2015 ACC/AHA/HRS Guideline for the Management of Adult Patients With Supraventricular Tachycardia

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society

WRITING COMMITTEE MEMBERS*
Richard L. Page, MD, FACC, FAHA, FHRS, Chair;
José A. Joglar, MD, FACC, FAHA, FHRS, Vice Chair;
Mary A. Caldwell, RN, MBA, PhD, FAHA; Hugh Calkins, MD, FACC, FAHA, FHRS*†;
Jamie B. Conti, MD, FACC*‡§; Barbara J. Deal, MD‡;
N.A. Mark Estes III, MD, FACC, FAHA, FHRS*‡; Michael E. Field, MD, FACC, FHRS‡;
Zachary D. Goldberger, MD, MS, FACC, FAHA, FHRS‡;
Stephen C. Hammill, MD, FACC, FHRS†; Julia H. Indik, MD, PhD, FACC, FAHA, FHRS†;
Bruce D. Lindsay, MD, FACC, FHRS*†; Brian Olshansky, MD, FACC, FAHA, FHRS*‡;
Andrea M. Russo, MD, FACC, FHRS*§; Win-Kuang Shen, MD, FACC, FAHA, FHRS‖;
Cynthia M. Tracy, MD, FACC‡; Sana M. Al-Khatib, MD, MHS, FACC, FAHA, FHRS,
Evidence Review Committee Chair‡

ACC/AHA TASK FORCE MEMBERS
Jonathan L. Halperin, MD, FACC, FAHA, Chair;
Glenn N. Levine, MD, FACC, FAHA, Chair-Elect;
Jeffrey L. Anderson, MD, FACC, FAHA, Immediate Past Chair¶;
Nancy M. Albert, PhD, RN, FAHA¶; Sana M. Al-Khatib, MD, MHS, FACC, FAHA;
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Federico Gentile, MD, FACC; Samuel Gidding, MD, FAHA; Mark A. Hlatky, MD, FACC;
John Ikonomidis, MD, PhD, FAHA; Jose Joglar, MD, FACC, FAHA;
Richard J. Kovacs, MD, FACC, FAHA¶; E. Magnus Ohman, MD, FACC¶;
Susan J. Pressler, PhD, RN, FAHA; Frank W. Sellke, MD, FACC, FAHA¶;
Win-Kuang Shen, MD, FACC, FAHA¶; Duminda N. Wijeysundera, MD, PhD

*Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry and other entities may apply; see Appendix 1 for recusal information. †HRS Representative. ‡ACC/AHA Representative. §ACC/AHA Task Force on Performance Measures Liaison. ‖ACC/AHA Task Force on Clinical Practice Guidelines Liaison. ¶Former Task Force member; current member during this writing effort.

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Preamble

Since 1980, the American College of Cardiology (ACC) and American Heart Association (AHA) have translated scientific evidence into clinical practice guidelines with recommendations to improve cardiovascular health. These guidelines, based on systematic methods to evaluate and classify evidence, provide a cornerstone of quality cardiovascular care.

In response to reports from the Institute of Medicine[1,2] and a mandate to evaluate new knowledge and maintain relevance at the point of care, the ACC/AHA Task Force on Clinical Practice Guidelines (Task Force) modified its methodology.[3–5] The relationships between guidelines, data standards, appropriate use criteria, and performance measures are addressed elsewhere.[4]

Intended Use

Practice guidelines provide recommendations applicable to patients with or at risk of developing cardiovascular disease. The focus is on medical practice in the United States, but guidelines developed in collaboration with other organizations may have a broader target. Although guidelines may inform regulatory or payer decisions, they are intended to improve quality of care in the interest of patients.

Evidence Review

Guideline Writing Committee (GWC) members review the literature; weigh the quality of evidence for or against particular tests, treatments, or procedures; and estimate expected health outcomes. In developing recommendations, the GWC uses evidence-based methodologies that are based on all available data.[4–6] Literature searches focus on randomized controlled trials (RCTs) but also include registries, nonrandomized

comparative and descriptive studies, case series, cohort studies, systematic reviews, and expert opinion. Only selected references are cited.

The Task Force recognizes the need for objective, independent Evidence Review Committees (ERCs) that include methodologists, epidemiologists, clinicians, and biostatisticians who systematically survey, abstract, and assess the evidence to address key clinical questions posed in the PICOTS format (P=population, I=intervention, C=comparator, O=outcome, T=timing, S=setting).[4,5] Practical considerations, including time and resource constraints, limit the ERCs to evidence that is relevant to key clinical questions and lends itself to systematic review and analysis that could affect the strength of corresponding recommendations. Recommendations developed by the GWC on the basis of the systematic review are marked "[SR]".

Guideline-Directed Medical Therapy

The term guideline-directed medical therapy refers to care defined mainly by ACC/AHA Class I recommendations. For these and all recommended drug treatment regimens, the reader should confirm dosage with product insert material and carefully evaluate for contraindications and interactions. Recommendations are limited to treatments, drugs, and devices approved for clinical use in the United States.

Class of Recommendation and Level of Evidence

The Class of Recommendation (COR; ie, the strength of the recommendation) encompasses the anticipated magnitude and certainty of benefit in proportion to risk. The Level of Evidence (LOE) rates evidence supporting the effect of the intervention on the basis of the type, quality, quantity, and consistency of data from clinical trials and other reports (Table 1).[5,7] Unless otherwise stated, recommendations are sequenced by COR and then by LOE. Where comparative data exist, preferred strategies take precedence. When >1 drug, strategy, or therapy exists within the same COR and LOE and no comparative data are available, options are listed alphabetically. Each recommendation is followed by supplemental text linked to supporting references and evidence tables.

Relationships With Industry and Other Entities

The ACC and AHA sponsor the guidelines without commercial support, and members volunteer their time. The Task Force zealously avoids actual, potential, or perceived conflicts of interest that might arise through relationships with industry or other entities (RWI). All GWC members and reviewers are required to disclose current industry relationships or personal interests from 12 months before initiation of the writing effort. Management of RWI involves selecting a balanced GWC and assuring that the chair and a majority of committee members have no relevant RWI (Appendix 1). Members are restricted with regard to writing or voting on sections to which their RWI apply. For transparency, members' comprehensive disclosure information is available online. Comprehensive disclosure information for the Task Force is also available online. The Task Force strives to avoid bias by selecting experts from a broad array of backgrounds representing different geographic regions, sexes, ethnicities, intellectual perspectives/biases, and scopes of clinical practice, and by inviting organizations and professional societies with related interests and expertise to participate as partners or collaborators.

Individualizing Care in Patients With Associated Conditions and Comorbidities

Managing patients with multiple conditions can be complex, especially when recommendations applicable to coexisting illnesses are discordant or interacting.[8] The guidelines are intended to define practices meeting the needs of patients in most, but not all, circumstances. The recommendations should not replace clinical judgment.

Clinical Implementation

Management in accordance with guideline recommendations is effective only when followed. Adherence to recommendations can be enhanced by shared decision making between clinicians and patients, with patient engagement in selecting interventions based on individual values, preferences, and associated conditions and comorbidities. Consequently, circumstances may arise in which deviations from these guidelines are appropriate.

Policy

The recommendations in this guideline represent the official policy of the ACC and AHA until superseded by published addenda, statements of clarification, focused updates, or revised full-text guidelines. To ensure that guidelines remain current, new data are reviewed biannually to determine whether recommendations should be modified. In general, full revisions are posted in 5-year cycles.[3,5]

Jonathan L. Halperin, MD, FACC, FAHA
Chair, ACC/AHA Task Force on Clinical Practice Guidelines

1. Introduction

1.1. Methodology and Evidence Review

The recommendations listed in this guideline are, whenever possible, evidence based. An extensive evidence review was conducted in April 2014 that included literature published through September 2014. Other selected references published through May 2015 were incorporated by the GWC. Literature included was derived from research involving human subjects, published in English, and indexed in MEDLINE (through PubMed), EMBASE, the Cochrane Library, the Agency for Healthcare Research and Quality, and other selected databases relevant to this guideline. The relevant data are included in evidence tables in the Online Data Supplement. Key search words included but were not limited to the following*: ablation therapy (catheter and radiofrequency; fast and slow pathway), accessory pathway (manifest and concealed), antiarrhythmic drugs, atrial fibrillation, atrial tachycardia, atrioventricular nodal reentrant (reentry, reciprocating) tachycardia, atrioventricular reentrant (reentry, reciprocating) tachycardia, beta blockers, calcium channel blockers, cardiac imaging, cardioversion, cost effectiveness, cryotherapy, echocardiography, elderly (aged and older), focal atrial tachycardia, Holter monitor, inappropriate sinus tachycardia,*

Table 1. Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care*

CLASS (STRENGTH) OF RECOMMENDATION	
CLASS I (STRONG)	Benefit >>> Risk
Suggested phrases for writing recommendations: ■ Is recommended ■ Is indicated/useful/effective/beneficial ■ Should be performed/administered/other ■ Comparative-Effectiveness Phrases†: ○ Treatment/strategy A is recommended/indicated in preference to treatment B ○ Treatment A should be chosen over treatment B	
CLASS IIa (MODERATE)	Benefit >> Risk
Suggested phrases for writing recommendations: ■ Is reasonable ■ Can be useful/effective/beneficial ■ Comparative-Effectiveness Phrases†: ○ Treatment/strategy A is probably recommended/indicated in preference to treatment B ○ It is reasonable to choose treatment A over treatment B	
CLASS IIb (WEAK)	Benefit ≥ Risk
Suggested phrases for writing recommendations: ■ May/might be reasonable ■ May/might be considered ■ Usefulness/effectiveness is unknown/unclear/uncertain or not well established	
CLASS III: No Benefit (MODERATE) *(Generally, LOE A or B use only)*	Benefit = Risk
Suggested phrases for writing recommendations: ■ Is not recommended ■ Is not indicated/useful/effective/beneficial ■ Should not be performed/administered/other	
CLASS III: Harm (STRONG)	Risk > Benefit
Suggested phrases for writing recommendations: ■ Potentially harmful ■ Causes harm ■ Associated with excess morbidity/mortality ■ Should not be performed/administered/other	

LEVEL (QUALITY) OF EVIDENCE‡	
LEVEL A	
■ High-quality evidence‡ from more than 1 RCT ■ Meta-analyses of high-quality RCTs ■ One or more RCTs corroborated by high-quality registry studies	
LEVEL B-R	(Randomized)
■ Moderate-quality evidence‡ from 1 or more RCTs ■ Meta-analyses of moderate-quality RCTs	
LEVEL B-NR	(Nonrandomized)
■ Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies ■ Meta-analyses of such studies	
LEVEL C-LD	(Limited Data)
■ Randomized or nonrandomized observational or registry studies with limitations of design or execution ■ Meta-analyses of such studies ■ Physiological or mechanistic studies in human subjects	
LEVEL C-EO	(Expert Opinion)
Consensus of expert opinion based on clinical experience	

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

junctional tachycardia, multifocal atrial tachycardia, paroxysmal supraventricular tachycardia, permanent form of junctional reciprocating tachycardia, pre-excitation, pregnancy, quality of life, sinoatrial node, sinus node reentry, sinus tachycardia, supraventricular tachycardia, supraventricular arrhythmia, tachycardia, tachyarrhythmia, vagal maneuvers (Valsalva maneuver), and *Wolff-Parkinson-White syndrome*. Additionally, the GWC reviewed documents related to supraventricular tachycardia (SVT) previously published by the ACC, AHA, and Heart Rhythm Society (HRS). References selected and published in this document are representative and not all-inclusive.

An independent ERC was commissioned to perform a systematic review of key clinical questions, the results of which were considered by the GWC for incorporation into this guideline. The systematic review report on the management of asymptomatic patients with Wolff-Parkinson-White (WPW) syndrome is published in conjunction with this guideline.[9]

1.2. Organization of the GWC

The GWC consisted of clinicians, cardiologists, electrophysiologists (including those specialized in pediatrics), and a nurse (in the role of patient representative) and included representatives from the ACC, AHA, and HRS.

1.3. Document Review and Approval

This document was reviewed by 8 official reviewers nominated by the ACC, AHA, and HRS, and 25 individual content reviewers. Reviewers' RWI information was distributed to the GWC and is published in this document (Appendix 2).

This document was approved for publication by the governing bodies of the ACC, the AHA, and the HRS.

1.4. Scope of the Guideline

The purpose of this joint ACC/AHA/HRS document is to provide a contemporary guideline for the management of adults with all types of SVT other than atrial fibrillation (AF). Although AF is, strictly speaking, an SVT, the term SVT generally does not refer to AF. AF is addressed in the 2014 ACC/AHA/HRS Guideline for the Management of Atrial Fibrillation (2014 AF guideline).[10] The present guideline addresses other SVTs, including regular narrow–QRS complex tachycardias, as well as other, irregular SVTs (eg, atrial flutter with irregular ventricular response and multifocal atrial tachycardia [MAT]). This guideline supersedes the "2003 ACC/AHA/ESC Guidelines for the Management of Patients With Supraventricular Arrhythmias."[11] It incorporates new and existing knowledge derived from published clinical trials, basic science, and comprehensive review articles, along with evolving treatment strategies and new drugs. Some recommendations from the earlier guideline have been updated as warranted by new evidence or a better understanding of existing evidence, whereas other inaccurate, irrelevant, or overlapping recommendations were deleted or modified. Whenever possible, we reference data from the acute clinical care environment; however, in some cases, the reference studies from the invasive electrophysiology laboratory inform our understanding of arrhythmia diagnosis and management. Although this document is aimed at the adult population (≥18 years of age) and offers no specific recommendations for pediatric patients, as per the reference list, we examined literature that included pediatric patients. In some cases, the data from noninfant pediatric patients helped inform this guideline.

In the current healthcare environment, cost consideration cannot be isolated from shared decision making and patient-centered care. The AHA and ACC have acknowledged the importance of value in health care, calling for eventual development of a Level of Value for practice recommendations in the "2014 ACC/AHA Statement on Cost/Value Methodology in Clinical Practice Guidelines and Performance Measures."[6] Although quality-of-life and cost-effectiveness data were not sufficient to allow for development of specific recommendations, the GWC agreed the data warranted brief discussion (Sections 10 and 11). Throughout this document, and associated with all recommendations and algorithms, the importance of shared decision making should be acknowledged. Each approach, ranging from observation to drug treatment to ablation, must be considered in the setting of a clear discussion with the patient regarding risk, benefit and personal preference. See Section 12 for additional information.

In developing this guideline, the GWC reviewed prior published guidelines and related statements. Table 2 contains a list of guidelines and statements deemed pertinent to this writing effort and is intended for use as a resource, thus obviating the need to repeat existing guideline recommendations.

2. General Principles

2.1. Mechanisms and Definitions

For the purposes of this guideline, SVT is defined as per Table 3, which provides definitions and the mechanism(s) of each type of SVT. The term SVT does not generally include AF, and this document does not discuss the management of AF.

2.2. Epidemiology, Demographics, and Public Health Impact

The epidemiology of SVT, including its frequency, patterns, causes, and effects, is imprecisely defined because of incomplete data and failure to discriminate among AF, atrial flutter, and other supraventricular arrhythmias. The best available evidence indicates that the prevalence of SVT in the general population is 2.29 per 1000 persons.[32] When adjusted by age and sex in the US population, the incidence of paroxysmal supraventricular tachycardia (PSVT) is estimated to be 36 per 100 000 persons per year.[32] There are approximately 89 000 new cases per year and 570 000 persons with PSVT.[32] Compared with patients with cardiovascular disease, those with PSVT without any cardiovascular disease are younger (37 versus 69 years; P=0.0002) and have faster PSVT (186 bpm versus 155 bpm; P=0.0006). Women have twice the risk of men of developing PSVT.[32] Individuals >65 years of age have >5 times the risk of younger persons of developing PSVT.[32]

Patients with PSVT who are referred to specialized centers for management with ablation are younger, have an equal sex distribution, and have a low frequency of cardiovascular disease.[33–47] The frequency of atrioventricular nodal reentrant tachycardia (AVNRT) is greater in women than in men. This may be due to an actual higher incidence in women, or it may reflect referral bias. In persons who are middle-aged or older, AVNRT is more common, whereas in adolescents, the prevalence may be more balanced between atrioventricular reentrant tachycardia (AVRT) and AVNRT, or AVRT may be more prevalent.[32] The relative frequency of tachycardia mediated by an accessory pathway decreases with age. The incidence of manifest pre-excitation or WPW pattern on ECG tracings in the general population is 0.1% to 0.3%. However, not all patients with manifest ventricular pre-excitation develop PSVT.[47–49] The limited data on the public health impact of SVT indicate that the arrhythmia is commonly a reason for emergency department and primary care physician visits but is infrequently the primary reason for hospital admission.[11,50,51]

Table 2. Associated Guidelines and Statements

Title	Organization	Publication Year (Reference)
Guidelines		
Atrial fibrillation	AHA/ACC/HRS	2014[10]
Stable ischemic heart disease	ACC/AHA/ACP/ AATS/ PCNA/ SCAI/STS	2014[12] 2012[13]
Valvular heart disease	AHA/ACC	2014[14]
Assessment of cardiovascular risk	ACC/AHA	2013[15]
Heart failure	ACC/AHA	2013[16]
Antithrombotic therapy for valvular heart disease	ACCP	2012[17]
Atrial fibrillation	ESC	2012[18] 2010[19]
Device-based therapy	ACC/AHA/HRS	2012[20]
Atrial fibrillation	CCS	2014[21] 2011[22]
Hypertrophic cardiomyopathy	ACC/AHA	2011[23]
Secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease	AHA/ACC	2011[24]
Adult congenital heart disease	ACC/AHA	2008[25]*
Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VII)	NHLBI	2003[26]
Statements		
Catheter ablation in children and patients with congenital heart disease	PACES/HRS	2015 (in press)[27]
Postural tachycardia syndrome, inappropriate sinus tachycardia, and vasovagal syncope	HRS	2015[28]
Arrhythmias in adult congenital heart disease	PACES/HRS	2014[29]
Catheter and surgical ablation of atrial fibrillation	HRS/EHRA/ECAS	2012[30]
CPR and emergency cardiovascular care	AHA	2010[31]*

*A revision to the current document is being prepared, with publication expected in late 2015.

AATS indicates American Association for Thoracic Surgery; ACC, American College of Cardiology; ACCP, American College of Chest Physicians; ACP, American College of Physicians; AHA, American Heart Association; CCS, Canadian Cardiovascular Society; CPR, cardiopulmonary resuscitation; ECAS, European Cardiac Arrhythmia Society; EHRA, European Heart Rhythm Association; ESC, European Society of Cardiology; HRS, Heart Rhythm Society; JNC, Joint National Committee; NHLBI, National Heart, Lung, and Blood Institute; PACES, Pediatric and Congenital Electrophysiology Society; PCNA, Preventive Cardiovascular Nurses Association; SCAI, Society for Cardiovascular Angiography and Interventions; and STS, Society of Thoracic Surgeons.

2.3. Evaluation of the Patient With Suspected or Documented SVT

2.3.1. Clinical Presentation and Differential Diagnosis on the Basis of Symptoms

Patients seen in consultation for palpitations often describe symptoms with characteristic features suggestive of SVT that may guide physicians to appropriate testing and a definitive diagnosis. The diagnosis of SVT is often made in the emergency department, but it is common to elicit symptoms suggestive of SVT before initial electrocardiogram/electrocardiographic (ECG) documentation. SVT symptom onset often begins in adulthood; in 1 study in adults, the mean age of symptom onset was 32±18 years of age for AVNRT, versus 23±14 years of age for AVRT.[52] In contrast, in a study conducted in pediatric populations, the mean ages of symptom onset of AVRT and AVNRT were 8 and 11 years, respectively.[53] In comparison with AVRT, patients with AVNRT are more likely to be female, with an age of onset >30 years.[49,54–56] AVNRT onset has been reported after the age of 50 years in 16% and before the age of 20 years in 18%.[57] Among women with SVT and no other cardiovascular disease, the onset of symptoms occurred during childbearing years (eg, 15 to 50 years) in 58%.[32] The first onset of SVT occurred in only 3.9% of women during pregnancy, but among women with an established history of SVT, 22% reported that pregnancy exacerbated their symptoms.[58]

SVT has an impact on quality of life, which varies according to the frequency of episodes, the duration of SVT, and whether symptoms occur not only with exercise but also at rest.[53,59] In 1 retrospective study in which the records of patients <21 years of age with WPW pattern on the ECG were reviewed, 64% of patients had symptoms at presentation, and an additional 20% developed symptoms during follow-up.[60] Modes of presentation included documented SVT in 38%, palpitations in 22%, chest pain in 5%, syncope in 4%, AF in 0.4%, and sudden cardiac death (SCD) in 0.2%.[60] Although this was a pediatric population, it provided symptom data that are likely applicable to adults. A confounding factor in diagnosing SVT is the need to differentiate symptoms of SVT from symptoms of panic and anxiety disorders or any condition of heightened awareness of sinus tachycardia (such as postural orthostatic tachycardia syndrome). In 1 study, the criteria for panic disorder were fulfilled in 67% of patients with SVT that remained unrecognized after their initial evaluation. Physicians attributed symptoms of SVT to panic, anxiety, or stress in 54% of patients, with women more likely to be mislabeled with panic disorder than men.[61]

When AVNRT and AVRT are compared, symptoms appear to differ substantially. Patients with AVNRT more frequently describe symptoms of "shirt flapping" or "neck pounding"[54,62] that may be related to pulsatile reversed flow when the right atrium contracts against a closed tricuspid valve (cannon a-waves). During 1 invasive study of patients with AVNRT and AVRT, both arrhythmias decreased arterial pressure and increased left atrial pressure, but simulation of SVT mechanism by timing the pacing of the atria and ventricles showed significantly higher left atrial pressure in simulated AVNRT than in simulated AVRT.[62] Polyuria is particularly common with AVNRT and is related to higher right atrial pressures and elevated levels of atrial natriuretic protein in patients with AVNRT compared with patients who have AVRT or atrial flutter.[63]

Table 3. Relevant Terms and Definitions

Arrhythmia/Term	Definition
Supraventricular tachycardia (SVT)	An umbrella term used to describe tachycardias (atrial and/or ventricular rates in excess of 100 bpm at rest), the mechanism of which involves tissue from the His bundle or above. These SVTs include inappropriate sinus tachycardia, AT (including focal and multifocal AT), macroreentrant AT (including typical atrial flutter), junctional tachycardia, AVNRT, and various forms of accessory pathway-mediated reentrant tachycardias. In this guideline, the term does not include AF.
Paroxysmal supraventricular tachycardia (PSVT)	A clinical syndrome characterized by the presence of a regular and rapid tachycardia of abrupt onset and termination. These features are characteristic of AVNRT or AVRT, and, less frequently, AT. PSVT represents a subset of SVT.
Atrial fibrillation (AF)	A supraventricular arrhythmia with uncoordinated atrial activation and, consequently, ineffective atrial contraction. ECG characteristics include: 1) irregular atrial activity, 2) absence of distinct P waves, and 3) irregular R-R intervals (when atrioventricular conduction is present). AF is not addressed in this document.
Sinus tachycardia	Rhythm arising from the sinus node in which the rate of impulses exceeds 100 bpm.
• Physiologic sinus tachycardia	Appropriate increased sinus rate in response to exercise and other situations that increase sympathetic tone.
• Inappropriate sinus tachycardia	Sinus heart rate >100 bpm at rest, with a mean 24-h heart rate >90 bpm not due to appropriate physiological responses or primary causes such as hyperthyroidism or anemia.
Atrial tachycardia (AT)	
• Focal AT	An SVT arising from a localized atrial site, characterized by regular, organized atrial activity with discrete P waves and typically an isoelectric segment between P waves. At times, irregularity is seen, especially at onset ("warm-up") and termination ("warm-down"). Atrial mapping reveals a focal point of origin.
• Sinus node reentry tachycardia	A specific type of focal AT that is due to microreentry arising from the sinus node complex, characterized by abrupt onset and termination, resulting in a P-wave morphology that is indistinguishable from sinus rhythm.
• Multifocal atrial tachycardia (MAT)	An irregular SVT characterized by ≥3 distinct P-wave morphologies and/or patterns of atrial activation at different rates. The rhythm is always irregular.
Atrial flutter	
• Cavotricuspid isthmus–dependent atrial flutter: typical	Macroreentrant AT propagating around the tricuspid annulus, proceeding superiorly along the atrial septum, inferiorly along the right atrial wall, and through the cavotricuspid isthmus between the tricuspid valve annulus and the Eustachian valve and ridge. This activation sequence produces predominantly negative "sawtooth" flutter waves on the ECG in leads 2, 3, and aVF and a late positive deflection in V1. The atrial rate can be slower than the typical 300 bpm (cycle length 200 ms) in the presence of antiarrhythmic drugs or scarring. It is also known as "typical atrial flutter" or "cavotricuspid isthmus–dependent atrial flutter" or "counterclockwise atrial flutter."
• Cavotricuspid isthmus–dependent atrial flutter: reverse typical	Macroreentrant AT that propagates around in the direction reverse that of typical atrial flutter. Flutter waves typically appear positive in the inferior leads and negative in V1. This type of atrial flutter is also referred to as "reverse typical" atrial flutter or "clockwise typical atrial flutter."
• Atypical or non–cavotricuspid isthmus–dependent atrial flutter	Macroreentrant ATs that do not involve the cavotricuspid isthmus. A variety of reentrant circuits may include reentry around the mitral valve annulus or scar tissue within the left or right atrium. A variety of terms have been applied to these arrhythmias according to the re-entry circuit location, including particular forms, such as "LA flutter" and "LA macroreentrant tachycardia" or incisional atrial re-entrant tachycardia due to re-entry around surgical scars.
Junctional tachycardia	A nonreentrant SVT that arises from the AV junction (including the His bundle).
Atrioventricular nodal reentrant tachycardia (AVNRT)	A reentrant tachycardia involving 2 functionally distinct pathways, generally referred to as "fast" and "slow" pathways. Most commonly, the fast pathway is located near the apex of Koch's triangle, and the slow pathway inferoposterior to the compact AV node tissue. Variant pathways have been described, allowing for "slow-slow" AVNRT.
• Typical AVNRT	AVNRT in which a slow pathway serves as the anterograde limb of the circuit and the fast pathway serves as the retrograde limb (also called "slow-fast AVNRT").
• Atypical AVNRT	AVNRT in which the fast pathway serves as the anterograde limb of the circuit and a slow pathway serves as the retrograde limb (also called "fast-slow AV node reentry") or a slow pathway serves as the anterograde limb and a second slow pathway serves as the retrograde limb (also called "slow-slow AVNRT").
Accessory pathway	For the purpose of this guideline, an accessory pathway is defined as an extranodal AV pathway that connects the myocardium of the atrium to the ventricle across the AV groove. Accessory pathways can be classified by their location, type of conduction (decremental or nondecremental), and whether they are capable of conducting anterogradely, retrogradely, or in both directions. Of note, accessory pathways of other types (such as atriofascicular, nodo-fascicular, nodo-ventricular, and fasciculoventricular pathways) are uncommon and are discussed only briefly in this document (Section 7).
• Manifest accessory pathways	A pathway that conducts anterogradely to cause ventricular pre-excitation pattern on the ECG.

(*Continued*)

Table 3. Continued

Arrhythmia/Term	Definition
• Concealed accessory pathway	A pathway that conducts only retrogradely and does not affect the ECG pattern during sinus rhythm.
• Pre-excitation pattern	An ECG pattern reflecting the presence of a manifest accessory pathway connecting the atrium to the ventricle. Pre-excited ventricular activation over the accessory pathway competes with the anterograde conduction over the AV node and spreads from the accessory pathway insertion point in the ventricular myocardium. Depending on the relative contribution from ventricular activation by the normal AV nodal/His Purkinje system versus the manifest accessory pathway, a variable degree of pre-excitation, with its characteristic pattern of a short P-R interval with slurring of the initial upstroke of the QRS complex (delta wave), is observed. Pre-excitation can be intermittent or not easily appreciated for some pathways capable of anterograde conduction; this is usually associated with a low-risk pathway, but exceptions occur.
• Asymptomatic pre-excitation (isolated pre-excitation)	The abnormal pre-excitation ECG pattern in the absence of documented SVT or symptoms consistent with SVT.
• Wolff-Parkinson-White syndrome	Syndrome characterized by documented SVT or symptoms consistent with SVT in a patient with ventricular pre-excitation during sinus rhythm.
Atrioventricular reentrant tachycardia (AVRT)	A reentrant tachycardia, the electrical pathway of which requires an accessory pathway, the atrium, atrioventricular node (or second accessory pathway), and ventricle.
• Orthodromic AVRT	An AVRT in which the reentrant impulse uses the accessory pathway in the retrograde direction from the ventricle to the atrium, and the AV node in the anterograde direction. The QRS complex is generally narrow or may be wide because of pre-existing bundle-branch block or aberrant conduction.
• Antidromic AVRT	An AVRT in which the reentrant impulse uses the accessory pathway in the anterograde direction from the atrium to the ventricle, and the AV node for the retrograde direction. Occasionally, instead of the AV node, another accessory pathway can be used in the retrograde direction, which is referred to as pre-excited AVRT. The QRS complex is wide (maximally pre-excited).
Permanent form of junctional reciprocating tachycardia (PJRT)	A rare form of nearly incessant orthodromic AVRT involving a slowly conducting, concealed, usually posteroseptal accessory pathway.
Pre-excited AF	AF with ventricular pre-excitation caused by conduction over ≥1 accessory pathway(s).

AF indicates atrial fibrillation; AT, atrial tachycardia; AV, atrioventricular; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; bpm, beats per minute; ECG, electrocardiogram/electrocardiographic; LA, left atrial; MAT, multifocal atrial tachycardia; PJRT, permanent form of junctional reciprocating tachycardia; PSVT, paroxysmal supraventricular tachycardia; SVT, supraventricular tachycardia; and WPW, Wolff-Parkinson-White.

True syncope is infrequent with SVT, but complaints of light-headedness are common. In patients with WPW syndrome, syncope should be taken seriously but is not necessarily associated with increased risk of SCD.[64] The rate of AVRT is faster when AVRT is induced during exercise,[65] yet the rate alone does not explain symptoms of near-syncope. Elderly patients with AVNRT are more prone to syncope or near-syncope than are younger patients, but the tachycardia rate is generally slower in the elderly.[66,67] The drop in blood pressure (BP) during SVT is greatest in the first 10 to 30 seconds and somewhat normalizes within 30 to 60 seconds, despite minimal changes in rate.[68,69] Shorter ventriculoatrial intervals are associated with a greater mean decrease in BP.[69] Studies have demonstrated a relationship between hemodynamic changes and the relative timing of atrial and ventricular activation. In a study of patients with AVNRT with short versus long ventriculoatrial intervals, there was no significant difference in tachycardia cycle length[70]; however, the induction of typical AVNRT caused a marked initial fall in systemic BP, followed by only partial recovery that resulted in stable hypotension and a reduction in cardiac output due to a decrease in stroke volume. In comparison, atypical AVNRT, having a longer ventriculoatrial interval, exhibited a lesser degree of initial hypotension, a complete recovery of BP, and no significant change in cardiac output.[70]

The contrasting hemodynamic responses without significant differences in heart rate during SVT confirm that rate alone does not account for these hemodynamic changes. Atrial contraction on a closed valve might impair pulmonary drainage and lead to neural factors that account for these observations. These findings were confirmed in a study performed in the electrophysiological (EP) laboratory: When pacing was used to replicate the timing of ventricular and atrial activation during SVT, the decrease in BP was greatest with simultaneous ventriculoatrial timing, smaller with a short vertriculoatrial interval, and smallest with a long ventriculoatrial interval.[71] An increase in central venous pressure followed the same trend. Sympathetic nerve activity increased with all 3 pacing modalities but was most pronounced with simultaneous atrial and ventricular pacing or a short ventriculoatrial interval.

In a study of the relationship of SVT with driving, 57% of patients with SVT experienced an episode while driving, and 24% of these considered it to be an obstacle to driving.[72] This sentiment was most common in patients who had experienced syncope or near-syncope. Among patients who experienced SVT while driving, 77% felt fatigue, 50% had symptoms of near-syncope, and 14% experienced syncope. Women had more symptoms in each category.

See Online Data Supplement 1 *for additional data on clinical presentation and differential diagnosis on the basis of symptoms.*

2.3.2. Evaluation of the ECG

Figures 1 to 6 provide representative ECGs, with Figure 1 showing ventricular tachycardia (VT) and Figures 2 to 5 showing some of the most common types of these SVTs.

A 12-lead ECG obtained during tachycardia and during sinus rhythm may reveal the etiology of tachycardia. For the patient who describes prior, but not current, symptoms of palpitations, the resting ECG can identify pre-excitation that should prompt a referral to a cardiac electrophysiologist.

A wide-complex tachycardia (QRS duration >120 ms) may represent either VT or a supraventricular rhythm with abnormal conduction. Conduction abnormalities may be due to rate-related aberrant conduction, pre-existing bundle-branch block seen in sinus rhythm, or an accessory pathway that results in pre-excitation (Table 4). The presence of atrioventricular (AV) dissociation (with ventricular rate faster than atrial rate) or fusion complexes–representing dissociation of supraventricular impulses from a ventricular rhythm–provides the diagnosis of VT (Figure 1). Other criteria are useful but not diagnostic. Concordance of the precordial QRS complexes such that all are positive or negative suggests VT or pre-excitation, whereas QRS complexes in tachycardia that are identical to those seen in sinus rhythm are consistent with SVT. Other, more complicated ECG algorithms have been developed to distinguish VT from SVT, such as the Brugada criteria, which rely on an examination of the QRS morphology in the precordial leads,[73] and the Vereckei algorithm, which is based on an examination of the QRS complex in lead aVR[74] (Table 5). The failure to correctly identify VT can be potentially life threatening, particularly if misdiagnosis results in VT being treated with verapamil or diltiazem. Adenosine is suggested in the "2010 AHA Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care–Part 8: Adult Advanced Cardiovascular Life Support" (2010 Adult ACLS guideline)[75] if a wide-complex tachycardia is monomorphic, regular, and hemodynamically tolerated, because adenosine may help convert the rhythm to sinus and may help in the diagnosis. When doubt exists, it is safest to assume any wide-complex tachycardia is VT, particularly in patients with known cardiovascular disease, such as prior myocardial infarction.

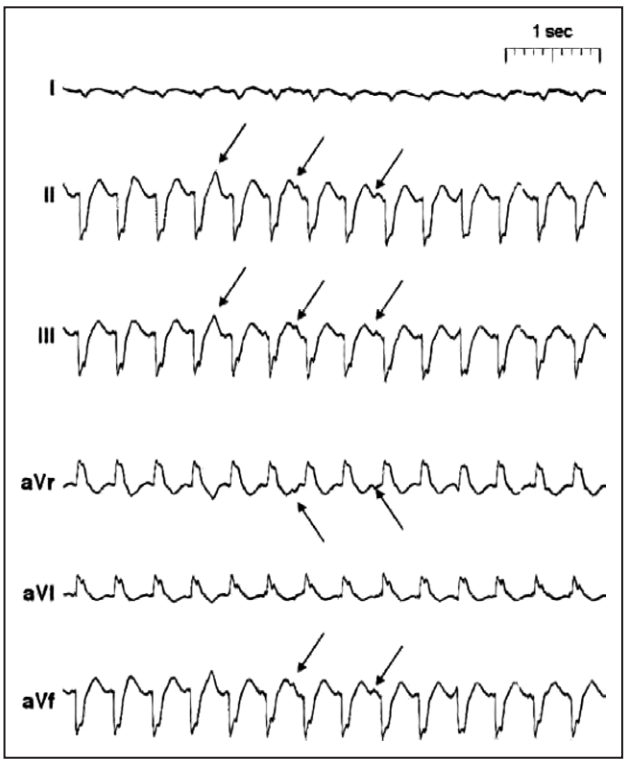

Figure 1. ECG showing AV dissociation during VT in a patient with a wide–QRS complex tachycardia. *P waves are marked with arrows. AV indicates atrioventricular; ECG, electrocardiogram; and VT, ventricular tachycardia. Reproduced with permission from Blomström-Lundqvist et al.[11]

For a patient presenting in SVT, the 12-lead ECG can potentially identify the arrhythmia mechanism (Figure 7). The tachycardia should first be classified according to whether there is a regular or irregular ventricular rate. An irregular ventricular rate suggests AF, MAT, or atrial flutter with variable AV conduction. When AF is associated with a rapid ventricular response, the irregularity of the ventricular response is less easily detected and can be misdiagnosed as a regular SVT.[76] If the atrial rate exceeds the ventricular rate, then atrial flutter or AT (focal or multifocal) is usually present (rare cases of AVNRT with 2:1 conduction have been described[77]).

If the SVT is regular, this may represent AT with 1:1 conduction or an SVT that involves the AV node. Junctional tachycardias, which originate in the AV junction (including the His bundle), can be regular or irregular, with variable conduction to the atria. SVTs that involve the AV node as a required component of the tachycardia reentrant circuit include AVNRT (Section 6: Figures 2 and 3) and AVRT (Section 7: Figures 4 and 6). In these reentrant tachycardias, the retrogradely conducted P wave may be difficult to discern, especially if bundle-branch block is present. In typical AVNRT, atrial activation is nearly simultaneous with the QRS, so the terminal portion of the P wave is usually located at the end of the QRS complex, appearing as a narrow and negative deflection in the inferior leads (a pseudo S wave) and a slightly positive deflection at the end of the QRS complex in lead V1 (pseudo R′). In orthodromic AVRT (with anterograde conduction down the AV node), the P wave can usually be seen in the early part of the ST-T segment. In typical forms of AVNRT and AVRT, because the P wave is located closer to the prior QRS complex than the subsequent QRS complex, the tachycardias are referred to as having a "short RP." They also have a 1:1 relationship between the P wave and QRS complex, except in rare cases of AVNRT in which 2:1 AV block or various degrees of AV block can occur. In unusual cases of AVNRT (such as "fast-slow"), the P wave is closer to the subsequent QRS complex, providing a long RP. The RP is also long during an uncommon form of AVRT, referred to as the permanent form of junctional reciprocating tachycardia (PJRT), in which an unusual accessory bypass tract with "decremental" (slowly conducting) retrograde conduction during orthodromic AVRT produces delayed atrial activation and a long RP interval.

A long RP interval is typical of AT because the rhythm is driven by the atrium and conducts normally to the ventricles. In AT, the ECG will typically show a P wave with a morphology that differs from sinus that is usually seen near the end of or shortly after the T wave (Figure 5). In sinus node reentry

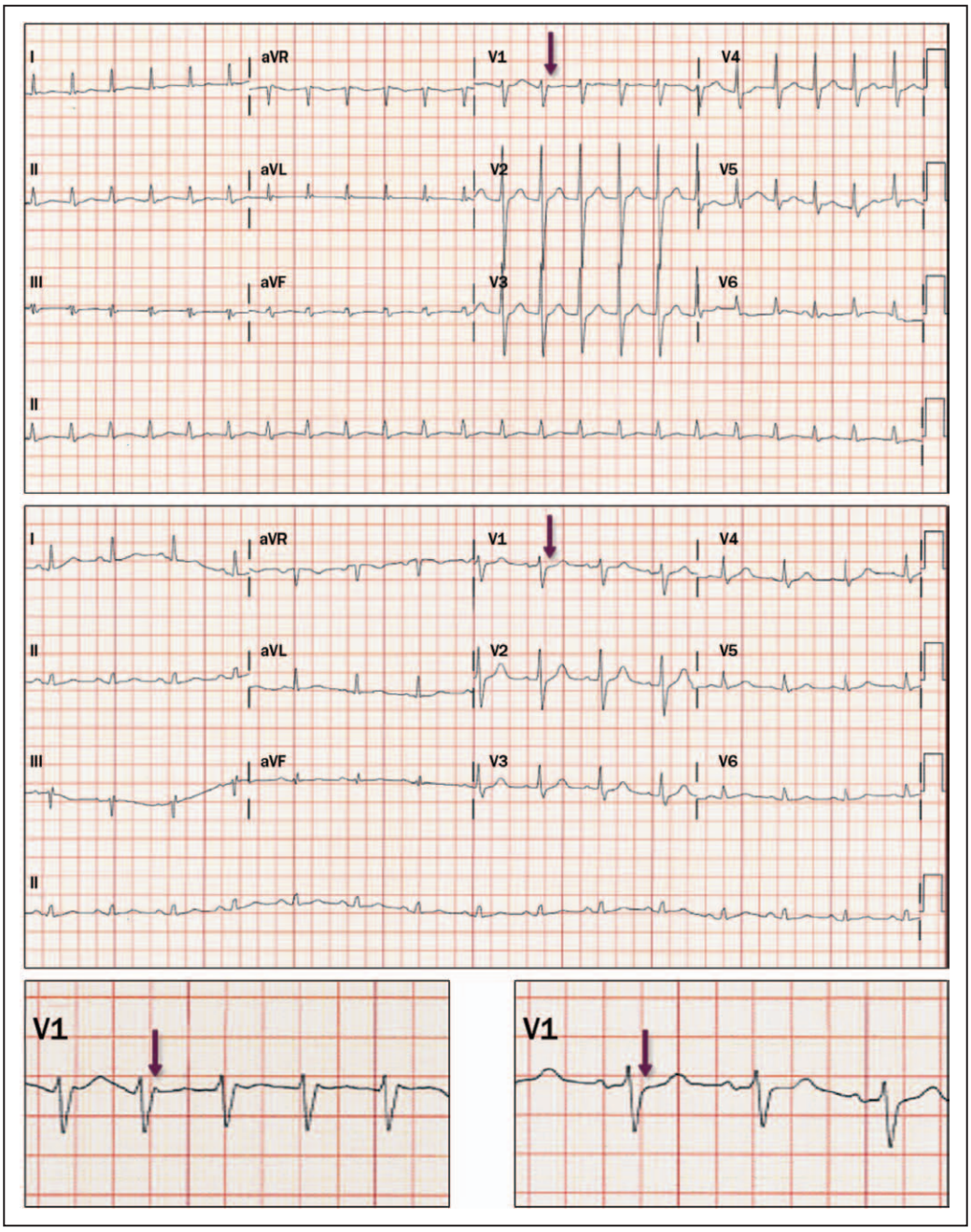

Figure 2. Typical AVNRT and normal sinus rhythm after conversion. **Upper panel**: The arrow points to the P waves, which are inscribed at the end of the QRS complex, seen best in the inferior leads and as a slightly positive R′ (pseudo r prime) in lead V1. The reentrant circuit involves anterograde conduction over a slow atrioventricular node pathway, followed by retrograde conduction in a fast atrioventricular node pathway. Typical AVNRT is a type of short RP tachycardia. **Middle panel**: When the patient is in sinus rhythm, the arrow indicates where the R′ is absent in V1. **Bottom panels**: Magnified portions of lead V1 in AVNRT **(left)** and sinus rhythm **(right)** are shown. AVNRT indicates atrioventricular nodal reentrant tachycardia.

tachycardia, a form of focal AT, the P-wave morphology is identical to the P wave in sinus rhythm.

2.4. Principles of Medical Therapy

See Figure 8 for the algorithm for acute treatment of tachycardia of unknown mechanism; Figure 9 for the algorithm for ongoing management of tachycardia of unknown mechanism; Table 6 for acute drug therapy for SVT (intravenous administration); and Table 7 for ongoing drug therapy for SVT (oral administration).

2.4.1. Acute Treatment: Recommendations

Because patients with SVT account for approximately 50 000 emergency department visits each year,[81] emergency physicians may be the first to evaluate patients whose tachycardia mechanism is unknown and to have the opportunity to diagnose the mechanism of arrhythmia. It is important to record a 12-lead ECG to differentiate tachycardia mechanisms according to whether the AV node is an obligate component (Section 2.3.2), because treatment that targets the AV node will not reliably terminate tachycardias

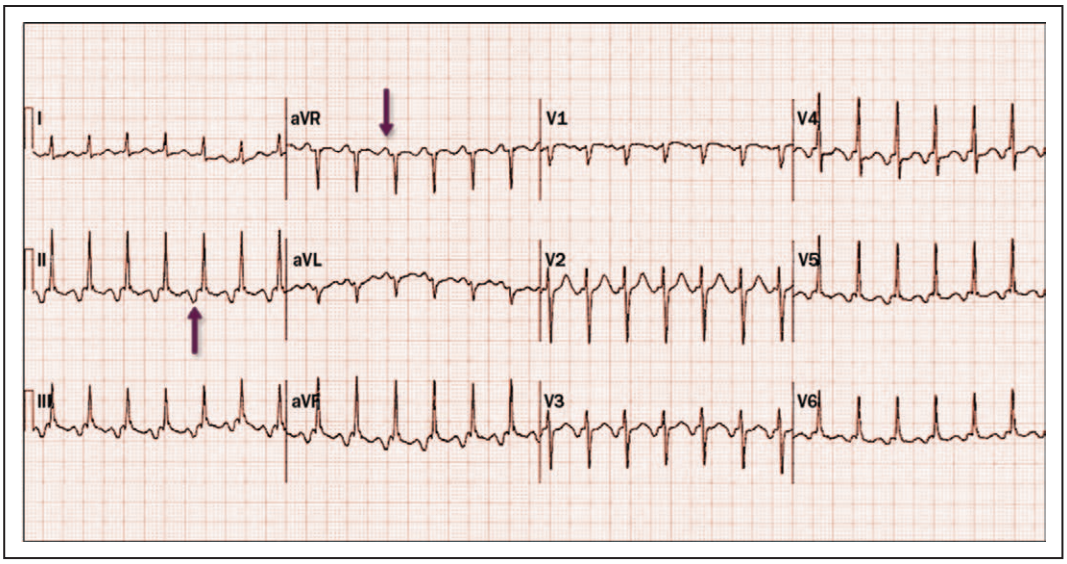

Figure 3. Atypical AVNRT. Arrows point to the P wave. The reentrant circuit involves anterograde conduction over a fast atrioventricular node pathway, followed by retrograde conduction in a slow atrioventricular node pathway, resulting in a retrograde P wave (negative polarity in inferior leads) with long RP interval. This ECG does not exclude PJRT or a low septal atrial tachycardia, which can appear very similar to this ECG. AVNRT indicates atrioventricular nodal reentrant tachycardia; ECG, electrocardiogram; and PJRT, permanent form of junctional reciprocating tachycardia.

that are not AV node dependent. Also, if the QRS duration is >120 ms, it is crucial to distinguish VT from SVT with aberrant conduction, pre-existing bundle-branch block, or pre-excitation (Table 4). In particular, the administration of verapamil or diltiazem for treatment of either VT or a pre-excited AF may lead to hemodynamic compromise or may accelerate the ventricular rate and lead to ventricular fibrillation.

Recommendations for Acute Treatment of SVT of Unknown Mechanism		
COR	**LOE**	**Recommendations**
I	B-R	**1. Vagal maneuvers are recommended for acute treatment in patients with regular SVT.[82–84]**
See Online Data Supplements 2 and 3.		For acute conversion of SVT, vagal maneuvers, including Valsalva and carotid sinus massage, can be performed quickly and should be the first-line intervention to terminate SVT. These maneuvers should be performed with the patient in the supine position. Vagal maneuvers typically will not be effective if the rhythm does not involve the AV node as a requisite component of a reentrant circuit. There is no "gold standard" for proper Valsalva maneuver technique but, in general, the patient raises intrathoracic pressure by bearing down against a closed glottis for 10 to 30 seconds, equivalent to at least 30 mm Hg to 40 mm Hg.[82,84] Carotid massage is performed after absence of bruit has been confirmed by auscultation, by applying steady pressure over the right or left carotid sinus for 5 to 10 seconds.[83,84] Another vagal maneuver based on the classic diving reflex consists of applying an ice-cold, wet towel to the face[85]; in a laboratory setting, facial immersion in water at 10°C (50°F) has proved effective in terminating tachycardia, as well.[86] One study involving 148 patients with SVT demonstrated that Valsalva was more successful than carotid sinus massage, and switching from 1 technique to the other resulted in an overall success rate of 27.7%.[82] The practice of applying pressure to the eyeball is potentially dangerous and has been abandoned.
I	B-R	**2. Adenosine is recommended for acute treatment in patients with regular SVT.[42,51,83,87–92]**
See Online Data Supplements 2 and 3.		Adenosine has been shown in nonrandomized trials in the emergency department or prehospital setting to effectively terminate SVT that is due to either AVNRT or AVRT, with success rates ranging from 78% to 96%. Although patients may experience side effects, such as chest discomfort, shortness of breath, and flushing, serious adverse effects are rare because of the drug's very short half-life.[93] Adenosine may also be useful diagnostically, to unmask atrial flutter or AT, but it is uncommon for adenosine to terminate these atrial arrhythmias.[91] It should be administered via proximal IV as a rapid bolus infusion followed by a saline flush. Continuous ECG recording during adenosine administration may help diagnostically and can also distinguish drug failure due to failure to terminate the arrhythmias versus successful termination with immediate arrhythmia reinitiation.
I	B-NR	**3. Synchronized cardioversion is recommended for acute treatment in patients with hemodynamically unstable SVT when vagal maneuvers or adenosine are ineffective or not feasible.[94]**
See Online Data Supplement 3.		Sinus rhythm must be promptly restored in patients with SVT who are hemodynamically unstable. The safety and effectiveness of cardioversion in the prehospital setting was analyzed in a cohort of patients with hemodynamically unstable SVT who had failed to convert with vagal maneuvers and intravenous pharmacological therapy, and cardioversion successfully restored sinus rhythm in all patients.[94] The 2010 adult ACLS guideline[75] advises synchronized cardioversion for any persistent SVT resulting in hypotension, acutely altered mental status, signs of shock, chest pain, or acute heart failure symptoms but recommends that adenosine be considered first if the tachycardia is regular and has a narrow QRS complex.

Recommendations for Acute Treatment of SVT of Unknown Mechanism (Continued)		
COR	LOE	Recommendations
I	B-NR	**4. Synchronized cardioversion is recommended for acute treatment in patients with hemodynamically stable SVT when pharmacological therapy is ineffective or contraindicated.[87,95]**
See Online Data Supplements 3 and 10.		Synchronized cardioversion is highly effective in terminating SVT (including AVRT and AVNRT), and when the patient is stable, this is performed after adequate sedation or anesthesia.[94] Most stable patients with SVT respond to pharmacological therapy, with conversion success rates of 80% to 98% for agents such as verapamil, diltiazem, or adenosine. In some resistant cases, a second drug bolus or higher dose of initial drug agent might prove effective.[87,96] Nevertheless, in rare instances, drugs may fail to successfully restore sinus rhythm, and cardioversion will be necessary. Synchronized cardioversion is inappropriate if the SVT is terminating and reinitiating spontaneously.
IIa	B-R	**1. Intravenous diltiazem or verapamil can be effective for acute treatment in patients with hemodynamically stable SVT.[87,89,92,97]**
See Online Data Supplements 2 and 3.		Intravenous diltiazem and verapamil have been shown to terminate SVT in 64% to 98% of patients. These drugs should be used only in hemodynamically stable patients. A slow infusion of either drug up to 20 minutes may lessen the potential for hypotension.[97] It is important to ensure that tachycardia is not due to VT or pre-excited AF because patients with these rhythms who are given diltiazem or verapamil may become hemodynamically unstable or may have accelerated ventricular rate, which may lead to ventricular fibrillation. These agents are especially useful in patients who cannot tolerate beta blockers or experience recurrence after conversion with adenosine. Diltiazem and verapamil are not appropriate for patients with suspected systolic heart failure.
IIa	C-LD	**2. Intravenous beta blockers are reasonable for acute treatment in patients with hemodynamically stable SVT.[96]**
See Online Data Supplement 2.		Evidence for the effectiveness of beta blockers in terminating SVT is limited. In a trial that compared esmolol with diltiazem, diltiazem was more effective in terminating SVT.[96] Nonetheless, beta blockers have an excellent safety profile, so it is reasonable to use intravenous beta blockers to attempt to terminate SVT in hemodynamically stable patients.

2.4.2. Ongoing Management: Recommendations

The recommendations and algorithm (Figure 9) for ongoing management, along with other recommendations and algorithms for specific SVTs that follow, are meant to include consideration of patient preferences and clinical judgment; this may include consideration of consultation with a cardiologist or clinical cardiac electrophysiologist, as well as patient comfort with possible invasive diagnostic and therapeutic intervention. Recommendations for treatment options (including drug therapy, ablation, or observation) must be considered in the context of frequency and duration of the SVT, along with clinical manifestations, such as symptoms or adverse consequences (eg, development of cardiomyopathy).

Recommendations for Ongoing Management of SVT of Unknown Mechanism		
COR	LOE	Recommendations
I	B-R	**1. Oral beta blockers, diltiazem, or verapamil is useful for ongoing management in patients with symptomatic SVT who do not have ventricular pre-excitation during sinus rhythm.[46,98,99]**
See Online Data Supplement 2.		Although many patients prefer to undergo potentially curative therapy with ablation, given its high success rate, and although ablation may be mandatory therapy for patients in certain occupations (eg, pilots, bus drivers), patients may prefer not to undergo ablation or may not have access to a cardiac electrophysiologist. In these latter cases, pharmacological therapy with AV nodal blockers is an appropriate option for long-term prophylactic therapy. Pharmacological therapy with verapamil (dosage up to 480 mg/day) has been studied in RCTs, with reductions documented in SVT episode frequency and duration as recorded by Holter monitoring or subjective episode frequency recording in diaries.[98] Evidence for beta blockers is limited. One small study randomized patients with SVT to digoxin (0.375 mg/day), propranolol (240 mg/day), or verapamil (480 mg/day), with 1 week of placebo washout between drug regimens.[99] Reduction in the number of episodes and duration of SVT (ascertained by diary and weekly 24-h Holter) was similar among the treatment groups, and all 3 medications were well tolerated.[99]
I	B-NR	**2. EP study with the option of ablation is useful for the diagnosis and potential treatment of SVT.[36,100–106]**
See Online Data Supplement 2.		EP testing with the option of ablation is useful as first-line therapy for treatment of symptomatic SVT, as it provides the potential for definitive cure without the need for chronic pharmacological therapy. Large registry studies report high success rates for ablation of both AVNRT and AVRT, with low frequency of potentially serious complications (Table 8).
I	C-LD	**3. Patients with SVT should be educated on how to perform vagal maneuvers for ongoing management of SVT.[82]**
See Online Data Supplement 2.		When properly performed, vagal maneuvers can terminate SVT, so patient education on this maneuver may help to avoid a more prolonged tachycardia episode and reduce the need to seek medical attention. Vagal maneuvers should be performed with the patient in the supine position. Patients can be taught to perform a Valsalva maneuver by forcefully exhaling against a closed airway for 10 to 30 seconds, equivalent to at least 30 mm Hg to 40 mm Hg.[82,84] Another vagal maneuver based on the classic diving reflex consists of applying an ice-cold, wet towel to the face.[85]
IIa	B-R	**1. Flecainide or propafenone is reasonable for ongoing management in patients without structural heart disease or ischemic heart disease who have symptomatic SVT and are not candidates for, or prefer not to undergo, catheter ablation.[45,46,107–112]**
See Online Data Supplement 2.		Several RCTs have demonstrated the efficacy of daily therapy with propafenone (450 mg/day to 900 mg/day) or flecainide (100 mg/day to 300 mg/day) to prevent recurrences of SVT in symptomatic patients.[45,46,107–112] In 1 RCT, the probability of 12 months of effective (defined as <2 attacks of arrhythmia) and safe treatment was 86% for propafenone and 93% for flecainide.[109] However, flecainide and propafenone have a risk of proarrhythmia in patients with structural heart disease or ischemic heart disease, so these drugs are contraindicated in these patient groups.[113] These drugs, though often effective, have potential side effects and as such should be reserved for patients for whom beta blockers, diltiazem, or verapamil are ineffective or cannot be prescribed.

Recommendations for Ongoing Management of SVT of Unknown Mechanism (Continued)		
COR	LOE	Recommendations
IIb	B-R	**1. Sotalol may be reasonable for ongoing management in patients with symptomatic SVT who are not candidates for, or prefer not to undergo, catheter ablation.[114]**
See Online Data Supplement 2.		Sotalol is a class III antiarrhythmic agent with beta-blocker properties. Unlike flecainide and propafenone, it can be used in patients with structural heart disease or ischemic heart disease. One study randomized patients with reentrant SVT (AVNRT or AVRT) or other atrial tachyarrhythmias (eg, AF, atrial flutter, AT) to sotalol at a dose of 80 mg or 160 mg twice daily or placebo and found significant reductions in recurrence risk, including for patients with reentrant SVT, with no proarrhythmic adverse effects.[114] Because of the potential for proarrhythmia, sotalol should be reserved for patients who are not candidates for catheter ablation and for whom beta blockers, diltiazem, or verapamil are ineffective or cannot be prescribed.
IIb	B-R	**2. Dofetilide may be reasonable for ongoing management in patients with symptomatic SVT who are not candidates for, or prefer not to undergo, catheter ablation and in whom beta blockers, diltiazem, flecainide, propafenone, or verapamil are ineffective or contraindicated.[107]**
See Online Data Supplement 2.		Dofetilide is a class III antiarrhythmic agent that, unlike sotalol, does not have beta-blocker properties. It may be reasonable in patients with structural heart disease or ischemic heart disease. In a trial of 122 patients randomized to dofetilide, propafenone, or placebo, the probability of remaining free of SVT after 6 months of treatment was 50% for dofetilide, 54% for propafenone, and 6% for placebo, with $P<0.001$ for either dofetilide or propafenone compared with placebo.[107] Because of the potential for proarrhythmia, dofetilide should be reserved for patients who are not candidates for catheter ablation and for whom beta blockers, diltiazem, flecainide, verapamil, or propafenone are ineffective or cannot be prescribed.
IIb	C-LD	**3. Oral amiodarone may be considered for ongoing management in patients with symptomatic SVT who are not candidates for, or prefer not to undergo, catheter ablation and in whom beta blockers, diltiazem, dofetilide, flecainide, propafenone, sotalol, or verapamil are ineffective or contraindicated.[115]**
See Online Data Supplement 2.		Evidence for amiodarone for the ongoing management of SVT is limited. The drug was evaluated in a small retrospective study and was found to be effective in suppressing AVNRT during outpatient follow-up.[115] Amiodarone is a second-line agent for patients who are not able to take beta blockers, diltiazem, dofetilide, flecainide, propafenone, sotalol, or verapamil given the toxicity and side effects that may develop with long-term amiodarone therapy.
IIb	C-LD	**4. Oral digoxin may be reasonable for ongoing management in patients with symptomatic SVT without pre-excitation who are not candidates for, or prefer not to undergo, catheter ablation.[99]**
See Online Data Supplement 2.		Evidence for the use of digoxin is limited. One small study randomized patients with SVT to digoxin (0.375 mg/day), propranolol (240 mg/day), and verapamil (480 mg/day), with 1 week of placebo washout between drug regimens.[99] Overall, episodes and duration of SVT (ascertained by diary and weekly 24-h Holter) were similar, and all 3 medications were well tolerated.[99] However, the dose of digoxin used was higher than that commonly used in clinical practice today, and in view of the risk of toxicity, digoxin should be reserved for patients who cannot take beta blockers, diltiazem, or verapamil or a class Ic agent (flecainide or propafenone) and must be used with caution in the presence of renal dysfunction. In some clinical studies, digoxin levels >1.2 ng/mL were associated with worse clinical outcomes, while levels <0.8 ng/mL were considered optimal; therefore, caution is advised.[116]

2.5. Basic Principles of Electrophysiological Study, Mapping, and Ablation

2.5.1. Mapping With Multiple and Roving Electrodes

An invasive EP study permits the precise diagnosis of the underlying arrhythmia mechanism and localization of the site of origin and provides definitive treatment if coupled with catheter ablation. There are standards that define the equipment and training of personnel for optimal performance of EP study.[141] EP studies involve placement of multielectrode catheters in the heart at ≥1 sites in the atria, ventricles, or coronary sinus. Pacing and programmed electrical stimulation may be performed with or without pharmacological provocation. Making a precise and correct diagnosis of the mechanism of SVT is the key to successful outcome, particularly when multiple arrhythmia mechanisms are possible; as such, appropriate diagnostic maneuvers should be performed before proceeding with ablation. By using diagnostic maneuvers during the EP study, the mechanism of SVT can be defined in most cases.[80,142] Complications of diagnostic EP studies are rare but can be life threatening.[143]

Cardiac mapping is performed during EP studies to identify the site of origin of an arrhythmia or areas of critical conduction to allow targeting of ablation. Multiple techniques have been developed to characterize the temporal and spatial distribution of electrical activation.[144] The simplest technique uses several multipole catheters plus a roving catheter that is sequentially positioned in different regions of interest and measures local activation time. Electroanatomic mapping systems and specialized multielectrode catheters, such as circular or multispline catheters, can map simultaneously from multiple sites and improve the speed and resolution of mapping.

2.5.2. Tools to Facilitate Ablation, Including 3-Dimensional Electroanatomic Mapping

Several tools have been developed to facilitate arrhythmia mapping and ablation, including electroanatomic 3-dimensional mapping and magnetic navigation. Potential benefits of these technologies include more precise definition or localization of arrhythmia mechanism, spatial display of catheters and arrhythmia activation, reduction in fluoroscopy exposure for the patient and staff, and shortened procedure times, particularly for complex arrhythmias or anatomy.[145] Disadvantages include higher cost, as well as additional training, support, and procedure preparation time. Several studies have demonstrated the advantages of electroanatomic mapping, with

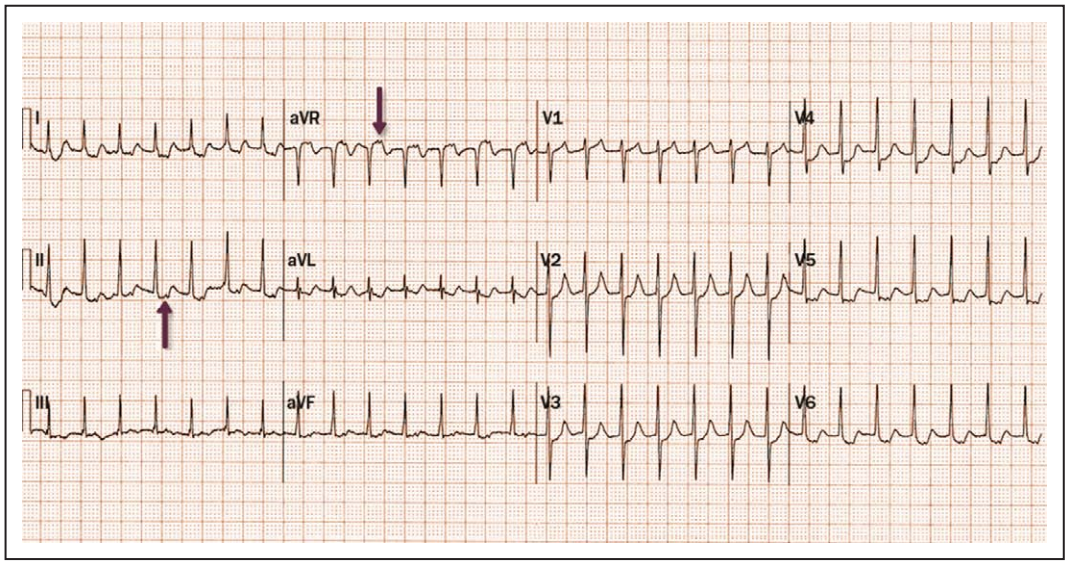

Figure 4. Orthodromic atrioventricular reentrant tachycardia. Arrows point to the P waves, which are inscribed in the ST-segment after the QRS complex. The reentrant circuit involves anterograde conduction over the atrioventricular node, followed by retrograde conduction over an accessory pathway, which results in a retrograde P wave with short RP interval.

success rates comparable to conventional approaches yet with significant reduction in fluoroscopy times.[145–148]

2.5.3. Mapping and Ablation With No or Minimal Radiation

Fluoroscopy has historically been the primary imaging modality used for EP studies. The use of ionizing radiation puts patient, operator, and laboratory staff at risk of the short- and long-term effects of radiation exposure. Attention to optimal fluoroscopic technique and adoption of radiation-reducing strategies can minimize radiation dose to the patient and operator. The current standard is to use the "as low as reasonably achievable" (ALARA) principle on the assumption that there is no threshold below which ionizing radiation is free from harmful biological effect. Alternative imaging systems, such as electroanatomic mapping and intracardiac echocardiography, have led to the ability to perform SVT ablation with no or minimal fluoroscopy, with success and complication rates similar to standard techniques.[147,149–152] Radiation exposure may be further reduced by using robotic or magnetic navigation of catheters that use a 3-dimensional anatomic tracking system superimposed on traditional fluoroscopy imaging. A reduced- fluoroscopy approach is particularly important in pediatric patients and during pregnancy.[153,154]

2.5.4. Ablation Energy Sources

Radiofrequency current is the most commonly used energy source for SVT ablation.[155] Cryoablation is used as an alternative to radiofrequency ablation to minimize injury to the AV node during ablation of specific arrhythmias, such as AVNRT, para-Hisian AT, and para-Hisian accessory pathways, particularly in specific patient populations, such as children and young adults. Selection of the energy source

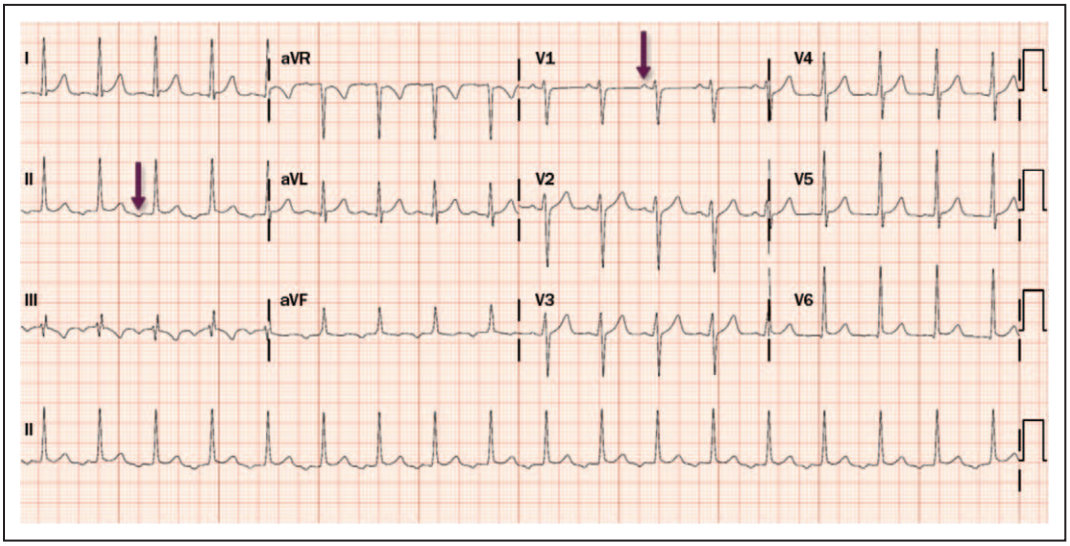

Figure 5. Atrial tachycardia. Arrows point to the P wave, which is inscribed before the QRS complex. The focus of this atrial tachycardia was mapped during electrophysiological study to an area near the left inferior pulmonary vein.

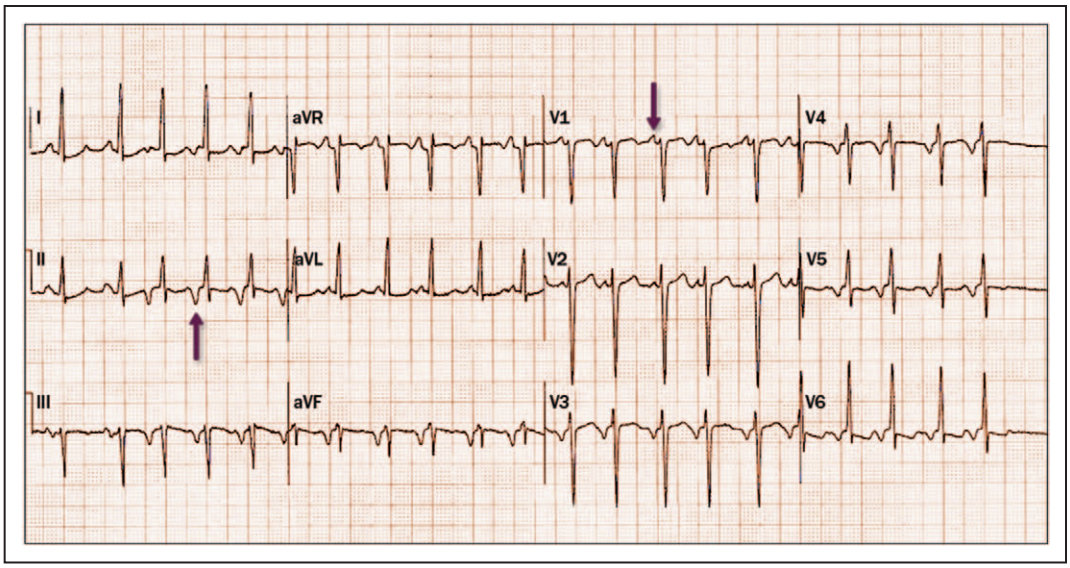

Figure 6. Permanent form of junctional reciprocating tachycardia (PJRT). Tachycardia starts after 2 beats of sinus rhythm. Arrows point to the P wave, which is inscribed before the QRS complex. The reentrant circuit involves anterograde conduction over the atrioventricular node, followed by retrograde conduction over a slowly conducting (or decremental) accessory pathway, usually located in the postero-septal region, to provide a retrograde P wave with long RP interval. This ECG does not exclude atypical AVNRT or a low septal atrial tachycardia, which can appear very similar to this ECG. AVNRT indicates atrioventricular nodal reentrant tachycardia; ECG, electrocardiogram; and PJRT, permanent form of junctional reciprocating tachycardia.

depends on operator experience, arrhythmia target location, and patient preference. Published trials, including a meta-analysis comparing radiofrequency ablation with cryoablation for treatment of AVNRT, have shown a higher rate of recurrence with cryoablation but lower risk of permanent AV nodal block.[156–158] The rate of AVNRT recurrence with cryoablation depends on the size of the ablation electrode and the endpoint used.[156,159] Ultimately, the choice of technology should be made on the basis of an informed discussion between the operator and the patient.

3. Sinus Tachyarrhythmias

In normal individuals, the sinus rate at rest is generally between 50 bpm and 90 bpm, reflecting vagal tone.[160–163] Sinus tachycardia refers to the circumstance in which the sinus rate exceeds 100 bpm. Sinus tachycardia may be appropriate in response to physiological stimuli or other exogenous factors or may be inappropriate when the heart rate exceeds what would be expected for physical activity or other circumstances. On the ECG, the P wave is upright in leads I, II, and aVF and is biphasic in lead V1. As the sinus rate increases, activation arises from more superior aspects of the right atrium, resulting in a larger-amplitude P wave in the inferior leads.

Table 4. Differential Diagnosis of Wide–QRS Complex Tachycardia

Mechanism
Ventricular tachycardia
SVT with pre-existing bundle-branch block or intraventricular conduction defect
SVT with aberrant conduction due to tachycardia (normal QRS when in sinus rhythm)
SVT with wide QRS related to electrolyte or metabolic disorder
SVT with conduction over an accessory pathway (pre-excitation)
Paced rhythm
Artifact

SVT indicates supraventricular tachycardia.

Table 5. ECG Criteria to Differentiate VT From SVT in Wide-Complex Tachycardia

Findings or Leads on ECG Assessed	Interpretation
QRS complex in leads V1-V6 (Brugada criteria)[73]	• Lack of any R-S complexes implies VT • R-S interval (onset of R wave to nadir of S wave) >100 ms in any precordial lead implies VT
QRS complex in aVR (Vereckei algorithm)[74]	• Presence of initial R wave implies VT • Initial R or Q wave >40 ms implies VT • Presence of a notch on the descending limb at the onset of a predominantly negative QRS implies VT
AV dissociation*	• Presence of AV dissociation (with ventricular rate faster than atrial rate) or fusion complexes implies VT
QRS complexes in precordial leads all positive or all negative (concordant)	• Implies VT
QRS in tachycardia that is identical to sinus rhythm[78]	• Suggests SVT
R-wave peak time in lead II[78]	• R-wave peak time ≥50 ms suggests VT

*AV dissociation is also a component of the Brugada criteria.[73]

AV indicates atrioventricular; ECG, electrocardiogram; SVT, supraventricular tachycardia; and VT, ventricular tachycardia.

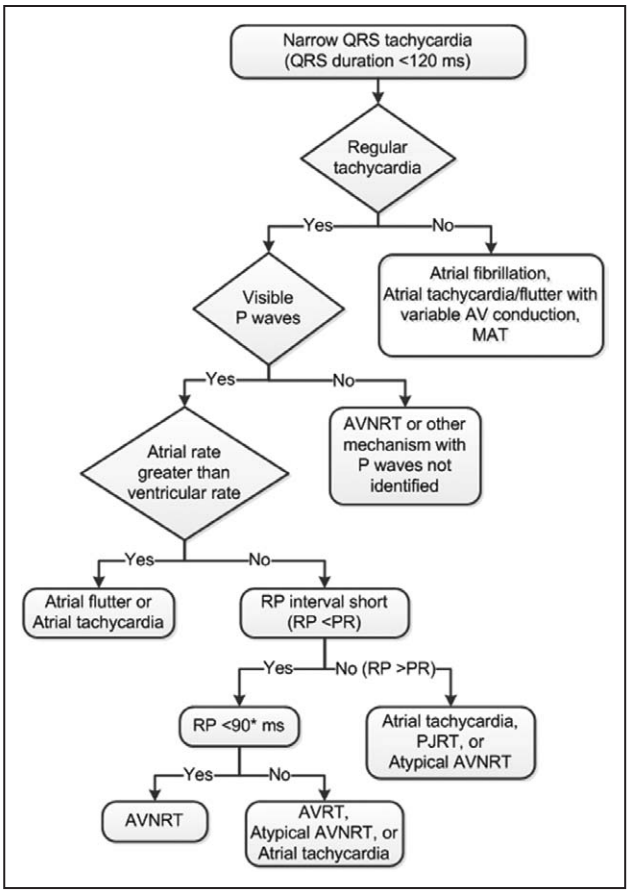

Figure 7. Differential diagnosis for adult narrow QRS tachycardia. Patients with junctional tachycardia may mimic the pattern of slow-fast AVNRT and may show AV dissociation and/or marked irregularity in the junctional rate. *RP refers to the interval from the onset of surface QRS to the onset of visible P wave (note that the 90-ms interval is defined from the surface ECG,[79] as opposed to the 70-ms ventriculoatrial interval that is used for intracardiac diagnosis [80]). AV indicates atrioventricular; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; ECG, electrocardiogram; MAT, multifocal atrial tachycardia; and PJRT, permanent form of junctional reentrant tachycardia. Modified with permission from Blomström-Lundqvist et al.[11]

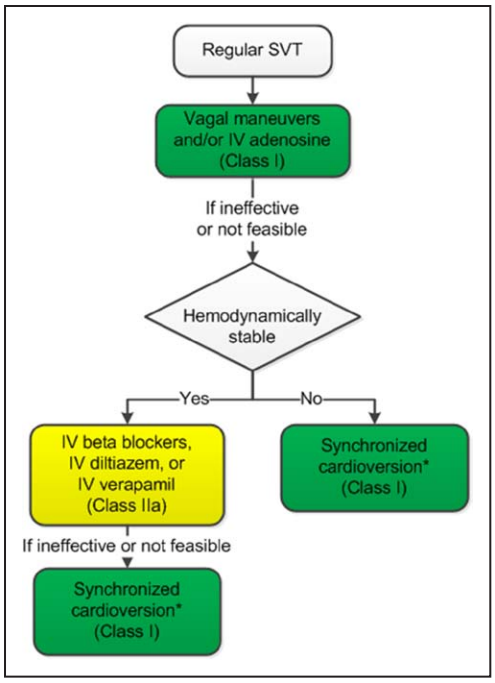

Figure 8. Acute treatment of regular SVT of unknown mechanism. Colors correspond to Class of Recommendation in Table 1; drugs listed alphabetically. *For rhythms that break or recur spontaneously, synchronized cardioversion is not appropriate. IV indicates intravenous; and SVT, supraventricular tachycardia.

3.1. Physiological Sinus Tachycardia

Sinus tachycardia is regarded as physiological when it is the result of appropriate autonomic influences, such as in the setting of physical activity or emotional responses. Physiological sinus tachycardia may result from pathological causes, including infection with fever, dehydration, anemia, heart failure, and hyperthyroidism, in addition to exogenous substances, including caffeine, drugs with a beta-agonist effect (eg, albuterol, salmeterol), and illicit stimulant drugs (eg, amphetamines, cocaine). In these cases, tachycardia is expected to resolve with correction of the underlying cause.

3.2. Inappropriate Sinus Tachycardia

Inappropriate sinus tachycardia (IST) is defined as sinus tachycardia that is unexplained by physiological demands at rest, with minimal exertion, or during recovery from exercise. Crucial to this definition is the presence of associated, sometimes debilitating, symptoms that include weakness, fatigue, lightheadedness, and uncomfortable sensations, such as heart racing. Patients with IST commonly show resting heart rates >100 bpm and average rates that are >90 bpm in a 24-hour period.[160] The cause of IST is unclear, and mechanisms related to dysautonomia, neurohormonal dysregulation, and intrinsic sinus node hyperactivity have been proposed.

It is important to distinguish IST from secondary causes of tachycardia, including hyperthyroidism, anemia, dehydration, pain, and use of exogenous substances and drugs of abuse. Anxiety is also an important trigger, and patients with IST may have associated anxiety disorders.[160] Structural heart disease, such as cardiomyopathies, must also be excluded, though the development of a cardiomyopathy secondary to sinus tachycardia is extremely rare.[164,165] IST must also be distinguished from other forms of tachycardia, including AT arising from the superior aspect of the crista terminalis and sinus node reentrant tachycardia (Section 4). It is also important to distinguish IST from postural orthostatic tachycardia syndrome, although overlap may be present within an individual. Patients with postural orthostatic tachycardia syndrome have predominant symptoms related to a change in posture, and treatment to suppress the sinus rate may lead to severe orthostatic hypotension. Thus, IST is a diagnosis of exclusion.

3.2.1. Acute Treatment

There are no specific recommendations for acute treatment of IST.

3.2.2. Ongoing Management: Recommendations

Because the prognosis of IST is generally benign, treatment is for symptom reduction and may not be necessary. Treatment

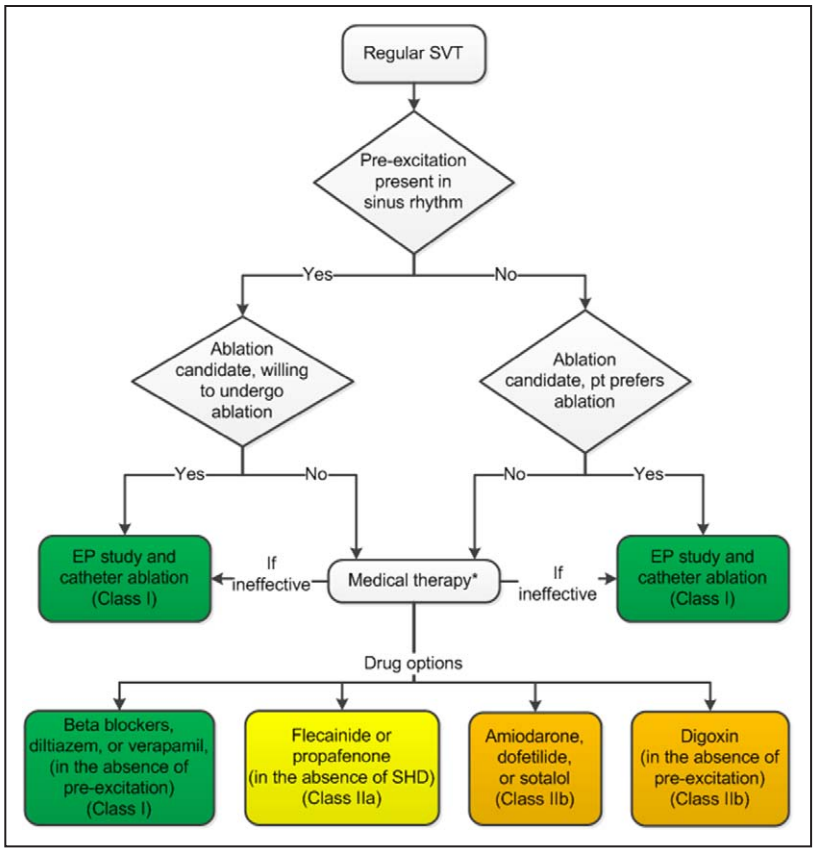

Figure 9. Ongoing management of SVT of unknown mechanism. Colors correspond to Class of Recommendation in Table 1; drugs listed alphabetically. *Clinical follow-up without treatment is also an option. EP indicates electrophysiological; pt, patient; SHD, structural heart disease (including ischemic heart disease); and SVT, supraventricular tachycardia.

of IST is difficult, and it should be recognized that lowering the heart rate may not alleviate symptoms. Therapy with beta blockers or calcium channel blockers is often ineffective or not well tolerated because of cardiovascular side effects, such as hypotension. Exercise training may be of benefit, but the benefit is unproven.

Ivabradine is an inhibitor of the "I-funny" or "If" channel, which is responsible for normal automaticity of the sinus node; therefore, ivabradine reduces the sinus node pacemaker activity, which results in slowing of the heart rate. On the basis of the results of 2 large, randomized, placebo-controlled trials, this drug was recently approved by the FDA for use in patients with systolic heart failure. In the BEAUTIFUL (Morbidity-Mortality Evaluation of the If Inhibitor Ivabradine in Patients With Coronary Disease and Left-Ventricular Dysfunction) study,[166] 10 917 patients with coronary disease and a left ventricular ejection fraction <40% were randomized to ivabradine or placebo. In the SHIFT (Systolic Heart Failure Treatment With the If Inhibitor Ivabradine) trial,[167] 6558 patients with a left ventricular ejection fraction ≤35% were randomized to ivabradine or placebo. In both of these trials, therapy with ivabradine resulted in additional heart rate reductions of 6 to 8 bpm and proved to be generally safe. The drug has no other hemodynamic effects aside from lowering the heart rate. As such, it has been investigated for use to reduce the sinus rate and improve symptoms related to IST.[168–176]

Radiofrequency ablation to modify the sinus node can reduce the sinus rate, with acute procedural success rates reported in the range of 76% to 100% in nonrandomized cohorts.[177–183] Ablation is typically performed with 3-dimensional electroanatomic or noncontact mapping techniques targeting sites of early activation with isoproterenol infusion, with or without use of intracardiac ultrasound–guided mapping to image the crista terminalis. Nonetheless, symptoms commonly recur after several months, with IST recurrence in up to 27% and overall symptomatic recurrence (IST or non-IST AT) in 45% of patients.[177,179,180,182] Complications can be significant and may include symptomatic sinus or junctional bradycardia necessitating pacemaker placement, phrenic nerve injury with paralysis of the right hemidiaphragm, and significant facial and upper-extremity swelling caused by narrowing of the superior vena cava/RA junction, which may rarely result in superior vena cava syndrome. In view of the modest benefit of this procedure and its potential for significant harm, sinus node modification should be considered only for patients who are highly symptomatic and cannot be adequately treated by medication, and then only after informing the patient that the risks may outweigh the benefits of ablation. Even more aggressive surgical methods to ablate or denervate the sinus node have been described, further highlighting the risks that highly symptomatic patients are willing to accept to find relief.[184] Effective patient communication is key for these patients.

Recommendations for Ongoing Management of IST		
COR	LOE	Recommendations
I	C-LD	**1. Evaluation for and treatment of reversible causes are recommended in patients with suspected IST.[160,185]**
See Online Data Supplements 4 and 5.		It is important to distinguish IST from physiological sinus tachycardia or focal AT from the high right atrium, which can have P-wave morphology similar to the sinus P wave. A careful history and physical examination, with further laboratory and imaging studies, are necessary to determine reversible causes of tachycardia, such as exogenous substances and drugs, infection, anemia, and hyperthyroidism. A focal AT would have sudden onset and termination, which would not be the case for IST.
IIa	B-R	**1. Ivabradine is reasonable for ongoing management in patients with symptomatic IST.[168–176]**
See Online Data Supplements 4 and 5.		In 1 small randomized crossover trial,[168] ivabradine given at a dosage of 2.5 to 7.5 mg twice daily significantly reduced daytime heart rate from 98.4±11.2 at baseline to 84.7±9.0, compared with 98.6±11.1 on placebo (P<0.001), and improved exercise tolerance and symptoms in patients with IST. Similar findings have been observed in several additional nonrandomized observational studies.[169–176] Furthermore, a significant number of patients in these studies reported complete resolution of symptoms, with persistent clinical benefit observed in some even after discontinuing the drug. In 1 observational study, ivabradine was more effective than metoprolol in reduction of the heart rate and amelioration of symptoms.[170] The drug is well tolerated, with an excellent safety profile demonstrated in 2 large RCTs in patients with heart failure.[166,167] Ivabradine can cause phosphenes, an enhanced brightness in a portion of the visual field; this side effect, which is usually transient, was reported in 3% of patients taking the drug in the SHIFT trial.[167]
IIb	C-LD	**1. Beta blockers may be considered for ongoing management in patients with symptomatic IST.[170,172]**
See Online Data Supplement 4 and 5.		Beta blockers are modestly effective in lowering the heart rate and improving symptoms that are due to IST. In a small nonrandomized observational cohort, metoprolol succinate titrated to a target of 95 mg daily lowered the heart rate over 4 weeks from a baseline.[172] In a small nonrandomized study comparing metoprolol with ivabradine, both agents reduced heart rate compared with baseline and improved exercise capacity.[170] Although effectiveness of beta blockers is modest and hypotension may limit dose, the overall safety of beta blockers warrants their use for treatment of symptomatic patients.
IIb	C-LD	**2. The combination of beta blockers and ivabradine may be considered for ongoing management in patients with IST.[172]**
See Online Data Supplement 4 and 5.		Some patients with IST may have particularly refractory symptoms, and single-drug efficacy may be limited. In a small observational study, the addition of ivabradine (7.5 mg twice daily) to metoprolol succinate (95 mg daily) reduced the heart rate from baseline to a greater extent than did metoprolol alone.[172] On combination therapy, symptoms related to IST were resolved in all patients, and the combined therapy was well tolerated. In the SHIFT and BEAUTIFUL studies, the majority of patients were taking the combination of ivabradine and a beta blocker, which was well tolerated.[166,167] Nevertheless, patients who are considered for combination therapy should be monitored closely for the possibility of excess bradycardia. Ivabradine can cause phosphenes, an enhanced brightness in a portion of the visual field; this side effect was reported in 3% of patients taking the drug in the SHIFT trial.[167]

4. Nonsinus Focal Atrial Tachycardia and MAT

See Figure 10 for the algorithm for acute treatment of suspected focal atrial tachycardia (AT) and Figure 11 for the algorithm for ongoing management of focal AT.

4.1. Focal Atrial Tachycardia

Focal AT is characterized as a fast rhythm from a discrete origin, discharging at a rate that is generally regular, and conducting in a centrifugal manner throughout the atrial tissue. Focal AT represents approximately 3% to 17% of the patients referred for SVT ablation.[49,122,186] The demographics of focal AT in the adult population will continue to change as SVTs are increasingly ablated at a younger age.

Focal AT can be sustained or nonsustained. The atrial rate during focal AT is usually between 100 and 250 bpm.[186] Presence and severity of symptoms during focal AT are variable among patients. Focal AT in the adult population is usually associated with a benign prognosis, although AT-mediated cardiomyopathy has been reported in up to 10% of patients referred for ablation of incessant SVT.[187,188] Nonsustained focal AT is common and often does not require treatment.

The diagnosis of focal AT is suspected when the ECG criteria are met (Section 2). Algorithms have been developed to estimate the origin of the focal AT from the P-wave morphology recorded on a standard 12-lead ECG.[189,190] In general, a positive P wave in lead V1 and negative P waves in leads I and aVL are correlated to ATs arising from the left atrium. Positive P waves in leads II, III, and aVF suggest that the origin of AT is from the cranial portion of either atria. Shorter P-wave duration is correlated to AT arising from the paraseptal tissue versus the right or left atrial free wall.[191] The precise location of the focal AT is ultimately confirmed by mapping during EP studies when successful ablation is achieved.[123–127,192–196] Focal AT has been localized to the crista terminalis, right or left atrial free wall or appendage, tricuspid or mitral annulus, paraseptal or paranodal areas, pulmonary veins, coronary sinus, and coronary cusps, but it originates more frequently from the right atrium than from the left atrium.[197,198]

The underlying mechanism of focal AT can be automatic, triggered activity, or microreentry, but methods to distinguish the mechanism through pharmacological testing or EP study are of modest value because of limited sensitivity and specificity.[123,199,200] An automatic AT can be transiently suppressed by adenosine or by overdrive pacing and may be terminated by beta blockers, diltiazem, or verapamil. Whereas a triggered AT can be terminated by adenosine or overdrive pacing, its response to beta blockers, diltiazem, or verapamil may be variable. A microreentrant AT can be induced and terminated by programmed stimulation, but its response to adenosine, beta blockers, diltiazem, or verapamil may depend on the location of the microreentrant circuit; the tachycardia can be terminated by these drugs if the microreentrant circuit involves tissue around the sinus node,

Table 6. Acute Drug Therapy for SVT, Intravenous Administration*

Drug	Initial Dose	Subsequent or Maintenance Dose	Potential Adverse Effects	Precautions (Exclude or Use With Caution) and Interactions
Nucleoside				
Adenosine	6-mg rapid IV bolus (injected into IV as proximal or as close to the heart as possible), administered over 1–2 s, followed by rapid saline flush	If no result within 1–2 min, 12-mg rapid IV bolus; can repeat 12-mg dose 1 time. The safe use of 18-mg bolus doses has been reported.[117]	Transient AV block, flushing, chest pain, hypotension, or dyspnea, AF can be initiated or cause decompensation in the presence of pre-excitation, PVCs/ventricular tachycardia, bronchospasm (rare), or coronary steal. Minor side effects are usually transient because of adenosine's very short half-life.	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Reactive airway disease • Concomitant use of verapamil or digoxin • WPW
Beta blockers				
Esmolol	500-mcg/kg IV bolus over 1 min	Infusion at 50–300 mcg/kg/min, with repeat boluses between each dosing increase	Hypotension, worsening HF, bronchospasm, bradycardia	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Decompensated systolic HF • Hypotension • Cardiogenic shock • Reactive airway disease • Renal dysfunction • Drugs with SA and/or AV nodal–blocking properties
Metoprolol tartrate	2.5–5.0-mg IV bolus over 2 min	Can repeat 2.5- to 5.0-mg IV bolus in 10 min, up to 3 doses	Hypotension, worsening HF, bronchospasm, bradycardia	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Decompensated systolic HF • Hypotension • Reactive airway disease • Drugs with SA and/or AV nodal–blocking properties
Propranolol	1 mg IV over 1 min	Can repeat 1 mg IV at 2-min intervals, up to 3 doses	Hypotension, worsening HF, bronchospasm, bradycardia	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Cardiogenic shock • Reactive airway disease • Decompensated HF • Hypotension • Hepatic or renal dysfunction • Drugs with SA and/or AV nodal–blocking properties
Nondihydropyridine calcium channel antagonists				
Diltiazem	0.25-mg/kg IV bolus over 2 min	Infusion at 5–10 mg/h, up to 15 mg/h	Hypotension, worsening HF in patients with pre-existing ventricular dysfunction, bradycardia, abnormal liver function studies, acute hepatic injury (rare)	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • WPW with AF/atrial flutter • Hypotension† • Decompensated systolic HF/LV dysfunction • Drugs with SA and/or AV nodal–blocking properties • Hepatic or renal dysfunction • Diltiazem is a substrate of CYP3A4 (major) and a moderate CYP3A4 inhibitor • Apixaban, itraconazole, bosutinib, ceritinib, cilostazol, cyclosporine, everolimus, ibrutinib, idelalisib, ivabradine, lomitapide, olaparib, posaconazole, ranolazine, rifampin, simeprevir, voriconazole

(*Continued*)

Table 6. Continued

Drug	Initial Dose	Subsequent or Maintenance Dose	Potential Adverse Effects	Precautions (Exclude or Use With Caution) and Interactions
Verapamil	5–10-mg (0.075–0. 15-mg/kg) IV bolus over 2 min	If no response, can give an additional 10 mg (0.15 mg/kg) 30 min after first dose; then infusion at 0.005 mg/kg/min	Hypotension, worsening HF in patients with pre-existing ventricular dysfunction, pulmonary edema in patients with hypertrophic cardiomyopathy, bradycardia	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Decompensated systolic HF/LV dysfunction • Drugs with SA and/or AV nodal–blocking properties • Hypotension† • Cardiogenic shock • WPW with AF/atrial flutter • Hepatic or renal dysfunction • Verapamil is a moderate CYP3A4 inhibitor and also inhibits P-glycoprotein • Contraindicated with dofetilide • Itraconazole, bosutinib, ceritinib, cilostazol, colchicine, cyclosporine, everolimus, dabigatran, edoxaban, flecainide, ibrutinib, ivabradine, olaparib, posaconazole, ranolazine, rivaroxaban, rifampin, silodosin, simeprevir, rivaroxaban, rifampin, simvastatin, topotecan, trabectedin, vincristine, voriconazole, grapefruit juice
Cardiac glycosides				
Digoxin	0.25–0.5-mg IV bolus	Can repeat 0.25-mg IV bolus, up to maximum dose of 1.0 mg over 24 h (ie, maximum loading dose 8–12 mcg/kg), given at 6–8-h intervals; maintenance dose based on patient's age, lean body weight, renal function, and concomitant drugs (IV 2.4–3.6 mcg/kg/d)	Anorexia, nausea, vomiting, visual changes and cardiac arrhythmias if digoxin toxicity (associated with levels >2 ng/mL, although symptoms may also occur at lower levels)	• Renal dysfunction • WPW with AF/atrial flutter • AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Drugs with AV nodal-blocking properties • Digoxin is a P-glycoprotein substrate • Dronedarone (reduce dose by at least 50%), amiodarone (reduce dose by 30%–50%) • Verapamil, clarithromycin, cyclosporine, erythromycin, flecainide, itraconazole, posaconazole, propafenone, voriconazole: Monitor digoxin levels • A large retrospective study suggested an increased risk in mortality in patients who were treated with digoxin for newly diagnosed AF or atrial flutter; although the data were collected from a population that was different from SVT patients, digoxin should be used with caution.[118]
Class III antiarrhythmic agents				
Amiodarone	150 mg IV over 10 min	Infusion at 1 mg/min (360 mg) over next 6 h; then 0.5 mg/min (540 mg) over remaining 18 h	Hypotension, bradycardia, phlebitis, QT prolongation, torsades de pointes (rare), increased INR	• Sinus or AV conduction disease (in absence of pacemaker) • Inflammatory lung disease (acute) • Hepatic dysfunction • Drugs with SA and/or AV nodal–blocking properties • Amiodarone is a substrate of and inhibits p-glycoprotein and CYP2C9 (moderate), CYP2D6 (moderate), and CYP3A4 (weak); amiodarone is a substrate for CYP3A4 (major) and CYP2C8 (major);amiodarone is an inhibitor of OCT2 • Reduce warfarin dose by 50% and reduce digoxin dose by 30%–50% • Agalsidase alfa, agalsidase beta, azithromycin, bosutinib, ceritinib, colchicine, dabigatran, edoxaban, flecainide, ivabradine, ledipasvir/sofosbuvir, lopinavir, lopinavir/ritonavir, lovastatin, nelfinavir, pazopanib, propafenone, simvastatin, ritonavir, rivaroxaban, saquinavir, sofosbuvir, topotecan, vincristine, grapefruit juice

(*Continued*)

Table 6. Continued

Drug	Initial Dose	Subsequent or Maintenance Dose	Potential Adverse Effects	Precautions (Exclude or Use With Caution) and Interactions
Ibutilide	Contraindicated when QTc >440 ms‡; 1 mg over 10 min (if ≥60 kg); if <60 kg, then 0.01 mg/kg	Can repeat 1 mg once, if the arrhythmia does not terminate within 10 min§	QT prolongation, torsades de pointes, AV block	• Prolonged QT interval • History of torsades de pointes • Avoid other QT interval–prolonging drugs • Concurrent administration of high-dose magnesium has been associated with enhanced efficacy and safety[119,120]

Note: For this reference table, drugs are presented in alphabetical order within the drug classes, not by COR and LOE.

*When 1 drug is used in combination with other drugs, appropriate dosing adjustments should be made with consideration of at least additive effects during dosage titration. All potential drug–drug interactions are not included in this list. For a more detailed list of drug–drug interactions, clinicians should consult additional resources.

†If hypotension is a consideration, a slow infusion of diltiazem (2.5 mg/min) or verapamil (1 mg/min) for up to 20 minutes may lessen the potential for hypotension.[92]

‡QTc calculation used the Bazett's Formula in most clinical studies. Patients should be observed with continuous ECG monitoring for at least 4 h after infusion or until QTc has returned to baseline.

§The infusion should be stopped as soon as the arrhythmia is terminated or in the event of sustained or nonsustained ventricular tachycardia or marked prolongation of QT or corrected QT interval.

AF indicates atrial fibrillation; AV, atrioventricular; BID, twice daily; COR, Class of Recommendation; HF, heart failure; INR, international normalized ratio; IV, intravenous; LOE, Level of Evidence; LV, left ventricular; PVC, premature ventricular contraction; QTc, corrected QT interval; SA, sinoatrial; SVT, supraventricular tachycardia; and WPW, Wolff-Parkinson-White.

whereas microreentrant ATs from other locations generally will not be terminated by these drugs.

Sinus node reentrant tachycardia is an uncommon type of focal AT that involves a microreentrant circuit in the region of the sinoatrial node, causing a P-wave morphology that is identical to that of sinus tachycardia (although this is not sinus tachycardia). Characteristics that distinguish sinus node reentry from sinus tachycardia are an abrupt onset and termination and often a longer RP interval than that observed during normal sinus rhythm. Sinus node reentry is characterized by paroxysmal episodes of tachycardia, generally 100 bpm to 150 bpm.[201–203] Confirmation of the reentrant mechanism requires an EP study. Induction of sinus node reentrant tachycardia during programmed stimulation, demonstration of entrainment, and localization of the tachycardia origin in the region of the sinus node are necessary to confirm the diagnosis.

4.1.1. Acute Treatment: Recommendations

RCTs of drug therapy for comparative effectiveness in patients with focal AT in the acute setting are not available. Many of the clinical outcomes are reported from small observational studies that included infants or pediatric patients.[204,205] The design or execution of these studies is frequently suboptimal because of the poorly defined inclusion criteria or variable clinical settings. Several studies included a mix of patients with congenital or postoperative AT, and some of these patients likely had macroreentrant AT. In many reports, the response to intravenous drug therapy was evaluated by EP study rather than in the clinical environment.[123,200,204–207] In the clinical setting, if the diagnosis is uncertain, vagal maneuvers may be attempted to better identify the mechanism of SVT.

Digoxin has not been well studied for focal AT. Intravenous class Ic drugs (eg, flecainide, propafenone) may be moderately effective in treating focal AT in the acute setting, as reported in earlier, small observational studies, although intravenous forms of IC drugs are not available in the United States. In patients with an implanted cardiac pacing device, it may be possible to perform overdrive pacing through the device, although close monitoring is required to prevent any significant adverse effect, such as pacing-induced AF or other atrial arrhythmias. Equipment should be available to provide support for cardioversion of AF if needed.

Recommendations for Acute Treatment of Suspected Focal Atrial Tachycardia		
COR	**LOE**	**Recommendations**
I	C-LD	**1. Intravenous beta blockers, diltiazem, or verapamil is useful for acute treatment in hemodynamically stable patients with focal AT.[123,204,205,207]**
See Online Data Supplement 6.		Intravenous beta blockers, diltiazem, or verapamil is recommended to treat focal AT. During EP study, propranolol or verapamil is moderately effective in either terminating the focal AT or slowing the ventricular rate in approximately 30% to 50% of the patients.[204,205] Although these agents are relatively safe, close monitoring is recommended during intravenous drug therapy to evaluate for hypotension or bradycardia.
I	C-LD	**2. Synchronized cardioversion is recommended for acute treatment in patients with hemodynamically unstable focal AT.[94,208]**
See Online Data Supplement 6.		Although minimum data are available on cardioversion of focal AT, synchronized cardioversion is a consideration in patients with drug-resistant arrhythmias associated with signs and symptoms of compromised hemodynamics. Termination of tachycardia is expected when a focal AT is of a microreentrant mechanism. Response of a triggered focal AT to cardioversion can be variable, whereas electrical cardioversion is not likely to be effective in focal AT with an automatic mechanism. In this latter case, antiarrhythmic drug therapy is usually required.

Recommendations for Acute Treatment of Suspected Focal Atrial Tachycardia (Continued)		
COR	LOE	Recommendations
IIa	B-NR	**1. Adenosine can be useful in the acute setting to either restore sinus rhythm or diagnose the tachycardia mechanism in patients with suspected focal AT.[123,200,207]**
See Online Data Supplement 6.		Adenosine is usually effective in terminating focal AT of a triggered mechanism but is not expected to be effective in reentrant focal AT.[207] Transient suppression can be observed in automatic focal AT. The observation of transient AV block with persistent AT can be helpful in making the diagnosis and differentiating focal AT from AVNRT and AVRT.
IIb	C-LD	**1. Intravenous amiodarone may be reasonable in the acute setting to either restore sinus rhythm or slow the ventricular rate in hemodynamically stable patients with focal AT.[205,206]**
See Online Data Supplement 6.		The therapeutic effect of intravenous amiodarone in the acute setting is likely mediated via blockade of the beta receptors or calcium channels. Amiodarone may be preferred in patients with reduced ventricular function or with a history of heart failure.
IIb	C-LD	**2. Ibutilide may be reasonable in the acute setting to restore sinus rhythm in hemodynamically stable patients with focal AT.[205,206]**
See Online Data Supplement 6.		The effectiveness of ibutilide for treatment of focal AT is unclear. In 1 study, intravenous ibutilide terminated AT of single atrial morphology in 19 of 39 patients (38.8%), but the proportions of patients with focal AT and macroreentrant AT were not differentiated in this study cohort.[206]

4.1.2. Ongoing Management: Recommendations

Recommendations for Ongoing Management of Suspected Focal Atrial Tachycardia		
COR	LOE	Recommendations
I	B-NR	**1. Catheter ablation is recommended in patients with symptomatic focal AT as an alternative to pharmacological therapy.[122–126,188,191–196,206]**
See Online Data Supplement 6.		A large number of nonrandomized cohort studies on focal AT ablation have accumulated in the past 2 decades. In a 2012 ablation registry provided by 74 voluntary medical centers in Spain, AT was found in 333 of 11 042 of the ablation procedures performed.[122] In experienced centers, when the AT can be induced in the laboratory, acute success rates above 90% to 95% have consistently been reported, with a complication rate of <1% to 2%.[122,123,125,196] See Table 8 for a summary of ablation efficacy, complications, and rate of recurrence. Although uncommon, focal AT-mediated cardiomyopathy should be recognized in patients presenting with heart failure, reduced ventricular function, and persistent tachycardia. In a case–control study of patients with AT, 10% of patients had evidence of cardiomyopathy.[125] The tachycardia in patients with cardiomyopathy was incessant and slower than in the patients without cardiomyopathy (cycle lengths 502 ms and 402 ms, respectively). Normal ejection fraction was restored in 97% of patients after successful ablation.[188]
IIa	C-LD	**1. Oral beta blockers, diltiazem, or verapamil are reasonable for ongoing management in patients with symptomatic focal AT.[123,204,205]**
See Online Data Supplement 6.		Data on long-term drug therapy of focal AT are limited to observational studies, and some studies did not provide clear inclusion criteria, so results for AT were combined with those for other mechanisms of SVT. Nevertheless, these drugs are moderately effective, with a low incidence of significant adverse effects.[123,204,205,209–214]
IIa	C-LD	**2. Flecainide or propafenone can be effective for ongoing management in patients without structural heart disease or ischemic heart disease who have focal AT.[209–213]**
See Online Data Supplement 6.		Small case series studies reported that focal AT suppression was achieved with flecainide in most patients.[209,210] In infants and children, propafenone is moderately effective in focal AT suppression during follow-up.[213] Flecainide and propafenone are generally tolerated by patients with focal AT. Combinations of a class Ic drug with a beta blocker, diltiazem, or verapamil may improve overall efficacy rates.
IIb	C-LD	**1. Oral sotalol or amiodarone may be reasonable for ongoing management in patients with focal AT.[188,211,215–219]**
See Online Data Supplement 6.		Several studies reported moderate efficacies of oral sotalol or amiodarone in maintaining sinus rhythm in long-term treatment in children.[188,211,215–219] Although most reports are in children, limited data suggest similar efficacy in adults.[218] Because of the risk of proarrhythmia and other complications, before use of these drugs, a balance between anticipated benefit of focal AT suppression and potential adverse effects of these drugs should be carefully considered.

4.2. Multifocal Atrial Tachycardia

MAT is defined as a rapid, irregular rhythm with at least 3 distinct morphologies of P waves on the surface ECG. It may be difficult to distinguish MAT from AF on physical examination or even on a single ECG tracing, so a 12-lead ECG is indicated to confirm the diagnosis. On the ECG, the atrial rate is >100 bpm (or >90 bpm, as defined in at least 1 report[220]). Unlike AF, there is a distinct isoelectric period between P waves. The P-P, P-R, and R-R intervals are variable. The mechanism of MAT is not well established. Although it is assumed that the variability of P-wave morphology implies a multifocal origin, there are very few mapping studies of MAT.[221] Similarly, the variability of the P-R interval may relate to decremental conduction through the AV node, as opposed to the origin of the P wave. Occasional responsiveness to verapamil suggests a triggered mechanism, but data are limited.[222]

MAT is commonly associated with underlying conditions, including pulmonary disease, pulmonary hypertension, coronary disease, and valvular heart disease,[223] as well as hypomagnesemia and theophylline therapy.[224] The first-line treatment is management of the underlying condition. Intravenous magnesium may also be helpful in patients with normal magnesium levels.[225] Antiarrhythmic medications in general are not helpful in suppression of multifocal AT.[226] Management often involves slowing conduction at the AV nodal level to control heart rate. Verapamil has been shown to have some efficacy in

Table 7. Ongoing Drug Therapy for SVT, Oral Administration*

Drug	Initial Daily Dose(s)	Maximum Total Daily Maintenance Dose	Potential Adverse Effects	Precautions (Exclude or Use With Caution) and Interactions
Beta blockers				
Atenolol	25–50 mg QD	100 mg QD (reduced dosing in patients with severe renal dysfunction)	Hypotension, bronchospasm, bradycardia	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Decompensated systolic HF • Hypotension • Reactive airway disease • Severe renal dysfunction • Drugs with SA and/or AV nodal–blocking properties
Metoprolol tartrate	25 mg BID	200 mg BID	Hypotension, bronchospasm, bradycardia	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Decompensated systolic HF • Hypotension • Reactive airway disease • Drugs with SA and/or AV nodal–blocking properties
Metoprolol succinate (long-acting)	50 mg QD	400 mg QD	Hypotension, bronchospasm, bradycardia	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Decompensated systolic HF • Hypotension • Reactive airway disease • Drugs with SA and/or AV nodal–blocking properties
Nadolol	40 mg QD	320 mg QD (reduced dosage with renal impairment)	Hypotension, bronchospasm, bradycardia	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Reactive airway disease • Cardiogenic shock • Decompensated HF • Hypotension • Renal dysfunction • Drugs with SA and/or AV nodal–blocking properties
Propranolol	30–60 mg in divided or single dose with long-acting formulations	40–160 mg in divided or single dose with long-acting formulations	Hypotension, worsening HF, bronchospasm, bradycardia	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Reactive airway disease • Decompensated systolic HF • Hypotension • Drugs with SA and/or AV nodal–blocking properties
Nondihydropyridine calcium channel antagonists				
Diltiazem	120 mg daily in divided or single dose with long-acting formulations	360 mg daily in divided or single dose with long-acting formulations	Hypotension, worsening HF in patients with pre-existing ventricular dysfunction, bradycardia, abnormal liver function studies, acute hepatic injury (rare)	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Hypotension† • Decompensated systolic HF/severe LV dysfunction • WPW with AF/atrial flutter • Drugs with SA and/or AV nodal–blocking properties • Diltiazem is a substrate of CYP3A4 (major) and a moderate CYP3A4 inhibitor • Apixaban, itraconazole, bosutinib, ceritinib, cilostazol, cyclosporine, everolimus, ibrutinib, idelalisib, ivabradine, lomitapide, olaparib, ranolazine, rifampin, simeprevir

(*Continued*)

Table 7. Continued

Drug	Initial Daily Dose(s)	Maximum Total Daily Maintenance Dose	Potential Adverse Effects	Precautions (Exclude or Use With Caution) and Interactions
Verapamil	120 mg daily in divided or single dose with long-acting formulations	480 mg daily in divided or single dose with long-acting formulations	Hypotension, worsening HF in patients with pre-existing ventricular dysfunction, pulmonary edema in patients with hypertrophic cardiomyopathy, bradycardia, abnormal liver function studies	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Decompensated systolic HF/severe LV dysfunction • Hypotension† • WPW with AF/atrial flutter • Verapamil is a moderate CYP3A4 inhibitor and also inhibits P-glycoprotein • Contraindicated with dofetilide • Itraconazole, bosutinib, ceritinib, cilostazol, colchicine, cyclosporine, everolimus, dabigatran, edoxaban, flecainide, ibrutinib, ivabradine, olaparib, ranolazine, rivaroxaban, rifampin, silodosin, simeprevir, rivaroxaban, rifampin, simvastatin, topotecan, trabectedin, vincristine, grapefruit juice
Cardiac glycosides				
Digoxin	*Loading*: 0.5 mg, with additional 0.125–0.25-mg doses administered at 6–8-h intervals until evidence of adequate effect (maximum dose 8–12 mcg/kg over 24 h)	0.25 mg QD *Maintenance*: 0.125–0.25 mg QD, with dosing based on patient's age, lean body weight, and renal function and drug interactions; occasionally down to 0.0625 mg in cases of renal impairment (trough serum digoxin level 0.5 to 1 ng/mL)	Bradycardia, heart block, anorexia, nausea, vomiting, visual changes and cardiac arrhythmias in cases of digoxin toxicity (associated with levels >2 ng/mL, although symptoms may also occur at lower levels)	• Renal dysfunction • WPW with AF/atrial flutter • AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Drugs with SA and/or AV nodal–blocking properties • Reduce dose by 30%–50% when administering with amiodarone and by 50% when administering with dronedarone • Monitor digoxin concentrations with verapamil, clarithromycin, erythromycin, itraconazole, cyclosporine, propafenone, flecainide
Class Ic antiarrhythmic agents				
Flecainide	50 mg every 12 h	150 mg every 12 h (PR and QRS intervals should be monitored. May consider monitoring flecainide plasma levels, keeping trough plasma levels below 0.7–1.0 mcg/mL)	Atrial flutter with 1:1 AV conduction‡, QT prolongation, torsades de pointes, worsening HF, bradycardia	• Sinus or AV conduction disease (in absence of pacemaker) • Cardiogenic shock • Avoid in structural heart disease (including ischemic heart disease) • Atrial flutter (unless concomitant AV nodal therapy to avoid 1:1 conduction) • Brugada syndrome • Renal dysfunction • Hepatic dysfunction • QT-prolonging drugs • Amiodarone, digoxin, ritonavir, saquinavir, tipranavir
Propafenone	150 mg every 8 h (immediate release); 225 mg every 12 h (extended release)	300 mg every 8 h (immediate release); 425 mg every 12 h (extended release) (PR and QRS interval should be monitored. Consider dosage reduction with hepatic impairment)	Atrial flutter with 1:1 AV conduction‡, QT prolongation, torsades de pointes, bradycardia, bronchospasm	• Sinus or AV conduction disease (in absence of pacemaker) • Cardiogenic shock • Hypotension • Reactive airway disease Avoid in structural heart disease (including ischemic heart disease) • Atrial flutter (unless concomitant AV nodal therapy to avoid 1:1 conduction) • Brugada syndrome • Hepatic dysfunction • QT-prolonging drugs • Drugs with SA and/or AV nodal–blocking properties • Amiodarone, ritonavir, saquinavir, tipranavir

(*Continued*)

Table 7. Continued

Drug	Initial Daily Dose(s)	Maximum Total Daily Maintenance Dose	Potential Adverse Effects	Precautions (Exclude or Use With Caution) and Interactions
Class III antiarrhythmic agents				
Amiodarone	400–600 mg QD in divided doses for 2–4 wk (loading dose); followed by 100–200 mg QD (maintenance dose)	Up to 1200 mg QD may be considered in an inpatient monitoring setting (loading dose); up to 200 mg QD maintenance (to minimize long-term adverse effects)	Bradycardia, QT prolongation, torsades de pointes (rare), gastrointestinal upset, constipation, hypothyroidism, hyperthyroidism, pulmonary fibrosis, hepatic toxicity, corneal deposits, optic neuritis, peripheral neuropathy, photosensitivity, adult respiratory distress syndrome after cardiac or noncardiac surgery (rare)	• Sinus or AV conduction disease (in absence of pacemaker) • Inflammatory lung disease • Hepatic dysfunction • Hypothyroidism, hyperthyroidism • Peripheral neuropathy • Abnormal gait/ataxia • Optic neuritis • Drugs with SA and/or AV nodal–blocking properties • Amiodarone is a substrate of and inhibits P-glycoprotein and CYP2C9 (moderate), CYP2D6 (moderate), and CYP3A4 (weak); amiodarone is a substrate for CYP3A4 (major) and CYP2C8 (major); amiodarone is an inhibitor of OCT2 • Reduce warfarin dose by 50%, and reduce digoxin dose by 30%–50% • Agalsidase alfa, agalsidase beta, azithromycin, bosutinib, ceritinib, colchicine, dabigatran, edoxaban, flecainide, ivabradine, ledipasvir/sofosbuvir, lopinavir, lopinavir/ritonavir, lovastatin, nelfinavir, pazopanib, propafenone, simvastatin, ritonavir, rivaroxaban, saquinavir, sofosbuvir, topotecan, vincristine, grapefruit juice
Dofetilide	500 mcg every 12 h (if CrCl >60 mL/min) 250 mcg every 12 h (if CrCl 40–60 mL/min) 125 mcg every 12 h (if CrCl 20 to <40 mL/min) Not recommended if CrCl <20 mL/min Adjust dose for renal function, body size, and age Initiate for minimum of 3 d in a facility that can provide continuous ECG monitoring and cardiac resuscitation Contraindicated if the baseline QTc interval or QTc >440 ms† or 500 ms in patients with ventricular conduction abnormalities	Repeat ECG 2–3 h after administering the first dose to determine QTc; if the QTc increased by >15% compared with baseline or if QTc is >500 ms† (550 ms in patients with ventricular conduction abnormalities), subsequent dosing should be down titrated by 50%; at 2–3 h after each subsequent dose, determine QTc (for in-hospital doses 2–5); if at any time after the second dose the QTc is >500 ms‖ (550 ms in patients with ventricular conduction abnormalities), dofetilide should be discontinued	QT prolongation, torsades de pointes	• Severe renal dysfunction (contraindicated if CrCl <20 mL/min) • Prolonged QT • History of torsades de pointes • Concomitant use of hydrochlorothiazide, cimetidine, dolutegravir, itraconazole, ketoconazole, megestrol, trimethoprim, prochlorperazine trimethoprim/sulfamethoxazole or verapamil, contraindicated • Avoid other QT-prolonging drugs
Sotalol	40–80 mg every 12 h (Patients initiated or reinitiated on sotalol should be placed in a facility that can provide cardiac resuscitation and continuous electrocardiographic monitoring for a minimum of 3 d). Contraindicated if the QTc† interval is >450 ms. CrCl should be calculated before dosing. If CrCl >60 mL/min, then dosing frequency is twice daily. If CrCl 40–60 mL/min, dosing interval is every 24 h. If CrCl <40 mL/min, should not be used.)	160 mg every 12 h (During initiation and titration, the QT interval should be monitored 2–4 h after each dose. If the QT interval prolongs to ≥500 ms, the dose must be reduced or the drug discontinued.)	QT prolongation, torsades de pointes, bradycardia, bronchospasm	• Prolonged QT • Renal dysfunction • Hypokalemia • Diuretic therapy • Avoid other QT-prolonging drugs • Sinus or AV nodal dysfunction (in absence of pacemaker) • Decompensated systolic HF • Cardiogenic shock • Reactive airway disease • Drugs with SA and/or AV–nodal blocking properties

(*Continued*)

Table 7. Continued

Drug	Initial Daily Dose(s)	Maximum Total Daily Maintenance Dose	Potential Adverse Effects	Precautions (Exclude or Use With Caution) and Interactions
Miscellaneous				
Ivabradine	5 mg BID	7.5 mg BID	Phosphenes, AF	• Concomitant drugs that can exacerbate bradycardia • Contraindicated in decompensated HF • Contraindicated if BP <90/50 mm Hg • Contraindicated in severe hepatic impairment • Hypertension • Ivabradine is a substrate of CYP3A4 (major) • Avoid use with concomitant strong CYP3A4 inhibitors (boceprevir, clarithromycin, indinavir, itraconazole, lopinavir/ritonavir, nelfinavir, ritonavir, saquinavir, telaprevir, posaconazole, voriconazole) • Avoid use with strong CYP3A4 inducers (carbamazepine, phenytoin, rifampin, St. John's wort) • Avoid use with diltiazem, verapamil, grapefruit juice

Note: For this reference table, drugs are presented in alphabetical order within the drug classes, not by COR and LOE.

*When 1 drug is used in combination with other drugs, appropriate dosing adjustments should be made with consideration of at least additive effects during dosage titration. All potential drug–drug interactions and adverse reactions are not included in this list. For a more detailed list of drug interactions and adverse responses, clinicians should consult additional resources; for example, www.crediblemeds.org may be consulted for potential prolongation of the QT interval.

†QTc calculation used the Bazett's Formula in most clinical studies.

‡Recommended given in conjunction with a beta blocker or nondihydropyridine calcium channel antagonist.

AF indicates atrial fibrillation; AV, atrioventricular; BID, twice daily; BP, blood pressure; CrCl, creatinine clearance; ECG, electrocardiogram/electrocardiographic; HF, heart failure; INR, international normalized ratio; LV, left ventricular; QD, once daily; QID, 4 times a day; QTc, corrected QT interval; SA, sinoatrial; SVT, supraventricular tachycardia; TID, 3 times a day; and WPW, Wolff-Parkinson-White.

patients with MAT who do not have ventricular dysfunction, sinus node dysfunction, or AV block[227,228]; although diltiazem has not been studied, it may provide a class effect with similar mechanism to verapamil. Beta blockers can be used with caution to treat MAT in the absence of respiratory decompensation, sinus node dysfunction, or AV block.[229,230] Amiodarone has been reported to be useful in 1 report.[231] Cardioversion is not useful in MAT.[223]

4.2.1. Acute Treatment: Recommendation

Recommendations for Acute Treatment of Multifocal Atrial Tachycardia		
COR	**LOE**	**Recommendation**
IIa	**C-LD**	**1. Intravenous metoprolol[229] or verapamil[232,233] can be useful for acute treatment in patients with MAT.**
See Online Data Supplement 7.		The mechanism of MAT can involve triggered activity, and treatment with intravenous verapamil can terminate the arrhythmia with moderate success. In 1 small study, intravenous verapamil converted MAT in 8 of 16 patients treated.[233] Alternatively, intravenous verapamil may acutely slow the ventricular response to MAT. The major potential side effect is hypotension.[233] The relatively cardioselective beta blocker metoprolol can also work by slowing the ventricular rate in MAT. Beta blockers are typically avoided in patients with severe underlying pulmonary disease, particularly those with bronchospasm; both beta blockers and verapamil are typically avoided in the presence of acute decompensated heart failure and/or hemodynamic instability.

4.2.2. Ongoing Management: Recommendations

Recommendations for Ongoing Management of Multifocal Atrial Tachycardia		
COR	**LOE**	**Recommendations**
IIa	**B-NR** **C-LD**	**1. Oral verapamil (*Level of Evidence: B-NR*) or diltiazem (*Level of Evidence: C-LD*) is reasonable for ongoing management in patients with recurrent symptomatic MAT.[227,230]**
See Online Data Supplement 8.		Long-term management of MAT frequently involves slowing of the ventricular response because arrhythmia termination is often not achievable. Verapamil has the advantage of not exacerbating pulmonary disease. Although it would be expected for diltiazem to have a similar effect, data on its use in patients with MAT are lacking. These drugs should not be used in patients with severe conduction abnormalities or sinus node dysfunction because those conditions can be exacerbated with these agents.

5. Atrioventricular Nodal Reentrant Tachycardia

See Figure 12 for the algorithm for acute treatment of AVNRT and Figure 13 for the algorithm for ongoing management of AVNRT.

AVNRT is the most common SVT. It is usually seen in young adults without structural heart disease or ischemic heart disease, and >60% of cases are observed in women.[49] The ventricular rate is often 180 bpm to 200 bpm but ranges from 110 bpm to >250 bpm (and in rare cases, the rate can be

Recommendations for Ongoing Management of Multifocal Atrial Tachycardia (Continued)		
COR	LOE	Recommendations
IIa	C-LD	**2. Metoprolol is reasonable for ongoing management in patients with recurrent symptomatic MAT.[226,229,230]**
See Online Data Supplements 7 and 8.		Beta blockers are typically avoided in the presence of acute decompensated heart failure or in patients with severe (particularly bronchospastic) pulmonary disease. However, metoprolol has been used in small studies in patients with serious pulmonary disease after correction of hypoxia or other signs of acute decompensation. In these studies, intravenous or oral metoprolol resulted in conversion to sinus rhythm or achieved rate control, and oral metoprolol was used for maintenance therapy.[226,230] Beta blockers are generally avoided in patients with severe conduction abnormalities or sinus node dysfunction.

<100 bpm).[54] The anatomic substrate of AVNRT is dual AV nodal physiology (Table 3).

AVNRT is often well tolerated and is rarely life threatening. Patients will typically present with the sudden onset of palpitations and possibly with shortness of breath, dizziness, and neck pulsations. Syncope is a rare manifestation of AVNRT. AVNRT may occur spontaneously or on provocation with exertion, coffee, tea, or alcohol.

5.1. Acute Treatment: Recommendations

Recommendations for Acute Treatment of AVNRT		
COR	LOE	Recommendations
I	B-R	**1. Vagal maneuvers are recommended for acute treatment in patients with AVNRT.[82–84,234,235]**
See Online Data Supplement 10.		For acute conversion of AVNRT, vagal maneuvers, including Valsalva and carotid sinus massage, can be performed quickly and should be the first-line intervention to terminate SVT. These maneuvers should be performed with the patient in the supine position. There is no "gold standard" for proper Valsalva maneuver technique, but in general, the patient raises intrathoracic pressure by bearing down against a closed glottis for 10 to 30 seconds, equivalent to at least 30 mm Hg to 40 mm Hg.[82,84] Carotid massage is performed after absence of bruit has been confirmed by auscultation, by applying steady pressure over the right or left carotid sinus for 5 to10 seconds.[83,84] Another vagal maneuver based on the classic diving reflex consists of applying an ice-cold, wet towel to the face[85]; in a laboratory setting, facial immersion in water at 10°C (50°F) has proved effective in terminating tachycardia, as well.[86] One study involving 148 patients with SVT demonstrated that Valsalva was more successful than carotid sinus massage, and switching from 1 technique to the other resulted in an overall success rate of 27.7%.[82] The practice of applying pressure to the eyeball is potentially dangerous and has been abandoned.
I	B-R	**2. Adenosine is recommended for acute treatment in patients with AVNRT.[42,51,91,236]**
See Online Data Supplements 9 and 10.		Adenosine can be considered as both a therapeutic and diagnostic agent in narrow-complex tachyarrhythmias. It will acutely terminate AVNRT in approximately 95% of patients and will unmask atrial activity in arrhythmias, such as atrial flutter or AT.[91,236]
I	B-NR	**3. Synchronized cardioversion should be performed for acute treatment in hemodynamically unstable patients with AVNRT when adenosine and vagal maneuvers do not terminate the tachycardia or are not feasible.[94,208]**
See Online Data Supplement 10.		Sinus rhythm must be promptly restored in patients with AVNRT who are hemodynamically unstable. The safety and effectiveness of cardioversion has been proven in patients with hemodynamically unstable SVT who had failed to convert with vagal maneuvers and intravenous pharmacological therapy.[94]
I	B-NR	**4. Synchronized cardioversion is recommended for acute treatment in hemodynamically stable patients with AVNRT when pharmacological therapy does not terminate the tachycardia or is contraindicated.[87,95]**
See Online Data Supplements 3 and 9.		Synchronized cardioversion is highly effective in terminating SVT (including AVRT and AVNRT).[94] Most stable patients with SVT respond to pharmacological therapy, with success rates of 80% to 98% for agents such as verapamil, diltiazem, or adenosine. In some resistant cases, a second drug bolus or higher dose of initial drug agent is often effective.[87,96] Nevertheless, in rare instances, drugs may fail to successfully restore sinus rhythm, necessitating synchronized cardioversion.
IIa	B-R	**1. Intravenous beta blockers, diltiazem, or verapamil are reasonable for acute treatment in hemodynamically stable patients with AVNRT.[96,237–240]**
See Online Data Supplement 10.		Intravenous diltiazem and verapamil are particularly effective in converting AVNRT to sinus rhythm. These drugs should be used only in hemodynamically stable patients. It is important to ensure the absence of VT or pre-excited AF, because patients with these rhythms may become hemodynamically unstable and develop ventricular fibrillation if administered diltiazem or verapamil. Diltiazem or verapamil should also be avoided in patients with suspected systolic heart failure. Evidence for the effectiveness of beta blockers to terminate AVNRT is limited. In a trial that compared esmolol with diltiazem, diltiazem was more effective in terminating SVT.[237] Nonetheless, beta blockers have an excellent safety profile, so it is reasonable to use them to attempt to terminate SVT in hemodynamically stable patients.
IIb	C-LD	**1. Oral beta blockers, diltiazem, or verapamil may be reasonable for acute treatment in hemodynamically stable patients with AVNRT.[241,242]**
See Online Data Supplement 9.		Overall, there are no data specifically studying the effect of oral beta-blocker monotherapy for the acute termination of AVNRT. However, 2 studies have demonstrated success with the combination of oral diltiazem and propranolol to terminate AVNRT or AVRT.[241,242] Oral beta blockers have an excellent safety profile, and administration (particularly in patients without intravenous access) can be performed in conjunction with vagal maneuvers.
IIb	C-LD	**2. Intravenous amiodarone may be considered for acute treatment in hemodynamically stable patients with AVNRT when other therapies are ineffective or contraindicated.[115]**
See Online Data Supplement 10.		In a small cohort study, intravenous amiodarone was effective in terminating AVNRT.[115] Long-term toxicity is not seen with intravenous amiodarone if given for a short period of time.

5.2. Ongoing Management: Recommendations

Recommendations for Ongoing Management of AVNRT		
COR	**LOE**	**Recommendations**
I	B-R	**1. Oral verapamil or diltiazem is recommended for ongoing management in patients with AVNRT who are not candidates for, or prefer not to undergo, catheter ablation.[98,99,243,244]**
See Online Data Supplements 9 and 10.		Both diltiazem and verapamil are well-tolerated and effective pharmacological alternatives to ablation for the ongoing treatment of patients with AVNRT.[98,243] When therapy with these agents is initiated, attention should be directed toward avoiding the potential for bradyarrhythmias and hypotension. Diltiazem and verapamil should also be avoided in patients with systolic heart failure.
I	B-NR	**2. Catheter ablation of the slow pathway is recommended in patients with AVNRT.[36,100–106,245–249]**
See Online Data Supplements 9 and 10.		Catheter ablation of AVNRT is regarded as first-line therapy for treatment of symptomatic AVNRT. It is potentially curative, and chronic pharmacological therapy is usually not needed after the procedure. Slow-pathway ablation (also called modification) is the preferred target during ablation of AVNRT. Large registry studies report the success rates of slow-pathway ablation to be >95%, with a <1% risk of AV block (Table 8).[36,100–102,246–248] Cryoablation of AVNRT is an alternative to radiofrequency ablation. Recent systematic reviews and trials randomizing patients to radiofrequency ablation versus cryoablation suggest an equivalent acute success rate, with a lower rate of AV block but a higher rate of recurrence during long-term follow-up.[156]
I	B-R	**3. Oral beta blockers are recommended for ongoing management in patients with AVNRT who are not candidates for, or prefer not to undergo, catheter ablation.[99]**
See Online Data Supplement 9.		Evidence for oral beta blockers is limited. One small study randomized patients with AVNRT and AVRT to digoxin (0.375 mg/day), propranolol (240 mg/day), or verapamil (480 mg/day), with 1 week of placebo washout between drug regimens.[99] Episodes and duration of tachyarrhythmia (ascertained by diary and weekly 24-h Holter) were similar among the treatment groups, and all 3 medications were well tolerated.
IIa	B-R	**1. Flecainide or propafenone is reasonable for ongoing management in patients without structural heart disease or ischemic heart disease who have AVNRT and are not candidates for, or prefer not to undergo, catheter ablation and in whom beta blockers, diltiazem, or verapamil are ineffective or contraindicated.[45,46,107–112,114,241,242,250,251]**
See Online Data Supplements 9 and 10.		In 1 RCT, the probability of 12 months of effective (defined as <2 attacks of arrhythmia) and safe treatment was 86% for propafenone and 93% for flecainide.[109] Flecainide and propafenone have a risk of proarrhythmia in patients with structural heart disease or ischemic heart disease and are contraindicated in these patient groups. In 1 nonrandomized study, flecainide was evaluated as "pill-in-the-pocket" therapy along with diltiazem or propranolol.[241,242] However, all patients were screened with EP studies, and only 5 patients were discharged on flecainide. As such, the merit of flecainide as "pill in the pocket" for outpatient therapy for AVNRT remains unclear.
IIa	B-NR	**2. Clinical follow-up without pharmacological therapy or ablation is reasonable for ongoing management in minimally symptomatic patients with AVNRT.[244]**
See Online Data Supplement 10.		In a prospective study of 93 adult patients with AVNRT who were followed for approximately 15 years, nearly half of minimally symptomatic patients who received no therapy (versus ablation or antiarrhythmic agents) improved over time and became asymptomatic.[244] Patients with a confirmed or suspected diagnosis of AVNRT who choose not to undergo catheter ablation or take medications should be educated about when to seek medical attention and be taught how to perform vagal maneuvers.
IIb	B-R	**1. Oral sotalol or dofetilide may be reasonable for ongoing management in patients with AVNRT who are not candidates for, or prefer not to undergo, catheter ablation.[107,114]**
See Online Data Supplement 9.		Unlike flecainide and propafenone, sotalol and dofetilide can be used in patients with structural heart disease or coronary artery disease.[113] Given the potential for significant QT prolongation and torsades de pointes, inpatient monitoring with serial ECGs is generally performed when these agents are initiated. Generally, these agents are reserved for patients who are unresponsive to, or are not candidates for, beta blockers, diltiazem, flecainide, propafenone, or verapamil.
IIb	B-R	**2. Oral digoxin or amiodarone may be reasonable for ongoing treatment of AVNRT in patients who are not candidates for, or prefer not to undergo, catheter ablation.[99,115]**
See Online Data Supplements 9 and 10.		One small study randomized patients with unspecified PSVT to digoxin (0.375 mg/day), propranolol (240 mg/day), or verapamil (480 mg/day), with 1 week of placebo washout.[99] Episodes and duration of PSVT (ascertained by diary and weekly 24-h Holter) were largely similar, and all 3 medications were well tolerated.[99] However, the dose of digoxin used was higher than that commonly used in clinical practice today. Amiodarone is effective in suppressing AVNRT during outpatient follow-up.[115] Given the potential adverse effects of digoxin and amiodarone, these agents are generally reserved as third-line therapy for patients who are unresponsive to, or are not candidates for, beta blockers, diltiazem, verapamil, flecainide, or propafenone.
IIb	C-LD	**3. Self-administered ("pill-in-the-pocket") acute doses of oral beta blockers, diltiazem, or verapamil may be reasonable for ongoing management in patients with infrequent, well-tolerated episodes of AVNRT.[241,242]**
See Online Data Supplement 9.		Two studies have demonstrated success with the combination of diltiazem and propranolol as a "pill-in-the-pocket" approach to acutely terminate PSVT caused by AVNRT, but the overall safety of self-administration of these medications remains unclear because episodes of syncope were observed.[241,242] If oral therapy with empiric beta blockers, diltiazem, or verapamil fails to terminate the tachyarrhythmia, patients should seek medical attention.

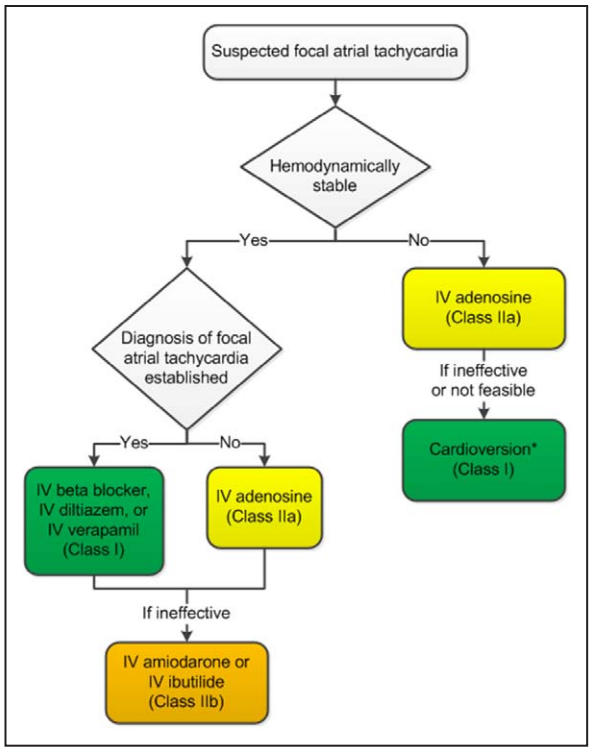

Figure 10. Acute treatment of suspected focal atrial tachycardia. Colors correspond to Class of Recommendation in Table 1; drugs listed alphabetically. *For rhythms that break or recur spontaneously, synchronized cardioversion is not appropriate. IV indicates intravenous.

6. Manifest and Concealed Accessory Pathways

Accessory pathways can be manifest or concealed; can conduct in the anterograde direction, retrograde direction, or both; and can be associated with several different supraventricular arrhythmias. Some anterograde pathways may place patients at risk of SCD. Typically, pathways directly connect the atrium and ventricle, bypassing the normal conduction through the AV node and His Purkinje system. The pathways are considered manifest if they conduct in the anterograde direction, demonstrating pre-excitation with a delta wave on the ECG. Manifest pathways occur in 0.1% to 0.3% of the population and may conduct in both the anterograde and retrograde directions or, less commonly, only in the anterograde direction.[252] Concealed pathways conduct only in the retrograde direction and therefore do not cause pre-excitation on the standard 12-lead ECG.

The most common tachycardia associated with an accessory pathway is orthodromic AVRT, with a circuit that uses the AV node and His Purkinje system in the anterograde direction, followed by conduction through the ventricle, retrograde conduction over the accessory pathway, and completion of the circuit by conduction through the atrium back into the AV node. Orthodromic AVRT accounts for approximately 90% to 95% of AVRT episodes in patients with a manifest accessory pathway. Pre-excited AVRT, including antidromic AVRT, accounts for 5% of the AVRT episodes in patients with a manifest pathway and involves conduction from the atrium to the ventricle via the accessory pathway, causing a pre-excited QRS complex. This is called antidromic AVRT tachycardia when the return reentrant conduction occurs retrogradely via the AV node. In rare cases of pre-excited AVRT, the return conduction occurs via a second accessory AV pathway. AF can occur in patients with accessory pathways, which may result in extremely rapid conduction to the ventricle over a manifest pathway, which increases the risk of inducing ventricular fibrillation and SCD. Other SVTs, such as AVNRT, AT, and atrial flutter, can also conduct rapidly over a manifest accessory pathway; in these instances, the pathway is considered a "bystander" because it is not part of the tachycardia circuit. Most accessory pathways have conduction properties similar to the myocardium and do not demonstrate decremental conduction. A unique form of AVRT involves a concealed accessory pathway, usually located in the posteroseptal region, with retrograde decremental conduction properties resulting in a form of orthodromic reentrant tachycardia termed PJRT. This tachycardia has deeply inverted retrograde P waves in leads II, III, and aVF, with a long RP interval due to the location and decremental conduction properties of the accessory pathway (Figure 6). The incessant nature of PJRT may result in tachycardia-induced cardiomyopathy that usually resolves after successful treatment. Another unusual accessory pathway is the atriofascicular fiber (also called a Mahaim fiber) that connects the right atrium to a fascicle of the distal right bundle branch and has decremental anterograde conduction while not allowing conduction in the retrograde direction; this pathway can allow reentrant tachycardia with a circuit that involves anterograde conduction over the accessory pathway with characteristic left bundle-branch block morphology and retrograde conduction through the AV node/His Purkinje system. Other rare accessory pathway connections that may participate in reentrant tachycardia are nodofascicular pathways (connecting the AV node to a fascicle) and nodoventricular pathways (connecting the AV node to the ventricular myocardium). Fasciculoventricular pathways, connecting a fascicle to the proximal right or left bundle branch, have also been described, although they have never been reported to participate in tachycardia. An EP study is necessary to establish the diagnosis of these rare accessory pathways.

The diagnosis of WPW syndrome is reserved for patients who demonstrate ventricular pre-excitation on their resting ECG that participates in arrhythmias. Rapid anterograde accessory pathway conduction during AF can result in SCD in patients with a manifest accessory pathway, with a 10-year risk ranging from 0.15% to 0.24%.[253,254] Unfortunately, SCD may be the first presentation of patients with undiagnosed WPW. Increased risk of SCD is associated with a history of symptomatic tachycardia, multiple accessory pathways, and a shortest pre-excited R-R interval of <250 ms during AF. The risk of SCD associated with WPW appears highest in the first 2 decades of life.[254–258] Antiarrhythmic drug treatment of

patients with orthodromic AVRT can be directed at either the accessory pathway or the AV node, as both are key portions of the reentrant circuit. AV nodal–blocking agents may be contraindicated in patients at risk of rapid conduction down the accessory pathway during AF. Catheter ablation strategies target the accessory pathway, with high success rates.

6.1. Management of Patients With Symptomatic Manifest or Concealed Accessory Pathways

See Figure 14 for the algorithm for acute treatment of orthodromic AVRT and Figure 15 for the algorithm for ongoing management of orthodromic AVRT.

6.1.1. Acute Treatment: Recommendations

Recommendations for Acute Treatment of Orthodromic AVRT		
COR	**LOE**	**Recommendations**
I	B-R	**1. Vagal maneuvers are recommended for acute treatment in patients with orthodromic AVRT.[42,75,235,259]**
See Online Data Supplements 11 and 12.		For acute conversion of orthodromic AVRT, vagal maneuvers, including Valsalva and carotid sinus massage, can be performed quickly and should be the first-line intervention to terminate SVT. These maneuvers should be performed with the patient in the supine position. There is no "gold standard" for proper Valsalva maneuver technique, but in general, the patient raises intrathoracic pressure by bearing down against a closed glottis for 10 to 30 seconds, equivalent to at least 30 to 40 mm Hg.[82,84] Carotid massage is performed after absence of bruit has been confirmed by auscultation, by applying steady pressure over the right or left carotid sinus for 5 to 10 seconds.[83,84] Another vagal maneuver based on the classic diving reflex consists of applying an ice-cold, wet towel to the face[85]; in a laboratory setting, facial immersion in water at 10°C (50°F) has proved effective in terminating tachycardia, as well.[86] One study involving 148 patients with SVT demonstrated that Valsalva was more successful than carotid sinus massage, and switching from 1 technique to the other resulted in an overall success rate of 27.7%.[82] The practice of applying pressure to the eyeball is potentially dangerous and has been abandoned.
I	B-R	**2. Adenosine is beneficial for acute treatment in patients with orthodromic AVRT.[42,260,261]**
See Online Data Supplements 11 and 12.		Adenosine is effective for conversion of orthodromic AVRT in 90% to 95% of patients, with minor and brief (<1 min) side effects occurring in approximately 30% of patients.[42,260,261] Patients often have atrial or ventricular premature complexes immediately after conversion that, on occasion, may induce further episodes of AVRT. In this situation, an antiarrhythmic drug may be required to prevent acute reinitiation of tachycardia. Because adenosine may precipitate AF that may then conduct rapidly to the ventricle and even cause ventricular fibrillation, electrical cardioversion should be available.
I	B-NR	**3. Synchronized cardioversion should be performed for acute treatment in hemodynamically unstable patients with AVRT if vagal maneuvers or adenosine are ineffective or not feasible.[75,262,263]**
See Online Data Supplement 10.		Synchronized cardioversion is highly effective in terminating AVRT.[75] Cardioversion avoids complications associated with antiarrhythmic drug therapy and should be considered early in the management of hemodynamically unstable patients. Patients often have atrial or ventricular premature complexes immediately after cardioversion that, on occasion, may induce further episodes of AVRT. In this situation, an antiarrhythmic drug may be required to prevent acute reinitiation of tachycardia.
I	B-NR	**4. Synchronized cardioversion is recommended for acute treatment in hemodynamically stable patients with AVRT when pharmacological therapy is ineffective or contraindicated.[87,95]**
See Online Data Supplements 3 and 10.		Synchronized cardioversion is highly effective in terminating SVT (including AVRT and AVNRT), and when the patient is stable, this is performed after adequate sedation or anesthesia.[94] Most stable patients with SVT respond to pharmacological therapy, with success rates of 80% to 98% for agents such as verapamil, diltiazem, or adenosine. In some resistant cases, a second drug bolus or higher dose of initial drug agent might prove effective.[87,96] Nevertheless, in rare instances, drugs may fail to successfully restore sinus rhythm.
I	B-NR	**5. Synchronized cardioversion should be performed for acute treatment in hemodynamically unstable patients with pre-excited AF.[75,94]**
See Online Data Supplement 10.		Synchronized cardioversion is highly effective in terminating pre-excited AF.[75] When AF occurs in patients with ventricular pre-excitation, if the accessory pathway has a short refractory period, this may allow for rapid pre-excited AV conduction; the resulting fast, often irregular, broad-complex tachycardia is often unstable and may lead to ventricular fibrillation. It is therefore important to achieve early restoration of sinus rhythm in these patients. Patients often have atrial or ventricular premature complexes immediately after cardioversion that, on occasion, may induce AVRT or recurrent pre-excited AF.
I	C-LD	**6. Ibutilide[264] or intravenous procainamide[265] is beneficial for acute treatment in patients with pre-excited AF who are hemodynamically stable.**
See Online Data Supplements 11 and 12.		Small observational studies support the use of ibutilide or intravenous procainamide for the treatment of pre-excited AF in patients who are not hemodynamically compromised.[264,265] Both medications can decrease ventricular rate by slowing conduction over the accessory pathway and have the additional benefit of possibly terminating AF.[264,265]
IIa	B-R C-LD	**1. Intravenous diltiazem, verapamil[42,260,266,267] (*Level of Evidence: B-R*), or beta blockers[268] (*Level of Evidence: C-LD*) can be effective for acute treatment in patients with orthodromic AVRT who do not have pre-excitation on their resting ECG during sinus rhythm.**
See Online Data Supplements 11 and 12.		Intravenous diltiazem or verapamil effectively terminate approximately 90% to 95% of AVRT episodes in patients without pre-excitation on their resting sinus-rhythm ECG, with drug-induced hypotension occurring in approximately 3% of patients.[42,260,266,267] Intravenous beta blockers have not been studied in clinical trials; however, clinical experience suggests they are useful for terminating AVRT, with a low risk of associated complications.[268]

Recommendations for Acute Treatment of Orthodromic AVRT (Continued)		
COR	LOE	Recommendations
IIb	B-R	**1. Intravenous beta blockers, diltiazem, or verapamil might be considered for acute treatment in patients with orthodromic AVRT who have pre-excitation on their resting ECG and have not responded to other therapies.[42,266,267,269]**
See Online Data Supplements 11 and 12.		Intravenous beta blockers, diltiazem, and verapamil have a risk of enhancing conduction over the accessory pathway if the AVRT converts to AF during administration of the medication. Should the patient have a rapidly conducting manifest accessory pathway, further enhancing accessory-pathway conduction during AF by shortening the refractory period (digoxin) or decreasing BP and increasing catecholamines (diltiazem, beta blockers, verapamil) may place the patient at risk of AF degenerating into a malignant ventricular arrhythmia. The ability to promptly perform electrical cardioversion must be available should AF with rapid ventricular conduction occur. Before intravenous beta blockers, diltiazem, and verapamil were available, intravenous digoxin was commonly used for acute treatment of patients with orthodromic AVRT who had pre-excitation on their resting ECG[270]; this agent is rarely used now because other agents are available and digoxin may put patients at risk of ventricular fibrillation.[271]
III: Harm	C-LD	**1. Intravenous digoxin, intravenous amiodarone, intravenous or oral beta blockers, diltiazem, and verapamil are potentially harmful for acute treatment in patients with pre-excited AF.[269,271–275]**
See Online Data Supplements 11 and 12.		Patients with pre-excited AF should not receive intravenous digoxin, intravenous amiodarone, or intravenous/oral beta blockers, diltiazem, or verapamil because these medications may enhance conduction over the accessory pathway, increase the ventricular rate, and increase the risk of provoking a life-threatening ventricular arrhythmia.[269,271–275] Digoxin increases the ventricular rate by shortening refractoriness of the accessory pathway, whereas amiodarone, beta blockers, diltiazem, and verapamil may increase the ventricular rate as a result of drug-induced hypotension with increased catecholamines. In addition, these medications may enhance conduction over the accessory pathway by slowing or blocking conduction through the AV node, preventing competitive concealed retrograde conduction into the accessory pathway.

6.1.2. Ongoing Management: Recommendations

Recommendations for Ongoing Management of Orthodromic AVRT		
COR	LOE	Recommendations
I	B-NR	**1. Catheter ablation of the accessory pathway is recommended in patients with AVRT and/or pre-excited AF.[103,254,276–282]**
See Online Data Supplements 11 and 12.		Several large series support the use of catheter ablation of the accessory pathway as first-line therapy in patients who have had AF and/or AVRT. These series report a success rate of approximately 93% to 95% and a 3% risk of major complications when patients are followed up for 6 months to 8 years[102,103,254,276–282] (Table 8). AF in younger patients is usually associated with the accessory pathway and is unlikely to occur after ablation; in contrast, older patients may have recurrence of AF from causes unrelated to the accessory pathway.[283,284] Catheter ablation is also effective for treating PJRT (Table 3) by ablating the concealed accessory pathway with a success rate of approximately 90%.[283,284] Catheter ablation of an atriofascicular (Mahaim) pathway is successful in preventing reentrant tachycardia in approximately 70% to 100% of patients.[285,286]
I	C-LD	**2. Oral beta blockers, diltiazem, or verapamil are indicated for ongoing management of AVRT in patients without pre-excitation on their resting ECG.[46,287]**
See Online Data Supplements 11 and 12.		Observational studies and clinical experience confirm that beta blockers, diltiazem, and verapamil are effective for preventing recurrent tachycardia in approximately 50% of patients without pre-excitation on their resting ECG (concealed accessory pathway) and are associated with a favorable side effect profile.[46,287]
IIa	B-R	**1. Oral flecainide or propafenone is reasonable for ongoing management in patients without structural heart disease or ischemic heart disease who have AVRT and/or pre-excited AF and are not candidates for, or prefer not to undergo, catheter ablation.[45,108,109,112,288]**
See Online Data Supplements 11 and 12.		Flecainide and propafenone are beneficial for the treatment of AVRT by directly slowing or blocking conduction over the pathway. These drugs are effective in approximately 85% to 90% of patients, with 30% reporting an absence of tachycardia.[45,108,109,112,288] Both drugs have a risk of proarrhythmia resulting in VT that is increased in patients with structural heart disease or ischemic heart disease; in such patients, these drugs are generally avoided. Side effects occur in up to 60% of patients, and approximately 20% discontinue the medications because of adverse effects.[45,108,109,112,288]
IIb	B-R	**1. Oral dofetilide or sotalol may be reasonable for ongoing management in patients with AVRT and/or pre-excited AF who are not candidates for, or prefer not to undergo, catheter ablation.[99,106]**
See Online Data Supplement 9.		Unlike flecainide and propafenone, sotalol and dofetilide can be used in patients with structural heart disease or coronary artery disease.[105] Given the potential for significant QT prolongation and torsades de pointes, inpatient monitoring with serial ECGs is generally performed when these agents are initiated.
IIb	C-LD	**2. Oral amiodarone may be considered for ongoing management in patients with AVRT and/or pre-excited AF who are not candidates for, or prefer not to undergo, catheter ablation and in whom beta blockers, diltiazem, flecainide, propafenone, and verapamil are ineffective or contraindicated.[289,290]**
See Online Data Supplements 11 and 12.		Small observational studies support the use of amiodarone for preventing recurrent AVRT, but long-term efficacy has not been reported.[289,290] Because of the important toxicity associated with long-term use of amiodarone, the drug is usually reserved for patients who are not candidates for catheter ablation and who have failed to respond to or have contraindications to other antiarrhythmic drugs.

Recommendations for Ongoing Management of Orthodromic AVRT (Continued)		
COR	LOE	Recommendations
IIb	C-LD	**3. Oral beta blockers, diltiazem, or verapamil may be reasonable for ongoing management of orthodromic AVRT in patients with pre-excitation on their resting ECG who are not candidates for, or prefer not to undergo, catheter ablation.[46,287]**
See Online Data Supplements 11 and 12.		One RCT supports the use of verapamil for prevention of orthodromic AVRT in patients with pre-excitation on their resting ECG (manifest accessory pathway).[46] There are no RCTs supporting the use of oral beta blockers or diltiazem for prevention of recurrent AVRT, although clinical experience suggests the drugs are effective, with a favorable side effect profile.[287] Patients with pre-excitation may develop AF during an episode of AVRT and be exposed to increased risk of rapid conduction over the accessory pathway while receiving beta blockers, diltiazem or verapamil, so these agents must be used with caution.[269] The decision to treat with these agents should follow a discussion of risks with the patient. Although evidence of poor anterograde conduction via the accessory pathway may be reassuring, rapid conduction in AF has been described even in the setting of intermittent anterograde conduction.[291]
IIb	C-LD	**4. Oral digoxin may be reasonable for ongoing management of orthodromic AVRT in patients without pre-excitation on their resting ECG who are not candidates for, or prefer not to undergo, catheter ablation.[292]**
See Online Data Supplement 12.		One small study reported the usefulness of oral digoxin in prevention of recurrent orthodromic AVRT in patients without pre-excitation on their resting ECG (concealed accessory pathway).[293] Digoxin has been used clinically for many years, but the low efficacy indicates its use would be best limited to patients who are not candidates for catheter ablation or prefer pharmacological therapy and have failed to respond to other antiarrhythmic drugs.
III: Harm	C-LD	**1. Oral digoxin is potentially harmful for ongoing management in patients with AVRT or AF and pre-excitation on their resting ECG.[271]**
See Online Data Supplement 12.		Digoxin shortens the refractory period of the accessory pathway, such that AF may induce ventricular fibrillation.[271] Even if AF has never been documented, AVRT may degenerate into AF. Thus, oral digoxin should not be used to treat patients with a manifest accessory pathway.

6.2. Management of Asymptomatic Pre-Excitation

6.2.1. PICOTS Critical Questions

See the ERC systematic review report, "Risk Stratification for Arrhythmic Events in Patients With Asymptomatic Pre-Excitation" for the complete evidence review on the management of asymptomatic pre-excitation,[9] and see Online Data Supplements 13, 14, and 15 for additional data on asymptomatic pre-excitation, which were reproduced directly from the ERC's systematic review. These recommendations have been designated with the notation SR to emphasize the rigor of support from the ERC's systematic review. PICOTS Question 1 did not provide adequate data for a recommendation; the other 3 PICOTS questions are addressed in the recommendations in Section 6.2.2.

As noted in Section 1.1, the recommendations in Section 6.3 are based on a separately commissioned systematic review of the available evidence, the results of which were used to frame our decision making. Full details are provided in the ERC's systematic review report.[9] The following 4 questions were considered by the ERC:

1. What is the comparative predictive accuracy of invasive EP study (without catheter ablation of the accessory pathway) versus noninvasive testing for predicting arrhythmic events (including SCD) in patients with asymptomatic pre-excitation?
2. What is the usefulness of invasive EP study (without catheter ablation of the accessory pathway) versus no testing for predicting arrhythmic events (including SCD) in patients with asymptomatic pre-excitation?
3. What is the usefulness of invasive EP study (without catheter ablation of the accessory pathway) or noninvasive EP study for predicting arrhythmic events (including SCD) in patients with asymptomatic pre-excitation?
4. What are the efficacy and effectiveness of invasive EP study with catheter ablation of the accessory pathway as appropriate versus noninvasive tests with treatment (including observation) or no testing/ablation as appropriate for preventing arrhythmic events (including SCD) and improving outcomes in patients with asymptomatic pre-excitation?

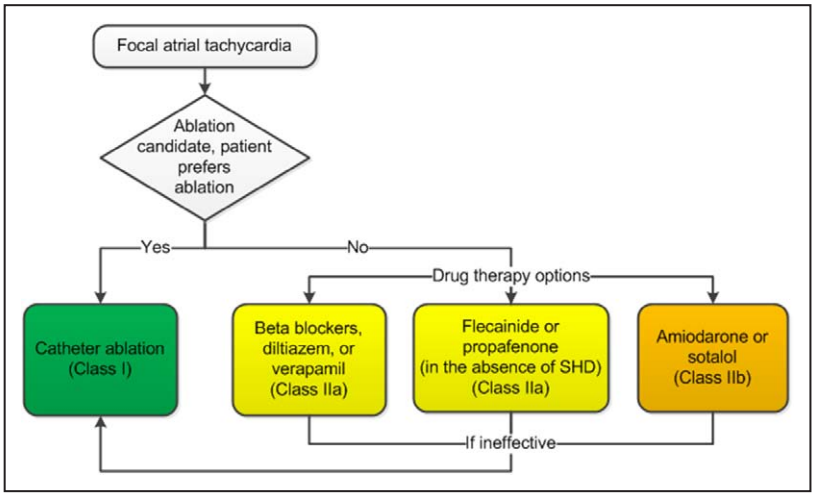

Figure 11. Ongoing management of focal atrial tachycardia. Colors correspond to Class of Recommendation in Table 1; drugs listed alphabetically. Pt indicates patient; and SHD, structural heart disease (including ischemic heart disease).

6.2.2. Asymptomatic Patients With Pre-Excitation: Recommendations

Recommendations for Management of Asymptomatic Patients With Pre-Excitation		
COR	**LOE**	**Recommendations**
I	B-NR [SR]	**1. In asymptomatic patients with pre-excitation, the findings of abrupt loss of conduction over a manifest pathway during exercise testing in sinus rhythm[294–297] *(Level of Evidence: B-NR)* [SR] or intermittent loss of pre-excitation during ECG or ambulatory monitoring[297] *(Level of Evidence: C-LD)* [SR] are useful to identify patients at low risk of rapid conduction over the pathway.**
	C-LD [SR]	
See Online Data Supplements 11 and 12.		Noninvasive testing has been shown to identify patients at low risk of developing rapid conduction over the accessory pathway and life-threatening ventricular arrhythmias in response to AF. The noninvasive findings that identify a pathway not capable of maintaining rapid conduction during AF include intermittent loss of conduction over the accessory pathway on the resting ECG or during ambulatory monitoring, or abrupt loss of pre-excitation during exercise testing (Figure 16).[294–297] The ECG should be evaluated closely to make certain the delta wave is truly absent, as accessory pathways, especially left lateral pathways, may demonstrate varying degrees of pre-excitation because of fusion between conduction over the accessory pathway and through the AV node. This may give the appearance of loss of pre-excitation if the subtle delta wave is not identified. Noninvasive tests have an approximately 90% positive predictive value and 30% negative predictive value for identifying pathways with life-threatening properties.[294,295,297]
IIa	B-NR [SR]	**1. An EP study is reasonable in asymptomatic patients with pre-excitation to risk-stratify for arrhythmic events.[254,256,298–301]**
See Online Data Supplements 11–15.		In the absence of symptoms, a clinical priority is identifying accessory pathways at increased risk of arrhythmic events, including rapid conduction during AF and development of life-threatening ventricular arrhythmias, with the most useful findings being the following: an R-R interval <250 ms between 2 pre-excited complexes during induced AF; the presence of multiple accessory pathways; the ability to induce sustained AVRT; the finding of AVRT precipitating pre-excited AF; and an accessory pathway refractory period <240 ms.[254,256,298,299,301] Malignant arrhythmias correlate more with the EP properties of the accessory pathway than with the presence or absence of symptoms. This approach is supported by the low risk of complications observed in an EP study in which complication rates among 2169 patients ranged from 0.09% to 1% and included pneumothorax and access site complications.[254]
IIa	B-NR [SR]	**2. Catheter ablation of the accessory pathway is reasonable in asymptomatic patients with pre-excitation if an EP study identifies a high risk of arrhythmic events, including rapidly conducting pre-excited AF.[254,302,303]**
See Online Data Supplements 11–15.		In a large prospective cohort study of 756 asymptomatic patients with close to 8 years of follow-up, 9% of patients developed malignant AF (shortest R-R interval ≤250 ms), and 2% developed ventricular fibrillation.[254] Malignant arrhythmias correlated more with high-risk EP properties of the accessory pathway than with the presence or absence of symptoms. Ablation of the accessory pathway(s) in high-risk patients was also examined in 1 RCT that enrolled 76 patients, showing that arrhythmic events (defined as symptomatic SVT, AF, and ventricular fibrillation in this study) occurred in 7% of patients who underwent ablation versus 77% who did not undergo ablation.[302] Another study that examined patients on the basis of whether an ablation was performed reported that none of the asymptomatic patients who had undergone ablation of the accessory pathway developed a malignant arrhythmia during 8 years of follow-up. The risk of complications with ablation ranged from 0.1% (complete heart block) to 0.9% (ablation-induced right bundle-branch block).[254] The risks and benefits of proceeding with ablation of pathways found not to have high-risk characteristics should be discussed thoroughly with patients in advance of the EP procedure.
IIa	B-NR [SR]	**3. Catheter ablation of the accessory pathway is reasonable in asymptomatic patients if the presence of pre-excitation precludes specific employment (such as with pilots).[103,254,276–282,302–304]**
See Online Data Supplements 11–15.		Patients with asymptomatic pre-excitation whose job activities would place them or others at risk if a hemodynamically significant arrhythmia occurred (such as airline pilots) are potential candidates for catheter ablation. Catheter ablation is associated with a success rate of approximately 95% and a 3% risk of major complications when patients are followed up for 6 months to 8 years.[103,254,276–282,302,303] Other documents advise EP study in asymptomatic athletes who engage in moderate- or high-level competitive sports.[305]
IIa	B-NR [SR]	**4. Observation, without further evaluation or treatment, is reasonable in asymptomatic patients with pre-excitation.[301,306–309]**
See Online Data Supplements 11–15.		Most observational cohort studies suggest that the great majority of adult patients with asymptomatic pre-excitation who do not undergo an ablation of the accessory pathway have a benign course with few clinically significant arrhythmic events occurring over time. This supports the recommendation that observation without medical therapy or ablation is a reasonable alternative because the risk of SCD is small and is seen mainly in children.[254,301,306–309] The choice to observe asymptomatic patients should be preceded by the patient being informed of the small risk of life-threatening arrhythmias developing in the absence of treatment, along with the success rate and complications associated with catheter ablation of the accessory pathway.

6.3. Risk Stratification of Symptomatic Patients With Manifest Accessory Pathways: Recommendations

Recommendations for Management of Symptomatic Patients With Manifest Accessory Pathways		
COR	**LOE**	**Recommendations**
I	B-NR C-LD	**1. In symptomatic patients with pre-excitation, the findings of abrupt loss of conduction over the pathway during exercise testing in sinus rhythm[294–297] *(Level of Evidence: B-NR)* or intermittent loss of pre-excitation during ECG or ambulatory monitoring[297] *(Level of Evidence: C-LD)* are useful for identifying patients at low risk of developing rapid conduction over the pathway.**
See Online Data Supplements 11–15.		An important consideration in the evaluation of patients with pre-excitation is determining risk of developing rapid conduction over the accessory pathway and life-threatening ventricular arrhythmias in response to AF. The noninvasive findings that identify a pathway incapable of maintaining rapid conduction during AF include intermittent loss of conduction over the accessory pathway on the resting ECG or during ambulatory monitoring or abrupt loss of pre-excitation during exercise testing.[294–297] The ECG should be evaluated closely to make certain the delta wave is truly absent, as accessory pathways (especially left lateral pathways) may demonstrate varying degrees of pre-excitation because of fusion between conduction over the accessory pathway and through the AV node, which may give the appearance of loss of pre-excitation if the subtle delta wave is not identified. Noninvasive tests have an approximately 90% positive predictive value and 30% negative predictive value for identifying pathways with life-threatening properties.[294,295,297] If noninvasive evaluation suggests that the accessory pathway conducts poorly in the anterograde direction, although risk of life-threatening events is likely lower, the EP study still may be useful because of patient symptoms.
I	B-NR	**2. An EP study is useful in symptomatic patients with pre-excitation to risk-stratify for life-threatening arrhythmic events.[254,256,298–300]**
See Online Data Supplements 11–15.		Most symptomatic patients with accessory pathways undergo catheter ablation, but in some instances, EP studies are performed to identify whether the patient is at increased risk of rapid conduction down the accessory pathway during AF and development of life-threatening ventricular arrhythmias. The most useful findings for risk stratification are an R-R interval <250 ms between 2 pre-excited complexes during induced AF; the presence of multiple accessory pathways; the finding of AVRT precipitating pre-excited AF; and an accessory pathway refractory period <240 ms.[254,256,298–300]

7. Atrial Flutter

See Figure 17 for a schematic depicting classification of atrial flutter/ATs; Figure 18 for the algorithm for acute treatment of atrial flutter; and Figure 19 for the algorithm for ongoing management of atrial flutter.

7.1. Cavotricuspid Isthmus–Dependent Atrial Flutter

Atrial flutter is a macroreentrant atrial arrhythmia characterized by regular atrial rate and constant P-wave morphology.

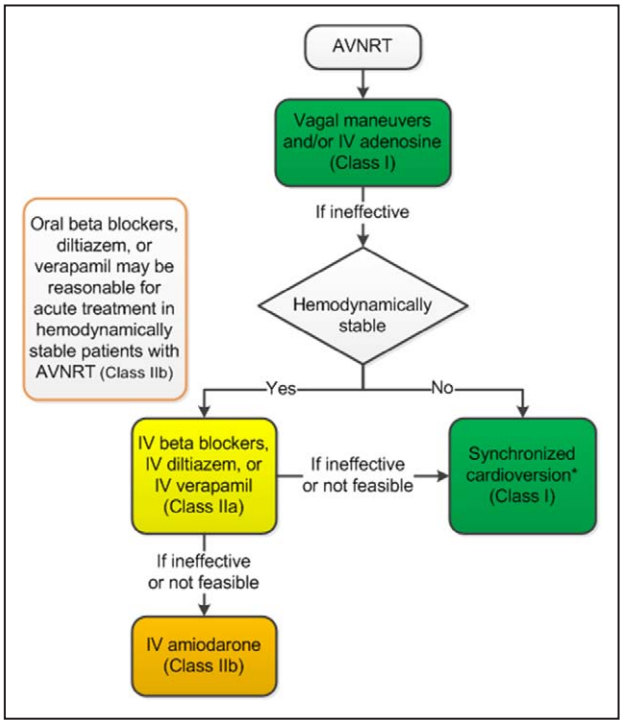

Figure 12. Acute treatment of AVNRT. Colors correspond to Class of Recommendation in Table 1; drugs listed alphabetically. *For rhythms that break or recur spontaneously, synchronized cardioversion is not appropriate. AVNRT indicates atrioventricular nodal reentrant tachycardia; and IV, intravenous.

When the atrial flutter circuit involves the cavotricuspid isthmus (CTI), it is labeled CTI-dependent atrial flutter. When CTI-dependent flutter involves a circuit that rotates around the tricuspid valve in a counterclockwise direction (up the septum and down the free wall), it is called "typical"; less commonly, the CTI-dependent flutter circuit rotates in a clockwise direction (sometimes called "reverse typical").[203] Counterclockwise CTI-dependent atrial flutter is characterized electrocardiographically by dominant negative flutter waves in the inferior leads (so-called "sawtooth waves") and a positive P wave in lead V1 at atrial rates of 250 bpm to 350 bpm (Figure 17). Clockwise isthmus-dependent flutter shows the opposite pattern (ie, positive flutter waves in the inferior leads and wide, negative flutter waves in lead V1) (Figure 17). Although the atrial rates for flutter typically range from 250 bpm to 330 bpm, the rates may be slower in patients with severe atrial disease or in patients taking antiarrhythmic agents or after unsuccessful catheter ablation.[310]

Atrial flutter can occur in clinical settings similar to those associated with AF, and atrial flutter can be triggered by AT or AF.[121,311] It is common for AF and atrial flutter to coexist in the same patient. After CTI ablation, 22% to 50% of patients have been reported to develop AF after a mean follow-up of 14 to 30 months, although 1 study reported a much higher rate of AF development, with 82% of patients treated by catheter ablation for atrial flutter manifesting AF within 5 years.[312] Risk factors for the manifesting AF after atrial flutter ablation include prior AF, depressed left ventricular function, structural heart disease or ischemic heart disease, inducible AF, and increased LA size.[121,312–316]

Atrial flutter may result from antiarrhythmic therapy of AF, particularly when flecainide, propafenone, or amiodarone is used for treatment of AF.[317,318] In those patients with atrial flutter resulting from antiarrhythmic therapy of AF, ablation of the CTI-dependent flutter may prevent recurrent flutter while antiarrhythmic therapy for AF is continued.[318]

Patients with atrial flutter are thought to have the same risk of thromboembolism as patients with AF; therefore,

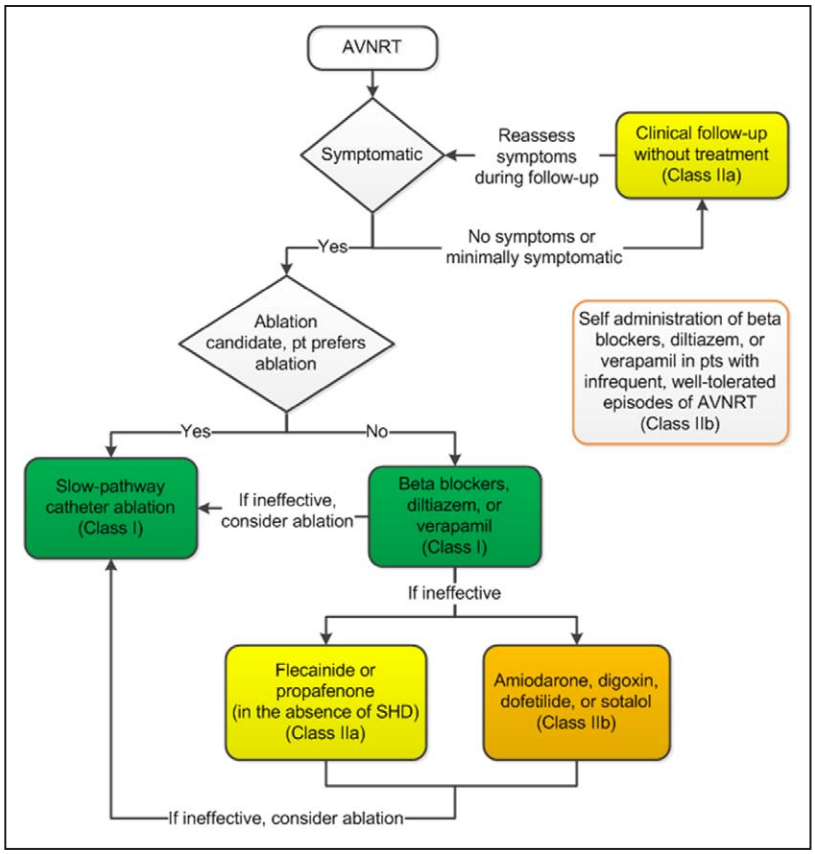

Figure 13. Ongoing management of AVNRT. Colors correspond to Class of Recommendation in Table 1; drugs listed alphabetically. AVNRT indicates atrioventricular nodal reentrant tachycardia; pt, patient; and SHD, structural heart disease (including ischemic heart disease).

recommendations for anticoagulation mirror those for patients with AF.[10,121,314] Similarly, the recommendations for anticoagulation with regard to either pharmacological or electrical cardioversion of patients with atrial flutter are the same as those for patients with AF, as discussed in the 2014 AF guideline (Section 6.1).[10]

7.2. Non–Isthmus-Dependent Atrial Flutters

Non–isthmus-dependent atrial flutter or atypical flutter describes macroreentrant ATs that are not dependent on conduction through the CTI. A variety of circuits have been described, including a path around the mitral annulus (perimitral flutter), re-entry involving the left atrial roof, and re-entry around regions of scarring in the right or left atrium. Non–isthmus-dependent atrial flutters often occur in patients with atrial scarring from prior heart surgery or ablation but also may occur in any form of heart disease or may be idiopathic.[134,140,319] Non–isthmus-dependent atrial flutters can coexist with CTI-dependent flutter or involve the presence of multiple atrial re-entry circuits.[133,320] The reentrant circuits are classified as either macroreentrant AT (large; often several centimeters or longer in diameter) or microreentrant AT (≤2 cm in diameter), which may be indistinguishable from focal AT.[321]

In the presence of substantial atrial disease, prior surgery, or prior radiofrequency catheter ablation, the ECG flutter-wave morphology is not a reliable predictor of whether the flutter circuit involves the CTI. Although an ECG with a typical flutter appearance has good predictive value for CTI-dependent flutter in a patient who has not undergone prior catheter ablation of AF, the ECG appearance is less useful in predicting the flutter circuit in a patient who has previously undergone AF ablation.[322–325] The presence of a positive or biphasic (but dominantly positive) deflection in V1, accompanied by deflections in other leads inconsistent with typical counterclockwise atrial flutter, suggests the presence of an atypical flutter (Figure 17). Definitive diagnosis requires EP study and intracardiac mapping.[326]

Catheter ablation of non–CTI-dependent flutter requires more extensive mapping than does ablation of CTI-dependent flutter, and success rates are lower (Table 8). The location of the circuit determines ablation approach and risks.

The substrate for macroreentrant atrial arrhythmias after cardiac surgery is atrial scarring from atriotomy incisions and cannulation sites and from the underlying myopathic process of the valve disease itself; this is sometimes referred to as incisional atrial reentrant tachycardia. The location of the reentrant circuit depends on the type of surgical approach, and common populations include patients who have undergone mitral valve surgery or have a repaired atrial septal defect.[327–330] These arrhythmias are also common after surgical or catheter ablation for AF.[331,332] Both single- and dual-loop circuits, as well as focal ATs, can be present. It is useful to review the procedural notes to identify the location of atrial incisions or prior ablation that can assist with future mapping and ablation.

The development of a microreentrant or macroreentrant left AT after AF ablation occurs in approximately 5% of patients.[330,333,334] This is less frequent if ablation is limited to pulmonary vein isolation. On the other hand, these arrhythmias

are more common in patients with longer-duration persistent AF or more dilated left atria or when linear ablation lesions are used.[333–338] Non–reentrant focal arrhythmias often originate at lesion edges or reconnected segments of prior isolated pulmonary veins.[333] Reisolation of the pulmonary vein and ablation of any nonpulmonary vein foci are often effective in treating these arrhythmias. Detailed activation and entrainment mapping of the tachycardia during a second procedure result in effective ablation in approximately 90% of patients.[335] Although right atrial CTI-dependent flutter may also occur, most of the tachycardias originate in the left atrium.

As with all types of atrial flutter, it may be very difficult to achieve rate control in patients with post–AF ablation non–CTI-dependent flutter (far more so than in patients with preablation AF). When the ventricular response cannot be controlled with common rate-control medications, attempts at restoration of sinus rhythm with pharmacological therapy and cardioversion are often required. Many of the atrial flutters that are observed during the first 3 months after catheter ablation or after cardiac surgery will not recur later on. For this reason, it is advised that attempts at ablation of atrial flutter after AF ablation be deferred until after the 3-month waiting period.[339] Rarely, pharmacological therapy and attempts at rhythm control with antiarrhythmic drug therapy fail to adequately control atrial flutter during the 3 months after AF ablation. In this situation, early repeat ablation is warranted.

7.3. Acute Treatment: Recommendations

Recommendations for Acute Treatment of Atrial Flutter		
COR	**LOE**	**Recommendations**
I	A	**1. Oral dofetilide or intravenous ibutilide is useful for acute pharmacological cardioversion in patients with atrial flutter.[119,340–346]**
See Online Data Supplements 16 and 17.		Pharmacological cardioversion of atrial flutter is generally less effective than synchronized cardioversion and carries the potential risk of proarrhythmia but can be an option when sedation is not available or not well tolerated or when indicated by patient preference. Intravenous ibutilide converts atrial flutter to sinus rhythm in approximately 60% of cases.[342] The major risk is torsades de pointes, which is more likely to occur in patients with reduced left ventricular ejection fraction. Patients receiving ibutilide should undergo continuous ECG monitoring during administration and for at least 4 hours after completion of dosing. Pretreatment with magnesium can increase the efficacy and reduce the risk of torsades de pointes.[119] Anticoagulation issues for chemical cardioversion are the same as those for electrical cardioversion of atrial flutter.[10]
I	B-R	**2. Intravenous or oral beta blockers, diltiazem, or verapamil are useful for acute rate control in patients with atrial flutter who are hemodynamically stable.[347–354]**
See Online Data Supplements 16 and 17.		It is often more difficult to achieve rate control for atrial flutter than for AF. Nonetheless, effective rate control may be achieved with beta blockers, diltiazem, or verapamil in patients with atrial flutter through a direct effect on the AV node. Hypotension is the main adverse effect. Intravenous diltiazem is the preferred intravenous calcium channel blocker for acute rate control because of its safety and efficacy.[351] Diltiazem and verapamil should be avoided in patients with advanced heart failure and in patients with heart block or sinus node dysfunction in the absence of pacemaker therapy. Verapamil and diltiazem also should not be used in patients with known preexcitation. The heart rate control achieved with beta blockers is similar to that seen with verapamil and diltiazem. The rate-slowing effect of beta blockers is largely related to reduction of sympathetic tone. Esmolol is generally the preferred intravenous beta blocker because of its rapid onset.[353] Care should be used in administering beta blockers for rate control in atrial flutter patients with decompensated heart failure or reactive airway disease.[355]
I	B-NR	**3. Elective synchronized cardioversion is indicated in stable patients with well-tolerated atrial flutter when a rhythm-control strategy is being pursued.[356–358]**
See Online Data Supplements 16 and 17.		Heart rates can be difficult to control in atrial flutter. Cardioversion for atrial flutter can be successful at lower energy levels than for AF.[356] Anticoagulation issues for cardioversion are the same as those for patients with AF and are addressed in the 2014 AF guideline.[10] Restoration of sinus rhythm is favored to avoid development of tachycardia-mediated cardiomyopathy, which is associated with a rapid ventricular response in atrial flutter.
I	B-NR	**4. Synchronized cardioversion is recommended for acute treatment of patients with atrial flutter who are hemodynamically unstable and do not respond to pharmacological therapies.[75,208,356,359]**
See Online Data Supplements 16 and 17.		The ventricular rate in atrial flutter can be difficult to control with pharmacological therapy. In patients with any signs or symptoms of hemodynamic compromise attributed to atrial flutter, synchronized cardioversion (with appropriate considerations with regard to anticoagulation) should be pursued without delay.
I	C-LD	**5. Rapid atrial pacing is useful for acute conversion of atrial flutter in patients who have pacing wires in place as part of a permanent pacemaker or implantable cardioverter-defibrillator or for temporary atrial pacing after cardiac surgery.[360–364]**
See Online Data Supplements 16 and 17.		Atrial pacing is effective at terminating flutter in >50% of cases.[364] Atrial pacing is more commonly applied in situations in which atrial wires are already in place, such as in the postoperative setting or in patients with programmable cardiac implanted electrical devices. A temporary pacing wire may also be placed and atrial pacing for termination of atrial flutter can be useful when sedation is contraindicated, or in the setting of digitalis toxicity, in which DC cardioversion is contraindicated. Pace-termination is performed by pacing the atrium at a rate starting approximately 5% to 10% above the atrial flutter rate to achieve atrial entrainment and by maintaining pacing for ≥15 seconds, with repeated attempts at incrementally faster rates (reducing the pacing cycle length by 5 to 10 ms until normal sinus rhythm or AF occurs.[364] When AF is precipitated, this is often more easily rate-controlled and may subsequently revert to sinus rhythm. Recommendations for anticoagulation with regard to pace-termination of atrial flutter are the same as those for chemical or electrical conversion of AF.

Recommendations for Acute Treatment of Atrial Flutter (Continued)		
COR	LOE	Recommendations
I	B-NR	**6. Acute antithrombotic therapy is recommended in patients with atrial flutter to align with recommended antithrombotic therapy for patients with AF.[365]**
See Online Data Supplements 16 and 17.		The risk of stroke associated with AF is well established, and several RCTs have demonstrated the efficacy of anticoagulation for stroke prevention in patients with additional risk factors.[366] Anticoagulation has also been shown to prevent stroke when administered during the weeks immediately before and after cardioversion.[367] Whether atrial flutter carries a risk of stroke similar to that in patients with AF has been debated in the past but is now supported by limited evidence from mechanistic, observational, and prospective studies that include patients primarily with atrial flutter.[365–369] Several reports have suggested that the risk of stroke in patients with atrial flutter is mitigated by anticoagulation. Meta-analysis of 13 studies of patients undergoing cardioversion of atrial flutter reported short-term stroke risks ranging from 0% to 7%, and the thromboembolism rate in patients with sustained flutter in 4 studies averaged 3% annually.[365] Other studies have reported similar risk and effectiveness of anticoagulation.[369] Therefore, on the basis of the available data, recommendations for antithrombotic therapy for patients with atrial flutter are similar to those for patients with AF.[10]
IIa	B-R	**1. Intravenous amiodarone can be useful for acute control of the ventricular rate (in the absence of pre-excitation) in patients with atrial flutter and systolic heart failure, when beta blockers are contraindicated or ineffective.[350,370,371]**
See Online Data Supplements 16 and 17.		Amiodarone may be useful for rate control in non–pre-excited atrial flutter because of its slowing of conduction through the AV node and prolongation of AV nodal refractoriness. Because it has less negative inotropic effect than beta blockers, diltiazem, and verapamil and may produce less hypotension, it may be preferred in critically ill patients or in those with tenuous hemodynamic stability. Because of potential toxicity, amiodarone should not be used for long-term rate control in most patients. Although unlikely, amiodarone may result in conversion of atrial flutter to sinus rhythm, so potential risks and benefits should be considered for patients with atrial flutter lasting ≥48 hours who are not adequately anticoagulated.[10] However, amiodarone is typically used for rate control only when other options are greatly limited. For patients with atrial flutter, antithrombotic therapy is recommended according to the same risk profile used for AF.

7.4. Ongoing Management: Recommendations

Recommendations for Ongoing Management of Atrial Flutter		
COR	LOE	Recommendations
I	B-R	**1. Catheter ablation of the CTI is useful in patients with atrial flutter that is either symptomatic or refractory to pharmacological rate control.[243,372–375]**
See Online Data Supplements 16 and 17.		Rate control can be difficult to achieve in atrial flutter, and a rhythm control strategy is often chosen. Catheter ablation of CTI-dependent atrial flutter is often preferred to long-term pharmacological therapy; in this rhythm, the CTI represents the optimal target for ablation because a line of ablation between the tricuspid valve annulus and inferior vena cava can effectively interrupt the circuit. A variety of techniques are applicable, including various catheter types, energy delivery systems, and mapping and visualization tools; generally, success depends on creation of a complete line of block and permanent interruption of conduction across the CTI (Table 8). Successful ablation is often heralded by intraprocedural interruption of the arrhythmia and subsequent EP demonstration of bidirectional block across the ablated tissue.
I	C-LD	**2. Beta blockers, diltiazem, or verapamil are useful to control the ventricular rate in patients with hemodynamically tolerated atrial flutter.[347–349]**
See Online Data Supplements 16 and 17.		In some circumstances of persistent atrial flutter or in patients who have infrequent reasonably well-tolerated episodes of atrial flutter, a rate-control strategy may be chosen. In atrial flutter, the relatively slower atrial rate compared with AF often paradoxically results in more rapid AV nodal conduction because there is less concealed AV nodal conduction. Therefore, achieving adequate rate control can be difficult. Higher doses of beta blockers, diltiazem, or verapamil, and often a combination of agents, may be needed to achieve adequate rate control. Beta blockers are generally preferred in patients with heart failure. Avoidance of beta blockers, diltiazem, and verapamil in patients with pre-excited atrial flutter is recommended, given the potential for accelerated ventricular rates degenerating to ventricular fibrillation, as has been reported to occur rarely in similar patients with AF.[274]
I	C-LD	**3. Catheter ablation is useful in patients with recurrent symptomatic non–CTI-dependent flutter after failure of at least 1 antiarrhythmic agent.[134,327]**
See Online Data Supplements 16 and 17.		No prospective RCTs have compared the efficacy or safety of antiarrhythmic drugs with that of catheter ablation for non–CTI-dependent atrial flutter. In general, catheter ablation of non–CTI-dependent atrial flutter is substantially more difficult than ablation of CTI-dependent flutter because the anatomic circuits are complex, are often not anatomically defined, and can be difficult to locate. Knowledge of the prior surgical or ablation approach and detailed activation and entrainment mapping of the tachycardia are useful during attempts at ablation (Table 8). The location of the circuit determines ablation approach and risks. Observational data support the relative effectiveness and safety of catheter ablation in experienced centers.[134,327] Many of the atrial flutters that are observed during the first 3 months after catheter ablation or cardiac surgery will not persist beyond the periprocedural period, so attempts at ablation can be deferred unless pharmacological therapy and/or cardioversion are unsuccessful.[327]

Recommendations for Ongoing Management of Atrial Flutter (Continued)		
COR	**LOE**	**Recommendations**
I	**B-NR**	**4. Ongoing management with antithrombotic therapy is recommended in patients with atrial flutter to align with recommended antithrombotic therapy for patients with AF.[365]**
See Online Data Supplements 16 and 17.		The risk of stroke associated with AF is well established, and several RCTs have demonstrated the efficacy of anticoagulation for stroke prevention in patients with additional risk factors.[366] Anticoagulation has also been shown to prevent stroke when administered during the weeks immediately before and after cardioversion.[367] Whether atrial flutter carries a risk of stroke similar to that in patients with AF has been debated in the past but is now supported by limited evidence from mechanistic, observational, and prospective studies that include patients primarily with atrial flutter.[365–369] Several reports have suggested that the risk of stroke in patients with atrial flutter is mitigated by anticoagulation. Meta-analysis of 13 studies of patients undergoing cardioversion of atrial flutter reported short-term stroke risks ranging from 0% to 7%, and the thromboembolism rate in patients with sustained flutter in 4 studies averaged 3% annually.[365] Other studies have reported similar risk and effectiveness of anticoagulation.[369] Therefore, on the basis of available data, recommendations for antithrombotic therapy for patients with atrial flutter are similar to those for patients with AF.[10]
IIa	**B-R**	**1. The following drugs can be useful to maintain sinus rhythm in patients with symptomatic, recurrent atrial flutter, with the drug choice depending on underlying heart disease and comorbidities:** **a. Amiodarone[376]** **b. Dofetilide[346,377]** **c. Sotalol[378]**
See Online Data Supplements 16 and 17.		In patients in whom ablation is not being considered because of contraindications (such as underlying medical illness) or because of patient preference, a variety of antiarrhythmic drugs are available. These drugs act by suppressing triggers and altering atrial tissue refractoriness. Individual properties of each drug need to be considered for proper use. Much of the data pertaining to use of amiodarone in management of atrial arrhythmias has been derived from use in patients with AF.[10] Few data are available for patients with atrial flutter. Amiodarone has significant toxicities, so it is used only when other treatments are contraindicated or ineffective. Nevertheless, administration is reasonable, particularly in patients with heart failure or significant underlying heart disease.[376] Dofetilide may be more effective than many other drugs but must be started in an inpatient setting.[346,377] The dose is adjusted on the basis of renal function, with close monitoring of the Q-T interval and subsequent monitoring for altered renal function. Sotalol, a class III antiarrhythmic, is generally well tolerated but is associated with typical beta blocker side effects, such as fatigue and bradycardia.[378] The major potential cardiac toxicity for both drugs is torsades de pointes.
IIa	**B-NR**	**2. Catheter ablation is reasonable in patients with CTI-dependent atrial flutter that occurs as the result of flecainide, propafenone, or amiodarone used for treatment of AF.[317,379–381]**
See Online Data Supplements 16 and 17.		Some patients with AF treated with propafenone, flecainide, or amiodarone will develop atrial flutter. In this circumstance, if flutter becomes the dominant arrhythmia, ablation of the CTI and continued use of the antiarrhythmic drug can decrease the incidence of atrial flutter and facilitate the pharmacological management of AF.[379,380]
IIa	**C-LD**	**3. Catheter ablation of the CTI is reasonable in patients undergoing catheter ablation of AF who also have a history of documented clinical or induced CTI-dependent atrial flutter.[381,382]**
See Online Data Supplements 16 and 17.		The indications for catheter ablation of AF are discussed in the 2014 AF guideline.[10] When AF and atrial flutter coexist, 1 randomized study demonstrated that at 1-year follow-up, greater success in terms of arrhythmia suppression and quality-of-life score resulted from AF ablation (with or without atrial flutter ablation) than from atrial flutter ablation alone.[381] It may be that AF ablation alone is sufficient to control both arrhythmias, although CTI ablation reduced the early postablation arrhythmia recurrence rate.[382]
IIa	**C-LD**	**4. Catheter ablation is reasonable in patients with recurrent symptomatic non–CTI-dependent flutter as primary therapy, before therapeutic trials of antiarrhythmic drugs, after carefully weighing potential risks and benefits of treatment options.[135]**
See Online Data Supplements 16 and 17.		No prospective RCTs have compared the efficacy or safety of antiarrhythmic drugs with that of catheter ablation for non–CTI-dependent atrial flutter. Observational data, however, support the relative effectiveness and safety of catheter ablation in experienced centers.[135,327] Many of the atrial flutters that are observed during the first 3 months after ablation or cardiac surgery will not persist beyond the periprocedural period, so attempts at ablation can be deferred unless attempts at pharmacological therapy or cardioversion are unsuccessful.[135]
IIb	**B-R**	**1. Flecainide or propafenone may be considered to maintain sinus rhythm in patients without structural heart disease or ischemic heart disease who have symptomatic recurrent atrial flutter.[383–385]**
See Online Data Supplements 16 and 17.		Data to support the recommendation for flecainide and propafenone for maintenance of sinus rhythm in patients with atrial flutter is derived from trials that pooled patients with AF and atrial flutter, with the vast majority of the patients having AF. It is therefore possible that these agents are not as effective for treating isolated atrial flutter as they are for AF.[386] Flecainide and propafenone may result in slowing of the atrial flutter cycle length, which may lead to a rapid 1:1 ventricular response.[387] Because of this, caution is advised with flecainide and propafenone in patients with atrial flutter at risk of 1:1 conduction. The risk may be reduced by coadministration of medications that slow AV nodal conduction, such as beta blockers, verapamil, or diltiazem.
IIb	**C-LD**	**2. Catheter ablation may be reasonable for asymptomatic patients with recurrent atrial flutter.[102,121,372]**
See Online Data Supplements 16 and 17.		Catheter ablation of atrial flutter is highly effective, with single-procedure success rates >90%[102] and an excellent safety profile.[102,121] In patients with recurrent atrial flutter, long-term maintenance of sinus rhythm is more likely with ablation than with pharmacological therapy.[372] Also, ablation may avoid potential development of tachycardia-mediated cardiomyopathy.

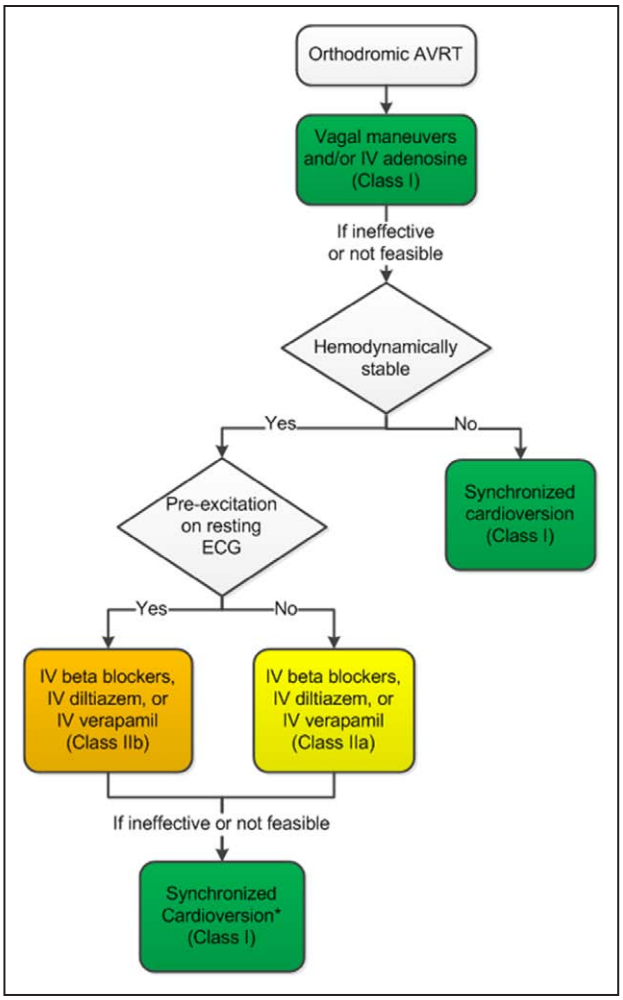

Figure 14. Acute treatment of orthodromic AVRT. Colors correspond to Class of Recommendation in Table 1; drugs listed alphabetically. *For rhythms that break or recur spontaneously, synchronized cardioversion is not appropriate. AVRT indicates atrioventricular reentrant tachycardia; ECG, electrocardiogram; and IV, intravenous.

8. Junctional Tachycardia

See Figure 20 for a representative ECG for junctional tachycardia and Figure 21 for the algorithm for ongoing management of junctional tachycardia.

Junctional tachycardia is a rapid, occasionally irregular, narrow-complex tachycardia (with rates typically of 120 bpm to 220 bpm) (Figure 20). AV dissociation (often isorhythmic) may be seen, and when present, excludes the misdiagnosis of AVRT and makes AVNRT highly unlikely. Other SVTs are often misdiagnosed and misclassified as junctional tachycardia because of the frequent absence of demonstrable P waves in reentrant rhythms. Furthermore, when it is irregular, junctional tachycardia may be misdiagnosed as AF or MAT. The mechanism for junctional tachycardia is enhanced (abnormal) automaticity from an ectopic focus in the AV junction (including the His bundle).[388]

Junctional tachycardia is uncommon in adults[388]; it is typically seen in infants postoperatively, after cardiac surgery for congenital heart disease; this is also known as junctional ectopic tachycardia. As such, there is limited evidence with regard to diagnosis and management of junctional tachycardia in adult patients. Adults with junctional tachycardia typically have a relatively benign course, whereas infants and children with acquired or congenital junctional tachycardia have a high rate of death due to heart failure or an uncontrollable, incessant tachyarrhythmia.

There are data to support the use of beta blockers, diltiazem, flecainide, procainamide, propafenone, and verapamil for the treatment of junctional tachycardia (see recommendations and references in Sections 8.1 and 8.2). The efficacy of amiodarone has been reported only in pediatric patients.[389,390] Digoxin has not been well established as chronic therapy for junctional tachycardia.

A related rhythm, nonparoxysmal junctional tachycardia (more commonly known as accelerated AV junctional rhythm), is far more common in adults than paroxysmal junctional tachycardia. The mechanism of nonparoxysmal junctional tachycardia is associated with automaticity or triggered activity. It occurs at a slower rate (70 bpm to 130 bpm) and is often due to digoxin toxicity[391] or myocardial infarction.[392,393] Treatment of this rhythm centers on addressing the underlying condition. In addition, there is some evidence that beta blockers,[394] intravenous adenosine, or verapamil[395] can terminate an accelerated junctional arrhythmia. A transient junction rhythm may be seen after slow-pathway ablation for AVNRT.[396]

8.1. Acute Treatment: Recommendations

Recommendations for Acute Treatment of Junctional Tachycardia		
COR	**LOE**	**Recommendations**
IIa	**C-LD**	**1. Intravenous beta blockers are reasonable for acute treatment in patients with symptomatic junctional tachycardia.[388]**
See Online Data Supplement 19.		In a series studying junctional tachycardia in adult patients, beta-blocker therapy—specifically intravenous propranolol—was found to be modestly effective in terminating and/or reducing the incidence of tachycardia.[388]
IIa	**C-LD**	**2. Intravenous diltiazem, procainamide, or verapamil is reasonable for acute treatment in patients with junctional tachycardia.[397]**
See Online Data Supplement 19.		There may be a limited role for intravenous diltiazem, procainamide, or verapamil in patients in whom beta blockers are ineffective. The literature supports the use of intravenous verapamil, alone or in combination with procainamide; less is known about diltiazem monotherapy.[397] The addition of procainamide to propranolol may be more effective than propranolol monotherapy.[388]

8.2. Ongoing Management: Recommendations

Recommendations for Ongoing Management of Junctional Tachycardia		
COR	LOE	Recommendations
IIa	C-LD	**1. Oral beta blockers are reasonable for ongoing management in patients with junctional tachycardia.[388]**
See Online Data Supplement 19.		Beta blockers are often used as first-line chronic therapy for junctional tachycardia because of the important proarrhythmic effects and long-term toxicity of other agents that have been shown to be effective.[389,398,399] When junctional tachycardia is paroxysmal, attention should be directed toward avoiding the potential for bradyarrhythmias and hypotension when beta-blocker therapy is initiated.
IIa	C-LD	**2. Oral diltiazem or verapamil is reasonable for ongoing management in patients with junctional tachycardia.[397]**
See Online Data Supplement 19.		Junctional tachycardia caused by enhanced automaticity may be suppressed as effectively by diltiazem and verapamil as by beta blockers. In 1 study of an adult patient on a regimen of oral verapamil, procainamide, and digoxin in combination for prophylactic therapy, junctional tachycardia could not be induced by either atrial or ventricular overdrive pacing, programmed electrical stimulation, or isoproterenol.[397] Less is known about oral diltiazem than verapamil, but it likely has a similar efficacy.
IIb	C-LD	**1. Flecainide or propafenone may be reasonable for ongoing management in patients without structural heart disease or ischemic heart disease who have junctional tachycardia.[398,399]**
See Online Data Supplement 19.		Studies supporting the use of flecainide for long-term control of junctional tachycardia were performed at a time when intravenous flecainide was given for acute control, followed by a transition to chronic oral therapy.[398] Although the only data for propafenone stem from case series in infants and children, given that flecainide and propafenone reduce automaticity from the ectopic focus in the AV junction, either agent is reasonable, provided patients do not have structural heart disease or ischemic heart disease.[213,400,401]
IIb	C-LD	**2. Catheter ablation may be reasonable in patients with junctional tachycardia when medical therapy is not effective or contraindicated.[131,132,396,402–405]**
See Online Data Supplement 19.		Radiofrequency ablation has been performed as a potentially curative therapy for junctional tachycardia since the early 1990s. However, in view of the reported 5% to 10% risk of AV block, catheter ablation is generally reserved for highly symptomatic patients in whom drug therapy has been ineffective or not tolerated (Table 8). Many practitioners use cryoablation as an alternative to radiofrequency ablation.[132] Given that it is often difficult to distinguish junctional tachycardia from AVNRT on the ECG, EP study with the goal of ablation may be a helpful diagnostic and potentially therapeutic intervention. Junctional tachycardia may be observed during and after slow-pathway ablation of AVNRT, because of irritation of the compact AV node.[406] This iatrogenic junctional tachycardia is transient and generally benign and can be distinguished from AVNRT through pacing maneuvers at EP study.[396,405] It is crucial to recognize this phenomenon at the time of EP study because attempts to ablate the junctional tachycardia are unnecessary and could result in AV block.

9. Special Populations

9.1. Pediatrics

As discussed in the Scope (Section 1.4), the present document is aimed at the adult population (≥18 years of age) and offers no specific recommendations for pediatric patients. Nevertheless, a brief discussion of SVT in pediatric patients is included below, highlighting major considerations with regard to SVT in younger patients, including adolescent patients.

SVT in young patients varies significantly from SVT in adult patients in terms of mechanism, risk of developing heart failure or cardiac arrest, risks associated with interventional therapy, natural history, and psychosocial impact. Approximately half of pediatric SVT presents in the first 4 months of life, with age-related peaks in occurrence subsequently at 5 to 8 years and after 13 years. Accessory pathway–mediated tachycardia accounts for >70% of SVT in infants, decreasing to approximately 55% in adolescents.[56,407–409] AVNRT increases with age, from 9% to 13% of SVT in infants, to 30% to 50% of SVT in teenagers. After 12 years of age, women are more likely to have AVNRT than men, and overall SVT is less frequent among African American and Hispanic patients than in the general pediatric population.[56] Atrial flutter is seen in some neonates and in older children is predominantly observed after congenital heart disease. AF is uncommon in childhood, accounting for <3% of supraventricular arrhythmias, and may be a consequence of AVRT or AVNRT in adolescents or may be associated with repaired congenital heart disease. Symptoms of SVT vary with age: gastrointestinal or respiratory findings in infants, chest or abdominal pain in the younger child, and palpitations in the adolescent. Congestive heart failure is present in up to 20% of infants and in older children with incessant tachycardia and in rare cases may necessitate mechanical cardiopulmonary support during initial therapy.[410]

Pre-excitation is present in 20% to 35% of children with SVT. The risk of ventricular fibrillation or SCD related to WPW in childhood is 1.3% to 1.6% and is highest in the first 2 decades of life.[60,254–257] The risk of cardiac arrest is higher in patients with AVRT precipitating AF, short accessory connection refractory periods, and posteroseptal accessory pathways.[60,254–257] Notably, the absence of prior symptoms does not preclude risk because cardiac arrest may be the initial manifestation of pre-excitation.[254,257,411] Risk stratification, such as with ambulatory 24-hour monitoring or treadmill exercise testing, is often considered for children with pre-excitation to assess persistence of pre-excitation.[412]

Pharmacological therapy of SVT in childhood is largely based on practice patterns because RCTs of antiarrhythmic medications in children are lacking. AV nodal–blocking drugs are widely used for the most common arrhythmias, AVRT, and

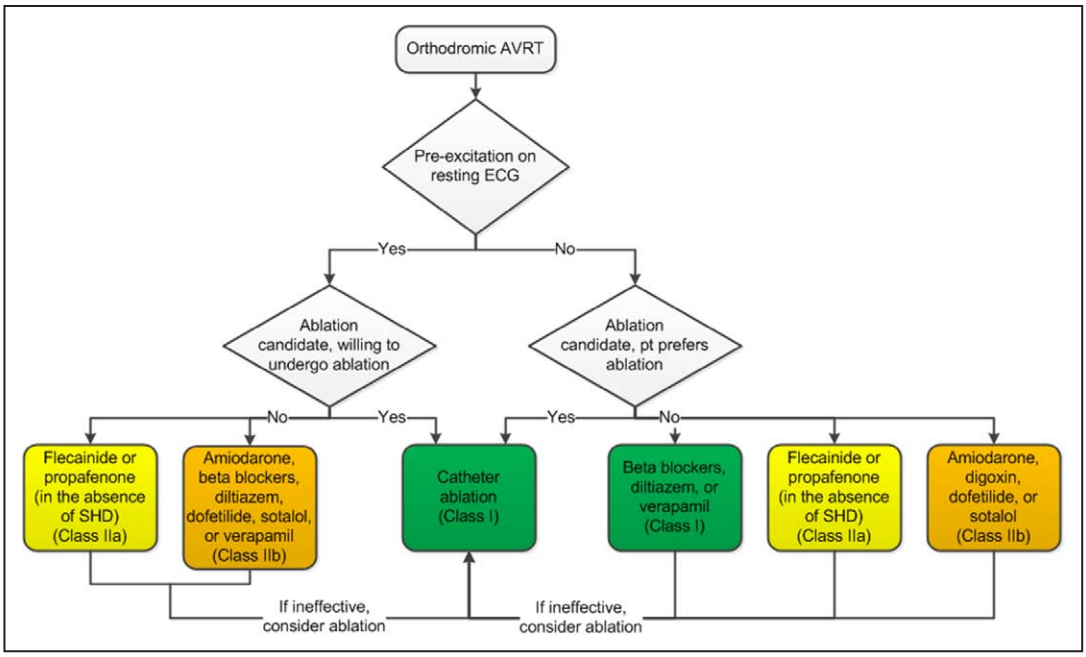

Figure 15. Ongoing management of orthodromic AVRT. Colors correspond to Class of Recommendation in Table 1; drugs listed alphabetically. AVRT indicates atrioventricular reentrant tachycardia; ECG, electrocardiogram; pt, patient; and SHD, structural heart disease (including ischemic heart disease).

AVNRT. Higher initial doses of adenosine are needed in children than in adults, with children receiving from 150 mcg/kg to 250 mcg/kg.[413–415] Digoxin and propranolol have similar efficacy in infants with SVT without pre-excitation.[416] Digoxin is avoided in the presence of pre-excitation because its use in infancy has been associated with SCD or ventricular fibrillation.[417,418] Amiodarone, sotalol, propafenone, or flecainide can be used for refractory SVT in infants. In older children presenting with SVT, beta-blocker therapy is most often the initial therapy used. Because of the rare occurrence of adverse events with flecainide, including in patients without structural heart disease, ischemic heart disease, or ventricular dysfunction, flecainide is not used as a first-line medication in children.[419]

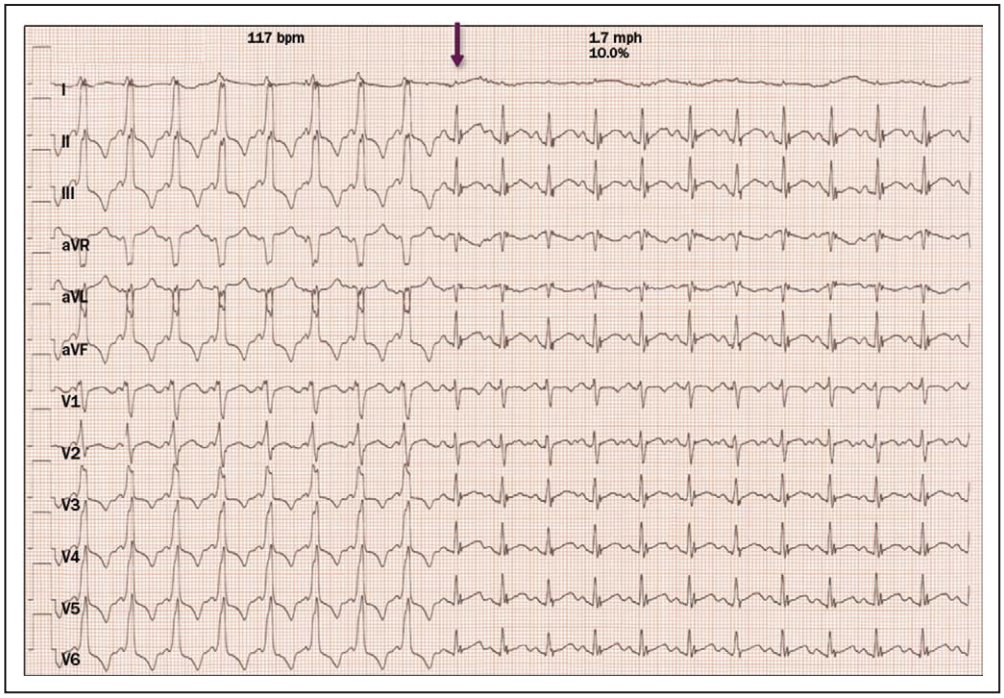

Figure 16. Abrupt loss of pre-excitation during exercise testing. During exercise treadmill testing, this patient abruptly lost pre-excitation at a heart rate of 117 bpm. Beginning abruptly with the beat under the arrow, the PR interval normalizes, and the QRS changes from pre-excited to narrow.

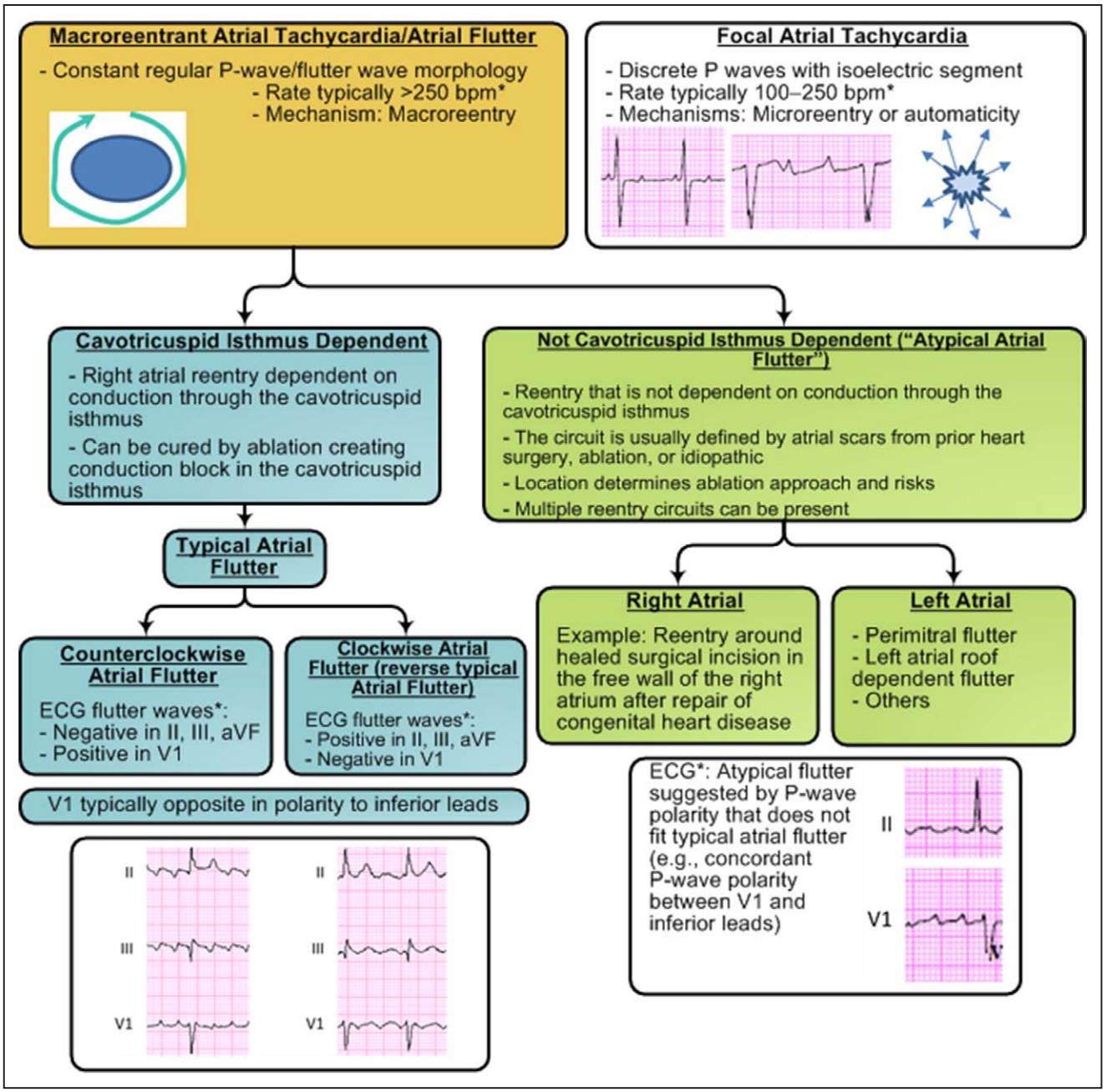

Figure 17. Classification of atrial flutter/atrial tachycardias. Diagram summarizing types of ATs often encountered in patients with a history of atrial fibrillation, including those seen after catheter or surgical ablation procedures. P-wave morphologies are shown for common types of atrial flutter; however, the P-wave morphology is not always a reliable guide to the re-entry circuit location or to the distinction between common atrial flutter and other macroreentrant ATs. *Exceptions to P-wave morphology and rate are common in scarred atria. bpm indicates beats per minute, and ECG, electrocardiogram.
Reproduced with permission from January et al.[10]

Catheter ablation can be successfully performed in children of all ages, with acute success rates comparable to those reported in adults.[281,282,420,421] Success rates are influenced by the presence of structural heart disease or ischemic heart disease and are highest in left-sided accessory pathways and lowest for AT. Complications were reported in 4% to 8% of the initial large series, with major complications in 0.9% to 3.2%, and complication rates were higher in patients weighing <15 kg.[281,420–422] The implications of complications, including AV block requiring pacing, perforation, and coronary artery or mitral valve injury, are profound in young patients.[423–425] In early series, death was reported in 0.12% of children with normal hearts and was associated with lower weight and increased number of ablation lesions.[426] Increased institutional experience, advanced mapping techniques, and use of cryoablation have reduced the incidence of complications, as well as the radiation exposure associated with the procedure. Although most centers perform elective ablation for children weighing >12 kg to 15 kg, ablation in younger or smaller children is generally reserved for those with medically refractory

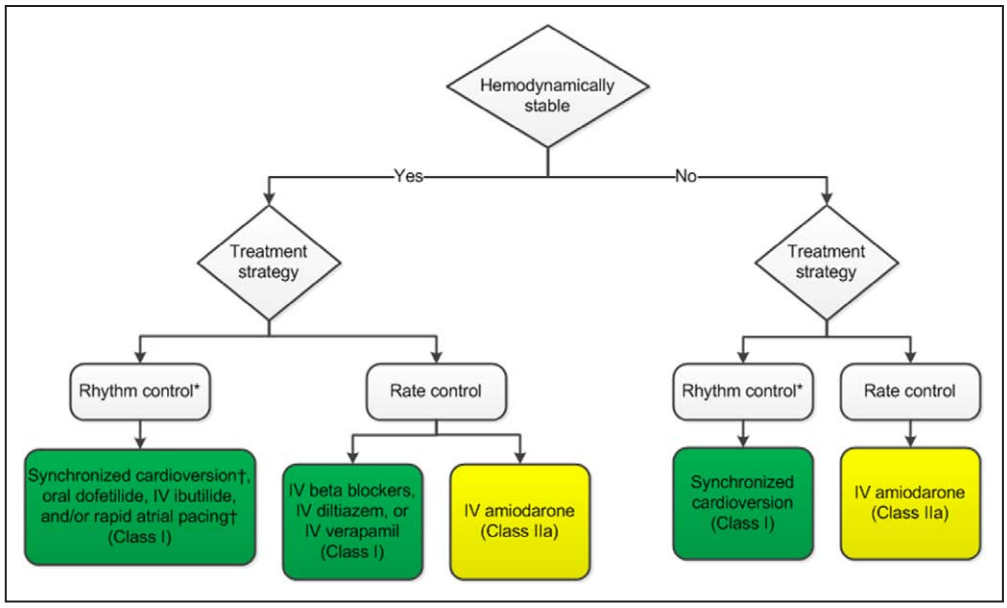

Figure 18. Acute treatment of atrial flutter. Colors correspond to Class of Recommendation in Table 1; drugs listed alphabetically. *Anticoagulation as per guideline is mandatory. †For rhythms that break or recur spontaneously, synchronized cardioversion or rapid atrial pacing is not appropriate. IV indicates intravenous.

SVT or tachycardia-induced cardiomyopathy or before surgery that may limit access for subsequent catheter-based procedures. Recurrence rates for SVT after successful procedures are higher than reported in large adult series, ranging from 7% to 17%; whether this reflects technical differences, natural history, or more long-term follow-up is unclear.[427–429] Recurrence is highest among right-sided accessory pathways, particularly anteroseptal or multiple pathways, and in AT in the setting of complex congenital heart disease.[427–429]

Junctional ectopic tachycardia occurs predominantly in very young patients either as a congenital form or, more commonly, after intracardiac repair of congenital heart disease. Nonpostoperative junctional tachycardia has been reported to respond to amiodarone or combination therapy including beta blockers, flecainide, procainamide, or propafenone.[130] Ablation for patients with refractory tachycardia or ventricular dysfunction has shown efficacy of 82% to 85%, but inadvertent AV block occurred in 18% and recurrence was seen in 14% of patients.[130] Postoperative junctional tachycardia occurs in 2% to 10% of young patients undergoing intracardiac surgery, particularly for ventricular or AV septal defects, tetralogy of Fallot, transposition of the great arteries, and Norwood procedures.[430,431] Treatment includes sedation with muscle relaxation, limitation of inotropic medications, reduction of core temperature to 34 to 35°C, atrial overdrive pacing, and procainamide or amiodarone infusions.[416,432–435] In general, postoperative junctional tachycardia resolves and does not require ongoing therapy.

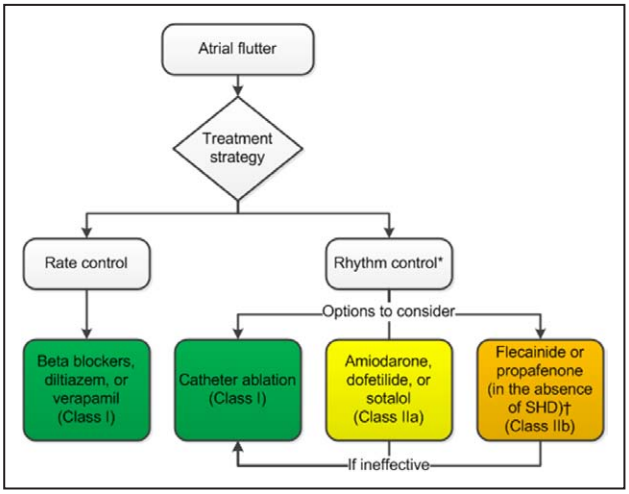

Figure 19. Ongoing management of atrial flutter. Colors correspond to Class of Recommendation in Table 1; drugs listed alphabetically. *After assuring adequate anticoagulation or excluding left atrial thrombus by transesophageal echocardiography before conversion. †Should be combined with AV nodal–blocking agents to reduce risk of 1:1 conduction during atrial flutter. AV indicates atrioventricular; SHD, structural heart disease (including ischemic heart disease).

Although this guideline focuses on adults, it should be noted that SVT may occur in the fetus and, if sustained, may put the fetus at risk of cardiovascular collapse manifested by hydrops. Mothers require safety monitoring by adult cardiologists during treatment. The most common mechanisms for fetal SVT are AVRT and atrial flutter.[436] Persistent SVT with hydrops carries a high mortality rate, and therefore, prompt and aggressive treatment is warranted. Maternal administration of antiarrhythmic agents has been shown to be effective through transplacental delivery. Flecainide, sotalol, and digoxin, alone or in combination, have demonstrated arrhythmia termination rates of 60% to 90%, depending on whether hydrops is present.[437,438] In cases refractory to the aforementioned drugs, maternal oral loading for 2 to 7 days with amiodarone may prove lifesaving.[439] Treatment of fetal SVT has provided safety data for treatment of arrhythmias in women during pregnancy, as addressed in Section 9.3.

Table 8. Success and Complication Rates for Ablation of SVT*

Arrhythmia	Acute Success	Recurrence Rate	Major Complications	References
Common SVTs				
AVNRT	96%–97%[102,103]	5%[103]	• Overall 3%[102] • PPM 0.7%[102] • Death 0%[102]	102,103
AVRT/accessory pathway	93%[102,103]	8%[103]	• Overall 2.8%[102] • PPM 0.3%[102] • Death 0.1%[102] • Tamponade 0.4%[102]	102,103
CTI-dependent atrial flutter	97%[102]	10.6% atrial flutter,[121] 33% atrial fibrillation[121]	• Overall 0.5%[102] • PPM 0.2%[102] • Pericardial effusion 0.3%[102]	102,103,121
Less common SVTs				
Focal AT	80%–100%	4%–27%	<1%–2%	122–129
JT	82%–85%	0–18%	0–18% CHB (overall complications N/A)	130–132
Non–CTI-dependent atrial flutter	73%–100%	7%–53%	0–7%	122,133–140

*Data in this table are derived from multiple observational studies and registries, and as such may not always reflect current practice.

AT indicates atrial tachycardia; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; CHB, complete heart block; CTI, cavotricuspid isthmus; JT, junctional tachycardia; N/A, not available; PPM, permanent pacemaker; and SVT, supraventricular tachycardia.

9.2. Patients With Adult Congenital Heart Disease

See Figure 22 for the algorithm for acute treatment of non–pre-excited SVT in adult congenital heart disease (ACHD) patients; and Figure 23 for the algorithm for ongoing management of non–pre-excited SVT in ACHD patients.

9.2.1. Clinical Features

SVT is observed in 10% to 20% of ACHD patients, and is associated with a significantly increased risk of heart failure, stroke, and SCD.[440–444] The most common mechanism of SVT in ACHD patients is macroreentrant AT (also called flutter), which accounts for at least 75% of SVT and frequently involves the CTI. Focal AT, AVNRT, and accessory pathway–mediated tachycardia each account for less than about 8% of SVT, whereas the incidence of AF is about 10% and increases with age.[133,445–449] AT occurs in 20% to 45% of adults with Ebstein anomaly, single-ventricle/Fontan procedures, tetralogy of Fallot, transposition of the great arteries, and atrial septal defects.[449–451]

The management of SVT in ACHD patients is influenced by the underlying cardiac anatomy and surgical repair, the current hemodynamic sequelae of the anatomy and repairs, and mechanism of SVT. The ventricular rate during SVT may be slowed because of variable AV conduction, which can result in a delay in recognizing tachycardia and the development of congestive failure. Recognition of severe forms of congenital heart disease, including unrepaired or palliated defects,

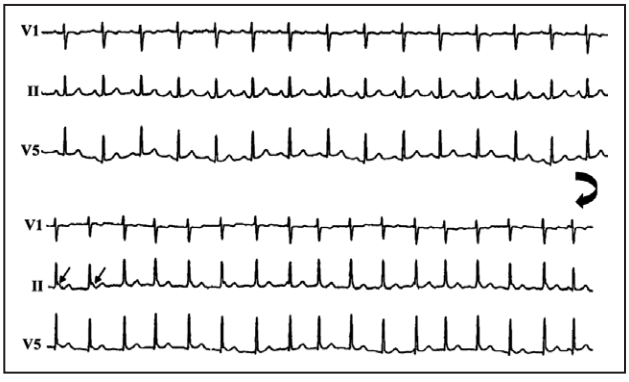

Figure 20. Surface electrocardiographic recording from leads VI, II, and V5 in a patient with junctional tachycardia. The **upper panel** shows sinus rhythm. The **lower panel** shows tachycardia onset with the characteristic finding of dissociation of the QRS and P waves (narrow arrows on P waves). The large arrow signifies continuous recording. Reproduced with permission from Blomström-Lundqvist et al.[11]

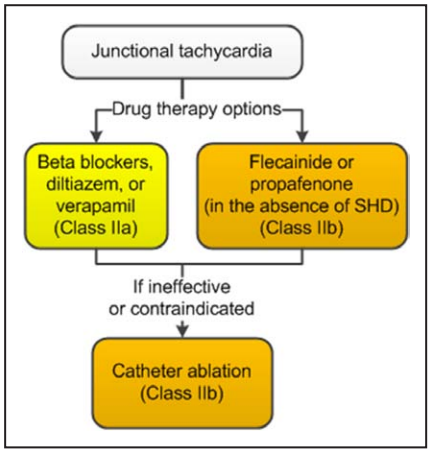

Figure 21. Ongoing management of junctional tachycardia. Colors correspond to Class of Recommendation in Table 1; drugs listed alphabetically. SHD indicates structural heart disease (including ischemic heart disease).

cyanotic heart disease, single or systemic right ventricles, or Ebstein anomaly, is essential to decision making during SVT treatment. In certain conditions, the presence of cyanosis or severe ventricular dysfunction requires consideration of high-risk cardioversion with resuscitation measures at hand; usually, this decision is made at centers with specialized expertise. Management of ACHD patients should be undertaken only in collaboration with a cardiologist who has specialized training or experience in managing such patients.

RCTs assessing antiarrhythmic medication efficacy are lacking. Beta-blocking medications offer the advantages of outpatient medication initiation and may provide protection from tachycardia-mediated hypotension or ischemia. Risks of proarrhythmia are increased with the use of sotalol, ibutilide, dofetilide, and particularly flecainide and require in-hospital initiation. Flecainide is associated with increased risk of SCD[419] and is reserved for patients without ventricular dysfunction who do not respond to other therapy. Sinus node dysfunction may contribute to the development of atrial arrhythmias and may become exacerbated with antiarrhythmic medications. Atrial antibradycardia pacing to maintain a consistent physiological heart rate may decrease the frequency of tachycardia episodes and may improve functional capacity.[364,370,371] Atrial antitachycardia pacing to terminate atrial reentry tachycardia is an effective approach when feasible.[364,370,371]

Overall acute success rates of catheter ablation procedures for SVT in ACHD patients range from 70% to 85%, with recurrences in 20% to 60% of patients within 2 years.[452–457] Catheter ablation is challenged by limitations of venous access to the heart, hypertrophied atrial tissue, multiple atrial reentrant circuits, and atrial baffles partitioning the coronary sinus and CTI to the pulmonary venous atrium. Because the CTI is involved in >60% of atrial reentry circuits, an initial strategy targeting this region is often used. Highest success rates are achieved in patients with atrial septal defects, approaching 90% to 100%, although subsequent AF has been reported in 11% to 30% of patients within 3 years.[330,449,458] Because of the need for sophisticated knowledge of anatomy, advanced mapping capability, cardiac anesthesia with careful periprocedural monitoring, and repeat ablations, such patients should be referred to centers with extensive experience in complex congenital heart disease ablations.

The development of atrial arrhythmias in ACHD patients is often an indicator of progressive hemodynamic changes, which require in-depth functional and hemodynamic assessment. Intervention for residual hemodynamic/structural defects may need to be planned as part of chronic arrhythmia management. Patients with Ebstein anomaly or repaired tetralogy of Fallot may have significant pulmonary regurgitation, tricuspid regurgitation, or both, which might benefit from reoperation. In some settings, integration of operative ablation techniques with hemodynamic repair may be optimal.

9.2.2. Acute Treatment: Recommendations

Recommendations for Acute Treatment of SVT in ACHD Patients		
COR	**LOE**	**Recommendations**
I	C-LD	**1. Acute antithrombotic therapy is recommended in ACHD patients who have AT or atrial flutter to align with recommended antithrombotic therapy for patients with AF.[365]**
See Online Data Supplements 16 and 17.		The risk of stroke associated with AF is well established, and several RCTs have demonstrated the efficacy of anticoagulation for stroke prevention in patients with additional risk factors.[366] Anticoagulation has also been shown to prevent stroke when administered during the weeks immediately before and after cardioversion.[31,367] Whether atrial flutter carries a risk of stroke similar to that in patients with AF has been debated in the past but is now supported by limited evidence from mechanistic, observational, and prospective studies that include patients primarily with atrial flutter.[365–369] Several reports have suggested that the risk of stroke in patients with atrial flutter is mitigated by anticoagulation. Meta-analysis of 13 studies of patients undergoing cardioversion of atrial flutter reported short-term stroke risks ranging from 0% to 7%, and the thromboembolism rate in patients with sustained flutter in 4 studies averaged 3% annually.[365] Other studies have reported similar risk and effectiveness of anticoagulation.[369] ACHD patients with nonfibrillatory atrial tachyarrhythmias appear to be at high risk, as well.[367,459] Therefore, on the basis of available data, recommendations for antithrombotic therapy for ACHD patients who also have AT or atrial flutter are similar to those for patients with AF.[10]
I	B-NR	**2. Synchronized cardioversion is recommended for acute treatment in ACHD patients and SVT who are hemodynamically unstable.[75,460]**
See Online Data Supplement 20.		A small observational study demonstrated safety and efficacy of synchronized cardioversion in ACHD patients, with sinus rhythm achieved in 94% of patients.[460] Guideline-directed medical therapy supports this treatment approach, stressing that electrical cardioversion is the safest and most effective way of treating SVT associated with hemodynamic instability and should be considered early in the management of such patients.[75] Modification of electrode pad placement may be necessary, by using an anterior-posterior configuration in patients with marked atrial enlargement or positioning strategically according to the individual arrhythmia and anatomic substrate, including consideration of the possibility of dextrocardia.
I	C-LD	**3. Intravenous diltiazem or esmolol (with extra caution used for either agent, observing for the development of hypotension) is recommended for acute treatment in ACHD patients and SVT who are hemodynamically stable.[461,462]**
See Online Data Supplement 21.		Very limited data exist on the use of calcium channel–blocking or beta-blocking medications for rate control or termination of AT or atrial flutter specifically associated with ACHD. Rate control of AT or atrial flutter with rapid AV conduction may be useful to improve hemodynamic status while planning conversion strategies. Patients with congenital heart disease, particularly single-ventricle physiology or systemic right ventricles, may not tolerate ventricular rates >120 bpm for many hours.[29] Either drug may be associated with the development of hypotension in up to 20% of patients.[462] Because of the high incidence of ventricular dysfunction in this population, particular attention should be given to monitoring the patient for development of hypotension, which would necessitate prompt dose adjustments or change of treatment strategy.
I	B-NR	**4. Intravenous adenosine is recommended for acute treatment in ACHD patients and SVT.[207,463–465]**
See Online Data Supplement 20.		Observational studies support the use of adenosine to terminate AVNRT, SVT using an accessory pathway, and some forms of focal AT. These mechanisms account for <25% of SVT in adults with repaired congenital disease.[207,463] Intravenous adenosine is unlikely to terminate atrial reentry tachycardia or atrial flutter, which represents >70% of SVT episodes in this population, but it may be diagnostic by producing transient AV block, which would make the atrial activity visible.[464,465]

Recommendations for Acute Treatment of SVT in ACHD Patients (Continued)		
COR	**LOE**	**Recommendations**
IIa	B-NR	**1. Intravenous ibutilide or procainamide can be effective for acute treatment in ACHD patients and atrial flutter who are hemodynamically stable.[466–468]**
See Online Data Supplement 20.		A small observational study reported that intravenous ibutilide was successful in conversion of 71% of acute episodes of atrial flutter in ACHD patients; torsades de pointes or nonsustained VT was reported in 2.7% of episodes.[468] Pretreatment with magnesium may reduce the incidence of postibutilide ventricular arrhythmias. Small studies support the use of intravenous procainamide as adjunctive therapy for acute therapy of atrial flutter because it improves efficacy of pacing conversion of atrial flutter.[466,467]
IIa	B-NR	**2. Atrial pacing can be effective for acute treatment in ACHD patients and SVT who are hemodynamically stable and anticoagulated as per current guidelines for antithrombotic therapy in patients with AF.[466,469–472]**
See Online Data Supplement 20.		Small observational studies support the efficacy of atrial pacing to successfully terminate 54% to 82% of acute episodes of AT or atrial flutter.[466,469–472] Atrial pacing is an effective alternative, particularly when concerns about the use of antiarrhythmic medications or significant sinus node dysfunction exist.
IIa	B-NR	**3. Elective synchronized cardioversion can be useful for acute termination of AT or atrial flutter in ACHD patients when acute pharmacological therapy is ineffective or contraindicated.[460]**
See Online Data Supplement 20.		ACHD patients are at increased risk of congestive heart failure and/or atrial thrombus formation with prolonged episodes of AT or atrial flutter. Pharmacological conversion in patients with complex anatomy, ventricular dysfunction, or prolonged QTc intervals may result in significant proarrhythmia or acute hemodynamic deterioration. Early assessment for cardiac thrombus with transesophageal echocardiogram followed by synchronized cardioversion may be preferable to prolonged or multiple attempts to achieve pharmacological cardioversion. Because of frequent coexistent sinus node dysfunction and ventricular dysfunction, the need for chronotropic or inotropic intervention should be anticipated, with appropriate personnel and support present. Modification of electrode pad placement may be necessary, by using an anterior-posterior configuration in patients with marked atrial enlargement or positioning strategically according to the individual arrhythmia and anatomic substrate, including consideration of the possibility of dextrocardia.
IIb	B-NR	**1. Oral dofetilide or sotalol may be reasonable for acute treatment in ACHD patients and AT and/or atrial flutter who are hemodynamically stable.[473,474]**
See Online Data Supplement 20.		Small observational studies support the use of oral dofetilide[474] or sotalol[473] to acutely convert AT to sinus rhythm in 70% to 85% of episodes of acute AT or atrial flutter. Proarrhythmic events are more commonly reported with dofetilide. One small study of 20 patients reported that 10% experienced torsades de pointes after dofetilide[474]; both proarrhythmic events occurred in patients with single-ventricle physiology. The risk of proarrhythmia or worsening ventricular function requires arrhythmia monitoring with use.

9.2.3. Ongoing Management: Recommendations

Recommendations for Ongoing Management of SVT in ACHD Patients		
COR	**LOE**	**Recommendations**
I	C-LD	**1. Ongoing management with antithrombotic therapy is recommended in ACHD patients and AT or atrial flutter to align with recommended antithrombotic therapy for patients with AF.[365]**
See Online Data Supplements 16 and 17.		The risk of stroke associated with AF is well established, and several RCTs have demonstrated the efficacy of anticoagulation for stroke prevention in patients with additional risk factors.[366] Anticoagulation has also been shown to prevent stroke when administered during the weeks immediately before and after cardioversion.[31,367] Whether atrial flutter carries a risk of stroke similar to that in patients with AF has been debated in the past but is now supported by limited evidence from mechanistic, observational, and prospective studies that include patients primarily with atrial flutter.[365–369] Several reports have suggested that the risk of stroke in patients with atrial flutter is mitigated by anticoagulation. Meta-analysis of 13 studies of patients undergoing cardioversion of atrial flutter reported short-term stroke risks ranging from 0% to 7%, and the thromboembolism rate in patients with sustained flutter in 4 studies averaged 3% annually.[365] Other studies have reported similar risk and effectiveness of anticoagulation.[369] ACHD patients with nonfibrillatory atrial tachyarrhythmias appear to be at high risk, as well.[367,459] Therefore, on the basis of available data, recommendations for antithrombotic therapy for ACHD patients who also have AT or atrial flutter are similar to those for patients with AF.[10]
I	C-LD	**2. Assessment of associated hemodynamic abnormalities for potential repair of structural defects is recommended in ACHD patients as part of therapy for SVT.[25,29]**
See Online Data Supplement 20.		The development of AT, atrial flutter, or AF in ACHD patients is often associated with progressive hemodynamic deterioration of the underlying disease. Surgical treatment of the hemodynamic problems does not eliminate atrial arrhythmias, and ablation of atrial arrhythmias alone could allow significant hemodynamic issues to progress and potentially deteriorate. Successful treatment involves assessing both the arrhythmia and the contributing hemodynamic changes and addressing both when indicated and feasible. Early experience in adults with unoperated atrial septal defects and atrial arrhythmias demonstrated the importance of an integrated approach for arrhythmia and hemodynamic problems; similar principles apply to patients with tetralogy of Fallot, Ebstein anomaly, and single-ventricle physiology; these patients are at highest risk of arrhythmia development, with concurrent hemodynamic abnormalities. For example, patients with ASD who underwent surgery before the age of 25 years had better long-term outcomes and a lower incidence of atrial arrhythmias than those who underwent surgery later in life.[475] Closure of significant atrial septal defects in adults even later in life improves morbidity and survival[476] but is associated with new (7%) or recurrent (60%) AT.[475] Arrhythmias still can be treated successfully when they develop later after surgical corrections; catheter ablation of atrial arrhythmias associated with ASD repair is highly successful, with acute success rates reported as 93% to 100%.[449,458,477] Therefore, patients with unoperated significant ASD and arrhythmias should undergo ablation of the AT, as well as closure of the ASD. The choice of catheter versus surgical approaches to therapy is determined by anatomic features of the ASD likely to be successfully addressed with a catheter approach. No randomized comparison trials of catheter versus surgical closure of ASD combined with arrhythmia intervention have been reported. Surgical closure of large ASDs combined with arrhythmia surgery for AT or fibrillation can be safely performed, with 6.5% occurrence of AF reported during 2 years of follow-up.[478]

Recommendations for Ongoing Management of SVT in ACHD Patients (Continued)		
COR	**LOE**	**Recommendations**
IIa	**B-NR**	**1. Preoperative catheter ablation or intraoperative surgical ablation of accessory pathways or AT is reasonable in patients with SVT who are undergoing surgical repair of Ebstein anomaly.[479–485]**
See Online Data Supplement 20.		The prevalence of SVT among patients with Ebstein anomaly was 33% in 1 large series, the highest noted among ACHD patients,[440] and increased with age. AT, atrial flutter, or AF develops in ≥50% of patients with Ebstein anomaly and significant tricuspid regurgitation. Right-sided accessory pathways are present in 15% to 30% of patients with Ebstein anomaly and may be multiple in up to ≥29% of those patients. Catheter ablation of accessory pathways in patients with Ebstein anomaly is associated with lower success rates than for other populations, acute success rate of 75% to 89% of procedures, with acute recurrence in 25% to 30%.[480,481] In a series of 83 adults undergoing arrhythmia surgery at the time of surgical repair of Ebstein anomaly, accessory pathways were present in 32%, and atrial flutter/fibrillation was noted in 54%,[483] with no recurrence of AP after surgery. Successful surgical ablation of accessory pathways has been reported in 92% to 100%.[483,484] In a series of patients undergoing right atrial maze procedures or isthmus ablation for atrial flutter/fibrillation in association with repair of Ebstein anomaly, freedom from recurrent flutter/fibrillation was 75% during 34 months of follow-up.[483] In a comparison study of combined operative arrhythmia surgery with repair, versus catheter ablation followed by surgical repair, the combined approach was effective in 94% of cases versus 76% of patients treated with the catheter approach alone.[484] In a series of patients undergoing repair of Ebstein anomaly, patients who underwent preoperative EP study with intraoperative ablation of arrhythmia substrate had lower risk of SCD than patients without arrhythmia intervention.[479] In patients with Ebstein anomaly undergoing planned surgical intervention, an integrated approach of arrhythmia intervention has been demonstrated to be safe and effective.
IIa	**B-NR**	**2. Oral beta blockers or sotalol therapy can be useful for prevention of recurrent AT or atrial flutter in ACHD patients.[218,447,486]**
See Online Data Supplement 20.		Beta blockers may decrease catecholamine-related triggers and provide AV nodal blockade during recurrent atrial arrhythmias. One study of adults with transposition of the great arteries and prior atrial switch repairs with implanted defibrillators demonstrated SVT preceding VT in 50% of patients; use of beta-blocker medications in this population was associated with decreased incidence of appropriate defibrillator shocks.[486] Observational studies on the use of sotalol in ACHD patients report freedom from recurrent AT in 41% to 46% of patients during short-term follow-up.[218,487,488] Use of either medication in the setting of significant sinus node dysfunction may exacerbate bradycardia and requires careful monitoring. Initiation of sotalol in this population is recommended during inpatient monitoring for proarrhythmia for 48 to 72 hours.
IIa	**B-NR**	**3. Catheter ablation is reasonable for treatment of recurrent symptomatic SVT in ACHD patients.[330,449,452,454,457,458,489–492]**
See Online Data Supplement 20.		Multiple observational and multicenter studies have demonstrated acute success rates between 65% and 100% for treatment of SVT associated with ACHD.[452,454,455,457,489,493,494] Acute success rates vary by tachycardia mechanism and type of congenital heart disease and repair. Success rates are highest for SVT associated with AVNRT (>80%),[490,494] accessory pathways (75% to 89% among patients with Ebstein anomaly),[480] or focal AT (80% to 100%).[492,494,495] Success rates for catheter ablation of AT or atrial flutter are significantly lower than that reported in patients without ACHD, with overall 65% to 82% acute success in mixed anatomic substrates,[452,454,455,457,493,494] but success rates have improved with advanced mapping and ablation techniques.[494] Acute success rates in ablation of AT or atrial flutter varies significantly by type of congenital heart disease, ranging from 93% to 100% in patients with repaired ASD,[330,449,458] 85% to 100% in atrial baffle repairs of transposition of the great arteries,[490,492] and 54% to 75% of univentricular heart or Fontan repairs.[457,490,495] Older age and presence of univentricular heart physiology was associated with decreased acute success rates in a series of 193 ablations of AT.[457] Recurrent AT has been reported in 20% to 85% of patients during short-term follow-up, with development of AF reported in 7% to 30% of patients.[330,449,454,493] Recurrent SVT may represent the same or a new reentrant circuit, and arrhythmia burden may be decreased by ablation procedures. Ablation procedures in patients with complex congenital heart disease are best performed in centers with advanced mapping techniques and expertise in congenital heart disease.[25,29,496]
IIa	**B-NR**	**4. Surgical ablation of AT or atrial flutter can be effective in ACHD patients undergoing planned surgical repair.[497–508]**
See Online Data Supplement 20.		In patients with symptomatic SVT undergoing planned surgical repairs of structural heart disease or ischemic heart disease, observation studies report that arrhythmia surgery can be integrated into the operation with high efficacy and without increased surgical morbidity.[497–500] In populations including those with tetralogy of Fallot/double-outlet right ventricle, tricuspid valve repairs, and ASD, rates of freedom from recurrent AT or atrial flutter have been reported as 73% to 93% without antiarrhythmic medications during medium-term follow-up of 2.5 to 10 years. Catheter ablation may be attempted in specialized centersbefore surgical Fontan repair. There are no RCTs comparing efficacy of catheter versus surgical ablation of AT or atrial flutter in patients with prior Fontan repairs. The incidence of AT or atrial flutter in patients with prior Fontan repairs approaches 60% and increases with advancing age. Catheter ablation success rates in this subset of patients are lower than for other lesions,[457] with acute success in 54% to 75%, and with recurrent AT in 27% to 50% of patients within 2 to 4 years[490,495]; death or transplantation was reported in 27% during follow-up. Several observational studies of surgical resection and ablation for AT or atrial flutter associated with Fontan conversion reported rates of freedom from AT of 12% to 16% during follow-up extending to 8 years[501–505]; death or transplantation was reported in 6% to 14% during follow-up. Performance of a modified right atrial maze procedure versus CTI ablation was associated with lower recurrence rates.[501] Alternatively, surgical repairs without arrhythmia intervention are associated with high recurrence rates of AT. Arrhythmia surgery can be combined with hemodynamic surgical revision with low mortality rate and improved medium-term freedom from arrhythmia recurrence and deathin this population.
IIb	**B-NR**	**1. Atrial pacing may be reasonable to decrease recurrences of AT or atrial flutter in ACHD patients and sinus node dysfunction.[472,509,510]**
See Online Data Supplement 20.		Small observational studies support the use of atrial pacing in patients with recurrent AT or atrial flutter to reduce the frequency of tachycardia episodes. The pacing rate is programmed to maintain atrial pacing for the majority of the time in patients with sinus node dysfunction, significantly reducing tachycardia recurrences to 11% in 1 study.[509,510] In addition, the implanted pacemaker can be used for termination of recurrent episodes of AT or atrial flutter.[472]

Recommendations for Ongoing Management of SVT in ACHD Patients (Continued)		
COR	LOE	Recommendations
IIb	B-NR	**2. Oral dofetilide may be reasonable for prevention of recurrent AT or atrial flutter in ACHD patients.[447,474,487,488]**
See Online Data Supplement 20.		Two small observational studies on the use of oral dofetilide for ACHD patients report a high rate of acute conversion of AT or atrial flutter, with longer-term efficacy of the drug (defined by either complete suppression or partial improvement of symptoms) ranging from 70% to 85%. The benefit was tempered by an association with torsades de pointes in 10%.[471,484] Although many patients continued to experience recurrence, these episodes were better tolerated and were of limited duration.[471,484] Because of the potential risk of proarrhythmia, dofetilide is usually a second-line medication after failure of beta blockers and sotalol. Initiation of oral dofetilide is recommended during 72-hour inpatient monitoring.
IIb	B-NR	**3. Amiodarone may be reasonable for prevention of recurrent AT or atrial flutter in ACHD patients for whom other medications and catheter ablation are ineffective or contraindicated.[447]**
See Online Data Supplement 20.		An observational study reported efficacy of amiodarone in maintaining sinus rhythm, although side effects were noted frequently, including thyroid disorders or AV block.[447] The risk of significant side effects increases with chronic use and with higher dosages; using the minimal effective chronic dosage is recommended. Observational studies reported thyroid disorders in 13% to 36% of ACHD patients receiving amiodarone; risk factors for thyrotoxicosis include female sex, cyanotic heart disease, low body mass index, prior Fontan procedure, or dosages >200 mg daily.[511,512] Amiodarone is recommended for short-term use or for patients for whom alternative therapy is not an option for prevention of recurrent AT.
III: Harm	B-NR	**1. Flecainide should not be administered for treatment of SVT in ACHD patients and significant ventricular dysfunction.[419]**
See Online Data Supplement 20.		There are no RCTs on the use of flecainide in ACHD patients and ventricular dysfunction. One retrospective study collected data on 579 young patients, 369 of whom received flecainide for the treatment of SVT. Efficacy for the treatment of SVT was 71%. Among 12 patients with cardiac arrest while receiving flecainide for SVT, 8 had congenital heart disease, and 7 of 8 had either mild to moderate ventricular dysfunction or systemic right- or single-ventricle anatomy. The risk associated with flecainide treatment of SVT associated with congenital heart disease appears to be highest among patients with complex heart disease or ventricular dysfunction.

9.3. Pregnancy

Pregnancy may confer an increased susceptibility to a variety of arrhythmias, even in the absence of underlying heart disease.[513] Pregnancy is also associated with an increased risk of arrhythmia exacerbation, such as more frequent and refractory tachycardia episodes, in patients with a pre-existing arrhythmic substrate.[514] An important consideration is that adverse maternal and fetal outcomes have been reported as a result of SVT in pregnancy.[515] Although there is potential toxicity to the fetus with certain pharmacological and nonpharmacological therapies, safe options exist to allow for treating most cases of maternal SVT effectively.

The literature on therapeutic options for the management of arrhythmias in pregnancy is generally limited to single case reports or small series and favors the use of older antiarrhythmic agents because of more abundant reports on the safe use of these drugs. Experience with use of drugs in pregnancy also comes from treating a variety of maternal and fetal conditions, not maternal SVT alone. Although all medications have potential side effects to both the mother and the fetus at any stage of pregnancy, if possible, drugs should be avoided in the first trimester, when risk of congenital malformations is greatest. The lowest recommended dose should be used initially, accompanied by regular monitoring of clinical response.

9.3.1. Acute Treatment: Recommendations

Recommendations for Acute Treatment of SVT in Pregnant Patients		
COR	LOE	Recommendations
I	C-LD	**1. Vagal maneuvers are recommended for acute treatment in pregnant patients with SVT.[235,516]**
See Online Data Supplement 20.		For acute conversion of SVT, vagal maneuvers, including Valsalva and carotid sinus massage, can be performed quickly and should be the first-line intervention to terminate SVT. These maneuvers should be performed with the patient in the supine position. Vagal maneuvers typically will not be effective if the rhythm does not involve the AV node as a requisite component of a reentrant circuit. There is no "gold standard" for proper Valsalva maneuver technique, but in general, the patient raises intrathoracic pressure by bearing down against a closed glottis for 10 to 30 seconds, equivalent to at least 30 mm Hg to 40 mm Hg.[82,84] Carotid massage is performed after absence of bruit has been confirmed by auscultation, by applying steady pressure over the right or left carotid sinus for 5 to 10 seconds.[83,84] Another vagal maneuver based on the classic diving reflex consists of applying an ice-cold, wet towel to the face[85]; in a laboratory setting, facial immersion in water at 10°C (50°F) has proved effective in terminating tachycardia, as well.[86] One study involving 148 nonpregnant patients with SVT demonstrated that Valsalva was more successful than carotid sinus massage, and switching from 1 technique to the other resulted in an overall success rate of 27.7%.[82] The practice of applying pressure to the eyeball is potentially dangerous and has been abandoned.
I	C-LD	**2. Adenosine is recommended for acute treatment in pregnant patients with SVT.[516]**
See Online Data Supplement 20.		When vagal maneuvers fail to terminate SVT, adenosine is a first-line drug option for pregnant patients.[516] Adverse effects to the fetus would not be expected, given that it is unlikely the drug will reach the fetal circulation because of adenosine's short half-life.[517] Maternal side effects, such as chest discomfort and flushing, are usually transient. The initial dose for adenosine is 6-mg rapid bolus IV. If this is ineffective, up to 2 subsequent infusions of 12 mg may be administered. Higher doses of adenosine may be necessary in some cases; safe administration of up to 24 mg has been reported.[518]
I	C-LD	**3. Synchronized cardioversion is recommended for acute treatment in pregnant patients with hemodynamically unstable SVT when pharmacological therapy is ineffective or contraindicated.[516]**
See Online Data Supplement 20.		Synchronized cardioversion has been reported to be safe at all stages of pregnancy. The electrode pads should be applied such that the energy source and trajectory are directed away from the uterus.[519] Fetal monitoring during cardioversion (if time allows) and during the immediate postcardioversion period is recommended.[519] Energy dosing for pregnant patients should be the same as in nonpregnant patients.[520]

Recommendations for Acute Treatment of SVT in Pregnant Patients (Continued)		
COR	LOE	Recommendations
IIa	C-LD	**1. Intravenous metoprolol or propranolol is reasonable for acute treatment in pregnant patients with SVT when adenosine is ineffective or contraindicated.[516]**
See Online Data Supplement 20.		Beta-adrenergic–blocking drugs are considered the first-line option for a variety of arrhythmias in pregnancy because there are extensive reports on their safe use from treating a variety of maternal conditions over many decades. A slow infusion would be less likely to cause hypotension.[516,517,521]
IIb	C-LD	**1. Intravenous verapamil may be reasonable for acute treatment in pregnant patients with SVT when adenosine and beta blockers are ineffective or contraindicated.[516]**
See Online Data Supplement 20.		Intravenous verapamil has been used effectively for the acute treatment of SVT in pregnant women; however, there is a higher risk of maternal hypotension with intravenous verapamil than with adenosine.[516] Reports on diltiazem use for acute SVT termination in pregnancy are more limited than for verapamil, yet similar effects are expected.[517]
IIb	C-LD	**2. Intravenous procainamide may be reasonable for acute treatment in pregnant patients with SVT.[522]**
See Online Data Supplement 20.		Intravenous procainamide has been used safely to treat a variety of maternal and fetal supraventricular and ventricular arrhythmias and can be effective when used for acute conversion.[517,522] Procainamide is generally best avoided as long-term therapy because it can cause a lupus-like syndrome, unless other options are contraindicated or ineffective.
IIb	C-LD	**3. Intravenous amiodarone may be considered for acute treatment in pregnant patients with potentially life-threatening SVT when other therapies are ineffective or contraindicated.[517,523]**
See Online Data Supplement 20.		Although intravenous amiodarone has been administered safely during pregnancy, multiple adverse effects to the fetus have also been reported.[523] An important concern is the possibility of fetal hypothyroidism, reported in approximately 17% of cases.[517,523] With an intravenous infusion for short-term use, side effects would be less of a concern, given that most toxicities are related to cumulative drug dose.

9.3.2. Ongoing Management: Recommendations

Recommendations for Ongoing Management of SVT in Pregnant Patients		
COR	LOE	Recommendations
IIa	C-LD	**1. The following drugs, alone or in combination, can be effective for ongoing management in pregnant patients with highly symptomatic SVT:** **a. Digoxin[437,517]** **b. Flecainide[437,517]** **c. Metoprolol[517,521]** **d. Propafenone[517]** **e. Propranolol[517,521]** **f. Sotalol[437,517]** **g. Verapamil[517]**
See Online Data Supplement 20.		If possible, antiarrhythmic drugs should be avoided in the first trimester, when risk of congenital malformations is greatest. Almost no reports exist on the use of newer antiarrhythmic drugs (such as dofetilide) during pregnancy, yet their use may be justified if the benefits outweigh the risk. The lowest recommended dose should be used initially, with dose adjustments made according to clinical response. For oral chronic prophylaxis, drugs such as metoprolol, propranolol, and digoxin are considered safe first-line agents because of their longer record of safety, yet caution is advised, given that therapy with beta blockers has been associated with intrauterine growth retardation.[517,524] This effect appears to be especially pronounced with atenolol, especially in mothers who received atenolol earlier in gestational age and who were treated for longer duration.[525] Flecainide and propafenone have been used effectively to treat a variety of maternal and fetal tachycardias, yet they are reserved for patients who have no underlying structural heart disease or ischemic heart disease.[113]
IIb	C-LD	**1. Catheter ablation may be reasonable in pregnant patients with highly symptomatic, recurrent, drug-refractory SVT with efforts toward minimizing radiation exposure.[526,527]**
See Online Data Supplement 20.		The risk of radiation exposure to the fetus is a concern with catheter ablation in pregnant patients, because high-dose ionizing radiation has been linked to excess malignancy and congenital malformations.[528] However, the fetal radiation dose for most common cardiovascular interventions is not likely to exceed the 50-mGy negligible-risk threshold dose for excess malignancy.[529] One study that used phantoms to simulate pregnancy estimated a low lifetime risk of malignancies from radiation exposure to the conceptus during a typical ablation procedure.[527] Furthermore, with current technologies such as electroanatomic mapping systems, catheter ablation procedures using minimal or even zero fluoroscopy have been described in pregnant women.[526] Thus, if a catheter ablation procedure is required in a pregnant woman, radiation-reduction technologies should be used, and the procedure should be avoided in the first trimester when the teratogenic risk is greatest.[528] Of note, shielding the fetus by covering the mother with a lead apron does not eliminate radiation to the fetus because most of the radiation to the fetus comes from scatter.
IIb	C-LD	**2. Oral amiodarone may be considered for ongoing management in pregnant patients when treatment of highly symptomatic, recurrent SVT is required and other therapies are ineffective or contraindicated.[517,523]**
See Online Data Supplement 20.		Although oral amiodarone has been administered safely during pregnancy, multiple adverse effects to the fetus have also been reported.[523] An important concern is the possibility of fetal hypothyroidism, reported in approximately 17% of cases.[517,523] Therefore, fetal monitoring for development of goiter with ultrasound and for signs of clinical hypothyroidism is advised. In addition, amiodarone has the potential for direct neurotoxicity, which may lead to neurodevelopmental abnormalities.[523]

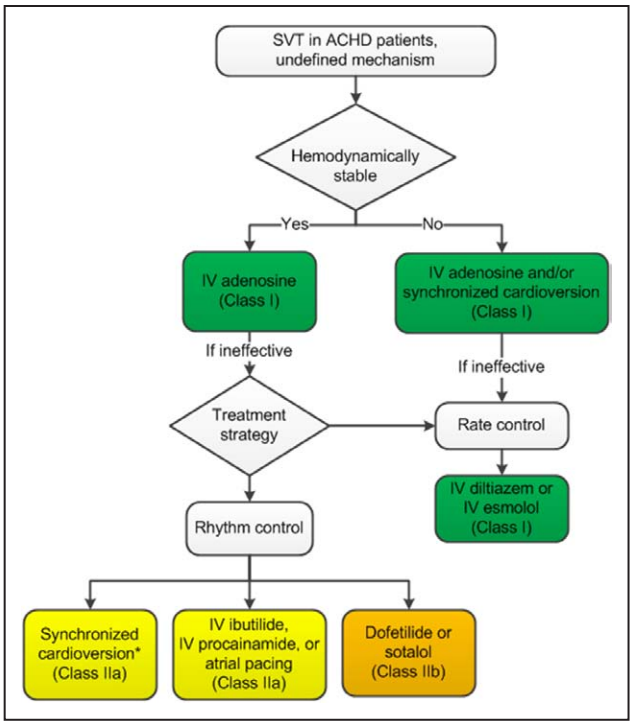

Figure 22. Acute treatment of SVT in ACHD patients. Colors correspond to Class of Recommendation in Table 1; drugs listed alphabetically. *For rhythms that break or recur spontaneously, synchronized cardioversion is not appropriate. ACHD indicates adult congenital heart disease; IV, intravenous; and SVT, supraventricular tachycardia.

9.4. SVT in Older Populations

9.4.1. Acute Treatment and Ongoing Management: Recommendation

The natural history of SVT is steadily changing because most patients with SVT undergo ablation at a younger age, but in general, the relative proportion of AT is higher in older populations, and AVNRT is more prevalent than AVRT among patients undergoing ablation.[49] Atypical atrial flutter and macroreentrant AT are on the rise as consequences of increasing AF ablation in this patient population, yet there are limited outcome data from RCTs for this segment of the population. Therapeutic decisions should be balanced between the overall risks and benefits of the invasive nature of ablation versus long-term commitment to pharmacological therapy.

10. Quality-of-Life Considerations

Patients with SVT may experience recurring symptoms that negatively impact their quality of life. Episodes of tachycardia can cause lightheadedness and syncope, which can become an obstacle to the performance of usual activities of daily living (eg, driving).[72] However, there are minimal data on the effect of treatment on the quality of life for patients with SVT. In 1 study that evaluated patients with SVT who underwent ablation or received medical therapy, questionnaires such as the 36-Item Short-Form Health Survey revealed improved quality-of-life scores in several categories, including physical role functioning (perceived disability from physical limitations), general health perceptions (perceived physical and mental health), and emotional role functioning (perceived disability from emotional limitations).[540] These improvements, measured at 1 to 5 years of follow-up, were greater in patients who underwent ablation than in those treated with medical therapy. Other literature, using domains from the 36-Item Short-Form Health Survey[541–543] and other quality- of-life questionnaires,[544–546] suggests that quality of life is improved after ablation for PSVT. However, these data carry important limitations, particularly a lack of an appropriate control group, small sample sizes, and referral bias. Furthermore, patients affected by PSVT carry different experiences. Therefore, firm conclusions cannot be drawn about the effect on quality of life provided by medical or ablation therapy, and no recommendations are provided.

See Online Data Supplement 22 *for additional data on quality-of-life considerations.*

11. Cost-Effectiveness

Given the rising costs of health care, there is a growing enthusiasm for incorporating economic appraisals of available therapies and resources into guidelines. The "2014 ACC/AHA Statement on Cost/Value Methodology in Clinical Practice Guidelines and Performance Measures"[6] called for development of Level of Value categories to accompany COR and LOE in future guidelines. Although basing recommendations on a cost-effectiveness approach to therapy is an important goal for the current and future healthcare economy, it also poses considerable challenges. For example, the cost of therapy, available technology, and practice patterns are highly dynamic, and there may

Recommendations for Acute Treatment and Ongoing Management of SVT in Older Populations		
COR	**LOE**	**Recommendation**
I	**B-NR**	**1. Diagnostic and therapeutic approaches to SVT should be individualized in patients more than 75 years of age to incorporate age, comorbid illness, physical and cognitive functions, patient preferences, and severity of symptoms.**[66,67,530–538]
See Online Data Supplement 20.		Data have consistently demonstrated that ablation is highly successful (>95%) in selected older patients.[66,67,531–536] Outcomes from 48 medical centers in Germany were reported among 3234 consecutive patients undergoing AVNRT ablation from 2007 to 2010; of the total, 259 patients (8%) were >75 years of age.[537] Acute success was achieved in 98.5% of the older patient group, similar to the 2 younger patient groups (98.7% for the group <50 years of age; 98.8% for the group 50 to 75 years of age). In this study, complication rates were low; hemodynamically stable pericardial effusion was observed in 2 of 259 patients (0.8%), and no pacemakers were needed in the older patient group. Similarly, additional studies from older patient cohorts have consistently shown that older patients have more comorbid medical conditions, have a higher incidence of structural heart disease or ischemic heart disease, and have more severe symptoms associated with SVT.[530,538,539] A few studies have shown that complications may be slightly higher in older patients than in younger patients, although the overall complications are low and acceptable.[530,538,539] These ablation outcome data should be balanced with the risks and benefits of pharmacological therapy when therapeutic options are reviewed with older patients.

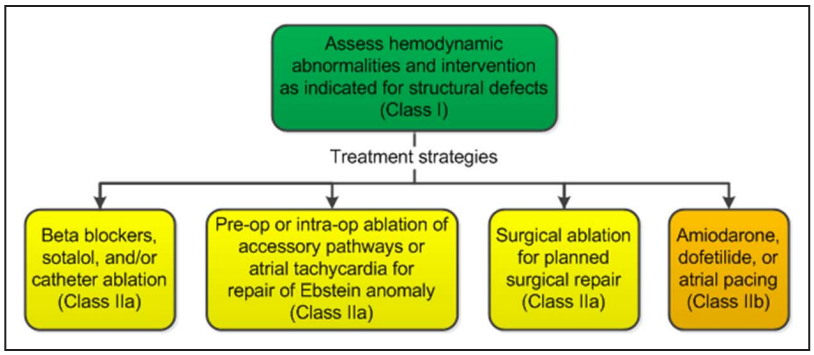

Figure 23. Ongoing management of SVT in ACHD patients. Colors correspond to Class of Recommendation in Table 1; drugs listed alphabetically. ACHD indicates adult congenital heart disease; intra-op, intraoperative; pre-op, preoperative; and SVT, supraventricular tachycardia.

be some cost associated with unintended harm or complications that result from any intervention. Furthermore, the approach toward evaluating the burden of cost in the literature is based on varied perspectives (eg, individual, third party, stakeholder, societal).

The small body of literature evaluating cost-effectiveness strategies in PSVT has traditionally centered on an evaluation of medical therapy versus catheter ablation. A rigorous cost-effectiveness Markov model was conducted in 2000 to compare radiofrequency ablation to medical management with generic metoprolol from the societal perspective.[105] The estimated population consisted of patients with AVNRT (approximately 65%) and AVRT. On the basis of this simulation, the authors concluded that, for symptomatic patients with monthly episodes of PSVT, radiofrequency ablation was the more effective and less expensive strategy when compared with medical therapy. An observational cohort study of patients with atrial flutter supported early ablation to significantly reduce hospital-based healthcare utilization and the risk of AF.[547]

These studies, along with other older literature, favor catheter ablation over medical therapy as the more cost-effective approach to treating PSVT and atrial flutter. However, the results of these studies were based on cost data and practice patterns that do not apply to the current environment and practice. Therefore, no recommendations are provided.

See Online Data Supplement 23 *for additional data on cost-effectiveness.*

12. Shared Decision Making

It is important that the patient be included in clinical decision-making processes, with consideration of his/her preferences and goals for therapy, as well as his/her unique physical, psychological, and social situation. In selected cases, personalized, self-directed interventions can be developed in partnership with the patient, such as vagal maneuvers and "pill-in-the-pocket" drug therapy.

Shared decision making is especially important for patients with SVT. As seen in this guideline, SVT treatment can be nuanced and requires expert knowledge of EP processes and treatment options. Treatment options are highly specific to the exact type of arrhythmia and can depend on certain characteristics of a particular arrhythmia (eg, whether there is pre-excitation). The various choices for therapy, including drugs, cardioversion, invasive treatment, or a combination thereof, can be confusing to the patient, so a detailed explanation of the benefits and risks must be included in the conversation.

Patients are encouraged to ask questions with time allotted for caregivers to respond. Providing a relaxed atmosphere, anticipating patient concerns, and encouraging patients to keep a notebook with questions could facilitate productive conversations.

It is also important that clinicians use lay terminology to explain treatment options to their patients. This involves a clear explanation of the risks and benefits of each recommendation, including how other comorbidities may impact each treatment option. Discussions with other physicians and healthcare providers caring for the patient will provide the broadest picture available. A full discussion about decisions for subsequent care and any further instructions is important to reinforce these issues before the patient leaves the healthcare setting. It is the responsibility of the physician and healthcare team to provide the patient with the best possible understanding of all management options in terms of risks, benefits, and potential effects on quality of life.

13. Evidence Gaps and Future Research Needs

SVTs, even with the exclusion of AF, are among the most common arrhythmias that require medical intervention. The decade before the publication of the "2003 ACC/AHA/ESC Guidelines for the Management of Patients With Supraventricular Arrhythmias"[11] was characterized by major shifts in understanding of the mechanism for SVT, as well as a sea change in management (because of catheter ablation). Since the early 2000s, there have been many iterative but important advances in pharmacological and invasive management for SVT. Catheter ablation is even better established, with a high degree of success and low complication rate, especially for the most common types of SVT, such as AVNRT and AVRT. Drug options, on the other hand, are relatively unchanged since publication of the 2003 guideline, perhaps relating to ongoing concern about potential adverse side effects of antiarrhythmic agents.

Areas of uncertainty remain, including interventions for which advanced technology is less important. For example, vagal maneuvers are recommended in many circumstances as first-line intervention in patients with SVT, but they are often ineffective. Furthermore, there is great variation in the way these maneuvers are administered. Therefore, research on the best technique of vagal maneuvers, with dissemination of the findings, is necessary. Clinical trials on

antiarrhythmic drugs for SVT have been limited, and data are often extrapolated from studies that primarily focused on management of patients with AF. The efficacy of a variety of drugs is likely to differ according to the tachycardia mechanism, and therefore differentiating the best drug for each individual arrhythmia is necessary; for example, the efficacy of class III agents might be markedly different in patients with AF than in patients with atrial flutter. Limited data exist on the optimal management of less common types of SVTs, such as junctional tachycardia and multifocal AT. Therefore, in view of significant gaps that remain with regard to optimal management of patients with SVT, we must consider the role of electronic medical records, registries, and national datasets to better acquire observational data when trials are not available or feasible. Multicenter registry studies would allow for expansion of our knowledge on the best pharmacological and nonpharmacological approaches to treat these arrhythmias. In collaboration with national societies, the National Institutes of Health, and the US Food and Drug Administration, registries could be developed across selected centers to gather important information on safety and long-term outcomes where data are lacking (just as such registries are being developed for AF ablation). Mandatory postmarket surveillance data collection on new drugs for SVT could also be considered by the US Food and Drug Administration as a condition for drug approval.

The mechanism and primary etiology of IST remains to be defined—advances here would provide a first step on finding better therapies for this disorder. It should be noted that medical advances have resulted in an increase in the number of patients with SVT in specific populations, such as in patients after ablation (especially AF), ACHD patients, and patients of advanced age. As the numbers of these often-complicated patients grow, opportunities arise to perform clinical research to guide future recommendations.

New pharmacological therapies are needed, especially for SVT in patients for whom ablation is not an option or has been unsuccessful. Newer drugs that selectively target atrial channels currently under investigation for patients with AF should be investigated for management of AT. Both mapping and ablation techniques need to be further investigated to maximize the likelihood of successful ablation with minimal risk. In the outpatient setting, the added value of new personal monitoring and implantable devices needs to be assessed, and studies of the impact of shared decision making with patients on outcomes are needed for personal monitoring innovations. Finally, we encourage investigation of quality-of-life improvement strategies, in addition to cost-effectiveness studies, for the management of SVT.

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KEY WORDS: AHA Scientific Statements ■ tachycardia, supraventricular ■ tachycardia, atrioventricular nodal reentry ■ Wolff-Parkinson-White syndrome ■ catheter ablation ■ tachycardia, ectopic atrial ■ tachycardia, ectopic junctional ■ atrial flutter ■ anti-arrhythmia agents ■ accessory atrioventricular bundle ■ Valsalva maneuver ■ tachycardia, reciprocating ■ electric countershock ■ heart defects, congenital ■ death, sudden ■ electrophysiologic techniques, cardiac ■ sinus tachycardia

Appendix 1. Author Relationships With Industry and Other Entities (Relevant)—2015 ACC/AHA/HRS Guideline for the Management of Adult Patients With Supraventricular Tachycardia (April 2014)

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
Richard L. Page, Chair	University of Wisconsin School of Medicine and Public Health—Chair, Department of Medicine	None	None	None	None	None	None	None
José A. Joglar, Vice Chair	University of Texas Southwestern Medical Center—Professor of Internal Medicine; Program Director, Clinical Cardiac Electrophysiology	None	None	None	None	None	None	None
Sana M. Al-Khatib	Duke Clinical Research Institute—Associate Professor of Medicine	None	None	None	None	None	None	None
Mary A. Caldwell	University of California San Francisco—Assistant Professor (Retired)	None	None	None	None	None	None	None
Hugh Calkins	Johns Hopkins Hospital—Professor of Medicine, Director of Electrophysiology	• Atricure • Boehringer Ingelheim • Daiichi-Sankyo	None	None	• St. Jude Medical†	None	None	All Sections except 2.4, 5.2, 6.1.2, 9.3.2, and 9.4.
Jamie B. Conti	University of Florida—Professor of Medicine, Chief of Cardiovascular Medicine	None	None	None	• Medtronic	• Boston Scientific‡ • Medtronic‡ • St. Jude Medical‡	None	All Sections except 2.4, 6.1.2, 9.3.2, and 9.4.
Barbara J. Deal	Feinberg School of Medicine, Northwestern University—Professor of Pediatrics; Ann & Robert H. Lurie Children's Hospital of Chicago—Division Head, Cardiology	None	None	None	None	None	None	None
N.A. Mark Estes III	Tufts University School of Medicine—Professor of Medicine	• Boston Scientific† • Medtronic • St. Jude Medical	None	None	• Boston Scientific	• Boston Scientific† • Medtronic† • St. Jude Medical†	None	All Sections except 2.4, 5.2, 6.1.2, 9.3.2, and 9.4.
Michael E. Field	University of Wisconsin School of Medicine and Public Health—Assistant Professor of Medicine, Director of Cardiac Arrhythmia Service	None	None	None	None	None	None	None
Zachary D. Goldberger	University of Washington School of Medicine—Assistant Professor of Medicine	None	None	None	None	None	None	None
Stephen C. Hammill	Mayo Clinic—Professor Emeritus of Medicine	None	None	None	None	None	None	None
Julia H. Indik	University of Arizona—Associate Professor of Medicine	None	None	None	None	None	None	None
Bruce D. Lindsay	Cleveland Clinic Foundation—Professor of Cardiology	• Biosense Webster • Boston Scientific • CardioInsight • Medtronic	None	None	None	• Boston Scientific† • Medtronic† • St. Jude Medical†	None	All Sections except 2.4, 5.2, 6.1.2, 9.3.2, and 9.4.
Brian Olshansky	University of Iowa Hospitals—Professor Emeritus of Medicine; Mercy Hospital Mason City—Electrophysiologist	• BioControl • Biotronik • Boehringer-Ingelheim • Boston Scientific-Guidant • Daiichi-Sankyo • Medtronic† • Sanofi-aventis	None	None	• Amarin (DSMB) • Boston Scientific (DSMB) • Sanofi-aventis (DSMB)	• Boston Scientific	None	All Sections except 2.4 and 9.4.
Andrea M. Russo	Cooper Medical School of Rowan University—Professor of Medicine; Cooper University Hospital—Director, Electrophysiology and Arrhythmia Services	• Biotronik • Boston Scientific • Medtronic • St. Jude Medical	None	None	• Medtronic†	• Biotronik‡ • Boston Scientific†	None	All Sections except 2.4, 5.2, 6.1.2, 9.3.2, and 9.4.

(*Continued*)

Appendix 1. Continued

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
Win-Kuang Shen	Mayo Clinic Arizona—Professor of Medicine; Chair, Division of Cardiovascular Diseases	None	None	None	None	None	None	None
Cynthia M. Tracy	George Washington University—Professor of Medicine; Associate Director Division of Cardiology, Director of Cardiac Services	None	None	None	None	None	None	None

This table represents the relationships of committee members with industry and other entities that were determined to be relevant to this document. These relationships were reviewed and updated in conjunction with all meetings and/or conference calls of the writing committee during the document development process. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or ownership of ≥$5,000 of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted.

According to the ACC/AHA, a person has a relevant relationship IF: a) the *relationship* or *interest* relates to the same or similar subject matter, intellectual property or asset, topic, or issue addressed in the *document*; or b) the *company/entity* (with whom the relationship exists) makes a drug, drug class, or device addressed in the *document*, or makes a competing drug or device addressed in the *document*; or c) the *person or a member of the person's household*, has a reasonable potential for financial, professional or other personal gain or loss as a result of the issues/content addressed in the document.

*Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry and other entities may apply.

†Significant relationship.

‡No financial benefit.

ACC indicates American College of Cardiology; AHA, American Heart Association; DSMB, data safety monitoring board; and HRS, Heart Rhythm Society.

Appendix 2. Reviewer Relationships With Industry and Other Entities (Relevant)—2015 ACC/AHA/HRS Guideline for the Management of Adult Patients With Supraventricular Tachycardia (March 2015)

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Eugene H. Chung	Official Reviewer—HRS	University of North Carolina School of Medicine—Associate Professor of Medicine	None	None	None	None	• Zoll Medical†	None
Timm L. Dickfeld	Official Reviewer—HRS	University of Maryland School of Medicine—Associate Professor of Medicine; Baltimore Veterans Affairs Medical Center—Director, Electrophysiology	• Biosense Webster	None	None	• Biosense Webster* • General Electric*	None	None
Samuel S. Gidding	Official Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	Nemours Cardiac Center—Division Chief of Cardiology; Jefferson Medical College—Professor of Pediatrics	None	None	None	None	None	None
Richard J. Kovacs	Official Reviewer—ACC Board of Trustees	Krannert Institute of Cardiology—Professor of Clinical Medicine	• Biomedical Systems*	None	None	• Siemens†	• AstraZeneca (DSMB) • MED Institute* • Eli Lilly (DSMB)* • Teva Pharmaceuticals	None
Byron K. Lee	Official Reviewer—AHA	University of California San Francisco—Professor of Medicine	• Biotronik • Boston Scientific • St. Jude Medical	None	None	• Zoll Medical*	• CarioNet*	• Defendant, Boehringer Ingelheim, 2013†

(*Continued*)

Appendix 2. Continued

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Gregory F. Michaud	Official Reviewer—AHA	Harvard Medical School—Assistant Professor	• Boston Scientific • Medtronic • St. Jude Medical	None	None	• Biosense Webster* • Boston Scientific* • St. Jude Medical*	None	None
Simone Musco	Official Reviewer—ACC Board of Governors	The International Heart Institute of Montana Foundation—Cardiology Research Investigator	None	• Bristol-Myers Squibb • Sanofi-aventis	None	None	None	None
Mohan N. Viswanathan	Official Reviewer—AHA	University of Washington School of Medicine—Assistant Professor of Medicine	• Biosense Webster • Siemens† • St. Jude Medical	None	None	• Medtronic*	None	None
Seshadri Balaji	Content Reviewer	Oregon Health and Science University—Professor of Pediatrics and Pediatric Cardiology, Director of Pacing and Electrophysiology	None	None	None	• Medtronic*	None	None
Nancy C. Berg	Content Reviewer—ACC Electrophysiology Section	Allina Health System	None	None	None	None	None	None
Noel G. Boyle	Content Reviewer—ACC Electrophysiology Section	University of California Los Angeles—Clinical Professor of Medicine	None	None	None	None	None	None
A. John Camm	Content Reviewer	St. George's University of London—Professor of Clinical Cardiology	• Bayer* • Biotronik • Boehringer Ingelheim • Boston Scientific • ChanRx • Daiichi-Sankyo • Medtronic • Menarini • Mitsubishi • Novartis† • Richmond Pharmacology* • Sanofi-aventis • Servier Pharmaceuticals* • St. Jude Medical • Takeda Pharmaceuticals • Xention	• Pfizer	None	None	None	None
Robert M. Campbell	Content Reviewer—ACC Adult Congenital and Pediatric Cardiology Section	Sibley Heart Center Cardiology—Director, Chief of Cardiac Services; Emory University School of Medicine—Division Director of Pediatric Cardiology, Professor of Pediatrics	None	None	None	None	None	None
Susan P. Etheridge	Content Reviewer—ACC Adult Congenital and Pediatric Cardiology Section	University of Utah—Training Program Director	None	None	None	None	None	None
Paul A. Friedman	Content Reviewer	Mayo Clinic—Professor of Medicine; Cardiovascular Implantable Device Laboratory—Director	• NeoChord	None	None	• Biotronik† • Medtronic • St. Jude Medical	• Preventice • Sorin*	None

(*Continued*)

Appendix 2. Continued

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Bulent Gorenek	Content Reviewer—ACC Electrophysiology Section	Eskisehir Osmangazi University—Professor and Vice Director, Cardiology Department	None	None	None	None	None	None
Jonathan L. Halperin	Content Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	Mt. Sinai Medical—Professor of Medicine	• AstraZeneca • Bayer Healthcare • Biotronik† • Boehringer Ingelheim† • Boston Scientific • Daiichi-Sankyo • Johnson & Johnson • Medtronic • Pfizer	None	None	None	None	None
Warren M. Jackman	Content Reviewer	University of Oklahoma Health Sciences Center—George Lynn Cross Research Professor Emeritus; Heart Rhythm Institute—Senior Scientific Advisor	• Biosense Webster* • Boston Scientific* • VytronUS*	• AtriCure* • Biosense Webster* • Biotronik* • Boston Scientific*	None	None	None	None
G. Neal Kay	Content Reviewer	University of Alabama—Professor Emeritus	None	None	None	None	None	None
George J. Klein	Content Reviewer	London Health Sciences Center—Chief of Cardiology	• Biotronik • Boston Scientific • Medtronic†	None	None	None	None	None
Bradley P. Knight	Content Reviewer	Northwestern University—Professor of Cardiology	• Boston Scientific • Medtronic	• Biosense Webster • Biotronik • Boston Scientific • Medtronic	None	None	None	None
John D. Kugler	Content Reviewer	University of Nebraska Medical Center—Division Chief of Pediatric Cardiology	None	None	None	None	None	None
Fred M. Kusumoto	Content Reviewer	Mayo Clinic—Professor of Medicine	None	None	None	None	None	None
Glenn N. Levine	Content Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	Baylor College of Medicine—Professor of Medicine; Director, Cardiac Care Unit	None	None	None	None	None	None
Marco A. Mercader	Content Reviewer	George Washington University—Associate Professor of Medicine	None	None	None	None	None	None
William M. Miles	Content Reviewer	University of Florida—Professor of Medicine, Silverstein Chair for Cardiovascular Education, Director of the Clinical Cardiac Electrophysiology Fellowship Program	None	None	None	None	• Medtronic (DSMB)	None
Fred Morady	Content Reviewer	University of Michigan—McKay Professor of Cardiovascular Disease	None	None	None	None	None	None
Melvin M. Scheinman	Content Reviewer	University of California San Francisco—Professor of Medicine	• Amgen • Biosense Webster • Biotronik* • Boston Scientific* • Gilead Sciences • Janssen Pharmaceuticals • Medtronic • St. Jude Medical	None	None	None	None	None

(*Continued*)

Appendix 2. Continued

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Sarah A. Spinler	Content Reviewer	University of the Sciences, Philadelphia College of Pharmacy—Professor of Clinical Pharmacy	• Portola Pharmaceuticals	None	None	None	None	None
William G. Stevenson	Content Reviewer	Brigham and Women's Hospital—Director, Clinical Cardiac Electrophysiology Program	• St. Jude Medical	None	None	None	None	None
Albert L. Waldo	Content Reviewer	University Hospitals—Associate Chief of Cardiovascular Medicine for Academic Affairs; Case Western Reserve University School of Medicine—Professor of Medicine	• AtriCure • Biosense Webster* • CardioInsight • ChanRx • Daiichi-Sankyo • Gilead Sciences • Pfizer • St. Jude Medical*	• Bristol-Myers Squibb* • Janssen Pharmaceuticals • Pfizer*	None	• Gilead Sciences*	None	None
Edward Walsh	Content Reviewer	Harvard Medical School—Professor of Pediatrics; Boston Children's Hospital—Chief, Division of Cardiac Electrophysiology	• Biosense Webster†	None	None	None	None	None
Richard C. Wu	Content Reviewer	University of Texas Southwestern Medical Center—Professor of Internal Medicine, Director of Cardiac Electrophysiology Lab	None	None	None	• Boehringer Ingelheim • Janssen Pharmaceutical • Medtronic	None	None

This table represents the relationships of reviewers with industry and other entities that were disclosed at the time of peer review and determined to be relevant to this document. It does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or ownership of ≥$5000 of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. A relationship is considered to be modest if it is less than significant under the preceding definition. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted. Names are listed in alphabetical order within each category of review.

According to the ACC/AHA, a person has a *relevant* relationship IF: a) the *relationship or interest* relates to the same or similar subject matter, intellectual property or asset, topic, or issue addressed in the *document*; or b) the *company/entity* (with whom the relationship exists) makes a drug, drug class, or device addressed in the *document*, or makes a competing drug or device addressed in the *document*; or c) the *person or a member of the person's household*, has a reasonable potential for financial, professional or other personal gain or loss as a result of the issues/content addressed in the *document*.

*Significant relationship.

†No financial benefit.

ACC indicates American College of Cardiology; AHA, American Heart Association; DSMB, data safety monitoring board; and HRS, Heart Rhythm Society.

Appendix 3. Abbreviations

ACHD	adult congenital heart disease
AF	atrial fibrillation
AT	atrial tachycardia
AV	atrioventricular
AVNRT	atrioventricular nodal reentrant tachycardia
AVRT	atrioventricular reentrant tachycardia
BP	blood pressure
CTI	cavotricuspid isthmus
ECG	electrocardiogram/electrocardiographic
ERC	Evidence Review Committee
EP	electrophysiological

Appendix 3. Continued

GWC	guideline writing committee
IST	inappropriate sinus tachycardia
MAT	multifocal atrial tachycardia
PJRT	permanent form of junctional reciprocating tachycardia
PSVT	paroxysmal supraventricular tachycardia
RCT	randomized controlled trial
SCD	sudden cardiac death
SVT	supraventricular tachycardia
VT	ventricular tachycardia
WPW	Wolff-Parkinson-White

2015 ACC/AHA/HRS Guideline for the Management of Adult Patients With Supraventricular Tachycardia: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society

Richard L. Page, José A. Joglar, Mary A. Caldwell, Hugh Calkins, Jamie B. Conti, Barbara J. Deal, N.A. Mark Estes III, Michael E. Field, Zachary D. Goldberger, Stephen C. Hammill, Julia H. Indik, Bruce D. Lindsay, Brian Olshansky, Andrea M. Russo, Win-Kuang Shen, Cynthia M. Tracy and Sana M. Al-Khatib
Evidence Review Committee Chair!

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Correction to: 2015 ACC/AHA/HRS Guideline for the Management of Adult Patients With Supraventricular Tachycardia: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society

In the article by Page et al, "2015 ACC/AHA/HRS Guideline for the Management of Adult Patients With Supraventricular Tachycardia: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society," which published online September 23, 2015, and appeared in the April 5, 2016, issue of the journal (*Circulation*. 2016;133;e506-e574. doi: 10.1161/CIR.0000000000000311), several corrections were needed.

1. On page e506, the title page, the order of footnote symbols for writing committee members' names has been amended to reflect the correct order of symbols in ACC/AHA house style.
2. On page e510, in section 2.2, right-hand column, first paragraph, the second sentence read, "The best available evidence indicates that the prevalence of SVT in the general population is 2.25 per 1,000 persons.[32]" It has been updated to read, "The best available evidence indicates that the prevalence of SVT in the general population is 2.29 per 1,000 persons.[32]"
3. On page e511, in section 2.3.1, right-hand column, third paragraph, the second sentence read, "Patients with AVNRT … when the atria contract against a closed tricuspid valve (cannon a-waves)." It has been updated to read, "Patients with AVNRT … when the right atrium contracts against a closed tricuspid valve (cannon a-waves)."
4. In the recommendation tables, a descriptive title was added to each table, relating it to the section in which it appears.
   - On page e516, in section 2.4.1, the recommendation table title reads, "Recommendations for Acute Treatment of SVT of Unknown Mechanism."
   - On page e517, in section 2.4.2, the recommendation table title reads, "Recommendations for Ongoing Management of SVT of Unknown Mechanism."
   - On page e523, in section 3.2.2, the recommendation table title now reads, "Recommendations for Ongoing Management of IST."
   - On page e526, in section 4.1.1, the recommendation table title now reads "Recommendations for Acute Treatment of Suspected Focal Atrial Tachycardia."
   - On page e527, in section 4.1.2, the recommendation table title now reads, "Recommendations for Ongoing Management of Suspected Focal Atrial Tachycardia."
   - On page e531, in section 4.2.1, the recommendation table title now reads, "Recommendations for Acute Treatment of Multifocal Atrial Tachycardia."
   - On page e531, in section 4.2.2, the recommendation table title now reads, "Recommendations for Ongoing Management of Multifocal Atrial Tachycardia."
   - On page e532, in section 5.1, the recommendation table title now reads, "Recommendations for Acute Treatment of AVNRT."

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- On page e533, in section 5.2, the recommendation table title now reads, "Recommendations for Ongoing Management of AVNRT."
- On page e535, in section 6.1.1, the recommendation table title now reads, "Recommendations for Acute Treatment of Orthodromic AVRT."
- On page e536, in section 6.1.2, the recommendation table title now reads, "Recommendations for Ongoing Management of Orthodromic AVRT."
- On page e538, in section 6.2.2, the recommendation table title now reads, "Recommendations for Management of Asymptomatic Patients With Pre-Excitation."
- On page e539, in section 6.3, the recommendation table title now reads, "Recommendations for Management of Symptomatic Patients With Manifest Accessory Pathways."
- On page e541, in section 7.3, the recommendation table title now reads, "Recommendations for Acute Treatment of Atrial Flutter."
- On page e542, in section 7.4, the recommendation table title now reads, "Recommendations for Ongoing Management of Atrial Flutter."
- On page e544, in section 8.1, the recommendation table title now reads, "Recommendations for Acute Treatment of Junctional Tachycardia."
- On page e545, in section 8.2, the recommendation table title now reads, "Recommendations for Ongoing Management of Junctional Tachycardia."
- On page e550, in section 9.2.2, the recommendation table title now reads, "Recommendations for Acute Treatment of SVT in ACHD Patients."
- On page e551, in section 9.2.3, the recommendation table title now reads, "Recommendations for Ongoing Management of SVT in ACHD Patients."
- On page e553, in section 9.3.1, the recommendation table title now reads, "Recommendations for Acute Treatment of SVT in Pregnant Patients."
- On page e554, in section 9.3.2, the recommendation table title now reads, "Recommendations for Ongoing Management of SVT in Pregnant Patients."
- On page e555, in section 9.4.1, the recommendation table title now reads, "Recommendations for Acute Treatment and Ongoing Management of SVT in Older Populations."

5. On page e517, table of "Recommendations for Ongoing Management of SVT of Unknown Mechanism," in the Class I, recommendation 2 supporting text, the second sentence read, "Large registry studies report high success rates for ablation of both AVNRT and AVRT, with infrequent but potentially serious complications (Table 8)." It has been updated to read, "Large registry studies report high success rates for ablation of both AVNRT and AVRT, with low frequency of potentially serious complications (Table 8)."
6. On page e520, Table 5, right-hand column of the table, "Interpretation," the first bullet point read, "Lack of any R-S complexes suggests VT." It has been updated to read, "Lack of any R-S complexes implies VT."
7. On page e522, in section 3.2.2, left-hand column, second paragraph, the first sentence read, "Ivabradine is an inhibitor…; therefore, ivabradine reduces the sinus node pacemaker activity that leads to slowing of the heart rate." It has been updated to read, "Ivabradine is an inhibitor…; therefore, ivabradine reduces the sinus node pacemaker activity, which results in slowing of the heart rate."
8. On page e523, in section 4.1, left-hand column, the section title read, "4.1. Focal AT." It has been updated to read, "4.1. Focal Atrial Tachycardia."
9. On pages e524 and e528, Tables 6 and 7, respectively, the left-hand column heading, "Drug," erroneously included a dagger symbol. This symbol has been deleted, and the other footnote symbols have been adjusted accordingly.
10. On page e534, in section 6, "Manifest and Concealed Accessory Pathways," right-hand column, second paragraph, the first sentence read, "The diagnosis of WPW syndrome is reserved for patients who demonstrate ventricular pre-excitation on their resting ECG and have associated SVT." It has been updated to read, "The diagnosis of WPW syndrome is reserved for patients who demonstrate ventricular pre-excitation on their resting ECG that participates in arrhythmias."
11. On page e541, in section 7.3, in the table of "Recommendations for Acute Treatment of Atrial Flutter," in the Class I, recommendation 2 supporting text, the third sentence read, "Hypotension is the chief adverse effect." It has been updated to read, "Hypotension is the main adverse effect."
12. On page e541, in section 7.3, in the table of "Recommendations for Acute Treatment of Atrial Flutter," Class I, recommendation 4 read, "4. Synchronized cardioversion is recommended for acute treatment of patients with atrial flutter who are hemodynamically unstable and do not respond to ptrun -1harmacological therapies.[75,208,356,359]" It has been updated to read, "4. Synchronized cardioversion is recommended for acute treatment of patients with atrial flutter who are hemodynamically unstable and do not respond to pharmacological therapies.[75,208,356,359]"

These corrections have been made to the current online version of the article, which is available at http://circ.ahajournals.org/content/133/14/e506.

Author Relationships With Industry and Other Entities (Comprehensive)—2015 ACC/AHA/HRS Guideline for the Management of Adult Patients With Supraventricular Tachycardia (April 2014)

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Richard L. Page (*Chair)*	University of Wisconsin School of Medicine and Public Health, Department of Medicine—Chair	None	None	None	None	• FDA Medical Device Advisory Board–Chair	None
Jose A. Joglar (*Vice Chair)*	University of Texas Southwestern Medical Center—Professor of Internal Medicine; Program Director, Clinical Cardiac Electrophysiology	None	None	None	None	None	None
Sana M. Al-Khatib	Duke Clinical Research Institute—Associate Professor of Medicine	None	None	None	• AHRQ* • NHLBI*	• Boston Scientific†‡ • DCRI • HRS Board of Trustees† • Medtronic†§	None
Mary A. Caldwell	University of California San Francisco—Assistant Professor (Retired)	None	None	None	None	None	None
Hugh Calkins	Johns Hopkins Hospital—Professor of Medicine, Director of Electrophysiology	• Atricure • Boehringer Ingelheim • Daiichi-Sankyo • Medtronic	None	None	• St. Jude Medical*	• HRS President†	• Defendant, sudden cardiac death, 2012
Jamie B. Conti	University of Florida—Professor of Medicine, Chief of Cardiovascular Medicine	None	None	None	• Medtronic	• Boston Scientific† • Medtronic† • St. Jude Medical†	None
Barbara J. Deal	Feinberg School of Medicine, Northwestern University—Professor of Pediatrics; Ann & Robert H. Lurie Children's Hospital of	None	None	None	None	None	None

	Chicago—Division Head, Cardiology						
N. A. Mark Estes	Tufts University School of Medicine—Professor of Medicine	• Boston Scientific* • Boston Scientific (Electrophysiology Fellows Educational Symposium)* • Medtronic • St. Jude Medical	None	None	• Boston Scientific	• Boston Scientific* • International Board of Heart Rhythm Examiners† • Medtronic* • St. Jude Medical*	None
Michael E. Field	University of Wisconsin School of Medicine and Public Health—Assistant Professor of Medicine, Director of Cardiac Arrhythmia Service	None	None	None	None	None	None
Zachary D. Goldberger	University of Washington School of Medicine—Assistant Professor of Medicine	• RubiconMD • Seattle Biomedical Research Institute	None	None	None	None	None
Stephen C. Hammill	Mayo Clinic—Professor Emeritus of Medicine	None	None	None	None	None	None
Julia H. Indik	University of Arizona—Associate Professor of Medicine	None	None	None	• NIH	• Boston Scientific†‡	None
Bruce D. Lindsay	Cleveland Clinic Foundation—Professor of Cardiology	• Biosense Webster • Boston Scientific • CardioInsight • Medtronic	None	None	None	• Boston Scientific* • Medtronic* • St. Jude Medical*	None
Brian Olshansky	University of Iowa Hospitals—Professor Emeritus of Medicine; Mercy Hospital Mason City—	• Arrhythmia Grand Rounds • BioControl • Biotronik • Boehringer-	None	• Executive Health Resources†	• Amarin (DSMB) • Boston Scientific (DSMB)	• Boston Scientific	• Defendant, event monitors, 2013 • Third party expert witness,

	Electrophysiologist	Ingelheim • Boston Scientific-Guidant • Combined Medicare Medicaid Services • Daiichi-Sankyo • Gerson Lehman • Lundbeck • Medtronic* • On-X Life Technologies • Sanofi-aventis • Thomas Reuters†			• Sanofi-aventis (DSMB)		cardiac arrest, 2012
Andrea M. Russo	Cooper Medical School of Rowan University—Professor of Medicine; Cooper University Hospital—Director, Electrophysiology and Arrhythmia Services	• Biotronik • Boston Scientific • Medtronic • St. Jude Medical	None	None	• Medtronic	• ABIM • Biotronik† • Boston Scientific* • HRS (Board of Trustees)† • UpToDate	None
Win-Kuang Shen	Mayo Clinic Arizona—Professor of Medicine; Chair, Division of Cardiovascular Diseases	None	None	None	None	• Circulation Arrhythmia and Electrophysiology Associate Editor	None
Cynthia M. Tracy	George Washington University—Professor of Medicine; Associate Director, Division of Cardiology and Director of Cardiac Services	None	None	None	• NIH	• George Washington Heart and Vascular Institute†	None

This table represents all relationships of committee members with industry and other entities that were reported by authors, including those not deemed to be relevant to this document, at the time this document was under development. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or ownership of ≥$5,000 of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted. Please refer to http://www.acc.org/guidelines/about-guidelines-and-clinical-documents/relationships-with-industry-policy for definitions of disclosure categories or additional information about the ACC/AHA Disclosure Policy for Writing Committees.

*Significant relationship.
†No financial benefit.
‡Relationship determined not relevant due to a "safe harbor" designation under the following requirements: a) the training is required (by FDA, professional organizations, and/or hospital certification committees) for privileging and/or for patient safety; b) the training is not available from a non-commercial entity; and c) expenses are not paid for by the sponsoring company.
§Dr. Al-Khatib's relationship with Medtronic was determine not relevant but is included in her comprehensive RWI for transparency. The training event was a self-funded, CME-equivalent presentation with no interaction from Medtronic. The presentation focused on a JAMA article on comparative-effectiveness research of ICDs compared to clinical practice.

ABIM indicates American Board of Internal Medicine; ACC, American College of Cardiology; AHA, American Heart Association; AHRQ, Agency for Healthcare Research and Quality; CME, certified medical education; DCRI, Duke Clinical Research Institute; DSMB, data safety monitoring board; FDA, Food and Drug Administration; HRS, Heart Rhythm Society; JAMA, *Journal of the American Medical Association*; NHLBI, National Heart, Lung, and Blood Institute; NIH, National Institutes of Health; and RWI, relationships with industry and other entities.

2015 SVT Guideline Data Supplements

Table of Contents

Methodology and Evidence Review

The recommendations listed in this guideline are, whenever possible, evidence based. An extensive evidence review was conducted in April 2014 that included literature published through September 2014. Other selected references published through May 2015 were incorporated by the writing committee. Literature included was derived from research involving human subjects, published in English, and indexed in MEDLINE (through PubMed), EMBASE, the Cochrane Library, the Agency for Healthcare Research and Quality, and other selected databases relevant to this guideline. The relevant search terms and data are included in Data Supplement evidence tables. Key search words included but were not limited to the following*: ablation therapy (catheter and radiofrequency; fast and slow pathway), accessory pathway (manifest and concealed), antiarrhythmic drugs, atrial fibrillation, atrial tachycardia, atrioventricular nodal reentrant (reentry, reciprocating) tachycardia, atrioventricular reentrant (reentry, reciprocating) tachycardia, beta blockers, calcium channel blockers, cardiac imaging, cardioversion, cost effectiveness, cryotherapy, echocardiography, elderly (aged and older), focal atrial tachycardia, Holter monitor, inappropriate sinus tachycardia, junctional tachycardia, multifocal atrial tachycardia, paroxysmal supraventricular tachycardia, permanent form of junctional reciprocating tachycardia, pre-excitation, pregnancy, quality of life, sinoatrial node, sinus node reentry, sinus tachycardia, supraventricular tachycardia, supraventricular arrhythmia, tachycardia, tachyarrhythmia, vagal maneuvers (Valsalva maneuver),* and *Wolff-Parkinson-White syndrome*.

Data Supplement 1. Nonrandomized Trials, Observational Studies, and/or Registries of Clinical Presentation and Differential Diagnosis Based on Symptoms – Section 2.3.1

Study Name, Author, Year	Study Type/ Design	Study Size	Inclusion/Exclusion Criteria	Primary Endpoint	Results/p Values	Summary/Conclusions
Sganzerla P 1989 (1) 2702964	Prospective, nonrandomized	16 AVNRT	All AVNRT	Relationship between hemodynamic changes associated w/ artificially induced arrhythmias and the EP properties of the related AV nodal reentry	Group 1 AVNRT w/ short RP Group 2 AVNRT w/ long RP No significant difference between the CLs of the two types of SVT (329 and 330-8 ms) Atypical SVT differed from the typical one by a significantly smaller initial decrease and a more rapid recovery of BP. In group 1, cardiac output and arterial pressure were lower in SVR higher and PAP equal. Contraction on a closed valve may be a factor resulting in impaired pulmonary drainage leading to neural factors w/ reduced cardiac output.	The induction of typical SVT (long AH) caused a marked initial fall in systemic BP w/ only a partial recovery, leading to stable hypotension and reduction of cardiac output owing to a decrease in stroke volume. On the contrary, in comparison to sinus rhythm, during the atypical SVT (long HA) a lesser degree of initial hypotension, a complete recovery of BP and no significant change in cardiac output were observed. The different hemodynamic response between the two types of SVT took place w/ the same increase in heart rate indicating that rate is not involved per se in the genesis of these circulatory changes. Simultaneous contraction more symptomatic for people.
Bhandari AK 1992 (2) 1636582	Prospective study	115 pts who were enrolled in a multicenter clinical trial of flecainide	Pts w/ SVT or AF or both, 49 had SVT	Determine whether sx recorded w/ transtelephonic monitoring correlated w/ SVT or AF	Among 49 pts w/ PSVT, 62.7% of symptomatic calls were associated w/ ECG-documented PSVT as compared w/ 6.6% of asymptomatic calls ($p<0.001$).	The sensitivity of a symptomatic call was 91% for PSVT
Leitch JW 1992 (3) 1537103	Prospective, nonrandomized	N=22	22 pts w/ SVT AVNRT 13 AVRT 8 AT 1 11 had a h/o syncope	Explore the mechanism of syncope during SVT	Lowest BP found in 1st 10 sec Compensated BP w/in 60 sec w/ minimal change in CL shorter and BP lower w/ upright tilt Comparison of the 7 pts w/ and the 15 pts w/o syncope. The only significant differences occurred in the extent of BP decrease during tachycardia (decrease in mean BP, 70±4 compared w/ 45+5 mm Hg; $p=0.01$) and in the frequency w/ which syncope occurred during passive tilt testing in sinus rhythm. The CL of tachycardia, in fact, tended to be longer in pts w/ syncope (311±10 compared w/ 290±+11 msec, $p=0.27$).	Syncope is associated w/ vasodepressor mechanism and is not directly related to the tachycardia CL
Lee SH 1995 (4) 7572623	Retrospective review	207 consecutive pts w/ h/o SVT	107 pts AP mediated, 100 pts w/ AVNRT	Determine effects of pregnancy on SVT	3.9% experienced first onset of SVT during pregnancy. Sx were exacerbated in 22% of pts w/ tachycardia in the pregnant and non-pregnant periods.	Pregnancy exacerbates SVT in some but not all pts.

Drago F 1996 (5) 8701888	Prospective, nonrandomized	N = 22 children	Ventriculoatrial interval <70 msec in 11 pts and >70 msec in 11	The aim of this study was to evaluate, by using transesophageal atrial pacing and recording, the clinical and EP features of reciprocating SVT at rest and during exercise and to determine the factors related to syncope during high adrenergic tone.	Group A = SVT, palpitations Group B = SVT near syncope Induced SVT via esoph pacing in both groups.	AVRT faster when induced during exercise Rate of SVT unrelated to sx of pre-syncope
Goyal R 1996 (6) 8831363	Observational	519 231 AVNRT 288 AVRT	AVNRT or AVRT	Assessment of age of onset	The mean age of sx onset was 32±18 y for AVNRT and 23±14 y for AP-mediated tachycardia. A significantly greater proportion of pts w/ AVNRT had the initial onset of sxs after the age of 20 y (AV nodal reen- trant tachycardia, 67% vs. AP, 41% (p<0.001)	There is a different mean age of sx onset for pts w/ AVNRT and AP-mediated tachycardia.
Abe H 1997 (7) 9392809	Prospective study of pts w/ SVT	N=32 13 AVNRT 4 atrial flutter 15 AVRT	32 consecutive pts w/ PSVT	Hypothesis was that pts w/ AVNRT would have more sx of diuresis because of higher right pressure	Increased diuresis in 12/13 (92%) of pts w/ AVNRT; 2/15 (13%) AVRT; and 1/4 atrial flutter w/ 2:1 AV conduction. Measured right atrial pressure and plasma ANP in 14 of 32 pts. RA pressure higher in AVNRT compared to the other tachycardias (16 vs. 5; p<0.01) and ANP levels also higher (215 vs. 63; p<0.001)	Sx of diuresis more common w/ AVNRT. The higher secretion of ANP may be the mechanism because there is a linear relationship between plasma ANP levels and atrial pressure
Lessmeier TJ 1997 (8) 9066458	Retrospective survey	119 consecutive pts	Limited to AVRT, AVNRT	Systematically evaluate the potential for SVT to simulate panic disorder	Criteria for panic disorder per DSM-IV were fulfilled in 67%. SVT unrecognized after initial medical evaluation in 59 (55%) including 41% of 32 w/ preexcitation. Physicians attributed sx to panic, anxiety orstress in 32 of the 59 (54%). SVT unrecognized a median of 3.3 y Women more likely to be labeled w/ panic than men (65% vs. 32% p<0.04 SVT diagnosed in 6 (9%) of 64 pts w/ Holters and 8 (47%) of 17 w/ event monitors (p=0.001)	SVT can mimic panic disorders and the diagnosis is often delayed by inappropriate rhythm detection techniques or missed preexcitation. Unrecognized SVT often attributed to psychiatric conditions. Perhaps misdiagnosis happens in women more often due to miscategorization of "feeling" in survey
Kalusche D 1998 (9)	Observational	395 pt w/ AVNRT 85 were >65 y	Limited to AVNRT	Main objective was to analyze risks and outcomes of	Elderly patents (mean 70.4 y) more often had syncope or presyncope w/ AVNRT (43.2% vs. 29.8%; P=0.05); had more	Elderly pts have more sxs, ER visits, and hospitalizations despite slower tachycardias. (Outcomes of ablation were no different.)

9812187				ablation, but they also characterized presenting sxs	hospitalizations and emergency department visits because of their sx 56.8 vs. 39.5% p,0.05 even though the CL was longer in the elderly (368 vs. 325 msec; P=0.0001)	
Orejarena LA 1998 (10) 9426034	Population epidemiologic research	Screened 50,000 Identified 1,763 w/ SVT	Limited to PSVT Standard ECG criteria for PSVT were employed: 1) paroxysmal, 2) normal QRS complex configuration or preexisting bundle branch block, 3) variation in successive RR intervals ≤40 msec, 4) ventricular rate 120 bpm, 5) no evidence of AV dissociation, and 6) no identifiable P waves preceding the QRS complex during tachycardia.	The aim was to determine the epidemiology and clinical significance of PSVT in the general population.	The prevalence was 2.25/1,000 persons and the incidence was 35/100,000 person-ys (95% CI: 23-47). Those w/ lone PSVT were younger (mean 37 vs. 69 y; p<0.0002), had a faster PSVT heart rate (mean 186 vs. 155 bpm; p<0.0006) and were more likely to have their condition first documented in the emergency room (69% vs. 30%; p<0.0377). The onset of sxs occurred during the childbearing y in 58% of females w/ lone PSVT vs. 9% of females w/ other cardio- vascular disease (p<0.0272). 21 incident pts (64%) had sxsconcordant w/ PSVT before initial ECG documentation. The probability of recurrence by the end of y 2 of f/u was 0.20 (95% CI: 0.06-0.35). There were no predictors of recurrence. For pts w/ a recurrence, all except one had their first recurrence w/in 12 mo of diagnosis and one had hemodynamic instability. 5 pts died during f/u, none due to PSVT	Approximately 89,000 new cases/y and 570,000 persons w/ PSVT in the United States.
Erdogan A 2001 (11) 11785371	Cohort survey	748 pts who underwent ablation responded to a survey	Limited to AVNRT	Analyze the medical h/o pts w/ AVNRT	Interval from onset of sx to ablation was 4.1 +/- 1.5 y. Mean age 55.4 female and 58.7 males. Only 6% had SHD. In females AVNRT appeared after age 50 in 16% and <age 20 in 18%. Women were more symptomatic. Women were more likely to delay ablation (average 7 y) (unknown whether this was due to personal preference or bias due to advice given)	High rate of pt w/ AVNRT begin in an older stage of life
Fitzsimmons PJ 2001 (12) 11526369	Retrospective review	238 aviators	Focused on manifest WPW	Report the natural h/o WPW in a nontertiary care population for the development of SCD and SVT	232 males, 6 women median age 35 (17-56) 11.7% had sx suggestive of SVT. 1 had syncope and 12 had near syncope. During f/u SVT occurred in 20.6%. SCD in 1 (0.02%)	Incidence of SVT is 1% per pt y. SCD risk low
Hamdan MH	Prospective	112	112 pts w/ pacemakers	Examine effect of	Decrease in BP greatest w/ simultaneous	SNA increases during all pacing modes

2001 (13) 11136692	analysis			atrial timing during simulated tachycardia on hemodynamic and neural responses.	pacing, less w/ short RP, and least w/ long RP Increase in CVP followed same trend SNA% increased w/ all three, but most pronounced w/ simultaneous AV and most w/ short RP Arterial baroreflex SNA correlated modestly w/ change in CVP	Decrease in BP and pulse pressure, which is directly related to the tachycardia rate, cardiac function, and AV synchrony. At any given rate, the timing of atrial systole has been shown to alter the hemodynamic response.
Razavi M 2005 (14) 16191112	Observational	N=17	AVNRT	Change in BP over time	BP decreased immediately after AVNRT initiation, w/ gradual recovery during the first 30 sec from 71.9±16.5 mm Hg to 86±13.8 mm Hg, p<0.01. When upright, the mean BP time course was similar, but mean BP recovery during AVNRT was slower	A short AV interval is associated w/ a greater mean BP decrease at the onset of tachycardia. These observations may explain clinical sxs immediately after the onset of AVNRT
Walfidsson U 2005 (15) 15733177	Survey of pts referred for ablation	301 pts 226 active drivers	Limited to AVRT and AVNRT	Evaluate the sx in pt w/ SVT and impact on driving	In 226 active drivers, fatigue 77%, dizziness 47%, diaphoresis 52%, near syncope 50%, and syncope14% reported w/ SVT. Women had more sxs for each category. 57% experienced SVT while driving and 42% had to stop because of it (during that episode). 24 pts considered SVT an obstacle to driving.	SVT is frequent while driving and can be associated w/ near syncope or syncope. Women seemed to have worse sxs. Pts w/ near syncope or syncope more likely to consider SVT an obstacle to driving
Drago F 2006 (16) 16835801	Observational	62 children	Limited to AVNRT.	Determine whether severity of sxs was related to EP characteristics	When pts w/ severe sxs were compared to those w/ mild sxs there was no difference in inducibility, CL of AVNRT, or the ERPs of the fast and slow pathways	The severity of sxs was not related to EP characteristics. -Although this study focused on children, the results are probably applicable to adults
Gonzalez-Torrecilla E 2009 (17) 19539146	Prospective analysis	370 consecutive pts who underwent EP study	AVRNT 262 (23 atypical) ORT 108 Excluded manifest preexcitation	Assess the independent predictive contribution to the ECG of clinical variables to distinguish major forms of SVT	370 consecutive pts ECG interpreted by 2 independent observers AVNRT more likely to be female, older age of onset (>30) Correct ECG interpretation more frequent in the AVRT group Rapid pounding in the neck more common w/ AVNRT (51% vs. 25%)	Age at the onset of sxs, sensation of rapid regular pounding in the neck during tachycardia, and female sex are the only significant clinical variables
Laurent G 2009 (18) 18775049	Mechanism of sx in SVT not understood. They evaluated VA timing	Survey included 152 pts w/ AVNRT and 80 w/ AVRT Hemodynamic	326 pts w/ a variety of clinically documented tachycardias (AVNRT, AVRT, VT, atrial flutter, AF completed a brief self-administered questionnaire regarding the occurrence of 5 sxs: “neck pounding,” chest pounding, palpitations, “shirt flapping,” and dizziness. This paper	Measured left atrial pressure during AVRT and simulated AVRT and AVNRT by the timing of pacing the atria and ventricles.	Sx of “shirt flapping” and “neck pounding” occur more frequently in AVNRT. Left atrial contractions during AV valve closure increase left atrial pressure and may explain the differences in sx between AVNRT and AVRT. Other sxs were about the same (chest pounding,	The sx of “shirt flapping” appears to be associated w/ pulsatile reversed flow in the pulmonary veins due to left atrial contraction against closed MV and is more common w/ AVNRT

		studies on 18 w/ AVRT and AVNRT	focuses on AVRT		palpitations, dizziness) Arterial pressures were significantly lower and left atrial pressures were significantly higher during native AVRT, simulated AVRT and AVNRT compared w/ sinus rhythm. Simulated AVRT created similar hemodynamic conditions as seen during native AVRT. Simulated AVNRT produced significantly higher left atrial pressure (peak and mean) than simulated AVRT.	
Walfridsson U 2009 (19) 19702600	QOL survey	97 AVNRT 79 AVRT	Focused on pts w/ AVRT and AVNRT	QOL scores	QOL scores were lower for pts w/ AVNRT compared to AVRT. Scores were affected by occurrence more than once a mo, arrhythmia duration, and whether sx occurred not only during exercise but also at rest.	The main conclusion was that QOL scores may direct therapy.
Kesek M 2011 (20) 21077786	Assessment of the U22 survey for clinical sxs before and after ablation	156 pts who underwent ablation of SVT	AVNRT and AVRT	QOL scores	Mean age 43.9 AVNRT vs. 57.1 AVRT Men 65% AVRT and 38% AVNRT 71% took medications prior to ablation	QOL scores using either the U22 or SF-36 improved after ablation.
Cain N 2013 (21) 23827401	Retrospective review	446 pts	Pts <21 w/ WPW (median age of diagnosis was 7y)	Modes of presentation	Modes of presentation included SVT (38%), palpitations (22%), chest pain (5%), syncope (4%), AF (0.4%), sudden death (0.2%), and incidental findings (26%); data were unavailable in 4%	64% had sxs at presentation, and an additional 20% developed sxs during f/u. There were 6 sudden deaths (1.3%), w/ an overall incidence of 1.1 per 1,000 pt-y in pts w/ structurally normal hearts and 27 per 1,000 pt-y in pts w/ associated heart disease. Although this was a pediatric study, it provides historical data that we can expect adults to describe.
Maryniak A 2013 (22) 23129107	Retrospective analysis	113	AVRT or AVNRT pts (9-13 y)	Evaluated cognitive and emotional development in a group of children and adolescents w/ AVRT and AVNRT.	Mean age AVRT 8 Meant age AVNRT 11 32% had hx syncope, more frequently w/ AVRT (37.5% vs. 24%; p=0.16) Deficiencies in cognitive function were prevalent. Anxiety levels increase w/ the appearance of sxs.	Both AVRT and AVNRT in childhood and adolescence can have a negative impact on cognitive and emotional development. Pts experiencing AVRT in the first y of life are likely to exhibit particularly severe deficits in cognitive function, including memory.

AF indicates atrial fibrillation; AP, accessory pathway; ANP, atrial natriuretic peptide; AT, atrial tachycardia; AV, atrioventricular; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; AT, atrial tachycardia; BP, blood pressure; bpm, beats per minute; CL, cycle length; CVP, central venous pressure; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders-IV; ECG, echocardiogram; EP, electrophysiological; ERP, effective refractory period; f/u, follow up; h/o, history of; MV, ??; ORT, orthodromic reentrant tachycardia; PAP, pulmonary arterial pressure; PSVT, paroxysmal supraventricular tachycardia; pt, patient; QOL, quality of life; RA, right arterial; SCD, sudden cardiac death; SF-36, Short-Form (36) Healt Survey; SHD, structural heart disease; SNA, sympathetic nerve activity; SVR, systemic valvular resistance; SVT, supraventricular tachycardia; sx, symptom; sx, symptom; U22 questionnaire, Umea 22 Arrhythmia Questions; VA, ventricular arrhythmia; VT, ventricular tachycardia; w/, with; and WPW, Wolff-Parkinson-White syndrome.

Data Supplement 2. Randomized Trials Comparing Principles of Acute and Chronic Therapy – Section 2.4

Study Name, Author, Year	Aim of Study	Study Type (Size, N)	Study Intervention Group (n)	Study Comparator Group (n)	Pt Population		Endpoints			P Values, OR: HR: RR: & 95% CI:	Study Limitations & Adverse Events
					Inclusion Criteria	*Exclusion Criteria*	*Primary Endpoint (efficacy) and Results*	*Safety Endpoint and Results*	*Secondary Endpoint and Results*		
Mauritson 1982 (23) 7065555	Effectiveness and safety of oral verapamil	11	Verapamil 240 mg/d followed by 480 mg/d (n=11)	Placebo	Symptomatic PSVT, ≥2 episodes/mo, ascertained by ECG AVNRT (n=7) AVRT (n=2 w/ WPW, n=3 w/ concealed AP)	CHF, severe hypertension, hypotension, VHD or CHD, renal/hepatic failure, SSS, AV block, atrial flutter, AF, AADs	Episodes/d (diary, Holter) Verapamil 0.1±0.1 ,0.3 ±0.5 Placebo 0.3±0.3 ,0.7 ±0.7 Duration(min) (diary, Holter) Verapamil 3±3 ,1±2 Placebo 27±5 ,67±111	Minor AEs in 6 pts on verapamil 5 pts required a total of 35 cardioversions for sustained tachycardia, 2 during verapamil, 33 during placebo (p<0.001) Programmed electrical stimulation performed at end of study to induce tachycardia. Caused sustained tachycardia in 9 on placebo, 2 on verapamil (p<0.01)	N/A	p<0.05 for primary endpoints	Oral verapamil safe and effective. Small sample size. Unclear which pt withdrew, so numbers of AVNRT vs. AVRT may be similar (i.e., 6 vs. 5).
Winniford 1984 (24) 6388299	Effect of AV nodal blockers for long-term therapy of PSVT	11	One mo of: Digoxin 0.375 mg/d Propranolol 240 mg/d Verapamil 480 mg/d	Direct comparison between all 3, w/ 1 wk of placebo washout	Symptomatic PSVT, ≥2 episodes/mo, ascertained by ECG	ECG evidence of preexcitation	Episodes and duration (ascertained by diary and weekly 24 h Holter), adverse effects, SDCs of each drug Episodes/wk	Mild side effects in 3/11 pts w/ digoxin and propranolol, and 5/11 w/ verapamil. All SDCs w/in normal reference range.	N/A	p=NS	Only verapamil had been studied in RCT prior to this (above) and given its proven efficacy, authors felt no need for placebo.

							(diary, Holter) Digoxin 2.3±3.1, 1.9±2.9 Propranolol 1.5±2.3 ,0.2±0.6 Verapamil 2.9±5.7 ,0.6 ±1.6 Duration(min) (diary, Holter) Digoxin 75±164, 47±157 Propranolol 60±112 ,1±1 Verapamil 56±148 ,1±1				Small series of pts. Unclear mechanism of PSVT (authors speculate all pts w/ AVRNT or oral rehydration therapy w/ concealed conduction.
Anderson 1986 (25) 2868645	Efficacy of esmolol in treatment of PSVT	71 Multicenter, double-blind, partial-crossover study	Esmolol (n=36)	Placebo (n=35)	"SVT" (HR>120) Note: AVNRT in 18% of subjects	VHD, AV block, SSS, significant electrolyte abnormality, precluding treatment w/ beta blockade, bronchial asthma, ventricular arrhythmias requiring drug therapy, cardiogenic shock, CHF (NYHA III-IV), renal or hepatic dysfunction, drug or alcohol abuse, on other beta-adrenergic blockers or calcium channel blockers w/in two half-lives of study entry	Therapeutic response: ≥20% reduction in HR, HR<100 bpm, or conversion to NSR. Therapeutic response to esmolol during the initial treatment period (72%) similar when esmolol was given as a second agent 4 pts (6%) converted to NSR In the 80% therapeutic response lost	Hypotension which occurred in12% on esmolol, 2% w/ placebo.	N/A	p=NS	Rapid onset and short of action of esmolol offer safe, effective therapy for acute treatment of pts w/ PSVT. Low numbers of pts w/ AVNRT.

							w/in 30 min following discontinuation of esmolol infusion				
Henthorn 1991 (26) 1898640	Flecainide for treatment of symptomatic PSVT (≥2 episodes)	34 8-wk crossover (after four episodes of PSVT or end of treatment period)	Flecainide (n=34)	Placebo (n=34)	PSVT	Syncope, angina, or transient cerebral events during PSVT, second or third degree AV block or had CHF (NYHA III-IV)	Freedom from symptomatic PSVT at 60 d: 79% events vs. 15% (p<0.001) Flecainide slowed symptomatic PSVT HR to 143±12 bpm from 178 ±12 on placebo in 7 pts who had events in the placebo and flecainide treatment phases (p<0.02)	Significantly more side effects w/ flecainide (p<0.05)	Flecainide vs. placebo: Recurrence: 8/34 vs. 29/34 (p<0.001). Median time to first event: 55 vs. 11 d (p<0.001) Median interval between episodes >55 vs. 12 d (p<0.001)	N/A	Despite participation of 19 medical centers, only 34 pts completed entire protocol and provided analyzable data. All pts tolerated flecainide, limiting generalizability. Transtelephonic monitoring does not permit assessment of proarrhythmia. 6/34 w/ AVNRT, confirmed by EP study, and 18/34 w/ unknown mechanism.
Pritchett 1991 (27) 1899432	Dose-response efficacy of flecainide in patents w/	42	Flecainide given in ascending order (25→50→100→150 mg bid) PSVT	Placebo inserted at random (alternating w/ flecainide) at 30 d intervals	PSVT, PAF, or paroxysmal atrial flutter	Syncope, angina, or transient cerebral events during PSVT, second or third degree AV block or had CHF (NYHA III-IV) .	Among 14 pts in Group 1 (PSVT) who qualified for efficacy analysis, 4 (29%) had no tachycardia while taking	Noncardiac adverse experiences were leading cause of premature study discontinuation during	N/A	N/A	Small sample size, short treatment period.

	PSVT, PAF, paroxysmal atrial flutter		(n=14, Group 1) PAF or parosysmal atrial flutter (n=28, Group 2)				placebo. Number w/ no tachycardia increased w/ progressively larger flecainide doses; w/ the 150 mg twice daily dose, 12 (86%) of 14 pts had no tachycardia (p<0.01 for overall differences among all treatments).	flecainide treatment periods (5 pts in Group 1 and 6 pts in Group 2).			
Pritchett 1991 (28) 2001087	Oral propafenone to prevent symptomatic PSVT Randomized, double-blind, placebo-controlled, crossover phase, w/ each treatment period lasting up to 60 d.	23	Propafenone (n=23)	Placebo (n=23)	PSVT (n=14) PAF (n=9)	Angina during tachycardia, pulmonary edema, neurologic sxs. PAF w/ WPW, on AADs	Compared w/ placebo, propafenone caused an increase in time to first recurrence of arrhythmia (p=0.004) PSVT: p=0.03 PAF: p=0.06 .	Cardiac AEs occurred only in pts w/ PAF (9/11): 2 w/ prolonged episode of AF, 1 w/ atrial flutter w/ a mean ventricular rate of 263 bpm recorded using the telephone monitor.	HR during recurrences, and not statistically different between propafenone and placebo	N/A	Propafenone efficacious in treating PSVT and PAF. Major limitation in not knowing how many pts had AVNRT. .
Anderson 1994 (29) 8074041	Long-term efficacy of flecainide (≥6	49	PSVT (n=21) PAF (n=28)	Placebo	Pts enrolled from 3 prior studies evaluating short-term flecainide efficacy	Syncope, angina, or transient cerebral events during PSVT, second or third degree AV block or had CHF (NYHA III-	-Number of pts w/o attacks -Time to first attack -Interval	No pt experienced proarrhythmia, MI, or died during chronic efficacy study.	N/A	N/A	Supports flecainide for chronic therapy of PSVT.

	mo)					IV)	between attacks -Average frequency of attacks, -Ventricular rate during attacks. PSVT pts: Of 17 efficacy evaluable pts, 14 (82%) had no SVT attacks during the chronic efficacy study compared w/ 4 (24%) w/ no attacks during placebo therapy at baseline (p=0.013). Time to first arrhythmia attack and time between attacks increased during chronic therapy w/ flecainide compared w/ placebo treatment (p=0.008 and p=0.012, respectively) Rates of attack/d not significantly different (p=0.130)				Small numbers of pts w/ PSVT, and PSVT not specifically defined.

							No PSVT pts w/ ventricular arrhythmias				
Chimienti 1995 (30) 8682031	Compare the long-term safety of flecainide and propafenone	335	SVT: flecainide 100 mg (n = 72) PAF: flecainide 200 mg (n = 97)	SVT: propafenone 450 mg (n=63) PAF: propafenone 450 mg (n=103).	SVT (n=135) PAF (n=200)	LVEF <35%, AV block, QRS >140 msec, SSS, persistent AF (episodes >72 h), VT (episodes >30 sec), NYHA III-IV, ischemic heart disease, hypertrophic cardiomyopathy, hypotension, valvular disease, renal/hepatic insufficiency, thyroid disease, AADs	ITT analysis (probability of 12 mo safe and effective tx) PSVT: 93% for flecainide and 86% for propafenone (p=0.24) PAF: 77% for flecainide and 75% for propafenone (p=0.72)	12 pts on flecainide reported 16 cardiac AEs, of whom 6 discontinued the treatment. 7 propafenone pts had 8 cardiac AEs, of whom 5 discontinued the treatment. (1 case of VT on propafenone 2 cases of AF w/ rapid ventricular response on flecainide	N/A	N/A	Both flecainide and propafenone were safe in the long-term treatment of pts w/ PSVT. Only one-third of pts had SVT.
UK Propafenone PSVT Study Group 1995 (31) 7586356	Efficacy and tolerability of propafenone at 600 mg and 900 mg daily doses (given bid). 2 consecutive crossover periods	100	Propafenone 300 mg bid Propafenone 300 mg tid	Placebo	PSVT (n=52) PAF (n=48) 75 pts in low-dose phase: 45 PSVT, 30 PAF 59 pts advanced to high-dose phase: 34 PSVT, 25 PAF ≥2 symptomatic episodes by transtelephonic monitoring	PSVT w/ hemodynamic collapse, LVEF ≤25%, recent MI or unstable angina; hepatic/renal failure, SSS, AV block, AADs, female pts of childbearing potential, COPD, myasthenia gravis.	Placebo vs. propafenone: PSVT, low-dose: Arrhythmia recurrence or AE RR: 6.8 (95% CI: 2.2-21.2; p<0.001), Arrhythmia recurrence RR: 7.4 (95% CI: 2.3-23.3, p<0.001). PSVT, high-dose: Arrhythmia recurrence or AE RR: 2.2 (95%	More pts experienced more AEs during propafenone (900 mg >600 mg). Most common adverse events during PSVT and PAF groups were related to the gastrointestinal and neuropsychiatric systems. Total numbers of adverse events on propafenone were 46 and 56 in the low-dose	1 episode of wide-complex tachycardia was documented during propafenone therapy	Propafenone at 600 mg is effective and well tolerated. A larger dose of 900 mg causes more AEs but may be more effective in those who can tolerate it	Sequential design (not randomized after low-dose phase) so population is not generalizable at 900 mg dose. Not powered for mortality. Limited in that PSVTs included AVNRT, AT, or AVRT.

							CI: 0.9-5.3, p=NS); Arrhythmia recurrence RR: 15.0 (95: CI: 2.0-113, p=0.009).	and high-dose PSVT group and 67 and 74 in the low-dose and high-dose PAF groups, respectively.			
Dorian 1996 (32) 8607397	Compare oral flecainide to verapamil in preventing PSVT recurrence	121 pts at 32 sites	Flecainide (n=63) (50 mg bid increased to max of 300 mg/d) AVNRT(n=17) AVRT(n=6) Unspecified (n=40)	Verapamil (n=58) (80 mg tid increased to max of 480 mg/d) AVNRT(n=10) AVRT(n=7) Unspecified (n=41)	PSVT, requiring therapy, majority w/ ≥2 attacks per mo AVNRT AVRT Unspecified PSVT but w/ clinical diagnosis of PSVT	Coexisting PAF, prior MI/UA, NYHA Class III-IV, AV block, preexcitation, AADs	86% of all flecainide 73% of all verapamil pt-mo occurred w/ 0-1 attack 19 (30%) pts on flecainide vs. 7 (13% of verapamil completed the trial (>270 d) w/o symptomatic attacks (p= 0.026) f/u 8.1 ±5.1 mo for flecainide and 7.5± 5.4 mo w/ verapamil	19% of flecainide group vs. 24% verapamil discontinued due to adverse effects (p=NS). Most common sx: flecainide: dizziness, concentration, sleep, nausea Verapamil: dyspnea, fatigue, HF sx	N/A	These agents confer potential benefit in pts who are not candidates for RFA	N/A
Wanless 1997 (33) 9124166	Sotalol in treatment of PSVT	126	Sotalol 80 mg (n=35) AVNRT (23%) Sotalol 160 mg (n=46) AVNRT (22%)	Placebo (n=45) AVNRT (24%)	Recurrent symptomatic PSVT were eligible for enrollment. AVNRT PAF Paroxysmal atrial flutter AVRT Paroxysmal AT	Decompensated CHF, asthma, chronic obstructive airways disease, second degree or third degree AV block, recent MI (<1 mo), recent coronary artery bypass graft surgery (<2 mo), unstable angina pectoris, bradycardia (<50 bpm), SSS, prolonged QTc interval (>0.45 sec), systemic hypertension	Time to recurrence of PSVT was less compared w/ placebo when receiving sotalol 80 mg (p=0.04) and sotalol 160 mg (p=0.0009). On subanalysis, sotalol was shown to be	No deaths, cases of ventricular proarrhythmia, CHF. Treatment of pts receiving sotalol were discontinued because of typical beta blocker side effects, including bradycardia, dyspnea, and fatigue.	N/A	N/A	Sotalol efficacious in the prophylaxis of PSVT. Study limited due to grouping of PSVTs.

						(diastolic BP >115 mm Hg), electrolyte imbalance, AADs	effective in the prophylaxis of both PAF (p=0.03) and paroxysmal reentrant arrhythmias (p=0.0003).				
Lim 1998 (34) 9437338	Efficacy of VM or CSM to terminate SVT in the ED	N=148 Randomized to VM first (62) or CSM first (86), then crossed-over to other therapy if first not effective	VM (blow into mouthpiece to achieve 40 mm Hg and sustain for at least 30 sec)	CSM (randomized first to left or then right CSM)	10 y of age or older	ECG w/ obvious atrial flutter, AF or sinus tachycardia, hemodynamically unstable (including poor cerebral perfusion, pulmonary edema or unstable angina). Pts w/ contraindications for CSM (h/o TIA, CVA, carotid bruit)	Conversion to SR	No adverse events directly related to VM or CSM. One pt was diagnosed w/ non-Q wave MI. 4 pts admitted for other medical problems (HF, pneumonia)	N/A	62 VM first, 19.4% conversion; 86 CSMc first, 10.5% conversion Crossover: to CSM, 14.0% conversion, and to VM w/ 16.9% conversion Total conversion rate (VM and CSM, including cross-overs): 27.7% No difference in efficacy between VM and CSM VM more effective in men, CSM more effective in older pts Recurrences w/in 2 h; 3 VM pts, 1 CSM pt	N/A
Gupta A 1999 (35) 10778689	Efficacy of IV diltiazem vs. esmolol for terminating PSVT	N=32 (study terminated prematurely due to superiority of diltiazem) Prospective randomized crossover, open-labeled	Esmolol 0.5 mg/kg twice in 5 min interval	Diltiazem 0.25 mg/kg twice in 5 min interval	SVT Hemodynamically tolerated in ICU	SHD; AT, AF or atrial flutter excluded	Conversion to SR	N/A	N/A	Diltiazem terminated SVT in all 16 pts where was first drug Esmolol terminated 4/16 (p<0.001 c/w diltiazem) and other 12 then terminated by diltiazem (total for diltiazem 28/28) Of the 28 pts responding to diltiazem a second dose was needed in 13. All 32 pts subsequently underwent EP study; 17 w/ AVNRT, 15 w/ AVRT. Diltiazem: first bolus converted 5/9 pts w/	Small trial, terminated early due to superiority of diltiazem.

										AVNRT, and 0/7 w/ AVRT (p<0.0001) Esmolol: equally ineffective for either tachycardia mechanism	
Alboni 2001 (36) 11216977	Effectiveness of self-administered flecainide or diltiazem /propranolol to terminate SVT	Randomized to placebo, flecainide (3 mg/kg), 120 mg diltiazem /80 mg propranolol on 3 different d for each pt N=33 (37 enrolled)	Flecainide (3 mg/kg) or 120 mg diltiazem w/ 80 mg propranolol	Placebo	Hemodynamically tolerated and long-lasting SVT confirmed by EP study to be reentrant (AVNRT or AVRT) Age 18-75, ≤5 episodes/y	Preexcitation, CAD, sinus <50 bpm, LVEF <50% or HF, recent MI, or stroke, need for long term beta blocker, calcium channel blocker, digoxin or AAD or h/o sustained atrial or VT	Conversion w/in 2 h: 52% placebo, 61% flecainide, 94% diltiazem/propranolol (p<0.001). Conversion faster w/ diltiazem/propranolol (p<0.001)	Hypotension, bradycardia	Over 17±12 mo treatment success f/u (SVT terminated in <2 h) in 81% of 26 diltiazem/propanolol pts, 80% of 5 flecainide pts % pts going to ED was 9% down from 100% of prior y (p<0.0001)	Adverse events: hypotension in 1 placebo, 2 flecainide and 1 diltiazem/propranolol pts; 3 had sinus <50 bpm (3 diltiazem/propranolol, 1 flecainide) 1 diltiazem/propranolol pt had syncope 5 pts ultimately referred for ablation	Unknown if outpt events that pts self-treated were indeed SVT and time to conversion assessed subjectively by pt Outpt management was not w/ placebo
Tendera 2001 (37) 11431663	Comparison of dofetilide to propafenone and placebo in the prevention of PSVT	122	Dofetilide (n=40) Propafenone (n=41)	Placebo (n=41)	18-75 y w/ ≥1 episode of PSVT w/in 6 wk documented by ECG	Pulmonary disease, myasthenia gravis, bundle branch block, resting bradycardia (<50 bpm), AV block, prolonged QTc, MI, unstable angina, recent sudden death, hematologic /hepatic/renal disease	After 6 mo of treatment, pts taking dofetilide, propafenone, and placebo had a 50%, 54%, and 6% probability, respectively, of remaining free of episodes of PSVT (p<0.001 for both dofetilide and propafenone vs. placebo). The hazard ratio for dofetilide vs. placebo was	19 of 40 pts (48%) treated w/ dofetilide and 21 of 41 (51%) treated w/ propafenone reported no AEs. No significant differences were noted between 3 groups in incidence of treatment-related adverse events or all-cause adverse events (p=0.73 and p=0.74, respectively).	Total number of episodes occurring during treatment, and type and frequency of sxs during episodes of PSVT before and during treatment Frequency of episodes lower in pts treated w/ dofetilide or propafenone thancompared to placebo. Active treatment did	N/A	Dofetilide is at least as safe and effective as propafenone as an alternative therapeutic option for the treatment of pts w/ PSVT. Limited in that PSVTs not specified.

							0.33 (95% CI: 0.18-0.61), and the hazard ratio for propafenone vs. placebo was 0.27 (95% CI: 0.14-0.51). Of 40 pts treated w/ dofetilide and propafenone, 23 (58%) and 25 (61%) had no recurring PSVT, compared w/ 16 (39%) in placebo group.		not alter distribution of sxs during a first episode of PSVT.		
Lim 2009 (38) 19261367	Efficacy and safety of slow infusion of calcium channel blockade vs. adenosine in the ED (RCT)	N=206	Slow infusion of calcium channel blocker: verapamil 1 mg/min to 20 mg total, or diltiazem 2.5 mg/min to 50 mg total If failed calcium channel blocker then given adenosine	Adenosine (6 mg followed by 12 mg if 6 mg ineffective) vs. (If adenosine ineffective after 12 mg they received a calcium channel blocker infusion)	10 y of age or older, SVT not converted by vagal maneuver	Impaired cerebral perfusion, subsequent diagnosis of non-SVT rhythm, pregnancy	Conversion to SR	Hypotension One pt that received calcium channel blocker became hypotensive	N/A	102 pts received calcium channel blocker and 98% converted to SR, 104 pts got adenosine, conversion was 86.5% (p=0.002) BP dropped by -13.0/-8.1 verapamil and -7.0/-9.4 for diltiazem. Recurrences w/in 2 h: 1 pt w/ diltiazem, 2 from adenosine group One pt that received calcium channel blocker became hypotensive	Slow infusion of verapamil or diltiazem was effective and well tolerated. Fall in BP transient. Unclear how many pts were excluded from analysis as a non-SVT rhythm was then identified – how did this cohort fair?
Smith 2013 (39) 23543578	Determine effectiveness of VM to terminat	Review of 3 RCTs: 1) Mehta D 1988 (40); 2)	N/A	N/A	N/A	N/A	Reversion to SR	Cardiovascular effects of VM (hypotension, bradycardia), mortality from VM, frequency	Failure to revert to SR followed by other therapies	Reversion success was 54.3% (19/35) in Mehta, 45.9% (61/133) in Wen and 19.4% in Lim (12/62)	Speculated that difference in conversion rates may be due to setting (ED vs. EP

	e SVT	Wen ZC 1998 (41); 3) Lim 1998 (34). Mehta and Wen studies were in a lab setting, Lim in ED setting						and severity of adverse events from VM		Heterogeneity between studies precluded a meta analysis; adverse effects not reported	lab)

AAD indicates antiarrhythmic drug; AE, adverse event; AF, atrial fibrillation; AP, accessory pathway; AT, atrial tachycardia; AV, atrioventricular; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; bid, two times per day; bpm, beats per minute; CAD, coronary artery disease; CHF, congestive heart failure; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CSM, carotid sinus massage; CVA, cerebral vascular accident; c/w, consistent with; ECG, electrocardiogram; ED, emergency department; EP, electrophysiological; f/u, follow up; HF, heart failure; h/o, history of; HR, heart rate; ICU, intensive care unit; ITT, insulin tolerance test; IV, intravenous; LVEF, left ventricular ejection fraction; MI, myocardial infarction; N/A, not applicable; NS, not significant; NSR, normal sinus rhythm; NYHA, New York Heart Association; PAF, paroxysmal atrial fibrillation; PSVT, paroxysmal supraventricular tachycardia; pt, patient; RCT, randomized controlled trial; RFA, radiofrequency ablation; RR, relative risk; SDC, serum drug concentration; SHD, structural heart disease; SR, sinus rhythm; SSS, sick sinus syndrome; SVT, supraventricular tachycardia; sx, symptom; TIA, transient ischemic attack; tid, three times per day; tx, treatment; UA, unstable angina; VHD, valvular heart disease; VM, Valsalva maneuver; VT, ventricular tachycardia; w/, with; w/o, without; and WPW, Wolff-Parkinson-White syndrome.

Data Supplement 3. Nonrandomized Trials, Observational Studies, and/or Registries of Principles of Acute and Chronic Therapy – Section 2.4

Study Name, Author, Year	Study Type/ Design	Study Size	Inclusion/Exclusion Criteria	Primary Endpoint	Results/p Values	Summary/Conclusions
Waxman 1980 (42) 7416025	Prospective cohort consisting of 33 pts in ED (group A) and 35 pts during EP study (Group B) to assess SVT termination using a protocol of successive vagal interventions until SVT terminated: a) L/R CSP (1-5 sec) b) multiple unilateral CSP c) edrophonium IV followed by CSP d)Valsalva (10 sec) e) edrophonium IV followed by Valsalva f) phenylephrine	N=68 (33 Group A-ED, 38 Group B- EP study)	SVT (AVNRT or AVRT (orthodromic). Overt WPW included.	Termination to SR	In all 68 pts SVT was terminated. 6 pts required phenylephrine. No complications. Post termination pauses was 1683± 66 ms In group B (EP study) pts, repeated trials were performed w/ overall 92% success in termination.	Data not broken down by group. However, text describes that 30/33 group A pts terminated SVT by a maneuver up to and including (e).
Rankin AC 1989 (43) 2789911	Cohort administered adenosine for either spontaneous tachycardia or induced	N=64 of which 54 pts had spontaneous tachycardia and 15 induced by programmed	Spontaneous and induced tachycardia in 16-79 y old pts	Termination to SR and diagnostic efficacy to identify atrial flutter or AT or VT	Adenosine terminated 46 of 48 episodes of narrow complex tachy Other tachycardias treated included wide	Adenosine effective for both diagnosis and treatment. Of note administration in wide complex tachycardia was safe. Early recurrences of arrhythmias seen in 35%.

		stimulation			complex (24 pts), Side effects: dysnea, chest pain, flushing, headache. No adverse hemodynamic effects High rate of recurrence (1/3)	
Cairns 1991 (44) 2064090	Observational cohort Adenosine to convert SR in ED setting	N=23	16 y or older presenting to ED in an 8 mo study period w/ sustained SVT, rate >140 bpm Exclusion: severe CHF, unstable angina, acute MI by ECG, hemodynamic compromise. Excluded sinus tachycardia, atrial flutter, AF, QRS >140 ms	Conversion to SR	2 pts after adenosine identified as not having SVT (a fluter, VT) 24 episodes of SVT in 21 pts of which 96% converted w/ adenosine (mean dose 10±6 mg) SVT recurred in 57% of episodes and other antiarrhythmic drugs then used to maintain SR. Adverse effects: 3 pts w/ chest pain, one pt w/ dyspnea but no adverse outcome	Adenosine highly effective in converted SVT but recurrences frequent
McCabe 1992 (45) 1554170	Prospective cohort Adenosine 6 mg , then 12 mg if ineffective, and 3rd dose of 12 mg if still ineffective	N=37, prehospital setting	18 y or older, w/ SVT assessed by paramedic, QRS <120 ms, rate 150-250 bpm Exclusion: hypersensitivity to adenosine or in extremis	Conversion to SR	26/37 in SVT (non-SVT rhythms were 5 AF, 4 sinus tach, 2 VT). 23/26 (88%) converted to SR 11 pts hypotensive at presentation in SVT and became stable upon conversion 9 pts had WCT and no hemodynamic compromise w/ adenosine	Small prospective series
Gausche 1994 (46) 8037382	Prospective cohort Adenosine 12 mg as initial dose, followed in 2 min of another 12 mg if no conversion	N=129, 106 w/ before and after strips Prehospital setting	18 y or older, w/ SVT assessed by paramedic. QRS <120 msec, rate >140 bpm. Exclusion: pregnancy, hypersensitivity to adenosine, sbp <80 mm Hg, or on carbamazepine	Conversion to SR	84/106 had SVT (AF in 13, ST in 5, atrial flutter in 2, and VT in 2 cases) 71/84 converted to SR (85%) and 4 needed second 12 mg dose Adverse effects: chest	Adenosine safe and effective in prehospital setting.

			or dipyridamole		pain (12), flushing (3), shortness of breath (2), nausea (1), anxiety (1), dizziness (1), headache (1)	
Madsen 1995 (47) 7741343	Nonrandomized, prospective 12 mo chart review of adenosine w/ comparison to historical cohort that received verapamil Pre-hospital setting (EMS) Verapamil up to 2 IV doses of 2.5 mg and 5 mg, or up to 2 doses of adenosine , 6 mg and 12 mg	N=73	Age >14 w/ paramedic assessment of narrow complex tachycardia (QRS <120, rate 160-240 bpm) 3/1990-2/1991 (verapamil) and 3/1991-2/1992 (adenosine) Pts had to be regarded as stable and first underwent Valsalva prior to administration of verapamil or adenosine by base hospital physician's order	Conversion to SR Also incidentally analyzed rate of ECG misinterpretation by EMS and base hospital physician	Verapamil given to 17 pts, of which 6 on subsequent review by cardiologist had AF, attach or sinus tach. 7/11 pts converted to SR (64%). Side effects in 5/17 pts (hypotension, NSVT, PACs) Adenosine: given to 64 pts, strips available for review in 56 pts. 24 pts on subsequent review by cardiologist had AF, attach, sinus tach, atrial flutter or VT. Of remaining 32 w/ true SVT that got adenosine, 78% converted to SR. Side effects: ventricular ectoic activity, 1st or 2nd degree AV block of <1 min, asystole (2-10 sec), chest pain, flushing, bronchospasm) Overall misinterpretation of the ECG occurred in 30/73 pts No difference in conversion rates between verapamil and adenosine	Misinterpretation of the ECG by paramedics and base hospital physician was common. But serious adverse events unlikely – no reported hemodynamic collapse from intervention. Conversion to SR by adenosine or verapamil similar (about 70%)
Brady 1996 (48) 8727628	Nonrandomized, prospective cohort w/ comparison to historical cohort Comparison of adenosine (prospective cohort) to verapamil (historical cohort)	N=211	Inclusion criteria: any age, narrow QRS tachycardia (120-300 bpm), or wide complex (120-300 bpm) who had received 2 doses of lidocaine, palpable pulse, IV in place. Exclusion: drug sensitivity, cardiac arrest, trauma etiology, for adenosine:	Conversion to SR	Adenosine: 87 of 105 pts received drug, 69% converted to SR Verapamil: 52 of 106 pts received drug, 88% converted to SR (p=0.1) Adverse events: adenosine: 4 pts (chest pain, dyspnea, prolonged	Adenosine and verapamil both effective in out of hospital setting to convert SVT. Rhythms were still commonly misidentified by EMS

			prior cardiac transplant, treatment w/ carbamazepine or dipyridamole Exclusion for verapamil: sbp <90, pulmonary edema, LV dysfunction, age <2 y, WCT		brady, VT) Verapamil: 4 pts (hypotension, VT, VF) – 2 pts had received verapamil for WCT and both had hemodynamic collapse Noted that EMS commonly misinterpreted non-SVT rhythms as SVT (including AF, ST, VT)	
Luber 2001 (49) 11146016	Observational cohort (retrospective chart review) Outcomes of pts treated for SVT in ED, including recurrence rates, from 1993-1996	N=111	Narrow complex tachycardia (QRS <120 ms), no P waves, rate 120-300 bpm. 1993-1996, single center	Recurrence of SVT Descriptive percentages of therapies given, pt demographics	Therapies given: adenosine (41%), Valsalva (22%), Calcium channel blocker (14%), beta blockers (4%), cardioversion (1%). 79 pts (71%) discharged from ED, mean age of 49, mean ED stay of 3.8 h, and 3 pts had recurrent SVT w/in 24 h 32 pts (29%) admitted to hospital, mean age 65, 6 pts (19%) had recurrent SVT in the hospital. SVT recurrence more likely in admitted pts (p<0.05), older pts (p<0.01) or h/o cardiac disease (p<0.01)	Largely a descriptive paper.
Roth A 2003 (50) 12586276	Prospective cohort study	84	PSVT 77% AF 23%	Effectiveness of DC cardioversion in pts who did not respond promptly to vagal maneuvers that were tried first and then tried again after intravenously administered medical treatment w/ 1 of the following intravenously administered drugs: adenosine,verapamil, digoxin, and/or procainamide. All study pts were hemodynamically compromised but did not require cardiopulmonary resuscitation.	DC cardioversion resulted in successful converson to sinus rhythm in all pts after 103 electrical attempts, using 118±69 Joules. No complications; all but 1 pt (w/ pulmonary edema and cardiogenic shock) discharged alive w/in 7 d of hospitalization.	Use of DC cardioversion to restore sinus rhythm can be safely and efficaciously applied in the prehospital setting in pts who are hemodynamically compromised but do not require cardiopulmonary resuscitation.

Chronic therapy of SVT (exclude WPW and preexcitation, but include if concealed AP)						
Neuss H 1988 (51) 3136637	Open label trial of chronic po flecainide to pts that first given IV dose in EP lab. Pts w/ WPW (concealed or overt) or AVNRT.	63 pts (47 WPW of which 8 concealed, 36 w/ AVNRT) Mean f/u 22.8 mo	WPW (overt or concealed) or AVNRT, previously refractory or intolerant to other antiarrhythmic drugs, verapamil or beta blockade) IV flecainide given during SVT induced at EP study (100 mg over 5 min)	Drug efficacy and tolerance based upon diary EP study also repeated while on therapy	In AVNRT pts (31) – mean observation of 23 mo, mean flecainide dose 257 mg/d, effective in 20 pts and reduced episodes in 4 other pts. Worsening of attacks seen in 2 pts. Adverse effects: visual, nervousness, dizziness, taste, hallucinations, vomiting. Therapy discontinued in 3 pts (AVNRT group)	Flecainide effective in reducing subjective episodes – among pts w/ AVNRT was effective in 20/31 pts.
Cockrell JL 1991 (52) 1898629	Open-label, uncontrolled trial of long term efficacy of flecainide	63 pts. mean f/u 24 mo	All pts w/ AV reentry	Drug efficacy and tolerance	Flecainide prevented or slowed AVRT in 44 pts. who were then followed and 33 (75%) w/ no adverse effects. Isuprel reversed the effects in 11/21 pts. Overall, 33 of 63 pts responded to and tolerated flecainide. 11 pts stopped due to adverse effects.	Flecainide moderately helpful in about 50% of pts over 2 y.
Jackman WM 1992 (53) 1620170	Prospective observational cohort	80	Symptomatic AVNRT undergoing RFA of slow-pathway	Successful ablation w/ intact AV nodal conduction, guided by atrial slow-path potentials	RFA abolished or modified slow-pathway conduction in 78/80 pts w/o affecting normal AVN conduction. Mean (+/- SD) f/u of 15.5 mo w/o recurrence.	Early report of success of RFA of slow-path conduction guided by atrial slow-path potentials—led to slow-pathway ablation being preferred method. Provided evidence that atrial insertions of fast and slow path are anatomically distinct.
Gambhir DS 1996 (54) 8682552	Prospective cohort study	9	All pts w/ symptomatic AVNRT, recurrent palpitations for 2-12 y EP study performed, IV amiodarone then oral therapy subsequently EP study repeated 1.5-3 mo later	No pts reported sxs of tachycardia during mean f/u of 65 d on oral amiodarone IV amiodarone terminated AVNRT in 7/9 pts (retrograde FP in 4/7 and anterograde SP in 3/7) Not inducible on PES after oral therapy, largely to due to prolonging refractoriness in atrium and ventricle, and depressing conduction through FP	No pts reported sxs of tachycardia during mean f/u of 65 d on oral amiodarone IV amiodarone terminated AVNRT in 7/9 pts (retrograde FP in 4/7 and anterograde SP in 3/7) Not inducible on PES after oral therapy, largely to due to prolonging	Small series of pts, but all w/ AVNRT Oral therapy w/ amiodarone is effective in suppressing AVNRT. IV amiodarone is effective in acute therapy. EP study efficacy.

					refractoriness in atrium and ventricle, and depressing conduction through FP	
Spector P 2009 (55) 19699343	Systematic review and meta-analysis to evaluate the safety and efficacy of RFA of AVNRT, AP-mediated, and atrial flutter.	For AVNRT and AP-mediated: 39 primary studies w/ 49 treatment arms in 7,693 pts.	Previous reviews or meta-analyses; animal or in vitro studies; subjects aged <18 y or mixed populations of which >15% were pediatric pts; f/u of <7 d; not studies of RFA; alternative energy sources used for ablation; AV junction ablation w/ pacemaker implantation; <40 pts per arrhythmia or ablation technique; published only in abstract form; published before 1990; and published in languages other than English, Spanish, French, Italian, German, and Portuguese.	SVT (AVNRT and AP-mediated) Single- and multiple-procedure success, arrhythmia recurrence, repeat ablation, adverse events, and death	Single-procedure success: 93.2% (95% CI 90.8-95.5%). Multiple-procedure success: 94.6% (95% CI 92.4- 96.9). Post-ablation arrhythmia: 5.6% (95% CI 4.1-7.2%). Repeat ablation: 6.5% (95% CI 4.7-8.3%) All-cause mortality: 0.1% Adverse events: 2.9%	First meta-analysis of RFA for AVNRT, AVRT (AP-mediated). Demonstrates high efficacy rates and low rates of complications.
Bohnen M 2011 (56) 21699857	Prospective observational cohort, single center Incidence and predictors for major complications of catheter ablation	1676 procedures	All pts undergoing ablation in a 2 y period (2009-2011) at a high volume center for variety of arrhythmias (SVT, AF, VT due to SHD or idiopathic)	Complications assessed over 30 d post-procedure.	524 SVT ablations performed of which major complications (total 0.8%) included perforation (n=1), pseudoaneurysm (groin, n=2), pulmonary edema (1). No instances of conduction system damage	Total major complication rate for SVT ablation below 1% in this contemporary prospective study.
Outcomes (Registry Data)						
Hindricks G 1993 (57) 8131762	Prospective cohort	4398	AT/atrial flutter (n=141, 3.2%) AVJ (n=900, 20.5%) AVNRT (n=815, 18.5%) AVRT: (n = 2222, 50.5%) VT (n=320, 7.3%).	Incidence of complications	Complications occurred in 223 pts (5.1%) overall AT/atrial flutter: 5.0% AVJ: 3.2% AVNRT: 8.0% AVRT: 4.4% VT: 7.5% Complications more in AVNRT RFA compared to AVJ or AP ablation (p<0.001) Complications more in VT	Early report showing high incidence of complications after AVNRT ablation.

					compared to AVJ (p<0.002) or AP (p<0.02)	
Hindricks G 1996 (58) 8682135	Prospective cohort	4463	AVNRT (n=880)	Incidence of AV block	AV block (4/ 880, 4.7%). AV block higher in fast pathway ablation (19/361, 5.3%, p<0.05) 6.3% in centers w/ limited experience in RFA (≤30 pts treated, p<0.05), and higher in these low-volume centers for both slow and fast pathway ablation (p<0.05)	Early report showing 5% incidence of AV block after RFA for AVNRT, and higher w/ fast pathway ablation.
Calkins H 1999 (59) 9892593	Prospective cohort	1050 (previously enrolled in RFA clinical trial)	RFA of AVNRT, AP, or AVJ AVNRT (n=373) AP (n=500) AVJ (n=121)	Efficacy and safety of RFA w/ long-term f/u.	Overall success: 95% Overall recurrence 6% Success: AVNRT: 97% AP: 93% AVJ: 100% Recurrence: AVNRT: 5% AP: 8% AVJ: 2% Predictors of success: -AVNRT OR: 3.94 (95%CI: 1.93-8.04; p=0.0002) -Left free wall AP OR: 3.09 (95% CI: 1.46-6.53; p=0.0003) -Experience of ablation center (>39 pts) OR: 2.39 (95% CI: 1.21-4.71; p=0.012) Joint predictors of mortality: -EF (p=0.003) -SHD (p=0.016) -AVJ ablation (p=0.048)	Shows RFA is a favorable option w/ low risk of complications and recurrence, and identifies pts who are at risk. Per-protocol analysis
Cheng	Comparison of cost	Symptomatic	RFA:	Perspective: societal	W/ monthly episodes of	RDA improves quality of life and

2000 (60) 11103056	effectiveness of RFA w/ medical management of PSVT	pts w/ 4.6 unscheduled visits/y for arrhythmia while on long-term drug therapy	Estimated population: AVNRT: 65% AVRT w/ concealed AP: 30% Efficacy estimates: AVNRT: 97% AVRT w/ concealed AP: 93% Recurrence estimates: AVNRT: 5% AVRT w/ concealed AP: 8% Drug efficacy: 60%	Outcomes: costs (office visit, annual drug rx, EP study, RFA, PPM, PPM replacement) QALY Life-years Marginal cost-effectiveness ratios	PSVT, RFA most effective and least expensive option RFA reduced lifetime medical expenditures by $27,940 compared w/ long-term pharmacologic therapy Lifetime costs: RFA: $61,880 Long-term drug rx: $89,820 Episodic drug rx: $143,530 RFA improved quality-adjusted life expectancy by 3.10 QALYs.	reduces costs when treating highly symptomatic pts. Effects in less symptomatic not studies
Scheinman MM 2000 (61) 10879389	Prospective cohort study (NASPE registry)	3,357	Ablation of AVNRT, AP, AVJ, atrial flutter, AT, IST, VT, idiopathic VT AVNRT (n=1,197 [35.6%) AVJ (n=646) AP (n=654) AT (n=216) Atrial flutter (n=447) IST (n=40)	Efficacy and safety of RFA w/ long-term f/u.	AVNRT Success: 96.1% Complications: 2% AVJ: Success: 96% Complications: 25 pts Recurrence:3.5% AP: Success: 94-96% Complications: 31 pts total Recurrence: 4.6% AT: Success: 51-79% Complications:5 total Recurrence:15.2% Atrial flutter: Success: 86% Complications:12 pts Recurrence:14.7% IST: Success: 71%	Large series reporting success of RFA, and stratification by age group confirms safety and efficacy in elderly pts, as well as by type of facility (teaching vs. community).

					Complications:2 pts Recurrence:10%	

AF, atrial fibrillation; AT, atrial tachycardia; AP, accessory pathway; AV, atrioventricular; AVJ, atrioventricular junction; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; bpm, beats per minute; CHF, congestive heart failure; CI, confidence interval; CSP, carotid sinus pressure; DC, direct current; ECG, electrocardiogram; ED, emergency department; EF, ejection fraction; EMS, emergency medical services; EP, electrophysiological; FP, fast pathway; f/u, follow up; h/o, history of; IST, inappropriate sinus tachycardia; IV, intravenous; LV, left ventricular; MI, myocardial infarction; NASPE, North American Society of Pacing and Electrophysiology; NSVT, non-sustained ventricular tachycardia; OR, odds ratio; PAC, premature atrial complex; PES, programmed electrical stimulation; PPM, prosthesis-patient mismatch; PSVT, paroxysmal supraventricular tachycardia; pt, patient; QALY, quality-adjusted life year; RFA, radiofrequency ablation; rx, prescription; sbp, systolic blood pressure; SD, standard deviation; SHD, structural heart disease; SP, slow pathway; SR, sinus rhythm; ST, sinus tachycardia; SVT, supraventricular tachycardia; VF, ventricular fibrillation; VT, ventricular tachycardia; WCT, wide complex tachycardia; w/, with; and WPW, Wolff-Parkinson-White syndrome.

Data Supplement 4. Randomized Trials Comparing Sinus Tachyarrhythmias – Section 3

Study Name, Author, Year	Aim of Study	Study Type (Size, N)	Study Intervention Group (n)	Study Comparator Group (n)	Pt Population		Endpoints			P Values, OR: HR: RR: & 95% CI:	Study Limitations & Adverse Events
					Inclusion Criteria	*Exclusion Criteria*	*Primary Endpoint (efficacy) and Results*	*Safety Endpoint and Results*	*Secondary Endpoint and Results*		
BEAUTIFUL 2008 (62) 18757088	To determine if HR lowering w/ ivabradine reduces cardiovascular death and morbidity in pts w/ coronary disease and LV systolic dysfunction	Randomized, double blind placebo controlled, parallel group. Multicenter 10,917 pts enrolled. Intention to treat analysis	Ivabradine 5 mg increased to 7.5 mg bid	Placebo	Coronary artery disease, LVEF <40% Age ≥55, or ≥18 if diabetic Sinus rhythm, HR≥60 bpm Angina and HF sxs stable over 3 mo prior to enrollment on stable doses of at least 1 mo of conventional medical therapy	MI or coronary revascularization w/in prior 6 mo Stroke/TIA in prior 3 mo Pacemaker or ICD VHD needing surgery w/in 3 y Sick sinus syndrome, long QT, complete heart block, uncontrolled HTN, NYHA IV Other medications w/ strong CYP P450 3A4 inhibition	Composite of cardiovascular death, hospital admission for acute MI, hospital admission for new onset or worsening HF	N/A	Mortality Cardiac death (MI, HF, due to cardiac procedure Cardiovascular death Hospital admit for acute MI or unstable angina Coronary revascularization Hospital admit for HF Hospital admit for acute MI	Median f/u 19 mo. Baseline mean HR 71.6±9.9 bpm, lowered at 12 mo by 6 bpm and by 5 bpm at 24 mo corrected for placebo Primary endpoint unchanged by ivabradine For pts w/ HR of 70 bpm or higher, ivabradine reduced admit to hospital for fatal and non fatal MI and coronary revascularization (secondary endpoints) 87% were on beta blockers No difference in serious adverse events between pts treated w/ ivabradine or placebo	Heart rate reduction not a specified endpoint of the trial, though is reported. Not an IST population but trial does demonstrate safety of ivabradine in a high risk population in a large, randomized, placebo controlled trial Heart rate reduction modest but baseline heart rates are lower compared to

											an IST population.
SHIFT 2010 (63) 20801500	To determine if HR lowering w/ ivabradine improves outcomes in HF	Randomized, double-blind, placebo-controlled, parallel-group. Multicenter trial that enrolled 6558 pts.	Ivabradine 5-7.5 mg bid	Placebo	Age ≥18 in sinus w/ resting HR of ≥70 Stable HF sxs over prior 4 wk Prior hospital admit for HF in previous 12 mo LVEF ≤35% On optimum, stable medical therapy over prior 4 wk	CHD Primary severe valvular disease Recent MI (<2 mo) Pacing for ≥40%/d AF/atrial flutter Symptomatic hypotension Pts not allowed to receive non-dihydropyridine calcium channel blocker, class I anti-arrhythmic or strong inhibitor of CYP3A4	Composite of cardiovascular death or hospital admission for worsening HF. Intention to treat analysis	N/A	Composite cardiovascular death or hospital admit for worsening HF in pts receiving at least 50% of target daily dose of beta blocker (metoprolol target dose = 150 mg/d) All cause death Any CV death Hospital admit (any) CV hospital admit Death from HF Composite of CV death, hospital admit for worsening HF, hospital admit for non-fatal MI	Median f/u 22.9 mo. HR at 28 d decreased by 15.4±10.7 bpm in ivabradine c/w baseline and by 10.9 (CI 10.4-11.4) bpm c/w placebo. At 1 y, HR reduction was 9.1 (CI 8.5-9.7) bpm c/w placebo, and at study end 8.1 (CI 7.5-8.7) bpm c/w placebo Primary endpoint reached in 24% of ivabradine group and 29% of placebo (p<0.0001), driven by difference in hospital admission for HF and death due to HF. Fewer serious adverse events in ivabradine group (p=0.025). 5% of ibabradine pts w/ symptomatic bradycardia compared to 1% of placebo (p<0.0001). Visual side effects (phosphenes) in 3% of ivabradine group vs. 1% of placebo (p<0.0001)	Heart rate reduction not a specified endpoint of the trial, though is reported. Not an IST population but trial does demonstrate safety of ivabradine in a high risk population in a large, randomized, placebo controlled trial HR reduction modest but baseline heart rates are lower compared to an IST population.
Cappato R 2012 (64) 22981555	To determine the effectiveness of ivabradine to	Double blind, randomized, placebo controlled	Ivabradine (2.5-7.5 mg twice daily) for 6 wk then 7 d washout then crossover to placebo for 6	Placebo for 6 wk then 7 d washout then crossover to ivabradine for 6 wk (n = 9)	Mean resting dtime HR >95 on Holter or >25 bpm symptomatic rise in HR from supine to standing or in response to stress	Underlying SHD (excluded by echocardiogram), SVT, orthostatic hypotension, compensatory sinus tachycardia, on	Sx resolution from 7 sx indicators	N/A	HR measurements (rest, exercise), exercise capacity	Ivabradine: >70% sx elimination (RR: 0.25; 95% CI: 0.18-0.34; p<0.001), resting heart rate reduced (p=0.011), and during exertion (p=0.001) and increased	Duration of therapy short (6 wk), some pts did not improve in sxs despite heart rate

	reduce sxs due to IST	crossover (N = 21)	wk (n = 10)			antiarrhythmic therapy, renal or hepatic insufficiency, on inhibitor of CYP3A4				exercise performance	reductions. Long term effectiveness and safety not studied.

AF indicates atrial fibrillation; bid, two times per day; bpm indicates beats per min; CI, confidence interval; CPY3A4, cytochrome p450 3A4; CV, cardiovascular; c/w, consistent with; f/u, follow up; HF, heart failure; HR, heart rate; LV, left ventricular; LVEF, left ventricular ejection fraction; MI, myocardial infarction; IAST, inappropriate sinus tachycardia; N/A, not available; pt, patient; RR, relative risk; SHD, structural heart disease; sx, symptom; TIA, transient ischemic attack; and w/, with.

Data Supplement 5. Nonrandomized Trials, Observational Studies, and/or Registries of Sinus Tachyarrhythmias – Section 3

Study Name, Author, Year	Study Type/ Design	Study Size	Inclusion/Exclusion Criteria	Primary Endpoint	Results/p Values	Summary/Conclusions
Lee RJ 1995 (65) 7586260	Prospective observational	16 pts (12 w/ SAN modification and 4 w/ SAN ablation)	Symptomatic, medically refractory pts w/ IST undergoing RFA enrolled Procedure: - Activation mapping (point-by-point) - Mapping guided by fluoroscopy or ICE (to visualize crista) - Isoproterenol F/u tests: - Autonomic blockade (intrinsic HR) w/ propranolol + atropine before and after ablation - ETT - Holter	Procedural success: SAN modification: at least 25% reduction in sinus HR under same conditions of catecholamine infusion w/ either retention of normal P wave axis or low atrial escape Total SAN ablation: reduction in HR >50% of tachycardia HR w/ junctional escape	Mean f/u = 20.5±0.4 mo SAN modification: - Procedural success 12/12 (100%) pts - 2 recurrences during F/U 7.1±1.7 mo Total SAN ablation: - Procedural success 4/4 (100%) pts - No recurrences at F/U Complications: - 2 pts PPM (both had total SAN ablation) - 1 pt transient right diaphragmatic paralysis - 1 pt transient SVC syndrome	- SAN modification is feasible and should be considered as alternative to complete AV junction ablation in pts w/ disabling sxs of IST that is refractory to medical therapy. -SAN modification may be aided by ICE.
Rakovec P 2009 (66) 19998013	Consecutively treated cohort	13	Resting HR on ECG >100 bpm Normal thyroid function, SHD excluded by echocardiogram	Evaluation at baseline (ECG, Holter) and after 2 wk on ivabradine 15 mg/d (repeat Holter)	11 women, 2 men, mean age 42±8 y 7/13 were pretreated w/ beta blockers. Mean HR decreased from 94±10 to 74.6±5.2 bpm w/ ivabradine (12 pts whose prior therapy could be discontinued or did not have prior therapy drug therapy). In 10 pts where min and max HR could be determined, the max HR decreased from 150.3±13.4 bpm to 120.6± 9.8 bpm and min HR decreased from 66.7±9.6 to 54.8±6.9. P<0.001 for all HR comparisons (paired t tests). One pt on metoprolol 300 mg/d switched to 15 mg of ivabradine and decrease of 4 bpm noted.	Limitation – small cohort, no meaningful comparisons to beta blockade could be made.
Calo L	Prospective,	18	Inclusion: Symptomatic IST,	Stress test ECG for	Mean and maximal HR on Holter reduced	Ivabradine lowers HR and improves sxs

2010 (67) 20621618	nonrandomized consecutively enrolled cohort		Exclusion: secondary causes of tachycardia, SHD (echocardiogram performed) Beta blockers and non-dihydropyridine calcium channel blockers interrupted before study	evaluation of sxs, maximal load, basal HR, maximal HR. Evaluation of stress ECG and 24-h Holter made at baseline, 3 mo, 6 mo Pts treated w/ ivabradine 5 mg-7.5 mg twice daily	compared to baseline at 3 or 6 mo ($p<0.001$) and at 6 mo compared to 3 mo ($p=0.02$) Resting and Maximal HR on stress test reduced and increased achieved maximal load	over 3 to 6 mo. Limitation – non-randomized, small cohort
Kaplinsky E 2010 (68) 20544616	Prospective, observational cohort	4	Resting HR ≥100, mean HR ≥90 on 24-h Holter Also noted: not previously treated w/ beta blocker or verapamil. SHD and secondary causes of tachycardia excluded	Evaluation at baseline, wk 1, 2, 3 and 4 and 2nd and 3rd mo. At 3 mo, Holter, ETT and QOL questionnaire performed. Ivabradine initiated at 5 mg bid, increased to 7.5 mg bid after first wk.	Ivabradine decreased resting HR from mean of 106.5±3 at baseline to 88.5 ±2 at wk 1 and 77 ±3 by wk 2 and 73.7 ±13 at mo 3. Holter monitor determined mean, max and minimum HR also reduced by 15-24% compared to baseline, exercise time increased, QOL improved.	Limitation- small cohort
Zellerhoff S 2010 (69) 20859616	Prospective observational cohort	10	Pts had failed or refused conventional therapy (beta blocker, calcium channel blocker, class IC AAD). Blood count, electrolytes and TSH normal. SHD excluded. EP study performed in 3 pts to exclude SVT. One pt w/ prior ablation of sinus node and pacemaker and another pt w/ prior ablation.	Ivabradine 5 mg-7.5 mg bid, w/ additional beta blocker therapy in 3 pts and monotherapy in 7 pts. 72-h Holter at baseline and during therapy. Sx assessment performed by telephone at mean f/u of 16±9 mo	Ivabradine reduced max and mean HR (baseline, max heart = 176±45, mean 84±11. On ivabradine max HR was 137 ±36 and mean 74±8 bpm, $p<0.05$. Min HR not significantly changed Of 8 pts contacted on followup at 16±9 mo, sxs improved in 3 pts and completely resolved in 5 pts.	Limitation – small cohort
Benezet-Mazuecos J 2013 (70) 23510001	Non randomized prospectively enrolled cohort	24	Inclusion: symptomatic pts diagnosed w/ IST at single institution (2009-2012) IST defined as resting dtime HR >100; excessive increase in HR w/ activity. Two Holters to confirm IST Exclusion: secondary cause of tachycardia	Comparison of baseline to 6 mo of mean, minimal, and maximal HR on Holter, and sxs assessed by SF-36 Health Survey (Secondary – assessment at 1 y and asked to stop treatment and reevaluate by Holter after 1 mo washout) Pts treated w/ ivabradine 5 mg-7.5 mg	At 6 mo, maximal HR, mean HR, and minimal HR reduced ($p<0.05$). SF-36 mean score improved on ivabradine ($p<0.001$) At 1 y 10 pts accepted to stop ivabradine w/ 2 pts continued to have IST criteria	At 6 mo ivabradine improved HR indices and sxs. Stopping ivabradine at 1 y showed HR continued to be in normal range in 8/10 pts. Limitation – non randomized, small cohort. Unclear given that pts that stopped the drug at 1 y no longer met criteria for IST that cohort itself may have consisted of pts w/ milder forms of IST or did not truly have IST.

				bid		
Ptaszynski P 2013 (71) 22772053	Prospective, nonrandomized cohort	20 (pts treated first w/ metoprolol for 4 wk, then ivabradine for 4 wk)	resting HR>100, or mean HR >90 bpm during 24-h Holter Antiarrhythmic therapy discontinued at least 4 wk prior Secondary causes for tachycardia and SHD were excluded	Aim: Evaluate safety and efficacy of ivabradine compared to metoprolol	Mean and resting HR lower w/ both metoprolol and ivabradine compared to baseline (p<0.001) Exercise capacity (METS) on ETT improved w/ both metoprolol and ivabradine compared to baseline (p<0.001) Sxs reduced more w/ ivabradine compared to metoprolol (p<0.05) 70% treated w/ ivabradine were free of sxs related to IST Side effects: Metoprolol – hypotension in 30%, asymptomatic sinus bradycardia (40-50 bpm) in 25%	Ivabradine and metoprolol both reduced HR. Ivabradine better tolerated and improved sxs to greater extent Limitation – short term (4 wk therapy per treatment), small sample size, nonrandomized w/o crossover; no washout period between drugs
Ptaszynski P 2013 (72) 23078130	Prospective, nonrandomized cohort	14	Inclusion: IST w/ resting HR ±100 bpm in sitting position and average HR ±90 bpm in 24-h Holter, following successful slow pathway ablation for AVNRT. Pts had also received at least 3 mo of beta blocker therapy Exclusion: secondary cause of tachycardia and SHD	Evaluation at baseline, 1 mo and 2 mo of therapy w/ ivabradine (5 mg -7.5 mg bid). Resting ECG, 24-h Holter to determine resting, mean, maximum HR, and evaluation of rhythm from Holter corresponding to sxs. ETT performed at baseline, 4 wk and 8 wk Questionnaire to assess sxs before and after 30 and 60 d – EHRA score	Mean resting HR at 30 and 60 d reduced compared to baseline (p<0.001) 24-h Holter w/ reduced mean and mean HR during daily activity (p<0.001). Improved exercise capacity w/ ivabradine (p<0.001) Reduced sxs w/ no severe sxs in any pts by 2 mo	At 2 mo severe sxs were eliminated in all pts. Limitation – No long term data for efficacy or if IST resolved
Ptaszynski P 2013 (73) 23426376	Prospective, observational cohort	20	Inclusion: IST w/ resting HR ≥100 bpm in sitting position and average HR ≥90 bpm in 24-h Holter. Pts previously treated w/ beta blockers or verapamil w/o effect or poorly tolerated Exclusion: secondary cause of tachycardia and SHD; postural orthostatic tachycardia or h/o orthostatic intolerance	Received metoprolol succinate 47.5 mg - 95 mg daily for first 4 wk, then ivabradine added 5 mg- 7.5 mg twice daily for additional 4 wk (combination therapy) Holter and ETT performed baseline, 4 wk, and 8 wk. Sxs assessed by questionnaire (EHRA score)	Resting HR: baseline 114.4±7.5, at 4 wk 97.3 ±14.4 and 8 wk 90.5 ±13.3 bpm, P<0.001. Mean and maximal HR on Holter monitor also lower in combination therapy compared to either baseline or monotherapy w/ beta blockade (P<0.001). Exercise capacity also increased. After 1 mo of combined therapy no pts reported IST related sxs	Limitation – no long term data

Kang KT 2014 (74) 25015944	Retrospective chart review (10 pediatric centers)	249 pts	Pediatric patient with focal AT (median age at diagnosis: 7.2 y), diagnosed based on ECG, 24-h Holter, or event monitor data consistent w/ EP criteria. 168 pts received antiarrhythmic medications (44 different medication combinations), including 154 pts as initial therapy and 14 pts after initial management with catheter ablation. Median duration of first-line therapy was 89 d.	Characterization of current management strategies for focal AT in children	Resolution of focal AT in 89% (including spontaneous resolution w/o catheter ablation in 34%). -antiarrhythmic medications used for initial therapy with control of focal AT in 72% (BB were most common, 53%, and most effective, 42%). 34% of the 154 pts w/ first-line therapy along achieved complete suppression or rate control of focal AT. 9 pts had serious AE while on antiarrhythmic medications. -catheter ablation successful in 109 of 134 pts (81%). -53 of 72 pts (74%) presenting at age <3 y had spontaneous resolution (including 50 pts aged <1 y). Spontaneous resolution observed in 18 of 129 pts >5 y. -Cardiomyopathy observed in 28%. 80% of pts with cardiomyopathy had focal AT resolution at last f/u. Lower recurrence rates when electroanatomic mapping techniques are used vs. conventional mapping techniques (16% vs. 35%; p=0.02).	Focal AT is managed successfully in most children. Many pts control focal AT with medications, but catheter ablation is used for most pts and successful for all ages.Spontaeous resolution is common, emphasizing delayed ablation in this group. Limitations: -retrospective study, variable f/u duration (median 2.1 y) and available data.
Case series						
Callans DJ 1999 (75) 10334440	Case series	10 pts (13 procedures)	Symptomatic, drug refractory pts referred for RFA of IST Procedure: - Primarily anatomic-based using ICE guidance, but also activation mapping for confirmation (point-by-point or electroanatomic w/ Carto) - Isoproterenol infusion	Procedural success: - -Abrupt decrease (≥30 bpm) in sinus rate during RF lesion delivery - Sudden appearance of superiorly directed p wave morphology (negative P in lead III) - Persistence of these features despite isoproterenol up to 4 mcg/min for at least 30 min following final RF lesion	11/13 (85%) procedures successful Local circumferential swelling w/ reduction in diameter of SVC-RA junction to 12.6±3.3 mm (24% reduction, p=0.0001) Complications – “none” - Reduction in diameter of SVC-RA junction by ≥30% compared w/ baseline observed in 5 pts; no pts had clinical signs for SVC syndrome. - Small adherent thrombi in 4 pts - 1 pt ppm (after complete SN ablation)	Conclusions: - RFA for IST can cause considerable swelling and narrowing of SVC-RA junction. - ICE might be useful in preventing excessive tissue swelling that could lead to complications.
Man KC 2000 (76) 10676693	Case series	29 pts	Consecutive, drug refractory, symptomatic pts who underwent RFA of IST Procedure: - Activation mapping (point-by-point)	Procedural success: Reduction of baseline sinus rate to <90 bpm, and a 20% or greater reduction in sinus rate	Procedural success 22/29 (76%) pts Sxs due to IST recurred in 6/22 (27%) at mean f/u 4.4±3 mo Additional procedures in 3 pts	RFA is at best only modestly effective for managing pts w/ IST.

			- Isoproterenol infusion 1-2 mcg/min	during infusion of isoproterenol.	Overall success 19/29 (66%) pts over long-term Complications in 2/29 (7%) pts - Sinus pauses/near-syncope (ppm) - Paralysis of right hemidiaphragm	
Marrouche NF 2002 (77) 11897449	Case series	39 pts	Inclusions: "Debilitating" IST (no prior drugs in 6 pts) Exclusions: - Prior sinoatrial node ablation at other center - F/u <2 y - POTS Procedure: - Mapping at baseline and after isoproterenol (or aminophylline) - Earliest site of activation by 3D electroanatomic mapping targeted - Autonomic testing (10 pts w/ resting HR >100) - tested response to esmolol before ablation - ETT before and after ablation - ICE to verify crista	Procedural success: HR drop below 120 bmp during isoproterenol 2 mcg/min alone or in combination w/ aminophylline (Look for SN acceleration during RFA delivery) When endpoint achieved, then recreated 3D map of RA Observe for recovery of HR for 45 to 60 min after last ablation	Sinoatrial node successfully modified in all pts (100%) Drop in mean HR from 99 ±14 bpm to 72±8 bpm, p<0.01 Shift in caudal activation along crista terminalis on 3D map was more pronounced after RFA than during esmolol (23 ±11 mm vs. 7±5 mm, p<0.05) No pt underwent ppm after mean f/u 32±9 mo. 21% of pts experienced recurrence of IST and were successfully re-ablated Complications: SVC syndrome (1 pt), requiring dilation	3D mapping provides an effective tool to monitor and guide RFA for IST. (Seems to eliminate excessive destruction of SN and reduce or eliminate risk of complete SN ablation.) Difference in caudal shift seen after esmolol and following sinoatrial node modification suggests that adrenergic hypersensitivity is not the only mechanism responsible for IST.
Lin D 2007 (78) 17338721	Case series	7 pts	Medically refractory IST referred for ablation Procedure: - Non-contact mapping (Endocardial Solutions, Ensite array, 4 mm Chilli Cooled Ablation system) - Isoproterenol 1-10 mcg/min - Intrinsic HR evaluated w/ BB and atropine	Endpoint: Decrease in HR of ≥25% off isoproterenol and associated change in P wave morphology in III and AVF from positive to a flat or negative defection c/w more inferior origin	Procedural success: 100% Complications: 1 pt ppm (symptomatic junctional bradycardia requiring ppm 2 wk after procedure) – but also had prior RFA	Non-contact mapping in conjunction w/ saline-cooled ablation for SN modification may provide effective HR control for treatment of IST.
Frankel DS 2012 (79) 22471900	Case series	33 pts	Consecutive, drug refractory, symptomatic Procedure: - Evolved from anatomic approach using ICE to EP approach using multi-electrode mapping (St. Jude Ensite or Biosense Webster) - Isoproterenol	Procedural endpoint: - Decrease of >25% in resting HR, w/ blunted HR response to isoproterenol and shift of P wave morphology from positive to flat or negative in leads III and AVF - Cranial to caudal shift in site of earliest RA activation pre and post SAN modification was	F/u 2.0±1.5 y - 18% recurrent IST - 27% developed non-IST tachyarrhythmia (42% had non-IST arrhythmia prior to SAN modification) 2 deaths (unrelated) during long-term f/u: - 1 mechanical fall - 1 pulseless electrical activity (end-stage cardiomyopathy) Complications (long-term): 12% required ppm for SAN dysfunction	Non-IST tachyarrhythmias are common in pts w/ IST before and after SAN modification, and are often responsible for sxs during f/u.

				measured using mapping system (later y)		
Takemoto M 2012 (80) 22333369	Case series	6 pts	Consecutive, drug refractory, "debilitating" Procedure: - Non-contact mapping (St. Jude Ensite) - Break-out sites also identified as earliest sites that showed rS pattern w/ sudden increase in peak negative potential on noncontact unipolar electrogram - Isoproterenol 2-5 mcg/min	Procedural endpoint: When break-out sites observed at heart rate >100 bpm moved from the tall P wave zone to the normal P wave zone, w/ and w/o IV isoproterenol	F/U 29±2 mo Procedural success 6/6 (100%) 1 y F/U: 0 recurrences 1 ½ y: 1/6 pts had recurrence of IST and underwent repeat RFA w/ success Also showed improvement of HR on Holter, BNP, NYHA functional class, exercise tolerance, and time to achieve HR of 130 bpm on ETT post-ablation Complications: none	Non-contact mapping can be used to safely and effectively treat IST.
Huang HD 2013 (81) 23313383	Case report using stellate ganglion block	1	34 y old woman previously treated w/ verapamil, beta blockers, clonidine Baseline mean HR (Holter) 104 bpm. Tilt table hr increased from 86 to 104 bpm at 2 min (70 deg) Stellate ganglion block performed (transient Horner syndrome) (right, then left 2 d later)	Following bilateral stellate ganglion block, Holter w/ mean HR of 73 bpm. Last f/u at 4 mo w/ resting HR of 87 bpm.	Following bilateral stellate ganglion block, Holter w/ mean HR of 73 bpm. Last f/u at 4 mo w/ resting HR of 87 bpm.	Mechanisms for lasting effect unclear as anesthetic agent used has half-life of 4-5 h

AAD indicates antiarrhythmic drug; AVNRT, atrioventricular nodal reentrant tachycardia; bid, two times per day; BNP, B-type natriuretic peptide; bpm indicates beats per min; c/w, consistent with; ECG, electrocardiogram; EHRA, European Heart Rhythm Association; EP, electrophysiological; ETT, exercise tolerance test; f/u, follow up; h/o, history of; HR, heart rate; ICE, intracardiac echocardiography; IST, inappropriate sinus tachycardia; IV, intravenous; METS, metabolic equivalents; NYHA, New York Heart Association; POTS, postural orthostatic tachycardia syndrome; PPM, prosthesis-patient mismatch; pt, patient; QOL, quality of life; RF, radiofrequency; RFA, radiofrequency ablation; SF, short form; SHD, structural heart disease; SN, sinus node; SVC, superior vena cava; SVC-RA, superior vena cava-right atrial; SVT, supraventricular tachycardia; sx, symptom; w/, with; and w/o, without.

Data Supplement 6. Nonrandomized Trials, Observational Studies, and/or Registries of Focal Atrial Tachycardia – Section 4.1

Study Name, Author, Year	Study Type/ Design	Study Size	Inclusion/Exclusion Criteria	Primary Endpoint	Results/p Values	Summary/Conclusions
Gillette PC 1977 (82) 902384	Observational	7 children (6 wks to 9 y of age)	Sustained automatic AT taken to EP lab	Programmed stimulation and drug testing	1 responded to digoxin, 3 responded to propranolol and digoxin; diphenylhydantoin in one and reserpine in1	Newborn and pediatric population
Creamer JE 1985 (83) 3966957	Case report	3 (23, 33 and 57 y of age, all man)	Symptomatic persistent AT	Acute (IV) and long term (oral) response to flecainide	All responded acutely and on long term f/u from 3 mo to 3 y	Case report demonstrating flecainide is effective in focal AT in selected pts.
Kunze KP 1986 (84) 3082957	Observational	5 pts (mean age 37)	Chronic symptomatic ectopic AT failed 4 other antiarrhythmic drugs including amiodarone and verapamil	Assess acute and long term outcomes w/ encainide and flecainide therapy	4/5 pts had complete suppression of AT by encainide and 1/5 had significant reduction at a mean f/u of 8 mo. 3/5 pts did not tolerate encainide. These pts responded to	One of the more comprehensive mechanism-based investigation in human subjects. Differentiation of mechanisms is based on best established criteria although overlaps between

					flecainide w/o any side effects	reentry and trigger are present; drug response was not specific. It is not apparent whether these were micro- or macro-reentry circuits. Ablation targeted the earliest activation, suggesting micro-reentry.
Lucet V 1987 (85) 3122689	Observational	30 children, age 3 mo to 20 y	All pts treated w/ propafenone for a mean period of 14 mo	Clinical outcomes on propafenone therapy	Study cohorts: chronic AT (8), junctional arrhythmia (9), ventricular arrhythmia (13). Propafeone was "more effective" than amiodarone in 3 pts w/ chronic AT and as effective as amiodarone in 2. Side effects were present in 27%, although "generally well tolerated".	There is significant limitation of the study due to the observational nature of the study design and mix of different arrhythmias.
Mehta AV 1988 (86) 3339178	Observational	10 infants and children; median age 6 mo, range from new born to 7.5 y	Met ECG critieria for ectopic AT	Acute and long term response to a sequence of drug testing. One pt underwent surgical ablation; one pt underwent catheter ablation	Digoxin did not suppress any AT but did slow the ventricular rate by 5-20% in 8 pts. IV propranolol was effective in AT suppression in 3/5 pts; oral propranolol was effective in 2/5. Class Ia and Ib antiarrhythmic agents were not effective in AT suppression and worsened the ventricular rate. IV amiodarone was effective in 3 /4 pts and oral amiodarone was effective in one pt. During f/u (10-28 mo), AT resolved in 4 pts and was well controlled in 4 pts. Surgical and catheter ablation was each performed in one pts	This small study was conducted in new born and very young children
Colloridi V 1992 (87) 1729843	Case study	5 pediatric pts	Ectopic AT was met by ECG criteria	Pts failed a mean of three drugs	Sotalol was added to digoxin; AT was suppressed in all 5 pts	A small case series study showing effect of sotalol on AT in pediatric pts
von Bernuth G 1992 (88) 1396817	Observational	21 infants and children	Automatic AT was documented by Holter and ECG; 12 were incessant, 7 were repetitive, 2 were undefined; 16/21 were symptomatic	All pts were treated w/ 1-8 antiarrhythmic drugs (median 3)	Amiodarone was most effective followed by class Ic drugs: flecainide and propafenone. During a median f/u of 2.5 y (range from 4 mo to 21 y), 12 were in sinus rhythm, 5 were w/o any drugs. Nine pts were still on antiarrhythmic drugs; all were intermittent except one	Small observational study in the pediatric population
Chen SA 1994 (89) 8087935	Observational	36 (57+/-13 y of age)	Sustained AT referred to the EP lab for ablation	Programmed stimulation, drug testing, Valsalva, monophasic AP recording and ablation to assess AT mechanisms	20/36 had reentrant AT, 9/36 triggered (DAD) 7/36 automatic Immediate success 40/41 (98%) Recurrence 2/40 (5%) in 18 mons f/u 2 failed RF, both were triggered	One of the earlier more comprehensive mechanism-based investigation in human subjects. Differentiation of mechanisms is based on best established criteria although overlaps between reentry and trigger are present; drug response was not specific. It is not apparent whether these were micro- or macro-reentry circuits. Ablation targeted the earliest activation, suggesting micro-reentry.
Engelstein ED	Observational	27 pts Automatic (7 pts,	Pts were referred for electrophysiology study (25 pts; 17 for symptomatic SVT, 7	Mechanism of tachycardia was	Adenosine terminated all sinus node reentry tachycardia (6/6), triggered	These earlier observations established our current understanding of potential mechanisms

1994 (90) 8205677		age 34+/- 18); sinus node reentry (6 pts, age 58+/- 16); atrial flutter (8 pts, age 62+/- 8); intra-atrial reentry (5 pts, age 70 +/- 8); triggered tachycardia (1 pt, age 79)	for VT, 1 for syncope) or cardioversion (2 pts w/ atrial flutter)	confirmed during electrophysiology study. Response to adenosine was assessed according to EP study determined mechanisms	tachycardia (1/1). Adenosine transiently suppressed automatic AT (7/7); it had not effect on reentry tachycardia (13/13)	of AT and drug effects as predicted by underlying mechanisms.
Heusch A 1994 (91) 7527342	Observational	72 children, mean age was 34 mo (range 0-192)	All pts were treated w/ propafenone	AT or junctional tachycardia were in 10/72 pts (14%). Other arrhythmias including AV reentrant tachycardia (32 pts, 44%), atrial flutter (16 pts, 22%), atrial reentry tachycardia (3 pts, 4%) and ventricular arrhythmias (11 pts, 16%).	Propafenone was effective in controlling atrial or junctional ectopic tachycardia in 83%. Of the entire study cohorts, better outcomes were observed in pts w/ normal hearts and in whom onset of arrhythmias was pre-natal.	A mix of many different arrhythmias renders interpretation of results difficult. The study population is young children, many w/ congenital heart conditions
Janousek J 1998 (92) 9605053	European, retrospective and multicenter study	722 infants and children from 27 European centers coordinated by the Working Group on Pediatric Arrhythmias and Electrophysiology of the Association of European Pediatric Cardiologist	All pts were treated w/ oral propafenone	Safety outcomes	Ectopic AT was in 66/722 study cohort. Other arrhythmias included reentrant SVT (388), junctional ectopic tachycardia (39), atrial flutter (21), ventricular premature complexes (140), VT (78) and other (39). 249/722 had SHD. Adverse events included sinus node dysfunction (4), complete heart block (2), SVT proarrhythmia (2), accelerated ventricular rate during atrial flutter (1), ventricular arrhythmias (5), unexplained syncope (1). Cardiac arrest occurred in 6 (0.6%, 2 had WPW, 3 had SHD)	A large retrospective multicenter study on the safety of propafenone in the pediatric population.
Kalman JM 1998 (93) 9462592	Observational	23 pts, 27 RA tachycardia	17 female, age 41 +/- 14 y; h/o AT suspected from RA; point to point mapping w/ 5 mm tip steerable catheter	ICE localization of AT origin; outcomes of RFA	23/27 localized to RA; 4 were from right superior pulmonary vein; other sites include posterior septum, coronary sinus os, RAA; 18/27 (67%) were on the CT; 26/27 successful ablation (96%); all visualized by ICE	Visual confirmation by ICE of ablation site; high prevalence of AT originating from cristae terminalis
Markowitz SM 1999	Observational	30 pts (age 55 +/- 18 y)	Referred to EP study for evaluation and treatment of tachycardia	Assess response to adenosine according to EP study	Adenosine terminated 14/17 focal AT and transiently suppressed the other 3 pts. Only 1/13 macrorenetrant tachycardia was	This study highlighted the challenges remain in differentiating automatic vs. triggered focal AT. The proportion of focal AT terminated by

(94) 10355690				determined mechanisms	terminated by adenosine. The termination occurred in the slow of conduction w/ decrementing properties. Verapamil terminated all of the focal ATs when tested	adenosine (presumably due to triggered activity) is significantly different from the report from Englestein 1994, from the same lab.
Morton JB 2001 (95) 11405398	Observational	9 pts from 64 consecutive pts underwent RFA for RA AT	6 male, 50 +/- 20 y; AT from CT; point to point steerable catheter	Mapping and localization of AT to CT	34/67 (51%) from CT; 8 (12%) from CS; 10 (15%) para-Hisian; 9 (13%) from TA. 8/9 were successfully ablated; 1 was not inducible	AT originating from CT is common
Kistler PM 2003 (96) 12821250	Observational	7 pts/ 172 consecutive pts w/ focal AT	AT from mitral annulus Point to point mapping	Mapping and ablation need to make note how they figured out where it was coming from	All mapped to left fibrous trigone and mitral-aortic continuity; P wave low amplitude in precordial leads, biphasic, negative followed by positive; 100% success rate	Mitral annular origin is less common
Kistler PM 2003 (97) 14557361	Observational	27 pts w/ 28 ATs	AT from pulmonary veins; 39 +/- 16 y; point to point mapping w/ or w/o Lasso	Mapping and ablation	Right superior pumonlary vein 11, left superior pulmonary vein 11, left inferior pulmonary vein 5, right inferior pulmonary vein 1; 26/28 were ostia; 100% successful; 4 recurrence; 25/28 were focal; 3/28 segmental	28/172 consecutive focal ATs (16%) from pulmonary vein; high success rate; majority at ostia
Gonzalez MD 2004 (98) 15533857	Observational	10 pts/35 consecutive pts (28%)	AT from mitral-aortic continuity	Mapping and ablation	Tachycardia CL 340 msec +/- 56; local e-P – 44 msec +/- 14; 100% successful	Provided a brief discussion on mouse embryo and the specialized conduction system in near the mitral-aortic continuity region
Kistler PM 2005 (99) 15862424	Observational	13 pts (of 193 w/ focal AT)	7 female; 41 +/- 6 y; AT from tricuspid annulus (TA); point to point mapping	Mapping and localization of AT to TA	Negative p wave in all inferior leads; negative or isoelectric in V1, positive in avL; 11/13 successfully ablated; 2 noninducible; no recurrence in 25 mo	13/ 193 (6.7%) of all AT are from coronary sinus os.
Eidher U 2006 (100) 16650262	Observational	38 pts, 49 episodes of AT	"monomorphic" AT, excluded typical atrial flutter and AF; likely included macro-reentry atypical flutter	Ibutilide conversion to SR in the acute setting	19/49 (38.8%) conversion	Inclusion does not differentiate focal AT from macro-reentry AT; conversion rate appear to be lower than atrial flutter and AF.
Ouyang F 2006 (101) 16814658	Observational	9 pts; 6 failed previous "para-Hisian" ablation; 6 female	NCC AT	Location and ablation	Local egram preceded His local A by 12 msec; no H on the ablation catheter; all ablation was successful w/o recurrence Age 54 +/- 12, range 32-66	One of the earlier observational studies reported AT localized to NCC and successfully ablated; highlights mapping NCC early if AT appears para-Hisian
Roberts-Thomson KC 2007 (102) 17286568	Observational	10 pts (of 261 w/ focal AT)	9 male, 39 =+/- 20 y; AT from RAA; point to point mapping w/ 4 mm tip deflectable catheter	Mapping and localization to RAA	P wave negative in V1; low amplitude or positive in inferior leads; acute success rate in 100%, no recurrence	RAA AT is less common 10/261 (3.8%)
Medi C 2009 (103) 19422986	Case control	30 pts w/ cardriomyopathy vs. 301 w/o cardiomyopathy	AT induced cardiomyopathy	Outcome assessment	AT induced caridomyopathy 10% (30/301); incessant, younger (39 +/- 22 vs. 51 +/- 17, 60% males vs. 38%), longer tachycardia CL (502 msec vs. 402 msec); LVEF was restored in 97% pts	Prevalence of AT induced cardiomyopathy 10% in all AT pts; RFA is highly successful in restore LVEF
Liu X	Case control	13 study pts	AT origination from NCC	Local e-gram,	Wide initial activation patter in the right	Presence of "para-Hisian AT" should raise

2010 (104) 20797494		15 PAF/PVI 25 PAF		activation sequence, electroanatomical mapping, histology, and P-wave morphology	atrium (RA), left atrium (LA) from the parahistian area; earliest activation in the NCC; no atrial myocardium in the NCC; NCC was adjacent to the atrial para-septal tissue	awareness of close anatomical relationship to atrial –paraseptal tissue and NCC Early mapping and ablation in the NCC may increase ablation success and reduce complications P wave morphology may not differentiate NCC-AT from left atrial or RA paraseptal AT
Biviano AB 2012 (105) 21967474	Observational	24, 14 female, age 48+/- 18	Focal left atrial AT; no prior h/o AF	Location and short term ablation outcome	CL 347 msec (190-510 msec); CS, septum (5), free wall, MVA, roof, LAA, ligament of Marshall and PV (6) Immediate success 19/22 ATs	A good observational study on the distribution of left atrial AT location; contemporary techniques; no major complications; success rate is consistent w/ the literature
de Loma-Osorio A 2013 (106) 24774111	Spanish registry from 74 centers, voluntary	333 of 11042 procedures (3%)	Registry included all ablation procedures from 2012	Ablation outcomes	Acute success rate 284/333 (85.3%); RA 61%, 36% in LA; complications 7/333 (2.1%), 1 permanent pacemaker, 2 vascular, 4 pericardial effusion	One of the few national registries
Mano H 2013 (107) 23595943	Case control	6 study cohorts, 12 controls	Anatomical substrate for NCC-AT vs. AVNRT	Comparing P wave duration, PQ, intracardiac intervals and local anatomy between NCC-AT and AVNRT	P wave duration, PQ and AH intervals were longer in NCC-AT than AVNRT; AS (aortic roof to IVS angle) angle was steeper and IVS was thicker	Interesting details, but not sure how useful for clinical practice

AF indicates atrial fibrillation; AP, accessory pathway; AT, atrial tachycardia; AV, atrioventricular; AVNRT, atrioventricular nodal reentrant tachycardia; CL, cycle length; CT, crista terminalis; DAD, delayed afterdepolarizations; ECG, electrocardiogram; EP, electrophysiological; f/u, follow up; h/o, history of; ICE, intracardiac echocardiography; IV, intravenous; IVS, intraventricular septum; LA, left atrial; LAA, left atrial appendage; LVEF, left ventricular ejection fraction; MVA, mitral valve area; NCC, non-coronary cusp; pt, patient; PV, pulmonary vein; RA, right atrial; RF, radiofrequency; RFA, radiofrequency ablation; SHD, structural heart disease; SR, sinus rhythm; SVT, supraventricular tachycardia; VT, ventricular tachycardia; w/, with; w/o, without; and WPW, Wolff-Parkinson-White syndrome.

Data Supplement 7. Randomized Trials Comparing Multifocal Atrial Tachycardia – Section 4.2

Study Name, Author, Year	Aim of Study	Study Type (Size, N)	Study Intervention Group (n)	Study Comparator Group (n)	Pt Population		Endpoints			P Values, OR: HR: RR: & 95% CI:	Study Limitations & Adverse Events
					Inclusion Criteria	*Exclusion Criteria*	*Primary Endpoint (efficacy) and Results*	*Safety Endpoint and Results*	*Secondary Endpoint and Results*		
Arsura E 1989 (108) 3052051	To determine efficacy of verapamil, metoprolol or placebo	Randomized, double-blind, placebo-controlled study of verapamil and	9 pts verapamil, 9 pts metoprolol	10 pts given placebo (2 pts given placebo on both days)	MAT diagnosed via ECG.	Reversible precipitants of MAT (hypoxia, electrolyte abnormalities, anemia, acidosis, and serum digoxin or theophylline levels outside therapeutic range) – if corrected and pt continued to	Conversion to sinus rhythm, a decline in the ventricular rate of ≥15%, or decline in ventricular rate to <100 bpm	N/A	Repeat physical exam and arterial blood gas values.	2/10 (20%); 4/9 (44%); 8/9 (89%) showed a response to placebo, verapamil, or metoprolol, respectively Mean slowing of ventricular rate was 3.4, 7.3, and 24.5% for placebo, verapamil, and metoprolol, respectively	Metoprolol appears more effective than verapamil in treating MAT. Caution must be exercised in selecting pts

	in MAT	metoprolol in treatment of MAT; 13 pts (4 male, 9 female)				have MAT, able to participate. CHF; SBP <100 mm Hg; bronchospasm; h/o greater than first-degree heart block; bifascicular block; altered sinus node function; hypersensitivity to either age; estimated survival time <72 h; use of either study agent w/in preceding 72 h				(p<0.01 for metoprolol vs. placebo). Five pts who had a response to metoprolol had failed to have a response to verapamil.	
McCord JK 1998 (109) 9462615	To assess the use of IV Mg for MAT in pts w/ COPD	Randomized; 14 pts	9 pts received 2 grams over 5 min and 10 g over 5 h	5 pts received Placebo	Pts w/ COPD and MAT	Cr ≥2.0 mg/dL, intolerance to IV infusion	Rhythm assessment at 5 h Pts treated w/ magnesium had a slowing of heart rate from 130 to 99 beats per min Placebo- no effect on HR. NSR at end of infusion in 7/9 treated w/ Mg vs. 1/5 w/ placebo.	N/A	N/A	N/A	Caregivers not blinded. Small sample size with no control group.

BP indicates blood pressure; CI, confidence interval; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; Cr, creatinine; ECG, electrocardiogram; HR, heart rate; IV, intravenous; MAT, multifocal atrial tachycardia; N/A, not applicable; OR, odds ratio; pt, patient; RR, relative risk; and SBP, systolic blood pressure.

Data Supplement 8. Nonrandomized Trials, Observational Studies, and/or Registries of Multifocal Atrial Tachycardia – Section 4.2

Study Name, Author, Year	Study Type/ Design	Study Size	Inclusion/Exclusion Criteria	Primary Endpoint	Results/p Values	Summary/Conclusions
Iseri LT 1985 (110) 4050650	Observational	8	8 pts w/ MAT received 7-12 Gm IV mag over 5 h	NSR	N/A	MAT was successfully converted to sinus rhythm or sinus tachycardia in seven pts. MAT rhythm (at slow rate) persisted in one pt.
Hazard PB 1987 (111)	Observational, active treatment w/	25	25 pts w/ MAT that was complicating severe cardiopulmonary illness	Observed its effect on heart rate and rhythm, BP, and arterial blood	All pts showed slowing of heart rate, averaging 54.0±4.0 bpm (p<0.001)	Metoprolol is effective in the management of MAT.

3792010	metoprolol			gase	pH and PaCO2 were unaltered; mean PaO2 increased by 12.2 +/- 5.8 torr (p<0.05)	

B indicates blood pressure; bpm, beats per minute; MAT, multifocal atrial tachycardia; N/A, not applicable; NSR, normal sinus rhythm; PaCO2, partial pressure of carbon dioxide; pt, patient; and w/, with.

Data Supplement 9. Randomized Trials Comparing Atrioventricular Nodal Re-Entrant Tachycardia – Section 5

Study Name, Author, Year	Aim of Study	Study Type (Size, N)	Study Intervention Group (n)	Study Comparator Group (n)	Pt Population		Endpoints			P Values, OR: HR: RR: & 95% CI:	Study Limitations & Adverse Events
					Inclusion Criteria	*Exclusion Criteria*	*Primary Endpoint (efficacy) and Results*	*Safety Endpoint and Results*	*Secondary Endpoint and Results*		
Pharmacological Therapy											
Waxman HL 1981 (112) 7447203	Effectiveness of IV verapamil	50	Group 1 (n=20) w/ AF or flutter Group 2 (n=30) PSVT (AVNRT in 8 pts),	N/A	PSVT w/ AF, atrial flutter, PSVT	N/A	Control of ventricular response in group 1, restoration of sinus rhythm in group 2 In Group 1 low-dose verapamil (0.075 mg/kg body weight) decreased the mean ventricular rate from 146 to 114 bpm (p<0.01) compared to a decrease of 145 to 132 bpm (p<0.01) after placebo. In Group 2, 14/29 pts converted to sinus rhythm after low-dose verapamil,	N/A	N/A	N/A	Verapamil results in a clinically significant slowing of the ventricular response in AF or atrial flutter and is superior to placebo for conversion of PSVT to sinus rhythm

							9/15 after high-dose verapamil (0.15 mg/kg), and 1/24 after placebo (p<0.01).				
Mauritson DR 1982 (23) 7065555	Effectiveness and safety of oral verapamil	11	Verapamil 240 mg/d followed by 480 mg/d (n=11)	Placebo	Symptomatic PSVT, ≥2 episodes/mo, ascertained by ECG AVNRT (n=7) AVRT (n=2 w/ WPW, n=3 w/ concealed AP)	CHF, severe hypertension, hypotension, VHD or CHD, renal/hepatic failure, SSS, AV block, atrial flutter, AF, AADs	Episodes/wk (diary, Holter) Verapamil 0.1±0.1 ,0.3 ±0.5 Placebo 0.3±0.3 ,0.7 ±0.7 Duration (min) (diary, Holter) Verapamil 3±3 ,1±2 Placebo 27±5 ,67±111	Minor AEs in 6 pts on verapamil 5 pts required a total of 35 cardioversions for sustained tachycardia, 2 during verapamil, 33 during placebo (p<0.001) PES performed at end of study to induce tachycardia. Caused sustained tachycardia in 9 on placebo, 2 on verapamil (p<0.01)	N/A	p<0.05 for primary endpoint	Oral verapamil safe and effective. Small sample size. Unclear which pt withdrew, so numbers of AVNRT vs. AVRT may be similar (i.e., 6 vs. 5).
Winniford MD 1984 (24) 6388299	Effect of AV nodal blockers for long-term therapy of PSVT	11	One mo of: Digoxin 0.375 mg/d Propranolol 240 mg/d Verapamil 480 mg/d	Direct comparison between all 3, w/ one wk of placebo washout	Symptomatic PSVT, ≥2 episodes/mo, ascertained by ECG	ECG evidence of preexcitation	Episodes and duration (ascertained by diary and weekly 24-h Holter), adverse effects, SDCs of each drug Episodes/wk (diary, Holter) Digoxin 2.3±3.1, 1.9±2.9 Propranolol 1.5±2.3,	Mild side effects in 3/11 pts w/ digoxin and propranolol, and 5/11 w/ verapamil. All SDCs w/in normal reference range.	N/A	p=NS	Only verapamil had been studied in RCT prior to this (above), and given its proven efficacy, authors felt no need for placebo. Small series of pts. Unclear mechanism of

							0.2±0.6 Verapamil 2.9±5.7, 0.6±1.6 Duration (min) (diary, Holter) Digoxin 75±164, 47±157 Propranolol 60±112, 1±1 Verapamil 56±148, 1±1				PSVT (authors speculate all pts w/ AVRNT or ORT w/ concealed conduction.
Yeh SJ 1984 (113) 3964710	Effect of diltiazem and propranolol as pill-in-the-pocket	15	Combination diltiazem 120 mg/propranolol 160 mg vs. placebos	Direct comparison on 2 consecutive d	Inducible PSVT AVRT (n=13) AVNRT (n=2)	N/A	W/ placebo PSVT lasted 164±89 min; 4 pts had spontaneous conversion. W/ diltiazem and propranolol PSVT lasted 39±49 min (p<.001). 14 pts had spontaneous conversion in an average of 27 ±15 min. None of the 14 pts had electrical reinduction of sustained PSVT after conversion. Outpatient f/u w/ 50/51 conversion of PSVT w/in 21±16 min, f/u of 5.6 mo.	The heart rate was 87±16 bpm before and 59±10 bpm at 90 min after diltiazem and propranolol (p<0.001). The systolic and diastolic pressures were, respectively, 111±11 and 77±10 mm Hg before and 88 + 9 and 66 + 9 mm Hg after diltiazem and propranolol (p<0.001)	N/A	N/A	Single dose of diltiazem/propranolol terminated acute PSVT Limited due to EP study efficacy and low numbers of AVNRT pts. Not placebo controlled.
Anderso	Efficacy	71	Esmolol	Placebo	"SVT" (HR>120)	VHD, AV block,	Therapeutic	Hypotension	N/A	p=NS	Rapid onset

n S 1986 (25) 2868645	of esmolol in treatment of PSVT	Multicenter, double-blind, partial-crossover study	(n=36)	(n=35)	Note: AVNRT in 18% of subjects	SSS, significant electrolyte abnormality, precluding treatment w/ beta blockade, bronchial asthma, ventricular arrhythmias requiring drug therapy, cardiogenic shock, CHF (NYHA III-IV), renal or hepatic dysfunction, drug or alcohol abuse, on other beta-adrenergic blockers or calcium channel blockers w/in two half-lives of study entry	response: ≥20% reduction in HR, HR<100 bpm, or conversion to NSR. Therapeutic response to esmolol during the initial treatment period (72%) similar when esmolol was given as a second agent 4 pts (6%) converted to NSR In the 80% therapeutic response lost w/in 30 min following discontinuation of esmolol infusion	which occurred in12% on esmolol, 2% w/ placebo.			and short of action of esmolol offer safe, effective therapy for acute treatment of pts w/ PSVT. Low numbers of pts w/ AVNRT.
*DiMarco JP 1990 (114) 2193560	Evaluate dose responses of adenosine in terminating PSVT	359 total in both protocols (n=201)	Sequential IV bolus doses of adenosine (3, 6, 9, 12 mg) (n=137)	Saline placebo (n=64)	PSVT	Severe CHF, unstable angina, recent MI, severe valvular regurgitation, intracardiac shunts, sleep apnea, current methylxanthine or dipyridamole use	Adenosine terminated acute episodes of PSVT, vs. placebo: 3 mg: 35.2% vs. 8.9% 6 mg 62.3% vs. 10.7% 9 mg: 80.2% vs. 14.3% 12 mg: 91.4% vs. 16.1%	Adenosine caused mild, transient side effects in 36% of pts (flushing, chest pain/pressure, hypotension, dyspnea)	N/A	p<0.0001	Overall efficacy of adenosine high, especially w/ increasing doses
*DiMarco	Compar	359 total	6-12 mg	5-7.5 mg of	PSVT	Severe CHF,	Cumulative	Adenosine	N/A	N/A	Overall

JP 1990 (114) 2193560	e adenosine to verapamil in terminating PSVT	in both protocols (n=158)	adenosine (n=77)	verapamil. (n=81)		unstable angina, recent MI, severe valvular regurgitation, intracardiac shunts, sleep apnea, current methylxanthine or dipyridamole use	response rates Adenosine: 6 mg: 57.4 12 mg: 93.4% Verapamil: 5 mg: 81.3% 7.5 mg: 91.4%	caused mild, transient side effects in 36% of pts			efficacy of adenosine is similar to verapamil, but onset of action is more rapid.
Henthorn RW 1991 (26) 1898640	Flecainide for treatment of symptomatic PSVT (≥2 episodes)	34 8-wk crossover (after four episodes of PSVT or end of treatment period)	Flecainide (n=34)	Placebo (n=34)	PSVT	Syncope, angina, or transient cerebral events during PSVT, second or third degree AV block or had CHF (NYHA III-IV)	Freedom from symptomatic PSVT at 60 d: 79% events vs. 15% (p<0.001) Flecainide slowed symptomatic PSVT HR to 143±12 bpm from 178 ±12 on placebo in 7 pts who had events in the placebo and flecainide treatment phases (p<0.02)	Significantly more side effects w/ flecainide (p<0.05)	Flecainide vs. placebo: Recurrence: 8/34 vs. 29/34 (p<0.001). Median time to first event: 55 vs. 11 d (p<0.001) Median interval between episodes >55 vs. 12 (p<0.001)	N/A	Despite participation of 19 medical centers, only 34 pts completed entire protocol and provided analyzable data. All pts tolerated flecainide, limiting generalizability. Transtelephonic monitoring does not permit assessment of proarrhythmia 6/34 w/ AVNRT, confirmed by EP study, and 18/34 w/ unknown mechanism.
Pritchett EL 1991 (27) 1899432	Dose-response efficacy of	42	Flecainide given in ascending order (25→50→10	Placebo inserted at random (alternating w/ flecainide) at	PSVT, PAF, or paroxysmal atrial flutter	Syncope, angina, or transient cerebral events during PSVT, second or third degree AV block or	Among 14 pts in Group 1 who qualified for efficacy analysis, 4	Noncardiac adverse experiences were leading cause of	N/A	N/A	Small sample size, short treatment period.

	flecainide in patents w/ PSVT, PAF, paroxysmal atrial flutter		0→1150 mg twice daily) PSVT (n=14, Group 1) PAF or parosysmal atrial flutter (n=28, Group 2)	30 d intervals		had CHF (NYHA III-IV) .	(29%) had no tachycardia while taking placebo. Number w/ no tachycardia increased w/ progressively larger flecainide doses; w/ the 150 mg twice daily dose, 12 (86%) of 14 pts had no tachycardia (p<0.01 for overall differences among all treatments).	premature study discontinuation during flecainide treatment periods (5 pts in Group 1 and 6 pts in Group 2).			
Pritchett EL 1991 (28) 2001087	Oral propafenone to prevent symptomatic PSVT Randomized, double-blind, placebo-controlled, crossover phase, w/ each treatment period lasting up to 60 d.	23	Propafenone (n=23)	Placebo (n=23)	PSVT (n=14) PAF (n=9)	Angina during tachycardia, pulmonary edema, neurologic sxs. PAF w/ WPW syndrome, on AADs	Compared w/ placebo, propafenone caused an increase in time to first recurrence of arrhythmia (p=0.004) PSVT: p=0.03 PAF: p=0.06 .	Cardiac AEs occurred only in pts w/ PAF (9/11): 2 w/ prolonged episode of AF, 1 w/ atrial flutter w/ a mean ventricular rate of 263 bpm recorded using the telephone monitor.	N/A	N/A	Propafenone efficacious in treating PSVT and PAF. Major limitation in not knowing how many pts had AVNRT. .
Dougherty AH 1992	Efficacy and safety of	87 AVNRT	Diltiazem	Placebo	Induction of PSVT w/ PES, required to have a rate of 120	Pts w/ severe congestive heart failure, sinus node	Conversion to sinus rhythm occurred in 4	N/A	Most frequent adverse	N/A	IV diltiazem in doses of 0.15, 0.25 and 0.45

(115) 1510006	IV diltiazem	(n=25) AVRT (n=60) AT (n=2)			bpm and to persist for 115 min.	dysfunction, pregnancy, myocardial infarction w/in 2 wk of study, or hypotension (SBP <90 mm Hg)	of 14 pts (29%) w/ 0.05 mg/kg of diltiazem, 16 of 19 (84%) w/ 0.15 mg/kg, 13 of 13 (100%) w/ 0.25 mg/kg, and 14 of 17 (82%) w/ 0.45 mg/kg compared w/ 6 of 24 (25%) treated w/ placebo. Conversion rates in groups receiving doses of 0.15 to 0.45 mg/kg of diltiazem were superior to that in the placebo group (p<0.001). Time to conversion was 3.0±2.6 min in responding diltiazem pts compared w/ 5.9±6.1 min in responding control pts.		response to diltiazem was hypotension (7 of 63 pts); however, only 4 pts had sxs related to hypotension.		mg/kg is effective and safe for acute management of PSVT.
Anderson JL 1994 (29) 8074041	Long-term efficacy of flecainide (≥6 mo)	49 PSVT (n=21) PAF (n=28)	Flecainide	Placebo	Pts enrolled from 3 prior studies evaluating short-term flecainide efficacy (2 above, Pritchett and Henthorn—one [Anderson, 1989]) not tabulated above due to PAF-only	Syncope, angina, or transient cerebral events during PSVT, second or third degree AV block or had CHF (NYHA III-IV)	-Number of pts w/o attacks -Time to first attack -Interval between attacks -Average	No pt experienced proarrhythmia, MI, or died during chronic efficacy study.	N/A	N/A	Supports flecainide for chronic therapy of PSVT. Small numbers of pts w/ PSVT,

					population)		frequency of attacks, -Ventricular rate during attacks. PSVT pts: Of 17 efficacy evaluable pts, 14 (82%) had no SVT attacks during the chronic efficacy study compared w/ 4 (24%) w/ no attacks during placebo therapy at baseline (p=0.013). Time to first arrhythmia attack and time between attacks increased during chronic therapy w/ flecainide compared w/ placebo treatment (p=0.008 and p=0.012, respectively) Rates of attack/d not significantly different (p=0.130) No PSVT pts w/ ventricular arrhythmias				and PSVT not specifically defined.

Chimienti M 1995 (30) 8682031	Compare the long-term safety of flecainide and propafenone	335	AVNRT: flecainide 100 mg (n = 72) PAF: flecainide 200 mg (n = 97)	AVNRT: propafenone 450 mg (n=63) PAF: propafenone 450 mg (n=103).	PAF (n-200) AVNRT (n=135)	LVEF <35%, AV block, QRS >140 msec, SSS, persistent AF (episodes >72 h), VT (episodes >30 sec), NYHA III-IV, ischemic heart disease, hypertrophic cardiomyopathy, hypotension, valvular disease, renal/hepatic insufficiency, thyroid disease, AADs	ITT analysis PSVT: 93% for flecainide and 86% for propafenone (p=0.24) PAF: 77% for flecainide and 75% for propafenone (p=0.72)	12 pts on flecainide reported 16 cardiac AEs, of whom six discontinued the treatment. 7 propafenone pts had 8 cardiac AEs, of whom 5 discontinued the treatment. (1 case of VT on propafenone 2 cases of AF w/ rapid ventricular response on flecainide	N/A	N/A	Both flecainide and propafenone were safe in the long-term treatment of pts w/ PSVT. Limited in that only one-third of pts w/ AVNRT.
UK Propafenone PSVT Study Group 1995 (31) 7586356	Efficacy and tolerability of propafenone at 600 and 900 mg daily doses (given twice daily). 2 consecutive crossover periods	100	Propafenone 300 mg bid Propafenone 300 mg tid	Placebo	PSVT (n=52) PAF (n=48) 75 pts in low-dose phase: 45 PSVT, 30 PAF 59 pts advanced to high-dose phase: 34 PSVT, 25 PAF ≥2 symptomatic episodes by transtelephonic monitoring	PSVT w/ hemodynamic collapse, LVEF ≤25%, recent MI or unstable angina; hepatic/renal failure, SSS, AV block, AADs, female pts of childbearing potential, COPD, myasthenia gravis.	Placebo vs. propafenone: Relative risks, PSVT, low-dose: Arrhythmia recurrence or AE 6.8 (95% CI: 2.2-21.2; p<0.001) Arrhythmia recurrence 7.4 (95% CI: 2.3-23.3; p<0.001) Relative risks, PSVT, high-dose: Arrhythmia recurrence or AE 2.2 (95% CI: 0.9-5.3;	More pts experienced more adverse events during propafenone (900 mg>600 mg). Most common adverse events during PSVT and PAF groups were related to the gastrointestinal and neuropsychiatric systems. Total numbers of adverse events on propafenone were 46 and 56 in the low-dose and high-dose PSVT group and 67 and 74	1 episode of wide-complex tachycardia was documented during propafenone therapy	N/A	Propafenone at 600 mg is effective and well tolerated. A larger dose of 900 mg causes more adverse effects but may be more effective in those who can tolerate it. Sequential design (not randomized after low-dose phase) so population is not generalizable at 900 mg dose. Not powered

							p=NS) Arrhythmia recurrence 15.0 (95% CI: 2.0-113; p=0.009)	in the low-dose and high-dose PAF groups, respectively.			for mortality. Limited in that PSVTs included AVNRT, AT, or AVRT.
Wanless RS 1997 (33) 9124166	Sotalol in treatment of PSVT	126	Sotalol 80 mg (n=35) AVNRT (23%) Sotalol 160 mg (n=46) AVNRT (22%)	Placebo (n=45) AVNRT (24%)	Recurrent symptomatic PSVT were eligible for enrollment. AVNRT PAF Paroxysmal atrial flutter AVRT Paroxysmal AT	Decompensated CHF, asthma, chronic obstructive airways disease, second degree or third degree AV block, recent myocardial infarction (<1 mo), recent coronary artery bypass graft surgery (<2 mo), unstable angina pectoris, bradycardia (<50 bpm), SSS, prolonged QTc interval (>0.45 sec), systemic hypertension (diastolic pressure >115 mm Hg), electrolyte imbalance, AADs	Time to recurrence of PSVT was less compared w/ placebo when receiving sotalol 80 mg (p=0.04) and sotalol 160 mg (p=0.0009). On subanalysis, sotalol was shown to be effective in the prophylaxis of both PAF (p=0.03) and paroxysmal reentrant arrhythmias (p=0.0003).	No deaths, cases of ventricular proarrhythmia, CHF. Treatment of pts receiving sotalol were discontinued because of typical BB side effects, including bradycardia, dyspnea, and fatigue.	N/A	N/A	Sotalol efficacious in the prophylaxis of PSVT. Study limited due to grouping of PSVTs.
Gupta A 1999 (35) 10778689	IV diltiazem and esmolol in acute therapy of PSVT	32 (initially 50 enrolled, but trial stopped early)	Hemodynamically tolerated PSVT	N/A	Two sequential doses w/ a 5 min interval of either drug were administered before crossover. Diltiazem was given in a dose of 0.25 mg/kg while the esmolol dose was 0.5 mg/kg.	N/A	Diltiazem terminated PSVT in all the 16 pts in whom it was given as the first drug. The 12 pts who did not respond to esmolol were also effectively treated w/ diltiazem. 28/28 pts	No significant adverse effects were seen.	N/A	N/A	IV diltiazem is highly effective and safe for terminating PSVT. When the first bolus is ineffective, the second bolus given after 5 min usually succeeds. Esmolol in the dose of 0.5 mg/kg has

							responded to diltiazem while only 4/16 pts responded to esmolol (p<0.001) Of the 28 pts who responded to diltiazem, in 13 pts the second bolus of diltiazem worked after the first one had failed.				poor efficacy for terminating PSVT, even when 2 boluses are administered.
Alboni P 2001 (36) 11216977	Pill-in-the-pocket approach to management of PSVT, well-tolerated	33	Flecainide (n=33) Diltiazem/ propranolol (n=33)	Placebo (n=33)	AVNRT and AVRT confirmed by EP study Well-tolerated (no sxs of dyspnea, syncope, presyncope, no interference w/ normal activities Infrequent (≤5 episodes/y) w/ ≥1 ED visit/y PSVT documented by ECG	Preexcitation, CAD, resting bradycardia <50 bpm, LVEF <50%, h/o HF, severe "general diseases," recent MI or CVA, acute illness, need for AADs, h/o sustained atrial/ventricular tachyarrhythmias	Conversion to sinus rhythm occurred w/in 2 h in 52%, 61%, and 94% of pts on placebo, flecainide and diltiazem/ propranolol, respectively (p<0.001) The conversion time was shorter after diltiazem/ propranolol (32±22 min) than after placebo (77±42 min, p<0.001) or flecainide (74± 37 min, p<0.001). 26 pts discharged on	Four pts (1 placebo, 1 diltiazem/ propranolol, and 2 flecainide) had hypotension and four (3 diltiazem/ propranolol and 1 flecainide) a sinus rate <50 bpm following SVT interruption	N/A	N/A	Use of these agents is efficacious in acute therapy, both w/ in-hospital and outpt therapy. However, only 4/5 pts discharged on flecainide. Complications not trivial and all pts pre-tested w/ EP study.

							diltiazem/ propranolol and 5 on flecainide. During 17±12 mo f/u, treatment successful in 81% of diltiazem/ propranolol pts and in 80% of flecainide pts (all the arrhythmic episodes were interrupted out-of-hospital w/in 2 h). In remaining pts, a failure occurred during ≥1 episodes because of drug ineffectiveness or drug unavailability. During f/u, the percentage of pts calling for emergency room assistance was significantly reduced as compared to the y before enrollment (9% vs. 100%, p<0.0001).				
Tendera M 2001	Comparison of dofetilide	122	Dofetilide (n=40)	Placebo (n=41)	18-75 y w/ ≥1 episode of PSVT w/in 6 wk documented by ECG	Pulmonary disease, myasthenia gravis, BBB, resting	After 6 mo of treatment, pts taking	19 of 40 pts (48%) treated w/ dofetilide	N/A	N/A	Dofetilide is at least as safe and effective

(37) 11431663	to propafenone and placebo in the prevention of PSVT		Propafenone (n=41)			bradycardia (<50 bpm), AV block, prolonged QTc, MI, unstable angina, recent sudden death, hematologic /hepatic/renal disease	dofetilide, propafenone, and placebo had a 50%, 54%, and 6% probability, respectively, of remaining free of episodes of PSVT (p<.001 for both dofetilide and propafenone vs. placebo). The hazard ratio for dofetilide vs. placebo was 0.33 (95% CI: 0.18-0.61), and the hazard ratio for propafenone vs. placebo was 0.27 (95% CI: 0.14-0.51). Of 40 pts treated w/ dofetilide and propafenone, 23 (58%) and 25 (61%) had no recurring PSVT, compared w/ 16 (39%) in placebo group.	and 21 of 41 (51%) treated w/ propafenone reported no adverse events. No significant differences were noted between 3 groups in incidence of treatment-related adverse events or all-cause adverse events (p=0.73 and p=0.74, respectively).			as propafenone as an alternative therapeutic option for the treatment of pts w/ PSVT. Limited in that PSVTs not specified.
Catheter Therapy (including cyroablation vs. RFA studies)											
Langberg JJ 1993 (116)	Slow vs. fast path ablation for	50	Anterior (n=22) Up to 1 h or 10 RF	Posterior (n=28) Up to 1 h or	AVNRT	None stated	Primary success rates, anterior vs. posterior	One pt w/ RBBB during an anterior lesion	N/A	N/A	Posterior (slow path) approach to RF

8491010	AVNRT		applications before alternative technique	10 RF applications before alternative technique			(55% vs. 68%, p=NS) All pts who failed initial approach were successfully treated by alternative technique w/o developing high-grade AV block	One pt w/ complete AV block complete during posterior lesion			modification of AV node is as effective as the anterior (fast path) approach, and both techniques associated w/ a low risk of complications. Limiting to 1 h or 10 attempts may underestimate success rates.
Kalbfleisch SJ 1994 (117) 8113557	Comparison of anatomic vs. EGM mapping for AVNRT ablation (slow path)	50	Anatomic (n=25) sequential RF energy applications (up to 12) delivered along tricuspid annulus from level of the coronary sinus ostium to His bundle	EGM mapping (n= 25) Target sites along posteromedial tricuspid annulus near coronary sinus ostium	AVNRT	None stated	Anatomic vs. mapping: Effective in 84 vs. 100% (p=0.1) 4 w/ an ineffective anatomic approach had a successful outcome w/ mapping approach	N/A	ITT analysis Mapping vs. anatomic: Time required for ablation: (28±21 vs. 31±31 min, p=0.7) Duration of fluoroscopy: (27±20 vs. 27±18 min, p=0.9) Mean number of RF applications: (6.3±3.9 vs. 7.2±8.0, p=0.6)	N/A	The anatomic and mapping approaches for ablation of the slow AV nodal pathway are comparable in efficacy and duration. Generalizability limited, and applicable only to technique described (e.g., authors cite not applicable for expanded anatomic approach or an EGM mapping approach that required the presence of a slow pathway potential).

											Small sample; probability of detecting a 20% difference in efficacy between two techniques only 0.67.
Kopelman HA 2003 (118) 12633642	Efficiency of conventional fluoroscopic and electroanatomic mapping (CARTO) in guiding catheter ablation of AVNRT	20	Electroanatomic mapping (n=10)	Fluoroscopic mapping (n=10)	AVNRT	None stated	Electroanatomic vs. fluoroscopy: Fluoroscopic duration: 12.6±6.8 vs. 35.9±18.3 min, p<0.001 Fluoroscopic exposure (0.7±0.5 vs. 9.6±5.0 min; p<0.001 Total procedure time: 83.6±23.6 vs. 114±19.3 min, p=0.008 Total fluoroscopic exposure: 4.2±1.4 vs. 15.9±-6.4 min, p<0.001 Number of RF applications: 2.7±1.6 vs. 5±2.8, p=0.018, Duration of RF: 165.3±181.6	No acute or long-term 8.9±2.2 mo) complications or arrhythmia recurrence in either group	N/A	N/A	Electroanatomic mapping offers significantly shorter procedure and fluoroscopy times, improving the efficiency of the procedure and reducing X-ray exposure. Small sample size, curious lack of side effects. Cost higher w/ electroanatomical mapping catheter, but likely offset by potential for improved efficiency, pt throughput and X-ray exposure from reductions in procedure and fluoroscopy times.

							vs. 341±177.7 sec, p=0.013 Total energy delivery: 24.3±3.1 vs. 28.7±4.5 watts, p=0.042				
Kimman GP 2004 (119) 15589641	CA vs. RFA	63	CA (n=30)	RFA (n=33)	AVNRT	None stated	Procedural success achieved in 91% RFA and 93% CA	N/A	Median number of CA applications lower than RFA (p<0.005) Both fluoroscopy and procedural times were comparable	N/A	CA useful for treatment of tachyarrhythmias near the compact AV node. Questionable whether lack of junctional rhythm is seen w/ CA makes this approach safer than RFA, as authors remark.
Zrenner B 2004 (120) 15589640	CA vs. RFA for AVNRT	200	CA (n=100)	RFA (n=100)	AVNRT	N/A	Cumulative incidence of primary endpoint (a combination of procedural failure, permanent complete AV block and AVNRT recurrence) higher in the CA group, p=0.03	Transient AV block was encountered in 18% pts in the CA group and in 8% in RF group (p<0.04) 21 episodes of transient AV block occurring during cryomapping (n = 4) or CA (n = 17) and 8 episodes during RF applications. The duration of transient AV	Procedural success defined as elimination of slow pathway or noninducibility of AVNRT CA vs. RFA 97% vs. 98%	N/A	Early pilot study (first prospective randomized investigation comparing CA w/ RFA of AVNRT) showing CA associated w/ a comparable acute success rate but a higher recurrence rate as compared w/ RFA in pts w/ AVNRT.

								block ranged from 2-420 s in CA group and from 2-180 s in RF group			
Kardos A 2007 (121) 18214124	Test the feasibility of cryomapping during AVNRT and AVRT Note: ablation performed only if cryomapping terminated the tachycardia w/o prolongation of AV conduction	30 AVNRT n=17 AVRT n=13 Randomized after dx of AVRT or AVNRT made 9 APS in CA, 4 in RF	CA (n=13)	RFA (n=17)	AVNRT or AVRT w/ anteroseptal pathway	AVRT w/ a posteroseptal, left-sided, or right free wall AP	CA vs. RFA Overall acute success rate: 85 vs. 82.4%, p=0.43	CA: in one pt, ablation not attempted because of AV prolongation RFA: two pts w/ temporary second-degree AV block	CA vs. RFA Long-term success rate (12 mo f/u) similar between the two groups Fluoroscopy and the procedure time similar (p=0.37 and p=0.14, respectively). Mean number of applications: 2 (1-6) vs. 7 (1-41), p=0.002	N/A	First study to assess ICE mapping guided ablation in a prospective randomized method. Cryomapping a feasible method to determine exact location of APs and of slow pathway during tachycardia. Cryomapping performed during tachycardia causes less ablation lesions w/o increasing procedure and fluoroscopy times. Pediatric pts eligible and pts in CA group younger (median age 20 vs. 44). No control, and arguably 2 groups not

											comparable because RF not safe during tachycardia when substrate located near AV node. LocaLisa system used in CA and RF groups, thus improving performance c/w "conventional" RFA.
CRYANO Study 2010 (122) 21098435	CA vs. RFA for AVNRT	509	CA (n=251)	RFA (n=258)	AVNRT	Prior AVNRT ablation CHD, prior pacemaker implantation, pregnancy, and inability to follow study protocol	Immediate ablation failure, permanent AV block, and AVNRT recurrence during a 6-mo f/u CA vs. RFA 12.6% vs. 6.3%, p=0.018) Immediate ablation success: 96.8% vs. 98.4%, p=NS Permanent AV block: 0% vs. 0.4%, p=NS AVNRT recurrence: 9.4% vs.	N/A (AV block in primary endpoint)	CA vs. RFA. Procedure duration (138±54 vs. 123±48 min, p=0.0012) Device problems: 13 vs. 2 pts, p=0.033) Pain perception lower in the cryoablation group. p<0.001	N/A	CA for AVNRT is as effective as RFA over short term but associated w/ higher recurrence rate at 6-mo f/u. Risk of permanent AV block does not differ significantly between CA and RFA. Potential benefits of CA relative to ablation safety and pain perception offset by longer procedure

							4.4%; P=0.029				times, more device problems, and a high recurrence rate.
Rodriguez-Entem FJ 2013 (123) 23080326	Efficacy of CA vs. RFA	119	CA (n=60)	RFA (n=59)	AVNRT	N/A	Acute procedural success achieved in 98% CA group and 59 100% in RFA group	One pt in RFA group underwent complete AV block and pacemaker implantation	CA vs. RFA Over a mean f/u period of 256.6 d, there was a significant difference in AVNRT recurrence (15 vs. 3.4%, p=0.03).	N/A	CA of AVNRT is a clinically effective alternative to RF ablation, w/ excellent acute success rate. Despite a slightly higher rate of recurrence during long-term f/u, CA may be considered first-line approach, especially in younger people.

*Two protocols tested in same study.

AAD indicates antiarrhythmic drug; AE, adverse effect; AF, atrial fibrillation; AP, accessory pathway; APS, acute procedureal success; AT, atrial tachycardia; AV, atrioventricular; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; BBB, bundle branch block; bid, two times per day; bpm indicates beats per min; CA, cryoablation; CAD, coronary artery disease; CHF, congestive heart failure; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CVA, cerebral vascular accident; c/w, consistent with; ECG, electrocardiogram; ED, emergency department; EGM, electrogram; EP, electrophysiological; f/u, follow up; HF, heart failure; h/o, history of; HR, heart rate; ICE, intracardiac echocardiography; ITT, intention to treat; IV, intravenous; LVEF, left ventricular ejection fraction; MI, myocardial infarction; N/A, not applicable; NS, not significant; NSR, normal sinus rhythm; NYHA, New York Heart Association; ORT, orthodromic reciprocating tachycardia; PAF, paroxysmal atrial fibrillation; PES, programmed electrical stimulation; PSVT, paroxysmal supraventricular tachycardia; pt, patient; RBBB, right bundle branch block; RCT, randomized controlled trial; RF, radiofrequency; RFA, radiofrequency ablation; sbp, systolic blood pressure; SDC, serum drug concentration; SSS, sick sinus syndrome; SVT, supraventricular tachycardia; sx, symptom; tid, three times per day; VHD, valvular heart disease; VT, ventricular tachycardia; w/, with; w/o, without; and WPW, Wolff-Parkinson-White syndrome.

Data Supplement 10. Nonrandomized Trials, Observational Studies, and/or Registries of Atrioventricular Nodal Re-Entrant Tachycardia – Section 5

Study Name, Author, Year	Study Type/ Design	Study Size	Inclusion/Exclusion Criteria	Primary Endpoint	Results/p Values	Summary/Conclusions
Vagal Maneuvers/Cardioversion						
Mehta D 1988 (40) 2897005	Prospective cohort study comparing 4 vagal maneuvers: right CSM, left	35	AVNRT (n=11) AVRT (n=24) EP study to induce SVT by PES	Termination of at least 2 of 3 episodes of induced SVT	Vagal maneuvers terminated tachycardia in 22 (63%) pts.	Valsalva most effective vagal maneuver for terminating PSVT. Limited in that study conducted

	CSM, face immersion in water, Valsalva maneuver		Excluded AADs taken 72 h prior to admission (amiodarone stopped prior to 3 mo), no AADs during admission		Valsalva maneuvers in supine position in 19 pts (54%), right CSM in 6 (17%), left CSM in 2 (5%), and face immersion in 6 (17%). (p<0.001 for difference). Vagal maneuvers more effective in pts w/ AVRT than AVNRT (79% vs. 27%, p<0.01) Pts w/ AVRT terminated by a vagal maneuver were significantly younger (p<0.001) than those w/ AVRT who did not respond to vagal maneuver; no such age difference seen w/ AVNRT	during EP study.
Wen ZC 1998 (41) 9851958	Prospective cohort study	133	AVRT (n=85) AVNRT (n=48) EP study to induce PSVT by PES Excluded atrial flutter, AF organic heart disease or other systemic diseases involving the autonomic function (e.g., diabetes), those who could not blow into an aneroid manometer to maintain a pressure of 35 mm Hg for 20 sec, and those w/ unstable hemodynamics during tachycardia.	Termination of PSVT	Vagal maneuvers more effective in terminating AVRT than AVNRT (53 vs. 33%, p<0.05). AVNRT: vagal maneuvers terminated tachycardia in antegrade slow pathway (14%) or in retrograde fast pathway (19%). Baroreflex sensitivity was poorer but isoproterenol sensitivity test better in pts w/ AVNRT.	Vagal maneuvers effective, more so for AVRT. Limited in that study conducted during EP study.
Roth A 2003 (50) 12586276	Prospective cohort study	84	PSVT 77% AF 23%	Effectiveness of DC cardioversion in pts who did not respond promptly to vagal maneuvers that were tried first and then tried again after intravenously administered medical treatment w/ 1 of the following intraveneously administered drugs: adenosine, verapamil, digoxin, and/or procainamide. All study pts were hemodynamically compromised but did not require cardiopulmonary resuscitation.	DC cardioversion resulted in successful converson to sinus rhythm in all pts after 103 electrical attempts, using 118±69 Joules. No complications; all but one pt (w/ pulmonary edema and cardiogenic shock) discharged alive w/in 7 d of hospitalization.	Use of DC cardioversion to restore sinus rhythm can be safely and efficaciously applied in the prehospital setting in pts who are hemodynamically compromised but do not require cardiopulmonary resuscitation.
Pharmacological Therapy						
Rinkenberger	Prospective cohort	28	AVNRT (n=6)	Effect of IV and oral verapamil	IV verapamil terminated AVNRT in	IV verapamil effective in acute

RL 1980 (124) 7418184	study		AVRT (n=6) AF/atrial flutter (15) AT(n=3)		all 6 pts Oral verapamil given to 19/28 pts, 7 reported improvement in sxs after 19 mo f/u (shorter frequency and shorter duration)	termination, while oral verapamil has selective efficacy.
Das G 1988 (125) 2905710	Prospective cohort study	113	Pts w/ PSVT (HR >100).	Efficacy and safety of esmolol. Also investigated feasibility of transferring pts from esmolol to alternate oral AADs w/o loss of therapeutic response.	95 (84%) achieved therapeutic response (reduction in heart rate of 15% or more or conversion to sinus rhythm). 93% achieved therapeutic response at esmolol doses of 200 micrograms/kg/min or lower. (88%) pts successfully transferred to oral AADs. Most frequent adverse effect observed during the study was hypotension, which resolved quickly (16±14 min)	Esmolol effective in HR reduction or convertion to NSR, and majority of pts successfully treated w/ esmolol can be safely and effectively transferred to oral AADs.
Rankin AC 1989 (43) 2789911	Cohort study	64	94 episodes of sustained, regular tachycardia; 40 pts w/ 64 episodes of narrow complex tachycardia (9 induced at EP study)	Efficacy of IV adenosine	Adenosine restored sinus rhythm in 25 pts 46/48 pts) w/ "junctional tachycardia," found to be due to AVRT or AVNRT	Not specific for AVNRT (defined AVRT and AVNRT as "junctional tachycardia"
Amsterdam EA 1991 (126) 1880230	Prospective cohort study	16	AF (n=11) Atrial flutter (n=2) PSVT (n=2) MAT (n=1)	In 13 responders (81%), mean ventricular rate decreased from 134±6 to 106±7 bpm 10 min after metoprolol administration and controlled for 40-320 min w/o further therapy. Metoprolol reduced ventricular rate by >15% in 11 (69%) of 16 pts, including 9 (82%) of 11 pts w/ AF. In one w/ AF and one w/ PSVT, ventricular rate was reduced by >12%	Hypotension, occurring in five pts, was the most frequent side effect but was transient and readily managed.	Metoprolol was rapidly effective in controlling ventricular rate in a majority of pts w/ supraventricular tachyarrhythmias. Limited data for AVNRT.
Cairns CB 1991 (44) 2064090	Observational cohort	23	Conversion to SR 16 y or older presenting to ED in an 8 mo study period w/ sustained SVT, rate >140 bpm Exclusion: severe CHF, unstable angina, acute MI by ECG, hemodynamic compromise. Excluded sinus tachycardia, atrial flutter, AF, QRS >140 ms	Adenosine to convert SR in ED setting	2 pts after adenosine identified as not having SVT (atrial flutter, VT) 24 episodes of SVT in 21 pts of which 96% converted w/ adenosine (mean dose 10±6 mg) SVT recurred in 57% of episodes and other antiarrhythmic drugs then used to maintain SR. Adverse effects: 3 pts w/ chest pain, one pt w/ dyspnea but no adverse	Adenosine highly effective in converted SVT but recurrences frequent

					outcome	
Musto B 1992 (127) 1615792	Prospective cohort study	35 9 pts w/ AVNRT (Age 10-23)	Recurrent PSVT documented by ECG; no h/o VT or AF, well-tolerated PSVT not induced by stress 9 total pts w/ AVNRT, remainder w/ AVRT	Termination of PSVT by flecainide.	PSVT terminated in 6/9.	Pts prescreened w/ EP study. Non-randomized study, and limited number of pts w/ AVNRT.
Gambhir DS 1995 (128) 7558090	Prospective cohort study	26	All pts w/ symptomatic PSVT, recurrent palpitations for 1-13 y EP study performed, IV flecainide given and then EP study repeated 20-30 min later w/ IV flecainide	Effective in terminating all pts w/ AVNRT, 11/12 w/ AVRT Time to termination both similar (146±70 vs. 149±29 sec, AVNRT vs. AVRT) AVNRT reinducible in one pt w/ AVNRT, 4 pts w/ AVRT Selective depression of retrograde limb	N/A	IV flecainide effective and safe for acute episodes of AVNRT and AVRT Oral therapy presumed to be effective given effects in preventing reinducibility. EP study efficacy.
Gambhir DS 1996 (54) 8682552	Prospective cohort study	9	All pts w/ symptomatic AVNRT, recurrent palpitations for 2-12 y EP study performed, IV amiodarone then oral therapy subsequently EP study repeated 1.5-3 mo later	No pts reported sxs of tachycardia during mean f/u of 65 d on oral amiodarone IV amiodarone terminated AVNRT in 7/9 pts (retrograde FP in 4/7 and anterograde SP in 3/7) Not inducible on PES after oral therapy, largely to due to prolonging refractoriness in atrium and ventricle, and depressing conduction through FP	N/A	Small series of pts, but all w/ AVNRT Oral therapy w/ amiodarone is effective in suppressing AVNRT. IV amiodarone is effective in acute therapy. EP study efficacy.
Glatter KA 1999 (129) 10051297	Retrospective cohort study	229	PSVT during EP study AVRT (n=59) Typical AVNRT (n=82) Artypical AVNRT (n=13) PJRT (n=12) AT (n=53) IST (n=10)	Determining the mechanism of PSVT w/ adenosine response	Adenosine of limited value in determining mechanism of PSVT 100% of pts w/ AVNRT, AVRT, atypical AVNRT, and PJRT terminated w/ adenosine	N/A
Ablation						
Jackman WM 1992 (53) 1620170	Prospective observational cohort	80	Symptomatic AVNRT undergoing RFA of slow-pathway	Successful ablation w/ intact AV nodal conduction, guided by atrial slow-path potentials	RFA abolished or modified slow-pathway conduction in 78/80 pts w/o affecting normal AVN conduction. Mean (±SD) f/u of 15.5 mo w/o recurrence.	Early report of success of RFA of slow-path conduction guided by atrial slow-path potentials—led to slow-pathway ablation being preferred method. Provided evidence that atrial insertions of fast and slow path are anatomically

						distinct.
Kay GN 1992 (130) 1572026	Prospective observational cohort	34	Slow pathway ablation (n=30) Fast pathway ablation (n=4)	Antegrade conduction over the fast pathway remained intact in all 30 pts after successful selective slow pathway ablation There was no statistically significant change in the atrio-His interval (68.5±21.8 msec before and 69.6±23.9 msec after ablation) or AV Wenckebach rate (167±27 beats per min before and 178±50 beats per min after ablation) after slow path ablation	3 complications in two pts, including an episode of pulmonary edema and the development of spontaneous AV Wenckebach block during sleep in one pt after slow pathway ablation and the late development of complete AV block in another pt after fast pathway ablation. Over a mean f/u period of 322±73 d, AVNRT recurred in three pts, all of whom were successfully treated w/ a second ablation.	Early report suggesting benefits of slow pathway ablation over fast pathway ablation.
Bogun F 1996 (131) 8837581	Prospective observational cohort	7 w/ noninducible AVNRT compared w/ 34 w/ inducible AVNRT	Spontaneous but noninducible AVNRT (w/ evidence of dual AV nodal physiology at EP study)	All evidence of dual AV node pathways was eliminated in six pts, and dual AV node physiology remained present in one pt. During a mean f/u period of 15±10 mo (range 8 to 27), no pt had a recurrence of symptomatic tachycardia (success rate 95%).	N/A	Slow pathway ablation may be clinically useful in pts w/ documented but noninducible PSVT who have evidence of dual AV node pathways First recommendation that slow pathway ablation be indicated in pts w/ spontaneous PSVT w/ dual AV node physiology but noninducible PSVT in EP study. Small sample size.
D'Este D 2005 (132) 16814416	Prospective cohort study	93	Pts w/ AVNRT prospectively followed for mean 13.2 y, compare outcomes of ablation (n=18) vs. AADs (n=24) vs. no therapy (n=38) AADs: flecainide, propafenone, verapamil, sotalol, atenolol, diltiazem	At f/u, asymptomatic for 3 y: Ablation: 100% AADs: 60.8% No therapy: 44.7% Untreated pts who became asymptomatic had a shorter duration of sxs before enrolment (3.7±1.5 vs. 7.1±3.6 y, p<0.05) and a shorter mean length of tachycardia episodes (3.8±2.4 vs. 42.6±17.8 min, p<0.02) than pts from same group who remained symptomatic	3 pts died, 10 lost to f/u	During a long-term f/u a considerable number of untreated pts w/ AVNRT become asymptomatic. Suggests that pts w/ infrequent and minor sxs may be able to be treated conservatively (i.e., no ablation or AADs. Study directly evaluates AVNRT and suggests efficacy of ablation over AADs. Limitations that the results are sx based.
Spector P 2009 (55) 19699343	Systematic review and meta-analysis to evaluate the safety and efficacy of RFA of AVNRT,	For AVNRT and AP-mediated: 39 primary studies w/ 49 treatment arms in 7,693 pts	Previous reviews or meta-analyses; animal or in vitro studies; subjects aged <18 y or mixed populations of which >15% were pediatric pts; f/u of <7 d; not studies of RFA; alternative energy sources used for	SVT (AVNRT and AP-mediated) Single- and multiple-procedure success, arrhythmia recurrence, repeat ablation, adverse events,	Single-procedure success: 93.2% (95% CI: 90.8-95.5%). Multiple-procedure success: 94.6% (95% CI: 92.4- 96.9).	First meta-analysis of RFA for AVNRT, AVRT (AP-mediated). Demonstrates high efficacy rates and low rates of complications.

	AP-mediated, and atrial flutter.		ablation; AV junction ablation w/ pacemaker implantation; <40 pts per arrhythmia or ablation technique; published only in abstract form; published before 1990; and published in languages other than English, Spanish, French, Italian, German, and Portuguese.	and death	Post-ablation arrhythmia: 5.6% (95% CI: 4.1-7.2%). Repeat ablation: 6.5% (95% C:I 4.7-8.3%) All-cause mortality: 0.1% Adverse events: 2.9%	
Outcomes (Registry Data)						
Hindricks G 1993 (57) 8131762	Prospective cohort	4398	AT/atrial flutter (n=141, 3.2%) AVJ (n=900, 20.5%) AVNRT (n=815, 18.5%) AVRT: (n = 2222, 50.5%) VT (n=320, 7.3%).	Incidence of complications	Complications occurred in 223 pts (5.1%) overall AT/atrial flutter: 5.0% AVJ: 3.2% AVNRT: 8.0% AVRT: 4.4% VT: 7.5% Complications more in AVNRT RFA compared to AVJ or AP ablation (p<0.001) Complications more in VT compared to AVJ (p<0.002) or AP (p<0.02)	Early report showing high incidence of complications after AVNRT ablation.
Hindricks G 1996 (58) 8682135	Prospective cohort	4463	AVNRT (n=880)	Incidence of AV block	AV block (4/ 880, 4.7%). AV block higher in fast pathway ablation (19/361, 5.3%, p<0.05) 6.3% in centers w/ limited experience in RFA (≤30 pts treated, p<0.05), and higher in these low-volume centers for both slow and fast pathway ablation (p<0.05)	Early report showing 5% incidence of AV block after RFA for AVNRT, and higher w/ fast pathway ablation.
Calkins H 1999 (59) 9892593	Prospective cohort	1050 (previously enrolled in RFA clinical trial)	RFA of AVNRT, AP, or AVJ AVNRT (n=373) AP (n=500) AVJ (n=121)	Efficacy and safety of RFA w/ long-term f/u.	Overall success: 95% Overall recurrence 6% Success: AVNRT: 97% AP: 93% AVJ: 100% Recurrence:	Shows RFA is a favorable option w/ low risk of complications and recurrence, and identifies pts who are at risk. Per-protocol analysis

					AVNRT: 5% AP: 8% AVJ: 2% Predictors of success: -AVNRT OR: 3.94 (95% CI: 1.93-8.04; p=0.0002) -Left free wall AP OR: 3.09 (95% CI: 1.46-6.53; p=0.0003) -Experience of ablation center (>39 pts) OR: 2.39 (95% CI: 1.21-4.71; p=0.012) Joint predictors of mortality: -EF (p=0.003) -SHD (p=0.016) -AVJ ablation (p=0.048)	
Scheinman MM 2000 (61) 10879389	Prospective cohort study (NASPE registry)	3,357	Ablation of AVNRT, AP, AVJ, atrial flutter, AT, IST, VT, idiopathic VT AVNRT (n=1,197 [35.6%) AVJ (n=646) AP (n=654) AT (n=216) Atrial flutter (n=447) IST (n=40)	Efficacy and safety of RFA w/ long-term f/u.	AVNRT Success: 96.1% Complications: 2% AVJ: Success: 96% Complications: 25 pts Recurrence: 3.5% AP: Success: 94-96% Complications: 31 pts total Recurrence: 4.6% AT: Success: 51-79% Complications: 5 total Recurrence: 15.2% Atrial flutter: Success: 86% Complications: 12 pts Recurrence: 14.7% IST: Success: 71% Complications: 2 pts Recurrence: 10%	Large series reporting success of RFA, and stratification by age group confirms safety and efficacy in elderly pts, as well as by type of facility (teaching vs. community).

Special Ablation Techniques						
Friedman PL 2004 (133) 15851143	Multicenter prospective study	157 (166 initially enrolled)	AVNRT (n=101) AVRT (n=44) AF (n=12)	Efficacy of cryomapping/ablation	Acute success overall 83% Success in AVNRT 91%, 69% AVRT and 67% AVJ (p<0.001) Per-protocol: Success in AVNRT 93%, 77% for AVRT and 67% for AVJ Long-term success after 6 mo 91% overall, 94% for AVNRT Cryomapping successfully identified ablation targets in 64% of pts, effects completely reversible w/in minutes in 94% of attempts	Acute success lower for CA compared to studies in RFA, but w/ no difference in long-term outcomes or arrhythmia recurrence. Later reports show improved success.
de Sisti A 2011 (134) 22017562	Systematic review	22 studies w/ 2,654 pts	Cryoablation for AVNRT compared to RFA	Overall success 95% (95% CI: 85-99%), but recurrence rate 11% (95% CI: 2-20%). RFA recurrence rate reported at 3-5%.	N/A	Cryoablation effective and safe, but lower long-term clinical efficacy compared to RFA.
Hanninen M 2013 (135) 24016223	Systematic review and meta-analysis	14 studies (5 RCTs), 5,617 pts (1990-2012). 3 studies pediatric	Pts w/ AVNRT treated w/ cryoablation vs. RFA (81%)	AVNRT recurrence (>2 mo post procedure; acute procedural failure and AV block requiring pacing	Acute failure w/ cryoablation was nonsignificantly slightly higher than w/ RFA (RR: 1.44; p=0.12). Long-term recurrence higher w/ cryoablation (RR: 3.66; p=0.0002) RFA associated w/ permanent AV block in 0.75% of pts, none w/ cryoablation (p=0.01).	Although late-recurrence more common w/ cryoablation than w/ RFA, avoidance of permanent AV block is advantageous
Santangeli P 2014 (136) 24293174	Systematic review and meta-analysis	14 studies (9 observational) w/ 2,340 pts (1980-2013)	Pts w/ AVNRT treated w/ CA (54%) vs. RFA (46%)	Successful ablation, procedural time, fluoroscopy time, complications	Acute success in 88% w/ RFA, vs. 83% treated w/ CA (OR: 0.72; p=0.16) RFA associated w/ shorter total procedure time (p=0.004), but slightly longer fluoroscopy time (p=0.002). Permanent AV block occurred in 0.9% RF case, none in CA cases (OR: 3.60; p=0.035). Freedom from recurrent AVNRT (10.5 mo median f/u) 97% in RF group vs. 90.9% in the CA group (OR: 0.40; p< 0.001).	RF significantly reduces the risk of long-term arrhythmia recurrence compared to cryoablation, but is associated w/ a higher risk of permanent AV block. No significant difference in acute success.

AAD indicates antiarrhythmic drug; AF, atrial fibrillation; AP, accessory pathway; AT, atrial tachycardia; AV, atrioventricular; AVJ, atrioventricular junction; AVN, atrioventricular node; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; bpm, beats per min; CA, cryoablation; CHF, congestive heart failure; CSM, carotid sinus massage; DC, direct current; ECG, electrocardiogram; ED, emergency department; EF, ejection fraction; EP, electrophysiological; FP, fast pathway; f/u, follow up; HR, heart rate; IST, inappropriate sinus tachycardia; IV, intravenous; MAT, multifocal atrial tachycardia; N/A, not applicable; NASPE, North American Society of Pacing and Electrophysiology; OR, odds ratio; PES, programmed electrical stimulation; PJRT, permanent junctional reciprocating tachycardia; PSVT, paroxysmal supraventricular tachycardia; pt, patient; RFA, radiofrequency ablation; RR, relative risk; SD, standard deviation; SHD, structural heart disease; SP, slow pathway; SR, sinus rhythm; SVT, supraventricular tachycardia; sx, symptom; VT, ventricular tachycardia; w/, with; and w/o, without.

Data Supplement 11. Randomized Trials Comparing Manifest and Concealed Accessory Pathways – Section 6.1

Study Name, Author, Year	Aim of Study	Study Type (Size, N)	Study Intervention Group (n)	Study Comparator Group (n)	Pt Population		Endpoints			P Values, OR: HR: RR: & 95% CI:	Study Limitations & Adverse Events
					Inclusion Criteria	*Exclusion Criteria*	*Primary Endpoint (efficacy) and Results*	*Safety Endpoint and Results*	*Secondary Endpoint and Results*		
Henthorn RW 1991 (26) 1898640	Double blind placebo controlled crossover trial of flecainide	34 pts	8 wk on flecainide	8 wk on placebo	13 w/ AVRT 7 w/ AVNRT 3 w/ AT 28 unknown	Syncopy, angina, and/or neurological sxs during tachycardia. Second or third degree AV block. NYHA CHF class III, IV	Flecainide superior to placebo. Flecainide associated w/ 79% freedom from PSVT and placebo 15% p<0.001. Median time to 1st PSVT 11 d in placebo group and 55 d in flecainide group. Flecainide slowed PSVT to 143±12 bpm from 178±12 bpm on placebo.	Side effects: flec 63% and placebo 36%. All not significant.	Flecainide was well tolerated.	Flecainide associated w/ 79% freedom from PSVT and placebo 15% p<0.001. Median time to 1st PSVT 11 d in placebo group and 55 d in flecainide group. Flecainide slowed PSVT to 143±12 bpm from 178±12 bpm on placebo. Side effects on flec 63% and placebo 36%. All not significant.	Study period was brief
Pritchett EL 1991 (28) 2001087	Double blind placebo controlled crossover trial of propafenone	33 pts	60 d on propafenone	60 d on propafenone	16 pts w/ PSVT and 17 w/ PAF. Not clear number of AP	NYHA class III or IV HF. Second or third degree AV block. Sxs of syncope, angina, neurological events during tachycardia.	Well-designed study showing propafenone superior to placebo. Propafenone prolonged the recurrence rate of	No serious side effects	N/A	Time to first recurrence prolonged for the propafenone group, p=0.004.	The study was brief and not clear how many AP pts studied.

							arrhythmia and was 20% the recurrence rate of placebo.				
UK Propafenone Study Group 1995 (31) 7586356	Double blind, placebo controlled study of propafenone	100 pts	Propafenone	Placebo	PSVT 52 pts AF 48 pts Unclear if any AP pts	Documented second or third degree AV block. Class III or IV HF. Sxs of syncope, angina, during tachycardia	Arrhythmia recurrence. Relative risk of treatment failure for placebo compared to propafenone was 6.8 (95% CI: 2.2-21.2; p<0.001; n=45) for PSVT and 6.0 (95% CI: 1.8-20.0; p=0.004) for AF.	One episode of wide QRS tachy.	Not applicable	Relative risk of treatment failure for placebo compared to propafenone was 6.8 (95% CI: 2.2-21.2; p<0.001; n=45) for PSVT and 6.0 (95% CI: 1.8-20.0; p=0.004) for AF.	Unusual study design.
Dorian P 1996 (32) 8607397	Randomized multicenter study of verapamil vs. flecainide for treatment of PSVT	121 pts	Verapamil	Flecainide	63 pts on flecainide and 58 verapamil. Followed for 8.1±5.1 and 7.5±5.4 mo, respectively.	Prior AF, atrial flutter, myocardial infarction, unstable angina. NYHA Class III or IV CHF. Second or third degree AV block.	86% of flecainide pt-mo and 73% of verapamil pt-mos w/ 0 or 1 episode of PSVT.	N/A	N/A	30% on flecainide and 13% on verapamil were free of PSVT (p=0.026)	Flecainide and verapamil were moderately effective for the prevention of PSVT.

AF indicates atrial fibrillation; AP, accessory pathway; AT, atrial tachycardia; AV, atrioventricular; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; bpm, beats per min; CHF, congestive heart failure; CI, confidence interval; HF, heart failure; N/A, not applicable; NYHA, New York Heart Association; PAF, paroxysmal atrial fibrillation; PSVT, paroxysmal supraventricular tachycardia; pt, patient; sx, symptom; and w/, with.

Data Supplement 12. Nonrandomized Trials, Observations Studies, and/or Registires of Manifest and Concealed Accessory Pathways – Section 6.1

Study Name, Author, Year	Study Type/ Design	Study Size	Inclusion/Exclusion Criteria	Primary Endpoint	Results/p Values	Summary/Conclusions
Risk Stratification of Symptomatic Patients with Manifest Pathways						
Klein GJ 1979 (137) 492252	Observational study of pts w/ WPW and VF	25	25 WPW pts w/ VF compared to 73 pts w/o	Comparing EP findings	Pts w/ WPW and VF had higher prevalence of AVRT (14/25 vs. 18/73, p=0.004) and multiple APs (5/25 vs. 4/73; p=0.012). The shortest preexcited RR was less in VF pts (mean RR 180 vs. 240	WPW pts w/ h/o VF had more rapid AF (mean RR 180 msec) and increased prevalence of AVRT and multiple APs compared to control.

					msec; p<0.0001) as was the mean RR (mean 269 vs. 340 msec; p<0.0001).	
Rinne E 1987 (138) 3630940	Observational study of clinical vs. induced rhythms	126	WPW pts w/ clinical AVRT and AF	Relation between clinical and induced arrhythmias	The shortest RR of clinical AF compared w/ the induced AF (r=0.72; p<0.00001). AVRT CL was similar (r=0.79; p<0.00001). 41% of pts w/ clinical AVRT had AF induced w/ shortest RR <250 msec.	There was good reproducibility between clinical and induced AF and AVRT. Clinical AVRT pts were at high risk for rapid AF at EP study.
Sharma AD 1987 (139) 3598007	Observational study comparing noninvasive and EP study	67	WPW pts w/ noninvasive and EP testing	Comparing findings of noninvasive tests and EP tests.	EP study (AF w/ shortest RR<250 msec) identified 7/9 pts w/ clinical VF. Continuous preexcitation during exercise testing had a sensitivity of 80%, specificity of 28.6% and predictive accuracy of 11.8%.	EP testing was more accurate than stress testing in predicting WPW pts at risk for VF. Stess testing had high sensitivity.
Gaita F 1989 (140) 2773792	Observational study of accuracy of noninvasive tests	65	Consecutive WPW pts studied w/ procainamide, stress testing and EP. 15 pts were asymptomatic; 50 had sxs.	Comparison of noninvasive tests to EP findings.	24 pts had high risk AF (shortest RR <250 msec, AP ERP<250 msec). Persistence of the delta wave during stress testing has a sens of 96%, spec of 17% to identify high-risk pts (PPV 40% and NPV 88%).	Stress tests and IV procainamide tests had good sensitivity and NPV but low specificity and PPV for identifying high risk WPW pts
Beckman KJ 1990 (141) 2303633	Observational study of ability of EP study to predict arrhythmic events	42	WPW pts w/ no sxs up to clinical AVRT/AF.	Assessing if EP findings predicted clinical events	During a f/u of 7.5±4.9 y, showed the only variables that correlated w/ subsequent arrhythmia were h/o documented arrhythmias before EP study (p<0.01) and inducible AVRT at EP study (p<0.05).	H/o arrhythmia and inducible arrhythmia predict subsequent events.
Pappone C 2012 (142) 22215859	Observational study identifying risk factors in symptomatic WPW pts	369	WPW pts followed to assess predictive factors from EP study	Evaluate the predictors of malignant rhythms	Mean f/u 42.1±10 mo. 29 pts w/ malignant arrhythmias, 168 asymptomatic on f/u, 172 w/ AVRT/AF. Malignant arrhythmia pts had shorter AP ERP (p<0.001), AVRT triggering AF (p<0.001), and multiple APs.	Short AP ERP, AVRT triggering AF, were independent predictors of malignant arrhythmias.
Spar DS 2012 (143) 22221954	Observational study of the utility of exercise testing	76 pediatric pts <22 y.	WPW pts w/ exercise and EP testing	Exercise test results compared to EP findings	11 pts w/ sudden loss of delta, 18 gradual, and 47 no loss during exercise. Of pts w/ 1:1 AP conduction <270 msec, none in sudden loss group and 18 in no loss group. Pts in gradual loss group more likely to have a left sided AP.	Pts w/ sudden loss of preexcitation during exercise had longer 1:1 conduction when the AP blocked and none had 1:1 over the AP <270 msec.
Wackel P 2012 (144) 22978820	Observational study of long term f/u of noninvasive tests	24 pediatric pts <22 y	WPW pts w/ Holter, stress test, ECG and EP	Noninvasive test results compared to EP findings	24 pts w/ at least one noninvasive test showing loss of preexcitation. 2 of the 24 had rapid AP conduction (1:1 over AP <260 msec). The noninvasive tests had a PPV of 92% and a NPV of 31%. 16 of 24 had loss of delta during stress test and none of those had rapid conduction at EP.	Small study showed loss of preexcitation during noninvasive testing had a high PPV and specificity for slow AP conduction during EP.
Pappone C 2014 (145) 25052405	Prospective single center registry of WPW pts	2169 pts	All pts w/ a manifest AP underwent EP study±RF. Followed 8 y	Both asymptomatic and symptomatic pts studied at EP to identify risk factors for VF	1001 pts (550 asymptomatic) did not undergo RF and 1168 (550 asymptomatic) underwent RF. F/u of 8 y. VF occurred in 1.5% of the no-RF group (mean age 11 y) and no VF occurred in the RF treated group (p<0.001). VF was associated w/ a short ERP of the AP w/ an optimal cut-off of 240 msec (p<0.001) and AVRT initiating AF (p<0.001).	Large single center registry showing that EP findings identified pts w/ a manifest AP at high risk for VF and the risk was eliminated w/ ablation.
Acute Treatment						
Sellers TD 1977 (146) 872319	Acute EP study of IV digitalis effects on AF in WPW	21 pts	WPW pts w/ AF induced during EP study and given IV digitalis	Safety for AF in WPW	Digitalis shortened the CL of the shortest preexcited RR in 6/21 pts increased the CL in 7/21 pts and had no effect in 5/21. Digitalis directly related to onset of AF degenerating to VF in 9/21	This study is old but highlights the risk of digitalis in WPW pts w/ AF

					pts. Each of these 9 had a shortest RR <230 msec during AF baseline.	
Sellers TD 1977 (147) 830205	Single center study of IV procainamide and quinidine in WPS pts w/ induced	33 pts	All pts w/ a manifest AP and induced AF	IV procainamide studied to assess effects on conduction during AF	IV procainamide prolonged the shortest RR between preexcited complexes during AF by 20-70 msec in 15 of 21 pts and no change in 6 pts.	IV procainamide prolonged the shortest RR between preexcited complexes in induced AF
Hamer A 1981 (148) 7223599	Single center study of IV verapamil in pts w/ AVRT	19 pts	All pts had AVRT: 12 w/ a manifest and 7 w/ a concealed AP	IV verapamil to assess EP changes and effects on AVRT	IV verapamil prolonged refractoriness and delayed conduction in the AV node but no effect on the AP. Sustained AVRT initiated in 15 pts and terminated by verapamil in 13 pts.	IV verapamil was effective in terminating AVRT
Hombach V 1981 (149) 7206601	Acute EP study of IV atenolol for treatment of induced PSVT	18 pts	Mixed group: 5 w/ AVRT, 2 w/ AVNRT, 6 w/ atrial flutter, 6 w/ AT, 1 w/ VT	IV atenolol given for treatment of induced PSVT	Atenolol was effective in preventing pacing induced AVRT in 3 of 5 pts w/ WPW.	Small study published in Klin Wochenschr showing IV atenolol prevented reinduction of AVRT in 3 of 5 pts.
Scheinman BD 1982 (150) 6812745	Case report	1 pt	WPW pt w/ AF	IV amiodarone given to treat AF	The ventricular rate during AF increased from 170 to 230 bpm	IV amiodarone accelerated the rate of AF in a pt w/ WPW
Morady F, et al., 1987 (151) 2439997	Observational study of IV propranolol administered during AF	10 pts	All pts w/ preexcited AF.	The effects of IV propranolol during preexcited AF were assessed.	AF terminated in 3 of the 10 pts. The mean ventricular rate during preexcited AF was slowed by 15-56 bpm in 6 pts; no effect in 3 pts; and increased from 203 to 267 bpm in 1 pt.	The authors concluded that IV propranolol should not be used in pts w/ preexcited AF if most QRS complexes are preexcited.
Schutzenberger W, et al., 1987 (152) 3610399	Case report	1 pt	WPW pt w/ AF	IV amiodarone given to treat AF	IV amiodarone accelerated the rate of preexcited AF	IV amiodarone accelerated the rate of AF in a pt w/ WPW
Huycke EC 1989 (153) 2918157	IV Diltiazem vs. placebo for the termination of PSVT	54 pts 20 pts AVNRT 34 pts AVRT (19 pts w/ manifest and 15 w/ concealed APs)		Safety and efficacy for termination of AVNRT and AVRT	PSVT terminated in 90% of pts w/ diltiazem and 19% w/ placebo. 100% of AVNRT pts converted and 81% of AVRT pts converted. Side effects: adverse effects in 6%.	IV diltiazem is safe and effective for treatment of AVRT
DiMarco JP 1990 (114) 2193560	Placebo controlled study of the acute treatment of PSVT w/ adenosine and IV verapamil	359 pts	PSVT pts given adenosine, placebo, or verapamil for termination. 36% had AVNRT and 64% had AVRT. 22% of pts had manifest APs.	Safety and efficacy of adenosine for PSVT	Dose ranging study. IV adenosine doses of 6, 9, 12 mg converted 62.3%, 80.2%, and 91.4% of PSVT. Placebo converted 10.7%, 14.3%, and 16.1% w/ 4-dose sequence. In trial 2, adenosine 6 mg followed by 12 mg had success of 57.4% and 93.4% (average time to termination 30 sec). AVNRT success 92% and AVRT success 97%. 61 total pts received adenosine. IV verapamil 5 mg followed by 7.5 mg if necessary was successful in 81.3% and 91.4%. 95% pts w/ AVNRT and 96% pts w/ AVRT were successfully converted w/ verapamil. 64 total pts received verapamil; manifest pts not excluded.	Both IV adenosine and IV verapamil effective for acute treatment of AVNRT and AVRT.

					Side effects: 36% w/ adverse effects lasting <1 min. Severe side effects in 2.3% including flushing, chest pain, and dyspnea.	
Furlong R 1995 (154) 7605518	Acute prospective case series study of adenosine for termination of PSVT	31 pts	PSVT of undocumented mechanism	Adenosine given prehospital for management of PSVT	31 pts w/ PSVT, 28 (90%) converted to sinus after the first (16) or second or third (13) dose. No significant complications reported	Adenosine was effective for treating PSVT (unclear how many pts had AVRT)
Boriani G 1996 (155) 8644602	Case report	1 pt	WPW pt w/ AF	IV amiodarone given to treat AF	IV amiodarone given to treat WPW w/ preexcited AF resulted in VF	IV amiodarone resulted in ventricular fibrillation
Wen ZC 1998 (41) 9851958	Acute study of vagal maneuvers for termination of PSVT	133 pts	Mixed group w/ PSVT: 85 w/ AVRT	Effects of vagal maneuvers on PSVT termination	Of 85 pts w/ AVRT, vagal maneuvers terminated 53%	Vagal maneuvers terminate 53% of pts w/ AVRT
Glatter KA 2001 (156) 11602497	Acute study of IV ibutilide in pts w/ WPW + AF	22 pts	WPW pts w/ AF at time of EP study	EP properties, safety and AF termination	Ibutilide terminated AF in 95%. In 18 additional pts ibutilide prolonged the AP ERP from 275±40 to 320±60 msec p<0.01. No placebo arm.	Ibutilide sass safe and effective terminating AF is WPW.
Shiraishi H 2002 (157) 12135176	Case report	1 pt	Pt w/ a concealed pathway and AVRT	IV verapamil given to treat AVRT	IV verapamil terminated AVRT the pt developed non-sustained polymorphic VT. Authers did EP study and mechanism unknown.	IV verapamil terminated AVRT in pt w/ concealed pathway but non-sustained polymorphic VT then developed
Neumar RW, et al., 2010 (158) 20956224	AHA ACLS Guidelines	N/A	Acute treatment of pts w/ bradycardia and tachycardia	Expert developed guidelines	Reviews role of direct current electrical cardioversion, vagal maneuvers and antiarrhythmic drug therapy for the treatment of supraventridular tachycardia in the emergency department including WPW w/ AF and SVT	Electrical cardioversion recommended for the treatment of WPW w/ AF or SVT and hemodynamic instability
Delaney B 2011 (159) 20926952	Meta-analysis of the efficacy of adenosine vs. verapamil for treatment of stable PSVT	692 pts/events	PSVT of undocumented mechanism	8 trials included that compared verapamil and adenosine	Adenosine converted 90.8% and verapamil 89.9%. More minor side effects w/ adenosine. More hypotension w/ verapamil (3.7% vs. 0.6%).	Both adenosine and verapamil were effective for termination of PSVT. Verapamil had more associated hypotension.
Smith GD, et al., 2013 (39) 23543578	Cochrane Database review of randomized trials of Valsalva	316 pts i	All pts w/ SVT. Number of pts w/ AVRT was not specified.	Valsalva compared to "other" vagal maneuvers	The reversion of SVT to sinus rhythm following Valsalva in the 3 studies was 19.4%, 45.9%, and 54.3%	Valsalva was effective in converting SVT to sinus rhythm.
Long-Term Pharmacological Treatment						
Sellers TD 1977 (146) 872319	Acute EP study of IV digitalis effects on AF in WPW	21 pts	WPW pts w/ AF induced during EP study and given IV digitalis	Safety for AF in WPW	Digitalis shortened the CL of the shortest preexcited RR in 6/21 pts increased the CL in 7/21 pts and had no effect in 5/21. Digitalis directly related to onset of AF degenerating to VF in 9/21 pts. Each of these 9 had a shortest RR <230 msec during AF baseline.	This study is old but highlights the risk of digitalis in WPW pts w/ AF
Bauernfeind RA, et al., 1980 (160)	Single center study of multiple drugs given IV and then	21 pts studied acutely; 18 pts followed 6-50	All pts w/ AV node reentry	Drug efficacy at minimal f/u of 6 mo	Pts were tested w/ IV drug to determine if the drug prevented induction of AVNRT. Successful pts were then treated long term w/ oral drugs. 18 pts	Small number of pts on each medication showing moderate success.

7438370	long term for AV node reentry	mo			followed at least 6 mo, 72% w/o recurrence: 3 of 5 pts on digoxin only; 2 of 3 pts on digoxin plus propranolol; 4 of 4 pts on propranolol only; 1 of 3 pts on procainamide; and 3 of 3 pts on quinidine only.	
Sakurai M 1983 (161) 6837416	Single center study of IV and oral verapamil for PSVT	15 pts studied acutely and followed 3 to 31 mo (mean 15 mo)	AVNRT in 4 and AVRT in 11 (all w/ a concealed AP)	Drug efficacy at minimal f/u of 3 mo	13 pts followed 3-31 (mean 15) mo w/ 8 having no recurrent PSVT and 5 having decreased frequency and duration. Mild constipation in 4.	Small, uncontrolled study of oral verapamil for PSVT including some pts w/ AVRT
Feld GK 1984 (162) 6707383	EP testing after amiodarone loading and then long term f/u	10 pts EP test at ≥4 wk	All pts w/ AP and AVRT	Assessment of EP properties	9 pts no longer had inducible AVRT. 1 pt had nonsustained AVRT. AP ERP increased by 20% anterograde p<0.05 and 40% retrograde p<0.02 symptomatic control of arrhythmia during 20 mo. 1 pt stopped due to side effects	Amiodarone had favorable effects on AP and long-term rhythm control. Small number of pts
Feld GK 1988 (163) 3336964	EP testing and long term assessment of amiodarone	10 pts Acute EP study and mean 30 mo f/u	All pts w/ WPW and AF w/ a rapid ventricular response	EP measurement of drug effect and long term f/u of rhythm control	EP study—amiodarone prolonged the AP ERP 38% (p<0.01) and atrial ERP 34% (p<0.01). Amiodarone prolonged the mean RR 90% and minimum RR 104% (p<0.01) during AF. Long-term f/u—no AF or VF. SVT in 1 who went to surgery. 1 serious and 5 minor side effects	Amiodarone was safe and effective preventing AF in a small number of pts although side effect were significant.
Chimienti M 1995 (30) 8682031	Open label, no placebo comparison of flecainide vs. propafenone	335 pts 12 mo mean f/u	PSVT 135 PAF 200 Unclear number of AVRT or WPW	Arrhythmia recurrence	Probability of 12 mo safe and effective treatment for PSVT was 93% for flecainide and 86% for propafenone p=0.24. For AF it was 77% for flecainide and 75% for propafenone p=0.72. One VT on propafenone, Two rapid AF on flecainide	Propafenone and flecainide had similar efficacy for PSVT and AF
Hopson JR 1996 (164) 8607395	Open-label multicenter trial of flecainide	151 pts 1 y	PSVT 67 PAF 67 CAF 17, unclear number of AVRT or WPW	Arrhythmia recurrence	At 1 y of treatment, 87% of PSVT, 73% of PAF, and 56% of CAF had improved symptomatically. Proarrhythmia is 3, CHF in 7. 65% w/ visual sx or headache	Poor study design, flecainide effective but important cardiac events. Study done before results of CAST known.
Catheter Ablation: Ablation of Standard APs						
Jackman WM 1991 (165) 2030716	Observational study of RF ablation and short term f/u for WPW	166	166 WPW pts w/ 177 pathways	Acute ablation success and at 8 mo	AP conduction eliminated in 164 of 166 pts (99%) by a median of 3 RF applications. F/u at 8±5.4 mo showed preexcitation or AVRT returned in 15 pts who underwent a 2nd RF. EP study at 3±9 mo after RF in 75 pts verified absence of AP. 3 pts (1.8%) w/ complications – AV block, cardiac tamponade, pericarditis.	Large series reporting success and safety of RF for treating AP in WPW.
Calkins H 1992 (166) 1555278	Observational study of RF in WPW	250	183 pts w/ manifest AP and 84 concealed. Failed 2.0+/-1.6 AADs	Acute, 3 mo EP study, and 10±4 mo success	250 pts w/ 267 APs. 94% w/ both acute success and free of tachycardia at 10 mo. 4% w/ complications: MI-1, AV block-3, valve damage-1, TIA-1, vascular-2	Large series reporting success and safety of RF in pts w/ APs
Kugler J 1994	Observational multicenter study of	652	615 APs	Acute and short-term f/u 13.5 mo	Success highest in left free wall APs (89%), high volume centers; lowest in right free wall AP's	Large multicenter series, RF acceptable treatment for AP w/

(167) 8164700	RF ablations in young pts SVT				(69%), pt weight >80 kg, or presence of CHD. Recurrence in 12-40%, higher in right free wall AP or presence of CHD. 3.7%; one procedural death; AV block, pericardial eff/usion; higher if weight <15 kg; One post procedural death in 5 wk old infant w/ torn mitral valve.	attention to pt age and body weight and center experience.
Calkins H 1999 (59) 9892593	Multicenter observational study of RF using Atakr for PSVT	1050	500 pts w/ AP; 373 w/ AVNRT; 121 of AV junction	Acute and long term safety and f/u.; median f/u 6.3 mo	Acute AP success 93% for single APs and 86% for multiple APs. 7.8% of pts w/ AP had a recurrence. 3% w/ major complication and 8.2% minor. Death-3, stroke-2, AV block-10, tamponade-6, valve damage-1, MI-1	Large series showing good acute success, 8% recurrence, and major complications in 3%. This is the most accurate study listing complications.
Dagres N 1999 (168) 10581141	Observational study of RF for APs	519	All pts w/ APs	Acute and long term f/u at 22.6±12.4 mo	398 pts responded to f/u questionnaire. 85.4% asymptomatic and 10.6% taking AADs. 41% of pts w/ failed ablations were asymptomatic.	Large series reporting good long term success w/ RF for APs
Schlapfer J 2001 (169) 11259148	Observational study of RF for APs followed long term	180	Pts. w/ APs undergoing RF failing 1.75+/- 1.25 AADs	Long-term f/u at a median of 48.1 mo	All pts has successful procedure. Pts followed median of 48.1 mo—79% remained asymptomatic. 10% required further RF' or meds. 4% w/ procedure complications: vascular-5, valve perforation-1, TIA-2	Large study of acute RF success w/ 21% having sxs by 4 y but only 10% requiring additional therapy.
Belhassen B 2007 (170) 17491219	Observational study of RF for APs	508	508 pts w/ 535 APs.	Acute and long term RF results 85±43 mo f/u	46.8% manifest and 44.4% concealed. 572 procedures in the 508 pts. Acute RF success 93.1% and multiple RF 95.3%. 9.9% recurrence after 1st RF. At 85 mo f/u, 94.9% cure. 2 major complications—pericardial effusion, MI	Large series showing long-term success and safety of RF for APs.
Pappone C, et al., 2014 (145) 25052405	Prospective single center registry of WPW pts	2169 pts	All pts w/ a manifest AP underwent EP±RF. Followed 8 y	Both asymptomatic and symptomatic pts studied at EP to identify risk factors for VF	1001 pts (550 asymptomatic) did not undergo RF and 1168 (550 asymptomatic) underwent RF. F/u of 8 y. VF occurred in 1.5% of the no-RF group (mean age 11 y) and no VF occurred in the RF treated group (p<0.001). VF was associated w/ a short ERP of the AP w/ an optimal cut-off of 240 msec (p<0.001) and AVRT initiating AF (p<0.001).	Large single center registry showing that EP findings identified pts w/ a manifest AP at high risk for VF and the risk was eliminated w/ ablation.

AAD indicates antiarrhythmic drugs; ACLS, Advanced Cardiovascular Life Support; AF, atrial fibrillation; AHA, American Heart Association; AP, accessory pathway; AT, atrial tachycardia; AV, atrioventricular; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; bpm, beats per min; CAF, chronic atrial fibrillation; CHF, congestive heart failure; CL, cycle length; EP, electrophysiological; ERP, effective refractory period; f/u, follow up; h/o, history of; IV, intravenous; MI, myocardial infarction; N/A, not applicable; NPV, negative predictive value; PAF, paroxysmal atrial fibrillation; PPV, positive predictive value; PSVT, paroxysmal supraventricular tachycardia; pt, patient; FR, radiofrequency; RVR, rapid ventricular response; SVT, supraventricular tachycardia; sx, symptom; TIA, transient ischemic attack; VF, ventricular fibrillation; w/, with; w/o, without; and WPW, Wolff–Parkinson-White syndrome.

Data Supplement 13. Summary of Included Studies – ERC Report (Section 6.2)

Study (Author, Year)	Study Design	Sample Size (N)	Participant Characteristics	Inclusion Criteria	Exclusion Criteria

Milstein S 1986 (171) 3706161	Uncontrolled prospective cohort study. All pts underwent an EP study.	42	• Mean age (±SD) 36 y (±12 y); age range 7-77 y • Gender: 21 (50%) men and 21 (50%) women • SHD: ---	• WPW pattern seen on a routine ECG. These pts were considered asymptomatic because they had neither documented arrhythmias nor a h/o sustained palpitations	---
Satoh M 1989 (172) 2466266	Uncontrolled observational cohort study. All pts underwent an EP study.	95 (34 asymptomatic and 61 symptomatic pts)	• Mean age (± SD) 32 y (± 19 y) • Male 73% • SHD 13% • Intermittent preexcitation 23%	• WPW pattern • Asymptomatic (neither documented tachycardia, nor a h/o palpitations suggestive of paroxysmal tachycardia.)	---
Klein GJ 1989 (173) 2710202	Uncontrolled prospective observational study. All pts underwent an EP study.	29	• Age (±SD): 50 y (±18 y) in the preexcitation lost subgroup 39 y (±11 y) in the preexcitation persistent subgroup • Gender: 17/29 (58.6%) men, 12/29 (41.4%) women • SHD: ---	• Asymptomatic WPW ECG pattern • No documented tachycardia and no h/o sustained tachycardia.	---
Leitch JW 1990 (174) 2225373	Uncontrolled prospective observational study. All pts underwent an EP study.	75	• Mean age (± SD) 34 y (± 13 y), age range 7-77 y • Male 44 (59%) • SHD 5/75 (7%): (1 w/ CAD, 2 w/ cardiomyopathy, 1 w/ VHD, 1 w/ Ebstein's anomaly)	• Asymptomatic w/ WPW ECG pattern	• All pts underwent sx-limited exercise stress testing and 24-h Holter monitoring and were excluded from the study if SVT was documented at any time. • Other specific exclusions were intermittent preexcitation either at rest or during exercise testing and EP study.
Brembilla-Perrot B 2001 (175) 11707045	Uncontrolled prospective observational study. All pts underwent testing w/ transesophageal stimulation.	92	• Mean age (±SD): 34 y (±15 y), age range 11-69 y • 68 men, 24 women • No SHD	• Asymptomatic WPW ECG pattern • No documented tachycardia and no h/o sustained tachycardia	• Documentation of SVT at any time
Pappone C 2003 (176) 12535816	Uncontrolled prospective observational study. All pts underwent an EP study.	212	• Mean age of overall population (± SD): 35.8 y (± 20.5 y), age range 7-63 y. Gender in overall population: N/A. SHD in overall population was present in 10/212 (5%) (5 w/ MVP, 2 w/ HCM, 3 w/ hypertension) • Mean age (±SD) of the 162 pts w/ complete f/u 33.6 y (±14.3 y), age range 7-63 y. Male 105/162 (65%).	• Asymptomatic WPW pattern was found either incidentally at routine examination or during a medical check-up before admission to a competitive sport or a high-risk occupation	---

			SHD was present in 4/162 (3 w/ MVP, 1 w/ HCM)		
Pappone C 2003 (177) 14602878	Combined RCT and prospective observational cohort study. All pts underwent EP study. Pts w/ inducible arrhythmia on EP study who were ≤35 y were randomized to ablation vs. no ablation. The remaining pts were followed as an observational cohort.	224 (EP study identified 76 high-risk pts who were then enrolled in a RCT and 148 low-risk pts enrolled in a prospective observational cohort study)	• Median (IQR) age 23 y (15-30 y) for ablation group and 22 y (15-30 y) for no ablation group. Male sex 53% in ablation arm and 47% in no ablation group. No SHD in either group. • Median (IQR) age for observational cohort 36 y (27-48 y). Male sex 59% in this cohort. SHD 7%.	• Ventricular preexcitation documented by 12-lead ECG • Absence of arrhythmia-related sxs	• Participation in other investigational protocols • Age <13 y • Pregnancy • Concomitant medical conditions
Santinelli V 2009 (178) 19808453	Uncontrolled prospective observational study. All pts underwent an EP study	293	• Median age (IQR) 36 y (28-48 y) • Male 61%	• Incidental WPW pattern on ECG • Asymptomatic based on an accurate history	• Participation in other research studies
Pappone C 2014 (145) 25052405	Uncontrolled prospective observational study. All pts underwent an EP study. They reported data by treatment w/ catheter ablation.	2169 (756 asymptomatic and 550 asymptomatic and w/ no ablation and 1413 symptomatic pts)	• Median age 19 y, male preponderance among asymptomatic pts (63%). • SHDs were found in 1.5% of asymptomatic pts	• Asymptomatic and symptomatic pts w/o prior ablation or documented life-threatening arrhythmias who consented to undergo a baseline EP study	---

CAD indicates coronary artery disease; ECG, electrocardiogram; EP, electophysiological; HCM, hypertrophic cardiomyopathy; IQR, interquartile range; MVP, mitral valve prolapse; N/A, not applicable; pt, patient; RCT, randomized controlled trial; SD, standard deviation; SHD, structural heart disease; SVT, supraventricular tachycardia; sx, symptom; VHD, valvular heart disease; w/, with; w/o, without; WPW, Wolff-Parkinson-White syndrome; and ---, not available.

Data Supplement 14. Comparators and Outcomes – ERC Report (Section 6.2)

Study (Author, Year)	Study Groups	Results of Noninvasive Testing	Results of Invasive EP Study	Acute Outcome of Catheter Ablation	Clinical Outcomes of Interest	Duration of F/u	Loss to F/u
Milstein S 1986 (171) 3706161	Group 1: Asymptomatic WPW pattern	N/A	43 APs in 42 asymptomatic pts. Mean ERP of AP was 333±106 msec in asymptomatic pts vs. 298± 42 msec in asymptomatic pts (p<0.025). Mean shortest RR interval during AF 277±48 msec in the asymptomatic groups vs. 247±51 msec in the symptomatic group (p<0.025). Sustained AVRT could be induced in only 1 pt.	No ablation	1 pt died of metastatic carcinoma after 43 mo, 1 pt died suddenly after he had agreed to participate in the study but before EP study could be performed. 4 pts received propranolol because of undocumented "skipped beats." All other pts remained asymptomatic.	29±18 mo	None
Klein GJ 1989 (173) 2710202	Group 1: Invasive EP study w/o catheter ablation	N/A	28/29 (97%) pts had only 1 AP and 1/29 (3%) pts had more than 1 AP. The mean (± SD) ERP of pathway(s) at baseline 334 msec (±105 msec) on the	No ablation	Sustained PSVT 2/29 (7%) (during 36-79 mo); 27/29 (93%) remained asymptomatic; 9/29 (31%) lost WPW pattern on ECG.	36-79 mo	None

			initial study and 301 msec (±78 msec) on the f/u study. The shortest RR interval (±SD) during induced AF was 266 msec (±39 msec). Sustained AF was induced in 2/29 (7%) pts on the initial study and 11/29 (38%) pts on the f/u study.				
Satoh M 1989 (172) 2466266	Group 1: Asymptomatic pts w/ WPW pattern	Intermittent preexcitation on ECG recording 23%	Number of pts w/ multiple APs not reported. Baseline mean ERP of AP was 288±29 msec in asymptomatic pts. Shortest RR in AF not reported. AVRT induced in 6/34 (18%) pts in the asymptomatic group, sustained AF was induced in 2/34 (6%) of asymptomatic pts.	No ablation	Group 1: no events Group 2: 2 pts w/ symptomatic WPW syndrome had VF and were resuscitated successfully	Mean 15 mo (range 2 to 47 mo)	---
Leitch JW 1990 (174) 2225373	Group 1: Invasive EP study w/o catheter ablation	N/A	At baseline, the median ERP of the AP was 293 msec (IQR 280-310 msec), and the median retrograde ERP of the AP was 288 msec (IQR 240-320 msec). The median shortest RR interval during preexcited AF was 274 msec (IQR 240-325 msec) in 72 pts, was ≤250 msec in 23 pts and was ≤200 msec in 8 pts. AVRT was induced in 12/75 (16%) and sustained AF was induced in 23/75 (31%).	No ablation	3/75 (4%) died of noncardiac causes, 1/75 (1%) pt died suddenly after initial consultation but before EP study was done. 5/75 (7%) developed symptomatic AVRT. 1/75 (1%) developed symptomatic AF. The presence of sustained AVRT at EP study did not differentiate pts who remained asymptomatic from pts who became symptomatic. Only 1 (4%) pt developed clinical AF of the 23 pts in whom AF was induced at EP study.	Median 4.3 y (range 1-9 y)	None
Brembilla-Perrot B 2001 (175) 11707045	Group 1: Transesophageal stimulation	All pts had 24-h Holter and stress test performed prior to study entry and only those w/o supraventricular arrhythmia were included	The number of APs found was not reported. The ERP of pathway(s) at baseline and during isoproterenol infusion were not reported. Shortest RR interval (<250 msec) during induced AF was present in 20/92 (22%) pts. Atrial tachyarrhythmia was induced in 27% of pts.	No ablation	3/92 (3%) pts developed symptomatic AF several y later. Of these 3 pts, 1 presented w/ AF and then VF 1 d after an aortic aneursymectomy. Among the 42 pts considered to have a benign form of WPW syndrome, there was no clinical event, except a death related to an accident.	---	---
Pappone C 2003 (176) 12535816	Group 1: Invasive EP study w/o catheter ablation	N/A	17/162 (10%) had multiple APs. Baseline mean (± SD) ERP 275.2 msec (± 33.8 msec). Isoproterenol mean (± SD) ERP 246.1 msec (± 30.5 msec). Shortest RR in AF not	No ablation	129/209 (62%) remained asymptomatic at the end of follow- up, whereas 33 (16%) developed arrhythmic events: SVT in 25, AF in 8, documented VF in 3/209 (aborted sudden death in 2 (both had developed sxs due to AF) and sudden	37.7±16.1 mo; range 14 to 60 mo	3/212 (1.4%) 47/212 who ref/used the 5-y EP study were excluded from the analysis

			reported 47/162 (29%) had inducible arrhythmia: nonsustained AF in 17, sustained AF in 19, inducible AVRT that degenerated into totally preexcited sustained AF in 11.		death in 1/209)		
Pappone C 2003 (177) 14602878	Group 1: Ablation Group 2: No ablation Group 3: Low-risk group followed as an observational cohort	N/A	15/37 (41%) pts in the ablation group had inducible AVRT. In 8 additional pts, AVRT degenerated into sustained AF. The median number of RF applications was 9 (range, 5 to 22).	Ablation was acutely successful in all pts. Complications related to EP study (2 pneumothoraxes and 1 large femoral hematoma) developed in 3 (1%) pts. An ablation-related complication (permanent right bundle-branch block) developed in 1/37 (3%) pt w/ an anteroseptal AP.	2/37 (5%) pts in the ablation group had an arrhythmic event found on EP study to be due to AVNRT in both pts. W/in a mean of 15 mo, 21/35 (60%) pts in the no ablation group had an arrhythmic event which was SVT in 15 pts, AF in 5 pts, and VF (not preceded by sxs) in 1 pt. Among the high-risk controls (group 2), the 5-y rate of arrhythmic events was 77% vs. 7% in the ablation group. In the observational cohort, sxs of SVT developed in 6 pts and 20 pts lost ventricular preexcitation.	Ablation group median f/u 27 mo, range 9-60 mo. Control group median f/u 21 mo, range 8-60 mo.	None
Santinelli V 2009 (178) 19808453	Group 1: Invasive EP study w/o catheter ablation	N/A	Anterograde ERP of AP ≤250 msec was present in 39/293 (13%) pts. Multiple APs were found in 13 (4%) pts. Inducible arrhythmia was found in 47 (16%) pts.	No ablation	262/293 (89%) pts did not experience arrhythmic events, remaining totally asymptomatic, whereas 31/293 (11%) pts had an arrhythmic event, which was potentially life-threatening in 17 of them. Potentially life-threatening tachyarrhythmias resulted in resuscitated cardiac arrest (1 pt), presyncope (7 pts), syncope (4 pts), or dizziness (5 pts).	Median duration of f/u after EP study was 67 mo (range 8 to 90)	---
Pappone C 2014 (145) 25052405	Group 1: Asymptomatic pts w/ WPW pattern (they presented data on symptomatic pts and by whether or not catheter ablation of the AP was done), but the groups were not matched and selection bias was not adjusted for)	---	No ablation: Multiple APs in 59 (6%), median (IQR) ERP of AP 280 msec (250-300 msec). Inducible AVRT triggering AF on EP study was found in 47 (5%) of pts. W/ Ablation: Multiple APs in 80 (7%), median ERP (IQR) of AP 280 msec (250-300 msec). Inducible AVRT triggering AF on EP study was found in 73 (6%) of pts.	206/756 asymptomatic pts were treated w/ ablation; ablation was successful in 98.5%.	No ablation: during a median f/u of 22 mo VF occurred in 13/550 (2%) asymptomatic pts (almost exclusively in children). During a median f/u of 46.5 mo, 48/550 (9%) additional asymptomatic pts experienced malignant arrhythmias 86/756 (11%) of the asymptomatic pts developed benign arrhythmias (AVRT and AF). W/ ablation: no pt developed malignant arrhythmias or VF over the 8 y of f/u.	Median 96 mo	No ablation: completeness of f/u was 99.8% at 1 y and 92.3% at the end of the study W/ ablation: completeness of f/u was 95.5% at 1 y and 90.2% at the end of the study

AF indicates atrial fibrillation; AP, accessory pathway; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventrial reentrant tachycardia; ECG, echocardiogram; EP, electrophysiological; ERP, effective refractory period; f/u, follow up; IQR, interquartile range; N/A, not applicable; pt, patient; RF, radiofrequency; SD, standard deviation; SVT, supraventricular tachycardia; VF, ventricular fibrillation; w/, with; w/o, without; WPW, Wolf-Parkinson-White syndrome; and ---, not available.

Data Supplement 15. Quality Assesment of Included Studies – ERC Report (Section 6.2)

Study (Author, Year)	Representativeness of the Cohort	Selection of a Nonexposed Cohort	Ascertainment of Exposure	Demonstration that Outcome of Interest was not Present at Enrollment	Independent Blind Assessment of Outcomes	Was Follow Up Long Enough for Outcomes to Occur?	Adequacy of Follow Up of Cohort (Including Loss to Follow Up)	Precision of Findings
Milstein S 1986 (171) 3706161	Yes	N/A (all pts underwent EP study)	All pts underwent EP study	Yes	---	Yes	Yes	Imprecise due to small sample size
Klein GJ 1989 (173) 2710202	Yes	N/A (no comparator group)	All pts underwent EP study	2/29 had SVT between scheduling EP study and when EP study was performed	---	Yes	Yes	N/A (no comparator group)
Satoh M 1989 (172) 2466266	Yes	N/A (all pts underwent EP study)	All pts underwent EP study	Yes	---	Yes	---	Imprecise (no events)
Leitch JW 1990 (174) 2225373	Questionable	N/A (no comparator group)	All pts underwent EP study	Yes	---	Yes	Yes	N/A (no comparator group)
Brembilla-Perrot B 2001 (175) 11707045	Yes	N/A (no comparator group)	All pts underwent EP study	Reasonable based on the absence of sxs. Pts had to have a normal ECG, exercise stress test and 24-h Holter monitor	---	Uncertain as duration of f/u was not reported	F/u and loss to f/u were not reported	N/A (no comparator group)
Pappone C 2003 (176) 12535816	Questionable	N/A (no comparator group)	All pts underwent EP study	Yes	---	Yes	Questionable	N/A (no comparator group)
Pappone C 2003 (177) 14602878	Questionable	Yes	Yes	Reasonable based on the absence of sxs	The events were reviewed by an independent committee whose members were unaware of the pts' treatment assignments	Yes	Yes	Fairly precise w/ 95% CI: 0.02-0.33 for arrhythmic events and 95% CI: 0.002-0.104 for event-free survival
Santinelli V 2009 (178) 19808453	Questionable	N/A (no comparator group)	All pts underwent EP study	Yes	---	Yes	---	N/A (no comparator group)
Pappone C 2014 (145) 25052405	Questionable	N/A (no comparator group)	All pts underwent EP study	Yes	---	Yes	---	N/A (no comparator group)

CI indicates confidence intervals; ECG, echocardiogram; EP, electrophysiological; f/u, f/u; N/A, not applicable; pt, patient; SVT, supraventricular tachycardia; sx, symptom; w/, with; and ---, not available.

Data Supplement 16. Randomized Trials Comparing Atrial Flutter – Section 7

Study Name, Author, Year	Aim of Study	Study Type (Size, N)	Study Intervention Group (n)	Study Comparator Group (n)	Pt Population		Endpoints			P Values, OR: HR: RR: & 95% CI:	Study Limitations & Adverse Events
					Inclusion Criteria	*Exclusion Criteria*	*Primary Endpoint (efficacy) and Results*	*Safety Endpoint and Results*	*Secondary Endpoint and Results*		
Platia EV 1989 (179) 2564725	The effects of esmolol, an ultrashort-acting beta blocker, and verapamil were compared in controlling ventricular response in 45 pts w/ AF or atrial flutter	Randomized, parallel, open-label study. 45 pts	Esmolol (n = 21)	Verapamil (n = 24)	Pts w/ either new onset (less than 48 h, n = 31) or old onset (greater than 48 h, n = 14) of AF or flutter w/ rapid ventricular rate	Uncontrolled CHF, SSS w/o pacemaker, h/o intolerance to beta blockers or ca-channel blockers, AMI <3 d, impaired renal and hepatic function, SVT other that AF or atrial flutter, digitalis toxicity, SBP <100 mm Hg unless it was usual	Drug efficacy was measured by ventricular rate reduction and conversion to sinus rhythm. HR declined w/ esmolol from 139 to 100 bpm and w/ verapamil from 142 to 97 bpm. 50% of esmolol-treated pts w/ new onset of arrhythmias converted to NSR vs. 12% w/ verapamil.	N/A	N/A	HR decline w/ esmolol (p<0.001); HR decline w/ verapamil (p<0.001). Conversion w/ esmolol vs. verapamil (<0.03).	Mild hypotension both groups
Salerno DM 1989 (180) 2650517	study evaluates the effectiveness and safety of IV diltiazem for the treatment of AF and atrial	Double-blind, parallel, randomized, placebo-controlled. 113 pts w/ AF or flutt	IV diltiazem 0.25 mg/kg/2 min followed 15 min later by 0.35 mg/kg/2 min if the first dose was tolerated but ineffective. If a pt did not respond, the code was broken and the pt was	Identical placebo	113 pts w/ AF or flutter, a ventricular rate greater than or equal to 120 bpm and systolic BP greater than or equal to 90 mm Hg.	Severe HF	Of 56 pts, 42 (75%) randomized to receive diltiazem responded to 0.25 mg/kg and 10 of 14 responded to 0.35 mg/kg, for a total response rate of 52 of 56 pts (93%),	Mild hypotension	N/A	Response to diltiazem vs. placebo (p<0.001)	IV diltiazem was rapidly effective for slowing the ventricular response in most pts w/ AF or atrial flutter. BP decreased slightly. Side effects were mild.

	flutter.		allowed to receive open-label diltiazem if placebo had been given.				whereas 7 of 57 pts (12%) responded to placebo.				
Van Gelder IC 1989 (181) 2511744	Efficacy and safety of flecainide acetate in the maintenance of sinus rhythm after electrical cardioversion of chronic AF or atrial flutter.	81 pts	N/A	N/A	Chronic AF or flutter	Age <16 or >80 y; CHF or angina pectoris > III (NYHA); MI <2 y, flecainide intolerance, BBB, SSS w/o pacemaker, antiarrhythmics, severe systemic disease	Multiple regression analysis showed New York Heart Association class I for exercise tolerance (p=0.0004) and flecainide treatment (p=0.01) to be the main factors increasing the arrhythmia-free episode. However, Mantel-Cox lifetable analysis did not reveal significant differences between arrhythmia-free survival curves of both treatment groups. In the flecainide-treated group, 9% of pts experienced side effects, mostly related to negative dromotropic effects. The incidence of ventricular proarrhythmia	N/A	N/A	N/A	9% of pts treated w/ flecainide had adverse events (e.g,sinus arrest, AV block, rate related LBBB). Moderate doses of flecainide (not >300 mg) recommended after cardioversion

							in this group of pts was low.				
Suttrop MJ 1990 (182) 2123909	Cardioversion w meds: Single blind randomized study of IV propafenone (2 mg/kg per 10 min) vs. flecainide (2 mg/kg per 10 min)	50 pts w/ AF or atrial flutter	AF or flutter Group A- 20 pts w/ AF treated w/ propafenone Group C- 5 pts w/ atrial flutter treated w/ proopafenone	AF or flutter Group B-20 pts w/ AF treated w/ flecainide Group D- 5 pts w/ atrial flutter treated w/ flecainide	AF or atrial flutter <6 mo w/ ventricular rate >100 bpm at rest w/ no HF signs	Conduction disturbances more that 1st degree AV block, on class I antiarrythmics, WPW syndrome, SSS, AMI, Hyperthyroidism, cardiac surgery <2 wks, atrial enlargement, w/ AF or atrial flutter w/o appropriate anticoagulants, body weight >100 kg	Conversion to NSR w/in 1 H 11/20 (55%)pts w/ AF treated w/ propafenone 18/20 (90%)pts w/ AF treated w/ flecainide (p<0.02) 2/5 (40%) pts w/ atrial flutter treated w/ propafenone 1/5 (20%) pts w/ atrial flutter treated w/ flecainide. P=NS	QRS lengthening (83±15 to 9920 msec) was observed only in the pts treated w/ flecainide (p<0.001).	N/A	Conversion from AF w/ flecainide vs. propafenone (p<0.02). Conversion from atrial flutter w/ fleainidec vs. propafenone (p=NS). Transient AE flecainide vs. propafenone more common (p<0.001)	Flecainide 2 mg/kg in 10 min is more effective than propafenone for conversion of AF to NSR but not for conversion of flutter. Few AE w/ propafenone- may be related to low dose.
Ellenbogen KA 1991 (183) 1894861	To demonstrate the safety and efficacy of a continuous IV diltiazem infusion for 24 h heart rate control	Randomized, double-blind, parallel, placebo-controlled	IV diltiazem vs. placebo	Placebo	Pts >18 y w/ AF or atrial flutter w/ duration >24 h and HR >120 bpm	Severe CHF, sinus node dysfunction, 2nd or 3rd degree AV block, WPW syndrome or hypotension	Therapeutic response (ventricular response <100 bpm, ≥20% decrease in heart rate from baseline or conversion to NSR 74% vs. 0%	N/A	N/A	p<0.001	IV diltiazem is safe and effective at slowing heart rate in AF or flutt
Van Gelder IC 1991 (184) 2058558	Cardioversion: reassess prospectively the immediate and long-term	246 pts	Multivariate analysis to identify factors predicting short- and long-term arrhythmia outcome following DC	N/A	AF or atrial flutter	Sinus rhythm, unstable HF, cardiogenic shock, severs systemic disease, SSS, AMI, contraindication to anticoagulants	Cardioversion successful in 70% of pts w/ AF and in 96% of pts w/ flutter. Stepwise logistic regression	N/A	N/A	Arrhythmia duration (p<0.001); AF vs. atrial flutter (p<0.02) and age (p<0.05) influenced DCV rates. MVanalysis showed arrhythmia type (p=0.0008), functional class (p=0.002) and presence of	Predictors for successful cardioversion include flutter vs. AF. FC, age and rheumatic heart disease affect

	results of direct-current electrical cardioversion in chronic AF or atrial flutter, and to determine factors predicting clinical outcome of the arrhythmia after direct-current cardioversion		cardioversion				analysis revealed that arrhythmia duration, type of arrhythmia and age independently influenced conversion rate. 42 and 36% of pts remained in sinus rhythm during 1 and 2 y, respectively. Multivariate regression analysis revealed that the type of arrhythmia), low precardioversion functional class and the presence of nonrheumatic mitral valve disease independently increased the length of the arrhythmia-free episode. Rheumatic heart disease shortened this period.			nonrheumatic disease (p=0.03) increased arrhythmia free period. Rheumatic heart disease decreased arrhythmia free period (p=0.03)	cardioversion.
Kingma JH 1992 (185) 1510000	Cardioversion w meds: Single-blind randomized study design.	90	Conversion to NSR w/in 1 hr of start of infusion: First 40: flecainide and verapamil assessed	Conversion to NSR w/in 1 hr of start of infusion: Second 50: flecainide and propafenone compared	Consecutive pts w/ AF or flutter	More than 1st degree AV block, class I antiarrhtyhmics, WPW syndrome, SSS, AMI, hyperthyroidism, cardiac surgery <2 wk, left atrial enlargement with AF	Conversion to NSR in: 32/37 (86%) AF w/ flecainide 11/20 (55%) AF w/ PPF In recent onset AF,	QRS widening occurred in flecainide-treated pts (83±15 to 99±20 msec; p<0.001), but not after propafenone	N/A	Recent onset AF flecainide more effective than propafenone at conversion ((p<0.05) Flutter conversion no difference in conversion w/ flecainide vs. propafenone (p=NS) Verapamil ineffective.	Flecainide is more effective than propafenone at converting recent onset AF, but not flutter. Verapamil

	Efficacy and safety of IV propafenone (2 mg/kg per 10 min) vs. flecainide (2 mg/kg per 10 min) vs. verapamil 10 mg in 1 min.in pts w/ AF or flutt					or atrial flutter >2 d w/o appropriate anticoagulants, body weight >100 kg	flecainide conversion 24/25 (96%) vs. 8/14 (57%) propafenone, p<0.05. 1/8 (13%) atrial flutter w/ flecainide 2/5 (40%) atrial flutter propafenone, p=NS Overall verapamil 1/20 (5%)	(83±11 to 86±12 msec).		QRS widening more common w/ flecainide than propafenone (p<0.001)	was not effective at converting AF or atrial flutter w/in 1 hr
Roberts SA 1993 (186) 8362772	Clinical effectiveness and cost of digoxin at controlling HR in AF and atrial flutter in prospective , observational study at 18 academic centers	115 pts	Assessed time to HR control w/ digoxin	N/A	18 y AF or atrial flutter w/ ventricular rates ≥ 120 BPM	NYHA class III, IV, HF, surgery, AMI	The median time to ventricular rate control (i.e., resting ventricular rate <100 bpm, decrease in ventricular rate of >20%, or sinus rhythm) was 11.6 h from the first dose of digoxin for all evaluable pts (n = 105) and 9.5 h for those only receiving digoxin (n = 64). Before ventricular rate control, the mean ±SD dose of	N/A	N/A	N/A	Observational study

							digoxin administered was 0.80±0.74 mg, and a mean of 1.4±1.8 serum digoxin concentrations were ordered per pt.				
Tucker KJ 1993 (187) 8343321 *Pace terminati on*	Prospective randomized clinical trial: Comparison of safety and efficacy of transesophageal atrial pacing vs. DC cardioversion in pts on medical therapy.	21 consec pts	Group A- 11 pts treated w/ TAP	Group B- 10 pts treated w/ DC cardioversion	Consecutive pts w/ flutter - HD stable. - Had failed 1A or 1C antiarrhythmic therapy -All pts received digoxin to control HR to <100 BPM	N/A	NSR achieved w/ intervention Group A- 8/11 TAP pts Group B- 9/10 DC cardioversion pts P= 0.31	Nonsustained VT was more frequent in DC cardioversion Group A- 0/11 TAP Group B 6/10 DC cardioversion P=0.02	N/A	P=0.31 NSR in TAP vs. DC cardioversion NSVT p= 0.02 Group A vs. B	TAP is safe and effective and was well tolerated and is as efficacious as DC cardioversion
Ellenbogen KA 1995 (188) 7801862	To demonstrate the efficacy of various doses of IV diltiazem for heart rate control	Open label, dose titration study. 84 pts w/ AF, atrial flutter, or both	Bolus dose of diltiazem followed by continuous infusion w/ monitoring of heart rate and BP	N/A	84 consecutive pts w/ AF or flutter, or both, received an IV bolus dose of diltiazem followed by a continuous infusion of diltiazem at 5, 10, and 15 mg/h.	>18 y, women of child-bearing age, SSS, 3rd degree AV block, WPW, hypotensive SBP <90 mm Hg, allergic to diltiazem.	94% of pts (79 of 84) responded to the bolus dose w/ a >20% reduction in HR from baseline, a conversion to sinus rhythm, or a heart rate <100 bpm. 78	Statistically significant change in BP before and after 20 mg bolus during infusion. NS difference in BP, after infustion at h 0, 1, 2, 4, 8, and 10.	N/A	Continuous infusion 10 h response at 5 mg/h (95% CI for 5 mg/h: 36-59; 95% CI for 10 mg/hr: 57-79%)	IV diltiazem is safe and effective at slowing heart rate in AF or flutter. Treatment related symptomatic hypotension (3.5-13% w/ hypotension)

							pts received the continuous infusion. After 10 h of infusion, 47% of pts had maintained response w/ the 5 mg/h infusion, 68% maintained response after the infusion was titrated to 10 mg/h, and 76% after titration from the 5 and 10 mg/h infusion to the 15 mg/h dose. For the 3 diltiazem infusions studied, mean (±SD) heart rate was reduced from a baseline value of 144±14 bpm to 98±19, 107±25, 107±22, 101±22, 91±17, and 88±18 bpm at infusion times 0, 1, 2, 4, 8, and 10 h, respectively. By the end of the infusion, 18% of pts (14 of 78) had conversion to sinus rhythm				was most common.
Hou ZY	Cardiove	51	Randomly	Amiodarone	Potentially useful for a	Recent-onset,	Heart rate	amiodarone	N/A	Amiodarone reduced	Demonstrated

1995 (189) 7671898	rsion w meds: Randomized, open label, digoxin-controlled study to observe efficacy and safety of dosing regimen of amiodarone in recent-onset, persistent AF and atrial flutter w/ ventircular rates >130 BPM.		assigned to either IV amiodarone (n=26) or digoxin (n=24) Amiodarone infused over 24 h (decreasing doses/h) Digoxin inf/used-0.013 mg/kg in 3 divided doses	vs. digoxin	recommendation	persistent, AF and flutter w/ ventricular rates above 130 beats.	control: Mean HR in amiodarone group decreased from 157 ± 20 to 122± 25 BPM in 1 hr (p<0.05) and further stabilized to 96±25 BPM after 6 h (p<0.05). Fewer HR reductions in digoxin group (p<0.05)	infusion was prematurely aborted in two pts due to severe bradycardia and death after conversion in one pt and aggravation of HF in the other		HR significantly more than digoxin at 1 and 6 h (p<0.05 both time frames)	HR control w/ amiodarone.
Sung RJ 1995 (190) 7900626	Cardioversion w meds Multicenter, randomized, double-blind, placebo controlled study: Placebo vs. sotalol	93	Two phased study: Phase 1: randomized placebo infusion vs. 1.0 or 1.5 mg/kg IV sotalol. (30 min observation) Phase 2: if not converted or if HR not fall to <100, 1.5 mg/kg sotalol given	Phase 1 sotalol vs. placebo Phase 2 no comparetor	Spontaneous or induced SVT (n=45) or atrial flutter/fibrillation (n=48)	N/A	SVT phase 1 conversion to NSR 2/14 (14%) w/ placebo SVT phase 1 conversion to NSR 10/15 (67%) sotalol 1.0 mh/kg (p<0.05 vs. placebo) SVT phase 1 conversion to NSR 10/15 (67%) sotalol 1.5 mg/kg (p<0.05 vs.	N/A	N/A	Phase 1 SVT sotalol 1.0 mg/kg and 1.5 mg/kg vs. placebo, sotalol superior (p<0.05 for each dose) Phase 1 sotalol vs. placebo conversion of AF 1.0 mg/kg and 1.5 mg kg not different (p=NS for both doses)	Sotalol was effective at terminating SVT but not AF

							placebo) SVT open label 7/17 (41%) conversion to NSR w/ 1.5 mg/kg sotalol AF phase 1 conversion to NSR 2/14 (14%) w/ placebo AF phase 1-2/11 (11%) conversion to NSR w/ 1.0 mg/kg sotalol (p=NS vs. placebo) AF phase 1-2/16 (13%) to NSR 1.5 mg/kg sotalol (p=NS vs. placebo)				
Doni F 1996 (191) 8945077	Pace termination (randomized): Comparison of TAP in Type 2 atrial flutter w/ or w/o propafenone	12 pts w/ type 2 atrial flutter	12 pts w/ type 2 flutter randomized to 2 groups: Group A- TAP on no meds	Group B- TAP 2 h after propafenone 600 mg	Mean age = 59 y. Symptomatic atrial flutter, all pts had negative P waves in leads II, III, and aVF.	N/A	NSR achieved in Group A-0/6 (no meds) Group B- 4/6 on PPF	Flutter CL: propafenone slowed flutter cycle: 219±33 vs. 168±8 msec, p<0.05	N/A	NSR in Group A vs. Group B (P<0.05). Flutter cycle legth propafenone vs. no meds, p<0.05	Propafenone facilitated pace termination in those pts in whom a slowing of flutter CL occurred but not in those w/ unchanged atrial flutter CL
Ellenbogen KA 1996 (192) 8752805	Cardioversion w meds: Randomized to single IV dose Efficacy	200 pts AF or atrial flutter 3H-90 d	Pts randomized to single IV dose vs. placebo 159 randomized to ibutilde: 41 at 0.005	41 randomized to placebo	AF or A flutter 3 h- 90 d	Childbearing age, MI <3 m, class I and III antiarrhythmics discontinued for 5 half lives, AF >3 d, anticoags >2 wk before ibutilide	Conversion to NSR during or w/in 60 min of infusion: 24% conversion to NSR in drug treated group	Polymorphic VT occurred in 3.6%	N/A	Placebo and 0.005 mg/kg ibutilide vs. all other groups lower success (p<0.05). No other statistic	Ibutilide can rapidly terminate AF and flutter

	of IV ibutilide vs. placebo for AF or flutter – dose respons e study.		mg/kg 40 at 0.10 mg/kg 38 at 0.015 mg/kg 40 at 0.025 mg/kg				vs. 3% in placebo. Conversion rates at successive doses: 12%, 33%, 45%, 46%.				
Stambler BS 1996 (193) 8840852	Multicent er study . Safety and efficacy study Varying doses of ibutilide	226 133 AF 133 atrial flutter	Randomized to up to 2 10-min doses Ibutilide separated by 10 min. Ibutilide doses= 1.0 and 0.5 mg or 1.0 and 1.0 mg.	This was compared to placebo.	AF and atrial flutter. Arrhythmia of 3 h to 45 d duration	Pt could not be <18 y, weight >300lbs, h/o of torsade, on ibutilide previously, MI, cardiac surgery <30 d, have digoxin toxicity, hyperthyroidism, not on class I	Conversion rates were: 47% w/ ibutilide vs. 2% w/ placebo (p<0.001) Efficacy in flutter >AF: 63% vs. 31%, p<0.001 In AF (but not flutter) conversion rates higher in those w/ shorter duration arrhythmia The 2 ibutilide dosing regimens did not differ in conversion efficacy (44% vs. 49%).	Polymorphic VT in 8.3% (15 pts) (3 required cardioversion, 12 did not)	N/A	Ibutilide vs. placebo (p<0.001) Efficacy in flutter vs. AF: (p<0.001) No difference in conversion at different doses (p=NS)	Ibutilide in repeated doses is effective in terminating AF and flutter
Volgman AS 1998 (194) 9581743	Cardiove rsion w meds: Multicent er study-compare efficacy and safety of ibutilide vs. procaina mide for	127	Conversion to NSR: randomized to either 2 10 min infusions of 1 mg ibutilide separated by 10 min vs. 3 successive 10 mg- /IV infusions of 400 mg	(Ibutilide vs. procainamide)	2 h to 90 d AF or flutter	N/A	120 evaluated for efficacy of conversion in 1.5 h: 35/60 (58%) ibutilide to NSR 11/60 (18.3%) procain converted to NSR (p=0.0001) Flutter-	PMVT- 1 pt in ibutilide group Hypotension- 7 pt in procainamide group	N/A	Ibutilide more successful at conversion n 1.5 h vs. procainamide (p<0.0001) Flutter: ibutlide superior to procain (p=0.001) AF- ibutilide superior to procain (p=0.005	Ibutilide was superior to procainamide at converting either AF or flutt. Hypotension was major AE for procainamide. Low incidence of serious proarrhythmia

	conversion of recent onset AF or flutt		procainamide 120 pts eval for efficacy: 60 received ibutilide 60 received proc				ibutilide significantly more effective than procain (76% 13/17 vs. 4% 3/22; p=0.001. AF- ibutilide significantly more effective than procain (51% 22/43 vs. 21% 8/38; p=0.005.				wth ibutilide.
Vos MA 1998 (195) 10078083	Cardioversion w meds: Randomized to receive one of 2 doses of ibutilde or DL sotalol. To compare safety and efficacy	308 pts: 251 AF, 57 atrial flutter.	Three treatment groups: 99 received 1 mg ibutilide 106 received 2 mg ibutilide 103 received 1.5 mg/kg DL-Sotalol	N/A	AF or flutter: Duration 3 h - 45 d	Hyperthyroidism, UA, bronchospasm, MI or cardiac surgery <30 ds, 2 and 3rd degree AV block, BBB, WPW, torsade de pointes	Conversion to NSR w/in 1 hr of treatment. Both drugs were more effective w/ atrial flutter than fib. Ibutilide was more effective than DL-sotalol achieving SNR in atrial flutter in: 70% and 56% vs. 19%. High dose ibutilide was more effective than DL-Sot in AF (44% vs. 11%) and than low dose ibutilide (44% vs. 20%, p<0.01)	Bradycardia (6.5%) and hypotension (3.7%) were more common side effects w/ DL-sotalol. Of 211 pts given ibutilide, two (0.9%) who received the higher dose developed polymorphic VT, one of whom required direct current cardioversion	N/A	High dose I more effective than. DL Sotalol and than low dose I in AF (p<0.01)	Ibutilide was more effective than DL sotalol. Duration of atrial flutter or AF was predictor of success.
Benditt DG 1999 (196) 10496434	Prospective dose finding study	Randomized	Sotalol 80 BID (59) Sotalol 120 BID (63) Sotalol 160 BID (62) Placebo (69)	N/A	50 pts - outpatient 134 pts - inpatient SHD 57%	H/o torsade de pointes, CHF, QI >450 msec, hypokalemia, hypomagenesemia, bradycardia.	Time to first recurrent symptomatic AF and/or atrial flutter after reaching drug steady	No cases of VT/VF/torsade QT>520 ms in 7 pts (4 in 120 mg BID and 3 in 160 mg BID) Premature	N/A	N/A	It is unrealistic to define efficacy in tx of AF and atrial flutter. HF pts for AF

							state (p=0.004, significant longer time to recurreance for sotalol 120 mg BID vs. placebo)	discontinuation due to AEs 25% inpatients, but 6% of outpatients (bradycardia predominantly)			and atrial flutter not evaluated.
Doni F 2000 (197) 17033455	Pace terminati on of atrial flutter via trans esophag eal pacing. Randomi zed to 4 groups	80	Randomized to 4 groups: A) Short bursts (5 sec) atrial pacing w/o drug B) Short bursts (5 sec) atrial pacing after propafenone 600 mg C) Long burst (30 sec) atrial pacing w/o drug D) Long burst (30 sec) atrial pacing after propafenone 600 mg	N/A	Atrial flutter- new onset	N/A	Successful flutter pace termination in: 20% 55% 50% 85%	N/A	N/A	(p<0.05: C vs. A) (p<0.05: D vs. B). (p<0.05: B vs. A and D vs. C) No other stats provided	Propafenone + long bursts of atrial pacing was best at terminating atrial flutter
Natale A 2000 (198) 10841241	Multicent er prospect ive randomi zed compari son of antiarrhy thmic therapy vs. first-line RF ablation in pts w/ atrial flutter.	61	Group 1: 30 randomized to drug therapy	Group 2: 31 randomized to RFA	Inclusion: At least two symptomatic episodes of atrial flutter in the last four mo. .	Exclusion:1) prior evidence of AF (AF); 2) the presence of significant left atrial enlargement (≥4.5 cm); and 3) previous treatment w/ antiarrhythmic medications	1) Rehospitalizat ion: medication group- 63% required one or more rehospitalizati ons, vs. post-RF ablation, 22% of pts were rehospitalized (p<0.01). 2) Post RF ablation, 29% developed AF vs. 53% of pts receiving	N/A	N/A	1) Rehospitalization more common w/ meds (p<0.01) 2) AF more common post RFA than meds (p<0.05) 3) Sense on well being improved w/ RFA but not meds (change in scoe p<0.01)	RF ablation could be considered a first-line therapy due to the better success rate and impact on QOL, the lower occurrence of AF and the lower need for rehospitalizati on at f/u.

							medications (p<0.05). 3) Sense of well being (pre-RF 2.0±0.3 vs. post-RF 3.8±0.5, p<0.01) and function in daily life (pre-RF 2.3±0.4 vs. post-RF 3.6±0.6, p<0.01) improved after ablation, but did not change significantly in pts treated w/ drugs.				
Delacretaz E 2001 (199) 11345382	Ablation: Single center, non-randomized trial comparing ablation of multi IART circuits in adults w/ CHD guided by entrainment mapping w/ and w/o 3D electroanatomic mapping	20 pts (47 circuits)	To define an approach for mapping and ablation, combining anatomy, activation sequence data and entrainment mapping. a) 7 pts w/ ablation guided by entrainment mapping only	b)13 pts w/ ablation guided by entrainment and 3D electroanatomic mapping	N/A	Recurrent IART refractory to meds. Late post repair of CHD	Overall 38 (81%) of 47 IARTs successfully ablated. In f/u ranging from 3-46 mo: a)16 (80%) of 20 pts remains free of recurrence b)Success similar in both groups but fluoroscopy time decreased from 60 +/- 30 to 24 +/- 9 min/procedure w/ addition of 3D electroanatomic mapping	N/A	N/A	No statistical analysis	Entrainment mapping combined w/ 3D electroanatomic mapping allows delineation of complex re-entry circuits and critical isthmuses as targets for RFA as a satisfactory treatment modality for IARTs related to CHD.
Delle	To	Randomi	IV diltiazem	N/A	Critically ill pts w/	N/A	Sustained	Bradycardia or	Uncontrolled	1° endpoint: NS	The study

Karth G 2001 (200) 11395591	compare the efficacy of IV diltiazem bolus/infusion vs. IV amiodarone bolus vs. IV amiodarone bolus/infusion for immediate (4 h) and 24-h rate control during AF	zed prospective, controlled	bolus/infusion vs. IV amiodarone bolus vs. IV amiodarone bolus/infusion		recent-onset AF w/ ventricular rate >120 bpm		heart rate reduction ≥30% w/in 4 h 70% vs. 55% vs. 75%	hypotension 35% vs. 0% vs. 5%	tachycardia 0% vs. 45% vs. 5%	2° endpoint p<0.00016 Safety endpoint p=0.01	speaks about rate control during recent AF or atrial flutter in really sick pts.
DIAMOND 2001 (201) 11457747	RCT, double-blind To evaluate the efficacy of dofetilide to maintain SR in pt w/ LV dysfunction	506 pts	Dofetilide 500 mcg/d (249)	Placebo (257)	Inclusion: Persistent AF associated w/ either HF or recent acute MI Dose reduction for renal insufficiency BBB), K <3.6 or >5.5, CrCl <20 mL/min	Exclusion: HR: <50 bpm, QTc >460 msec (500 msec w/	Probability of maintaining SR at 1 y 79% dofetilide 42% w/ placebo (p<0.001)	No effect on all-cause mortality Dofetilide associated w/ reduced rate of rehospitalization	N/A	Torsade de pointes occurred in 4 dofetilide pts (1.6%)	Subjects not stratified by rhythm. Differences in population, Lft atrial size, LV diastolic dysfunction, and MR could have influenced results.
Gallagher MM 2001 (202) 11691530	Cardioversion: design a more efficient protocol for the electrical cardiove	1838 attempts at cardioversion of AF and 678 attempts at	Analyzed the effects of different energy deliveries at terminating either AF or atrial flutter in pts w/	N/A	AF or atrial flutter undergoing DC cardioversion	N/A	Conversion rates were: a) AF of >30 d duration = 5.5% at <200 J; 35% at 200 J and 56% at 360 J. b) atrial	N/A	N/A	For AF >180 d, initial use of a 360 J shock was associated w/ the eventual use of less electrical energy than w/ an initial shock of ≤100 J (581±316 J vs. 758±433 J, p<0.01, Mann-Whitney U test).	An initial energy setting of ≥360 J can achieve cardioversion of AF more efficiently in pts than traditional

	rsion of atrial arrhythmias	cardioversion of flutter	arrhythmias of varying duration.				flutter= 68% at 100 J c) AF of >30 d duration, shocks of <200 J = 6.1% d) AF >180 d= 2.2% at 200 J				protocols, particularly w/ AF of longer duration.
Wazni O 2003 (203) 14610012	Randomized study comparing combined pulmonary vein-left atrial junction disconnection and cavotricuspid isthmus ablation vs. pulmonary vein-left atrial junction disconnection alone in pts presenting w/ typical atrial flutter and AF.	108	Consecutive pts w/ documented symptomatic AF and typical atrial flutter were randomly assigned to have PV-LAJ disconnection combined w/ CTI ablation (group 1, n=49) or PV-LAJ disconnection alone (group 2, n=59).	PV-LAJ disconnection combined w/ CTI ablation (group 1, n=49) or PV-LAJ disconnection alone	Preablation proof of both atrial flutter and AF on ECG, 1 documented episode of typical atrial flutter while not on antiarrhythmics	N/A	W/in the first 8 wk after ablation, 32 of the group 2 pts had typical atrial flutter documented, whereas none was seen in group 1. Twenty of these 32 converted to sinus rhythm after initiating AADs. Twelve were cardioverted, and AADs were started. After 8 wk, all AADs were stopped, and only 3 pts continued to have recurrent sustained typical atrial flutter that was eliminated by CTI ablation. Beyond 8 wk of f/u, 7 pts in group 1 and 6 pts in group 2 (14% and 11%, respectively) continued to	N/A	N/A	N/A	Isolating of all 4 pulmonary vs. is challenging. No f/u beyond 1 y.

							have AF. Ten of these 13 pts underwent a repeat PV-LAJ disconnection procedure and were cured. The remaining 3 remained in normal sinus rhythm while taking AADs.				
LADIP Trial 2006 (204) 17030680	Randomized study comparing amiodarone and RF ablation after the first episode of symptomatic atrial flutter	104 pts w/ atrial flutter:	group I= 52 pts treated w/ RFA as 1st line	Group2 treated w/ cardioversion and amiodarone as 1st line	1 episode of symptomatic typical atrial flutter	N/A	Recurrence of flutter: 3.8% after RFA vs. 29.5% w/ amiodarone and cardioversion; p<0.0001	Complications of treatment: Five complications (10%) were noted in group II (SSS in 2, hyperthyroidism in 1, and hypothyroidism in 2) and none in group I (0%) (P=0.03).	long-term risk of subsequent AF (AF): 25% after RFA vs. 18% after amiodarone and cardioversion (p=NS)	RFA reduced recurrences of flutter vs. amiodarone and caridoversion (p<0.0001) RFA not different than amiodarone and cardioversion at occurrence of AF (p=NS). Fewer complications w/ RFA than amiodarone + cardioversion (p=0.03)	RFA should be considered first line therapy even after 1 recurrence of atrial flutter
Kuniss M 2009 (205) 19959115	Prospective randomized comparison of durability of bidirectional conduction block in the cavotricuspid isthmus in pts after	191	Cryoablation Do people use this for atrial flutter ablation?	Vs. standard RFA	Inclusion: 1. One episode of ECG-documented typical atrial flutter symptomatic w/ eligibility for ablation treatment 2. Age between 18 and 80 y 3. Written informed consent for the ablation procedure and the invasive f/u procedure after 3 mo.	Exclusion: atypical flutter	Acute success rates: 91% (83/91) in the RF group vs. 89% (80/90) in the cryoablation group (P=NS). Invasive 2) f/u 3 mo EP study available for 60 pts in the RF group and 64 pts in cryoablation group. 3) Persistent	N/A	Secondary end-point-pain perception during ablation was significant lower in the cryoablation group (*P*<0.001)	Acute success RFA vs. cryoablation (p=NS) Pesristent BCB-cryoablation inferior to RFA (p<0.014)	Persistence of BCB in pts treated w/ cryoablation reinvestigated after 3 mo is inferior to that pts treated w/ RF ablation, as evidenced by the higher recurrence rate of common atrial flutter seen in this study.

	ablation of common atrial flutter using cryotherm y and RF energy: The CRYOTIP study						BCB confirmed in 85% of the RF group vs. 65.6% of the cryoablation group. 4)The primary end-point= nonpersistence of BCB block was seen in 15% of the RF group vs. 34.4% of the cryoablation group (P<0.014).				
Steinwender C 2009 (206) 19136164	Randomized placebo controlled Trial: Assess pretreatment w/ magnesium for conversion w/ Ibutilide: Randomized 117 pts (58 w/ and 59 w/o pre-injection of magnesium; 65 w/ typical atrial flutter and 52 w/	117- 65 typical flutter; 52 atypical flutter	2 randomized groups: Group 1) 4 g of IV magnesium sulfate	Vs. Group 2) placebo immediately before administration of a maximum dose of 2 mg of ibutilide fumarate	Typical and atypical atrial flutter	N/A	1) TAF: pre-injection IV magnesium improved efficacy of ibutilide for conversion (85% w/ magnesium vs. 59% w/ placebo, p=0.017). Atypical atrial flutter: no significant difference in conversion rates between pts receiving magnesium vs. placebo (48% vs. 56%,p=0.189)	No effect of magnesium on QTc interval. QTc intervals at 30 min after ibutilitde did not differ between patients w/ and w/o ventricular ectopy	N/A	Preinjcention w/ Mg superior for conversion w/ ibutilide in trypical atrial flutter (p=0.017) Preinjection w/ Mg for conversion w/ ibutilide no different (p=NS) Preinjection wih Mg did not affect QT (no statistic offered)	Pre-injection of magnesium significantly enhances the efficacy of ibutilide for the conversion of typical atrial flutter but not of atypical atrial flutter.

	atrypical atrial flutter.										
Bastani H 2012 (207) 22927662	Randomized comparison in pts w/ typical atrial flutter. RFA- 3.5 mm open-irrigated-tip catheter and Cryoablation a 9 F, 8 mm tip catheter. Ablation endpoint was bidirectional CTI block.	153	Ablation RFA- 3.5 mm open-irrigated-tip catheter (N= 75)	Cryoablation a 9 F, 8 mm tip catheter (N=78)	Inclusion: Pts w/ a h/o AF included if they had predominant atrial flutter under chronic treatment w/ class I or III antiarrhythmic agents.	Exculsion: (i) prior ablation for atrial flutter; (ii) atrial flutter related to recently undergone surgery, hyperthyroidism or other severe disease; (iii) inability to adhere w/ the study protocol; (iv) pregnancy; (v) predominant AF; and (vi) contraindication to warfarin.	Primary endpoint: demonstration of long-term efficacy defined as no symptomatic recurrence of atrial flutter at the 6-mo f/u. Success rate at 6-mo f/u was 93% (73 of 78) for Cryoablation vs. 97% (73 of 75) for RF (p= 0.86).	safety assessed by the rate of periprocedural complications, procedure and fluoroscopy times, and the level of pain experienced by the pt during the ablation procedure Procedural time was longer in the cryoablation group (152±54 min) than the RF group (116±41 min) (P<0.001). Cryoablation was less painful compared w/ RF (mean VAS-Cryoablation 0.7±1.2 vs. VAS-RF 4.6±2.0; P<0.001).	Secondary end-points: acute ablation success defined as bidirectional CTI-block; Acute success rate 92% for cryoablation vs. 95% for RF (p=0.58).	1) Acute success rate for Cryoablation vs. RF (p=0.58). 2) Procedural time was longer in the Cryoablation group vs. RF group (p<0.001). 3) Cryoablation was less painful compared vs. RF (p<0.001). 4) Success rate at 6-mo f/u was no different for Cryoablation vs. RF (P= 0.86). No major adverse events occurred in any group.	Cryoablation is not inferior to RFA for typical flutter
Mohantys 2013 (208) 23572499	Single-blind, randomized study- Examined the impact of different ablation	360 pts w/ documented AF and atrial flutter	Blinded and randomized to group 1, AF±atrial flutter ablation (n=182), or group 2, atrial flutter ablation only (n=178). AF recurrence was evaluated	AF ± atrial flutter ablation vs. atrial flutter ablation only	1 antiarrhythmic and preablation evidence of typical atrial flutter by 12-lead surface ECG.	<18 or >85 y old, previous ablation, left atrium size ≥5 cm, or contraindication to oral anticoagulation	At 21±9 mo of f/u, 117 in group 1 (64%) and 34 in group 2 (19%) were arrhythmia free (P<0.001). In group 1, scores on	N/A	N/A	Group 1 vs. Group 2 p<0.001	Questionnaires didn't address comorbidities, smaller sample size

	strategies on AF recurrence and QOL in coexistent AF and atrial flutter.		w/ event recording and 7-d Holter at 3, 6, 9, and 12-mo f/us. QOL was assessed at baseline and at the 12-mo f/u w/ 4 questionnaires.				most quality-of-life subscales showed significant improvement at f/u, whereas group 2 pts derived relatively minor benefit.				

AAD, antiarrhythmic drug; AE, adverse events; AF, atrial fibrillation; AMI, acute myocardial infarction; AV, atrioventricular; BBB, bundle branch block; BCB, bidirectional conduction block; bid, two times per day; BP, blood pressure; bpm, beats per min; CHD, congenital heart disease; CHF, congestive heart failure; CI, confidence interval; CL, cycle length; CrCl, creatinine clearance; CTI, cavotricuspid isthmus; DC, direct current; ECG, electrocardiogram; EP, electrophysiological; f/u, follow up; HF, heart failure; h/o, history of; HR, heart rate; IART, intraatrial reentrant tachycardia; IV, intravenous; LBBB, left bundle branch block; LV, left ventricular; MI, myocardial infarction; MR, mitral regurgitation; N/A, not applicable; NS, non-significant; NSR, normal sinus rhythm; NSVT, non-sustatined supraventricular tachycardia; NYHA, New York Heart Association; pt, patient; PV-LAJ, pulmonary vein-left atrial junction; QTc, corrected QT interval; RCT, randomized controlled trial; RF, radiofrequency; RFA, radiofrequency ablation; SBP, systolic blood pressure; SD, standard deviation; SHD, structural heart disease; SR, sinus rhythm; SSS, sick sinus syndrome; SVT, supraventricular tachycardia; TAP, transesophageal atrial pacing; tx, transplant; VAS, visual analog scale; VF, ventricular fibrillation; VT, ventricular tachycardia; w/, with; w/o, without; and WPW, Wolff-Parkinson-White syndrome.

Data Supplement 17. Nonrandomized Trials, Observational Studies, and/or Registries of Atrial Flutter – Section 7

Study Name, Author, Year	Study Type/ Design	Study Size	Inclusion/Exclusion Criteria	Primary Endpoint	Results/p Values	Summary/Conclusions
Van Gelder IC 1989 (181) 2511744	Persistent AF and atrial flutter after cardioversion randomized to flecainide or no therapy to reduce recurrence	81 pts (16 pts with atrial flutter – 6 in flecainide group and 10 in control group)	Inclusion: Persistent AF and atrial flutter referred for cardioversion. All pts w/ atrial flutter received verapamil 240 mg daily to reduce 1:1 AV conduction. Exclusion: <16 y or >80 y, CHF, angina, MI <2 y before, bifascicular block or bundle branch block, sick sinus syndrome without pacemaker, severe systemic disease	Arrhythmia-free survival after cardioversion	No significant difference in arrhythmia free survival. However, it postponed time to arrhythmia recurrence. Adverse effects: 9% flecainide group experience side effects. 3 pts in flecainide group required pacemaker (2 w/ symptomatic sinus arrest and 1 with AV block). 1 pt had increase ventricular ectopy burden requiring discontinuation.	No significant difference in arrhythmia free survival in pts w/ persistent AF or atrial flutter. However, it postponed time to arrhythmia recurrence after cardioversion.
Pietersen 1991 (209) 1900978	Randomized, placebo controlled cross over design trial flecainide 150 mg bid vs. placebo. Pts received 3 mo of therapy w/ another 3 mo of crossover therapy.	43 pts	Inclusion: Paroxysmal AF or atrial flutter >3 episodes <3 mo prior to enrollment Exclusion: CHF, reduced LV fractional shortening, WPW, syncope, thyroid disease, sinus node dysfunction w/o pacer, more than isolated PVC's	Number of symptomatic recurrences	Outcome: Significant reduction in number of episodes with flecainide treatment (p<0.002). Adverse events: 1 pt developed 1:1 conduction of atrial flutter. 1 sudden death in flecainide group (bathing in the cold Norway sea after drinking alcohol). Other minor adverse events occurred in 74% (mostly visual changes, dizziness, and GI side effects) resulting in 2 withdrawals.	Flecainide significantly redcuced the number of recurrent episodes of AF or flutter.

Aliot E 1996 (210) 8607394	Randomized, open-label, long-term, parallel, comparative multicenter study comparing propafenone to flecainide	97 pts (5 with atrial flutter)	Inclusion: adults with paroxysmal AF or atrial flutter on ECG or Holter Exclusion: MI, recent heart surgery, VT, CHF, PR >280 ms, QRS >150 ms, sinus node dysfunction or heart block in absence of pacemaker	Proportion of pts remaining on therapy at 1 y	0.619 remained on flecainide 1 y 0.469 propafenone Adverse events: 1 death in propafenone group. 8.5% flecainide experienced neurological side effects, 16% propafenone group GI side effects	In paroxysmal AF and paroxysmal atrial flutter, flecainide and propafenone not significantly different. Too few pts with atrial flutter to draw conclusions. Rate of side effects was greater with propafenone.
Baker 1996 (211) 8800118	Single center trial evaluating efficacy of anatomically based RFA ablation for the treatment of IART in pts w/ previous atrial surgery	14 pts	H/o atrial surgery and clinical intraatrial reentrant tachycardia	Freedom from recurrence of IART	Successfully terminated in 13 pts (93%). Six pts required repeat ablation for recurrence. Twelve (86%) remained free of IART at 7.5 mo.	RFA is effective technique for IART in pts w/ previous atrial surgery
Kalman JM 1996 (212) 8565168	Single center observation cohort study to evaluate the success of RFA for IART in CHD using targeted ablation of critical isthmus	18 pts	IART and repaired CHD	Acute success	Successful termination in 15 pts (21 arrhythmias). During f/u (mean 17 mo), 11 pts (61%) remained free of recurrence (2 remained on antiarrhythmic drug)	Describes early experience w/ targeted RF to critical isthmus in pts w/ repaired CHD. Successful ablation IART can be achieved w/ ablation to critical isthmus of conduction.
Triedman 1997 (213) 9316535	Single center retrospective trial evaluating the short and mid term efficacy of RFA for IART in CHD	45 pts	Pts w/ CHD w/ IART undergoing RFA Non-isthmus dependent flutter instead of IART	Freedom from recurrence of IART	73% acutely successful. Recurrence 53% during mean f/u of 17.4 mo. Seven underwent repeat ablation.	Early experience w/ RFA for IART in CHD reduced events in population of pts. However, recurrence was frequent often w/ new IART circuits.
Huang DT 1998 (214) 9607453	Single center trial assessing efficacy of combining pharmacologic and simple ablative therapies in treating AF in small targeted subset of pts	13 pts w/ AF who converted to electrocardiographic atrial flutter during anti-arrhythmic treatment	"Typical" atrial flutter in 11 pts and "atypical" atrial flutter in 2 suggested by surface ECG. Intracardiac mapping and entrainment studies found 9 pts w/ CCW isthmus dependent atrial flutter and remaining 4 had complex activation patterns.	Successful ablation w/o recurrence at mean f/u 14.3±6.9 mo	All 9 pts w/ typical atrial flutter had successful ablation and 88.9% maintained sinus rhythm in f/u period (while continued on antiarrhythmic drugs) None of 4 pts w/ complex activation patterns had successful ablation	In pts who experience conversion of AF to typical isthmus dependent flutter during anti-arrhythmic drug therapy, ablation and continuation of pharmacologic therapy is effective in maintaining sinus rhythm.
Chan DP 2000 (215) 10982544	Single center study assessing the importance of atrial flutter isthmus in post-	19 postoperative CHD pts w/ IART	All study pts underwent EP study w/ entrainment mapping of atrial flutter isthmuses to determine PPIs. RFA performed at identified isthmus to create line of block.	Successful ablation	21 IARTS identified in 19 pts Atrial flutter isthmus part of circuit in 15 of 21 (71.4%) Sites near atrial incisions or suture lines in remaining 6 of 21	When IART occurs late after repair of CHD, atrial flutter isthmus may be part of reentrant circuit and should be evaluated as a target for ablation.

	operative IART				Ablation successful in 19 of 21 (90.4%) of IARTs and in 14 of 15 cases of at the atrial flutter isthmus (93.3%)	
Jais 2000 (216) 10869265	Single center retrospective observational trial to assess efficacy of mapping guided RFA	22 pts	Pts w/ persistent left atrial flutter predominantly in pts w/ SHD. 18 (81%) failed amiodarone.	Acute success and mid-term f/u	Complete activation map achieved in 17/22 pts. 20 pts (90%) in sinus rhythm at the end of procedure. 7 pts required 2 procedures and 1 pt required 3 procedures. During mean 15 mo f/u, 16 pts (73%) remained free of recurrence (2 remained on antiarrhythmic).	Describes various left atrial reentrant circuits and demonstrated feasibility of mapping guided RFA
Reithmann C 2000 (217) 10775011	Single center trial assessing catheter ablation of CTI on amiodarone-induced atrial flutter and subsequent incidence of AF in comparison to CTI ablation of regular typical atrial flutter	92 consecutive pts w/ typical atrial flutter who underwent CTI ablation	3 groups 28 pts w/o h/o AF 10 pts w/ atrial flutter following amiodarone treatment for PAF 54 pt w/ AF and atrial flutter	Successful CTI ablation w/ bidirectional block eliminating atrial flutter and recurrence of AF during mean f/u 8±3 mo	Successful ablation achieved in 90% of amiodarone-treated pt's and 93% of pts w/o amiodarone therapy Recurrence of AF occurred in 20% amiodarone treated pts which was similar to pts w/o preexisting AF (25%) and markedly lower than pts w/ atrial flutter plus preexisting PAF (76%)	CTI ablation w/ bidirectional block and continuation of amiodarone therapy is effective for treatment of atrial flutter due to amiodarone therapy for PAF. Hybrid therapy belongs in this guideline? Yes. Merit a rec? Yes.
Akar JG 2001 (218) 11499727	Single center study assessing the coexistence of IART and IDAF in pts w/ SVTs after surgical correction of CHD	16 consecutive pts diagnosed w/ both IART and IDAF	IART and IDAF diagnosed by standard criteria and entrainment mapping. 7 pts had classic atrial flutter morphology on surface ECG, whereas 9 had atypical morphology	Successful ablation w/o procedural complication or recurrence at mean f/u of 24 mo	Successful ablation performed in 13 of 14 (93%) IART and 9 of 10 (90%) IDAF circuits. 1 IART recurrence otherwise none reported at 24 mo Slow conduction zone involved region of right atriotomy scar in 12 of 14 (86%) IART circuits No procedural complications	IDAF and IART are the most common and commonly coexistant mechanisms of atrial re-entrant tachyarrhythmias in pts w/ surgically corrected CHD. Majority of IART circuits involve lateral RA and may be successfully ablated by lesion extending to IVC.
Nakagawa 2001 (219) 11156882	Characterize the circuit of IART in pts w/ repaired CHD and evaluate success of RFA of w/in channels defined by electroanatomic mapping	13 pts w/ 15 IARTs	Pts w/ repaired CHD and IART	Acute and medium term success	Ablation acutely eliminated inducibility of all 15 IARTs. During f/u of median 13.5 mo, 13 pts (81%) remained free of recurrence. Large area of low voltage scar identified in all pts w/ macroreentrant tachycardias.	RFA of IART in pts w/ repaired CHD using electroanatomic mapping and targeting channels has a reasonable success rate.
Deal BJ 2002 (220)	Retrospective non-randomized comparison of	23 pts	Pts undergoing Fontan revision w/ AT Maybe shouldn't be in here since	Inducibility at f/u EP and long-term freedom from	Inducibility of AT: 62% inferomedial RA ablation 7% modified RA MAZE	Modified RA maze procedure is superior to anatomic isthmus block in treating reentrant AT in postoperative Fontan pts

12147539	cryoablation of inferomedial RA vs. extensive modified RA maze in pts undergoing Fontan revision w/ AT		surgical; may be more recent papers breaking down the differences by types of CHD	recurrence of AT	P<0.02 Freedom from AT (mean 43 mo f/u): 62% inferomedial RA ablation 0% modified RA MAZE P<0.001	
Spector P 2010 (55) 19699343	Meta-analysis of ablation of atrial flutter and SVT.	A meta-analysis of 21 studies RFA in atrial flutter:18 primary studies w/ 22 treatment arms and 1,323 pts)	N/A	Evaluate the safety and efficacy of RFA of typical atrial flutter and AV node-dependent SVT in adult pts	Single-procedure success for atrial flutter was 91.7% (95% CI: 88.4%-94.9%). Multiple-procedure success was 97.0% (95% CI: 94.7%-99.4%). Postablation arrhythmia was noted in 13.2% of pts (95% CI: 7.5%-18.9%), while repeat ablation was reported in 8% (95% CI: 4.5%-11.4%).	RFA for the treatment of pts w/ atrial flutter and SVT report high efficacy rates and low rates of complications. 70% of pts who got ablation didn't need it; interrelationship for AF and atrial flutter. When to ablate? → discussion. AF ablation covered in consensus document. Drive by protein disulfide isomerase vs. drive by flutter ablation. Both ways.
Coffey JO 2013 (221) 23385050	Retrospective multicenter cohort study to assess the efficacy of RFA on atypical atrial flutter/AT	91 pts w/ 171 ATs (1.9 / pt)	Pts w/ atypical atrial flutter/AT in pts w/ prior catheter ablation for AF, MAZE or other cardiac surgery, or idiopathic scar. Pts w/ on CTI-dependent flutter were excluded.	Acute and long-term success	Acute success was 97% for non-septal AT and 77% for septal AT. Long-term success rates 82% in pts w/ no septal AT and 67% in pts w/ 1 or more septal AT. Long-term success rates were 75%, 88%, and 57% for pts w/ ATs associated w/ prior catheter ablation, cardiac sugery/MAZE or idiopathic scar, respectively.	High-density activation mapping combined w/ selective entrainment mapping allows for reasonable successful RFA of non-CTI dependent ATs occurring after AF ablation, cardiac surgery, or in the setting of idiopathic scar.
Ghali WA 2005 (222)	Systematic review and meta-analysis of observational studies that investigated risk of thromboembolism associated with atrial flutter.	The meta analysis included 13 studies on embolic risk around time of cardioversion that included 1546 patients. For chronic risk, there were 14 studies involving 17,691 patients.	MEDLINE, EMBASE, bibliographies, and consultation with clinical experts were used to identify studies that report the risk of thromboembolism associated with attempted cardioversion and longer-term risk in patients with atrial flutter.	Risk of thromboembolism associated with atrial flutter around time of cardioversion or over the long term in chronic atrial flutter.	Around the time of cardioversion, the risk of thromboembolic events ranged from 0% to 7.3% depending of clinical factors. Lower event rates were observed in patients taking anticoagulants. The long term risk rate of thromboembolism was approximately 3% with sustained atrial flutter.	The findings of this systematic review strongly suggest that atrial flutter does indeed impart a risk of thromboembolism.

AF indicates atrial fibrillation; AT, atrial tachycardia; AV, atrioventricular; bid, two times per day; CCW, counter-clockwise; CHD, congenital heart disease; CHF, congestive heart failure; CI, confidence interval; CTI, cavotricuspid isthmus; ECG, electrocardiogram; EP, electrophysiological; f/u, follow up; GI, gastrointestinal; h/o, history of; IART, intraatrial reentrant tachycardia; IDAF, isthmus-dependent atrial flutter; IVC, inferior vena cava; LV, left ventricular; MI, myocardial infarction; N/A, not applicable; PAF, paroxysmal atrial fibrillation; PPI, postpacing interval; pt, patient; PVC, premature ventricular contraction; RA, right atrial; RF, radiofrequency; RFA, radiofrequency ablation; SHD, structural heart disease; SVT, supraventricular tachycardia; w/, with; w/o, without; and WPW, Wolff-Parkinson-White syndrome.

Data Supplement 18. Randomized Trials for Junctional Tachycardia – Section 8

Study Name, Author, Year	Aim of Study	Study Type (Size, N)	Study Intervention Group (n)	Study Comparator Group (n)	Pt Population		Endpoints			P Values, OR: HR: RR: & 95% CI:	Study Limitations & Adverse Events
					Inclusion Criteria	*Exclusion Criteria*	*Primary Endpoint (efficacy) and Results*	*Safety Endpoint and Results*	*Secondary Endpoint and Results*		
Mamchur SE 2012 (223) 22978723	Assess the risk of AV block during ablation of parahisian ectopic foci prior to ablation by high-amplitude pace mapping.	RCT (N=20)	Ablation at site where high-amplitude (15-30 mA) pacing revealed absence of His capture (wide QRS complexes) (n=11)	Ablation performed in conventional manner (n=9)	Pts w/ parahisian ectopic foci (i.e., pts w/ focal JT)	Pts w/ SHD	Group 1: Ablation (standard approach) effective in 6/11 (55%); Group 2: Ablation effective w/ high amplitude pacing in 9/9 (100%), p=0.02	Group 1: 27% AV block; Group 2: no complications, p=0.09	Late recurrence of ectopic activity similar in both groups, p=NS	Group 1: Ablation effective in 6/11 (55%); Group 2: Ablation effective in 9/9 (100%), p=0.02. Group 1: 27% AV block; Group 2: no complications, p=0.09. Late recurrence of ectopic activity similar in both groups, p=NS.	Small sample, generalizability unclear. Cannot use method for ectopic focus in right coronary sinus or the aorta.

AV indicates atrioventricular; NS, non-significant; pt, patient; RCT, randomized controlled trial; SHD, structural heart disease; and w/, with.

Data Supplement 19. Nonrandomized Trials, Observational Studies, and/or Registries of Junctional Tachycardia – Section 8

Study Name, Author, Year	Study Type/ Design	Study Size	Inclusion/Exclusion Criteria	Primary Endpoint	Results/p Values	Summary/Conclusions
Pharmacological Therapy						
Ruder 1986 (224) 3698238	Case report	n=5	5 adult pts w/ JT (one pt refused drug therapy)	Control or eradication of arrhythmia	All pts responded to beta-blockers (nadolol, propranolol), and best response w/ beta-blockers w/ procainamide.	First report of JT in adults. Good response to beta-blockers. Only 4/5 pts underwent EP study to definitively identify junctional origin.
Cook 1988 (225) 1951023	Case report	n=1	19 y w/ refractory JT	Flecainide therapy for JT refractory to AV nodal blockers, burst atrial or ventricular pacing	Flecainide 150 mg bid successful in restoring SR	First report of successful treatment of "incessant" JT w/ class Ic agent.
Kuck 1988 (226)	Case series	n=3	16 total pts w/ ectopic atrial tachyarrhythmia in study, 2 spontaneous JT (not inducible),	Flecainide and encainide therapy for JT	Flecainide effective in 2 pts w/ spontaneous JT (200 and 300 mg/d). Pt w/ incessant JT had prolongation	Encainide arm not valid for guidelines, but flecainide results valid for treatment of spontaneous JT. Builds on Cook's data above.

3144166			1 incessant JT		of H-V interval and hypotension.	
Villain 1990 (227) 2184944	Multicenter study; pediatric population	n=26	Infants w/ JT	AAD therapy in congenital JT, w/ success defined as HR <150 bpm, partial success as HR >150 bpm w/ sx relief	Combinations of digoxin, propranolol, amiodarone, quinidine, flecainide, chlorpromazine, phenytoin. 10 pts treated w/ amiodarone monotherapy —6 successes, 2 partial successes, 2 failures. One death in f/u. Amiodarone combination therapy less effective.	Amiodarone monotherapy is effective for congenital JT, but associated w/ some mortality. Authors comment that ablation should be reserved for drug-refractory JT. Digoxin ineffective in rate control, and may be harmful--specifically, incriminated in producing VF in 4 wk old child; and atrial tachycardia and then atrial flutter in 10 d old infant.
Paul 1992 (228) 1527301	Case series; pediatric population	n=4	Infants w/ congenital JT	Propafenone therapy for congenital JT	Effective at restoring SR w/ doses of 300 mg/m^2 w/ f/u ranging 1-36 mo	Efficacy of propafenone in pediatric population can avoid need for ablation in young population, and early toxicity of amiodarone.
Heusch 1994 (91) 7527342	Retrospective cohort study; pediatric population	n=3	72 pediatric pts w/ supraventricular arrhythmias treated w/ propafenone, only 3 pts had JT	Efficacy of propafenone in suppressing supraventricular arrhythmia	Successful in 2/3 pts w/ JT	Supports results of Paul et al for use of propafenone, despite small subset of pts w/ JT.
Raja P 1994 (229) 7946778	Retrospective cohort study; pediatric population	n=16	Postoperative (CHD) JET	Efficacy of amiodarone for rate control	Mean HR of 200 bpm, reduced to mean 153-170 in 24-h f/u	Amiodarone effective in HR and hemodynamic control for postoperative JT.
Lee 1999 (230) 10392383	Prospective cohort study	n=17 (age 12-83)	Pts developed JT during EP study, and all inducible w/ isoproterenol	Effect of adenosine and verapamil in catecholamine-inducible JT	Adenosine terminated rhythm in all pts, 11 w/ transient AV block. IV verapamil terminated rhythm in all 10 pts given the drug	Supports treatment of JT due to enhanced automaticity w/ adenosine and verapamil. Presence of AV block w/ adenosine suggests differential effect on automaticity and AV conduction. Age range spans pediatric and adult.
Sarubbi 2002 (231) 12117855	Retrospective cohort study	n = 9, age 2-6 mo	5/9 pts w/ family h/o JT; 6/9 w/ decreased ventricular function	Effects of digoxin, propafenone, amiodarone	Digoxin alone ineffective; propafenone alone effective in 2/9 pts; amiodarone in combination w/ propafenone or flecainide effective in 6 pts	Digoxin or propafenone alone ineffective; Amiodarone effective as part of combination therapy w/ propafenone; or flecainide; genetic contribution noted.
Ablation Therapy						
Scheinman MM 1994 (232) 8074039	Case series	n=8	Adult pts w/ JT	RFA of JT	6/8 w/ JT underwent ablation, 2 underwent AVJ ablation. Only 2 w/ preserved AV conduction.	Early report establishing that RF ablation may be successful therapy for JT.
Hamdan M 1996 (233) 8960595	Case series	n=11	Pts w/ JT (age 1-66)	RFA of JT	RFA successful w/o complications in 9/11 pts (82%). 7/9 successful w/ ablation at site of earliest atrial activation and 2 pts required empiric lesions in posteroseptal area due to lack of VA conduction. CHB developed in 1 pt, and RFA failed in 1 pt. F/u 1-20 mo.	RF ablation a largely successful strategy in series of pts, half of which were adults.
Law IH 2006 (234)	Retrospective cohort study; pediatric	n=6 (range 7-36 y,	All pts who underwent cryoablation for symptomatic, non-postoperative JT,	Efficacy and safety of cryoablation for JT	4 pts had no JT at end of procedure. All 5 pts who underwent procedure were free of JT on up to 2 y of f/u.	Early report of cryoablation of JT, safe and effective (except w/ proximity to His-Purkinje system), and may confer long term benefit.

16876738	population	median 8 y)	refractory to AADs (primarily beta-blockers), at 2 hospitals.			This study studied a small number of primarily pediatric pts at two institutions. Pharmacologic therapy not attempted in all pts. One pt had an ectopic focus proximal to His-Purkinje, and cryomapping resulted in transient CHB, so cryoablation not performed.
EP Study Diagnosis						
Meiltz A 2006 (235) 16627404	Retrospective cohort, multicenter	n=49	Adults w/ PJRT confirmed at EP study, both paroxysmal (53%) and incessant	Describe results of RFA in adults w/ PJRT	RFA successful in 94% w/o complications, and long term success 100% w/o AADs, w/ 49 mo mean f/u.	Rare report of PJRT in adults only, so results pertinent to guidelines, and support RF ablation as first line therapy.
Padanilam BJ 2006 (236) 19007691	Prospective cohort study	n=39	Adults w/ AVNRT, JT, or "clinically indeterminate."	To distinguish JT or AVNRT based on specific responses to PACs delivered at different phases of the tachycardia cycle	PACs introduced during His refractoriness did not affect tachycardia. Earlier PACs preexcite the immediate His and ventricle, w/o terminating tachycardia, confirming JT. For AVNRT, 61% sensitivity, 100% specificity; for JT, 100% sensitivity and specificity.	The response to PACs during tachycardia can distinguish JT from AVNRT w/ 100% specificity and high sensitivity. However, PACs introduced during His refractoriness can lead to misdiagnosis of JT as AVNRT if dual AV nodal physiology is present. Furthermore, if double ventricular responses are present, a PAC during AVNRT can advance the His w/ continuation of the tachycardia, misdiagnosed as JT.
Srivathsan K 2007 (237) 17916156	Retrospective cohort study	n=35	Typical AVNRT and evidence of JT during EP study and/or ablation	To assess the utility of delta H-A interval (difference in the H-A intervals observed during tachycardia and basal RV pacing to differentiate AVNRT and JT—delta HA = HA during pacing minus HA during tachycardia. (Helps to distinguish whether H-A interval represents true his conduction to the atria, or whether atria and His activated simultaneously from common focal source.)	Average H-A interval was -10 msec during AVNRT and 9 msec during JT ($p<0.00001$). Delta HA ≥0 has sensitivity/specificity of 89%/83%, PPV/NPV 84%/88% for diagnosis of JT.	Delta HA is a useful metric that can aid differentiation of AVNRT and JT during EP study. Utility in that JT ablation confers high risk of AV block. Limited in that spontaneous JT may be mechanistically different from JT seen w/ slow path modification.
Fan R 2011 (238) 21220046	Prospective cohort study	n=21	Adult pts referred to a single center for EP study and subsequent AVNRT ablation.	To investigate whether the tachycardia response to atrial overdrive pacing at a CL shorter than the tachycardia CL can elucidate whether the tachycardia is JT or AVNRT.	The paced AH interval was shorter for JT compared w/ AVNRT (86±19 msec vs. 338±59 msec, $p<0.0001$). The mean CL of JT longer compared w/ AVNRT (614±118 msec vs. 373±65 msec, $p<0.0001$)	Atrial overdrive pacing during tachycardia can help to rapidly differentiate JT from AVNRT (transiently suppresses JT, entrains AVNRT). Diagnosis of JT made on clinical grounds, although JT only observed post-ablation. Potential for misdiagnosis of AVNRT as JT. Included only spontaneous JT after AVNRT ablation (excluded "clinical" JT, i.e. not due to AVNRT ablation).

AAD indicates antiarrhythmic drug; AV, atrioventricular; AVJ, atrioventricular junction; AVNRT, atrioventricular nodal reentrant tachycardia; bid, two times per day; bpm, beats per min; CHB, complete heart block; CHD, congenital heart disease; CL, cycle length; EP, electrophysiological; f/u, follow up; h/o, history of; HR, heart rate; IV, intravenous; JET, junctional ectopic tachycardia; JT, junctional tachycardia; NPV, negative predictive value; PAC, premature atrial contractions; PJRT, permanent junctional reciprocating tachycardia; PPV, positive predictive value; pt, patient; RFA, radiofrequency ablation; SR, sinus rhythm; sx, symptom; VA, ventriculoatrial; VF, ventricular fibrillation; w/, with; and w/o, without.

Data Supplement 20. Nonrandomized Trials, Observational Studies, and/or Registries of Special Populations – Section 9

Study Name, Author, Year	Study Type/ Design	Study Size	Inclusion/Exclusion Criteria	Primary Endpoint	Results/p Values	Summary/Conclusions
Pediatrics: Epidemiology						
Lundberg A 1982 (239) 7122164	Retrospective, single center	49	49 babies SVT in infancy, 40 SVT, 9 atrial flutter/AF 86% males F/u mean 24 y	SVT recurrence after infancy	Males w/ WPW: 60% recurrence. Pts w/o WPW: 30% recurrence	Recurrent SVT after infant SVT: 30-60%
Deal BJ 1985 (240) 3964800	Retrospective multicenter	90	90 babies WPW and SVT ≤4 mo of age. SHD 20%. AVRT, one atrial flutter, no AF. Mean f/u 6.5 y.	WPW outcomes infants w/ SVT	Cardioversion success 87%, chronic digoxin 85 pts. Deaths: 4.4%, 2 w/o SHD: all receiving digoxin. One no SHD developed cardiomyopathy thought due to recurrent high dose cardioversions.	Mortality 4.4%, (2 no SHD), all receiving digoxin. 1/3 pts developing wide QRS tachycardia died.
Perry JC 1990 (241) 2229769	Retrospective, single center	140	140 pts WPW w/ SVT <18 y old. CHD 37%--23% of CHD = Ebstein's. Multiple AC: 12%.	SVT recurrences vs. age w WPW	SVT age ≤2 mo: 31% recurrent SVT, average age 8 y. SVT > age 5 y: 78% recurrent SVT during mean f/u 7 y.	SVT recurs more frequently in pts w/ first episode ≥ age 5 y.
Wu MH 1994 (242) 7850817	Retrospective, single center	90	90 pts w/ SVT <15 y old, median f/u 215 mo. CHF 16%. Stroke 1 pt.	Recurrent SVT vs. age onset SVT	SVT age 1-5 y: 40% recurrent SVT prenatal SVT lowest risk recurrent SVT, followed by age <1 y, then 1-5 y; onset >5 y highest risk.	First SVT ≥5 y: highest risk for recurrent SVT vs. age 1-5 y, or age <1 y
Riggs TW 1999 (243) 10393395	Retrospective, single center	70	70 pediatric pts w/ SVT, vs. WPW and age. Recurrent SVT: 29% w/ SVT <1 y, vs. 94% w/ SVT onset >1 y.	Risk recurrent SVT in young pts	Only sig predictor of recurrent SVT was age at presentation WPW not significant multivariate. 11	First SVT after age 1 y: high likelihood recurrent SVT vs. onset SVT <1 y (OR: 34.6).
Tortoriello TA 2003 (244) 14583354	Retrospective, single center	150	All pts SVT <1 y 1/1984-12/00.	Risk recurrent SVT in young pts vs. preexcitation	Pts w/ preexcitation: 88% recurrent SVT, vs. 17% w/o WPW. WPW pts more likely to require multiple drugs.	Presence of WPW associated w/ increased risk recurrent SVT
Gilljam T 2008 (245) 18489621	Retrospective, single center	109	109 pts SVT <30 d, 1971-1997. SVT = AVRT or AVNRT	Outcomes neonatal SVT	Freedom from arrhythmia: 52% 1 y, 82% 5 y, 83% 10 y. Recurrence 31% WPW vs. 6% no overt WPW.	Mortality 2.7% related to arrhythmia/CHF. Recurrences higher overt WPW, multiple meds, or >6 d to obtain initial arrhythmia control.
Santinelli V 2009 (246) 19147045	Prospective, single center	184	1995-2005, 184 pts ≤12 y (median 10 y, 8-12 y) w/ asymptomatic WPW evaluated and followed, median 57 mo.	Natural h/o asymptomatic WPW in children	72% remained asymptomatic. 28% sxs: 10% considered "POTS life-threatening": cardiac arrest 1.6%; Syncope 1.6%	Cardiac arrest 1.6% Multivariate risk: APERP ≤240 msec (p=.001) And multiple AC (p= .001)
Salerno JC 2011 (247) 21418251	Retrospective multi-center review	1755	Reviewed hospital databases 41 children's hospitals between 1/03-9/08 Discharge dx SVT, age <25 y	Case fatality	Overall 68 deaths (4%) 6% w/ SHD died vs. 1% of pts w/o SHD Case fatality increased in: Age <1 mo, OR: 2.41 (95% CI: 1.35-4.32) SHD, OR: 2.67 (95% CI: 1.22-5.80) Cardiomyopathy, OR: 6.72 (95% CI: 1.79-25.28) regardless of SHD	Case fatality in absence of SHD is low, 1%, Vs. 6% in presence of SHD Case fatality highest in cardiomyopathy regardless of presence of SHD
Cain N	Retrospective, single	446	446 pts WPW; median age dx 7	Natural h/o WPW	During f/u: additional 20% developed sx.	Sudden death: 1.3%

2013 (21) 23827401	center		y, 61% male, 9% SHD. Presentation: 64% w/ sxs--SVT 38%; chest pain or palps 27%; syncope 4%, AF 0.4%; cardiac arrest 0.2%.		54% SVT, AF 1.6%. Pts dx ≤3 mo, 35% WPW resolved, vs. 5.8% dx >3 mo. Sudden death 1.3%, 2.8/1000 pt y.	No heart disease: 1.1/1000 pt y SHD: 27/1000 pt y.
Pediatrics: Mechanisms of SVT						
Garson A 1981 (248) 7258098	Retrospective, single center	103	Intracardiac EP study in pts 2 d-17 y, mean 4.2 y.	Determine mechanisms of SVT in young pts w/ clinical SVT	AVRT 50%, AVNRT 24%, AT 21% 55% of AP tachycardia w/ manifest WPW	Predominance of AP mediated tachycardia in young pts
Ko JK 1992 (249) 1561973	Retrospective, single center	137	EP study (TEP 110, intracardiac 14, both 13) performed in pts <18 y of age, excluding significant heart disease or neuromuscular disorders	Determine mechanism of SVT in young pts w/ clinical SVT	AVRT 73%, AT 14%, AVNRT 13%.	AVNRT rarely present <2 y of age; AVRT and AT occurred throughout childhood
Weindling SN 1996 (250) 8554021	Retrospective, single center	112	SVT in infants, 7/85-3/93.	Mechanism of SVT in infants w/ SVT	AVRT 77%, AVNRT 9%, Atrial reentry 10%, ectopic atrial 4%. 106 pts treated: 70% digoxin, propranolol, or both, Class I or III used in 12% each. 8% ablation failed med rx: 1/9 died related to ablation (VF after discharge). Overall mortality 4.4%, 4/5 w/ SHD.	Ablation for medically refractory SVT. Neonate w/o SHD died related to complications of ablation. Recommends ablation for rare infants: fail aggressive med rx, rx comp by ventricular dysfunction, severe sx, complex SHD.
Gross GJ 1998 (251) 9794351	Retrospective, single center	15	Infants AVNRT <1 y mean age 58 d, 5/15 after CHD palliation. Typical AVNRT 14/15. Mean f/u 45 mo.	Outcome of AVNRT in first y of life	Digoxin: 87%, successful 38%. 40% digoxin + propranolol, successful 4/6. Class III in 3 pts: 2/3 RFA: ages 4.1 and 6.7 y.	All pts alive and well, minority syx beyond infancy. Digoxin questionalble benefit. AVNRT remained inducible in asymptomatic pts.
Anand RG 2009 (252) 19925541	Retrospective, multicenter	3556	Registry of pediatric EP reviewed for pts undergoing ablation for SVT between 1999-2004. Ages <7 y: 378; 7-12: 964; 12-21 y: 2214; males 55%; white 82%	Assess influence of age, gender, ethnicity on SVT	AP: 68%; decreased w/ increasing age AVNRT 32% In age 12-21 y, females more likely to have AVNRT than AP Black and Hispanic pts had less SVT than representation in population; whites more SVT than population.	Proportion of SVT due to AP decreases w/ increasing age. After age 12 y, females more likely to have AVNRT than males. More whites in registry than expected based on population.
Brembilla Perrot 2013 (253) 23609066	Retrospective, single center	140	Sxs of palpitations/SVT w/ normal ECG, underwent transesophageal pacing. Mean age 15±3 y	Utility of TEP to identify SVT in pts w/o preexcitation	59% AVNRT, AVRT 37%, AT 0.7%, VT 3%. High risk antegrade conduction over AP >240 bpm baseline or >290 bpm isoproterenol found in 1.4%.	Preexcitation found in 13.5% w/ atrial pacing.
Pediatrics: SVT Pharmacological Therapy						
Pfammatter JP 1998 (254) 9504781	Retrospective single center	26	SVT in infants <4 mo of age Mean age presentation 7 d SHD 31%; WPW 35% All AVRT	Digoxin for neonatal SVT	Digoxin successful: 65% Failure 27% Mean f/u 54 mo, 73% no meds no recurrences; 8% recurrent SVT	Digoxin success 65% 73% no early recurrences 8% symptomatic recurrences
Villain E 1998 (255)	Retrospective single center	141	SVT <1 y of age, 77% <1 mo. Digoxin first med in 114 pts, 81%; Amiodarone used after	Infant SVT: digoxin and amiodarone outcomes	Digoxin effective 65%; amiodarone 97%. Total amiodarone used in 58 pts, no pro-arrhythmia, increase TSH 10%. .	Digoxin: VF in 3 pts, (2/3 WPW) in hospital; one additional baby died at 3 mo, digoxin, no SHD. Total 4 CA on digoxin:

10223132			failure of digoxin (combo: 26%) or first: 19%. (solo 16%).		Adverse events 6 pts w/ digoxin: VF in 3 pts	3.5%. Amiodarone safer, more effective than digoxin.
Losek JD 1999 (256) 9922414	Multicenter prospective and retrospective	82	82 pts w/ 95 episodes SVT ≤18 y, in pediatric ED. 25 episodes <1 y of age. 10% SHD. Adenosine doses: low 0.1 mg/kg, medium 0.1-0.2 mg/kg, high ≥0.3 mg/kg.	Adenosine for pediatric SVT	Adenosine success 72%; AV node-dependent SVT success 79%. Successful dose: low 6%, medium 62%, high 32%.	Adenosine cardioversion 72%; low dose rarely effective.
Dixon J 2005 (257) 16243875	Retrospective single center	35	SVT rx w/ adenosine 1/98-5/03. 53 episodes. 23 infants, 12 children <16 y.	Dosing of adenosine to terminate SVT	Adenosine efficacy vs. dose: Infants: 50 mcg/kg, 9%, 150 mcg/kg, 35%; median effective 200 mcg/kg. Children: 50 mcg/kg: 9%,100 mcg/kg: <50%. median effective dose 150 mcg/kg	Adenosine in recommended dose has low efficacy, <10%. Recommend minimum dose 100 mcg/kg children, 150-200 mcg/kg infants.
Chang PM 2010 (258) 20194798	Retrospective single center	37	Refractory SVT: 40 episodes, 37 pts. 7/04-8/06. Median 34 d, 0-19 y. 65 SHD. IV procainamide: 50, Amiodarone 158 pts. AVRT 11, IART 18, EAT 11. Median dose amiodarone 2.5 mg/kg; procainamide 10 mg/kg.	IV procainamide vs. amiodarone for terminating SV12	Success: full + partial: Procainamide 71%, amiodarone 34%. Full success, Procainamide 50%, amiodarone 15%.	IV procainamide more efficacious than IV amiodarone for acute termination of SVT
Diza-Parra S 2014 (259) 24849273	Retrospective, single center	26	Ped ED: 44 episodes SVT in 26 pts, mean age 3.1 y. 1/07-12/11. Adenosine given to 89%, increasing dosages.	Efficacy of adenosine pediatric SVT	Adenosine efficacy 75%. 30% responded to single dose, mean 112 mcg/kg; 41% 2 doses, mean response dose 188 mcg/kg; 24% 3 doses, mean response dose 249 mcg/kg. 66% discharged home.	Mean effective dose of adenosine 173 mcg/kgm, higher than usual recommended dose. Mean number doses 1.7.
Pediatrics: JET Risk Factors						
Batra AS 2006 (260) 16391972	Retrospective, single center	336	336 consecutive pts surg for CHD/1 y. JET 8%, 27/336 pts	Identify risk factors for postop JET	Highest risk: TGA arterial switch, 23%; AVSD 21%; Norwood, 20%. JET pts younger, longer CPB times, hgher iinotrope schore, longer ischemic time	JET incidence 8%.
Andreasen JB 2008 (261) 18196218	Retrospective single center, case-control	874	874 pts <16 y, CHD surgery 1/98-12/05 Among JET pts: 26% had VSD closure; more often in pts w/ high RACHS score; 25% had surgery NOT near the AVN.	Identify risk factors for postop JET	Incidence 10.2%, CPB >90 min (OR: 2.6); high inotropes (OR: 2.6); high postop CK-MB (OR: 3.1). Mortality increased: 13.5% vs. 1.7%; 12 deaths. Prolonged LOS.	Rx protocol: sedation/electrolytes; reduced inotropes; reduced core temp to 34-35 d C; muscle relaxation, IV amiodarone.
Borgman KY 2012 (262) 21740877	Retrospective Single center,	36	CHD pts developing JET postop compared w/ CHD pts w/o JET	Assess genetic polymorphism in CHD pts who develop postop JET	Risks for JET postop included, age, inotrope score, bypass time, crossclamp time. ACE I/D genotype associated w/ 2-fold increase in risk for JET.	ACE I/D polymorphism may be risk factor for JET
Makhoul M 2013 (263) 22987106	Single center, retrospective, matched cohorts	54	Pts <21 y, CHD surgery 1/06-6/10 Emory. Narrow QRS tach >150 bpm. Identified JET in 54, incidence 1.4%out of 2450 pts undergoing CPB. One death in each group, 1.8%.	JET risk factors	↑risk: weight <4 kg, CPB >100 min; postop lactic acid >20 mg/dL. Rx: ↓ surface cooling core temp 35 d C, ↓exogenous catech; optimize sedation: used in 96%. Atrial overdrive pacing used 74%. Amiodarone 78%, Procainamide 9%;	Lower mortality and incidence JET than prior studies. Study not designed to assess drug efficacy.

					esmolol 6%.	
Pediatrics: JET Therapy						
Pfammatter JP 1995 (264) 7677480	Retrospective single center	6	Postop JET treated w/ hypothermia. 6 consecutive pts, surface cooling to rectal temperature 32-34 d C; sedated, vent. Cooling maintained 24-88 h.	Assess rx postop JET w/ hypothermia	Mean interval Dx JET and start hypothermia 4 h. JET rate ↓from 219 to 165 bpm mean.	Early institution moderate hypothermia effective in lowering HR
Walsh EP 1997 (265) 9120158	Prospective, single center	71	Staged rx for JET 1986-1994. 71 pts, HR >170 bpm. Stages: ↓catecholamines; correct feve; atrial pacing; digoxin; phenytoine or propranolol or verap; procaine or hypothermia; combine procainamide + hypothermia	Assess rx JET postop	Success: reduce HR <170 w/in 2 h. Treatment success 70/71 pts. JET associated w/ young age, transient AV block, VSD closures	Only correction of fever and combined procainamide + hypothermia efficacious.
Laird WP 2003 (266) 12370794	Retrospective, single center	11	11 pediatric postop CHD pts w/ JET, mean HR 203 bpm. IV amiodarone 5 mg/kg x2 given, followed by infusion 10-15 mg/kg/d for 48-72 h.	Amiodarone efficacy for postop JET	Amiodarone in higher dose (10 mg/kg vs. 5 mg/kg) achieved control more rapids. Hypotension/bradycardia 2 pts.	Amiodarone 10 mg/kg IV effective for rapid control of postop JET; continuous infusion necessary.
Plumpton K 2005 (267) 15831155	Retrospective, single center	15	15 postop pediatric CHD pts, JET, median 2.6 mo. JET rates 182-229 bpm, median 192 bpm. IV amiodarone	Amiodarone efficacy for postop JET	Amiodarone controlled tachycardia, median time 4.5 h, median dose 5.9 mg/kg. Hypotension or bradycardia in 2 pts.	Amiodarone controlled post-op JET rapidly.
Haas NA 2008 (268) 19026806	Prospective observational	71	71 of 2106 CPB pts repair CHD received amiodarone for postop atrial (70) or ventricular (7) tachycardia. Median age 3 mo. JET 37, ectopic AT 10, atrial flutter 8, AF 1, IART 1. Early rx: w/in 60 min of arrhythmia detection vs. >60 min. Protocol: reduce inotropes, correct lytes; IV amiodarone. Dose 5 mg/kg over 1-4 h, infusion 5-15 mcg/kg/min. Repeat boluses; infusion 5-10 mg/kg/d.	Assess response of postop tachycardia to IV amiodarone	Early rx postop tachycardia reduced rate (156 vs. 300 bpm, p<0.01); time to control (400 vs. 1038 min, p<0.001), reduced dose (28 vs. 67 mg, p<0.025), and ICU LOS (3.3 vs. 5.3 d, p<0.01).	Early RX w/ amiodarone (60 min) significant improved outcomes.
Collins KK 2009 (269) 19232902	Multicenter retrospective	94	Non postoperative JET, median age 0.8 y, range fetus – 16 y). . Time frame 1969-2008. CHF 16%. *VA dissociated 56%,* 1:1 VA 32%; both 3%, NOS 9%. Median f/u 4.5 y.	Assess outcomes of rx for non postop JET in pediatric pts	Medications used in 89%; 62% ≥2 medications. Amiodarone used 60%, alone in 20%, combo w/ beta blocker (15%), procainamide, dif, flecainide, propafenone. Ablation: indication CHF or refractory to medications; elective 15%. RF 17, cryoablation 27, efficacy 82 vs. 85%, p=NS; recurrence 13-14%; inadvertent CHB 18% of RF pts. AV node ablation 3%, pacer 14%.	Amiodarone effective in 60%; Ablation: 47%: efficacy 82-85%, recurrence 13-14%, 18% inadvertent CHB in RF pts; 3% underwent intentional ablation AVN. Pacers 14% of ablation pts.

					Deaths 4%, all age ≤6 mo. 70% no chronic medical rx for JET.	
Kovacikova L 2009 (270) 19632422	Retrospective single center	40	Postop CHD pts IV amiodarone 2 mg/kg boluses, continuous infusion 10=15 mcg/kg/min	Assess IV amiodarone as rx for postop JET	Amiodarone effective 45%; SR in 7, decreased HR 11; allowed effective atrial pacing w/ AV synchrony. Failure of amiodarone associated w/ higher AV oxygen saturation difference, lower body temp.	Amiodarone achieved SR in 45% as first line; recommend in combo w/ hypothermia.
Pediatrics: EP Study/Risk						
Klein GJ 1979 492252 (137)	To assess risk of VF in WPW pts.	73	WPW + h/o VF vs. preexcitation, WPW pts w/ no h/o VF	VF	These pts also had high prevelance of reciprocating tachycardia and AF (14 of 25 vs. 18 of 73 [P=0.004]) and multiple APs (5 of 25 vs. four of 73 [P=0.012]). WPW + h/o AF and tachycardia demonstrate rapid conduction over AP during AF.	VF was initial manifestation of WPW in 10% of pts: ages 8,9, 16 y.
Timmermans C 1995 (271) 7653450	Retrospective, single center	15	15/690 pts w/ WPW referred 1/79-2/95 presented w/ cardiac arrest. 53% not known to have WPW. EP study done to assess AP characteristics.	Characterize WPW pts w/ arrest	VF initial manifestation in 8 pts. 10/15 exercising. 7 pts known ORT/AF. 9/11 EP study: AP ERP≤250 msec. Multiple AP not a risk.	VF 2.2% of series; all under age 45 y, half under age 30y.
Ceresnak SR 2012 (272) 22324823	Retrospective, multi-center	30	1147 pts w/ WPW underwent EP study; 30 pts (2.6%) w/ ADT. Mean age 16±3 y.	Assess EP characteristics of pts w/ ADT	7% w/ CHD 13% more than one AP Left sided AP 53%; right 47% often septal High risk in 17 pts (57%)	ADT rare in children w/ WPW undergoing ablation, 2.6% 57% w/ ADT had high risk characteristics
Brembilla Perot B 2013 (273) 23148120	Retrospective, single center	63	807 pts w/ WPW underwent EP study; ADT induced in 63 pts (8%) Ages	Assess EP characteristics of pts w/ WPW and ADT	Pts w/ ADT more likely to have AF induction (41 vs. 24%, p<.002), and high risk characteristics (22 vs. 12%, p<.02) No difference in age, gender, clinical presentation, ORT	Clinical outcome did not differ in pts w/ ADT; older pts less likely to have high risk characteristics
Pappone C 2014 (145) 25052405	Prospective single center	2169	2169 pts w/ WPW, 8 y prospective study. 1001: no RFA; 1168: RFA. EP study in all. Median f/u 96 mo. 92% f/u.	Assess VF or malignant arrhythmias in WPW	In no RFA group, 1.5% experienced VF, vs. 0.4% in no RFA group. VF: 13/15 were children, median age 11 y. Associated w/ short AP ERP (APERP <240 msec) (P <0.001) and AVRT initiating AF, but no sxs. Posteroseptal AP more common among VF pts. VF w/ exertion in 4, at rest in 11.	1.5% VF, almost all in children; risk higher in asymptomatic pts 13/15 pts w/ VF <15 y; 2 age 32 y.
Pediatrics: Ablation						
Kugler JD 1994 (167) 8164700	Retrospective, multi-center	652	652 pts underwent 725 ablation procedures between 1/91-9/92, Median age 13.5 y, 84% no SHD	Assess outcomes and complications of ablation in young pts	Success rates: AVRT and AVNRT 83%; highest in LFW AP and ↑institutional experience; lower in RFW AP, structural heart disease, body weight >80 kg. Complications 4.8%, higher in very low weight <15 kg and less institutional experience	Uncontrolled, voluntary registry
Kugler J	Retrospective, multi-	4135	46 centers, pts 0.1-20.9 y	Determine safety and	Success rates: AVRT 90%, higher left	Ablation evolving into treatment of choice

1997 (274) 9399718	center		undergoing ablation 1/91-9/15/96 88% no SHD 58% performed due to family/pt choice	efficacy of ablation in childhood	>right, 95 vs. 86%; AVNRT 96%; Mean fluoroscopy time 47.6±40 min; Major complications 3.2% Deaths 4 pts, 1 immediate, 3 late (2 infant deaths) Freedom from recurrence at 3 y: AP 77%, AVNRT 71%.	for SVT in older pts Deaths in 2 infants noted Higher recurrence than adult pts, but possibly due to higher f/u.
Schaffer msec 2000 (275) 10980215	Retrospective multicenter	10	Rviewed 4651 cases in Pediatric RFCA Registry; deaths 0.22% 5/4092 w/ normal hearts 0.12%	Assess incidence/causes of death	Deaths: all in left sided AP; mural injury, perforation, thromboembolism, vent arrhythmia Weight 32.7 kg vs. 55.6 kg (p=.023) Number of lesions 26.3 vs. 8.7, (p=.019)	Mortality 0.12-0.22% in left sided AP ablations; lower weight, greater number of lesions
Blaufox AD 2001 (276) 11733398	Retrospective multicenter	137	Reviewed Pediatric RFCA Registry, 1989-1999, age ≤18 mo, median 0.7 y, weight median 10 kg. 152 procedures, CHD 36%.	Outcomes ablation in age ≤18 mo	Success 87.6%, vs. 90.6%, NS Major comps 4.6% vs. 2.9%, p=.17	No difference in success or complications ≤18 mo
Blaufox AD 2004 (277) 14764175	Retrospective single center	18	18 RFA in pts <15 kg 1/88-8/01; median weight 5.7 kg, age 5.8 mo; 4 CHD, 4 CHF	Outcomes ablation <15 kg	ORT 9, MAT 1, VT 4; success all AP; no recur. Complications 3/18 myocardial infarct 1 occluding left circ, CHF, mitral valve replacement; torn mitral leaflet 1	Complications 16% associated w/ RF dose indexed for body size (duration and number) Mitral valve replacement
Van Hare G 2004 (278) 15250858	Prospective, multi-center	481	Pts ≤16 y, w/o significant heart disease, w/ AVRT or AVNRT; compared w/ cohort-eligible registry pts, N =504	Assess success rates and complications in age <16 y	Acute success: 96%, highest in left sided AP; left 98% vs. right 91% Complications 4.2%; no deaths; AV block 1.2% in AVNRT or septal AC	High success rates for AVNRT or AVRT w/o CHD
Van Hare G 2004 (279) 15851152	Prospective, multi-center	481	481 pts w/ AVRT or AVNRT, excluding pts w/ significant heart disease Ages 0.1-16 y Followed at 2,6,12 mo following ablation	Assess recurrence following successful ablation	Recurrence at 2,6, 12 mo was 7, 9.2, and 10.7% Recurrence highest right septal AP 24.6%, RFW 15.8%, LFW 9.3%, left septal 4.8%; AVNRT 4.8% vs. 12.9% for AP at 12 mo	Recurrence after initially successful ablation occurs commonly in children, 10.7% Recurrence less common for AVNRT 4.8%, most common for right sided AP >25% at one y
Aiyagari R 2005 (280) 16132307	Retrospective, single center	69	All pts ≤20 kg undergoing ablation between 1/94-1/03 Group 1, <15 kg, 25 pts Group 2, 15.1-20 kg, 44 pts	Compare safety and efficacy of ablation in pts <15 kg vs. 15.1-20 kg	SHD more common in pts <15 kg 28% vs. 7%, p<0.01. No difference in mechanism SVT, number lesions, temperature, procedure time, success rates 91% vs. 89%. Major complications 8% in Group 1, 2.3% Group 2, p=0.39.	Outcomes similar between groups Complications 8% in smaller children, although not statistically significant
Lee PC 2007 (281) 17461876	Retrospective, single center	228	228 pts 5-18 y old undergoing ablation 12/89 to 8/05 Mean age 9±7 y; mean f/u 86±38 mo	Assess results of ablation in pediatric pts 5-18 y	AVRT 61%, AVNRT 29%, AT 5%, atrial flutter 5%. Success rates 92% AVRT, 97% AVNRT, 82% AT, 91% atrial flutter. Complications 8.7%, major 0.9% AV block; Recurrence 4.7%	AVRT incidence higher than in adults; Success rates lowest for AT 82%; other mechanisms 91-97%. Complications 8.7%, recurrence 4.7%

Chiu SN 2009 (282) 19609044	Retrospective single center	27	27/210 pts underwent RF at age <6 y. Median age 4.4 y (8 mo-5.9 y). Median weight 15 kg (6.6-30 kg). AVRT 55%, atrial flutter 19%, AVNRT 15%. SHD 33%.	Outcomes ablation <6 y.	Indications: drug refractory SVT, or tach-induced cardiomyopathy. Acute success 93%, recurrence 7.4%.	Acute success 93%, recurrence 7.4%. CHB 3.7% in 5 y old.
Schneider HE 2009 (283) 19324303	Prospective, single center	212	212 pts ages <21 y undergoing ablation for SVT underwent selective coronary angiography before and 30 min after RFA or cryoablation; CHD present in 15% Median age 12 y (0.3-20.4 y) Median weight 47 kg (5.5–130 kg)	Assess incidence of coronary injury following ablation	AP 53%; AVNRT 40%, both 7% Coronary artery narrowing identified in 2/117 pts (1.7%) w/ AP, both in posteroseptal region.	Coronary artery injury present in 1.7% of AP ablations: both in posteroseptal region Consider coronary angiography w/ ablation in posteroseptal region
Kantoch MJ 2011 (284) 21621374	Retrospective single center	34	1995-2009, 34 pts <2y of age, RFA 42 procedures in 31 pts, mean wt 7.4 kg; 17/34 CHF; 3 pts ECMO	Outcomes ablation <2 y	AVRT 19, Focal 6, atrial flutter 1, VT 3, JET 2 Acute success 74% vs. 91% >2y No recurrence mean 7.3 y Major complications 4/34 children; CHB, pacer in 6 wk old infant; RFA occusion x 2,	Major complications 11.8% vs. 0.7% in >2 y of age
Buddhe S 2012 (282) 22452328	Retrospective single center	155	1/05-12/09, 155 pts ablation for SVT. Mean age 13.4±3.7 y. 22% African American. RF 107, Cryoablation 11, Both 97. AVRT 74%, AVNRT 17%; SNRT 5%, His bundle reentry 4%. . Median f/u 41 mo.	Outcomes ablation during longer f/u	Acute success 98%; 5 y f/u 83% success. Recurrences higher w/ right anterior-anteroseptal AC (33%), multiple (27%), or broad distribution. Recurrence not statistical different RF (14%) vs. Cryoablation (22%) or both (20%)	17% recurrence WPW or SVT during mean f/u 38 mo. Recurrences higher vs. age, 11.7 y vs. 13.6 y ($p<0.05$).
Pediatrics: QOL & Cost Effectiveness						
Garson A 1997 (285) 9395176	Cost modeling	N/A	Cost-effectiveness modeling for ablation vs. medications or surgery for WPW treatment in pts age 5-21 y	Identify long term cost effectiveness of treatment strategies	Ablation cost 39% of surgical rx, and 57% of medical management. Estimated mortality ablation 0.15% = 10% of medical rx, and 28% of surgical rx Morbidity ablation = 32% of medications, and 36% of surgery	Catheter ablation has lower cost, mortality and morbidity than either medical rx or surgery, and is treatment of choice for the child 5 y of age or older w/ WPW and SVT.
Pfammatter JP 2004 (286) 15093993	Retrospective, single center	88	Compare drug therapy vs. ablation as first line in 2 time periods: 1989-94, N = 40, and 1995-2000, N = 48. Early time period: medications only Later ablation as first line in 16/48 pts.	Assess impact of ablation as first line therapy for SVT in pts >5 y of age	Over time, number of SVT episodes (3.7 to 2), duration of meds (15 mo to 4.6 mo, $p<0.05$) and numbers of cardioversions declined (1.1/pt to 0.2, $p<0.05$)	Use of ablation as first line treatment in pts over age 5 y results in fewer episodes of SVT and cardioversions
Strieper M 2010 (287) 21106019	Prospective, single group, pre-test-posttest design	27	Consecutive pts w/ SVT referred for catheter ablation between 10/04 – 6/06. Pre and 6 mo post ablation. Ages 5-18 y.	Assess impact of ablation on QOL scores	Pre test lowest scores in social and physical functioning; post test greatest improvement in physical functioning. Significant improvement in all QOL scores following successful elimination of SVT	Significant improvement in all QOL scores following successful elimination of SVT

Wood KA 2010 (288) 20109982	Prospective, single group, pre-test-posttest design	52	Consecutive pts w/ SVT referred for catheter ablation ≥13 y, Mean age 41±17 y, range 13-85 y Female 65% AVNRT 57%, AVRT 31%, AT 12%	Comparison of QOL, sxs before and after ablation procedure for SVT	All sxs decreased but not completely eliminated at 1 mo f/u Improvements in palpitations, p=0.001, Fatigue, p=0.001, Dizziness, p<0.01, resp or chest pressure p<0.001 QOL improvements in number, severity and impact of sxs, p<0.001	All sxs improved after ablation, women reported larger changes in sxs and QOL than men
CHD: Incidence of SVT						
Engelfriet P 2005 (289) 15996978	Retrospective, multicenter	4110	CONCOR national registry >8600 pts ACHD >17y of age: Pts w/ ACHD of 8 major types seen in 1998, w/ complete f/u to 2003: (ASD, VSD, TGA, TOF, single ventricle, coarctation, Marfan's, cyanotic heart disease); followed until 12/2003	assess endocarditis, arrhythmias, vascular events	Median age 27.9 y, (21.7-38.6y), 79% <50 y old median f/u 5.1 y (3.6-5.7 y); SVA occurred in TOF 20%, TGA 26%; ASD 28%, Fontan 45%	Young population w/ ACHD, overall 18% developed SVA
Verheugt C 2008 (290) 18559697	Retrospective, multicenter	7414	CONCOR registry, Netherlands, >8600 pts ACHD >17 y old 1/02-1/08; assess outcomes frequencies	Is gender associated w/ outcomes in ACHD	Median age 35 y (17-91); males 50.2%; median f/u 2.7 y; frequencies of arrhythmias 22-44%; females 12% lower risk arrhythmia, NS; females higher risk for pulmonary HTN	15% developed SVA during f/u 2.7 y
Bouchardy 2009 (291) 19822808	Retrospective multicenter	38,428	Adult registry Canada; ACHD median age 42 y; 1983-2005; 5812 pts AT	Assess risk of developing atrial arrhythmias as adult	Prevalence 15.1% AT; impact: 20 y risk for 20 y old 7%, 50 y old 38%; adverse event HR 2.5; mortality 1.47; stroke, CHF 2.21	>50% severe CHD developed AT by age 65 y; 2-3↑ death, stroke, CHF
Trojnarska O 2009 (292) 19437395	Retrospective, multicenter	1304	National Polish registry, ACHD pts followed 1995-2004; mean age 29.4±10.6 y, mean f/u 3.5±1.8 y	Assess outcomes of SVA	SVA developed in 10.3% of pts; multivariable predictors; presence of HF (HR: 4.66) CHD complexity (HR: 2.31), age (HR: 1.32) gender NS	10.3% developed SVA Increased w/ CHF, complex CHD, increasing age
Bernier M 2010 (293) 20691314	Retrospective multicenter	71,467	Quebec database; ACHD ≥18 y; study period 1/88–12/05; ACHD pts *arrhythmia free* by age 18 y in 1/1988	assess risk of developing AT vs. type CHD	11% developed SVA; 30 y risk for 18 y old: 18% for right sided CHD, 11% for left sided herat disease	ACHD pts arrhythmia free by age 18 y: risk greater in pts w/ right-sided disease vs. left-sided
Khairy P 2010 (294) 20713900	Retrospective, multicenter	566	AARCC (Alliance for Adult Research in Cong Card); 11 centers; ACHD ages ≥18 y; study period 9/07-10/08	Assess arrhythmia prevalence in TOF adults	Mean age 36.8±12 y; f/u; Prevalence SVA 20.1%; risk factors reentrant AT: right atrial enlargement (OR: 6.2); HTN (OR: 2.3), number of cardiac surgeries (OR: 1.4); ventricular arrhythmias 14.6%	20.1% of TOF w/ SVA
Cuypers JA 2013 (295) 23886606	Retrospective single center	85	135 pts, Netherlands; surgical ASD closure <15 y of age, (mean 7.5± 3.5 y) between 1968-1980; f/u on 131 pts	Assess SVA development late after ASD closure	Mean f/u 35 y (30-41 y), 16% developed SVA; 12% developed AF	16% AT in f/u ASD
Valente AM 2014	Multicenter, prospective	873	Repaired TOF Median age 24.4 y, undergoing standard eval ECG,	Assess TOF primary outcome of VT or death	SVA developed in 11% (7% atrial flutter, 4% AF); total 3.7% death or VT; Risk for	TOF pts develop SVA in 11%; SVA significant risk factor for VT or sudden

(296) 24179163			Exercise, MRI		VT or sudden death included ↑RV mass (HR: 5.04), ↓LVEF (HR: 3.34) or h/o atrial arrhythmia (HR: 3.65)	death, HR: 3.65
CHD: Mechanisms of SVT						
Collins KK 2000 (297) 11053709	Retrospective, single center	88	ACHD, 110 AT macro-reentry circuits, median age 23.4 y, repaired CHD: TGA/atrial repair, 17%,; biventricular CHD 27%; Fontan 49%, other 7	Sites of successful ablation for AT	Non-Fontan: CTI 57-67%, lateral RA wall 22-43%, anterior RA 11%. Fontan pts: isthmus 15%, lateral RA 53%, anterior 25%, septum 7%	CTI involved in right AT in ~60% non-Fontan AT; Fontan multiple RA circuits esp lateral RA wall
Akar JG 2001 (218) 11499727	Retrospective single center	16	Consecutive repaired ACHD pts, EP study & ablation, mean ages 32±18 y; 24 circuits. Mean f/u 24 mo ASD/VSD 9; TOF 3, UVH 4. ECG: 44% typical atrial flutter; 56% atypical.	Frequency of typical atrial flutter vs. IART in CHD	19% typical atrial flutter only; 37% IART alone; 44% both atrial flutter/IART; Isthmus dependent 86% IART; 92% successful ablation; only failure=Fontan	44% both atrial flutter and IART: Surface ECG did not predict mechanism 7% recurrence 2 y.
Delacretaz E 2001 (199) 11345382	Retrospective, single center	20	47 Atrial reentry circuits mapped in 20 pts, repaired CHD, ASD 10, TOF 6; mean age 43 ±15 y	Assess sites of reentry circuits	Lateral RA wall 40%, CTI 38%; ASD patch 17%. Acute success 80% pts; mean f/u 19 mo, 20% recurrence.	ALL RA macro-reentry, largely ASD or TOF pts; Circuits in 3 sites: lateral RA wall ≅ CTI
De Groot NM 2006 (298) 16648056	Retrospective single center	43	43 consecutive pts repaired ACHD undergoing EP study/ablation for SVT, mean age 37 y,	Assess mechanism of SVT and success of ablations	IART 77% including scar-related 43%, CTI 34%; Focal 16%; AF 3%. Ablation success 70% IART, atrial flutter,focal 100%	RA macro-reentry: 77% Focal 16% AF 3%
Mah DY 2011 (299) 21539636	Retrospective, single center	58	Repaired TOF or DORV pts, 1/97 to 3/10; 58 pts w/ 127 AT circuits, mean age 35 y	Assess atrial reentry circuits in TOF	RA reentry 75%; focal/ectopic 13%; AF 12%; CTI 53% of IART; CTI and lateral RA wall = 85% of IART; AT ablation acute success 90%; 34% recurrence w/in 3 y	13% focal; AF 12%; IART 75%: Of IART 53% involve isthmus; acute success high, recurrence moderate; target both isthmus and lateral RA wall
Koyak Z 2013 (300) 23993125	Retrospective multicenter	92	ACHD pts, CONCOR Dutch database; First onset SVT 1/08-1/11 mean age 51±16 y; AF/atrial flutter >80%; septal defects 50%, left sided CHD 21%.	Mech of SVT in ACHD	Mechanism of SVT described as AF 68%, atrial flutter 14%, AVNRT 8%, "AT" 7%, unspecified 3%	AF 68%, atrial flutter 14% AVNRT 8% AT ? focal 7%
Wasmer K 2013 (301) 23540398	Retrospective, single center	54	54 pts repaired ASD, mean age 47.3 y at study, 11/95-12/01, 2 pts w/ AF, 10 no inducible AT: 42 pts studied; f/u 7.7 y	Assess RA reentry circuits in ASD	CTI dependent 69%, of which 40% were clockwise; scar related 17%, both 12%; CTI ablation performed in non-inducible/AF; acute success ~90%; 60% arrhythmia free at 7.7 y	ASD Ablation aimed at CTI highly successful; 11% developed AF
CHD: Pharmacological Therapy						
Fish FA 1991 (302) 1906902	Retrospective multi-center	455	455/579 rx for SVT (79%); 369 pts rx flecainide (81%) . encainide 19%, Mean age of flecainide death or CA: 9.9 y, range 4d-26 y	Pro-arrhythmia, cardiac arrest or death w/ flecainide/encainide in young pts	Overall death/CA; 25 pts; 18/25 w/ CHD; Flecainide for SVT: efficacy 7.1%, proarrhythmia 7.4%; cardiac arrest 2.3%; 12 pts cardiac arrest; 8/12 CHD: 7/8 mild-mod ventricular dysfunction or single vent or systemic RV Flecainide efficacy SVT 70%; pro-	Flecainide rx SVT + CHD: 8.3% death or CA. vs. 0.3% w/o CHD. Deaths flecainide + CHD, average 16.1 y 4 flecainide deaths in structurally normal hearts, 3 of 4 normal function.

					arrhythmia 7.4%;	
Thorne SA 1999 (303) 10402444	Retrospective single center	92	ACHD, mean age 34.9 y, receiving amiodarone for ≥6 mo; case-control group. Mean duration 3 y, mean dose 191 mg	Review side effects of chronic oral amio	36% developed thyroid dysfunction: 19 hyper, 14 hypothyroid. Sig risk factors: Female gender (OR: 3.0) cyanotic HD (OR: 7.0); Fontan (OR :4.0); dosage >200 mg/d (OR: 4.0)	Pts w/ CHD at higher risk for amiodarone adverse effects, especially women, cyanosis, Fontan, or dose >200 mg
Pass RH 2000 (304) 11009280	Retrospective single center	10	IV diltiazem for AT w/ rapid response. Includes 3 adults w/ AT and repaired CHD, ages 18-21 y.	Efficacy diltiazem for AT	Diltiazem 0.25 mg/kg over 5 min + infusion 0.11 mg/kg/h. HR median 166 pre-treatment, fell to 23 bpm w/in 10 min. No HTN.	Diltiazem effectively decreased ventricular rate w/in 10 min.
Hoyer AW 2007 (305) 17669084	Retrospective single center	19	15 w/ CHD, 4 w/ normal hearts. 74 episodes of atrial flutter 4 AF. Median age 16 y.	Evaluate efficacy of ibutilide	71% successful cardioversion; No symptomatic bradycardia. 1 TdP, 1 NSVT	W/ careful monitoring, ibutilide can be an effective tool for cardioversion of flutter.
Khairy P 2008 (306) 19808416	Retrospective multicenter	37	37 pts w/ intra-atrial baffle repair of TGA, 7 sites, ages 28±7.6 y, w/ AICD: primary prevention 62%, secondary 38%.	ICD and outcomes TGA	Annual rates approximately shock: 0.5% primary, 6% secondary. SVT preceded VT in 50%.	Lack of beta-blockers use: HR: 16.7; beta-blockers seem protective for SVT initiating VT
Miyazaki A 2008 (307) 18931451	Retrospective single center	27	44 ACHD, mean age 23±12 y, f/u 13±12 mo; oral sotalol 2002-2007; 27 pts SVT	Efficacy & safety sotalol in ACHD	Overall 41% control; for SVT 52% complete control; Not effective for AF	AT w/ AF risk factor for rx failure, OR: 18.3 One death 34 y old, AT + AF
Rao SO 2009 (308) 18653253	Prospective, non-randomized	19	19 pts ACHD, mean age 20 y; present in AT, given oral sotalol 2 mg/kg as inpatients	Sotalol for conversion	Focal AT 21%, IART 79%; 84% conversion w/in 98-145 min; 75% of focal and 87% IART. One fatality after 2 d: thromboembolism.	High efficacy 84% for oral sotalol in ACHD acute conversion of AT
Wells R 2009 (309) 19691680	Retrospective multicenter	20	ACHD pts, 4 institutions, 7 y, rx w/ dofetilide, median age 30 y, 19-53 y.11/20 pts Fontan surgeries. AF 4, IART 13, AF + IART 3. Dosage 125-500 mcg bid. Median f/u ~ 12 mo.	Dofetilide efficacy AT in ACHD	Conversion to SR: 85%. Torsades de pointes: 10%, immediate. Recurrent AT: 65%. 55% taking dofetilide at 1 y.	Dofetilide effective acute termination of AT (85%) w/ 10% Torsades de pointes. 65% recurrent AT in 12 mo. ie 35% control AT x 1 y.
Garnock-Jones KP 2012 (310) 22191799	Meta-analysis of databases		MEDLINE, EMBASE, and AdisBases databases searched for esmolol and tachycardia, and heart surgery, through 11/2011.	Review of databases using esmolol	Includes comparison trials w/ other meds: placebo, propranolol, diltiazem, ibutilide, for treatment of SVT and for prophylaxis during heart surgery	Hypotension in 2-40% of SVT pts. Resulted in discontinuation in 3-23%
Koyak Z 2013 (300) 23993125	Retrospective multicenter	92	ACHD pts, CONCOR databse; First onset SVT 1/08-1/11 mean age 51±16 y; AF/atrial flutter >80%; septal defects 50%, left sided CHD 21%. Sotalol used in 34%, (mean dose 156 mg)) and amiodarone 15%,(mean dose 350 mg)	Long term efficacy of AA meds	90% achieved sinus rhythm. 84% rx w/ chronic oral agents; f/u 2.5±1.4 y; 45% free from SVT. Sotalol or Amiodarone: significantly fewer recurrences, (HR: 0.5); 22% adverse events; all amiodarone pts w/ side effects, thyroid 80%, AVB 20%.	Class III agents sotalol and amiodarone more efficacious in maintaining SR; sotalol considered as first choice med Relatively high dose amiodarone associated w/ significant adverse events
Banchs JE 2014	Prospective non randomized	13	ACHD, 4 TOF, 1 pulmonary atresia, 2 ASD, 1 dextro-TGA ; 2	Dofetilide efficacy and safety for AT in ACHD	Mechanism of SVT described as AF, atrial flutter or AT	Dofetilide well tolerated, Effective for conversion in 70%

(311) 23947935			L-TGA, 2 tricuspid atresia, 1 asd and vsd, 1 vsd pulmonary atresia, 1 noncompaction; mean age 40±11; median f/u 16 mo		70% conversion 15% control of recurrences Average time to recurrence 5.5 mo 39% ddischarge medication due to recurrence	Recurrence still frequent.
Stan MN 2014 (312) 22518347	Retrospective single center	23	ACHD pts developing amiodarone-induced thyrotoxicosis after ≥3 mo amiodarone, Mayo Clinic 1987-2009; median f/u 3.1 y.	Identify incidence and risk factors amiodarone thyrotoxicosis	13.6% (23/169) ACHD pts developed amiodarone thryrotoxicosis.	Highest Risk: low BMI <21, cyanotic heart disease
CHD: Atrial Pacing						
Olshansky B 1988 (313) 3339174	Retrospective single center	12	Rapid atrial pacing ≥15 sec at ≥10 msec shorter than AT, 12 adult pts, mean 55 y, 2/12 ACHD: VSD, VSD +ASD; mean atrial CL 233 msec	Conversion rates of AT/atrial flutter w/ rapid atrial pacing	2/12 converted w/ rapid atrial pacing 10 pts received procaine then repeat rapid atrial pacing: successful in 10 pts	Procaine needed to assist RAP conversion in pts w/ ACHD
Silka MJ 1990 (314) 2305688	Retrospective single center	21	21 pts, CHD, AT or VT and anti-bradycardia pacing. Mean age 11 y (2-19 y)	Assess impact of anti-brady pacing on frequency of AT	14 pts w/ AT. Prevention of bradycardia by pacing: significant decrease in SVT (p=0.008) and VT	SVT reduced, but not atrial flutter
Ragonese P 1997 (315) 9455751	Retrospective single center	18	18 ACHD pts, recurrent late IART, implanted atrial pacemakers programmed for atrial pacing >80% of time.	Atrial anti-brady pacing effect on IART recurrence	Recurrent AT in 29% in first 6 mo. Late recurrences in 11%; 83% arrhythmia free, 2 pts on AA meds.	Chronic atrial pacing reduced IART recurrences to 11%. One late sudden death.
Brockmeier K 2002 (316) 12539114	Retrospective single center	39	62 conversions in 39 pts, 31 postop CHD, median age 12.5 y (0.1-33 y); "typical atrial flutter 21", median CL 235 msec	TEP conversion of AT in CHD	81% successful conversions w/ TEP; 19% underwent CDDV Used AEST 4-6 x (CL-20) to minimum 120 msec; mA 24-28	TEP converted 81% atrial flutter or ART
Stephenson EA 2003 (317) 14516898	Retrospective multicenter	28	ATP in 28 ACHD pts, age 30 ±18 y. Medtronic AT500 pacer. ≥2 episodes AT in 12 mo. Mean f/u 10 mo.	ATP detection and termination of AT	57% of pts had AT after implant, mean 54 episodes.	ATP efficacy for termination: 54%.
CHD: DC Cardioversion						
Ammash NM 2012 (318) 20934227	Retrospective single center	63	63 ACHD underwent 80 DCCV 6/00-7/03. Flutter most common 46%. f/u 387 d	Outcome of DCCV	DCCV successful in 94%. 60% ACHD pts recurred during f/u all cause mortality was 11% during one y f/u.	DCCV safe and effective in ACHD. Recurrence rate is 60%/1 y; AF predicted recurrence, and spontaneous echocardiography contrast in LA
CHD: Catheter Ablation - NOS						
Triedman JK 1995 (319) 7828297	Retrospective single center	10	10 consecutive ACHD pts, median age 18.4 y (12-43 y). Fontan 6, TGA atrial 2, 2 biVS. 30 IART circuits. Ablate 22 circuits. Median f/u 4 mo.	ACHD ablation outcomes	Circuits in 4 areas of RA. 77% acute success (circuits) 50% recurrence short term	77% acute success, 50% recurrence short term 4 mo
Kalman JM 1996 (212) 8565168	Retrospective single center	18	18 consecutive ACHD pts, 26 IART circuits, mean age 26 ±15 y map & Ablation 1992-1995. ASD 50%, Fontan 22%, TGA	ACHD ablation outcomes	Acute success 83% Fontan 50% success	Acute success 83%, 50% asymptomatic, no medications during f/u. 33% recurrence, plus 7% AF

			atrial switch 22%, Rastelli 5%; conventional mapping, f/u mean 17 mo.			
Tanner H 2004 (320) 15851168	Multicenter retrospective	36	36 consecutive ACHD pts, median age 46 y. ASD 20, TOF 8, TGA 5, VSD 1, UVH 1, cc-TGA 1. Mean f/u 17 mo	ACHD ablation outcomes	52 IART circuits; 48 ablations. 65% CTI dependent. 27% incisional, 8% LA. Acute success: 87%.	87% acute success ablation ACHD (2 ventricles predominantly) 25% on chronic AA meds 92% free of recurrence 14% developed AF
Lukac P 2005 (321) 15851267	Retrospective single center	52	52/83 pts postop ACHD, median age 36 y ASD 21, TOF 11, TGA 9; UVH 4, VSD 2 Median f/u 27 mo	ACHD ablation outcomes	CTI dependent 71% Fontan pts multiple circuits;lateral RA wall	CTI dependent 71%-most common, except in Fontan pts 31% chronic AA meds 24% recurrence 13% died or OHT
De Groot NM 2010 (322) 20194797	Retrospective single center	53	Ablation in 53 ACHD pts, age 38±15 y.	Examine characteristics of recurrences after ablation ACHD	Atrial flutter 51%; IART 42%; Focal 9%. Acute success 65%; recurrence 59% w/in one y. Repeat ablation 15: 7 similar mechanism. f/u: 5± 3 y: death 9%; AA meds 57%; 31% recurrent AT	ACHD: High recurrence 59%; 57% meds; 9% death Recurrent AT may be different mechanism.
Yap SC 2010 (323) 21029876	Retrospective single center	130	193 ablations performed in ACHD 130 pts, mean age 40 ±13 y; median f/u 3.4 y. Type of CHD ASD 21%, TGA 18%; UVH 20%; TGA 18%, other 12%	Acute & long term outcomes ablation of IART in ACHD	Acute success 69%; 5% major comps; pacers 3%; 62% discharged on AA meds; IART recurrence: 4 y =51%; repeat ablation 35%; death 4%. Older age and Fontan palliation predictors of recurrence.	Differential outcomes of ablation based on type of CHD: in Fontan pts, 4 y r freedom from recurrence 15% vs.~42% in ASD, TOF, Mustard
Ueda A 2013 (324) 23685536	Retrospective single center	116	Ablation 116 ACHD pts, mean age 41 y; 154 procedures, 228 circuits using remote navigation, 3D mapping. F/u mean 20 mo, Group A: manual mappping/ablation; B: remote navigation; C: remote navigation +difficult access.	Assess outcomes ablation ACHD	Compare simple vs. complex lesions or complex vascular access. AVNRT 5-13%; AVRT 4-7%; Focal 11-26%; atrial flutter 11-39%; IART 23-45%; AF 6-18%. No difference acute success 82-91%, recurrence 20-24%.	ACHD population: ablation Acute success >80%; 20-25% recurrence w/in 20 mo
CHD: Catheter Ablation – ASD						
Teh AW 2011 (325) 21208243	Retrospective single center	20	Ablation AT after ASD repair; mean age 53±13 y; post ASD closure interval 29±15 y.	ASD Outcome atrial flutter ablation in	All CTI dependent atrial flutter; + other circuits. Acute success 100%; 25% repeat abl at 13 mo. F/u 3.2±1.6 y, 30% documented AF; stroke 5%; 35% AF intervention	Excellent acute ablation success ASD: 100%; 25% recur-repeat ablation, 30% AF in 3 y of f/u
Wasmer K 2013 (301) 23540398	Retrospective single center	54	Consecutive Repaired ASD pts underwent EP study & ablation, mean age 47 y. Mean 22 y postop. f/u in 83%, 7.7 y. Mean AT CL 270 msec.	ASD ablation & mechanisms of AT	AT at EP study in 78%: RA macroreentry in 100%; CTI dependent 69%; typical atrial flutter 41%. 10% not inducible. CTI ablation in AF or non-inducible. Ablation acute success: 93%	93% acute success ablation ASD. 4% recurred w/ different mechanism. 60% arrhythmia free during f/u 11% developed AF
Scaglione M 2014 (326) 24843050	Retrospective single center	46	46 repaired ASD pts, mean age 49 y; 89% secundum ASD. ECG atrial flutter 48%, atypical atrial flutter 35%, AT 17%. 41%	ASD mechanisms & ablation outcomes	Typical AF: 48%, atypical 35%, AT 17%. CTI dependent 26%, 74% atriotomy dependent; Ablation acute success 100%; recur 24%	ALL RA macro-reentry; no focal. High success ablation for ASD: 100%, 24% recurrence 20% repeat ablations

			also AF. Onset AT 19±12 y postop. Complete f/u, 7.3 y		Recur same mechanism w/ gaps. 70% atypical atrial flutter had ECG concordance.	
CHD: Catheter Ablation – Ebstein's						
Cappato R 1996 (327) 8759079	Retrospective single center	21	Ebstein pts w/ AVRT: EP study + attempted RFA. 34 right sided AP in 21 pts. Mean age 28±14 y. Mean f/u 22 mo.	Ebstein's ablation outcomes	76% acute success ablation AP. 24% recurrent SVT (5 pts, including 4/5 w/ acute success)—4/16 successful ablations-rec SVT=	Cath ablation success 76%; 25% recurrence in 22 mo in pts w/ acutely successful ablation.
Reich JD 1998 (328) 9869537	Retrospective multi-center	65	65 Ebstein's pts, age 9.8±5.4 y, 82 accessory connections: 62% right, 34% septal, 4% left; only 52% w/ single AP; 9% AP plus atrial tachycardia; 9% non-AP tachycardia.	Ebstein's ablation outcomes	Acute success 75-89%. Mild tricuspid regurgitation and BSA <1.7 predicted acute success.	SVT related to AC 82%; 18% other atrial tachycardia mechanisms.
CHD: Catheter Ablation – UVH						
De Groot NM 2009 (329) 19808474	Retrospective single center	19	19 Pts w/ UVH, age 29±9 y; 41 SVT circuits;	Procedural outcomes of ablation in UVH	Mechanisms: IART 73%; Typical atrial flutter 10%; Focal 15%; AF 2%. Acute ablation success: 73% IART; 75% atrial flutter; 100% focal f/u 53±34 mo: 16% died; 11% transplant	UVH pts: Acute success ~78% Death or OHT : 27% Recurrence: 27% by 53 mo
Yap SC 2012 (330) 22035149	Retrospective single center	11	Ablation in Fontan pts vs. 30 other ACHD pts; atriopulmonary and AV Fontan, mean age 33±0 y.	Assess AT substrate after Fontan surgery	Fontan pts larger RA (p<.001), larger low-voltage area (p=.01). Acute success Fontan 54% vs. 83% other CHD (p=.04). F/u 2.3±1.6 y, IART recurrence 47%.	Fontan pts lower acute success vs. other ACHD high recurrence 47% at 2.3 y all pts; Fontan 50 ±19%, vs. 32 ±10% non-Fontan pts at 2 y Larger RA size and low voltage areas predicted IART recurrence
Correa R 2015 (331) 25583982	Retrospective single center	32	52 consectutive pts underwent 57 EP studies 2006-2012. Mean age 18.4±11.8 y, all with TCPC type Fontans. 32 ablations, 31 for SVT. VT induced in 5/52 pts studied. No f/u in 19%. In others, median f/u 18 mo.	Procedural outcomes of ablation in UVH.	47 procedures w/ 54 defined SVT mechanisms. IART 46%, AVNRT 24%, focal 15%, AP 7%, twin AVN 7%. Additional 21 undefined AT. Ablation for SVT acute success 80%. Two major adverse events 6%: death, pulmonary embolus. 50% recurrence short term, improved arrhythmia scores.	78% acute success for SVT. 50% recurrence short term; improved arrhythmia scores. 6% major adverse cardiac events.
CHD: Catheter Ablation – TGA						
Jones DG 2013 (332) 23219079	Retrospective single center	9	AT ablations TGA Mustard; 9 procedures, 12 circuits between 2007-2012, median age 38 y (18-56 y), used Carto and irrigated tips. Median f/u 15 mo.	Ablation outcomes TGA atrial switch pts	Transbaffle puncture in all. AT mechs: CTI dep: 75%, focal 25% (pulmonary venous ¾). Acute success 100%; 25% recurrence w/in 16 mo. Death 11% (1/9); recurrent AT w/ CHF. ICD's in 3/9.	Ablation in pulmonary venous atrium needed in all pts. Acute success 100%, recurrence 25% short-term.
Wu J 2013 (333) 23355133	Retrospective single center	26	Ablation in 26 TGA pts s/p atrial switch repairs, mean age 28.7±6.7 y; 34 ablation procedures.	Assess outcomes ablation in TGA atrial switch pts	34 AT: IART 88%; AVNRT 12%. Acute success 85% of circuits. Mean f/u 34±24 mo, 30% recurrence IART.	TGA atrial switch: high acute success, 34% recurrence <3 y
CHD: Surgical therapy						

Pressley JC 1992 (334) 1394922	Retrospective, single center	38	38 pts, WPW and Ebstein anomly, surgical AP ablation and repair. Mean age 26.3 ±12.3 y, 1968-88. Compared to 384 pts undergoing AP surgery w/o Ebstein. 76% documented AVRT; 42% AF. F/u 6.2± 3.8 y.	Assess surgical impact AP ablation during Ebstein repair.	Mult AP 50%, right sided 79%, posteroseptal 58%, left 7.9%. Surgery mortality 5.3%, both <15 y old. 28/38 surgery repair + AP ablation; Successful AP ablation: 95%. 82% NS arrhythmias during f/u.	Pts w/ Ebstein anomaly improved after surgery w/ AP ablation. Late AF reduced from 42% to 9%, p<.001.
Misaki T 1995 (335) 8523883	Retrospective, single center	42	42 pts WPW = Ebstein, surgery 1973-1993. Mean age 35±14 y. 52 APs, 48 right or posteroseptal. Division of AP at surgery; 35 TV operation.	Assess outcome WPW surgery in Ebstein	All 52 AP successfully rx at surg. 2 reops due to SVT: additional AP. Hospital mortality 7.1%. no late deaths f/u mean 94 mo	N/A
Theodoro DA 1998 (336) 9456109	Retrospective, single center	18	18 ACHD pts mean age 34.9 y underwent RA Maze for AT/atrial flutter or AF: Ebstein 15, tricuspid regurgitation 2, ASD1. Mean f/u 8 mo.	Assess outcome RA maze in ACHD	No early deaths. Early postop SVT 3. RA maze performed, even in pts w/ AF.	Inclusion RA maze in ACHD pt w/ RA dilatation and AT is effective in eliminating or reducing AT.
Huang CJ 2000 (337) 11145402	Retrospective, single center	30	30 pts w/ Ebstein:surg repair 1973-1997. Preop EP study performed in 11 after 1980: surg ablation performed in 10/11: WPW 4, AVNRT 2, atrial flutter/AF 3, VT1.	Assess survival difference w/ op ablation Ebstein.	No mort in ablated pts. 7/30 died: 1-infection, 6 died suddenly. None of 6 sudden deaths underwent preop EP study.	Detailed preop EP study in Ebstein: "mandatory": Aggressive surg intervention for arrhythmia may reduce risk of sudden death.
Mavroudis C 2001 (338) 11689789	Retrospective, single center	40	40 Fontan conversions w/ arrhythmia surgery; mean age 18.7±9 y. All pts w/ AT; AF in 15.	Assess impact of arrhythmia surgery on AT in Fontan	Isthmus ablation 10 pts, RA Maze 16, Biatrial maze 14. No mortality. Mean f/u 2.5±1.9 y, OHT 7.5%. Arrhythmia recurrence 12.5%	Largely AP Fontan population; arrhythmia recurrence 12.5% at 2.5 y
Deal BJ 2002 (220) 12147539	Retrospective, single center	23	Comparison isthmus ablation (8) w/ RA maze (15) in AP Fontan pts w/ AT; median age 10.9 y (2-33 y)	Assess efficacy of operative ablation techniques Fontan.	Isthmus ablation: 62% recurrent AT; f/u 5.6 y RA maze: no recurrence, f/u 2.8 y	RA maze superior to isthmus ablation in Fontan pts
Khositseth A 2004 (339) 15573066	Retrospective single center	83	83129 adult Ebstein pts w/ SVT underwent arrhy procedure w/ surgery for Ebstein. 41: AP, mean age 18 y; 7 AVNRT, mean 18 y ; 48 atrial flutter/AF (RA maze 38, isthmus 10), mean 33 y.	Assess arrhythmia surgery in Ebstein	Incidence SVT: atrial flutter/AF 54%, AP 32%, AVNRT 8%. Surgical outcomes: AP or AVNRT: 0 recurrence 48 mo; Atrial flutter/AF 75% freedom from recurrence at 34 mo.	Arrhy surg interventions should be added to surgical repair Ebstein in pts w/ SVT: AP, AVNRT, or atrial flutter/AF. AS AT present in 54% and increases w/ age, recommend AT surgery as well as AP surgery.
Bockeria L 2005 (340) 16179193	Retrospective, single center	53	53 pts, Ebstein + SVT, mean age 21.6±10.7 y. Surgery + operative ablation: 32 pts; preop RFablation later surg: 21 pt. WPW 26, AVNRT 3, focal 3.	Assess combined arrhythmia surgery in Ebstein vs. RFA + surgery.	Mortality 3.1% in combined ablation operation vs. 0% in 2 staged. Efficacy: Surgery ablation 94% op vs. 76% catheter. Surgery efficacy WPW 92%, AVNRT 100%, focal 66%.	Combined operative ablation + surg repair showed improved AT elimination vs. catheter ablation approach followed by surgery.
Giamberti A 2006 (341) 16996928	Retrospective, single center	15	15 ASD pts, >40 y, surgical closure ASD w/ intraop RF ablation. All SVT: 8 AF, 7 AT/atrial flutter. 2002-2004. RA	Assess op ablation AT in ASD pts	No mortality, one pacemaker. AF recurrentce 6.5%, no AT recurrence.	Rec add intraop RF ablation to surgical ASD closure, safe & effective.

			Maze 8, biatrial cox maze iii 7 pts. F/u mean 24 mo.			
Karamlou T 2006 (342) 16631673	Retrospective, single center	249	1969-2005, TOF or DORV pts undergoing reop for PVR or TVR; AT in 41 pts. Median age 23 y. Assess RA maze vs. no maze on late outcome.	Assess impact of RA ablation on arrhythmia outcomes TOF.	Atrial flutter: isthmus ablation; AF RA maze. AT recurrence: ablation pts, 9%, vs. 78% AT occurence in non-ablation; 7.5 y. AT pts older, longer QRS duration	RA Maze at time of surgery improved long term AT free status. QRS duration >160 msec predicted risk of AT in TOF
Stulak JM 2006 (343) 16631672	Retrospective, single center	99	1993-2003, 99 pts RA maze w/ ACHD repair. Median age 43 y. *Did not distinguish between AT and AF.* Ebsteins 47, TR 19, UVH 11, ASD 8, TOF 8, other 6.	Impact arrhythmia surgery on AT: ACHD.	6% early mortality. 28% early AT Arrhythmia recurrence 7%, f/u 2.7 y; AA medications 55%.	ACHD: 55% on AA meds; 93% not in AT at 2.7 y
Mavroudis C 2007 (344) 17954046	Retrospective, single center	111	1994-2007, 111 Fontan conversions w/ arrhythmia surgery; mean age 22.5 y. Mainly AP Fontan.	Assess arrhythmia recurrence, survival Fontan	Early mortality 0.9%, late death/OHT 11%. Late AT 13.5%, f/u 7.9 y	Late AT in Fontan 13.5% at ~ 8 y;
Giamberti A 2008 (345) 17689722	Retrospective, single center	50	50 ACHD adults undergoing surgery; mean age 39 y. 31 RA Maze, 13 biatrial, 6 VT ablations.	Assess surgical arrhythmia outcome ACHD.	Mortality 4%; Mean f/u 28 mo: 4/48 on medications; 43 sinus rhythm, 4 recurrent AF	ACHD: 86% sinus rhythm, no medications during short term f/u
Mavroudis C 2008 (346) 18721574	Retrospective, single center	100	Arrhythmia operations, 11 no HD; 89 associated CHD (33 UVH); mean age 15.9 y. SVT 87, VT 13	Assess surgical arrhythmia outcome ACHD	Mechs AT: ART 45, AF 11, AC 19, AVNRT 6, Focal 6; early mortality 3%, late death/OHT 6%; 10 y Freedom from AT 85%, 68% VT	Freedom from AT at 10 y: 85% in mixed population ACHD
Aboulhosn J 2010 (347) 21087427	Retrospective, single center	27	27 atriopulm Fontan adults converted to TCPC; 67% extracardiac. 89% w/ atrial tach. 21/27 w/ arrhythmia surg: RA 12, RA + LA 9. Mean age 30 y (18-52 y) Mean f/u 4.2 y.	Assess arrhythmia recurrence after Fontan arrhythmia surgery.	Operative mortality 7.4%. Arrhythmia recurrence 14% (3/21) PLE 3; 1 died 27 mo postop, 2 resolved.	Recurrrent AT in 14% w/ 4 y f/u
Gutierrez SD 2013 (348) 23280242	Retrospective, single center	24	24 ACHD pts w/ AA undergoing surgery, mean age 40.9 y; incorporated cox maze procedure. 2004-2010. TOF 8, AVSD 4; RVOT repair 10, TV repair 8, ASD 7. Mean F/u 2.8 y, (.1-5.7 y).	Assess outcome of cox maze procedure in ACHD	Preop AT: 19, AF 5. Mortality: 16.5%, (12.5% early, 1 late) 74% of survivors arrhythmia free.	Pts w/ CHD and atrial arrhythmias, majority free of arrhythmias w Cox Maze procedure.
Terrada T 2013 (349) 24887891	Retrospective, single center	25	25 consecutive pts undergoing Fontan conversion 1/04-3/12. Mean age 21 6.3 y. 24/25 underwent arrhyth surg: RA maze 15, isthmus 3, biatrial 6. Mean f/u 21 mo(11-86 mo)	Assess outcome Fontan arrhythmia surgery.	Late AT recurrence 12.5% Operative mortality: 0. 16/25 no pacemaker implanted. 5 pts reoperation to implant pacer.	Recurrent AT 12. 5%,
Said SM 2014 (350) 24786860	Retrospective, single center	70	70 Fontan pts underwent Fontan conversion 1994-2011. Median age 23 y (4-46 y) AT present 89%	Assess outcome Fontan arrhythmia surgery.	Late Recurrent AT in 16% of pts w/ arrhythmia surgery Operative mortality 14%. 10 y survival 67%	Late Recurrent AT in 16%

			TCPC intra-atrial 59%; extracardiac 26%, Lateral tunnel 16%. 49/70 arrhythmia surgery. Mean f/u 5 y.		Periop death predictors: Age >27 y, AV valve regurgitation, males. PLE improved in 1/7 pts.	
Pregnancy: Acute Conversion of AV Node-Dependent Tachycardia						
Ghosh N 2011 (351) 21272431	Review of all reports published 1950-2010 on acute termination of SVT	138 pts	Variety of drugs. Most common adenosine w/ 58 cases. Also electrical DCCV 18 cases	Successful termination of SVT	Adenosine was most successful at terminating SVT. Beta blockers and verapamil second, led to more hypotension. Antiarrhythmic drugs not very effective.	Variety of interventions was reported on acute termination of SVT. Most common adenosine w/ 58 cases. Also electrical DCCV 18 cases, verapamil 16 cases and beta blockers 13 cases. Diversity of antiarrhythmic drugs as well. Most effective was adenosine w/ 84% success, followed by beta blockers and verapamil. Cardioversion safe.
Pregnancy: Catheter Ablation						
Damilakis J 2001 (352) 11514375	Conceptus radiation dose and risk determination for catheter ablation procedures.	20	20 women of childbearing ages who underwent ablation procedures	Estimation of radiation dose using phantom pregnancy	Typical dose to conceptus was <1 mGy	A typical ablation procedure results in very small increase in risk of harmful effects to the conceptus.
Berruezo A 2007 (353) 17897139	Case report of ablation w/ low radiation exposure	2 pts	Pt w/ drug refractory SVT; ablation of SVT w/ radiation dosimeter	Successful ablation; adverse effects	All pathways eliminated successfully	Both pts treated, fetus dose was very low, below dangerous limit.
Szumowski 2010 (354) 20158563	Observational, multicenter report experience w/ ablation of SVT in pregnancy	9 pts	Pt w/ severe SVT refractory to medical therapy; ablation w/ low radiation exposure	Successful ablation; adverse effects	All pathways eliminated successfully	All pts treated successfully, w/ either no radiation at all to very low dose.
Pregnancy: Prophylactic Antiarrhythmic Drug Therapy						
Wen Z 1998 (41) 9851958	Prospective cohort study	133	AVRT (n=85) AVNRT (n=48) EP study to induce PSVT by PES Excluded atrial flutter, AF organic heart disease or other systemic diseases involving the autonomic function (e.g., diabetes), those who could not blow into an aneroid manometer to maintain a pressure of 35 mm Hg for 20 sec, and those w/ unstable hemodynamics during tachycardia.	Termination of PSVT	Vagal maneuvers more effective in terminating AVRT than AVNRT (53 vs. 33%, p<0.05). AVNRT: vagal maneuvers terminated tachycardia in antegrade slow pathway (14%) or in retrograde fast pathway (19%). Baroreflex sensitivity was poorer but isoproterenol sensitivity test better in pts w/ AVNRT.	Vagal maneuvers effective, more so for AVRT. Limited in that study conducted during EP study.
Lydakis C 1999	Retrospective study on the effect of	78	Atenolol given to 78 pregnant women and compared to other	Comparison of adverse effects to fetal growth	Increased risk of fetal growth retardation	Possible increased risk of fetal growth retardation on atenolol compared to other

(355) 10371362	Atenolol and other drugs on fetal growth		drugs.			drugs, risk related to duration of treatment.
Von Dadelszen P 2000 (356) 10675164	Metanalysis of different drugs, mainly beta blockers, inpregnancy	3773	Meta analysis of different drugs for pregnancy induced HTN to try to determine if growth retardation is due to drugs or disease.	The association of treatment-induced difference in mean arterial pressure with measures of fetoplacental growth	Relationship was observed between fall in MAP and growth retardation, but was not related to drugs.	Beta blockers mainly safe during pregnancy, growth retardation likely due to fall in BP.
Bartalena 2001 (357) 11263469	Review of case reports when amiodarone was given during pregnancy	64	Review of case reports when amiodarone was given. There were 64 identified and effect on babies was reported.	Adverse effects documented on progeny of mothers who received amiodarone.	Hypothyroidism reported in 17%, which most of the time was transient. Some developmental disabilities seen even in euthyroid.	Maternal use of amiodarone can cause hypothyroidism in progeny and occasionally neurodevelopmental abnormalities.
Qasqas SA 2004 (358) 15191632	Review article on all cardiovascular drugs in pregnancy.	N/A	This is a review article.	N/A	All drugs are describe in detail and references made to all case reports.	This is a comprehensive compendium of all antiarrhythmic agents give during pregnancy.
Jaeggi ET 2011 (359) 21931080	Nonrandomized multicenter comparison of different drugs administered for transplacental therapy of fetal SVT	159	The authors reviewed 159 consecutive referrals w/ fetal SVT (n=114) and AF (n=45). Of these, 75 fetuses w/ SVT and 36 w/ AF were treated nonrandomly w/ transplacental flecainide (n=35), sotalol (n=52), or digoxin (n=24) as a first-line agent.	Effectiveness of different drugs reported.	Flecainide and digoxin were superior to sotalol for fetal SVT.	This was a study for fetal SVT, but showed that flecainide sotalol and digoxin are well tolerated in pregnant women.
SVT in the Elderly						
Chen SA 1995 (360) 7490388	Observational	66 pts w/ AVRT and AVNRT w/ initial sx onset after age 65 vs. 440 pts w/ sxs onset before age 30	All pts underwent EP study and RFA; 4 mm tip temperature control deflectable catheter	Compare clinical characteristics in the older vs. younger grooups	Older group: 32/66 had AVRT, 34/66 had AVNRT Younger group: 283/440 AVRT, 157/444 AVNRT Sxs of syncope and cardioversion were similar between two age groups; older pts had more atrial and ventricular ectopic beats on Holter; dispersion of anterograde ERP was greater in older pts; Success rate was 97-98% in all groups; Recurrence was similar (6-7%; f/u duration was not stated in the paper); complications were significantly higher (13-14% in older pts than younger pts (1%) (for AVRT: 2 arterial thrombosis, 1 TIA, 1 DVT; for AVNRT: 1 DVT, 1 AV block)	Greater dispersion of ERP and increased atrial and ventricular ectopic beats may explain the later onset of sxs in older pts.
Chen SA 1996 (361) 8540455	Observational	3966 consecutive EP study and 2593 ablation procedures	Tertiary referral center in Taiwan, 1987 – 1994 4 mm tip temperature control deflectable catheter	Risk factors associated w/ complications	Overall complications, RFA vs. EP study, 3.1% vs. 1.1% (p 0.00002); Older (≥65 y) vs. younger, 2.2% vs. 0.5% (p 0.0002) for EP study and 6.1% vs. 2.0% for RFA. Older age and presence of systemic	Data suggest older age is an independent risk for EP study and RFA. These data are somewhat out dated. Older pts had more co-morbidities and the presence of systemic diseases (co-morbidities) is an

					disease are independent predictors for complications. Complications included pericardial eff/usion, tamponade, AVB, vascular injury, systemic emboli)	independent predictor of acute complications.
Boulos M 1998 (362) 9708674	Observational	271 consecutive pts	AVNRT from a single center undergoing RFA, 1991 – 1995. 4 mm tip deflectable catheter were used to map and ablate	Slow pathway ablation	Acute success rate 98.1%, recurrence rate 4.1%; CHB 2.2%, 2% for pts <65 y of age, 8% in older pts; Older age is associated w/ higher risk of CHB.	Data are historical. The focus was on AVB complicating slow pathway ablation; no other complications were reported.
Kalusche 1998 (9) 9812187	Retrospective cohort study	395 pts undergoing AVNRT RFA. 85 (22%) ≥65 y (mean 70 y).	Consecutive pts from a single center in Germany, 1992 – 1997 9 pts were excluded due to more than one tachycardia inducible 4 mm tip temperature controlled deflectable catheter	Clinical presentation and outcomes in young vs. elderly during AVNRT ablation	Similar to younger pts, elderly more often had organic heart disease (CAD w/ or w/o MI,19.3% vs. 2.6%; P<0.02), syncope or presyncope w/ AVNRT (43.2% vs. 29.8%; P<0.05). 17.5% vs. 6.5% (P<0.05) the fast pathway approach was chosen as the first therapy. The overall success rate (96.8% vs. 95.3%) and recurrence rate (5.8% vs. 4.9%) were similar in both pt groups. Details of complications not listed: "minor complications such as hematoma; severe complications such as need of a PM" (2 in older group, 1 in younger group); f/u 2-68 mo.	Elderly pts have more severe sxs and more comorbid illnesses, but RFA safe.
Zado 2000 (363) 10676694	Prospective cohort study	695 pts were divided into: ≥80 y (n=37), 60-79 (n=275), and <60 y (n=383)	Ablation for SVT, VT (only 8% VT, 43% His ablation)	Determine whether catheter ablation is safe and effective in pts >80 y.	Overall success rate 95% (e groups (97% ≥80 y; 94% 60-79 y; 95%, <60 y). The overall complication rate for the entire group was 2.6%; no difference in complication rates among the groups (0%, ≥80 y; 2.2%, 60 to 79 y; 3.1%, <60 y)	RFA safe in elderly. However ,only 37 pts were >80 y.
Li YG 2001 (364) 11133214	Observational	18 pts among 346 pts w/ prolong PR at baseline	Slow pathway ablation in pts w/ AVNRT 4 mm tip temperature control deflectable catheter	Late occurrence of AVB after complete short pathway ablation in AVNRT	18/346 pts w/ prolong PR before RFA, age 62±7; Holters were obtained before, 1 d, 1 wk, 1, 3, 6 mo after ablation. Incidence of delayed AVB occurred in 6/18 pts w/ preexisting PR prolongation; antepgrade ERP was longer in the study group	Risk of AVB is increased after short pathway ablation in pts w/ pre-existing PR prolongation. These data have not been confirmed in the contemporary era.
Porter MJ 2004 (365) 15851189	Observational	1754 consecutive pts, 1856 PSVT from a single center 1991-2003	PSVT undergoing RFA; exclude IAST, flutter and fibrillation, age <5 Mapping and ablation techniques were not described.	Age and gender correlation to PSVT	Mean age 49±19 (5-96), women 62%; AVNRT 1042 (56%), AVRT 500 (27%), AT 315 (17%); AVRT decreases w/ age in both genders; AVNRT and AT increased w/ older age; majority (54.6%) of AVRT were men; majority of AVNRT and AT were women; In women, 63% had AVNRT, 20% AVRT and 17% AT; in men, 45% AVNRT, 39% AVRT, 17% AT	SVT is age and gender dependent in this single center study among pts referred for RFA. It is unknown whether this reflects the epidemiology in the general population due to the evolution of ablation from 1990 – current and whether referral bias, specifically related to age. This is an age and gender dependent mechanism study; not an outcome study
Rostock 2005 (366) 15946358	Retrospective cohort study	<75 y (n=508) and pts ≥75 y (n=70)	All pts w/ symptomatic AVNRT referred for slow-pathway ablation	Determine whether catheter ablation is safe and effective in pts ≥75 y.	Preexisting prolonged PR interval was present in 3.3 vs. 37% in pts <75 vs. older, p<0.0001). Following successful slow-pathway ablation, no induction of an AV	Slow-pathway ablation in elderly pts effective and safe and should be considered as first line therapy in this pt population. Challenges evidence that

					block was observed in >75 y group. No recurrences occurred pts ≥75 y.	preexisting PR prolongation found to be associated w/ a higher risk of developing a delayed high-degree AV block.
Kihel J 2006 (367) 16687422	Observational, case control	42 pts ≥75 y vs. 234 pts <75 y	Consecutive pts w/ AVNRT from a single center in France, 1997 – 2004. 4 mm tip deflectable catheters were used for mapping and ablation	Determine whether catheter ablation is safe and effective comparing older vs. younger pts	Success rate 100% in the elderly vs. 99.6% in the younger pts; 1 minor complication of groin hematoma occurred in older pts (2.4%), 4 (1.7%) in younger pts including one PE, one pericardial effusion, 2 hematoma. Recurrent was 0 in older pts, 3.4% in the younger pts (p 0.5) F/u duration was 28 mo and 35 mo in older and younger groups, respectively.	Catheter ablation for AVNRT is reasonable w/ high success rate and low complication rate. The data are more contemporary. No difference between older and younger groups.
Dagres N 2007 (368) 17434888	Observational	131 consecutive pts ≥80 y old undergoing ablation	Consecutive pts from 3 centers: Greece, Germany and Switzerland, 1998 – 2004 "Temperature guided" approach	Determine pt characteristics and ablation outcomes	Flutter most common (54%), AVNRT 22%, AF 18%. 52% had SHD. AVN ablation was performed in pts w/ AF. Overall success rate was 97% w/ one pts had a CVA after isthmus ablation for flutter. Minor complications such as hematoma occurred in 3.1% of study population	In selected elderly pts, ablation is highly successful for flutter, AVNRT and AVN ablation. More than half of the elderly pts have SHD when undergoing RFA. The consistent theme w/ other contemporary studies is that elderly have more co-morbid conditions but the overall ablation outcomes are highly successful w/ acceptable low complications. None of these studies are randomized studies; selection bias cannot be excluded.
Haghjoo M 2007 (369) 17069836	Observational case control	268 consecutive pts underwent RFA for AVNRT; 2001 - 2005	Dichotomized at 65 y of age	Ablation outcomes	156/112 : younger/older; CL longer in older pts; success rate, complications, the recurrences were similar between older and younger pts	No significant differences in outcomes between the two age groups dichotomized at 65 y of age
Pedrinazzi C 2007 (370) 17823861	Observation	Total of 605 pts	Consecutive pts undergoing RFA for all arrhythmias in a single center in Italy, 2000-2005 4 mm tip temperature control deflectable catheter	RFA outcomes	Older pts had more co-morbidities; 69% <70 y of age, 24% 70-79 y, 7% ≥80 y; complications were similar 1.2 vs. 1.4 vs. 2%; Complications included pneumothorax, pericardial eff/usion, and hematoma; success rates were similar 92 vs. 88 vs. 88%; recurrence was followed up to 12 mo; AT and flutter had higher recurrence rate than AVNRT or AVRT	Outcomes of RFA for SVT and VT were similar in younger and older pt groups. No major complications
Yangni N'Da' O 2008 (371) 18477940	Observational	141/816 (17%) elderly >70 y of age admitted for recurrent SVT	Paroxysmal junctional tachycardia actually included AVNRT and AVRT Temperature controlled catheter	Clinical outcomes after RFA	In the acute setting: Cardiac decompenstation 10, syncope 26, ACS 14, vascular event 5; typical AVNRT 73%; atypical AVNRT more common in older pts than in younger pts (15% vs. 4%); ablation was performed in 79% of the older pts vs. 57% in the younger pts; complications more common 7% vs. 2.5% in older pts; more AF induced during study (19% vs. 5%)	Older pts have more severe sxs associated w/ SVT at baseline; Atypical AVNRT is more common in older pts. Complications are higher in older pts. Very difficult paper to understand; did not specifically, or clearly, state the types of complications.
Hoffman BA	German registry; 48	3234 consecutive	AVNRT pts: >50 y	Acute and long term	No differences were observed among the	Catheter ablation for AVNRT is highly

2011 (372) 21315834	trial centers in Germany	pts undergoing AVNRT ablation from 3/2007 to 5/2010	Group 1, n=1,268 [39.2%]; median age 40 y (95% CI: 30.0–45.0 y), 74.1% women, Group 2 50–75 y old (n=1,707 [52.8%]; 63.0 y [95% CI: 58.0–69.0] y, 63.0% women) Group 3 >75 y old (n =259 [8.0%]; 79.0 [95% CI: 77.0–82.0] y, 50.6% women).	success rate, complications and recurrence	three groups w/ regard to primary CA success rate (98.7% vs. 98.8% vs. 98.5%; *P=0.*92) Hemodynamically stable pericardial eff/usion occurred in five group 2 (0.3%) and two group 3 (0.8%) pts but in none of the group 1 (*P=0.*05) pts AV block requiring permanent pacemaker implantation occurred in two pts in group 1 (0.2%) and six pts in group 2 (0.4%) but none in group 3 (*P*= 0.41) During a median f/u of 511 d, recurrence rate was 5.7% in all pts	effective and safe and does not pose an increased risk for complete AV block in pts over 75 y of age, despite a higher prevalence of structural heart disease.
Ghali WA 2005 (222)	Systematic review and meta-analysis of observational studies that investigated risk of thromboembolism associated with atrial flutter.	The meta analysis included 13 studies on embolic risk around time of cardioversion that included 1546 patients. For chronic risk, there were 14 studies involving 17,691 patients.	MEDLINE, EMBASE, bibliographies, and consultation with clinical experts were used to identify studies that report the risk of thromboembolism associated with attempted cardioversion and longer-term risk in patients with atrial flutter.	Risk of thromboembolism associated with atrial flutter around time of cardioversion or over the long term in chronic atrial flutter.	Around the time of cardioversion, the risk of thromboembolic events ranged from 0% to 7.3% depending of clinical factors. Lower event rates were observed in patients taking anticoagulants. The long term risk rate of thromboembolism was approximately 3% with sustained atrial flutter.	The findings of this systematic review strongly suggest that atrial flutter does indeed impart a risk of thromboembolism.

AA indicates antiarrhythmic; AARCC, Allicance for Adult Research in Congential Cardiology; AC, atrioventricular connections; ACE I/D, angiotensin converting enzyme insertion/deletion; ACHD, adult congenital heart disease; ACS, acute coronary syndrome; ADT, antidromic tachycardia; AF, atrial fibrillation; AICD, automatic implantable cardioverter defibrillator; AP, accessory pathway; APERP, accessory pathway effective refractory period; ART, atrioventricular tachycardia; ASD, atrioventricular septal defect; AT, atrial tachycardia; ATP, antitachycardia pacing; AVB, atrioventricular block; AVN, atrioventricular node; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; AVSD, atrioventricular septal defects; BMI, body mass index; bpm, beats per min; BP, blood pressure; BSA, body surface area; CAD, coronary artery disease; cc-TGA, congenitally corrected transposition of the great arteries; CHD, congenital heart disease; CHF, congestive heart failure; CK-MB, creatinine kinase myocardial enzyme; CL, cycle length; CONCOR, Interuniversity Cardiology Institute of the Netherlands and the Netherlands Heart Foundation; CPB, cardiopulmonary bypass; CTI, cavotricuspid isthmus; CVA, cerebral vascular accident; DCCV, direct current cardioversion; DOVR, double outlet right ventricle; DVT, deep vein thrombosis; dx, diagnosis; EAT, ectopic atrial tachycardia; ECG, electrocardiogram; ECMO, extracorporeal membrane oxygenation; ED, emergency department; EP, electrophysiological; ERP, effective refractory period; f/u, follow up; HF, heart failure; h/o, history of; HR, heart rate; HTN, hypertension; IART, intraatrial reentrant tachycardia; IAST, inappropriate sinus tachycardia; ICD, implantable cardioverter defibrillator; ICU, intensive care unit; intraop, intraoperative; IV, intravenous; JET, junctional ectopic tachycardia; LA, left atrium; LFW, left free wall; LOS, length of stay; LVEF, left ventricular ejection fraction; MAP, mean arterial pressure; MAT, multifocal atrial tachycardia; MI, myocardial infarction; MRI, magnetic resonance imaging; NOS, nitric oxide synthase; NS, non-significant; NSVT, nonsustained ventricular tachycardia; OHT, orthotopic herat transplant; OR, odds ratio; ORT, orthodromic tachycardia; PES, programmed electrical stimulation; PLE, protein-losing enteropathy; postop, postoperative; POTS, postural tachycardia syndrome; preop, preoperative; PSVT, paroxysmal supraventricular tachycardia; pt, patient; QOL, quality of life; RA, right atrium; RACHS, risk adjustment for congenital heart surgery; RF, radiofrequency; RFA, radiofrequency ablation; RFCA, radiofrequency catheter ablation; RFW, right free wall; RV, right ventricular; RVOT, right ventricular outflow tract; rx, therapy; SHD, structural heart disease; s/p, status post; SR, sinus rhythm; SVA, supraventricular arrhythmia; SVT, supraventricular tachycardia; sx, symptom; TCPC, total cavopulmonary connection; TEP, transesophageal pacing; TGA, transposition of the great arteries; TIA, transischemic attack; TOF, tetralogy of Fallot; TSH, thyroid stimulating hormone; TV, tricuspid valve; UVH, univentricular heart; VA, ventriculoatrial; VF, ventricular fibrillation; VSD, ventricular septal defect; VT, ventricular tachycardia; w/, with; w/o, without; and WPW, Wolff-Parkinson-White syndrome.

Data Supplement 21. Randomized Trials Comparing Special Populations – Section 9

Study Name, Author, Year	Aim of Study	Study Type (Size, N)	Study Intervention Group (n)	Study Comparator Group (n)	Pt Population		Endpoints			P Values, OR: HR: RR: & 95% CI:	Summary/Conclusions
					Inclusion Criteria	*Exclusion Criteria*	*Primary Endpoint (efficacy) and Results*	*Safety Endpoint and Results*	*Secondary Endpoint and Results*		
Saul JP 2005 (373) 16316969	IV amiodarone efficacy/ safety	Multicenter randomized double-blind (N=61)	Ages <16 y, median 1.6 y. SVT 26, JET 31. 71% SHD.	Dosages: low 1 mg/kg, medium 5 mg/kg, high 10 mg/kg, plus 47 h maintenance. 30 d f/u.	N/A	Ages <16 y, median 1.6 y, SVT 26, JET 31. 71% SHD.	Amidarone use <3 mo, drug intereaction w/ amiodarone, imminent death, intentional hypothermia to <35 degrees C	Endpoint: time to success. Success low 47%, medium 80%, high 73%.	Adverse events 87%, 5 deaths, 2 related to drug: profound hypotension medium and high dose.	N/A	Medium or high dose effective 2.1-2.6 h. Efficacy JET 67-83%. SVT 33-89%.
Lim SH 2009 (38) 19261367	Compare efficacy of bolus adenosine vs. slow calcium channel blockers in ED rx SVT	Prospective randomized trial (N=206). Mean ages 48.3±18.6 y.	104 pts; adenosine 6 mg followed by 12 mg given as needed. Stopped w/ SVT conversion	102 pts infusion verapamil 1 mg/min to max 20 mg, or dilitazem 2.5 mg/min to max 50 mg. Stopped w/ SVT conversion.	Pts ≥10 y in ED w/ narrow QRS tachycardia, ECG dx SVT, not converting w/ vagal maneuvers.	N/A	Conversion to SR: calcium channel blockers 98% vs. adenosine 86.5% (RR: 1/13; p= 0.002)	N/A	Drop in BP more common in calcium blockers group, mean SBP ↓13-7 mm Hg vs. no change w/ adenosine.	N/A	Calcium channel blockers effective and safe alternative to adenosine for conversion SVT; implications for cost.
Manrique AM 2010 (374) 19819469	Assess magnesium sulfate supplementation during CPB on risk of JET	Randomized, double-blind, controlled trial (N=99)	2/05-8/06, pts <17 y undergoing CPB repair CHD randomized to receive MgSO4 during rewarming	Placebo: 3 groups: Mg 25 mg/kg, 50 mg/kg or placebo.	Pts from birth-17 y w/ elective cardiac surgery.	Pts with Mg supplements for malnutrition, sepsis, pancreatitis, neonates.	Total incidence JET 7.0%. JET incidences: Placebo 31%, low Mg 10%; higher Mg 0%.	N/A	N/A	Younger age <1 mo, complex CHD Aristotle score ≥4, prior CHF correlated w/ JET.	MgSO4 reduced incidence of postop JET
Sanatani S 2012 (375) 2296243	Compare digoxin vs. propranolol for	Multicenter randomized double-	Digoxin (27)	Propranolol (34)	Infants <4 mo w/ SVT, AVRT or AVNRT.	Excluding manifest WPW.	Recurrent SVT. 27 digoxin, 34 propranolol SVT recurred	No deaths, no serious adverse events.	Time to recurrence, adverse events. No first	N/A	No difference between digoxin and propranolol in preventing

1	control of infant SVT	blind (N=61)					19% digoxin, 31% propranolol (p=0.25, NS). Recurrence free status 79% digoxin, 67% propranolol, NS.		recurrence after 10 d.		recurrent SVT. As recurrences did not occur >110 d, may not need prolonged rx.

AVNRT indicates atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; BP, blood pressure; CHD, congenital heart disease; CHF, congestive heart failure; CPB, cardiopulmonary bypass; dx, diagnosis; ECG, echocardiogram; ED, emergency department; IV, intravenous; JET, junctional ectopic tachycardia; N/A, not applicable; NS, non-significant; pt, patient; rx, therapy; SBP, systolic blood pressure; SHD, structural heart disease; SR, sinush rhythm; SVT, supraventricular tachycardia; w/, with; and WPW, Wolff-Parkinson-White syndrome.

Data Supplement 22. Nonrandomized Trials, Observational Studies, and/or Registries of Quality-of-Life Considerations – Section 10

Study Name, Author, Year	Study Type/ Design	Study Size	Inclusion/Exclusion Criteria	Primary Endpoint	Results/p Values	Summary/Conclusions
Lau CP 1995 (376) 7770362	QOL and exercise capacity in pts w/ PSVT due to AP treated medically vs. ablation	N=55 Random allocation to ablation vs. medical therapy	Pts w/ PSVT (including WPW) on stable medications for 3 mo Randomly selected for ablation or continuing medical therapy	QOL questionnaire and ETT performed at baseline and every 3 mo for 1 y Assessed PSVT frequency/duration of episodes; hemodynamic disturbance, presence of preexcited AF	46 pts selected for ablation and 9 for medical therapy 36/46 successfully ablated, and they improved in QOL at 3 mo post ablation (total scores on General Health Questionnaire, Somatic Symptoms Inventory and Sickness Impact Profile) P<0.01for all 3 Improvements held at 1 y Exercise capacity increased from 13.1±5.5 to 14.9 ±4.5 min at 3 mo after successful ablation (p<0.002) (due mostly to suppressing exercised induced PSVT). Medical group or those w/ unsuccessful ablation had no change in QOL or exercise capacity	While pts randomly assigned to ablation vs. medical therapy, only 9 pts allocated to medical therapy Population – WPW, not other forms of PSVT
Bubien RS 1996 (377) 8840848	Prospective cohort study, QOL of PSVT	188	AVNRT (n=59) AVRT (n=46) AF s/p AVJ ablation (n=22) Atrial flutter/AT (n=22) VT (n=10)	RFA associated w/ significant improvement in QOL sustained over 6 mo (p<0.005). RFA followed by improved	N/A	Overall demonstrates benefit of RFA on variety of arrhythmias. Tried to minimize response bias w/ anonymous mail surveys, self-reporting

			QOL before, compared w/ 1 and 6 mo after RFA using SF-36 and disease-specific sx checklist—Frequency and Severity Scale	performance of ADLs and a marked decrease in number of visits to physicians and emergency rooms in the 6 mo after RFA compared w/ 6 mo before. Pt's perception of impact of arrhythmias on health improved after ablation, maintained between 1 and 6 mo after ablation. 90% of pts indicated that heart rhythm problems influenced health perception at baseline, and declined to 59% at 1 mo and 58% at 6 mo.		methods may be confounded by under-reporting of undesirable characteristics and over-reporting of socially desirable behaviors.
*Bathina MN 1998 (378) 9732885	Prospective comparison of the impact of QOL and CE between RFA and pharmacologic therapy for PSVT	79 w/ newly-documented PSVT Average number of drugs 1.35/pt (CCB, BB, most common)	Exclusions: drug-refractory pts, prior treatment, AF, atrial flutter, preexcitation	SF-36 used to measure QOL after 12-mo f/u	RFA vs. medication Bodily pain: 63±24 vs. 81±20 p<0.005 General health: 69±21 vs. 79±21 p<0.05 Vitality: 55±21 vs. 66±22 p<0.05 Role emotion: 78±36 vs. 94±17 p<0.05 Ablation resulted in complete amelioration of sxs in 33% vs. 74%.	First study to prospectively evaluate QOL and resource utilization between RFA vs. medical therapy. Both effective, but RFA improves QOL to a greater extent.
Larson msec 1999 (379) 10468092	Retrospective single center evaluation	161 pts w/ RFA for drug-refractory AVNRT	Not specified	Duke Activity Status Index used for physical function, Symptom Checklist—Frequency and Severity Scale, both used in telephone survey	Mean number of sxs declined from 5.8→3.1 (p<0.001) Moderate-severe sxs declined 4.6→1.1 (p<0.0001) Urgent care visits declined from mean of 4.6→0.4/y (p<0.001) Heath score increased from mean of 56.6→77.3 (p<0.0001)	RFA effective in improving QOL. Although single center, Kaiser is a large health care system. Susceptible to recall bias

					Pt utility increased from mean of 0.71 to 0.88 (p<0.0001)	
*Goldberg AS 2002 (380) 11988206	Prospective comparison on long-term effects of QOL between RFA and pharmacologic therapy for PSVT	83 pts w/ newly-diagnosed symptomatic PSVT Average number of drugs 1.49/pt (BB most common) 39 w/ initial RFA, 44 w/ initial medical therapy (of which 22/44 underwent RFA)	Referred specifically for ablation Excluded AF and atrial flutter AVNRT (67%) AVRT w/ AP (28%) AT (5%)	SF-36 used to measure QOL after 1-y and 5-y f/u At 5-y f/u, both RFA and pharmacologic therapy w/ improved scores (cumulative p<0.05 and p<0.001, respectively) RFA significantly improved in physical function, physical role, emotional role, mental health (p<0.05) At 5-y f/u, there was greater sx reduction in RFA group (p<0.01) compared to medical therapy Improvement in sxs who underwent initial RFA or cross-over to RFA after 5 y, compared to medical therapy (p<0.05) Over 5 y, the average cumulative cost for pts in the ablation therapy group was $7,507± $1,098. The cumulative cost for pts in medical therapy group was significantly lower than in pts initially treated w/ ablation therapy: $6,249±$1,421, p<0.05.	N/A	RFA was associated w/ higher QOL in all health concepts at 1 y; this improvement was sustained in the physical function, emotional role, physical role, and mental health subsets at 5 y. Cost estimated to be higher in RFA group. Offers 5 y f/u and includes pts who were not drug-refractory.
Walfridsson U 2005 (15) 15733177	Impact of PSVT on perceived ability to drive	N=301 Interview w/ structured questions	Pts referred for ablation, of which 226 were active drivers	N/A	Sxs among drivers (irrespective of driving): fatigue 77%, dizziness 47%, cold sweat (52%), near syncope (50%), syncope (14%). Women more symptomatic than men (p<0.05). 57% had sxs while driving, 42% of those pts needed to stop driving and 24 pts regarded their tachycardia as an obstacle to driving, w/ correlation (p<0.001) if near syncope was a sx	PSVT common while driving. Correlation of near syncope as sx w/ deciding that PSVT was obstacle to driving.
Meissner A 2009	QOL pre-post RFA	309	AVNRT (n=230) AVRT (n=66)	QOL following ablation, measured w/ SF-36 and Symptom Checklist-	F/u 4.5±1.3 y	Large series w/ long-term f/u.

(381) 19158961			AT (n=13)	Frequency and Severity Scale	QOL significantly improved in AVNRT (p<0.0005) and AVRT (p<0.04); AT p=NS Pre-RFA sxs of tachycardia (91.5%), increased incidence of tachycardia episodes over time (78.1%), anxiety (55.5%), reduced physical capacity in daily life (52%) significantly improved post RFA (p<0.0001)	
Walfridsson U 2009 (19) 19702600	QOL Survey	Pts w/ AVRT and AVNRT referred for RFA	AVNRT (n=97) AVRT (n=79)	QOL scores measured by SF-36 and EuroQol, and disease-specific questions, compared w/ reference group	QOL scores were significantly lower for pts w/ AVNRT compared to AVRT in several SF-36 measures (physical functioning, general health, and bodily pain) as w/ EuroQol. Scores significantly affected by occurrence >once a mo, arrhythmia duration, and whether sxs occurred not only during exercise but also at rest	Arrhythmia recurrence important to consider when setting priorities for treatment w/ RFA.
Wood KA 2010 (288) 20109982	QOL pre-post RFA	52	AVNRT (n=30) AVRT (n=16) AT (n=6)	QOL following ablation, measured w/ Patient Perception scale, 3 subscales of SF-36, 2 subscales from Medical Outcomes Study, disease-specific measures	Significant improvement in most sxs post-ablation (p<0.05) No sxs completely eliminated at one mo f/u Effect greater in women	Ablation improves QOL on several measures, both generic and PSVT-specific measures. Short f/u.
Yildrim O 2010 (382) 23280027	QOL pre-post RFA	50	AVNRT (n=28) AVRT (n=22)	WHOQOL-BREF and STAI domains	Prior to RFA, greater than average anxiety score (p<0.05) All items significantly improved post-RFA—anxiety, QOL, and health satisfaction scores	RFA improves anxiety and QOL. Limited by 3 mo f/u, but consistent w/ prior work.
Farkowski MM 2014 (383) 24919538	Prospective cohort, gender-related differences in outcomes pre-post RFA	64	AVNRT (n=40, 32 women, 8 men) AVRT (n=26, 11 women, 15 men) (2 pts did not complete f/u)	QOL measured by PPAQ, EQ-5D-3L	41 women completed survey. No significant baseline differences except AVNRT prevalence, and HRQOL by gender Women reported higher severity of sxs on PPAQ than men (p<0.001) At 2 mo after RFA, women	Small but significant gender-related difference in outcome of RFA in pts w/ AVNRT or AVRT measured w/ a disease-specific instrument No significant difference in QOL or access to healthcare resources between women and men.

					reported higher severity of sxs (p=0.02) on PPAQ and more heart skipping than men (p=0.0014) No significant difference in healthcare resource utilization during the y preceding RFA AADs more often prescribed to women pre-procedure (p=0.022)	

*Study addressed both CE and QoL

AAD indicates antiarrhythmic drug; ADL, activities of daily living; AF, atrial fibrillation; AP, accessory pathway; AT, atrial tachycardia; AVJ, atrioventricular junction; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; BB, beta blocker; CCB, calcium channel blocker; CE, cost effectiveness; EQ-5D-3L, EuroQol Research Foundation questionnaire; ETT, exercisetreadmill test; f/u, follow up; HRQOL, health-related quality of life; N/A, not applicable; PPAQ, Patient Perception of Arrhythmia Questionnaire; PSVT, paroxysmal supraventricular tachycardia; pt, patient; QOL, quality of life; RFA, radiofrequency ablation; SF-36, Short Form (36) Health Survey; s/p, status post; STAI, State and Trait Anxiety Inventory; sx, symptom; VT, ventricular tachycardia; w/, with; WHOQOL-BREF, World Health Organization Quality of Life Scale; and WPW, Wolff-Parkison-White syndrome.

Data Supplement 23. Nonrandomized Trials, Observational Studies, and/or Registries of Cost Effectiveness – Section 11

Study Name, Author, Year	Study Type/ Design	Study Size	Inclusion/Exclusion Criteria	Primary Endpoint	Results/p Values	Summary/Conclusions
De Buitlier M 1990 (384) 2371949	Retrospective cohort study to evaluate CE of AP RFA c/w surgical ablation	22	Pts w/ APs who underwent RFA or surgical ablation (n=11 RFA) (n=11 surgical ablation)	Health care cost, w/ secondary endpoint LOS	RFA success: 73% (all w/ posteroseptal AP) Surgical success: 100% (right, left lateral, posteroseptal AP) RFA LOS 6±2 d Surgical LOS 8±4 d RFA cost: 14,116±4,493 c/w 34,175±5,434 in surgical group (p<0.0001). Mean time lost from work or school was 10± 5 d in RFA group c/w 60±16 d in surgical group (p<0.01).	1988 dollars RFA of APs substantially lower in cost and LOS c/w surgical ablation.
De Buitlier M 1991 (385) 1746469	Retrospective cohort study to evaluate CE of AP RFA c/w surgical ablation	50	Pts w/ APs who underwent RFA or surgical ablation (n=25 RFA, 1990) (n=25 surgical ablation, 1989)	Health care cost, w/ secondary endpoint LOS	Success rate was 96% for both groups. Mean LOS was 3±1 d in RFA group and 9±4 d in surgical group (p<0.0001). RFA total cost $14,919 c/w $53,265 in the surgical group (p<0.0001).	1990/1991 dollars RFA of APs substantially lower in cost and LOS c/w surgical ablation.
Kalbfleisch	Retrospective review	15	Symptomatic AVNRT who	RFA cost of $15,893 would be	N/A	1991 dollars

SJ 1992 (386) 1593054	to establish cost-advantage of RFA for AVNRT		underwent RFA	advantageous after 10 y in pts who visit ED once per y (in study medical therapy more expensive after 2 y due to frequent ED visits in study population). Perspective: pt Outcomes: annual charges		Early report using hospital charges showing cost advantage of RFA for AVNRT Medical therapy at the time more expensive given drugs may not have been at generic prices.
Hogenhuis W 1993 (387) 8222191	CE of management in WPW	Markov model, none-specified, but costs estimated from convenience sample of 13 pts	N/A	Evaluation of 5 different strategies: -observation - observation until SCD -therapy guided by noninvasive monitoring, -initial RFA -initial surgical ablation Perspective: largely pt-perspective Outcomes: QALY and mortality, using Markov Model	RFA yields life expectancy greater than or equal to other strategies 40 y-old pt: Observation: $2360 RFA: $5,150-6,250 Surgery: $15,120 Observation w/ RFA at cardiac arrest: $16,860 Drug therapy: $20,250 In cardiac arrest survivors and pts who have had PSVT/AF w/ hemodynamic compromise, RFA should both prolong survival and save resources For pts w/ PSVT/AF w/o hemodynamic compromise, the marginal cost-effectiveness of attempted RFA ranges from $6,600 per QALY gained for 20-y old pts to $19,000 per QALY gained for 60-y old pts. For asymptomatic pts, RFA costs from $174,000 per QALY gained for 20-y old pts to $540,000 per QALY gained for 60-y old pts	Supports RFA in WPW syndrome who survive cardiac arrest or who experience PSVT/AF. but also supports the current practice of observing asymptomatic pts
Kalbfleisch SJ 1993 (388) 8436736	Prospective cohort study to evaluate safety, feasibility, and cost of AP RFA as an outpt	137	Exclusion: <13 or >70 y, anteroseptal AP, obesity, or clinical indication for hospitalization	RFA of AP cost as outpt procedure	97% success rate, w/ 73% performed as outpatients. In 70 cases the pt was discharged the d of ablation, and in 30 cases the pt required a short (≤18 h) overnight stay due to scheduling issues. Mean duration of observation was 4.8±1.5 h for outpts and 15±1.4 h for pts who underwent overnight hospitalization.	Outpt ablation of AP, w/ possible overnight observation, is feasible in low-risk pts

					Mean cost of the procedure was $10,183±$1,082 in 30 pts studied for cost analysis. 22 outpts vs. 8 overnight pts : Total charges: $9,873 vs. $11,034 (p<0.01) Professional fees: $6,163 vs. $6,286 (p=NS) Hospital charges: $3,710 vs. $4,748 (p<0.01) 2 pts w/ complications: femoral artery pseudoaneurysm notes 3-4 wk after procedure, one in outpt, one after 13 h overnight stay.	
Kertes PJ 1993 (389) 8240167	CE of RFA compared to AADs in Australia	26	AVNRT (n=16) WPW (n=10)	Mean cost of RFA $4067, c/w AAD of $700/ y *NOTE: these are likely Australian dollars, although authors do not specify* Extrapolating over 20 y and allowing for an annual 5% inflation factor, RFA becomes cost saving in 5.5 y Over 20 y, AAD estimated at 4-5 times more expensive than RF Perspective: pt and societal perspective Outcomes: cost analysis w/ "cost-saving" criterion used to define effectiveness, on the assumption that RFA is at least as effective as AADs in long-term control of PSVT; authors used annual charges	N/A	RFA more cost-effective than AADs. Limited to Australian population, but results consistent w/ other series. Used pt data in constructing cost-analysis, not simulation.
Ikeda T 1994 (390) 7823285	Prospective cohort, CE evaluation of CE of RFA for PSVT	20	Symptomatic PSVT, on AADs, all w/ successful RFA AVNRT (n=5)	Mean total charge for ablation 982,806 yen and 5.7 times the outpt charges in the previous y	N/A	Small study, limited to Japan, but suggests RFA effective and reduces medical costs.

			WPW (n=15)	Mean total life-expectancy charges w/ AADs were estimated at 7,064,726 yen, 41.0 times the outpt charges Total RFA charge 14% of total estimated charges of estimated lifetime medical treatment w/o RFA (p<0.001) Perspective: pt-perspective, societal component Outcomes: total life-expectancy charges, total ablation charges		Utilizes hospital charges, and not a cost-simulation model.
*Bathina MN 1998 (378) 9732885	Prospective comparison of the impact of QOL and CE between RFA and pharmacologic therapy for PSVT	79 w/ newly-documented PSVT Average number of drugs 1.35/pt (CCB, BB, most common)	Exclusions: drug-refractory pts, prior treatment, AF, atrial flutter, preexcitation	SF-36 and direct costs Perspective: pt-perspective Outcomes: direct hospital charges	RFA vs. medication Potential long-term costs similar, but w/ specific assumptions about ED visits, pharmacologic costs will exceed RFA	First study to prospectively evaluate QOL and resource utilization between RFA vs. medical therapy. Cumulative cost of medical therapy equal to, or less than RFA. This is in contrast to studies by Cheng and Ikeda, which have stronger methodology.
Cheng CH 2000 (60) 11103056	Comparison of CE of RFA w/ medical management of PSVT	Symptomatic pts w/ 4.6 unscheduled visits/y for arrhythmia while on long-term drug therapy	RFA: Estimated population: AVNRT: 65% AVRT w/ concealed AP: 30% Efficacy estimates: AVNRT: 97% AVRT w/ concealed AP: 93% Recurrence estimates: AVNRT: 5% AVRT w/ concealed AP: 8% Drug efficacy: 60%	Perspective: societal Outcomes: Costs (office visit, annual drug rx, EP study, RFA, PPM, PPM replacement) QALY Life-ys Marginal CE ratios	W/ monthly episodes of PSVT, RFA most effective and least expensive option RFA reduced lifetime medical expenditures by $27,940 compared w/ long-term pharmacologic therapy Lifetime costs: RFA: $61,880 Long-term drug rx: $89,820 Episodic drug rx: $143,530 RFA improved quality-adjusted life expectancy by 3.10 QALYs.	RFA improves QOL and reduces costs when treating highly symptomatic pts. Effects in less symptomatic not studies
Dewland TA 2013 (391) 24983868	Observational cohort	Pts w/ atrial flutter in the California HCUP database, 2005-2009 (n=33,004), median f/u 2/1 y	Exclusion: Non-California residence, concomitant AF, missing admission date data	Whether catheter ablation of atrial flutter associated w/ reductions in healthcare utilization, AF, or CVA	2,733 (8.2%) underwent catheter ablation. Atrial flutter ablation (in 8.2% of pts) lowered adjusted risk of inpt hospitalization and ED visits (p<0.001); overall hospital-based healthcare utilization (p=0.001); and 11% reduction in AF(p=0.01). Risk of CVA not reduced after ablation (p=0.57).	Robust registry data supports early atrial flutter ablation to significantly reduce hospital-based healthcare utilization and risk of AF.

*Study addressed both CE and QoL

AAD indicates antiarrhythmic drug; AF, atrial fibrillation; AP, accessory pathway; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular tachycardia; BB, beta blocker; CCB, calcium channel blocker; CE, cost effectiveness; CVA, cerebrovascular accident; c/w, consistent with; ED, emergency department; EP, electrophysiological; HCUP, Healthcare Cost and Utilization Project; LOS, length of stay; N/A, not applicable; NS, non-significant; PPM, permanent pacemaker; PSVT, paroxysmal supraventricular tachycardia; pt, patient; QALY, quality-adjusted life year; QOL, quality of life; RF, radiofrequency; RFA, radiofrequency ablation; rx, therapy; SCD, sudden cardiac death; SF-36, Short Form (36) Heatlh Survey; w/, with; and w/o, without.

Appendix 1. Acute Drug Therapy for SVT, Intravenous Administration*

Drug†	Initial Dose	Subsequent or Maintenance Dose	Potential Adverse Effects	Precautions (Exclude or Use With Caution) and Interactions
Nucleoside				
Adenosine	6-mg rapid IV bolus (injected into IV as proximal or as close to the heart as possible), administered over 1–2 s, followed by rapid saline flush	If no result within 1–2 min, 12-mg rapid IV bolus; can repeat 12-mg dose 1 time. The safe use of 18-mg bolus doses has been reported (392).	Transient AV block, flushing, chest pain, hypotension, or dyspnea, AF can be initiated or cause decompensation in the presence of pre-excitation, PVCs / ventricular tachycardia, bronchospasm (rare), or coronary steal. Minor side effects are usually transient because of adenosine's very short half-life.	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Reactive airway disease • Concomitant use of verapamil or digoxin • WPW
Beta blockers				
Esmolol	500-mcg/kg IV bolus over 1 min	Infusion at 50–300 mcg/kg/min, with repeat boluses between each dosing increase	Hypotension, worsening HF, bronchospasm, bradycardia	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Decompensated systolic HF • Hypotension • Cardiogenic shock • Reactive airway disease • Renal dysfunction • Drugs with SA and/or AV nodal–blocking properties
Metoprolol tartrate	2.5–5.0-mg IV bolus over 2 min	Can repeat 2.5- to 5.0-mg IV bolus in 10 min, up to 3 doses	Hypotension, worsening HF, bronchospasm, bradycardia	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Decompensated systolic HF • Hypotension • Reactive airway disease • Drugs with SA and/or AV nodal–blocking properties
Propranolol	1 mg IV over 1 min	Can repeat 1 mg IV at 2-min intervals, up to 3 doses	Hypotension, worsening HF, bronchospasm, bradycardia	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Cardiogenic shock • Reactive airway disease • Decompensated HF • Hypotension • Hepatic or renal dysfunction • Drugs with SA and/or AV nodal–blocking properties
Nondihydropyridine calcium channel antagonists				
Diltiazem	0.25-mg/kg IV bolus over 2 min	Infusion at 5–10 mg/h, up to 15 mg/h	Hypotension, worsening HF in patients with pre-existing ventricular dysfunction, bradycardia, abnormal	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • WPW with AF / atrial flutter • Hypotension‡ • Decompensated systolic HF/LV

			liver function studies, acute hepatic injury (rare)	dysfunction • Drugs with SA and/or AV nodal–blocking properties • Hepatic or renal dysfunction • Diltiazem is a substrate of CYP3A4 (major) and a moderate CYP3A4 inhibitor • Apixaban, itraconazole, bosutinib, ceritinib, cilostazol, cyclosporine, everolimus, ibrutinib, idelalisib, ivabradine, lomitapide, olaparib, posaconazole, ranolazine, rifampin, simeprevir, voriconazole
Verapamil	5–10-mg (0.075–0.15-mg/kg) IV bolus over 2 min	If no response, can give an additional 10 mg (0.15 mg/kg) 30 min after first dose; then infusion at 0.005 mg/kg/min	Hypotension, worsening HF in patients with pre-existing ventricular dysfunction, pulmonary edema in patients with hypertrophic cardiomyopathy, bradycardia	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Decompensated systolic HF/ LV dysfunction • Drugs with SA and/or AV nodal–blocking properties • Hypotension‡ • Cardiogenic shock • WPW with AF / atrial flutter • Hepatic or renal dysfunction • Verapamil is a moderate CYP3A4 inhibitor and also inhibits P-glycoprotein • Contraindicated with dofetilide • Itraconazole, bosutinib, ceritinib, cilostazol, colchicine, cyclosporine, everolimus, dabigatran, edoxaban, flecainide, ibrutinib, ivabradine, olaparib, posaconazole, ranolazine, rivaroxaban, rifampin, silodosin, simeprevir, rivaroxaban, rifampin, simvastatin, topotecan, trabectedin, vincristine, voriconazole, grapefruit juice
Cardiac glycosides				
Digoxin	0.25–0.5-mg IV bolus	Can repeat 0.25-mg IV bolus, up to maximum dose of 1.0 mg over 24 h (i.e., maximum loading dose 8–12 mcg/kg), given at 6–8-h intervals; maintenance dose based on patient's age, lean body weight, renal function, and concomitant drugs (IV 2.4–3.6 mcg/kg/d)	Anorexia, nausea, vomiting, visual changes and cardiac arrhythmias if digoxin toxicity (associated with levels >2 ng/mL, although symptoms may also occur at lower levels)	• Renal dysfunction • WPW with AF / atrial flutter • AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Drugs with AV nodal-blocking properties • Digoxin is a P-glycoprotein substrate • Dronedarone (reduce dose by at least 50%), amiodarone (reduce dose by 30%–50%) • Verapamil, clarithromycin, cyclosporine, erythromycin, flecainide, itraconazole, posaconazole, propafenone, voriconazole: Monitor digoxin levels • A large retrospective study suggested an increased risk in mortality in patients who were treated with

				digoxin for newly diagnosed AF or atrial flutter; although the data were collected from a population that was different from SVT patients, digoxin should be used with caution (393).
Class III antiarrhythmic agents				
Amiodarone	150 mg IV over 10 min	Infusion at 1 mg/min (360 mg) over next 6 h; then 0.5 mg/min (540 mg) over remaining 18 h	Hypotension, bradycardia, phlebitis, QT prolongation, torsades de pointes (rare), increased INR	• Sinus or AV conduction disease (in absence of pacemaker) • Inflammatory lung disease (acute) • Hepatic dysfunction • Drugs with SA and/or AV nodal–blocking properties • Amiodarone is a substrate of and inhibits p-glycoprotein and CYP2C9 (moderate), CYP2D6 (moderate), and CYP3A4 (weak); amiodarone is a substrate for CYP3A4 (major) and CYP2C8 (major);amiodarone is an inhibitor of OCT2 • Reduce warfarin dose by 50% and reduce digoxin dose by 30%–50% • Agalsidase alfa, agalsidase beta, azithromycin, bosutinib, ceritinib, colchicine, dabigatran, edoxaban, flecainide, ivabradine, ledipasvir/sofosbuvir, lopinavir, lopinavir/ritonavir, lovastatin, nelfinavir, pazopanib, propafenone, simvastatin, ritonavir, rivaroxaban, saquinavir, sofosbuvir, topotecan, vincristine, grapefruit juice
Ibutilide	Contraindicated when QTc >440 ms‖; 1 mg over 10 min (if ≥60 kg); if <60 kg, then 0.01 mg/kg	Can repeat 1 mg once, if the arrhythmia does not terminate within 10 min§	QT prolongation, torsades de pointes, AV block	• Prolonged QT interval • History of torsades de pointes • Avoid other QT interval–prolonging drugs • Concurrent administration of high-dose magnesium has been associated with enhanced efficacy and safety (206, 394)

Note: For this reference table, drugs are presented in alphabetical order within the drug classes, not by COR and LOE.
*When 1 drug is used in combination with other drugs, appropriate dosing adjustments should be made with consideration of at least additive effects during dosage titration. All potential drug–drug interactions are not included in this list. For a more detailed list of drug–drug interactions, clinicians should consult additional resources.
‡If hypotension is a consideration, a slow infusion of diltiazem (2.5 mg/min) or verapamil (1 mg/min) for up to 20 minutes may lessen the potential for hypotension (38).
§The infusion should be stopped as soon as the arrhythmia is terminated or in the event of sustained or nonsustained ventricular tachycardia or marked prolongation of QT or corrected QT interval.
‖QTc calculation used the Bazett's Formula in most clinical studies. Patients should be observed with continuous ECG monitoring for at least 4 h after infusion or until QTc has returned to baseline.

AF indicates atrial fibrillation; AV, atrioventricular; BID, twice daily; CrCl, creatinine clearance; ECG, electrocardiogram/electrocardiographic; HF, heart failure; INR, international normalized ratio; LV, left ventricular; QD, once daily; QID, four times a day; QTc, corrected QT interval; SA, sinoatrial; SVT, supraventricular tachycardia; TID, 3-times a day; and WPW, Wolff-Parkinson-White.

Appendix 2. Ongoing Drug Therapy for SVT, Oral Administration*

Drug†	Initial Daily Dose(s)	Maximum Total Daily Maintenance Dose	Potential Adverse Effects	Precautions (Exclude or Use With Caution) and Interactions
Beta blockers				
Atenolol	25–50 mg QD	100 mg QD (reduced dosing in patients with severe renal dysfunction)	Hypotension, bronchospasm, bradycardia	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Decompensated systolic HF • Hypotension • Reactive airway disease • Severe renal dysfunction • Drugs with SA and/or AV nodal–blocking properties
Metoprolol tartrate	25 mg BID	200 mg BID	Hypotension, bronchospasm, bradycardia	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Decompensated systolic HF • Hypotension • Reactive airway disease • Drugs with SA and/or AV nodal–blocking properties
Metoprolol succinate (long-acting)	50 mg QD	400 mg QD	Hypotension, bronchospasm, bradycardia	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Decompensated systolic HF • Hypotension • Reactive airway disease • Drugs with SA and/or AV nodal–blocking properties
Nadolol	40 mg QD	320 mg QD (reduced dosage with renal impairment)	Hypotension, bronchospasm, bradycardia	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Reactive airway disease • Cardiogenic shock • Decompensated HF • Hypotension • Renal dysfunction • Drugs with SA and/or AV nodal–blocking properties
Propranolol	30–60 mg in divided or single dose with long-acting formulations	40–160 mg in divided or single dose with long-acting formulations	Hypotension, worsening HF, bronchospasm, bradycardia	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Reactive airway disease • Decompensated systolic HF • Hypotension • Drugs with SA and/or AV nodal–blocking properties
Nondihydropyridine calcium channel antagonists				
Diltiazem	120 mg daily in divided or single dose with long-acting formulations	360 mg daily in divided or single dose with long-acting formulations	Hypotension, worsening HF in patients with	• AV block greater than first degree or SA node dysfunction (in absence of

			pre-existing ventricular dysfunction, bradycardia, abnormal liver function studies, acute hepatic injury (rare)	pacemaker) • Hypotension‡ • Decompensated systolic HF / severe LV dysfunction • WPW with AF / atrial flutter • Drugs with SA and/or AV nodal–blocking properties • Diltiazem is a substrate of CYP3A4 (major) and a moderate CYP3A4 inhibitor • Apixaban, itraconazole, bosutinib, ceritinib, cilostazol, cyclosporine, everolimus, ibrutinib, idelalisib, ivabradine, lomitapide, olaparib, ranolazine, rifampin, simeprevir
Verapamil	120 mg daily in divided or single dose with long-acting formulations	480 mg daily in divided or single dose with long-acting formulations	Hypotension, worsening HF in patients with pre-existing ventricular dysfunction, pulmonary edema in patients with hypertrophic cardiomyopathy, bradycardia, abnormal liver function studies	• AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Decompensated systolic HF / severe LV dysfunction • Hypotension‡ • WPW with AF / atrial flutter • Verapamil is a moderate CYP3A4 inhibitor and also inhibits P-glycoprotein • Contraindicated with dofetilide • Itraconazole, bosutinib, ceritinib, cilostazol, colchicine, cyclosporine, everolimus, dabigatran, edoxaban, flecainide, ibrutinib, ivabradine, olaparib, ranolazine, rivaroxaban, rifampin, silodosin, simeprevir, rivaroxaban, rifampin, simvastatin, topotecan, trabectedin, vincristine, grapefruit juice
Cardiac glycosides				
Digoxin	*Loading*: 0.5 mg, with additional 0.125–0.25-mg doses administered at 6–8-h intervals until evidence of adequate effect (maximum dose 8–12 mcg/kg over 24 h)	0.25 mg QD *Maintenance*: 0.125–0.25 mg QD, with dosing based on patient's age, lean body weight, and renal function and drug interactions; occasionally down to 0.0625 mg in cases of renal impairment (trough serum digoxin level 0.5 to 1 ng/mL)	Bradycardia, heart block, anorexia, nausea, vomiting, visual changes and cardiac arrhythmias in cases of digoxin toxicity (associated with levels >2 ng/mL, although	• Renal dysfunction • WPW with AF / atrial flutter • AV block greater than first degree or SA node dysfunction (in absence of pacemaker) • Drugs with SA and/or AV nodal–blocking properties • Reduce dose by 30%–50% when administering with amiodarone and by 50% when administering with

			symptoms may also occur at lower levels)	dronedarone • Monitor digoxin concentrations with verapamil, clarithromycin, erythromycin, itraconazole, cyclosporine, propafenone, flecainide
Class Ic antiarrhythmic agents				
Flecainide	50 mg every 12 h	150 mg every 12 h (PR and QRS intervals should be monitored. May consider monitoring flecainide plasma levels, keeping trough plasma levels below 0.7–1.0 mcg/mL)	Atrial flutter with 1:1 AV conduction§, QT prolongation, torsades de pointes, worsening HF, bradycardia	• Sinus or AV conduction disease (in absence of pacemaker) • Cardiogenic shock • Avoid in structural heart disease (including ischemic heart disease) • Atrial flutter (unless concomitant AV nodal therapy to avoid 1:1 conduction) • Brugada syndrome • Renal dysfunction • Hepatic dysfunction • QT-prolonging drugs • Amiodarone, digoxin, ritonavir, saquinavir, tipranavir
Propafenone	150 mg every 8 h (immediate release); 225 mg every 12 h (extended release)	300 mg every 8 h (immediate release); 425 mg every 12 h (extended release) (PR and QRS interval should be monitored. Consider dosage reduction with hepatic impairment)	Atrial flutter with 1:1 AV conduction§, QT prolongation, torsades de pointes, bradycardia, bronchospasm	• Sinus or AV conduction disease (in absence of pacemaker) • Cardiogenic shock • Hypotension • Reactive airway disease Avoid in structural heart disease (including ischemic heart disease) • Atrial flutter (unless concomitant AV nodal therapy to avoid 1:1 conduction) • Brugada syndrome • Hepatic dysfunction • QT-prolonging drugs • Drugs with SA and/or AV nodal–blocking properties • Amiodarone, ritonavir, saquinavir, tipranavir
Class III antiarrhythmic agents				
Amiodarone	400–600 mg QD in divided doses for 2-4 wk (loading dose); followed by 100–200 mg QD (maintenance dose)	Up to 1200 mg QD may be considered in an inpatient monitoring setting (loading dose); up to 200 mg QD maintenance (to minimize long-term adverse effects)	Bradycardia, QT prolongation, torsades de pointes (rare), gastrointestinal upset, constipation, hypothyroidism, hyperthyroidism, pulmonary fibrosis, hepatic	• Sinus or AV conduction disease (in absence of pacemaker) • Inflammatory lung disease • Hepatic dysfunction • Hypothyroidism, hyperthyroidism • Peripheral neuropathy • Abnormal gait / ataxia • Optic neuritis

			toxicity, corneal deposits, optic neuritis, peripheral neuropathy, photosensitivity, adult respiratory distress syndrome after cardiac or noncardiac surgery (rare)	• Drugs with SA and/or AV nodal–blocking properties • Amiodarone is a substrate of and inhibits p-glycoprotein and CYP2C9 (moderate), CYP2D6 (moderate), and CYP3A4 (weak); amiodarone is a substrate for CYP3A4 (major) and CYP2C8 (major); amiodarone is an inhibitor of OCT2 • Reduce warfarin dose by 50%, and reduce digoxin dose by 30%–50% • Agalsidase alfa, agalsidase beta, azithromycin, bosutinib, ceritinib, colchicine, dabigatran, edoxaban, flecainide, ivabradine, ledipasvir/sofosbuvir, lopinavir, lopinavir/ritonavir, lovastatin, nelfinavir, pazopanib, propafenone, simvastatin, ritonavir, rivaroxaban, saquinavir, sofosbuvir, topotecan, vincristine, grapefruit juice
Dofetilide	• 500 mcg every 12 h (if CrCl >60 mL/min) • 250 mcg every 12 h (if CrCl 40–60 mL/min) • 125 mcg every 12 h (if CrCl 20 to <40 mL/min) • Not recommended if CrCl <20 mL/min • Adjust dose for renal function, body size, and age • Initiate for minimum of 3 d in a facility that can provide continuous ECGmonitoring and cardiac resuscitation • Contraindicated if the baseline QTc interval or QTc >440 ms‖ or 500 ms in patients with ventricular conduction abnormalities	Repeat ECG 2–3 h after administering the first dose to determine QTc; if the QTc increased by >15% compared with baseline or if QTc is >500 ms‖ (550 ms in patients with ventricular conduction abnormalities), subsequent dosing should be downtitrated by 50%; at 2–3 h after each subsequent dose, determine QTc (for in-hospital doses 2–5); if at any time after the second dose the QTc is >500 ms‖ (550 ms in patients with ventricular conduction abnormalities), dofetilide should be discontinued	QT prolongation, torsades de pointes	• Severe renal dysfunction (contraindicated if CrCl <20 mL/min) • Prolonged QT • History of torsades de pointes • Concomitant use of hydrochlorothiazide, cimetidine, dolutegravir, itraconazole, ketoconazole, megestrol, trimethoprim, prochlorperazine trimethoprim/sulfamethoxazole or verapamil, contraindicated • Avoid other QT-prolonging drugs
Sotalol	40–80 mg every 12 h (Patients initiated or reinitiated on sotalol should be placed in a facility that can provide cardiac resuscitation and continuous electrocardiographic	160 mg every 12 h (During initiation and titration, the QT interval should be monitored 2–4 h after each dose. If the QT interval prolongs to ≥500 ms, the dose must be reduced or the drug	QT prolongation, torsades de pointes, bradycardia, bronchospasm	• Prolonged QT • Renal dysfunction • Hypokalemia • Diuretic therapy • Avoid other QT-prolonging drugs • Sinus or AV nodal

	monitoring for a minimum of 3 d. Contraindicated if the QTc‖ interval is >450 ms. CrCl should be calculated before dosing. If CrCl >60 mL/min, then dosing frequency is twice daily. If CrCl 40-60 mL/min, dosing interval is every 24 h. If CrCl <40 mL/min, should not be used.)	discontinued.)		dysfunction (in absence of pacemaker) • Decompensated systolic HF • Cardiogenic shock • Reactive airway disease • Drugs with SA and/or AV–nodal blocking properties
Miscellaneous				
Ivabradine	5 mg BID	7.5 mg BID	Phosphenes, AF	• Concomitant drugs that can exacerbate bradycardia • Contraindicated in decompensated HF • Contraindicated if BP <90/50 mm Hg • Contraindicated in severe hepatic impairment • Hypertension • Ivabradine is a substrate of CYP3A4 (major) • Avoid use with concomitant strong CYP3A4 inhibitors (boceprevir, clarithromycin, indinavir, itraconazole, lopinavir/ritonavir, nelfinavir, ritonavir, saquinavir, telaprevir, posaconazole, voriconazole) • Avoid use with strong CYP3A4 inducers (carbamazepine, phenytoin, rifampin, St. John's wort) • Avoid use with diltiazem, verapamil, grapefruit juice

Note: For this reference table, drugs are presented in alphabetical order within the drug classes, not by COR and LOE.
*When 1 drug is used in combination with other drugs, appropriate dosing adjustments should be made with consideration of at least additive effects during dosage titration. All potential drug–drug interactions and adverse reactions are not included in this list. For a more detailed list of drug interactions and adverse responses, clinicians should consult additional resources; for example, www.crediblemeds.org may be consulted for potential prolongation of the QT interval.
§Recommended given in conjunction with a beta blocker or nondihydropyridine calcium channel antagonist.
‖QTc calculation used the Bazett's Formula in most clinical studies.

AF indicates atrial fibrillation; AV, atrioventricular; BID, twice daily; BP, blood pressure; CrCl, creatinine clearance; ECG, electrocardiogram/electrocardiographic; HF, heart failure; INR, international normalized ratio; LV, left ventricular; QD, once daily; QID, 4 times a day; QTc, corrected QT interval; SA, sinoatrial; SVT, supraventricular tachycardia; TID, 3 times a day; and WPW, Wolff-Parkinson-White.

Appendix 3. Success and Complication Rates for Ablation of SVT*

Arrhythmia	Acute Success	Recurrence Rate	Major Complications	References
Common SVTs				
AVNRT	96%–97% (55, 59)	5% (59)	• Overall 3% (55) • PPM 0.7% (55) • Death 0% (55)	(55, 59)
AVRT / accessory pathway	93% (55, 59)	8% (59)	• Overall 2.8% (55) • PPM 0.3% (55) • Death 0.1% (55) • Tamponade 0.4% (55)	(55, 59)
CTI-dependent atrial flutter	97% (55)	10.6% atrial flutter (395), 33% atrial fibrillation (395)	• Overall 0.5% (55) • PPM 0.2% (55) • Pericardial effusion 0.3% (55)	(55, 59, 395)
Less common SVTs				
Focal AT	80%–100%	4%–27%	<1%–2%	(89, 93, 97, 99, 105, 106, 396, 397)
JT	82%–85%	0–18%	0–18% CHB (overall complications N/A)	(233, 234, 269)
Non–CTI-dependent atrial flutter	73%–100%	7%–53%	0–7%	(106, 211, 213, 215, 216, 218, 219, 221, 398)

*Data in this table are derived from multiple observational studies and registries, and as such may not always reflect current practice. AT indicates atrial tachycardia; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; CHB, complete heart block; CTI, cavotricuspid isthmus; JT, junctional tachycardia; N/A, not available; PPM, permanent pacemaker; and SVT, supraventricular tachycardia.

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