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.

References

1. Sganzerla P, Fabbiocchi F, Grazi S, et al. Electrophysiologic and haemodynamic correlates in supraventricular tachycardia. Eur Heart J. 1989;10:32-9.
2. Bhandari AK, Anderson JL, Gilbert EM, et al. Correlation of symptoms with occurrence of paroxysmal supraventricular tachycardia or atrial fibrillation: a transtelephonic monitoring study. The Flecainide Supraventricular Tachycardia Study Group. Am Heart J. 1992;124:381-6.
3. Leitch JW, Klein GJ, Yee R, et al. Syncope associated with supraventricular tachycardia. An expression of tachycardia rate or vasomotor response? Circulation. 1992;85:1064-71.
4. Lee SH, Chen SA, Wu TJ, et al. Effects of pregnancy on first onset and symptoms of paroxysmal supraventricular tachycardia. Am J Cardiol. 1995;76:675-8.
5. Drago F, Turchetta A, Calzolari A, et al. Reciprocating supraventricular tachycardia in children: low rate at rest as a major factor related to propensity to syncope during exercise. Am Heart J. 1996;132:280-5.
6. Goyal R, Zivin A, Souza J, et al. Comparison of the ages of tachycardia onset in patients with atrioventricular nodal reentrant tachycardia and accessory pathway-mediated tachycardia. Am Heart J. 1996;132:765-7.
7. Abe H, Nagatomo T, Kobayashi H, et al. Neurohumoral and hemodynamic mechanisms of diuresis during atrioventricular nodal reentrant tachycardia. Pacing Clin Electrophysiol. 1997;20:2783-8.
8. Lessmeier TJ, Gamperling D, Johnson-Liddon V, et al. Unrecognized paroxysmal supraventricular tachycardia. Potential for misdiagnosis as panic disorder. Arch Intern Med. 1997;157:537-43.
9. Kalusche D, Ott P, Arentz T, et al. AV nodal re-entry tachycardia in elderly patients: clinical presentation and results of radiofrequency catheter ablation therapy. Coron Artery Dis. 1998;9:359-63.
10. Orejarena LA, Vidaillet H, Jr., DeStefano F, et al. Paroxysmal supraventricular tachycardia in the general population. J Am Coll Cardiol. 1998;31:150-7.
11. Erdogan A, Schulte B, Carlsson J, et al. [Clinical characteristics of patients with AV-nodal reentrant tachycardia (AVNRT): modification by high frequency catheter ablation. Study of 748 patients after high frequency catheter ablation]. Med Klin (Munich). 2001;96:708-12.
12. Fitzsimmons PJ, McWhirter PD, Peterson DW, et al. The natural history of Wolff-Parkinson-White syndrome in 228 military aviators: a long-term follow-up of 22 years. Am Heart J. 2001;142:530-6.
13. Hamdan MH, Zagrodzky JD, Page RL, et al. Effect of P-wave timing during supraventricular tachycardia on the hemodynamic and sympathetic neural response. Circulation. 2001;103:96-101.
14. Razavi M, Luria DM, Jahangir A, et al. Acute blood pressure changes after the onset of atrioventricular nodal reentrant tachycardia: a time-course analysis. J Cardiovasc Electrophysiol. 2005;16:1037-40.
15. Walfridsson U, Walfridsson H. The impact of supraventricular tachycardias on driving ability in patients referred for radiofrequency catheter ablation. Pacing Clin Electrophysiol. 2005;28:191-5.
16. Drago F, Grutter G, Silvetti MS, et al. Atrioventricular nodal reentrant tachycardia in children. Pediatr Cardiol. 2006;27:454-9.
17. Gonzalez-Torrecilla E, Almendral J, Arenal A, et al. Combined evaluation of bedside clinical variables and the electrocardiogram for the differential diagnosis of paroxysmal atrioventricular reciprocating tachycardias in patients without pre-excitation. J Am Coll Cardiol. 2009;53:2353-8.
18. Laurent G, Leong-Poi H, Mangat I, et al. Influence of ventriculoatrial timing on hemodynamics and symptoms during supraventricular tachycardia. J Cardiovasc Electrophysiol. 2009;20:176-81.
19. Walfridsson U, Stromberg A, Janzon M, et al. Wolff-Parkinson-White syndrome and atrioventricular nodal re-entry tachycardia in a Swedish population: consequences on health-related quality of life. Pacing Clin Electrophysiol. 2009;32:1299-306.
20. Kesek M, Ronn F, Tollefsen T, et al. Symptomatic improvement after catheter ablation of supraventricular tachycardia measured by the arrhythmia-specific questionnaire U22. Ups J Med Sci. 2011;116:52-9.
21. Cain N, Irving C, Webber S, et al. Natural history of Wolff-Parkinson-White syndrome diagnosed in childhood. Am J Cardiol. 2013;112:961-5.
22. Maryniak A, Bielawska A, Bieganowska K, et al. Does atrioventricular reentry tachycardia (AVRT) or atrioventricular nodal reentry tachycardia (AVNRT) in children affect their cognitive and emotional development? Pediatr Cardiol. 2013;34:893-7.
23. Mauritson DR, Winniford MD, Walker WS, et al. Oral verapamil for paroxysmal supraventricular tachycardia: a long-term, double-blind randomized trial. Ann Intern Med. 1982;96:409-12.
24. Winniford MD, Fulton KL, Hillis LD. Long-term therapy of paroxysmal supraventricular tachycardia: a randomized, double-blind comparison of digoxin, propranolol and verapamil. Am J Cardiol. 1984;54:1138-9.
25. Anderson S, Blanski L, Byrd RC, et al. Comparison of the efficacy and safety of esmolol, a short-acting beta blocker, with placebo in the treatment of supraventricular tachyarrhythmias. The Esmolol vs Placebo Multicenter Study Group. Am Heart J. 1986;111:42-8.
26. Henthorn RW, Waldo AL, Anderson JL, et al. Flecainide acetate prevents recurrence of symptomatic paroxysmal supraventricular tachycardia. The Flecainide Supraventricular Tachycardia Study Group. Circulation. 1991;83:119-25.

27. Pritchett EL, DaTorre SD, Platt ML, et al. Flecainide acetate treatment of paroxysmal supraventricular tachycardia and paroxysmal atrial fibrillation: dose-response studies. The Flecainide Supraventricular Tachycardia Study Group. J Am Coll Cardiol. 1991;17:297-303.
28. Pritchett EL, McCarthy EA, Wilkinson WE. Propafenone treatment of symptomatic paroxysmal supraventricular arrhythmias. A randomized, placebo-controlled, crossover trial in patients tolerating oral therapy. Ann Intern Med. 1991;114:539-44.
29. Anderson JL, Platt ML, Guarnieri T, et al. Flecainide acetate for paroxysmal supraventricular tachyarrhythmias. The Flecainide Supraventricular Tachycardia Study Group. Am J Cardiol. 1994;74:578-84.
30. Chimienti M, Cullen MT, Jr., Casadei G. Safety of flecainide versus propafenone for the long-term management of symptomatic paroxysmal supraventricular tachyarrhythmias. Report from the Flecainide and Propafenone Italian Study (FAPIS) Group. Eur Heart J. 1995;16:1943-51.
31. A randomized, placebo-controlled trial of propafenone in the prophylaxis of paroxysmal supraventricular tachycardia and paroxysmal atrial fibrillation. UK Propafenone PSVT Study Group. Circulation. 1995;92:2550-7.
32. Dorian P, Naccarelli GV, Coumel P, et al. A randomized comparison of flecainide versus verapamil in paroxysmal supraventricular tachycardia. The Flecainide Multicenter Investigators Group. Am J Cardiol. 1996;77:89A-95A.
33. Wanless RS, Anderson K, Joy M, et al. Multicenter comparative study of the efficacy and safety of sotalol in the prophylactic treatment of patients with paroxysmal supraventricular tachyarrhythmias. Am Heart J. 1997;133:441-6.
34. Lim SH, Anantharaman V, Teo WS, et al. Comparison of treatment of supraventricular tachycardia by Valsalva maneuver and carotid sinus massage. Ann Emerg Med. 1998;31:30-5.
35. Gupta A, Naik A, Vora A, et al. Comparison of efficacy of intravenous diltiazem and esmolol in terminating supraventricular tachycardia. J Assoc Physicians India. 1999;47:969-72.
36. Alboni P, Tomasi C, Menozzi C, et al. Efficacy and safety of out-of-hospital self-administered single-dose oral drug treatment in the management of infrequent, well-tolerated paroxysmal supraventricular tachycardia. J Am Coll Cardiol. 2001;37:548-53.
37. Tendera M, Wnuk-Wojnar AM, Kulakowski P, et al. Efficacy and safety of dofetilide in the prevention of symptomatic episodes of paroxysmal supraventricular tachycardia: a 6-month double-blind comparison with propafenone and placebo. Am Heart J. 2001;142:93-8.
38. Lim SH, Anantharaman V, Teo WS, et al. Slow infusion of calcium channel blockers compared with intravenous adenosine in the emergency treatment of supraventricular tachycardia. Resuscitation. 2009;80:523-8.
39. Smith GD, Dyson K, Taylor D, et al. Effectiveness of the Valsalva Manoeuvre for reversion of supraventricular tachycardia. Cochrane Database Syst Rev. 2013;3:CD009502.
40. Mehta D, Wafa S, Ward DE, et al. Relative efficacy of various physical manoeuvres in the termination of junctional tachycardia. Lancet. 1988;1:1181-5.
41. Wen ZC, Chen SA, Tai CT, et al. Electrophysiological mechanisms and determinants of vagal maneuvers for termination of paroxysmal supraventricular tachycardia. Circulation. 1998;98:2716-23.
42. Waxman MB, Wald RW, Sharma AD, et al. Vagal techniques for termination of paroxysmal supraventricular tachycardia. Am J Cardiol. 1980;46:655-64.
43. Rankin AC, Oldroyd KG, Chong E, et al. Value and limitations of adenosine in the diagnosis and treatment of narrow and broad complex tachycardias. Br Heart J. 1989;62:195-203.
44. Cairns CB, Niemann JT. Intravenous adenosine in the emergency department management of paroxysmal supraventricular tachycardia. Ann Emerg Med. 1991;20:717-21.
45. McCabe JL, Adhar GC, Menegazzi JJ, et al. Intravenous adenosine in the prehospital treatment of paroxysmal supraventricular tachycardia. Ann Emerg Med. 1992;21:358-61.
46. Gausche M, Persse DE, Sugarman T, et al. Adenosine for the prehospital treatment of paroxysmal supraventricular tachycardia. Ann Emerg Med. 1994;24:183-9.
47. Madsen CD, Pointer JE, Lynch TG. A comparison of adenosine and verapamil for the treatment of supraventricular tachycardia in the prehospital setting. Ann Emerg Med. 1995;25:649-55.
48. Brady WJ, Jr., DeBehnke DJ, Wickman LL, et al. Treatment of out-of-hospital supraventricular tachycardia: adenosine vs verapamil. Acad Emerg Med. 1996;3:574-85.
49. Luber S, Brady WJ, Joyce T, et al. Paroxysmal supraventricular tachycardia: outcome after ED care. Am J Emerg Med. 2001;19:40-2.
50. Roth A, Elkayam I, Shapira I, et al. Effectiveness of prehospital synchronous direct-current cardioversion for supraventricular tachyarrhythmias causing unstable hemodynamic states. Am J Cardiol. 2003;91:489-91.
51. Neuss H, Schlepper M. Long-term efficacy and safety of flecainide for supraventricular tachycardia. Am J Cardiol. 1988;62:56D-61D.
52. Cockrell JL, Scheinman MM, Titus C, et al. Safety and efficacy of oral flecainide therapy in patients with atrioventricular re-entrant tachycardia. Ann Intern Med. 1991;114:189-94.
53. Jackman WM, Beckman KJ, McClelland JH, et al. Treatment of supraventricular tachycardia due to atrioventricular nodal reentry, by radiofrequency catheter ablation of slow-pathway conduction. N Engl J Med. 1992;327:313-8.

54. Gambhir DS, Bhargava M, Nair M, et al. Comparison of electrophysiologic effects and efficacy of single-dose intravenous and long-term oral amiodarone therapy in patients with AV nodal reentrant tachycardia. Indian Heart J. 1996;48:133-7.
55. Spector P, Reynolds MR, Calkins H, et al. Meta-analysis of ablation of atrial flutter and supraventricular tachycardia. Am J Cardiol. 2009;104:671-7.
56. Bohnen M, Stevenson WG, Tedrow UB, et al. Incidence and predictors of major complications from contemporary catheter ablation to treat cardiac arrhythmias. Heart Rhythm. 2011;8:1661-6.
57. Hindricks G. The Multicentre European Radiofrequency Survey (MERFS): complications of radiofrequency catheter ablation of arrhythmias. The Multicentre European Radiofrequency Survey (MERFS) investigators of the Working Group on Arrhythmias of the European Society of Cardiology. Eur Heart J. 1993;14:1644-53.
58. Hindricks G. Incidence of complete atrioventricular block following attempted radiofrequency catheter modification of the atrioventricular node in 880 patients. Results of the Multicenter European Radiofrequency Survey (MERFS) The Working Group on Arrhythmias of the European Society of Cardiology. Eur Heart J. 1996;17:82-8.
59. Calkins H, Yong P, Miller JM, et al. Catheter ablation of accessory pathways, atrioventricular nodal reentrant tachycardia, and the atrioventricular junction: final results of a prospective, multicenter clinical trial. The Atakr Multicenter Investigators Group. Circulation. 1999;99:262-70.
60. Cheng CH, Sanders GD, Hlatky MA, et al. Cost-effectiveness of radiofrequency ablation for supraventricular tachycardia. Ann Intern Med. 2000;133:864-76.
61. Scheinman MM, Huang S. The 1998 NASPE prospective catheter ablation registry. Pacing Clin Electrophysiol. 2000;23:1020-8.
62. Fox K, Ford I, Steg PG, et al. Ivabradine for patients with stable coronary artery disease and left-ventricular systolic dysfunction (BEAUTIFUL): a randomised, double-blind, placebo-controlled trial. Lancet. 2008;372:807-16.
63. Swedberg K, Komajda M, Bohm M, et al. Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study. Lancet. 2010;376:875-85.
64. Cappato R, Castelvecchio S, Ricci C, et al. Clinical efficacy of ivabradine in patients with inappropriate sinus tachycardia: a prospective, randomized, placebo-controlled, double-blind, crossover evaluation. J Am Coll Cardiol. 2012;60:1323-9.
65. Lee RJ, Kalman JM, Fitzpatrick AP, et al. Radiofrequency catheter modification of the sinus node for "inappropriate" sinus tachycardia. Circulation. 1995;92:2919-28.
66. Rakovec P. Treatment of inappropriate sinus tachycardia with ivabradine. Wien Klin Wochenschr. 2009;121:715-8.
67. Calo L, Rebecchi M, Sette A, et al. Efficacy of ivabradine administration in patients affected by inappropriate sinus tachycardia. Heart Rhythm. 2010;7:1318-23.
68. Kaplinsky E, Comes FP, Urondo LS, et al. Efficacy of ivabradine in four patients with inappropriate sinus tachycardia: a three month-long experience based on electrocardiographic, Holter monitoring, exercise tolerance and quality of life assessments. Cardiol J. 2010;17:166-71.
69. Zellerhoff S, Hinterseer M, Felix KB, et al. Ivabradine in patients with inappropriate sinus tachycardia. Naunyn Schmiedebergs Arch Pharmacol. 2010;382:483-6.
70. Benezet-Mazuecos J, Rubio JM, Farre J, et al. Long-term outcomes of ivabradine in inappropriate sinus tachycardia patients: appropriate efficacy or inappropriate patients. Pacing Clin Electrophysiol. 2013;36:830-6.
71. Ptaszynski P, Kaczmarek K, Ruta J, et al. Metoprolol succinate vs. ivabradine in the treatment of inappropriate sinus tachycardia in patients unresponsive to previous pharmacological therapy. Europace. 2013;15:116-21.
72. Ptaszynski P, Kaczmarek K, Ruta J, et al. Ivabradine in the treatment of inappropriate sinus tachycardia in patients after successful radiofrequency catheter ablation of atrioventricular node slow pathway. Pacing Clin Electrophysiol. 2013;36:42-9.
73. Ptaszynski P, Kaczmarek K, Ruta J, et al. Ivabradine in combination with metoprolol succinate in the treatment of inappropriate sinus tachycardia. J Cardiovasc Pharmacol Ther. 2013;18:338-44.
74. Kang KT, Etheridge SP, Kantoch MJ, et al. Current management of focal atrial tachycardia in children: a multicenter experience. Circ Arrhythm Electrophysiol. 2014;7:664-70.
75. Callans DJ, Ren JF, Schwartzman D, et al. Narrowing of the superior vena cava-right atrium junction during radiofrequency catheter ablation for inappropriate sinus tachycardia: analysis with intracardiac echocardiography. J Am Coll Cardiol. 1999;33:1667-70.
76. Man KC, Knight B, Tse HF, et al. Radiofrequency catheter ablation of inappropriate sinus tachycardia guided by activation mapping. J Am Coll Cardiol. 2000;35:451-7.
77. Marrouche NF, Beheiry S, Tomassoni G, et al. Three-dimensional nonfluoroscopic mapping and ablation of inappropriate sinus tachycardia. Procedural strategies and long-term outcome. J Am Coll Cardiol. 2002;39:1046-54.
78. Lin D, Garcia F, Jacobson J, et al. Use of noncontact mapping and saline-cooled ablation catheter for sinus node modification in medically refractory inappropriate sinus tachycardia. Pacing Clin Electrophysiol. 2007;30:236-42.
79. Frankel DS, Lin D, Anastasio N, et al. Frequent additional tachyarrhythmias in patients with inappropriate sinus tachycardia undergoing sinus node modification: an important cause of symptom recurrence. J Cardiovasc Electrophysiol. 2012;23:835-9.
80. Takemoto M, Mukai Y, Inoue S, et al. Usefulness of non-contact mapping for radiofrequency catheter ablation of inappropriate sinus tachycardia: new procedural strategy and long-term clinical outcome. Intern Med. 2012;51:357-62.

81. Huang HD, Tamarisa R, Mathur N, et al. Stellate ganglion block: a therapeutic alternative for patients with medically refractory inappropriate sinus tachycardia? J Electrocardiol. 2013;46:693-6.
82. Gillette PC, Garson A, Jr. Electrophysiologic and pharmacologic characteristics of automatic ectopic atrial tachycardia. Circulation. 1977;56:571-5.
83. Creamer JE, Nathan AW, Camm AJ. Successful treatment of atrial tachycardias with flecainide acetate. Br Heart J. 1985;53:164-6.
84. Kunze KP, Kuck KH, Schluter M, et al. Effect of encainide and flecainide on chronic ectopic atrial tachycardia. J Am Coll Cardiol. 1986;7:1121-6.
85. Lucet V, Do ND, Fidelle J, et al. [Anti-arrhythmia efficacy of propafenone in children. Apropos of 30 cases]. Arch Mal Coeur Vaiss. 1987;80:1385-93.
86. Mehta AV, Sanchez GR, Sacks EJ, et al. Ectopic automatic atrial tachycardia in children: clinical characteristics, management and follow-up. J Am Coll Cardiol. 1988;11:379-85.
87. Colloridi V, Perri C, Ventriglia F, et al. Oral sotalol in pediatric atrial ectopic tachycardia. Am Heart J. 1992;123:254-6.
88. von Bernuth G, Engelhardt W, Kramer HH, et al. Atrial automatic tachycardia in infancy and childhood. Eur Heart J. 1992;13:1410-5.
89. Chen SA, Chiang CE, Yang CJ, et al. Sustained atrial tachycardia in adult patients. Electrophysiological characteristics, pharmacological response, possible mechanisms, and effects of radiofrequency ablation. Circulation. 1994;90:1262-78.
90. Engelstein ED, Lippman N, Stein KM, et al. Mechanism-specific effects of adenosine on atrial tachycardia. Circulation. 1994;89:2645-54.
91. Heusch A, Kramer HH, Krogmann ON, et al. Clinical experience with propafenone for cardiac arrhythmias in the young. Eur Heart J. 1994;15:1050-6.
92. Janousek J, Paul T. Safety of oral propafenone in the treatment of arrhythmias in infants and children (European retrospective multicenter study). Working Group on Pediatric Arrhythmias and Electrophysiology of the Association of European Pediatric Cardiologists. Am J Cardiol. 1998;81:1121-4.
93. Kalman JM, Olgin JE, Karch MR, et al. "Cristal tachycardias": origin of right atrial tachycardias from the crista terminalis identified by intracardiac echocardiography. J Am Coll Cardiol. 1998;31:451-9.
94. Markowitz SM, Stein KM, Mittal S, et al. Differential effects of adenosine on focal and macroreentrant atrial tachycardia. J Cardiovasc Electrophysiol. 1999;10:489-502.
95. Morton JB, Sanders P, Das A, et al. Focal atrial tachycardia arising from the tricuspid annulus: electrophysiologic and electrocardiographic characteristics. J Cardiovasc Electrophysiol. 2001;12:653-9.
96. Kistler PM, Sanders P, Hussin A, et al. Focal atrial tachycardia arising from the mitral annulus: electrocardiographic and electrophysiologic characterization. J Am Coll Cardiol. 2003;41:2212-9.
97. Kistler PM, Sanders P, Fynn SP, et al. Electrophysiological and electrocardiographic characteristics of focal atrial tachycardia originating from the pulmonary veins: acute and long-term outcomes of radiofrequency ablation. Circulation. 2003;108:1968-75.
98. Gonzalez MD, Contreras LJ, Jongbloed MR, et al. Left atrial tachycardia originating from the mitral annulus-aorta junction. Circulation. 2004;110:3187-92.
99. Kistler PM, Fynn SP, Haqqani H, et al. Focal atrial tachycardia from the ostium of the coronary sinus: electrocardiographic and electrophysiological characterization and radiofrequency ablation. J Am Coll Cardiol. 2005;45:1488-93.
100. Eidher U, Freihoff F, Kaltenbrunner W, et al. Efficacy and safety of ibutilide for the conversion of monomorphic atrial tachycardia. Pacing Clin Electrophysiol. 2006;29:358-62.
101. Ouyang F, Ma J, Ho SY, et al. Focal atrial tachycardia originating from the non-coronary aortic sinus: electrophysiological characteristics and catheter ablation. J Am Coll Cardiol. 2006;48:122-31.
102. Roberts-Thomson KC, Kistler PM, Haqqani HM, et al. Focal atrial tachycardias arising from the right atrial appendage: electrocardiographic and electrophysiologic characteristics and radiofrequency ablation. J Cardiovasc Electrophysiol. 2007;18:367-72.
103. Medi C, Kalman JM, Haqqani H, et al. Tachycardia-mediated cardiomyopathy secondary to focal atrial tachycardia: long-term outcome after catheter ablation. J Am Coll Cardiol. 2009;53:1791-7.
104. Liu X, Dong J, Ho SY, et al. Atrial tachycardia arising adjacent to noncoronary aortic sinus: distinctive atrial activation patterns and anatomic insights. J Am Coll Cardiol. 2010;56:796-804.
105. Biviano AB, Bain W, Whang W, et al. Focal left atrial tachycardias not associated with prior catheter ablation for atrial fibrillation: clinical and electrophysiological characteristics. Pacing Clin Electrophysiol. 2012;35:17-27.
106. de Loma-Osorio F, Diaz-Infante E, ., et al. Spanish Catheter Ablation Registry. 12th Official Report of the Spanish Society of Cardiology Working Group on Electrophysiology and Arrhythmias (2012). Rev Esp Cardiol (Engl Ed). 2013;66:983-92.
107. Mano H, Okumura Y, Watanabe I, et al. Potential anatomic substrate of peri-atrioventricular nodal atrial tachycardia ablated from the noncoronary sinus of Valsalva. J Interv Card Electrophysiol. 2013;38:27-34.
108. Arsura E, Lefkin AS, Scher DL, et al. A randomized, double-blind, placebo-controlled study of verapamil and metoprolol in treatment of multifocal atrial tachycardia. Am J Med. 1988;85:519-24.

109. McCord JK, Borzak S, Davis T, et al. Usefulness of intravenous magnesium for multifocal atrial tachycardia in patients with chronic obstructive pulmonary disease. Am J Cardiol. 1998;81:91-3.
110. Iseri LT, Fairshter RD, Hardemann JL, et al. Magnesium and potassium therapy in multifocal atrial tachycardia. Am Heart J. 1985;110:789-94.
111. Hazard PB, Burnett CR. Treatment of multifocal atrial tachycardia with metoprolol. Crit Care Med. 1987;15:20-5.
112. Waxman HL, Myerburg RJ, Appel R, et al. Verapamil for control of ventricular rate in paroxysmal supraventricular tachycardia and atrial fibrillation or flutter: a double-blind randomized cross-over study. Ann Intern Med. 1981;94:1-6.
113. Yeh SJ, Lin FC, Chou YY, et al. Termination of paroxysmal supraventricular tachycardia with a single oral dose of diltiazem and propranolol. Circulation. 1985;71:104-9.
114. DiMarco JP, Miles W, Akhtar M, et al. Adenosine for paroxysmal supraventricular tachycardia: dose ranging and comparison with verapamil. Assessment in placebo-controlled, multicenter trials. The Adenosine for PSVT Study Group. Ann Intern Med. 1990;113:104-10.
115. Dougherty AH, Jackman WM, Naccarelli GV, et al. Acute conversion of paroxysmal supraventricular tachycardia with intravenous diltiazem. IV Diltiazem Study Group. Am J Cardiol. 1992;70:587-92.
116. Langberg JJ, Leon A, Borganelli M, et al. A randomized, prospective comparison of anterior and posterior approaches to radiofrequency catheter ablation of atrioventricular nodal reentry tachycardia. Circulation. 1993;87:1551-6.
117. Kalbfleisch SJ, Strickberger SA, Williamson B, et al. Randomized comparison of anatomic and electrogram mapping approaches to ablation of the slow pathway of atrioventricular node reentrant tachycardia. J Am Coll Cardiol. 1994;23:716-23.
118. Kopelman HA, Prater SP, Tondato F, et al. Slow pathway catheter ablation of atrioventricular nodal re-entrant tachycardia guided by electroanatomical mapping: a randomized comparison to the conventional approach. Europace. 2003;5:171-4.
119. Kimman GP, Theuns DA, Szili-Torok T, et al. CRAVT: a prospective, randomized study comparing transvenous cryothermal and radiofrequency ablation in atrioventricular nodal re-entrant tachycardia. Eur Heart J. 2004;25:2232-7.
120. Zrenner B, Dong J, Schreieck J, et al. Transvenous cryoablation versus radiofrequency ablation of the slow pathway for the treatment of atrioventricular nodal re-entrant tachycardia: a prospective randomized pilot study. Eur Heart J. 2004;25:2226-31.
121. Kardos A, Paprika D, Shalganov T, et al. Ice mapping during tachycardia in close proximity to the AV node is safe and offers advantages for transcatheter ablation procedures. Acta Cardiol. 2007;62:587-91.
122. Deisenhofer I, Zrenner B, Yin YH, et al. Cryoablation versus radiofrequency energy for the ablation of atrioventricular nodal reentrant tachycardia (the CYRANO Study): results from a large multicenter prospective randomized trial. Circulation. 2010;122:2239-45.
123. Rodriguez-Entem FJ, Exposito V, Gonzalez-Enriquez S, et al. Cryoablation versus radiofrequency ablation for the treatment of atrioventricular nodal reentrant tachycardia: results of a prospective randomized study. J Interv Card Electrophysiol. 2013;36:41-5.
124. Rinkenberger RL, Prystowsky EN, Heger JJ, et al. Effects of intravenous and chronic oral verapamil administration in patients with supraventricular tachyarrhythmias. Circulation. 1980;62:996-1010.
125. Das G, Tschida V, Gray R, et al. Efficacy of esmolol in the treatment and transfer of patients with supraventricular tachyarrhythmias to alternate oral antiarrhythmic agents. J Clin Pharmacol. 1988;28:746-50.
126. Amsterdam EA, Kulcyski J, Ridgeway MG. Efficacy of cardioselective beta-adrenergic blockade with intravenously administered metoprolol in the treatment of supraventricular tachyarrhythmias. J Clin Pharmacol. 1991;31:714-8.
127. Musto B, Cavallaro C, Musto A, et al. Flecainide single oral dose for management of paroxysmal supraventricular tachycardia in children and young adults. Am Heart J. 1992;124:110-5.
128. Gambhir DS, Bhargava M, Arora R, et al. Electrophysiologic effects and therapeutic efficacy of intravenous flecainide for termination of paroxysmal supraventricular tachycardia. Indian Heart J. 1995;47:237-43.
129. Glatter KA, Cheng J, Dorostkar P, et al. Electrophysiologic effects of adenosine in patients with supraventricular tachycardia. Circulation. 1999;99:1034-40.
130. Kay GN, Epstein AE, Dailey SM, et al. Selective radiofrequency ablation of the slow pathway for the treatment of atrioventricular nodal reentrant tachycardia. Evidence for involvement of perinodal myocardium within the reentrant circuit. Circulation. 1992;85:1675-88.
131. Bogun F, Knight B, Weiss R, et al. Slow pathway ablation in patients with documented but noninducible paroxysmal supraventricular tachycardia. J Am Coll Cardiol. 1996;28:1000-4.
132. D'Este D, Zoppo F, Bertaglia E, et al. Long-term outcome of patients with atrioventricular node reentrant tachycardia. Int J Cardiol. 2007;115:350-3.
133. Friedman PL, Dubuc M, Green MS, et al. Catheter cryoablation of supraventricular tachycardia: results of the multicenter prospective "frosty" trial. Heart Rhythm. 2004;1:129-38.
134. de Sisti A, Tonet J. Cryoablation of atrioventricular nodal reentrant tachycardia: a clinical review. Pacing Clin Electrophysiol. 2012;35:233-40.
135. Hanninen M, Yeung-Lai-Wah N, Massel D, et al. Cryoablation versus RF ablation for AVNRT: A meta-analysis and systematic review. J Cardiovasc Electrophysiol. 2013;24:1354-60.

136. Santangeli P, Proietti R, Di BL, et al. Cryoablation versus radiofrequency ablation of atrioventricular nodal reentrant tachycardia. J Interv Card Electrophysiol. 2014;39:111-9.
137. Klein GJ, Bashore TM, Sellers TD, et al. Ventricular fibrillation in the Wolff-Parkinson-White syndrome. N Engl J Med. 1979;301:1080-5.
138. Rinne C, Klein GJ, Sharma AD, et al. Relation between clinical presentation and induced arrhythmias in the Wolff-Parkinson-White syndrome. Am J Cardiol. 1987;60:576-9.
139. Sharma AD, Yee R, Guiraudon G, et al. Sensitivity and specificity of invasive and noninvasive testing for risk of sudden death in Wolff-Parkinson-White syndrome. J Am Coll Cardiol. 1987;10:373-81.
140. Gaita F, Giustetto C, Riccardi R, et al. Stress and pharmacologic tests as methods to identify patients with Wolff-Parkinson-White syndrome at risk of sudden death. Am J Cardiol. 1989;64:487-90.
141. Beckman KJ, Gallastegui JL, Bauman JL, et al. The predictive value of electrophysiologic studies in untreated patients with Wolff-Parkinson-White syndrome. J Am Coll Cardiol. 1990;15:640-7.
142. Pappone C, Vicedomini G, Manguso F, et al. Risk of malignant arrhythmias in initially symptomatic patients with Wolff-Parkinson-White syndrome: results of a prospective long-term electrophysiological follow-up study. Circulation. 2012;125:661-8.
143. Spar DS, Silver ES, Hordof AJ, et al. Relation of the utility of exercise testing for risk assessment in pediatric patients with ventricular preexcitation to pathway location. Am J Cardiol. 2012;109:1011-4.
144. Wackel P, Irving C, Webber S, et al. Risk stratification in Wolff-Parkinson-White syndrome: the correlation between noninvasive and invasive testing in pediatric patients. Pacing Clin Electrophysiol. 2012;35:1451-7.
145. Pappone C, Vicedomini G, Manguso F, et al. Wolff-Parkinson-white syndrome in the era of catheter ablation: insights from a registry study of 2169 patients. Circulation. 2014;130:811-9.
146. Sellers TD, Jr., Bashore TM, Gallagher JJ. Digitalis in the pre-excitation syndrome. Analysis during atrial fibrillation. Circulation. 1977;56:260-7.
147. Sellers TD, Jr., Campbell RW, Bashore TM, et al. Effects of procainamide and quinidine sulfate in the Wolff-Parkinson-White syndrome. Circulation. 1977;55:15-22.
148. Hamer A, Peter T, Platt M, et al. Effects of verapamil on supraventricular tachycardia in patients with overt and concealed Wolff-Parkinson-White syndrome. Am Heart J. 1981;101:600-12.
149. Hombach V, Braun V, Hopp HW, et al. Antiarrhythmic effects of acute betablockade with atenolol on supraventricular tachycardias at rest and during exercise. Klin Wochenschr. 1981;59:123-33.
150. Sheinman BD, Evans T. Acceleration of ventricular rate by fibrillation associated with the Wolff-Parkinson-White syndrome. Br Med J (Clin Res Ed). 1982;285:999-1000.
151. Morady F, DiCarlo LA, Jr., Baerman JM, et al. Effect of propranolol on ventricular rate during atrial fibrillation in the Wolff-Parkinson-White syndrome. Pacing Clin Electrophysiol. 1987;10:492-6.
152. Schutzenberger W, Leisch F, Gmeiner R. Enhanced accessory pathway conduction following intravenous amiodarone in atrial fibrillation. A case report. Int J Cardiol. 1987;16:93-5.
153. Huycke EC, Sung RJ, Dias VC, et al. Intravenous diltiazem for termination of reentrant supraventricular tachycardia: a placebo-controlled, randomized, double-blind, multicenter study. J Am Coll Cardiol. 1989;13:538-44.
154. Furlong R, Gerhardt RT, Farber P, et al. Intravenous adenosine as first-line prehospital management of narrow-complex tachycardias by EMS personnel without direct physician control. Am J Emerg Med. 1995;13:383-8.
155. Boriani G, Biffi M, Frabetti L, et al. Ventricular fibrillation after intravenous amiodarone in Wolff-Parkinson-White syndrome with atrial fibrillation. Am Heart J. 1996;131:1214-6.
156. Glatter KA, Dorostkar PC, Yang Y, et al. Electrophysiological effects of ibutilide in patients with accessory pathways. Circulation. 2001;104:1933-9.
157. Shiraishi H, Ishibashi K, Urao N, et al. Two cases of polymorphic ventricular tachycardia induced by the administration of verapamil against paroxysmal supraventricular tachycardia. Intern Med. 2002;41:445-8.
158. Neumar RW, Otto CW, Link MS, et al. Part 8: adult advanced cardiovascular life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2010;122:S729-S767.
159. Delaney B, Loy J, Kelly AM. The relative efficacy of adenosine versus verapamil for the treatment of stable paroxysmal supraventricular tachycardia in adults: a meta-analysis. Eur J Emerg Med. 2011;18:148-52.
160. Bauernfeind RA, Wyndham CR, Dhingra RC, et al. Serial electrophysiologic testing of multiple drugs in patients with atrioventricular nodal reentrant paroxysmal tachycardia. Circulation. 1980;62:1341-9.
161. Sakurai M, Yasuda H, Kato N, et al. Acute and chronic effects of verapamil in patients with paroxysmal supraventricular tachycardia. Am Heart J. 1983;105:619-28.
162. Feld GK, Nademanee K, Weiss J, et al. Electrophysiologic basis for the suppression by amiodarone of orthodromic supraventricular tachycardias complicating pre-excitation syndromes. J Am Coll Cardiol. 1984;3:1298-307.
163. Feld GK, Nademanee K, Stevenson W, et al. Clinical and electrophysiologic effects of amiodarone in patients with atrial fibrillation complicating the Wolff-Parkinson-White syndrome. Am Heart J. 1988;115:102-7.

164. Hopson JR, Buxton AE, Rinkenberger RL, et al. Safety and utility of flecainide acetate in the routine care of patients with supraventricular tachyarrhythmias: results of a multicenter trial. The Flecainide Supraventricular Tachycardia Study Group. Am J Cardiol. 1996;77:72A-82A.
165. Jackman WM, Wang XZ, Friday KJ, et al. Catheter ablation of accessory atrioventricular pathways (Wolff-Parkinson-White syndrome) by radiofrequency current. N Engl J Med. 1991;324:1605-11.
166. Calkins H, Langberg J, Sousa J, et al. Radiofrequency catheter ablation of accessory atrioventricular connections in 250 patients. Abbreviated therapeutic approach to Wolff-Parkinson-White syndrome. Circulation. 1992;85:1337-46.
167. Kugler JD, Danford DA, Deal BJ, et al. Radiofrequency catheter ablation for tachyarrhythmias in children and adolescents. The Pediatric Electrophysiology Society. N Engl J Med. 1994;330:1481-7.
168. Dagres N, Clague JR, Kottkamp H, et al. Radiofrequency catheter ablation of accessory pathways. Outcome and use of antiarrhythmic drugs during follow-up. Eur Heart J. 1999;20:1826-32.
169. Schlapfer J, Fromer M. Late clinical outcome after successful radiofrequency catheter ablation of accessory pathways. Eur Heart J. 2001;22:605-9.
170. Belhassen B, Rogowski O, Glick A, et al. Radiofrequency ablation of accessory pathways: a 14 year experience at the Tel Aviv Medical Center in 508 patients. Isr Med Assoc J. 2007;9:265-70.
171. Milstein S, Sharma AD, Klein GJ. Electrophysiologic profile of asymptomatic Wolff-Parkinson-White pattern. Am J Cardiol. 1986;57:1097-100.
172. Satoh M, Aizawa Y, Funazaki T, et al. Electrophysiologic evaluation of asymptomatic patients with the Wolff-Parkinson-White pattern. Pacing Clin Electrophysiol. 1989;12:413-20.
173. Klein GJ, Yee R, Sharma AD. Longitudinal electrophysiologic assessment of asymptomatic patients with the Wolff-Parkinson-White electrocardiographic pattern. N Engl J Med. 1989;320:1229-33.
174. Leitch JW, Klein GJ, Yee R, et al. Prognostic value of electrophysiology testing in asymptomatic patients with Wolff-Parkinson-White pattern. Circulation. 1990;82:1718-23.
175. Brembilla-Perrot B, Holban I, Houriez P, et al. Influence of age on the potential risk of sudden death in asymptomatic Wolff-Parkinson-White syndrome. Pacing Clin Electrophysiol. 2001;24:1514-8.
176. Pappone C, Santinelli V, Rosanio S, et al. Usefulness of invasive electrophysiologic testing to stratify the risk of arrhythmic events in asymptomatic patients with Wolff-Parkinson-White pattern: results from a large prospective long-term follow-up study. J Am Coll Cardiol. 2003;41:239-44.
177. Pappone C, Santinelli V, Manguso F, et al. A randomized study of prophylactic catheter ablation in asymptomatic patients with the Wolff-Parkinson-White syndrome. N Engl J Med. 2003;349:1803-11.
178. Santinelli V, Radinovic A, Manguso F, et al. Asymptomatic ventricular preexcitation: a long-term prospective follow-up study of 293 adult patients. Circ Arrhythm Electrophysiol. 2009;2:102-7.
179. Platia EV, Michelson EL, Porterfield JK, et al. Esmolol versus verapamil in the acute treatment of atrial fibrillation or atrial flutter. Am J Cardiol. 1989;63:925-9.
180. Salerno DM, Dias VC, Kleiger RE, et al. Efficacy and safety of intravenous diltiazem for treatment of atrial fibrillation and atrial flutter. The Diltiazem-Atrial Fibrillation/Flutter Study Group. Am J Cardiol. 1989;63:1046-51.
181. Van Gelder IC, Crijns HJ, Van Gilst WH, et al. Efficacy and safety of flecainide acetate in the maintenance of sinus rhythm after electrical cardioversion of chronic atrial fibrillation or atrial flutter. Am J Cardiol. 1989;64:1317-21.
182. Suttorp MJ, Kingma JH, Jessurun ER, et al. The value of class IC antiarrhythmic drugs for acute conversion of paroxysmal atrial fibrillation or flutter to sinus rhythm. J Am Coll Cardiol. 1990;16:1722-7.
183. Ellenbogen KA, Dias VC, Plumb VJ, et al. A placebo-controlled trial of continuous intravenous diltiazem infusion for 24-hour heart rate control during atrial fibrillation and atrial flutter: a multicenter study. J Am Coll Cardiol. 1991;18:891-7.
184. Van Gelder IC, Crijns HJ, Van Gilst WH, et al. Prediction of uneventful cardioversion and maintenance of sinus rhythm from direct-current electrical cardioversion of chronic atrial fibrillation and flutter. Am J Cardiol. 1991;68:41-6.
185. Kingma JH, Suttorp MJ. Acute pharmacologic conversion of atrial fibrillation and flutter: the role of flecainide, propafenone, and verapamil. Am J Cardiol. 1992;70:56A-60A.
186. Roberts SA, Diaz C, Nolan PE, et al. Effectiveness and costs of digoxin treatment for atrial fibrillation and flutter. Am J Cardiol. 1993;72:567-73.
187. Tucker KJ, Wilson C. A comparison of transoesophageal atrial pacing and direct current cardioversion for the termination of atrial flutter: a prospective, randomised clinical trial. Br Heart J. 1993;69:530-5.
188. Ellenbogen KA, Dias VC, Cardello FP, et al. Safety and efficacy of intravenous diltiazem in atrial fibrillation or atrial flutter. Am J Cardiol. 1995;75:45-9.
189. Hou ZY, Chang MS, Chen CY, et al. Acute treatment of recent-onset atrial fibrillation and flutter with a tailored dosing regimen of intravenous amiodarone. A randomized, digoxin-controlled study. Eur Heart J. 1995;16:521-8.
190. Sung RJ, Tan HL, Karagounis L, et al. Intravenous sotalol for the termination of supraventricular tachycardia and atrial fibrillation and flutter: a multicenter, randomized, double-blind, placebo-controlled study. Sotalol Multicenter Study Group. Am Heart J. 1995;129:739-48.
191. Doni F, Staffiere E, Manfredi M, et al. Type II atrial flutter interruption with transesophageal pacing: use of propafenone and possible change of the substrate. Pacing Clin Electrophysiol. 1996;19:1958-61.

192. Ellenbogen KA, Stambler BS, Wood MA, et al. Efficacy of intravenous ibutilide for rapid termination of atrial fibrillation and atrial flutter: a dose-response study. J Am Coll Cardiol. 1996;28:130-6.
193. Stambler BS, Wood MA, Ellenbogen KA, et al. Efficacy and safety of repeated intravenous doses of ibutilide for rapid conversion of atrial flutter or fibrillation. Ibutilide Repeat Dose Study Investigators. Circulation. 1996;94:1613-21.
194. Volgman AS, Carberry PA, Stambler B, et al. Conversion efficacy and safety of intravenous ibutilide compared with intravenous procainamide in patients with atrial flutter or fibrillation. J Am Coll Cardiol. 1998;31:1414-9.
195. Vos MA, Golitsyn SR, Stangl K, et al. Superiority of ibutilide (a new class III agent) over DL-sotalol in converting atrial flutter and atrial fibrillation. The Ibutilide/Sotalol Comparator Study Group. Heart. 1998;79:568-75.
196. Benditt DG, Williams JH, Jin J, et al. Maintenance of sinus rhythm with oral d,l-sotalol therapy in patients with symptomatic atrial fibrillation and/or atrial flutter. d,l-Sotalol Atrial Fibrillation/Flutter Study Group. Am J Cardiol. 1999;84:270-7.
197. Doni F, Manfredi M, Piemonti C, et al. New onset atrial flutter termination by overdrive transoesophageal pacing: effects of different protocols of stimulation. Europace. 2000;2:292-6.
198. Natale A, Newby KH, Pisano E, et al. Prospective randomized comparison of antiarrhythmic therapy versus first-line radiofrequency ablation in patients with atrial flutter. J Am Coll Cardiol. 2000;35:1898-904.
199. Delacretaz E, Ganz LI, Soejima K, et al. Multi atrial maco-re-entry circuits in adults with repaired congenital heart disease: entrainment mapping combined with three-dimensional electroanatomic mapping. J Am Coll Cardiol. 2001;37:1665-76.
200. Delle Karth G, Geppert A, Neunteufl T, et al. Amiodarone versus diltiazem for rate control in critically ill patients with atrial tachyarrhythmias. Crit Care Med. 2001;29:1149-53.
201. Pedersen OD, Bagger H, Keller N, et al. Efficacy of dofetilide in the treatment of atrial fibrillation-flutter in patients with reduced left ventricular function: a Danish investigations of arrhythmia and mortality on dofetilide (diamond) substudy. Circulation. 2001;104:292-6.
202. Gallagher MM, Guo XH, Poloniecki JD, et al. Initial energy setting, outcome and efficiency in direct current cardioversion of atrial fibrillation and flutter. J Am Coll Cardiol. 2001;38:1498-504.
203. Wazni O, Marrouche NF, Martin DO, et al. Randomized study comparing combined pulmonary vein-left atrial junction disconnection and cavotricuspid isthmus ablation versus pulmonary vein-left atrial junction disconnection alone in patients presenting with typical atrial flutter and atrial fibrillation. Circulation. 2003;108:2479-83.
204. Da Costa A, Thevenin J, Roche F, et al. Results from the Loire-Ardeche-Drome-Isere-Puy-de-Dome (LADIP) trial on atrial flutter, a multicentric prospective randomized study comparing amiodarone and radiofrequency ablation after the first episode of symptomatic atrial flutter. Circulation. 2006;114:1676-81.
205. Kuniss M, Vogtmann T, Ventura R, et al. Prospective randomized comparison of durability of bidirectional conduction block in the cavotricuspid isthmus in patients after ablation of common atrial flutter using cryothermy and radiofrequency energy: the CRYOTIP study. Heart Rhythm. 2009;6:1699-705.
206. Steinwender C, Honig S, Kypta A, et al. Pre-injection of magnesium sulfate enhances the efficacy of ibutilide for the conversion of typical but not of atypical persistent atrial flutter. Int J Cardiol. 2010;141:260-5.
207. Bastani H, Drca N, Insulander P, et al. Cryothermal vs. radiofrequency ablation as atrial flutter therapy: a randomized comparison. Europace. 2013;15:420-8.
208. Mohanty S, Mohanty P, Di BL, et al. Results from a single-blind, randomized study comparing the impact of different ablation approaches on long-term procedure outcome in coexistent atrial fibrillation and flutter (APPROVAL). Circulation. 2013;127:1853-60.
209. Pietersen AH, Hellemann H. Usefulness of flecainide for prevention of paroxysmal atrial fibrillation and flutter. Danish-Norwegian Flecainide Multicenter Study Group. Am J Cardiol. 1991;67:713-7.
210. Aliot E, Denjoy I. Comparison of the safety and efficacy of flecainide versus propafenone in hospital out-patients with symptomatic paroxysmal atrial fibrillation/flutter. The Flecainide AF French Study Group. Am J Cardiol. 1996;77:66A-71A.
211. Baker BM, Lindsay BD, Bromberg BI, et al. Catheter ablation of clinical intraatrial reentrant tachycardias resulting from previous atrial surgery: localizing and transecting the critical isthmus. J Am Coll Cardiol. 1996;28:411-7.
212. Kalman JM, VanHare GF, Olgin JE, et al. Ablation of 'incisional' reentrant atrial tachycardia complicating surgery for congenital heart disease. Use of entrainment to define a critical isthmus of conduction. Circulation. 1996;93:502-12.
213. Triedman JK, Bergau DM, Saul JP, et al. Efficacy of radiofrequency ablation for control of intraatrial reentrant tachycardia in patients with congenital heart disease. J Am Coll Cardiol. 1997;30:1032-8.
214. Huang DT, Monahan KM, Zimetbaum P, et al. Hybrid pharmacologic and ablative therapy: a novel and effective approach for the management of atrial fibrillation. J Cardiovasc Electrophysiol. 1998;9:462-9.
215. Chan DP, Van Hare GF, Mackall JA, et al. Importance of atrial flutter isthmus in postoperative intra-atrial reentrant tachycardia. Circulation. 2000;102:1283-9.
216. Jais P, Shah DC, Haissaguerre M, et al. Mapping and ablation of left atrial flutters. Circulation. 2000;101:2928-34.
217. Reithmann C, Hoffmann E, Spitzlberger G, et al. Catheter ablation of atrial flutter due to amiodarone therapy for paroxysmal atrial fibrillation. Eur Heart J. 2000;21:565-72.
218. Akar JG, Kok LC, Haines DE, et al. Coexistence of type I atrial flutter and intra-atrial re-entrant tachycardia in patients with surgically corrected congenital heart disease. J Am Coll Cardiol. 2001;38:377-84.

219. Nakagawa H, Shah N, Matsudaira K, et al. Characterization of reentrant circuit in macroreentrant right atrial tachycardia after surgical repair of congenital heart disease: isolated channels between scars allow "focal" ablation. Circulation. 2001;103:699-709.
220. Deal BJ, Mavroudis C, Backer CL, et al. Comparison of anatomic isthmus block with the modified right atrial maze procedure for late atrial tachycardia in Fontan patients. Circulation. 2002;106:575-9.
221. Coffey JO, d'Avila A, Dukkipati S, et al. Catheter ablation of scar-related atypical atrial flutter. Europace. 2013;15:414-9.
222. Ghali WA, Wasil BI, Brant R, et al. Atrial flutter and the risk of thromboembolism: a systematic review and meta-analysis. Am J Med. 2005;118:101-7.
223. Mamchur SE, Kurilin MY. High-amplitude pace mapping increases safety of radiofrequency catheter ablation of parahisian ectopic foci. Pacing Clin Electrophysiol. 2012;35:1458-63.
224. Ruder MA, Davis JC, Eldar M, et al. Clinical and electrophysiologic characterization of automatic junctional tachycardia in adults. Circulation. 1986;73:930-7.
225. Cook JR, Steinberg JS. An incessant form of junctional ectopic tachycardia in an adult responsive to a class 1C agent. Am Heart J. 1991;122:1487-9.
226. Kuck KH, Kunze KP, Schluter M, et al. Encainide versus flecainide for chronic atrial and junctional ectopic tachycardia. Am J Cardiol. 1988;62:37L-44L.
227. Villain E, Vetter VL, Garcia JM, et al. Evolving concepts in the management of congenital junctional ectopic tachycardia. A multicenter study. Circulation. 1990;81:1544-9.
228. Paul T, Reimer A, Janousek J, et al. Efficacy and safety of propafenone in congenital junctional ectopic tachycardia. J Am Coll Cardiol. 1992;20:911-4.
229. Raja P, Hawker RE, Chaikitpinyo A, et al. Amiodarone management of junctional ectopic tachycardia after cardiac surgery in children. Br Heart J. 1994;72:261-5.
230. Lee KL, Chun HM, Liem LB, et al. Effect of adenosine and verapamil in catecholamine-induced accelerated atrioventricular junctional rhythm: insights into the underlying mechanism. Pacing Clin Electrophysiol. 1999;22:866-70.
231. Sarubbi B, Musto B, Ducceschi V, et al. Congenital junctional ectopic tachycardia in children and adolescents: a 20 year experience based study. Heart. 2002;88:188-90.
232. Scheinman MM, Gonzalez RP, Cooper MW, et al. Clinical and electrophysiologic features and role of catheter ablation techniques in adult patients with automatic atrioventricular junctional tachycardia. Am J Cardiol. 1994;74:565-72.
233. Hamdan M, Van Hare GF, Fisher W, et al. Selective catheter ablation of the tachycardia focus in patients with nonreentrant junctional tachycardia. Am J Cardiol. 1996;78:1292-7.
234. Law IH, Von Bergen NH, Gingerich JC, et al. Transcatheter cryothermal ablation of junctional ectopic tachycardia in the normal heart. Heart Rhythm. 2006;3:903-7.
235. Meiltz A, Weber R, Halimi F, et al. Permanent form of junctional reciprocating tachycardia in adults: peculiar features and results of radiofrequency catheter ablation. Europace. 2006;8:21-8.
236. Padanilam BJ, Manfredi JA, Steinberg LA, et al. Differentiating junctional tachycardia and atrioventricular node re-entry tachycardia based on response to atrial extrastimulus pacing. J Am Coll Cardiol. 2008;52:1711-7.
237. Srivathsan K, Gami AS, Barrett R, et al. Differentiating atrioventricular nodal reentrant tachycardia from junctional tachycardia: novel application of the delta H-A interval. J Cardiovasc Electrophysiol. 2008;19:1-6.
238. Fan R, Tardos JG, Almasry I, et al. Novel use of atrial overdrive pacing to rapidly differentiate junctional tachycardia from atrioventricular nodal reentrant tachycardia. Heart Rhythm. 2011;8:840-4.
239. Lundberg A. Paroxysmal atrial tachycardia in infancy: long-term follow-up study of 49 subjects. Pediatrics. 1982;70:638-42.
240. Deal BJ, Keane JF, Gillette PC, et al. Wolff-Parkinson-White syndrome and supraventricular tachycardia during infancy: management and follow-up. J Am Coll Cardiol. 1985;5:130-5.
241. Perry JC, Garson A, Jr. Supraventricular tachycardia due to Wolff-Parkinson-White syndrome in children: early disappearance and late recurrence. J Am Coll Cardiol. 1990;16:1215-20.
242. Wu MH, Chang YC, Lin JL, et al. Probability of supraventricular tachycardia recurrence in pediatric patients. Cardiology. 1994;85:284-9.
243. Riggs TW, Byrd JA, Weinhouse E. Recurrence risk of supraventricular tachycardia in pediatric patients. Cardiology. 1999;91:25-30.
244. Tortoriello TA, Snyder CS, Smith EO, et al. Frequency of recurrence among infants with supraventricular tachycardia and comparison of recurrence rates among those with and without preexcitation and among those with and without response to digoxin and/or propranolol therapy. Am J Cardiol. 2003;92:1045-9.
245. Gilljam T, Jaeggi E, Gow RM. Neonatal supraventricular tachycardia: outcomes over a 27-year period at a single institution. Acta Paediatr. 2008;97:1035-9.
246. Santinelli V, Radinovic A, Manguso F, et al. The natural history of asymptomatic ventricular pre-excitation a long-term prospective follow-up study of 184 asymptomatic children. J Am Coll Cardiol. 2009;53:275-80.
247. Salerno JC, Garrison MM, Larison C, et al. Case fatality in children with supraventricular tachycardia in the United States. Pacing Clin Electrophysiol. 2011;34:832-6.

248. Garson A, Jr., Gillette PC. Electrophysiologic studies of supraventricular tachycardia in children. I. Clinical-electrophysiologic correlations. Am Heart J. 1981;102:233-50.
249. Ko JK, Deal BJ, Strasburger JF, et al. Supraventricular tachycardia mechanisms and their age distribution in pediatric patients. Am J Cardiol. 1992;69:1028-32.
250. Weindling SN, Saul JP, Walsh EP. Efficacy and risks of medical therapy for supraventricular tachycardia in neonates and infants. Am Heart J. 1996;131:66-72.
251. Gross GJ, Epstein MR, Walsh EP, et al. Characteristics, management, and midterm outcome in infants with atrioventricular nodal reentry tachycardia. Am J Cardiol. 1998;82:956-60.
252. Anand RG, Rosenthal GL, Van Hare GF, et al. Is the mechanism of supraventricular tachycardia in pediatrics influenced by age, gender or ethnicity? Congenit Heart Dis. 2009;4:464-8.
253. Brembilla-Perrot B, Moulin-Zinsch A, Sellal JM, et al. Impact of transesophageal electrophysiologic study to elucidate the mechanism of arrhythmia on children with supraventricular tachycardia and no preexcitation. Pediatr Cardiol. 2013;34:1695-702.
254. Pfammatter JP, Stocker FP. Re-entrant supraventricular tachycardia in infancy: current role of prophylactic digoxin treatment. Eur J Pediatr. 1998;157:101-6.
255. Villain E, Bonnet D, Acar P, et al. [Recommendations for the treatment of recurrent supraventricular tachycardia in infants]. Arch Pediatr. 1998;5:133-8.
256. Losek JD, Endom E, Dietrich A, et al. Adenosine and pediatric supraventricular tachycardia in the emergency department: multicenter study and review. Ann Emerg Med. 1999;33:185-91.
257. Dixon J, Foster K, Wyllie J, et al. Guidelines and adenosine dosing in supraventricular tachycardia. Arch Dis Child. 2005;90:1190-1.
258. Chang PM, Silka MJ, Moromisato DY, et al. Amiodarone versus procainamide for the acute treatment of recurrent supraventricular tachycardia in pediatric patients. Circ Arrhythm Electrophysiol. 2010;3:134-40.
259. Diaz-Parra S, Sanchez-Yanez P, Zabala-Arguelles I, et al. Use of adenosine in the treatment of supraventricular tachycardia in a pediatric emergency department. Pediatr Emerg Care. 2014;30:388-93.
260. Batra AS, Chun DS, Johnson TR, et al. A prospective analysis of the incidence and risk factors associated with junctional ectopic tachycardia following surgery for congenital heart disease. Pediatr Cardiol. 2006;27:51-5.
261. Andreasen JB, Johnsen SP, Ravn HB. Junctional ectopic tachycardia after surgery for congenital heart disease in children. Intensive Care Med. 2008;34:895-902.
262. Borgman KY, Smith AH, Owen JP, et al. A genetic contribution to risk for postoperative junctional ectopic tachycardia in children undergoing surgery for congenital heart disease. Heart Rhythm. 2011;8:1900-4.
263. Makhoul M, Oster M, Fischbach P, et al. Junctional ectopic tachycardia after congenital heart surgery in the current surgical era. Pediatr Cardiol. 2013;34:370-4.
264. Pfammatter JP, Paul T, Ziemer G, et al. Successful management of junctional tachycardia by hypothermia after cardiac operations in infants. Ann Thorac Surg. 1995;60:556-60.
265. Walsh EP, Saul JP, Sholler GF, et al. Evaluation of a staged treatment protocol for rapid automatic junctional tachycardia after operation for congenital heart disease. J Am Coll Cardiol. 1997;29:1046-53.
266. Laird WP, Snyder CS, Kertesz NJ, et al. Use of intravenous amiodarone for postoperative junctional ectopic tachycardia in children. Pediatr Cardiol. 2003;24:133-7.
267. Plumpton K, Justo R, Haas N. Amiodarone for post-operative junctional ectopic tachycardia. Cardiol Young. 2005;15:13-8.
268. Haas NA, Camphausen CK. Impact of early and standardized treatment with amiodarone on therapeutic success and outcome in pediatric patients with postoperative tachyarrhythmia. J Thorac Cardiovasc Surg. 2008;136:1215-22.
269. Collins KK, Van Hare GF, Kertesz NJ, et al. Pediatric nonpost-operative junctional ectopic tachycardia medical management and interventional therapies. J Am Coll Cardiol. 2009;53:690-7.
270. Kovacikova L, Hakacova N, Dobos D, et al. Amiodarone as a first-line therapy for postoperative junctional ectopic tachycardia. Ann Thorac Surg. 2009;88:616-22.
271. Timmermans C, Smeets JL, Rodriguez LM, et al. Aborted sudden death in the Wolff-Parkinson-White syndrome. Am J Cardiol. 1995;76:492-4.
272. Ceresnak SR, Tanel RE, Pass RH, et al. Clinical and electrophysiologic characteristics of antidromic tachycardia in children with Wolff-Parkinson-White syndrome. Pacing Clin Electrophysiol. 2012;35:480-8.
273. Brembilla-Perrot B, Pauriah M, Sellal JM, et al. Incidence and prognostic significance of spontaneous and inducible antidromic tachycardia. Europace. 2013;15:871-6.
274. Kugler JD, Danford DA, Houston K, et al. Radiofrequency catheter ablation for paroxysmal supraventricular tachycardia in children and adolescents without structural heart disease. Pediatric EP Society, Radiofrequency Catheter Ablation Registry. Am J Cardiol. 1997;80:1438-43.
275. Schaffer MS, Gow RM, Moak JP, et al. Mortality following radiofrequency catheter ablation (from the Pediatric Radiofrequency Ablation Registry). Participating members of the Pediatric Electrophysiology Society. Am J Cardiol. 2000;86:639-43.

276. Blaufox AD, Felix GL, Saul JP. Radiofrequency catheter ablation in infants </=18 months old: when is it done and how do they fare?: short-term data from the pediatric ablation registry. Circulation. 2001;104:2803-8.
277. Blaufox AD, Paul T, Saul JP. Radiofrequency catheter ablation in small children: relationship of complications to application dose. Pacing Clin Electrophysiol. 2004;27:224-9.
278. Van Hare GF, Javitz H, Carmelli D, et al. Prospective assessment after pediatric cardiac ablation: demographics, medical profiles, and initial outcomes. J Cardiovasc Electrophysiol. 2004;15:759-70.
279. Van Hare GF, Javitz H, Carmelli D, et al. Prospective assessment after pediatric cardiac ablation: recurrence at 1 year after initially successful ablation of supraventricular tachycardia. Heart Rhythm. 2004;1:188-96.
280. Aiyagari R, Saarel EV, Etheridge SP, et al. Radiofrequency ablation for supraventricular tachycardia in children < or =15 kg is safe and effective. Pediatr Cardiol. 2005;26:622-6.
281. Lee PC, Hwang B, Chen SA, et al. The results of radiofrequency catheter ablation of supraventricular tachycardia in children. Pacing Clin Electrophysiol. 2007;30:655-61.
282. Buddhe S, Singh H, Du W, et al. Radiofrequency and cryoablation therapies for supraventricular arrhythmias in the young: five-year review of efficacies. Pacing Clin Electrophysiol. 2012;35:711-7.
283. Schneider HE, Kriebel T, Gravenhorst VD, et al. Incidence of coronary artery injury immediately after catheter ablation for supraventricular tachycardias in infants and children. Heart Rhythm. 2009;6:461-7.
284. Kantoch MJ, Gulamhusein SS, Sanatani S. Short- and long-term outcomes in children undergoing radiofrequency catheter ablation before their second birthday. Can J Cardiol. 2011;27:523-9.
285. Garson A, Jr., Kanter RJ. Management of the child with Wolff-Parkinson-White syndrome and supraventricular tachycardia: model for cost effectiveness. J Cardiovasc Electrophysiol. 1997;8:1320-6.
286. Pfammatter JP, Pavlovic M, Bauersfeld U. Impact of curative ablation on pharmacologic management in children with reentrant supraventricular tachycardias. Int J Cardiol. 2004;94:279-82.
287. Strieper M, Leong T, Bajaj T, et al. Does ablation of supraventricular tachycardia in children with a structurally normal heart improve quality of life? Congenit Heart Dis. 2010;5:587-93.
288. Wood KA, Stewart AL, Drew BJ, et al. Patient perception of symptoms and quality of life following ablation in patients with supraventricular tachycardia. Heart Lung. 2010;39:12-20.
289. Engelfriet P, Boersma E, Oechslin E, et al. The spectrum of adult congenital heart disease in Europe: morbidity and mortality in a 5 year follow-up period. The Euro Heart Survey on adult congenital heart disease. Eur Heart J. 2005;26:2325-33.
290. Verheugt CL, Uiterwaal CS, van der Velde ET, et al. Gender and outcome in adult congenital heart disease. Circulation. 2008;118:26-32.
291. Bouchardy J, Therrien J, Pilote L, et al. Atrial arrhythmias in adults with congenital heart disease. Circulation. 2009;120:1679-86.
292. Trojnarska O, Grajek S, Kramer L, et al. Risk factors of supraventricular arrhythmia in adults with congenital heart disease. Cardiol J. 2009;16:218-26.
293. Bernier M, Marelli AJ, Pilote L, et al. Atrial arrhythmias in adult patients with right- versus left-sided congenital heart disease anomalies. Am J Cardiol. 2010;106:547-51.
294. Khairy P, Aboulhosn J, Gurvitz MZ, et al. Arrhythmia burden in adults with surgically repaired tetralogy of Fallot: a multi-institutional study. Circulation. 2010;122:868-75.
295. Cuypers JA, Opic P, Menting ME, et al. The unnatural history of an atrial septal defect: longitudinal 35 year follow up after surgical closure at young age. Heart. 2013;99:1346-52.
296. Valente AM, Gauvreau K, Assenza GE, et al. Contemporary predictors of death and sustained ventricular tachycardia in patients with repaired tetralogy of Fallot enrolled in the INDICATOR cohort. Heart. 2014;100:247-53.
297. Collins KK, Love BA, Walsh EP, et al. Location of acutely successful radiofrequency catheter ablation of intraatrial reentrant tachycardia in patients with congenital heart disease. Am J Cardiol. 2000;86:969-74.
298. de Groot NM, Zeppenfeld K, Wijffels MC, et al. Ablation of focal atrial arrhythmia in patients with congenital heart defects after surgery: role of circumscribed areas with heterogeneous conduction. Heart Rhythm. 2006;3:526-35.
299. Mah DY, Alexander ME, Cecchin F, et al. The electroanatomic mechanisms of atrial tachycardia in patients with tetralogy of Fallot and double outlet right ventricle. J Cardiovasc Electrophysiol. 2011;22:1013-7.
300. Koyak Z, Kroon B, de Groot JR, et al. Efficacy of antiarrhythmic drugs in adults with congenital heart disease and supraventricular tachycardias. Am J Cardiol. 2013;112:1461-7.
301. Wasmer K, Kobe J, Dechering DG, et al. Isthmus-dependent right atrial flutter as the leading cause of atrial tachycardias after surgical atrial septal defect repair. Int J Cardiol. 2013;168:2447-52.
302. Fish FA, Gillette PC, Benson DW, Jr. Proarrhythmia, cardiac arrest and death in young patients receiving encainide and flecainide. The Pediatric Electrophysiology Group. J Am Coll Cardiol. 1991;18:356-65.
303. Thorne SA, Barnes I, Cullinan P, et al. Amiodarone-associated thyroid dysfunction: risk factors in adults with congenital heart disease. Circulation. 1999;100:149-54.
304. Pass RH, Liberman L, Al-Fayaddh M, et al. Continuous intravenous diltiazem infusion for short-term ventricular rate control in children. Am J Cardiol. 2000;86:559-62, A9.

305. Hoyer AW, Balaji S. The safety and efficacy of ibutilide in children and in patients with congenital heart disease. Pacing Clin Electrophysiol. 2007;30:1003-8.
306. Khairy P, Harris L, Landzberg MJ, et al. Sudden death and defibrillators in transposition of the great arteries with intra-atrial baffles: a multicenter study. Circ Arrhythm Electrophysiol. 2008;1:250-7.
307. Miyazaki A, Ohuchi H, Kurosaki K, et al. Efficacy and safety of sotalol for refractory tachyarrhythmias in congenital heart disease. Circ J. 2008;72:1998-2003.
308. Rao SO, Boramanand NK, Burton DA, et al. Atrial tachycardias in young adults and adolescents with congenital heart disease: conversion using single dose oral sotalol. Int J Cardiol. 2009;136:253-7.
309. Wells R, Khairy P, Harris L, et al. Dofetilide for atrial arrhythmias in congenital heart disease: a multicenter study. Pacing Clin Electrophysiol. 2009;32:1313-8.
310. Garnock-Jones KP. Esmolol: a review of its use in the short-term treatment of tachyarrhythmias and the short-term control of tachycardia and hypertension. Drugs. 2012;72:109-32.
311. Banchs JE, Baquero GA, Nickolaus MJ, et al. Clinical efficacy of dofetilide for the treatment of atrial tachyarrhythmias in adults with congenital heart disease. Congenit Heart Dis. 2014;9:221-7.
312. Stan MN, Hess EP, Bahn RS, et al. A risk prediction index for amiodarone-induced thyrotoxicosis in adults with congenital heart disease. J Thyroid Res. 2012;2012:210529.
313. Olshansky B, Okumura K, Hess PG, et al. Use of procainamide with rapid atrial pacing for successful conversion of atrial flutter to sinus rhythm. J Am Coll Cardiol. 1988;11:359-64.
314. Silka MJ, Manwill JR, Kron J, et al. Bradycardia-mediated tachyarrhythmias in congenital heart disease and responses to chronic pacing at physiologic rates. Am J Cardiol. 1990;65:488-93.
315. Ragonese P, Drago F, Guccione P, et al. Permanent overdrive atrial pacing in the chronic management of recurrent postoperative atrial reentrant tachycardia in patients with complex congenital heart disease. Pacing Clin Electrophysiol. 1997;20:2917-23.
316. Brockmeier K, Ulmer HE, Hessling G. Termination of atrial reentrant tachycardias by using transesophageal atrial pacing. J Electrocardiol. 2002;35 Suppl:159-63.
317. Stephenson EA, Casavant D, Tuzi J, et al. Efficacy of atrial antitachycardia pacing using the Medtronic AT500 pacemaker in patients with congenital heart disease. Am J Cardiol. 2003;92:871-6.
318. Ammash NM, Phillips SD, Hodge DO, et al. Outcome of direct current cardioversion for atrial arrhythmias in adults with congenital heart disease. Int J Cardiol. 2012;154:270-4.
319. Triedman JK, Saul JP, Weindling SN, et al. Radiofrequency ablation of intra-atrial reentrant tachycardia after surgical palliation of congenital heart disease. Circulation. 1995;91:707-14.
320. Tanner H, Lukac P, Schwick N, et al. Irrigated-tip catheter ablation of intraatrial reentrant tachycardia in patients late after surgery of congenital heart disease. Heart Rhythm. 2004;1:268-75.
321. Lukac P, Pedersen AK, Mortensen PT, et al. Ablation of atrial tachycardia after surgery for congenital and acquired heart disease using an electroanatomic mapping system: Which circuits to expect in which substrate? Heart Rhythm. 2005;2:64-72.
322. de Groot NM, Atary JZ, Blom NA, et al. Long-term outcome after ablative therapy of postoperative atrial tachyarrhythmia in patients with congenital heart disease and characteristics of atrial tachyarrhythmia recurrences. Circ Arrhythm Electrophysiol. 2010;3:148-54.
323. Yap SC, Harris L, Silversides CK, et al. Outcome of intra-atrial re-entrant tachycardia catheter ablation in adults with congenital heart disease: negative impact of age and complex atrial surgery. J Am Coll Cardiol. 2010;56:1589-96.
324. Ueda A, Suman-Horduna I, Mantziari L, et al. Contemporary outcomes of supraventricular tachycardia ablation in congenital heart disease: a single-center experience in 116 patients. Circ Arrhythm Electrophysiol. 2013;6:606-13.
325. Teh AW, Medi C, Lee G, et al. Long-term outcome following ablation of atrial flutter occurring late after atrial septal defect repair. Pacing Clin Electrophysiol. 2011;34:431-5.
326. Scaglione M, Caponi D, Ebrille E, et al. Very long-term results of electroanatomic-guided radiofrequency ablation of atrial arrhythmias in patients with surgically corrected atrial septal defect. Europace. 2014.
327. Cappato R, Schluter M, Weiss C, et al. Radiofrequency current catheter ablation of accessory atrioventricular pathways in Ebstein's anomaly. Circulation. 1996;94:376-83.
328. Reich JD, Auld D, Hulse E, et al. The Pediatric Radiofrequency Ablation Registry's experience with Ebstein's anomaly. Pediatric Electrophysiology Society. J Cardiovasc Electrophysiol. 1998;9:1370-7.
329. de Groot NM, Lukac P, Blom NA, et al. Long-term outcome of ablative therapy of postoperative supraventricular tachycardias in patients with univentricular heart: a European multicenter study. Circ Arrhythm Electrophysiol. 2009;2:242-8.
330. Yap SC, Harris L, Downar E, et al. Evolving electroanatomic substrate and intra-atrial reentrant tachycardia late after Fontan surgery. J Cardiovasc Electrophysiol. 2012;23:339-45.
331. Correa R, Sherwin ED, Kovach J, et al. Mechanism and Ablation of Arrhythmia Following Total Cavopulmonary Connection. Circ Arrhythm Electrophysiol. 2015.

332. Jones DG, Jarman JW, Lyne JC, et al. The safety and efficacy of trans-baffle puncture to enable catheter ablation of atrial tachycardias following the Mustard procedure: a single centre experience and literature review. Int J Cardiol. 2013;168:1115-20.
333. Wu J, Deisenhofer I, Ammar S, et al. Acute and long-term outcome after catheter ablation of supraventricular tachycardia in patients after the Mustard or Senning operation for D-transposition of the great arteries. Europace. 2013;15:886-91.
334. Pressley JC, Wharton JM, Tang AS, et al. Effect of Ebstein's anomaly on short- and long-term outcome of surgically treated patients with Wolff-Parkinson-White syndrome. Circulation. 1992;86:1147-55.
335. Misaki T, Watanabe G, Iwa T, et al. Surgical treatment of patients with Wolff-Parkinson-White syndrome and associated Ebstein's anomaly. J Thorac Cardiovasc Surg. 1995;110:1702-7.
336. Theodoro DA, Danielson GK, Porter CJ, et al. Right-sided maze procedure for right atrial arrhythmias in congenital heart disease. Ann Thorac Surg. 1998;65:149-53.
337. Huang CJ, Chiu IS, Lin FY, et al. Role of electrophysiological studies and arrhythmia intervention in repairing Ebstein's anomaly. Thorac Cardiovasc Surg. 2000;48:347-50.
338. Mavroudis C, Backer CL, Deal BJ, et al. Total cavopulmonary conversion and maze procedure for patients with failure of the Fontan operation. J Thorac Cardiovasc Surg. 2001;122:863-71.
339. Khositseth A, Danielson GK, Dearani JA, et al. Supraventricular tachyarrhythmias in Ebstein anomaly: management and outcome. J Thorac Cardiovasc Surg. 2004;128:826-33.
340. Bockeria L, Golukhova E, Dadasheva M, et al. Advantages and disadvantages of one-stage and two-stage surgery for arrhythmias and Ebstein's anomaly. Eur J Cardiothorac Surg. 2005;28:536-40.
341. Giamberti A, Chessa M, Foresti S, et al. Combined atrial septal defect surgical closure and irrigated radiofrequency ablation in adult patients. Ann Thorac Surg. 2006;82:1327-31.
342. Karamlou T, Silber I, Lao R, et al. Outcomes after late reoperation in patients with repaired tetralogy of Fallot: the impact of arrhythmia and arrhythmia surgery. Ann Thorac Surg. 2006;81:1786-93.
343. Stulak JM, Dearani JA, Puga FJ, et al. Right-sided Maze procedure for atrial tachyarrhythmias in congenital heart disease. Ann Thorac Surg. 2006;81:1780-4.
344. Mavroudis C, Deal BJ, Backer CL, et al. J. Maxwell Chamberlain Memorial Paper for congenital heart surgery. 111 Fontan conversions with arrhythmia surgery: surgical lessons and outcomes. Ann Thorac Surg. 2007;84:1457-65.
345. Giamberti A, Chessa M, Abella R, et al. Surgical treatment of arrhythmias in adults with congenital heart defects. Int J Cardiol. 2008;129:37-41.
346. Mavroudis C, Deal BJ, Backer CL, et al. Arrhythmia surgery in patients with and without congenital heart disease. Ann Thorac Surg. 2008;86:857-68.
347. Aboulhosn J, Williams R, Shivkumar K, et al. Arrhythmia recurrence in adult patients with single ventricle physiology following surgical Fontan conversion. Congenit Heart Dis. 2010;5:430-4.
348. Gutierrez SD, Earing MG, Singh AK, et al. Atrial tachyarrhythmias and the Cox-maze procedure in congenital heart disease. Congenit Heart Dis. 2013;8:434-9.
349. Terada T, Sakurai H, Nonaka T, et al. Surgical outcome of Fontan conversion and arrhythmia surgery: Need a pacemaker? Asian Cardiovasc Thorac Ann. 2013;22:682-6.
350. Said SM, Burkhart HM, Schaff HV, et al. Fontan conversion: identifying the high-risk patient. Ann Thorac Surg. 2014;97:2115-21.
351. Ghosh N, Luk A, Derzko C, et al. The acute treatment of maternal supraventricular tachycardias during pregnancy: a review of the literature. J Obstet Gynaecol Can. 2011;33:17-23.
352. Damilakis J, Theocharopoulos N, Perisinakis K, et al. Conceptus radiation dose and risk from cardiac catheter ablation procedures. Circulation. 2001;104:893-7.
353. Berruezo A, Diez GR, Berne P, et al. Low exposure radiation with conventional guided radiofrequency catheter ablation in pregnant women. Pacing Clin Electrophysiol. 2007;30:1299-302.
354. Szumowski L, Szufladowicz E, Orczykowski M, et al. Ablation of severe drug-resistant tachyarrhythmia during pregnancy. J Cardiovasc Electrophysiol. 2010;21:877-82.
355. Lydakis C, Lip GY, Beevers M, et al. Atenolol and fetal growth in pregnancies complicated by hypertension. Am J Hypertens. 1999;12:541-7.
356. von Dadelszen P, Ornstein MP, Bull SB, et al. Fall in mean arterial pressure and fetal growth restriction in pregnancy hypertension: a meta-analysis. Lancet. 2000;355:87-92.
357. Bartalena L, Bogazzi F, Braverman LE, et al. Effects of amiodarone administration during pregnancy on neonatal thyroid function and subsequent neurodevelopment. J Endocrinol Invest. 2001;24:116-30.
358. Qasqas SA, McPherson C, Frishman WH, et al. Cardiovascular pharmacotherapeutic considerations during pregnancy and lactation. Cardiol Rev. 2004;12:201-21.
359. Jaeggi ET, Carvalho JS, De GE, et al. Comparison of transplacental treatment of fetal supraventricular tachyarrhythmias with digoxin, flecainide, and sotalol: results of a nonrandomized multicenter study. Circulation. 2011;124:1747-54.

360. Chen SA, Lee SH, Wu TJ, et al. Initial onset of accessory pathway-mediated and atrioventricular node reentrant tachycardia after age 65: clinical features, electrophysiologic characteristics, and possible facilitating factors. J Am Geriatr Soc. 1995;43:1370-7.
361. Chen SA, Chiang CE, Tai CT, et al. Complications of diagnostic electrophysiologic studies and radiofrequency catheter ablation in patients with tachyarrhythmias: an eight-year survey of 3,966 consecutive procedures in a tertiary referral center. Am J Cardiol. 1996;77:41-6.
362. Boulos M, Hoch D, Schecter S, et al. Age dependence of complete heart block complicating radiofrequency ablation of the atrioventricular nodal slow pathway. Am J Cardiol. 1998;82:390-1.
363. Zado ES, Callans DJ, Gottlieb CD, et al. Efficacy and safety of catheter ablation in octogenarians. J Am Coll Cardiol. 2000;35:458-62.
364. Li YG, Gronefeld G, Bender B, et al. Risk of development of delayed atrioventricular block after slow pathway modification in patients with atrioventricular nodal reentrant tachycardia and a pre-existing prolonged PR interval. Eur Heart J. 2001;22:89-95.
365. Porter MJ, Morton JB, Denman R, et al. Influence of age and gender on the mechanism of supraventricular tachycardia. Heart Rhythm. 2004;1:393-6.
366. Rostock T, Risius T, Ventura R, et al. Efficacy and safety of radiofrequency catheter ablation of atrioventricular nodal reentrant tachycardia in the elderly. J Cardiovasc Electrophysiol. 2005;16:608-10.
367. Kihel J, Da CA, Kihel A, et al. Long-term efficacy and safety of radiofrequency ablation in elderly patients with atrioventricular nodal re-entrant tachycardia. Europace. 2006;8:416-20.
368. Dagres N, Piorkowski C, Kottkamp H, et al. Contemporary catheter ablation of arrhythmias in geriatric patients: patient characteristics, distribution of arrhythmias, and outcome. Europace. 2007;9:477-80.
369. Haghjoo M, Arya A, Heidari A, et al. Electrophysiologic characteristics and results of radiofrequency catheter ablation in elderly patients with atrioventricular nodal reentrant tachycardia. J Electrocardiol. 2007;40:208-13.
370. Pedrinazzi C, Durin O, Agricola P, et al. Efficacy and safety of radiofrequency catheter ablation in the elderly. J Interv Card Electrophysiol. 2007;19:179-85.
371. Yangni NO, Brembilla-Perrot B. Clinical characteristics and management of paroxysmal junctional tachycardia in the elderly. Arch Cardiovasc Dis. 2008;101:143-8.
372. Hoffmann BA, Brachmann J, Andresen D, et al. Ablation of atrioventricular nodal reentrant tachycardia in the elderly: results from the German Ablation Registry. Heart Rhythm. 2011;8:981-7.
373. Saul JP, Scott WA, Brown S, et al. Intravenous amiodarone for incessant tachyarrhythmias in children: a randomized, double-blind, antiarrhythmic drug trial. Circulation. 2005;112:3470-7.
374. Manrique AM, Arroyo M, Lin Y, et al. Magnesium supplementation during cardiopulmonary bypass to prevent junctional ectopic tachycardia after pediatric cardiac surgery: a randomized controlled study. J Thorac Cardiovasc Surg. 2010;139:162-9.
375. Sanatani S, Potts JE, Reed JH, et al. The study of antiarrhythmic medications in infancy (SAMIS): a multicenter, randomized controlled trial comparing the efficacy and safety of digoxin versus propranolol for prophylaxis of supraventricular tachycardia in infants. Circ Arrhythm Electrophysiol. 2012;5:984-91.
376. Lau CP, Tai YT, Lee PW. The effects of radiofrequency ablation versus medical therapy on the quality-of-life and exercise capacity in patients with accessory pathway-mediated supraventricular tachycardia: a treatment comparison study. Pacing Clin Electrophysiol. 1995;18:424-32.
377. Bubien RS, Knotts-Dolson SM, Plumb VJ, et al. Effect of radiofrequency catheter ablation on health-related quality of life and activities of daily living in patients with recurrent arrhythmias. Circulation. 1996;94:1585-91.
378. Bathina MN, Mickelsen S, Brooks C, et al. Radiofrequency catheter ablation versus medical therapy for initial treatment of supraventricular tachycardia and its impact on quality of life and healthcare costs. Am J Cardiol. 1998;82:589-93.
379. Larson MS, McDonald K, Young C, et al. Quality of life before and after radiofrequency catheter ablation in patients with drug refractory atrioventricular nodal reentrant tachycardia. Am J Cardiol. 1999;84:471-3, A9.
380. Goldberg AS, Bathina MN, Mickelsen S, et al. Long-term outcomes on quality-of-life and health care costs in patients with supraventricular tachycardia (radiofrequency catheter ablation versus medical therapy). Am J Cardiol. 2002;89:1120-3.
381. Meissner A, Stifoudi I, Weismuller P, et al. Sustained high quality of life in a 5-year long term follow-up after successful ablation for supra-ventricular tachycardia. results from a large retrospective patient cohort. Int J Med Sci. 2009;6:28-36.
382. Yildirim O, Yontar OC, Semiz M, et al. The effect of radiofrequency ablation treatment on quality of life and anxiety in patients with supraventricular tachycardia. Eur Rev Med Pharmacol Sci. 2012;16:2108-12.
383. Farkowski MM, Pytkowski M, Maciag A, et al. Gender-related differences in outcomes and resource utilization in patients undergoing radiofrequency ablation of supraventricular tachycardia: results from Patients' Perspective on Radiofrequency Catheter Ablation of AVRT and AVNRT Study. Europace. 2014.
384. de Buitleir M, Bove EL, Schmaltz S, et al. Cost of catheter versus surgical ablation in the Wolff-Parkinson-White syndrome. Am J Cardiol. 1990;66:189-92.
385. de Buitleir M, Sousa J, Bolling SF, et al. Reduction in medical care cost associated with radiofrequency catheter ablation of accessory pathways. Am J Cardiol. 1991;68:1656-61.

386. Kalbfleisch SJ, Calkins H, Langberg JJ, et al. Comparison of the cost of radiofrequency catheter modification of the atrioventricular node and medical therapy for drug-refractory atrioventricular node reentrant tachycardia. J Am Coll Cardiol. 1992;19:1583-7.
387. Hogenhuis W, Stevens SK, Wang P, et al. Cost-effectiveness of radiofrequency ablation compared with other strategies in Wolff-Parkinson-White syndrome. Circulation. 1993;88:II437-II446.
388. Kalbfleisch SJ, el-Atassi R, Calkins H, et al. Safety, feasibility and cost of outpatient radiofrequency catheter ablation of accessory atrioventricular connections. J Am Coll Cardiol. 1993;21:567-70.
389. Kertes PJ, Kalman JM, Tonkin AM. Cost effectiveness of radiofrequency catheter ablation in the treatment of symptomatic supraventricular tachyarrhythmias. Aust N Z J Med. 1993;23:433-6.
390. Ikeda T, Sugi K, Enjoji Y, et al. Cost effectiveness of radiofrequency catheter ablation versus medical treatment for paroxysmal supraventricular tachycardia in Japan. J Cardiol. 1994;24:461-8.
391. Dewland TA, Glidden DV, Marcus GM. Healthcare utilization and clinical outcomes after catheter ablation of atrial flutter. PLoS One. 2014;9:e100509.
392. Domanovits H, Laske H, Stark G, et al. Adenosine for the management of patients with tachycardias-a new protocol. Eur Heart J. 1994;15:589-93.
393. Turakhia MP, Santangeli P, Winkelmayer WC, et al. Increased mortality associated with digoxin in contemporary patients with atrial fibrillation: findings from the TREAT-AF study. J Am Coll Cardiol. 2014;64:660-8.
394. Tercius AJ, Kluger J, Coleman CI, et al. Intravenous magnesium sulfate enhances the ability of intravenous ibutilide to successfully convert atrial fibrillation or flutter. Pacing Clin Electrophysiol. 2007;30:1331-5.
395. Perez FJ, Schubert CM, Parvez B, et al. Long-term outcomes after catheter ablation of cavo-tricuspid isthmus dependent atrial flutter: a meta-analysis. Circ Arrhythm Electrophysiol. 2009;2:393-401.
396. Natale A, Breeding L, Tomassoni G, et al. Ablation of right and left ectopic atrial tachycardias using a three-dimensional nonfluoroscopic mapping system. Am J Cardiol. 1998;82:989-92.
397. Goldberger J, Kall J, Ehlert F, et al. Effectiveness of radiofrequency catheter ablation for treatment of atrial tachycardia. Am J Cardiol. 1993;72:787-93.
398. Stevenson IH, Kistler PM, Spence SJ, et al. Scar-related right atrial macroreentrant tachycardia in patients without prior atrial surgery: electroanatomic characterization and ablation outcome. Heart Rhythm. 2005;2:594-601.