ACC/AHA/ESC Guidelines for the Management of Patients With Supraventricular Arrhythmias*

A Report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Supraventricular Arrhythmias)

Developed in Collaboration with NASPE-Heart Rhythm Society

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*This document does not cover atrial fibrillation, which is covered in the ACC/AHA/ESC guidelines on the management of patients with atrial fibrillation found on the ACC, AHA, and ESC Web sites.

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PREAMBLE

It is important that the medical profession play a significant role in critically evaluating the use of diagnostic procedures and therapies in the management or prevention of disease states. Rigorous and expert analysis of the available data documenting relative benefits and risks of those procedures and therapies can produce helpful guidelines that improve the effectiveness of care, optimize patient outcomes, and generally have a favorable effect on the overall cost of care by focusing resources on the most effective strategies.

The American College of Cardiology Foundation (ACCF), the American Heart Association (AHA) have jointly engaged in the production of such guidelines in the area of cardiovascular disease since 1980. The ACC/AHA Task Force on Practice Guidelines, whose charge is to develop and revise practice guidelines for important cardiovascular diseases and procedures, directs this effort. The Task Force is pleased to have this guideline cosponsored by the European Society of Cardiology (ESC). Experts in the subject under consideration have been selected from all three organizations to examine subject-specific data and write guidelines. The process includes additional representatives from other medical practitioner and specialty groups when appropriate. Writing groups are specifically charged to perform a formal literature review, weigh the strength of evidence for or against a particular treatment or procedure, and include estimates of expected health outcomes where data exist. Patient-specific modifiers, comorbidities and issues of patient preference that might influence the choice of particular tests or therapies are

considered as well as frequency of follow-up. When available, information from studies on cost is considered, but review of data on diagnostic or therapeutic efficacy and clinical outcomes is the primary basis for preparing recommendations in these guidelines.

The ACC/AHA Task Force on Practice Guidelines and the ESC Committee on Practice Guidelines make every effort to avoid any actual or potential conflict of interest that might arise as a result of an industry relationship or from personal biases of the writing panel. Specifically, all members of the writing panel were asked to provide disclosure statements of all such relationships that might be perceived as real or potential conflicts of interest. These statements are reported orally to all members of the writing panel during the first meeting and are updated as changes occur.

These practice guidelines are intended to assist physicians in clinical decision making by describing a range of generally acceptable approaches for the diagnosis and management of supraventricular arrhythmias. These guidelines attempt to define practices that meet the needs of most patients in most circumstances. The ultimate judgment regarding care of a particular patient must be made by the physician and the patient in light of all of the circumstances presented by that patient. There are circumstances in which deviations from these guidelines are appropriate.

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I. INTRODUCTION

A. Organization of Committee and Evidence Review

Supraventricular arrhythmias are a group of common rhythm disturbances. The most common treatment strategies include antiarrhythmic drug therapy and catheter ablation. Over the last decade, the latter has been shown to be a highly successful and often curative intervention. With the advent of new therapeutic interventions and sophisticated mapping tools, even very complex arrhythmias may be cured. To facilitate and optimize the management of patients with supraventricular arrhythmias, the ACCF, the AHA, and the ESC created a committee to establish guidelines for better management of these heterogeneous tachyarrhythmias. This document summarizes the management of patients with supraventricular arrhythmias with recommendations for diagnostic procedures as well as indications for antiarrhythmic drugs and/or nonpharmacologic treatments.

The panel was composed of physicians and scientists at university and community hospitals. Members were selected to represent experts from different European countries and from the United States and to include members of associations or working groups whose activities and fields of interest were related to the topic of the writing committee, including the ESC Working Groups on Arrhythmias, Cardiac Pacing, and Grown-Up Congenital Heart Diseases and the North American Society of Pacing and Electrophysiology (NASPE-Heart Rhythm Society). The writing committee was composed of six members representing the ACCF and the AHA, four members representing the ESC, and one member representing NASPE. The writing committee was chosen on the basis of willingness and availability to participate actively in meetings and the production of the final manuscript. Writing groups are specifically charged to perform a formal literature review, weigh the strength of evidence for or against a particular treatment or procedure, and estimate expected health outcomes where data exist. Patient-specific modifiers, comorbidities, and issues of patient preference that might influence the choice of particular tests or therapies are considered, as are frequency of follow-up and cost effectiveness. In controversial areas, or with regard to issues without evidence other than usual clinical practice, a consensus was achieved by agreement of the expert panel after thorough deliberations.

This document was peer reviewed by two official external reviewers representing the American College of Cardiology Foundation, two official external reviewers representing the American Heart Association, and two official external reviewers representing the European Society of Cardiology. The North American Society for Pacing and Electrophysiology-Heart Rhythm Society assigned one organizational reviewer to the guideline. In addition, 37 external content reviewers participated in the review representing the ACC/AHA Task Force on Practice Guidelines, the ESC Committee for Practice Guidelines, the ACCF Electrophysiology Committee, the AHA ECG/Arrhythmias Committee, the ESC Working Group on Arrhythmias, and the ESC Task Force on Grown-Up Congenital Heart Disease. See Appendix 2 for the names of all reviewers.

The document was approved for publication by the governing bodies of the ACCF, AHA, and ESC. These guidelines will be reviewed annually by the ESC and the ACC/AHA Task Force on Practice Guidelines and will be considered current unless they are revised or withdrawn from distribution.

The ACC/AHA/ESC Writing Committee to Develop Guidelines for the Management of Patients With Supraventricular Tachycardias conducted a comprehensive review of the relevant literature. Literature searches were conducted in the following databases: PubMed/Medline, EMBASE, the Cochrane Library (including the Cochrane Database of Systematic Reviews and the Cochrane Controlled Trials Registry), and Best Evidence. Searches were limited to English language sources and to human subjects. The references selected for this document are exclusively peer-reviewed papers that are representative but not all-inclusive.

Recommendations are evidence-based and derived primarily from published data. The level of evidence was ranked as follows:

Level A (highest): derived from multiple randomized clinical trials;

Level B (intermediate): Data are based on a limited number of randomized trials, nonrandomized studies, or observational registries;

Level C (lowest): Primary basis for the recommendation was expert consensus.

Recommendations follow the format of previous ACC/AHA guidelines for classifying indications, summarizing both the evidence and expert opinion.

Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective.

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.

Class IIa: Weight of evidence or opinion is in favor of usefulness/efficacy.

Class IIb: Usefulness/efficacy is less well established by evidence or opinion.

Class III: Conditions for which there is evidence and/or general agreement that the procedure or treatment is not useful/effective and in some cases may be harmful.

B. Contents of These Guidelines—Scope

The purpose of this joint ACC/AHA/ESC document is to provide clinicians with practical and authoritative guidelines for the management and treatment of patients with supraventricular arrhythmias (SVA). These include rhythms emanating from the sinus node, from atrial tissue (atrial flutter), and from junctional as well as reciprocating or accessory pathway-mediated tachycardia. This document does not include recommendations for patients with atrial fibrillation (AF) [see ACC/AHA/ESC Guidelines for the Management of Patients With Atrial Fibrillation (1)] or for pediatric patients with supraventricular arrhythmias. In this document, SVT is used to describe re-entrant arrhythmias involving the atrioventricular (AV) junction (atrioventricular nodal reciprocating tachycardia [AVNRT]), atrium [atrial tachycardia (AT)], or AV-reciprocating rhythms [atrioventricular reciprocating tachycardia (AVRT)]). For our purposes, the term "supraventricular arrhythmia" refers to all types of supraventricular arrhythmias, excluding AF, as opposed to SVT, which includes AVNRT, AVRT, and AT.

These guidelines first present a review of the definition, public health, epidemiology, general mechanisms, and clinical characteristics of SVT. The management of each specific tachycardia is then presented, including a review of the existing literature relating to drug versus catheter ablative therapy. The treatment algorithms include pharmacologic and nonpharmacologic antiarrhythmic approaches thought to be most appropriate for each particular condition. Overall, this is a consensus document that includes evidence and expert opinions from several countries. The pharmacologic and nonpharmacologic antiarrhythmic approaches discussed may, therefore, include some drugs and devices that do not have the approval of governmental regulatory agencies. Because antiarrhythmic drug dosages and drug half-lives are detailed in the ACC/AHA/ESC Guidelines for the Management of Patients With Atrial Fibrillation (1), they are not repeated in this document.

II. PUBLIC HEALTH CONSIDERATIONS AND EPIDEMIOLOGY

Supraventricular arrhythmias are relatively common, often repetitive, occasionally persistent, and rarely life threatening (2). The precipitants of supraventricular arrhythmias vary with age, gender, and associated comorbidity (3). While supraventricular arrhythmias are a frequent cause of emergency room (4,5) and primary care physician (6) visits, they are infrequently the primary reason for hospital admission (3,7).

Failure to discriminate among AF, atrial flutter, and other supraventricular arrhythmias has complicated the precise definition of this arrhythmia in the general population (8). The estimated prevalence of ischemic heart disease in the adult U.S. population is approximately tenfold greater than that of supraventricular arrhythmias (78 per 1000 vs. 6 to 8 per 1000, respectively) (9). The estimated prevalence of paroxysmal supraventricular tachycardia (PSVT) in a 3.5% sample of medical records in the Marshfield (Wisconsin, U.S.A.) Epidemiologic Study Area (MESA) was 2.25 per 1000 (10). The incidence of PSVT in this survey was 35 per 100 000 person-years (10).

Occurrence rates have been determined for various subtypes of supraventricular arrhythmia after acute myocardial infarction (11) or coronary artery bypass graft surgery (12) and in congestive heart failure (CHF) patients (13). The incidence rate of supraventricular arrhythmias among patients with CHF is 11.1% (13); paroxysms are more common in older patients, males, and those with longstanding CHF and radiographic evidence of cardiomegaly.

Age exerts an influence on the occurrence of SVT. The mean age at the time of PSVT onset in the MESA cohort was 57 years (ranging from infancy to more than 90 years old) (3). Among emergency room patients older than 16 years treated with intravenous (IV) adenosine for supraventricular arrhythmias diagnosed by surface electrocardiogram (ECG) criteria, 9% had atrial flutter and 87% had SVT (4); 70% of these patients (age 51 plus or minus 19 years) reported a history of cardiovascular disease. In the MESA population (10), compared to those with other cardiovascular disease, "lone" (no cardiac structural disease) PSVT patients without associated structural heart disease were younger (mean age equals 37 vs. 69 years), had faster heart rates (186 vs. 155 beats per minute [bpm]), and were more likely to present first to an emergency room (69 vs. 30%). The age at tachycardia onset is higher for AVNRT (32 plus or minus 18 years) than for AVRT (23 plus or minus 14 years) (14,15).

Hospitalization statistics for supraventricular arrhythmias are summarized in Tables 1 and 2. Of 144 512 discharges for

Table 1. Epidemiological Trends in U.S. Medicare Hospitalizations for Supraventricular Arrhythmias—1991 to 1998

Arrhythmia	Percent of Total 1998 Discharges*	Percent Change 1991–1998	Case Fatality Rate (%)	Average Length of Stay (days)	Average Medicare Reimbursement ($)
Atrial fibrillation	44.8	30.3	1.7	4.7	3559
Atrial flutter	5.2	27.6	1.3	4.5	3912
SVT	3.8	2.9	1	4.2	3802

*5% sample of Medicare Provider Analysis and Review (MEDPAR) and U.S. Health Care Financing Administration (HCFA) enrollee databases; total equals 144 512 discharges with ICD-9-CM codes 427.xx (supraventricular arrhythmia) and 426.xx (conduction disorders).

SVT indicates supraventricular tachycardia.

patients aged more than 65 years in the 1991 to 1998 U.S. Medicare Provider Analysis and Review (MEDPAR) files, hospitalizations and discharges for AF or atrial flutter occurred more frequently with advancing age (3), peaking in 75- to 84-year-old patients. The Healthcare Cost and Utilization Project (HCUP-3) database, a large, national inpatient sample of all payer data collected from diverse U.S. community hospitals (a 20% sample from 17 states), provides data comparable to MEDPAR for various supraventricular arrhythmia subsets (16). Supraventricular tachycardia hospital length-of-stay (3.1 vs. 4.2 days) and case fatality rates (0.8% vs. 1%) are slightly lower in the HCUP-3 dataset when compared to MEDPAR. Atrial flutter and PSVT represented 5.2% and 3.8%, respectively, of 1998 MEDPAR database admissions for supraventricular arrhythmias or conduction disorders (3), but only 0.1 to 0.11% of all 1996 HCUP-3 database hospital admissions (16).

Gender plays a role in the epidemiology of SVT. Female residents in the MESA population had a twofold greater relative risk (RR) of PSVT (RR equals 2.0; 95% confidence interval equals 1.0 to 4.2) compared to males (10). Fifty-eight percent (58%) of symptomatic "lone" PSVT episodes in MESA females without concomitant structural heart disease occurred in the premenopausal age group, as compared to only 9% of episodes in women with cardiovascular disease (10). Women accounted for the majority (64%) of 1999 U.S. short-stay, nonfederal hospital admissions for PSVT (ICD-9-CM 427.0) (17).

The only reported epidemiologic study of patients with atrial flutter (18) involved a selected sample of individuals treated in the Marshfield Clinic in predominantly white, rural mid-Wisconsin. Over 75% of the 58 820 residents and virtually all health events were included in this population database. In approximately 60% of cases, atrial flutter occurred for the first time associated with a specific precipitating event (ie, major surgery, pneumonia, or acute myocardial infarction). In the remaining patients, atrial flutter was associated with chronic comorbid conditions (ie, heart failure, hypertension, and chronic lung disease). Only 1.7% of cases had no structural cardiac disease or precipitating cause (lone atrial flutter). The overall incidence of atrial flutter was 0.088%; 58% of these patients also had AF. Atrial flutter alone was seen in 0.037%. The incidence of atrial flutter increased markedly with age, from 5 per 100 000 of those more than 50 years old to 587 per 100 000 over age 80. Atrial flutter was 2.5 times more common in men. If these findings were extrapolated to the general U.S. population, then approximately 200 000 new cases of atrial flutter would occur annually, a diagnosis that is made twice as often as PSVT (19).

III. GENERAL MECHANISMS OF SUPRAVENTRICULAR ARRHYTHMIA

A. Specialized Atrial Tissue

The sinoatrial (SA) node, atria, and AV node are heterogeneous structures (20). There is distinct electrophysiological specialization of tissues and cells within these structures. In the case of the nodes, cellular heterogeneity is a prominent feature. In the atria, cellular heterogeneity is not prominent, but there are marked complexities of tissue structure that have important implications for impulse propagation and the production of arrhythmias (21).

The SA node is a collection of morphologically and electrically distinct cells (22-28). The central portion of the sinus node, which houses the dominant pacemaking function, contains cells with longer action potentials and faster rates of phase 4 diastolic depolarization than other cardiac cells (28,29). The varied electrophysiological phenotypes of cells

Table 2. HCUP-3 National Inpatient Sample of U.S. Community Hospital Discharge Data—1996

Dysrhythmia	Percent of Total Discharges*	Mean Age (years)	Male (%)	Case Fatality Rate (%)	Average Length of Stay (days)	Average Hospital Charge ($)
Atrial fibrillation	0.78	70	46	1	3.8	7520
Atrial flutter	0.1	67	64	1	3.6	7895
SVT	0.11	62	39	0.8	3.1	8071

SVT indicates supraventricular tachycardia.

Source: Agency for Healthcare Policy Research (AHCPR) Center for Organization and Delivery Studies. Healthcare Cost and Utilization Project (HCUP-3) data for clinical classification software (CCS) categories 7.2.9.1, 3, 4, and 7 (1996).

within the sinus node are due to a distinctive pattern of ion channel expression in the different cell types. Differences in the electrophysiological properties of cells within the node and differences in the expression and distribution of intercellular ion channels or connexins insulate SA nodal tissue from the electrotonic influences of the surrounding atrial myocardium (27,29,30).

Heterogeneity of the action potential profiles in the atria has been described (21,31,32). The underlying ionic current basis for the spatial differences in atrial action potentials has also been described in animal models. In the right atrium of the dog, cells from the crista terminalis exhibit the longest action potential durations when compared to cells isolated from the appendage and pectinate muscles, which have intermediate duration action potentials and myocytes from the AV ring, which exhibit the shortest action potential duration. Differential expression of calcium and transient outward and delayed rectifier potassium currents produce the differences in the action potential profiles and durations (33). Shorter action potential durations are observed in the left compared with the right atrial myocytes, the result of more robust expression of the rapid component of the delayed rectifier potassium current in the left atrium (34).

Cellular recordings support the existence of distinct populations of cells in the mammalian AV node (35). Ovoid cells have a nodal (N- or NH-type) action potential configuration (ie, action potentials with slow [Ca channel–dependent] phase 0 upstrokes and prominent phase 4 diastolic depolarization). In contrast, rod-shaped cells have action potentials more similar to action potentials recorded in atrial myocytes (AN-type) with rapid Na channel–dependent upstrokes and little phase 4 diastolic depolarization (35). Differences in ion channel expression underlie the differences in the electrophysiological behavior of each of the cell types. Variation in cell phenotype and intercellular connectivity cause differences in tissue-level conduction velocity, refractory period, and automaticity.

B. General Mechanisms

All cardiac tachyarrhythmias are produced by one or more mechanisms, including disorders of impulse initiation and abnormalities of impulse conduction. The former are often referred to as automatic; the latter as re-entrant. Tissues exhibiting abnormal automaticity that underlie SVT can reside in the atria, the AV junction, or vessels that communicate directly with the atria, such as the vena cava or pulmonary veins (36-38). The cells with enhanced automaticity exhibit enhanced diastolic phase 4 depolarization and, therefore, an increase in firing rate compared with pacemaker cells. If the firing rate of the ectopic focus exceeds that of the sinus node, then the sinus node can be overdriven and the ectopic focus will become the predominant pacemaker of the heart. The rapid firing rate may be incessant (ie, more than 50% of the day) or episodic.

Triggered activity is a tachycardia mechanism associated with disturbances of recovery or repolarization. Triggered rhythms are generated by interruptions in repolarization of a heart cell called afterdepolarizations (Fig. 1). An afterdepolarization of sufficient magnitude may reach “threshold” and trigger an early action potential during repolarization. Delayed afterdepolarizations (DADs) have been described in a variety of mammalian atrial tissues and cells exposed to mechanical stress (39), digitalis, or neurohormonal stress (40-47). It has been suggested that multifocal atrial tachycardia (MAT) is the result of DAD-induced triggered automaticity (48,49). Early afterdepolarizations have also been observed in human atrial myocardium (50) and pulmonary vein myocytes (51).

The most common arrhythmia mechanism is re-entry. Indeed, the first proven re-entry circuit in humans was that composed of the atrium, AV node, ventricle, and accessory pathway in patients with AV re-entry tachycardia. Re-entry may occur in different forms. In its simplest form, it occurs as repetitive excitation of a region of the heart and is a result of conduction of an electrical impulse around a fixed obstacle in a defined circuit. This is referred to as re-entrant tachycardia, and there are several requirements for its initiation and maintenance. Initiation of a re-entrant tachycardia requires unidirectional conduction block in one limb of a circuit. Unidirectional block may occur as a result of acceleration of the heart rate or block of a premature impulse that impinges on the refractory period of the pathway. Slow conduction is usually required for both initiation and maintenance of a re-entrant tachycardia. In the case of orthodromic AV re-entry (ie, anterograde conduction across the AV node with retrograde conduction over an accessory pathway), slowed conduction through the AV node allows for recovery of, and retrograde activation over, the accessory pathway. A requirement for the maintenance of such a tachycardia is that the wavelength of the tachycardia (ie, the product of the conduction velocity and the refractory period) must be shorter than the pathlength of the circuit over which the impulse travels. Too long a wavelength or too short a pathlength will result in the extinction of the tachycardia as the activation wavefront impinges on the inexcitable refractory tail terminating propagation. The amount by which the pathlength exceeds the wavelength represents the excitable gap. Antiarrhythmic drugs may interrupt re-entrant tachycardia by altering the relationship between the pathlength and the wavelength. Drugs with class III action prolong refractoriness and, therefore, the wavelength, thereby eliminating the excitable gap (52,53). Alternatively, drugs with class I action may interfere with conduction, often in the region of slow conduction-producing bidirectional block and inability to initiate or maintain the tachycardia.

Re-entry is the mechanism of tachycardia in SVTs such as AVRT, AVNRT and atrial flutter; however, a fixed obstacle and a predetermined circuit are not essential requirements for all forms of re-entry. In functionally determined re-entry, propagation occurs through relatively refractory tissue and there is an absence of a fully excitable gap (54). Specific mechanisms are considered in the following sections.

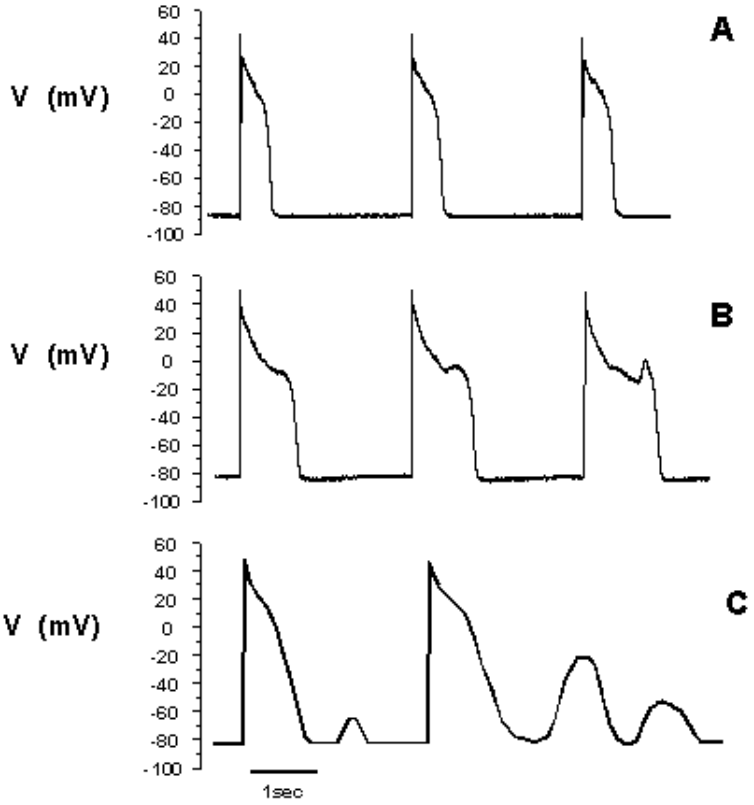

Figure 1. Afterdepolarizations from myocytes. Action potentials recorded before (A) and after (B) application of a potassium channel blocker. Potassium channel blockers lengthen action potential duration and encourage afterdepolarizations. The action potentials are prolonged in (B), and repolarization is interrupted by early afterdepolarizations (C). A series of DADs of decreasing amplitude occurs after completion of repolarization of the action potential, often in the setting of intracellular [Ca^{2+}] overload. DADs indicates delayed afterdepolarizations; mV, millivolts; sec, seconds.

IV. CLINICAL PRESENTATION, GENERAL EVALUATION, AND MANAGEMENT OF PATIENTS WITH SUPRAVENTRICULAR ARRHYTHMIA

A. General Evaluation of Patients Without Documented Arrhythmia

1. Clinical History and Physical Examination

Patients with paroxysmal arrhythmias are most often asymptomatic at the time of evaluation. Arrhythmia-related symptoms include palpitations; fatigue; lightheadedness; chest discomfort; dyspnea; presyncope; or, more rarely, syncope.

A history of arrhythmia-related symptoms may yield important clues to the type of arrhythmia. Premature beats are commonly described as pauses or nonconducted beats followed by a sensation of a strong heartbeat, or they are described as irregularities in heart rhythm. Supraventricular tachycardias occur in all age groups and may be associated with minimal symptoms, such as palpitations, or may present with syncope. The clinician should distinguish whether the palpitations are regular or irregular. Irregular palpitations may be due to premature depolarizations, AF, or MAT. The latter are most commonly encountered in patients with pulmonary disease. If the arrhythmia is recurrent and has abrupt onset and termination, then it is designated paroxysmal. Sinus tachycardia is, conversely, nonparoxysmal and accelerates and terminates gradually. Patients with sinus tachycardia may require evaluation for stressors such as infection or volume loss. Episodes of regular and paroxysmal palpitations with sudden onset and termination (also referred to as PSVT) most commonly result from AVRT or AVNRT. Termination by vagal maneuvers further suggests a re-entrant tachycardia involving AV nodal tissue (eg, AVNRT, AVRT). Polyuria is caused by release of atrial natriuretic peptide in response to increased atrial pressures from contraction of atria against a closed AV valve, which is supportive of a sustained supraventricular arrhythmia.

With SVT, syncope is observed in approximately 15% of patients, usually just after initiation of rapid SVT or with a prolonged pause after abrupt termination of the tachycardia (55). Syncope may be associated with AF with rapid conduction over an accessory AV pathway or may suggest concomitant structural abnormalities, such as valvular aortic stenosis, hypertrophic cardiomyopathy, or cerebrovascular disease. Symptoms vary with the ventricular rate, underlying heart disease, duration of SVT, and individual patient perceptions. Supraventricular tachycardia that is persistent for weeks to months and associated with a fast ventricular response may lead to a tachycardia-mediated cardiomyopathy (56-58).

Of crucial importance in clinical decision making is a clinical history describing the pattern in terms of the number of episodes, duration, frequency, mode of onset, and possible triggers.

Supraventricular tachycardia has a heterogeneous clinical presentation, most often occurring in the absence of detectable heart disease in younger individuals. The presence of associated heart disease should, nevertheless, always be sought and an echocardiogram may be helpful. While a physical examination during tachycardia is standard, it usually does not lead to a definitive diagnosis. If irregular cannon A waves and/or irregular variation in S_1 intensity is present, then a ventricular origin of a regular tachycardia is strongly suggested.

2. Diagnostic Investigations

A resting 12-lead ECG should be recorded and evaluated for the presence of abnormal rhythm, pre-excitation, prolonged QT interval, sinus tachycardia, segment abnormalities, or evidence of underlying heart disease. The presence of pre-excitation on the resting ECG in a patient with a history of paroxysmal regular palpitations is sufficient for the presumptive diagnosis of AVRT, and attempts to record spontaneous episodes are not required before referral to an arrhythmia specialist for therapy (Fig. 2). Specific therapy is discussed in Section V–A clinical history of irregular and paroxysmal palpitations in a patient with baseline pre-excitation strongly suggests episodes of AF, which requires immediate electrophysiological evaluation because these patients are at risk for sudden death (see Section V–D). The diagnosis is otherwise made by careful analysis of the 12-lead ECG during tachycardia (see Section IV). Therefore, patients with a history of sustained arrhythmia should always be encouraged to have at least one 12-lead ECG taken during the arrhythmia. Automatic analysis systems of 12-lead ECGs are unreliable and commonly suggest an incorrect arrhythmia diagnosis.

Indications for referral to a cardiac arrhythmia specialist include presence of a wide complex tachycardia of unknown origin. For those with narrow complex tachycardias, referral is indicated for those with drug resistance or intolerance as well as for patients desiring to be free of drug therapy. Because of the potential for lethal arrhythmias, all patients with Wolff-Parkinson-White (WPW) syndrome (ie, pre-excitation combined with arrhythmias) should be referred for further evaluation. All patients with severe symptoms, such as syncope or dyspnea, during palpitations also should be referred for prompt evaluation by an arrhythmia specialist. An echocardiographic examination should be considered in patients with documented sustained SVT to exclude the possibility of structural heart disease, which usually cannot be detected by physical examination or 12-lead ECG.

An ambulatory 24-hour Holter recording can be used in patients with frequent (ie, several episodes per week) but transient tachycardias (59-61). An event or wearable loop recorder is often more useful than a 24-hour recording in patients with less frequent arrhythmias (62). Implantable loop recorders may be helpful in selected cases with rare symptoms (ie, fewer than two episodes per month) associated with severe symptoms of hemodynamic instability (63).

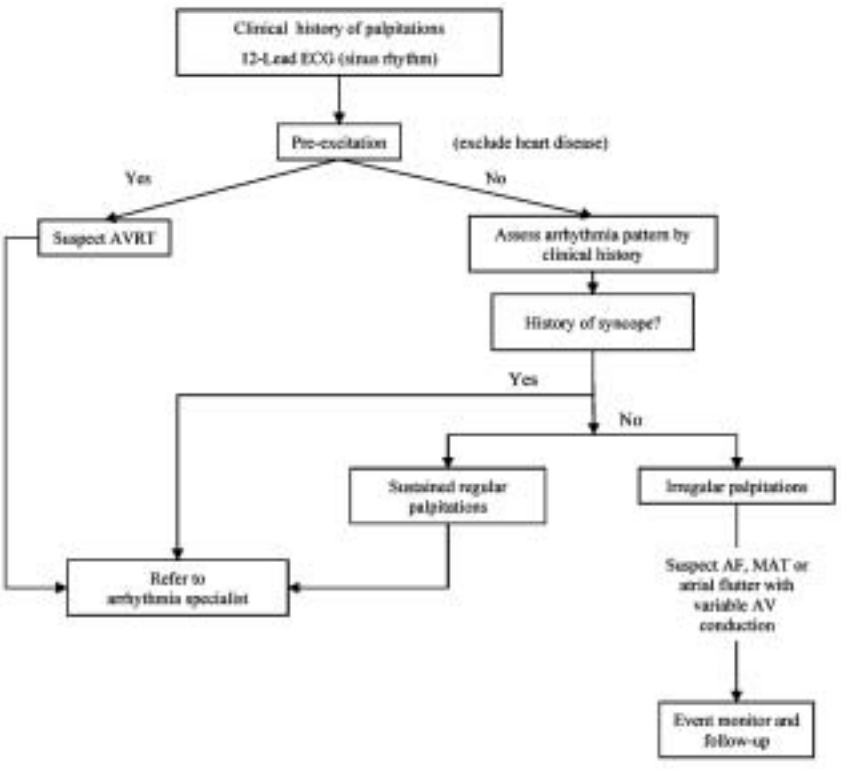

Figure 2. Initial evaluation of patients with suspected tachycardia. AVRT indicates atrioventricular reciprocating tachycardia; ECG, electrocardiogram.

Exercise testing is less often useful for diagnosis unless the arrhythmia is clearly triggered by exertion.

Transesophageal atrial recordings and stimulation may be used in selected cases for diagnosis or to provoke paroxysmal tachyarrhythmias if the clinical history is insufficient or if other measures have failed to document an arrhythmia. Esophageal stimulation is not indicated if invasive electrophysiological investigation is planned (64,65). Invasive electrophysiological investigation with subsequent catheter ablation may be used for diagnoses and therapy in cases with a clear history of paroxysmal regular palpitations. It may also be used empirically in the presence of pre-excitation or disabling symptoms (Fig. 2).

3. Management

The management of patients with symptoms suggestive of an arrhythmia but without ECG documentation depends on the nature of the symptoms. If the surface ECG is normal and the patient reports a history consistent with premature extra beats, then precipitating factors, such as excessive caffeine, alcohol, nicotine intake, recreational drugs, or hyperthyroidism, should be reviewed and eliminated (Table 3). Benign extrasystoles are often manifest at rest and tend to become less common with exercise.

If symptoms and the clinical history indicate that the arrhythmia is paroxysmal in nature and the resting 12-lead ECG gives no clue for the arrhythmia mechanism, then further diagnostic tests for documentation may not be necessary before referral for an invasive electrophysiological study and/or catheter ablation. Patients should be taught to perform vagal maneuvers. A beta-blocking agent may be prescribed empirically provided that significant bradycardia (less than 50 bpm) have been excluded. Due to the risk of proarrhythmia, antiarrhythmic treatment with Class I or Class III drugs should not be initiated without a documented arrhythmia.

Table 3. Predisposing or Precipitating Factors for Patients With Palpitations

Noncardiac Causes
Nicotine, alcohol, caffeine
Physical or mental stress
Hyperthyroidism
Premenstrual or menstrual
Electrolyte disturbance
Certain drugs (antiarrhythmic, antidepressant, antibiotic drugs; stimulants; antihistamines; appetite suppressants)
Anemia
Anxiety or hypovolemia
Fever, infection
Lack of sleep
Cardiac Causes
Coronary artery disease; old myocardial infarction, especially for ventricular tachycardias
Congestive heart failure
Cardiomyopathy
Valvular disease
Congenital heart disease
Other conditions that may cause myocardial scarring (ie, sarcoidosis, tuberculosis)
Primary electrical disorders (ie, long QT syndrome, Brugada syndrome)
Accessory pathways

B. General Evaluation of Patients With Documented Arrhythmia

1. Diagnostic Evaluation

Whenever possible, a 12-lead ECG should be taken during tachycardia but should not delay immediate therapy to terminate the arrhythmia if there is hemodynamic instability. At a minimum, a monitor strip should be obtained from the defibrillator, even in cases with cardiogenic shock or cardiac arrest, before direct current (DC) cardioversion is applied to terminate the arrhythmia.

a. Differential Diagnosis for Narrow QRS-Complex Tachycardia

If ventricular activation (QRS) is narrow (less than 120 milliseconds [ms]), then the tachycardia is almost always supraventricular and the differential diagnosis relates to its mechanism (Fig. 3) (66,67). If no P waves or evidence of atrial activity is apparent and the RR interval is regular, then AVNRT is most commonly the mechanism (Fig. 4). P-wave activity in AVNRT may be only partially hidden within the QRS complex and may deform the QRS to give a pseudo-R wave in lead V1 and/or a pseudo-S wave in inferior leads (Fig. 4). If a P wave is present in the ST segment and separated from the QRS by 70 ms, then AVRT is most likely. In tachycardias with RP longer than PR (Fig. 5), the most typical diagnosis is atypical AVNRT, permanent form of junctional reciprocating tachycardia (PJRT) (ie, AVRT via a slowly conducting accessory pathway), or AT (see Sections V–B, V–D, and V–E). Responses of narrow QRS-complex tachycardias to adenosine or carotid massage may aid in the differential diagnosis (Fig. 6) (68-70). A 12-lead ECG recording is desirable during use of adenosine or carotid massage. If P waves are not visible, then the use of esophageal pill electrodes can also be helpful.

b. Differential Diagnosis for Wide QRS-Complex Tachycardia

If the QRS is wide (greater than 120 ms), then it is important to differentiate between SVT and ventricular tachycardia (VT) (Fig. 7). Intravenous medications given for the treatment of SVT, particularly verapamil or diltiazem, may be deleterious because they may precipitate hemodynamic collapse for a patient with VT (71-73). Stable vital signs during tachycardias are not helpful for distinguishing SVT from VT. If the diagnosis of SVT cannot be proven or cannot be made easily, then the patient should be treated as if VT were present. Wide-QRS tachycardia can be divided into three groups: SVT with bundle-branch block (BBB) or aberration, SVT with AV conduction over an accessory pathway, and VT.

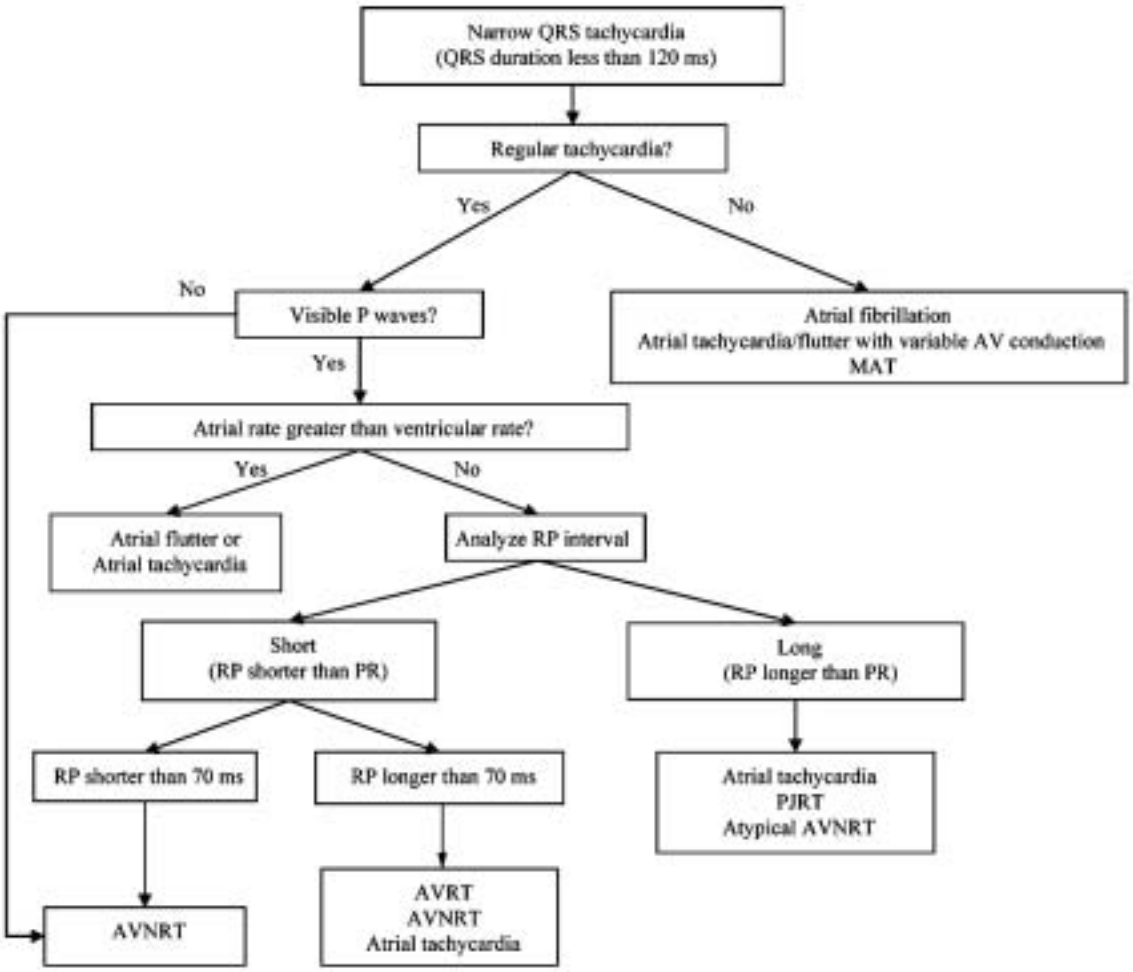

Figure 3. Differential diagnosis for narrow QRS tachycardia. Patients with focal junctional tachycardia may mimic the pattern of slow-fast AVNRT and may show AV dissociation and/or marked irregularity in the junctional rate. AV indicates atrioventricular; AVNRT, atrioventricular nodal reciprocating tachycardia; AVRT, atrioventricular reciprocating tachycardia; MAT, multifocal atrial tachycardia; ms, milliseconds; PJRT, permanent form of junctional reciprocating tachycardia; QRS, ventricular activation on electrocardiogram.

SUPRAVENTRICULAR TACHYCARDIA WITH BUNDLE-BRANCH BLOCK. Bundle-branch block may be pre-existing or may occur only during tachycardia when one of the bundle branches is refractory due to the rapid rate. Most BBBs are not only rate-related, but are also due to a long-short sequence of initiation. Bundle-branch block can occur with any supraventricular arrhythmia. If a rate-related BBB develops during orthodromic AVRT, then the tachycardia rate may slow if the BBB is ipsilateral to the bypass tract location.

SUPRAVENTRICULAR TACHYCARDIA WITH ATRIOVENTRICULAR CONDUCTION OVER AN ACCESSORY PATHWAY. Supraventricular tachycardia with AV conduction over an accessory pathway may occur during AT, atrial flutter, AF, AVNRT or antidromic AVRT. The latter is defined as anterograde conduction over the accessory pathway and retrograde conduction over the AV node or a second accessory AV pathway. A wide-QRS complex with left bundle-branch block (LBBB) morphology may be seen with anterograde conduction over other types of accessory pathways, such as atriofascicular, nodofascicular, or nodoventricular tracts.

VENTRICULAR TACHYCARDIA. Several ECG criteria have been described to differentiate the underlying mechanism of a wide-QRS tachycardia.

VENTRICULAR ARRHYTHMIA DISSOCIATION. Ventricular arrhythmia dissociation with a ventricular rate faster than the atrial rate generally proves the diagnosis of VT (Fig. 8) but is clearly discernible in only 30% of all VTs (74). Fusion complexes represent a merger between conducted sinus (or supraventricular complexes) impulses and ventricular depolarization occurring during AV dissociation. These complexes are pathognomonic of VT. Retrograde VA block may be present spontaneously or brought out by carotid massage. The demonstration that P waves are not necessary for tachycardia maintenance strongly suggests VT. P waves can be difficult to recognize during a wide-QRS tachycardia. Therefore, one should also look for evidence of VA dissociation on examination: irregular cannon A waves in the jugular venous pulse and variability in the loudness of the first heart sound and in systolic blood pressure (75). If P waves are not visible, then the use of esophageal pill electrodes can also be useful.

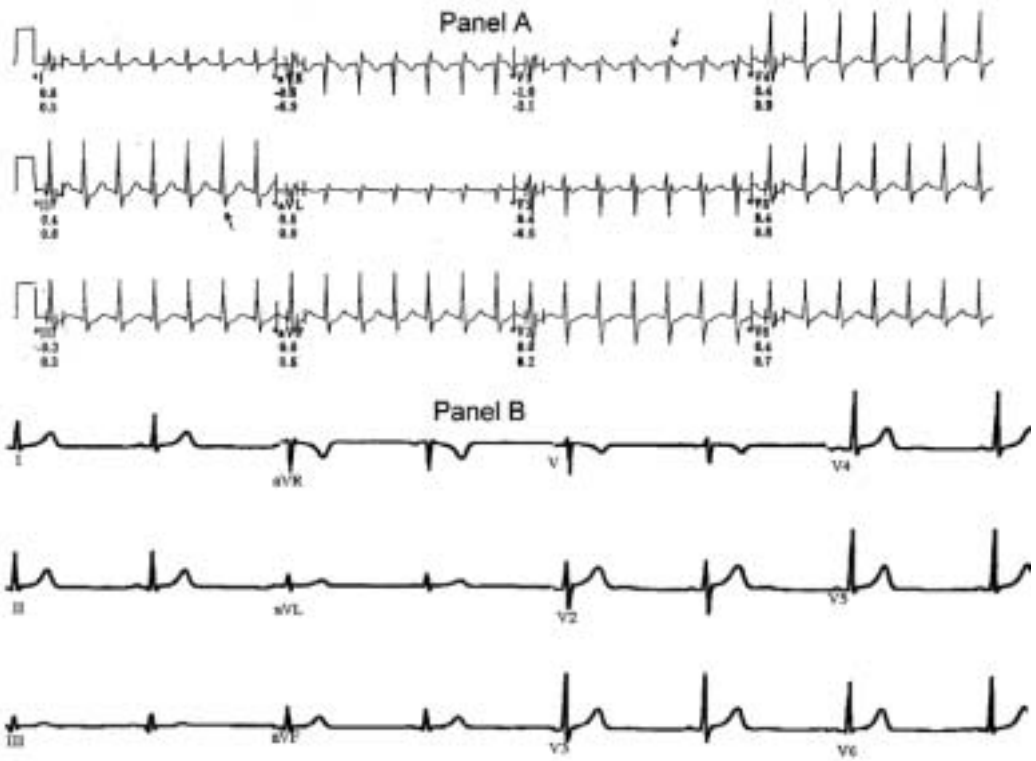

Figure 4. ECG pattern of typical AVNRT. Panel A: 12-Lead ECG shows a regular SVT recorded at an ECG paper speed of 25 mm/sec. Panel B: After conversion to sinus rhythm, the 12-lead ECG shows sinus rhythm with narrow QRS complexes. In comparison with Panel A: Note the pseudo r´ in V1 (arrow) and accentuated S waves in 2, 3, aVF (arrow). These findings are pathognomonic for AVNRT. AVNRT indicates atrioventricular nodal reciprocating tachycardia; ECG, electrocardiogram; mm/sec, millimeters per second; QRS, ventricular activation on ECG; SVT, supraventricular tachycardia.

WIDTH OF THE QRS COMPLEX. A QRS width of more than 0.14 seconds with right bundle-branch block (RBBB) or 0.16 seconds during LBBB pattern favors VT (74). The QRS width criteria are not helpful in differentiating VT from SVT with AV conduction over an accessory pathway. A patient with SVT can have a QRS width of more than 0.14 (RBBB) or 0.16 (LBBB) in the presence of either pre-existing BBB or AV conduction over an accessory pathway, or when class Ic or class Ia antiarrhythmic drugs are used.

CONFIGURATIONAL CHARACTERISTICS OF THE QRS COMPLEX DURING TACHYCARDIA. Leads V1 and V6 are helpful in differentiating VT from SVT (74,76,77).

- An RS (from the initial R to the nadir of S) interval longer than 100 ms in any precordial lead is highly suggestive of VT (78).
- A QRS pattern with negative concordance in the precordial leads is diagnostic for VT ("negative concordance" means that the QRS patterns in all of the pre cordial leads are similar, and with QS complexes). Positive concordance does not exclude antidromic AVRT over a left posterior accessory pathway (79).
- The presence of ventricular fusion beats indicates a ventricular origin of the tachycardia.

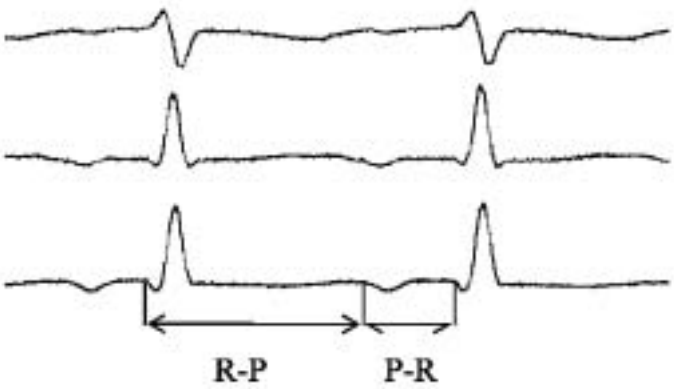

Figure 5. ECG tracing with limb leads I, II, and III, showing an RP (initial R to initial P) interval longer than the PR interval. The P wave differs from the sinus P wave. ECG indicates electrocardiogram.

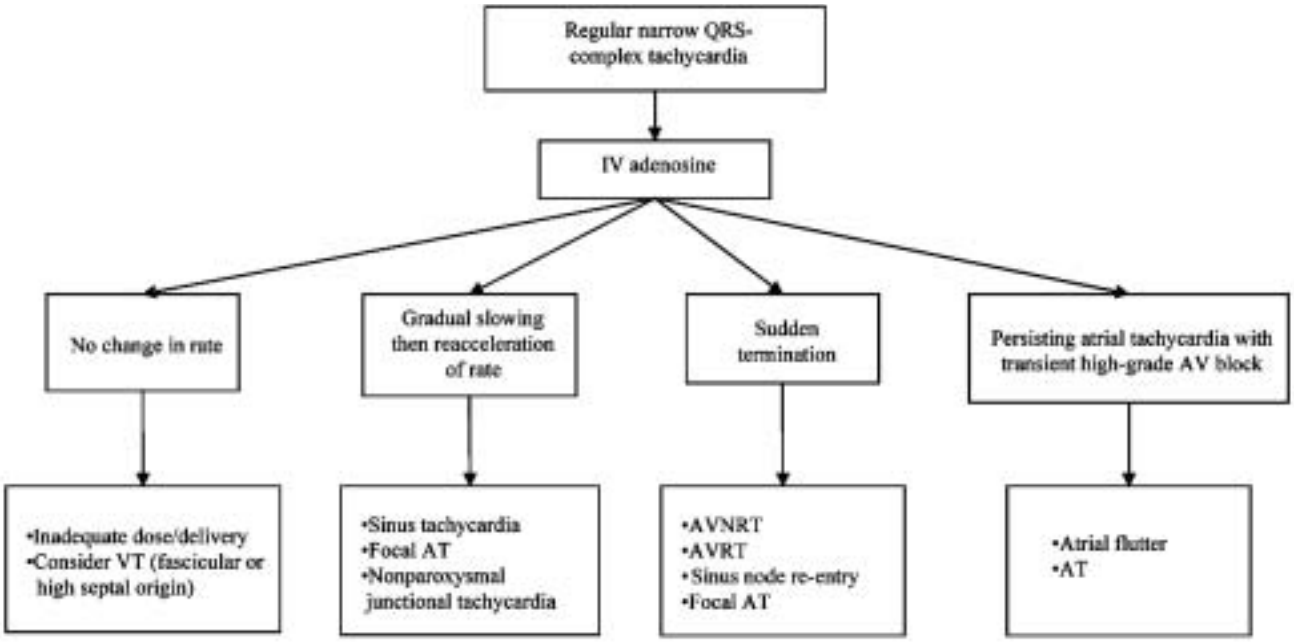

Figure 6. Responses of narrow complex tachycardias to adenosine. AT indicates atrial tachycardia; AV, atrioventricular; AVNRT, atrioventricular nodal reciprocating tachycardia; AVRT, atrioventricular reciprocating tachycardia; IV, intravenous; QRS, ventricular activation on electrocardiogram; VT, ventricular tachycardia.

- QR complexes indicate a myocardial scar and are present in approximately 40% of patients with VTs after myocardial infarction (80).

The width and morphologic criteria are less specific for patients taking certain antiarrhythmic agents and those with hyperkalemia or severe heart failure. Despite ECG criteria, patients presenting with wide QRS-complex tachycardia are often misdiagnosed (71,72,81). A positive answer to two inquiries, namely the presence of a previous myocardial infarct and the first occurrence of a wide QRS-complex tachycardia after an infarct, strongly indicates a diagnosis of VT (82).

2. Management

When a definitive diagnosis can be made on the basis of ECG and clinical criteria, acute and chronic treatment should be initiated on the basis of the underlying mechanism (see the sections on specific arrhythmias).

If the specific diagnosis of a wide QRS-complex tachycardia cannot be made despite careful evaluation, then the patient should be treated for VT. Acute management of patients with hemodynamically stable and regular tachycardia is outlined in Fig. 9.

The most effective and rapid means of terminating any hemodynamically unstable narrow or wide QRS-complex tachycardia is DC cardioversion.

a. Acute Management of Narrow QRS-Complex Tachycardia

In regular narrow QRS-complex tachycardia, vagal maneuvers (ie, Valsalva [83], carotid massage, and facial immersion in cold water), should be initiated to terminate the arrhythmia or to modify AV conduction. If this fails, IV antiarrhythmic drugs should be administered for arrhythmia termination in hemodynamically stable patients. Adenosine or nondihydropyridine calcium-channel antagonists are the drugs of choice (Fig. 7). The advantage of adenosine relative to IV calcium-channel or beta blockers relates to its rapid onset and short half-life. Intravenous adenosine is, therefore, the preferred agent except for patients with severe asthma. Patients treated with theophylline may require higher doses of adenosine for effect, and adenosine effects are potentiated by dipyridamole. In addition, higher rates of heart block may be seen when adenosine is concomittantly administered with carbamazepine. Longer-acting agents (eg, IV calcium-channel blockers or beta blockers [ie, verapamil/diltiazem or metoprolol]) are of value, particularly for patients with frequent atrial premature beats or ventricular premature beats, which may serve to trigger early recurrence of PSVT. Adenosine or DC cardioversion is preferred for those with PSVT in whom a rapid therapeutic effect is essential. Potential adverse effects of adenosine include initiation of AF (1 to 15%), which is usually transient, and may be particularly problematic for those with ventricular pre-excitation. Adenosine should be avoided in patients with severe bronchial asthma. It is important to use extreme care with concomitant use of IV calcium-channel blockers and beta blockers because of possible potentiation of hypotensive and/or bradycardic effects. An ECG should be recorded during vagal maneuvers or drug administration because the response may aid in the diagnosis even if the arrhythmia does not terminate (Fig. 6). Termination of the tachycardia with a P wave after the last QRS complex favors AVRT or AVNRT. Tachycardia termination with a QRS complex favors AT,

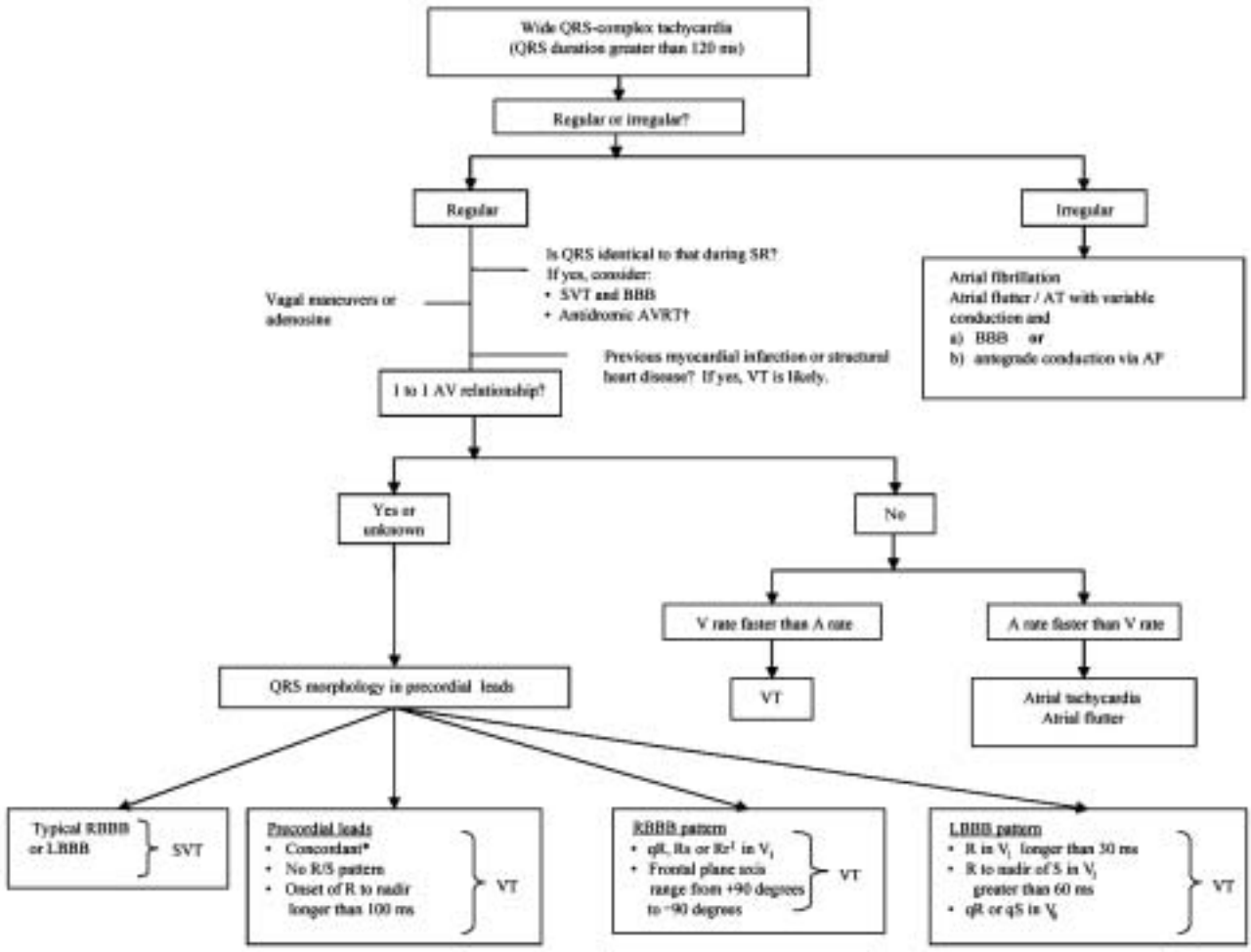

Figure 7. Differential diagnosis for wide QRS-complex tachycardia (greater than 120 ms). A QRS conduction delay during sinus rhythm, when available for comparison, reduces the value of QRS morphology analysis. Adenosine should be used with caution when the diagnosis is unclear because it may produce VF in patients with coronary artery disease and AF with a rapid ventricular rate in pre-excited tachycardias. Various adenosine responses are shown in Fig. 6. *Concordant indicates that all precordial leads show either positive or negative deflections. Fusion complexes are diagnostic of VT. †In pre-excited tachycardias, the QRS is generally wider (ie, more pre-excited) compared with sinus rhythm. A indicates atrial; AF, atrial fibrillation; AP, accessory pathway; AT, atrial tachycardia; AV, atrioventricular; AVRT, atrioventricular reciprocating tachycardia; BBB, bundle-branch block; LBBB, left bundle-branch block; ms, milliseconds; QRS, ventricular activation on ECG; RBBB, right bundle-branch block; SR, sinus rhythm; SVT, supraventricular tachycardias; V, ventricular; VF, ventricular fibrillation; VT, ventricular tachycardia.

which is often adenosine insensitive. Continuation of tachycardia with AV block is virtually diagnostic of AT or atrial flutter, excludes AVRT, and makes AVNRT very unlikely.

b. Acute Management of Wide QRS-Complex Tachycardia

Immediate DC cardioversion is the treatment for hemodynamically unstable tachycardias. If the tachycardia is hemodynamically stable and definitely supraventricular, then management is as described for narrow QRS-complex tachycardias (Fig. 6). For pharmacologic termination of a stable wide QRS-complex tachycardia, IV procainamide and/or sotalol are recommended on the basis of randomized but small studies (84,85). Amiodarone is also considered acceptable. Amiodarone is preferred, compared to procainamide and sotalol, in patients with impaired left ventricular (LV) function (86,87) or signs of heart failure. These recommendations are in accord with the current Advanced Cardiovascular Life Support guidelines (88). Special circumstances may require alternative therapy (ie, pre-excited tachycardias and VT caused by digitalis toxicity). For termination of an irregular wide QRS-complex tachycardia (ie, pre-excited AF), DC cardioversion is recommended. Or, if the patient is hemodynamically stable, pharmacologic conversion using IV ibutilide, flecainide, or procainamide is appropriate.

c. Further Management

After successful termination of a wide QRS-complex tachycardia of unknown etiology, patients should be referred to an arrhythmia specialist. Patients with stable narrow QRS-complex tachycardia, normal LV function, and a normal ECG during sinus rhythm (ie, no pre-excitation) may require no specific therapy. Referral is indicated for those with drug

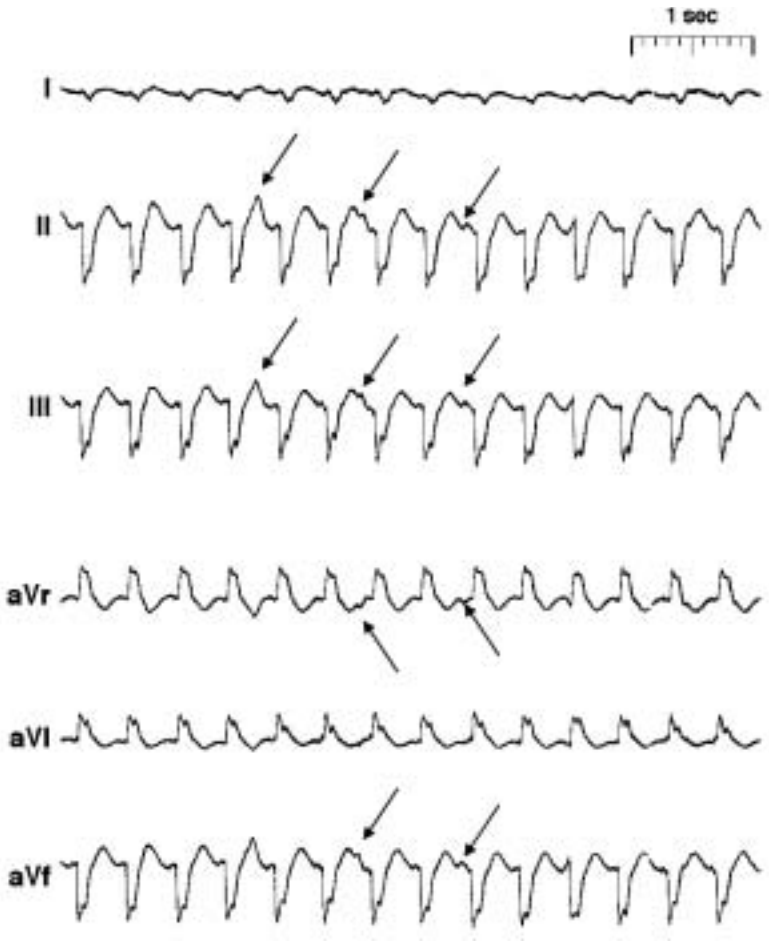

Figure 8. Electrocardiogram showing AV dissociation during VT in a patient with a wide QRS-complex tachycardia. The P waves are marked with arrows.

resistance or intolerance as well as for patients desiring to be free of lifelong drug therapy. When treatment is indicated, options include catheter ablation or drug therapy. Finally, because of the potential for lethal arrhythmias, all patients with WPW syndrome (ie, pre-excitation and arrhythmias) should be referred for further evaluation (89).

V. SPECIFIC ARRHYTHMIAS

A. Sinus Tachyarrhythmias

Sinus tachycardia usually occurs in response to an appropriate physiological stimulus (eg, exercise) or to an excessive stimulus (eg, hyperthyroidism). Failure of the mechanisms that control the sinus rate may lead to an inappropriate sinus tachycardia. Excessive sinus tachycardia may also occur in response to upright posture (postural orthostatic tachycardia syndrome [POTS]). A re-entry mechanism may also occur within, or close to, the sinus node, resulting in so-called sinus node re-entrant tachycardia, which is also sometimes known as SA re-entry.

1. Physiological Sinus Tachycardia

The normally innervated sinus node generates an impulse approximately 60 to 90 times per minute and responds to autonomic influences. Nevertheless, the sinus node is a versatile structure and is influenced by many other factors, including hypoxia, acidosis, stretch, temperature, and hormones (eg, tri-iodothyronine, serotonin).

a. Definition

Sinus tachycardia is defined as an increase in sinus rate to greater than 100 bpm in keeping with the level of physical, emotional, pathological, or pharmacologic stress. Pathological causes of sinus tachycardia include pyrexia, hypovolemia, or anemia, which may result from infections, malignancies, myocardial ischemia, congestive cardiac failure, pulmonary emboli, shock, and thyrotoxicosis. Drugs that induce sinus tachycardia include stimulants (eg, caffeine, alcohol, nicotine); prescribed compounds (eg, salbutamol, aminophylline, atropine, catecholamines); and certain recreational/illicit drugs (eg, amphetamines, cocaine, "ecstasy," cannabis) (100). Anticancer treatments, in particular anthracycline compounds such as doxorubicin (or Adriamycin) and daunorubicin, can also trigger sinus tachycardia as part of the acute cardiotoxic response that is predominantly catecholamine/histamine induced (101) or part of a late cardiotoxic response (102,103). Sinus tachycardia may signal severe underlying pathologies and often requires comprehen-

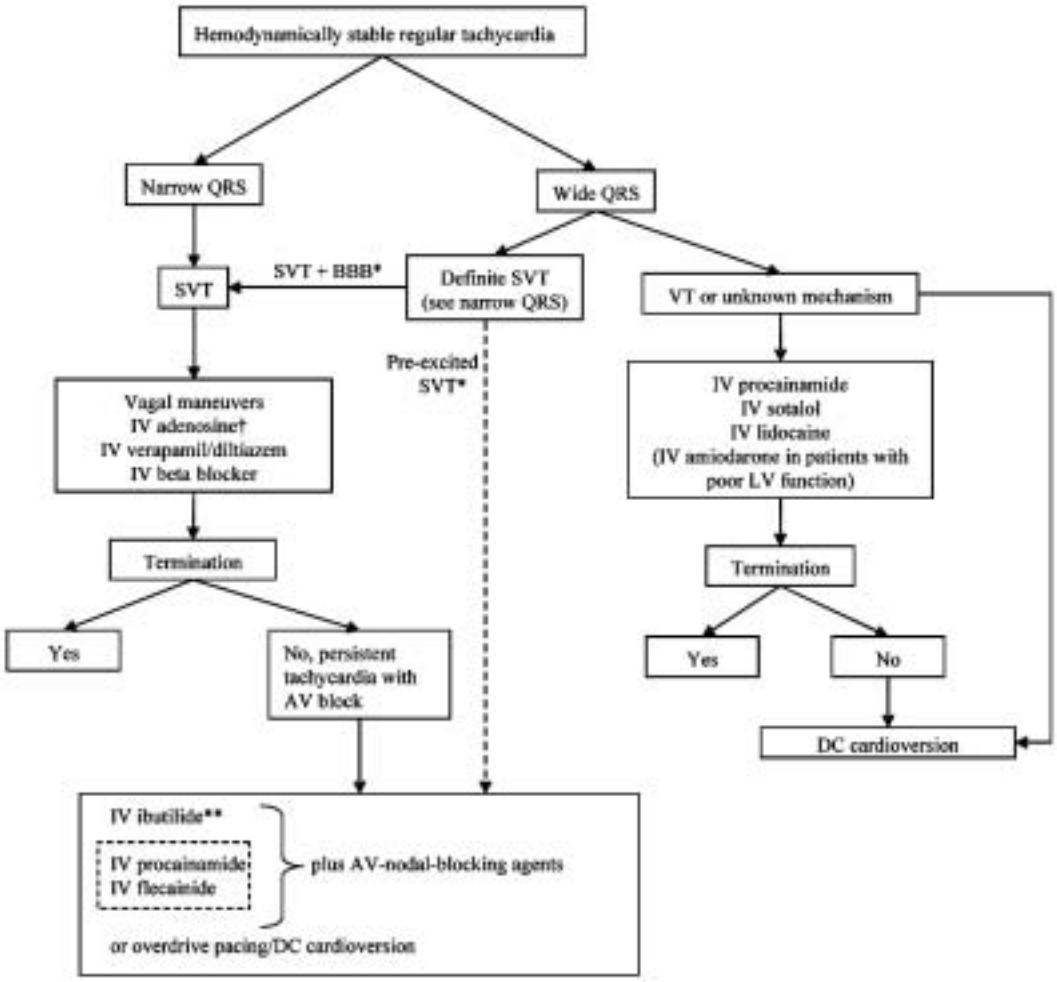

Figure 9. Acute management of patients with hemodynamically stable and regular tachycardia. *A 12-lead ECG during sinus rhythm must be available for diagnosis. †Adenosine should be used with caution in patients with severe coronary artery disease and may produce AF, which may result in rapid ventricular rates for patients with pre-excitation. **Ibutilide is especially effective for patients with atrial flutter but should not be used in patients with EF less than 30% due to increased risk of polymorphic VT. AF indicates atrial fibrillation; AV, atrioventricular; BBB, bundle-branch block; DC, direct current; ECG, electrocardiogram; IV, intravenous; LV, left ventricle; QRS, ventricular activation on ECG; SVT, supraventricular tachycardia; VT, ventricular tachycardia.

sive evaluation. Atrial and sinus tachycardias may be difficult to differentiate.

b. Mechanism

Sinus tachycardia results from physiological influences on individual pacemaker cells and from an anatomical shift in the site of origin of atrial depolarization superiorly within the sinus node (104). If current activity is one of several mechanisms by which phase 4 diastolic depolarization is hastened, therefore increasing the heart rate, then an increase in cyclic adenosine monophosphate triggers opening of ion channels responsible for the pacemaker, or funny current (i_f), resulting in a faster heart rate due to more rapid attainment of threshold potential.

c. Diagnosis

In normal sinus rhythm, the P wave on a 12-lead ECG is positive in leads I, II, and aVF and negative in aVR. Its axis in the frontal plane lies between 0 and +90; in the horizontal plane, it is directed anteriorly and slightly leftward and can, therefore, be negative in leads V1 and V2 but positive in leads V3 to V6. The PR interval is normally between 120 ms and 200 ms (220 ms in the elderly). The P waves have a normal contour, but a larger amplitude may develop and the wave may become peaked (105). Sinus tachycardia is nonparoxysmal, thus differentiating it from re-entry.

d. Treatment

The mainstay in the management of sinus tachycardias primarily involves identifying the cause and either eliminating or treating it. However, beta blockade can be extremely useful and effective for physiological symptomatic sinus tachycardia triggered by emotional stress and other anxiety-related disorders (106-113); for prognostic benefit after myocardial infarction (114-117); for the symptomatic and prognostic benefits in certain other irreversible causes of sinus tachycardias, such as congestive cardiac failure (118-120); and for symptomatic thyrotoxicosis in combination with carbima-

Recommendations for Acute Management of Hemodynamically Stable and Regular Tachycardia

ECG	Recommendation*	Classification	Level of Evidence	References
Narrow QRS-complex tachycardia (SVT)	Vagal maneuvers	I	B	
	Adenosine	I	A	(4,69,90)
	Verapamil, diltiazem	I	A	(91)
	Beta blockers	IIb	C	(92,93)
	Amiodarone	IIb	C	(94)
	Digoxin	IIb	C	
Wide QRS-complex tachycardia				
•SVT and BBB	See above			
•Pre-excited SVT/AF†	Flecainide‡	I	B	(95)
	Ibutilide‡	I	B	(96)
	Procainamide‡	I	B	
	DC cardioversion	I	C	
•Wide QRS-complex tachycardia of unknown origin	Procainamide‡	I	B	(84,97)
	Sotalol‡	I	B	(85)
	Amiodarone	I	B	(25,86)
	DC cardioversion	I	B	(98)
	Lidocaine	IIb	B	(85,97)
	Adenosine§	IIb	C	(99)
	Beta blockers¶	III	C	(98)
	Verapamil**	III	B	(73)
Wide QRS-complex tachycardia of unknown origin in patients with poor LV function	Amiodarone	I	B	(25,86)
	DC cardioversion, lidocaine	I	B	(98)

The order in which treatment recommendations appear in this table within each class of recommendation does not necessarily reflect a preferred sequence of administration. Please refer to text for details. For pertinent drug dosing information, please refer to the ACC/AHA/ESC Guidelines on the Management of Patients With Atrial Fibrillation.

*All listed drugs are administered intravenously.

†See Section V, specific section.

‡Should not be taken by patients with reduced LV function.

§Adenosine should be used with caution in patients with severe coronary artery disease because vasodilation of normal coronary vessels may produce ischemia in vulnerable territory. It should be used only with full resuscitative equipment available.

¶Beta blockers may be used as first-line therapy for those with catecholamine-sensitive tachycardias, such as right ventricular outflow tachycardia.

**Verapamil may be used as first-line therapy for those with LV fascicular VT.

AF indicates atrial fibrillation; BBB, bundle-branch block; DC, direct current; ECG, electrocardiogram; LV, left ventricular; QRS, ventricular activation on ECG; SVT, supraventricular

zole or propylthiouracyl while these palliative agents take effect (121,122). Nondihydropyridine calcium-channel blockers, such as diltiazem or verapamil, may be of benefit in patients with symptomatic thyrotoxicosis, if beta blockade is contraindicated (123).

2. Inappropriate Sinus Tachycardia

a. Definition

Inappropriate sinus tachycardia is a persistent increase in resting heart rate or sinus rate unrelated to, or out of proportion with, the level of physical, emotional, pathological, or pharmacologic stress.

b. Mechanism

The underlying pathological basis for inappropriate sinus tachycardia is likely to be multifactorial, but two main mechanisms have been proposed:

1. Enhanced automaticity of the sinus node (125)
2. Abnormal autonomic regulation of the sinus node with excess sympathetic and reduced parasympathetic tone (126,127)

It is unclear whether these mechanisms are a direct result of impaired neural input into the sinus node or whether they represent an inherent abnormality within the sinus node itself (128).

Recommendations for Treatment of Inappropriate Sinus Tachycardia

Treatment	Recommendation	Classification	Level of Evidence	References
Medical	Beta blockers	I	C	–
	Verapamil, diltiazem	IIa	C	–
Interventional	Catheter ablation-sinus node modification/elimination*	IIb	C	(133-135,137-141)

The order in which treatment recommendations appear in this table within each class of recommendation does not necessarily reflect a preferred sequence of administration. Please refer to text for details. For pertinent drug dosing information, please refer to the ACC/AHA/ESC Guidelines on the Management of Patients With Atrial Fibrillation.

*Used as a last resort.

c. Presentation

A high proportion of patients with inappropriate sinus tachycardia are healthcare professionals, and approximately 90% are female (129). The mean age of presentation is 38 plus or minus 12 years. Although the predominant symptom at presentation is palpitations, symptoms such as chest pain, shortness of breath, dizziness, lightheadedness, and presyncope have also been reported. The degree of disability can vary tremendously, from totally asymptomatic patients identified during routine medical examination to individuals who are fully incapacitated. Clinical examination and routine investigations allow elimination of a secondary cause for the tachycardia but are generally not helpful in establishing the diagnosis.

d. Diagnosis

Inappropriate sinus tachycardia is diagnosed on the basis of invasive and noninvasive criteria (128,129):

1. The presence of a persistent sinus tachycardia (heart rate greater than 100 bpm) during the day with excessive rate increase in response to activity and nocturnal normalization of rate, as confirmed by a 24-hour Holter recording
2. The tachycardia (and symptoms) is nonparoxysmal
3. P-wave morphology and endocardial activation identical to sinus rhythm
4. Exclusion of a secondary systemic cause (eg, hyperthyroidism, pheochromocytoma, physical deconditioning)

e. Treatment

The treatment of inappropriate sinus tachycardia is predominantly symptom driven. The risk of tachycardia-induced cardiomyopathy (130) in untreated patients is unknown but likely to be small.

Although no randomized, double-blinded, placebo-controlled clinical trials exist, beta blockers may be useful and should be prescribed as first-line therapy in the majority of these patients. Anecdotal evidence suggests that nondihydropyridine calcium-channel blockers, such as verapamil and diltiazem, are also effective (131). Specific bradycardic agents (eg, I_f inhibitor ivabradine) may be valuable, but these agents are still under investigation (132).

Sinus node modification by catheter ablation remains a potentially important therapeutic option in the most refractory cases of inappropriate sinus tachycardia (133). Potential adverse effects include pericarditis, phrenic nerve injury, superior vena cava (SVC) syndrome, or need for permanent pacing. A number of case reports have recorded successful surgical excision (134,135) or radiofrequency (RF) ablation of the sinus node (136-138). There is also a case report of successful obliteration of the sinus node artery for the management of this disorder (139). The diagnosis of POTS (see Section V–A, 3) must be excluded before considering ablation. In a retrospective analysis of 29 cases undergoing sinus node modification for inappropriate sinus tachycardia (140), a 76% acute success rate (22 out of 29 cases) was reported. The long-term success rate has been reported to be 25% to 65%.

3. Postural Orthostatic Tachycardia Syndrome

Postural orthostatic tachycardia syndrome is part of a wide spectrum of disorders that exhibit autonomic dysfunction (142). These include severe orthostatic hypotension in the presence of autonomic neuropathy and vasovagal syncope in the absence of other evidence of autonomic dysfunction. Postural orthostatic tachycardia syndrome manifests as an excessive orthostatic tachycardia without significant orthostatic hypotension in those without overt autonomic neuropathy. It is associated with numerous other symptoms, such as exercise intolerance, palpitations, weakness, and lightheadedness; most of these symptoms are also autonomically mediated (143-145).

a. Definition

Postural orthostatic tachycardia syndrome is the diagnosis applied to individuals who present with orthostatic intolerance (ie, symptoms on standing that are relieved by recumbency) in the presence of a demonstrable exaggerated, persistent postural sinus tachycardia (greater than 30 bpm from baseline or greater than 120 bpm) within 10 minutes of an upright tilt in the absence of postural hypotension and any demonstrable autonomic neuropathy.

b. Mechanism

Many mechanisms have been proposed for POTS. These range from idiopathic hypovolemia (146) and reduced circulating blood volume (147) to splanchnic bed blood pooling (148,149) and reduced red cell mass resulting from an

impaired erythropoietin response (150). There is little doubt that the etiology and pathophysiology of POTS is heterogeneous, although there are similar clinical characteristics (151). Two forms seem to predominate (152) The first is a central beta-hypersensitivity form in which the normal physiological baroreflex fails to terminate the tachycardia triggered by upright posture (153). In certain cases of this form of POTS, the basic abnormality responsible for the condition is a defective norepinephrine-transporter mechanism (154). This abnormality leads to a failure in the synaptic clearance of norepinephrine, resulting in an exaggerated sympathetic response to physiological stimuli. The second form of POTS, the so-called partial dysautonomic form, is seen in the majority of POTS patients. There appears to be a mild idiopathic peripheral autonomic neuropathy, wherein there is a failure of the peripheral vasculature to vasoconstrict appropriately during orthostatic stress, thereby resulting in an exaggerated tachycardia (145,155). This effect is likely to be due to partial sympathetic denervation, especially in the legs (156); arteries seem to be affected rather than veins (157). Emerging evidence suggests that there may be two further subgroups of this partial dysautonomic form-one that is centrally mediated and the other peripheral (158). There is, however, also evidence of autoantibodies to ganglionic nicotinic acetylcholine receptors in certain cases (159), and intrinsic sinus node abnormalities in others (160). In almost half of the cases of POTS, there may be a preceding viral illness; these patients have a better long-term prognosis than others (145,161).

c. Presentation

Patients with POTS present with palpitations, severe fatigue, exercise intolerance, presyncope, tremor, bowel hypomotility, and dizziness or lightheadedness. A significant proportion of patients also complain that they always feel cold and are unable to tolerate extreme heat (152). Furthermore, patients with POTS may be diagnosed as suffering from chronic fatigue syndrome (162). In fact, there appears to be a considerable overlap between the two ailments (163,164).

d. Diagnosis

1. Head-upright tilt testing exhibits an increase in heart rate of at least 30 bpm in the first 5 to 10 minutes or achieves heart rates well in excess of 120 bpm
2. Absence of orthostatic hypotension
3. Absence of a known cause of autonomic neuropathy
4. Provocation of orthostatic symptoms (165)

Patients with the central beta hypersensitivity form of POTS tend to have high serum catecholamine levels (ie, norepinephrine greater than 600 ng/ml) and exhibit an excessive increase in supine heart rate in response to a low-dose isoproterenol infusion (heart rate increase greater than 30 bpm with a 1-mcg/min infusion) (152).

e. Treatment

As POTS becomes better understood and appropriately classified, management will be targeted according to the underlying cause. At present, there is little controlled data on long-term efficacy of therapy. Nevertheless, for the vast majority of patients, the management of POTS is medical. The use of ablative procedures involving the sinus node has been shown to worsen the symptoms. In one study, a group of seven patients with symptoms of POTS demonstrated that, although sinus node modification resulted in a reduction in the basal heart rate in five out of the seven patients, their symptoms persisted and in some cases worsened (142). In fact, four out of the five cases required insertion of a permanent pacemaker. The medical management of POTS can be divided into nonpharmacologic and pharmacologic.

NONPHARMACOLOGIC. The mainstay of nonpharmacologic treatment for all patients with POTS is volume expansion. All patients need five to eight 8-ounce (240 ml) glasses of fluids daily and a high-salt diet (10 to 15 grams daily) (161). Sleeping with the head of the bed elevated four inches (10 to 16 cm) (166,167) increases vasopressin secretion and expands plasma volume. Resistance training combined with the use of physical countermaneuvers has also been recommended (167). Radiolabeled erythrocytes have been used to demonstrate significant lower limb venous pooling in a range of patients with orthostatic intolerance (168). This study also demonstrated that heart rates could be returned to normal and symptoms could be relieved by inflation of military antishock trousers (MAST) to 45 mm Hg while patients were upright (168). The use of thigh-length compression stockings is, therefore, advocated in POTS patients. Anke pressure should be at least 30 mm Hg (152).

PHARMACOLOGIC. No single agent is appropriate for all cases of POTS, and combination therapy may often be necessary. The agent of choice will depend on the nature of the orthostatic intolerance and the tolerability of the agent. Beta blockers can be effective in the central beta-hypersensitive and in the partial dysautonomic forms of POTS because of unopposed alpha-receptor–mediated increase in peripheral vascular resistance (161,169). Fludrocortisone with or without bisoprolol has also been shown to improve symptoms in patients in whom idiopathic hypovolemia is present (169,170), but this requires high salt intake and regular monitoring of plasma potassium levels. Fludrocortisone has also been effectively combined with sleeping in the head-up tilt position (166). Centrally acting (eg, methylphenidate, clonidine) or peripherally acting agents (eg, midodrine) have also been effectively used (171,172). Phenobarbital has also been successfully used for the hyperadrenergic form of POTS but with the potential hazard of dependence (173). Disturbances in central serotonin production and regulation have also been implicated in the pathogenesis of POTS, and serotonin-specific uptake inhibitors have been used with some effect (174). The advantage of peripheral agents is that they are free of the centrally induced undesired effects. Octreotide, a predominantly splanchnic vasoconstrictor, has been successfully

Recommendations for Treatment of Postural Orthostatic Tachycardia Syndrome

Treatment	Recommendation	Class	Level of Evidence	References
Medical				
•*Nonpharmacologic**	Increase salt and fluid intake	IIa	B	(161,171)
	Head-up tilt sleep	IIa	B	(166)
	Physical maneuvers	IIa	B	(167)
	Compression stockings	IIa	B	(168)
•*Pharmacologic**				
Mineralocorticoids	Fludrocortisone	IIa	B	(161,169)
Beta blockers	Bisoprolol	IIa	B	(161,169)
Beta blockers plus mineralocorticoids	Bisoprolol plus Fludrocortisone	IIa	B	(169)
Central sympatholytic agents	Clonidine	IIb	B	(171,172)
Peripherally acting	Midodrine	IIb	B	(171,175)
Centrally acting	Methylphenidate	IIb	C	(173)
Serotonin-specific reuptake inhibitor	Fluoxetine	IIb	C	(152)
Others	Erythropoietin	IIb	B	(176)
	Ergotamine/octroetide	IIb	B	(175)
	Phenobarbitone	IIb	C	(152)
Interventional				
•*Catheter ablation/ surgical*	Sinus node modification, catheter ablation	III	B	(142)

The order in which treatment recommendations appear in this table within each class of recommendation does not necessarily reflect a preferred sequence of administration. Please refer to text for details. For pertinent drug dosing information, please refer to the ACC/AHA/ESC Guidelines on the Management of Patients With Atrial Fibrillation.

*Combination therapy commonly required.

used, indicating that the splanchnic bed may also be an important site for blood pooling (175). In the most refractory cases, erythropoietin may be tried. Erythropoietin not only increases red cell mass but also has vasoconstrictor properties that may benefit certain patients. However, the evidence suggests that the patients most likely to respond to this therapy are those with orthostatic hypotension and not orthostatic tachycardia (150,176).

4. Sinus Node Re-entry Tachycardia

Although sinus node re-entry tachycardia was conceptualized as early as 1943 (177), it was only first demonstrated in the rabbit heart in 1968 (178). The phenomenon was first demonstrated during an electrophysiological study in a patient in 1985 (179).

a. Definition

Sinus node re-entry tachycardias arise from re-entrant circuits involving the sinus node's production of paroxysmal, often nonsustained bursts of tachycardia with P waves that are similar, if not identical, to those in sinus rhythm. They are usually triggered and terminated abruptly by an atrial premature beat.

b. Mechanism

Heterogeneity of conduction within the sinus node provides a substrate for re-entry (180,181), but it is still not known whether the re-entry circuit is isolated within the sinus node itself, whether perisinus atrial tissue is necessary, or whether re-entry around a portion of the crista terminalis is responsible. However, the fact that this arrhythmia, like AVNRT, responds to vagal maneuvers and adenosine suggests that sinus node tissue is involved in the re-entrant circuit (182).

c. Presentation

The incidence of sinus node re-entry tachycardia in patients undergoing electrophysiological study for SVT ranges between 1.8 and 16.9% (183) and up to 27% for those with focal AT (184). Contrary to popular belief, there is a high incidence of underlying organic heart disease in patients with sinus node re-entry tachycardia (185). Patients present with symptoms of palpitations, lightheadedness, and presyncope. Syncope is extremely rare, as the rates of the tachycardia are rarely higher than 180 bpm. An important clue for diagnosis is the paroxysmal nature of the attacks.

d. Diagnosis

Sinus node re-entry tachycardia is diagnosed on the basis of invasive and noninvasive criteria (128). Clinically, the following features are highly suggestive of this arrhythmia:

1. The tachycardia and its associated symptoms are paroxysmal.
2. P-wave morphology is identical to sinus rhythm with the vector directed from superior to inferior and from right to left.
3. Endocardial atrial activation is in a high-to-low and right-to-left pattern, with an activation sequence similar

to that of sinus rhythm.

4. Induction and/or termination of the arrhythmia occurs with premature atrial stimuli.
5. Termination occurs with vagal maneuvers or adenosine.
6. Induction of the arrhythmia is independent of atrial or AV-nodal conduction time.

e. Treatment

There have been no controlled trials of drug prophylaxis involving patients with sinus node re-entrant tachycardia. Clinically suspected cases of symptomatic sinus node re-entrant tachycardia may respond to vagal maneuvers, adenosine, amiodarone, beta blockers, nondihydropyridine calcium-channel blockers, or even digoxin. Patients whose tachyarrhythmias are well tolerated and easily controlled by vagal maneuvers and/or drug therapy should not be considered for electrophysiological studies (89). Electrophysiological studies are indicated for patients with frequent or poorly tolerated episodes of tachycardia that do not adequately respond to drug therapy and for patients in whom the exact nature of the tachycardia is uncertain and for whom electrophysiological studies would aid appropriate therapy. Radiofrequency catheter ablation of persistent sinus node re-entry tachycardias identified through electrophysiological study is generally successful (183,184,186-188).

B. Atrioventricular Nodal Reciprocating Tachycardia

1. Definitions and Clinical Features

Atrioventricular nodal reciprocating tachycardia is the most common form of PSVT. It is more prevalent in females; is associated with palpitations, dizziness, and neck pulsations; and is not usually associated with structural heart disease. Rates of tachycardia are often between 140 and 250 per minute.

Although the re-entrant circuit was initially thought to be confined to the compact AV node, a more contemporary view recognizes the usual participation of perinodal atrial tissue as the most common component of the re-entrant circuit (189). However, it has been shown convincingly that AVNRT may persist without participation of atrial tissue. Atrioventricular nodal reciprocating tachycardia involves reciprocation between two functionally and anatomically distinct pathways (190). In most cases, the fast pathway appears to be located near the apex of Koch's triangle. This triangle is bounded by the tendon of Tadaro superiorly, and the tricuspid annulus is the base. The slow pathway extends inferoposterior to the compact AV-node tissue and stretches along the septal margin of the tricuspid annulus at the level of, or slightly superior to, the coronary sinus.

During typical AVNRT, the fast pathway serves as the retrograde limb of the circuit, whereas the slow pathway is the anterograde limb (ie, slow-fast AV-node re-entry). After conduction through the slow pathway to the His bundle and ventricle, brisk conduction back to the atrium over the fast pathway results in inscription of the shorter duration (40 ms) P wave during or close to the QRS complex (less than or equal to 70 ms) (Fig. 4) often with a pseudo-r´ in lead V1 (see Fig. 3). Less commonly (approximately 5 to 10%), the tachycardia circuit is reversed such that conduction proceeds by an anterograde route over the fast pathway and by a retrograde route over the slow pathway (ie, fast-slow AV-node re-entry, or atypical AVNRT) producing a long R-P tachycardia (ie, atypical AVNRT) (191), but other circuits may also be involved. The P wave, negative in leads III and aVF, is inscribed prior to the QRS. Infrequently, both limbs of the tachycardia circuit are composed of slowly conducting tissue (ie, slow-slow AV-node re-entry), and the P wave is inscribed after the QRS (ie, RP interval greater than or equal to 70 ms).

2. Acute Treatment

Acute evaluation and treatment of the patient with PSVT are discussed in Sections IV–A and IV–B.

3. Long-Term Pharmacologic Therapy

In patients with common, recurrent sustained episodes of AVNRT who prefer long-term oral therapy instead of catheter ablation, a spectrum of antiarrhythmic agents is available. Standard therapy includes nondihydropyridine calcium-channel blockers, beta blockers, and digoxin (192,193). In patients without structural heart disease who do not respond to AV-nodal–blocking agents, the class Ic drugs flecainide and propafenone have become the preferred choice (194-197). In most cases, class III drugs, such as sotalol or amiodarone, are unnecessary (198,199). Class Ia drugs, such as quinidine, procainamide, and disopyramide, have limited appeal due to their multidosing regimens, modest efficacy, and adverse and proarrhythmic effects (200-202).

A major limitation in evaluating antiarrhythmic agents for treating AVNRT is the general absence of large multicenter, randomized, placebo-controlled studies. The diagnosis of the rhythm disturbance is often on the basis of the 12-lead ECG, but the correct diagnosis of AVNRT can be reliably assured only when confirmed by intracardiac recordings, which have, by necessity, limited the number of patients and centers willing to participate in studies. As a result, some of the information that follows is derived from extrapolation of data from studies in patients with PSVT, where AVNRT is not differentiated from AVRT.

a. Prophylactic Pharmacologic Therapy

CALCIUM-CHANNEL BLOCKERS, BETA BLOCKERS, AND DIGOXIN. Comments regarding the long-term efficacy of calcium-channel blockers, beta blockers, and digoxin taken orally in the management of AVNRT are limited by the small number of randomized patients studied. A small (11 patients), randomized, double-blinded, placebo-controlled trial showed that verapamil taken orally decreases the number and duration of both patient-reported and electrophysiologically-recorded episodes (203). A similar finding was

demonstrated with doses of 360 to 480 mg/day with a trend toward greater effect with higher doses; however, the study was underpowered to detect a modest difference (204).

Oral digoxin (0.375 mg/day), verapamil (480 mg/day), and propranolol (240 mg/day) showed similar efficacy in 11 patients in a randomized, double-blinded, crossover study. There was no difference among the drugs with respect to frequency or duration of PSVT (192).

CLASS I DRUGS. The data showing efficacy of procainamide, quinidine, and disopyramide are from the older literature and are derived from small studies. These drugs are rarely used for treating AVNRT today (200-202).

Long-term benefits of oral flecainide in AVNRT were initially shown in an open-labeled study. At doses between 200 and 300 mg/day, flecainide completely suppressed episodes in 65% of patients (195). Several double-blinded, placebo-controlled trials have confirmed the efficacy of flecainide for prevention of recurrences (194,205). Events are reduced when compared with placebo, with an increase in the median time to the first recurrence and a greater interval between attacks. Open-labeled, long-term studies suggest excellent chronic tolerance and safety. In patients without structural heart disease, 7.6% discontinued the drug due to a suboptimal clinical response, and 5% discontinued it because of noncardiac (usually central nervous system) side effects (206). Class Ic agents (ie, flecainide and propafenone) are contraindicated for patients with structural heart disease. Moreover, class Ic drugs are often combined with beta-blocking agents to enhance efficacy and reduce the risk of one-to-one conduction over the AV node if atrial flutter occurs.

Flecainide appears to have greater long-term efficacy than verapamil. Although both drugs (median doses 200 mg/day and 240 mg/day, respectively) demonstrated an equivalent reduction in the frequency of episodes, 30% of patients had complete suppression of all symptomatic episodes with flecainide, whereas 13% had complete suppression with verapamil (207). Discontinuation rates due to adverse effects were equivalent, 19% and 24%, respectively.

Propafenone is also an effective drug for prophylaxis of AVNRT. In a double-blinded, placebo-controlled trial, in which time to treatment failure was analyzed, the RR of treatment failure for placebo versus propafenone was 6.8 (208). A single-center, randomized, double-blinded, placebo-controlled study showed that propafenone (300 mg taken three times per day) reduces the recurrence rate to one fifth of that of placebo (197).

CLASS III DRUGS. Limited prospective data are available for use of class III drugs (eg, amiodarone, sotalol, dofetilide). Although many have been used effectively to prevent recurrences, routine use should be avoided due to their toxicities, including proarrhythmia (ie, torsades de pointes). A placebo-controlled trial found sotalol to be superior to placebo in prolonging time to recurrence of PSVT (199). With regard to dofetilide, a multicenter, randomized, placebo-controlled study showed that patients with PSVT had a 50% probability of complete symptomatic suppression with dofetilide over a 6-month follow up (500 mcg taken twice per day), whereas the probability of suppression in the control group was 6% (*P* less than 0.001). There were no proarrhythmic events (198). In this study, dofetilide was shown to be as effective as propafenone (150 mg taken three times per day).

There is a paucity of data regarding the effects of amiodarone on AVNRT (209). In one open-labeled study in the electrophysiology laboratory, IV amiodarone (5 mg/kg over 5 minutes) terminated tachycardia in seven out of nine patients. Treatment with oral amiodarone (maintenance dose 200 to 400 mg/day) for 66 plus or minus 24 days prevented recurrence and inducibility in all patients, with its predominant effect being the depression of conduction in the retrograde fast pathway (210). Of note, amiodarone has been shown to be safe in structural heart disease, particularly LV dysfunction.

b. Single-Dose Oral Therapy (Pill-in-the-Pocket)

Single-dose therapy refers to administration of a drug only during an episode of tachycardia for the purpose of termination of the arrhythmia when vagal maneuvers alone are not effective. This approach is appropriate to consider for patients with infrequent episodes of AVNRT that are prolonged (ie, lasting hours) but yet well tolerated (211). This approach obviates exposure of patients to chronic and unnecessary therapy between their rare arrhythmic events. It necessitates the use of a drug that has a short time to take effect (ie, immediate-release preparations). Candidate patients should be free of significant LV dysfunction, sinus bradycardia, or pre-excitation.

A single oral dose of flecainide (approximately 3 mg/kg) has been reported to terminate acute episodes of AVNRT in adolescents and young adults without structural heart disease (196), although it offered no benefit compared with placebo in other studies (211).

Single-dose oral therapy with diltiazem (120 mg) plus propranolol (80 mg) has been shown to be superior to both placebo and flecainide in sequential testing in 33 patients with PSVT in terms of conversion to sinus rhythm (211). Favorable results comparing diltiazem plus propranolol with placebo have also been reported by others (212). Hypotension and sinus bradycardia are rare complications. Single-dose therapy with diltiazem plus propranolol is associated with a significant reduction in emergency room visits in appropriately selected patients (211).

4. Catheter Ablation

Radiofrequency ablation for AVNRT originated in the observation that surgical dissection in discrete regions of the perinodal area could interrupt fast- or slow-pathway conduction (213,214). This finding led to the development of percutaneous, catheter-based techniques designed to modify or eliminate fast-pathway conduction. Energy (initially DC and later RF) was applied in the region of the apex of Koch's triangle, along the superior aspect of the tricuspid annulus

Recommendations for Long-Term Treatment of Patients With Recurrent AVNRT

Clinical Presentation	Recommendation	Class	Level of Evidence	References
Poorly tolerated AVNRT with hemodynamic intolerance	Catheter ablation	I	B	(189)
	Verapamil, diltiazem, beta blockers, sotalol, amiodarone	IIa	C	(189)
	Flecainide,* propafenone*	IIa	C	
Recurrent symptomatic AVNRT	Catheter ablation	I	B	(189)
	Verapamil	I	B	(203)
	Diltiazem, beta blockers	I	C	(192)
	Digoxin†	IIb	C	
Recurrent AVNRT unresponsive to beta blockade or calcium-channel blocker and patient not desiring RF ablation	Flecainide,* propafenone,* sotalol	IIa	B	(194,197-199,205,208)
	Amiodarone	IIb	C	(210)
AVNRT with infrequent or single episode in patients who desire complete control of arrhythmia	Catheter ablation	I	B	
Documented PSVT with only dual AV-nodal pathways or single echo beats demonstrated during electrophysiological study and no other identified cause of arrhythmia	Verapamil, diltiazem, beta blockers, flecainide,* propafenone*	I	C	
	Catheter ablation‡	I	B	
Infrequent, well-tolerated AVNRT	No therapy	I	C	(189)
	Vagal maneuvers	I	B	
	"Pill-in-the-pocket"	I	B	
	Verapamil, diltiazem, beta blockers	I	B	
	Catheter ablation	I	B	(227)

The order in which treatment recommendations appear in this table within each class of recommendation does not necessarily reflect a preferred sequence of administration. Please refer to text for details. For pertinent drug dosing information, please refer to the ACC/AHA/ESC Guidelines on the Management of Patients With Atrial Fibrillation.

*Relatively contraindicated for patients with coronary artery disease, LV dysfunction, or other significant heart disease.

†Often ineffective because pharmacological effects can be overridden by enhanced sympathetic tone.

‡Decision depends on symptoms.

AV indicates atrioventricular; AVNRT, atrioventricular nodal reciprocating tachycardia; LV, left ventricular; PSVT, paroxysmal supraventricular tachycardia; RF, radiofrequency.

(215,216). Success with this technique was associated with prolongation of the PR interval (ie, first-degree AV block), elimination of retrograde fast-pathway conduction, and non-inducibility of AVNRT. Success rates for this technique are approximately 90%. The major procedural risk is significant, 5 to 10% risk of complete AV block caused by proximity of the fast pathway to the His bundle (217).

Targeting the slow pathway along the posteroseptal region of the tricuspid annulus markedly reduces the risk of heart block and is the preferred approach. A prospective, randomized comparison of the fast- and slow-pathway approaches demonstrates equivalent success rates (218). Advantages of slow-pathway ablation include a lower incidence of complete AV block (1 vs. 8%) and the absence of the hemodynamic consequences of marked prolongation of the PR interval. Hence, slow pathway ablation is always used initially and fast pathway ablation is considered only when slow pathway ablation fails. Mapping to target discrete "slow-pathway" potentials was proposed originally (219), but an anatomical approach targeting the region between the coronary sinus ostium and the tricuspid annulus is also effective. A randomized study comparing an anatomical versus "slow-pathway potential-guided" approach showed no difference in success,

number of RF applications, duration of ablation or fluoroscopy, or complications (220).

In the fast-slow form of AVNRT, the slow pathway can be targeted directly by mapping the atrial exit site during tachycardia. In the slow-slow form of AVNRT, the retrograde slow pathway is likely to be composed of tissue originating from an extension of the AV node along the left side of the interatrial septum. Earliest retrograde atrial activation can be successfully and safely ablated within the ostium of the coronary sinus (221).

The NASPE Prospective Cardiac Ablation Registry included 1197 patients who underwent AV-nodal modification for AVNRT. Success was achieved in 96.1%, and the only significant complication was a 1% incidence of second-degree or third-degree AV block (222). These data have been confirmed by others (223). Atrioventricular block may complicate slow-pathway ablation due to posterior displacement of the fast pathway, superior displacement of the slow pathway (and coronary sinus), or inadvertent anterior displacement of the catheter during RF application. Pre-existing first-degree AV block does not appear to increase appreciably the risk of developing complete AV block (224), although caution is advised. The recurrence rate after ablation is approximately 3 to 7% (223,225,226).

Ablation of the slow pathway may be performed in patients with documented SVT (which is morphologically consistent with AVNRT) but in whom only dual AV-nodal physiology (but not tachycardia) is demonstrated during electrophysiological study (227). Because arrhythmia induction is not an available endpoint for successful ablation in this circumstance, the surrogate endpoint of an accelerated junctional rhythm during ablation is a good indication of slow-pathway ablation.

Slow-pathway ablation may be considered at the discretion of the physician when sustained (greater than 30 seconds) AVNRT is induced incidentally during an ablation procedure directed at a different clinical tachycardia.

Indications for ablation depend on clinical judgment and patient preference. Factors that contribute to the therapeutic decision include the frequency and duration of tachycardia, tolerance of symptoms, effectiveness and tolerance of antiarrhythmic drugs, need for lifelong drug therapy, and the presence of concomitant structural heart disease. Catheter ablation has become the preferred therapy, compared with long-term pharmacologic therapy, for management of patients with AVNRT. The decision to ablate or proceed with drug therapy as initial therapy is, however, often patient specific, related to lifestyle issues (eg, planned pregnancy, competitive athlete, recreational pilot), affected by individual inclinations or aversions with regard to an invasive procedure or the chronicity of drug therapy, and influenced by the availability of an experienced center for ablation. Because drug efficacy is in the range of 30 to 50%, catheter ablation may be offered as first-line therapy for patients with frequent episodes of tachycardia. Patients considering RF ablation must be willing to accept the risk, albeit low, of AV block and pacemaker implantation.

C. Focal and Nonparoxysmal Junctional Tachycardia

1. Focal Junctional Tachycardia

a. Definition

Abnormally rapid discharges from the junctional region have been designated by a number of terms, each of which has deficiencies. For example, some refer to these disorders as "junctional ectopic tachycardia." The problem with this term is redundancy because all pacemakers outside the sinus node are in fact ectopic. The term "automatic junctional tachycardia" suggests that the dominant mechanism is abnormal automaticity; however, mechanisms other than abnormal automaticity may be operative. The writing committee believes it reasonable to designate these arrhythmias as focal junctional tachycardia, which has a neutral connotation with regard to arrhythmic mechanism.

b. Diagnoses

The unifying feature of focal junctional tachycardias is their origin from the AV node or His bundle. This site of arrhythmia origin results in varied ECG manifestations because the arrhythmia requires participation of neither the atrium nor the ventricle for its propagation. The ECG features of focal junctional tachycardia include heart rates of 110 to 250 bpm and a narrow complex or typical BBB conduction pattern. Atrioventricular dissociation is often present (Fig. 10), although one-to-one retrograde conduction may be transiently observed. On occasion, the junctional rhythm is quite erratic, suggesting AF. Finally, isolated, concealed junctional extrasystoles that fail to conduct to the ventricles may produce episodic AV block by rendering the AV node intermittently refractory.

During electrophysiological study, each ventricular depolarization is preceded by a His bundle deflection (228,229). The precise electrophysiological mechanism of this arrhythmia is thought to be either abnormal automaticity or triggered activity based on its response to beta-adrenergic stimulation and calcium-channel blockade (230,231).

c. Clinical Features

Focal junctional tachycardia, also known as automatic or paroxysmal junctional tachycardia, is a very uncommon arrhythmia. It is rare in the pediatric population and even less common in adults. Under the common umbrella of "focal junctional tachycardia" are several distinct clinical syndromes. The most prevalent among these, so-called "congenital junctional ectopic tachycardia" and "postoperative junctional ectopic tachycardia," occur exclusively in pediatric patients and are, therefore, outside of the scope of this document.

Focal junctional tachycardia usually presents in young adulthood. It has been speculated that this form of arrhythmia is an adult extension of the pediatric disorder commonly termed "congenital junctional ectopic tachycardia." If this is

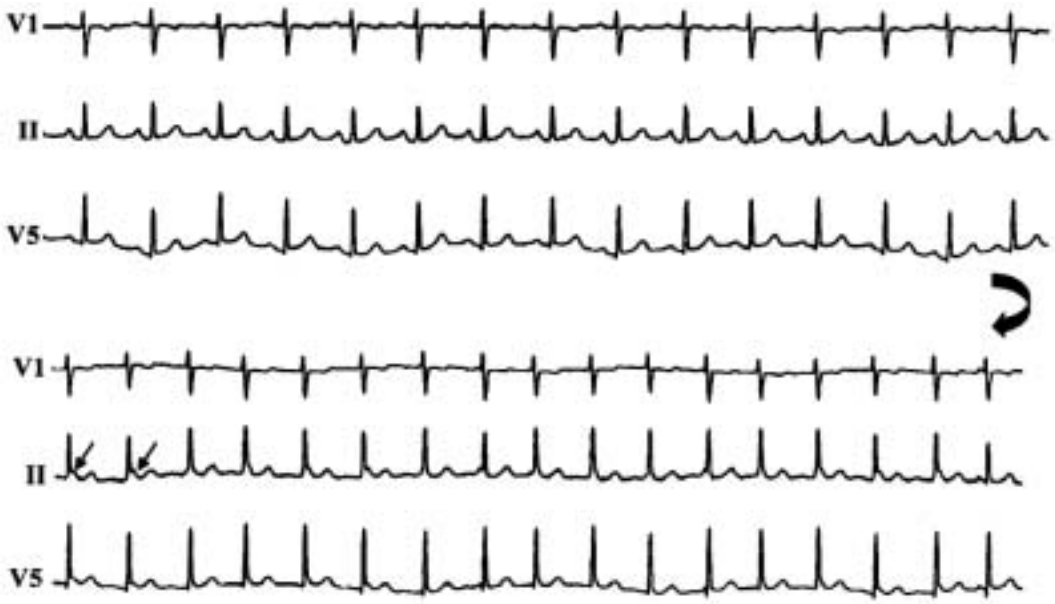

Figure 10. Surface ECG recording from leads V1, II, and V5 in a patient with focal junctional tachycardia. The upper panel shows sinus rhythm. The lower panel shows tachycardia onset with the characteristic finding of isorhythmic AV dissociation (arrows). The large arrow signifies continuous recording. AV indicates atrioventricular; ECG, electrocardiogram.

the case, then it appears to be more benign than is the pediatric form. This arrhythmia is usually exercise or stress related and may be found in patients with structurally normal hearts or in patients with congenital abnormalities, such as atrial or ventricular septal defects (230). The patients are often quite symptomatic and, if untreated, may develop heart failure, particularly if the tachycardia is incessant.

d. Management

Relatively little information is available about the response of rapid focal junctional tachycardia to suppressive drug therapy. Patients typically show some responsiveness to beta blockade. The tachycardia can be slowed or terminated with IV flecainide and shows some positive response to long-term oral therapy (232,233). Drug therapy is only variably successful, and ablative techniques have been introduced to cure tachycardia. Catheter ablation can be curative by destroying the foci adjacent to the AV node, but the procedure appears to be associated with risk (5 to 10%) of AV block (234-236).

In one series, 17 patients with focal junctional tachycardia were referred for electrophysiological testing and possible catheter ablation. Ten of 11 patients undergoing RF catheter ablation in this series had acute tachycardia elimination. Eight patients remained symptom free during follow-up (228). The related pediatric disorder has been successfully treated with propafenone (237), sotalol (238), and amiodarone (239,240), although the latter is limited by its slow onset of action.

2. Nonparoxysmal Junctional Tachycardia

a. Definition and Clinical Features

Nonparoxysmal junctional tachycardia is a benign arrhythmia that is characterized by a narrow complex tachycardia with rates of 70 to 120 bpm. The arrhythmia mechanism is thought to be enhanced automaticity arising from a high junctional focus (68) or in response to a triggered mechanism (241). It shows a typical "warm-up" and "cool-down" pattern and cannot be terminated by pacing maneuvers. The most important feature about this tachycardia is that it may be a marker for a serious underlying condition, such as digitalis toxicity (242), postcardiac surgery, hypokalemia, or myocardial ischemia. Other associated conditions include chronic obstructive lung disease with hypoxia, and inflammatory myocarditis. Unlike the more rapid form of focal junctional tachycardia, there is commonly one-to-one AV association. In some cases, particularly in the setting of digitalis toxicity, anterograde AV-nodal Wenckebach conduction block may be observed (241,243).

The diagnosis must be differentiated from other types of narrow complex tachycardia, including AT, AVNRT, and AVRT. Usually, the clinical setting in which the arrhythmia presents and the ECG findings allow the clinician to ascertain the arrhythmia mechanism. However, in some cases, the mechanism may be determined only with invasive electrophysiological testing.

b. Management

The mainstay of managing nonparoxysmal junctional tachycardia is to correct the underlying abnormality. Withholding digitalis when junctional tachycardia is the only clinical manifestation of toxicity is usually adequate. However, if ventricular arrhythmias or high-grade heart block are observed, then treatment with digitalis-binding agents may be indicated. It is not unusual for automatic activity from the AV node to exceed the sinus rate, leading to loss of AV synchrony. This should be regarded as a physiological condition, and no specific therapy is indicated. Persisting junctional tachycardia may be suppressed by beta blockers or calcium-channel blockers (68). In rare cases, the emergence of a junc-

Recommendations for Treatment of Focal and Nonparoxysmal Junctional Tachycardia Syndromes

Clinical Presentation	Recommendation	Class	Level of Evidence	References
Focal junctional tachycardia	Beta blockers	IIa	C	
	Flecainide	IIa	C	(232)
	Propafenone*	IIa	C	(237)
	Sotalol*	IIa	C	(238)
	Amiodarone*	IIa	C	(239,240)
	Catheter ablation	IIa	C	(228,234-236)
Nonparoxysmal junctional tachycardia	Reverse digitalis toxicity	I	C	(242,243)
	Correct hypokalemia	I	C	
	Treat myocardial ischemia	I	C	(244)
	Beta blockers, calcium-channel blockers	IIa	C	(68,245)

The order in which treatment recommendations appear in this table within each class of recommendation does not necessarily reflect a preferred sequence of administration. Please refer to text for details. For pertinent drug dosing information, please refer to the ACC/AHA/ESC Guidelines on the Management of Patients With Atrial Fibrillation.

*Data available for pediatric patients only.

tional rhythm is the result of sinus node dysfunction. Sympathetic stimulation of the AV-junction automaticity can lead to an AV-junctional rhythm that supersedes the sinus rhythm. In these cases, symptoms mimicking "pacemaker syndrome" may occur due to retrograde conduction from the AV junction to the atrium and resultant atrial contraction against closed AV valves, resulting in cannon A waves and possible hypotension. Atrial pacing is an effective treatment for this condition.

D. Atrioventicular Reciprocating Tachycardia (Extra Nodal Accessory Pathways)

Typical accessory pathways are extra nodal pathways that connect the myocardium of the atrium and the ventricle across the AV groove. Delta waves detectable on an ECG have been reported to be present in 0.15 to 0.25% of the general population (246,247). Pathway conduction may be intermittent. A higher prevalence of 0.55% has been reported in first-degree relatives of patients with accessory pathways (248). Accessory pathways can be classified on the basis of their location along the mitral or tricuspid annulus; type of conduction (decremental [ie, progressive delay in accessory pathway conduction in response to increased paced rates] or nondecremental); and whether they are capable of anterograde conduction, retrograde conduction, or both. Accessory pathways usually exhibit rapid, nondecremental conduction, similar to that present in normal His-Purkinje tissue and atrial or ventricular myocardium. Approximately 8% of accessory pathways display decremental anterograde or retrograde conduction (249). The term "permanent form of junctional reciprocating tachycardia" is used to refer to a rare clinical syndrome involving a slowly conducting, concealed, usually posteroseptal (inferoseptal) accessory pathway. This syndrome is characterized by an incessant SVT, usually with negative P waves in leads II, III, and aVF and a long RP interval (RP greater than PR).

Accessory pathways that are capable of only retrograde conduction are referred to as "concealed," whereas those capable of anterograde conduction are "manifest," demonstrating pre-excitation on a standard ECG. The degree of pre-excitation is determined by the relative conduction to the ventricle over the AV node-His bundle axis versus the accessory pathway. In some patients, anterograde conduction is apparent only with pacing close to the atrial insertion site, as, for example, for left-lateral-located pathways. Manifest accessory pathways usually conduct in both anterograde and retrograde directions (250). Those that conduct in the anterograde direction only are uncommon, whereas those that conduct in the retrograde direction are common.

The diagnosis of WPW syndrome is reserved for patients who have both pre-excitation and tachyarrhythmias. Among patients with WPW syndrome, AVRT is the most common arrhythmia, accounting for 95% of re-entrant tachycardias that occur in patients with an accessory pathway.

Atrioventricular re-entry tachycardia is further subclassified into orthodromic and antidromic AVRT. During orthodromic AVRT, the re-entrant impulse conducts over the AV node and the specialized conduction system from the atrium to the ventricle and utilizes the accessory pathway for conduction from the ventricle to the atrium. During antidromic AVRT, the re-entrant impulse travels in the reverse direction, with anterograde conduction from the atrium to the ventricle occurring via the accessory pathway and retrograde conduction over the AV node or a second accessory pathway. Antidromic AVRT occurs in only 5 to 10% of patients with WPW syndrome. Pre-excited tachycardias can also occur in patients with AT, atrial flutter, AF, or AVNRT, with the accessory pathway acting as a bystander (ie, not a critical part of the tachycardia circuit).

Atrial fibrillation is a potentially life-threatening arrhythmia in patients with WPW syndrome. If an accessory pathway has a short anterograde refractory period, then rapid repetitive conduction to the ventricles during AF can result in

a rapid ventricular response with subsequent degeneration to VF (251-253). It has been estimated that one third of patients with WPW syndrome also have AF (254). Accessory pathways appear to play a pathophysiological role in the development of AF in these patients, as most are young and do not have structural heart disease. Rapid AVRT may play a role in initiating AF in these patients. Surgical or catheter ablation of accessory pathways usually eliminates AF as well as AVRT (255,256).

1. Sudden Death in WPW Syndrome and Risk Stratification

The incidence of sudden cardiac death in patients with WPW syndrome has been estimated to range from 0.15 to 0.39% (253) over 3- to 10-year follow-up (257,258). It is unusual for cardiac arrest to be the first symptomatic manifestation of WPW syndrome (253). Conversely, in about half of the cardiac arrest cases in WPW patients, it is the first manifestation of WPW syndrome (258). Given the potential for AF among patients with WPW syndrome and the concern about sudden cardiac death resulting from rapid pre-excited AF, even the low annual incidence of sudden death among patients with WPW syndrome is of note and supports the concept of liberal indications for catheter ablation.

Studies of WPW syndrome patients who have experienced cardiac arrest have retrospectively identified a number of markers that identify patients at increased risk (251,258-262). These include 1) a shortest pre-excited R-R interval less than 250 ms during spontaneous or induced AF, 2) a history of symptomatic tachycardia, 3) multiple accessory pathways, and 4) Ebstein's anomaly. A high incidence of sudden death has been reported in familial WPW syndrome. This familial presentation is, however, exceedingly rare (263). Several noninvasive and invasive tests have been proposed as useful in risk-stratifying patients for sudden death risk. The detection of intermittent pre-excitation, which is characterized by an abrupt loss of the delta wave and normalization of the QRS complex, is evidence that an accessory pathway has a relatively long refractory period and is unlikely to precipitate VF (264). The loss of pre-excitation after administration of the antiarrhythmic drug procainamide has also been used to indicate a low-risk subgroup (262). Noninvasive tests are considered inferior to invasive electrophysiological assessment for risk of sudden cardiac death. For this reason, noninvasive tests currently play little role in patient management.

2. Acute Treatment

The approach to acute evaluation and management during a sustained regular tachycardia is addressed in Sections IV–A and IV–B. The approach to acute termination of these arrhythmias generally differs from that used for long-term suppression and prevention of further episodes of SVT.

a. Special Considerations for Patients With Wide-Complex (Pre-excited) Tachycardias

In patients with antidromic tachycardia, drug treatment may be directed at the accessory pathway or at the AV node because both are critical components of the tachycardia circuit. Atrioventricular nodal–blocking drugs would, however, be ineffective in patients who have anterograde conduction over one pathway and retrograde conduction over a separate accessory pathway because the AV node is not involved in the circuit. Adenosine should be used with caution because it may produce AF with a rapid ventricular rate in pre-excited tachycardias. Ibutilide, procainamide, or flecainide, which are capable of slowing the conduction through the pathway, are preferred.

Pre-excited tachycardias occurring in patients with either AT or atrial flutter with a bystander accessory pathway may present with a one-to-one conduction over the pathway. Caution is advised against AV-nodal–blocking agents, which would obviously be ineffective in this situation. Antiarrhythmic drugs, which prevent rapid conduction through the bystander pathway, are preferable, even if they may not convert the atrial arrhythmia. Similarly, it is preferable to treat pre-excited AF by IV ibutilide, flecainide, or procainamide.

Patients with AVNRT and pre-excited tachycardia with a bystander accessory pathway may respond to AV-nodal–blocking drugs, which are usually discouraged because of the risk of AV-nodal blockade and acceleration of ventricular rate if AF occurs.

3. Long-Term Pharmacologic Therapy

Antiarrhythmic drugs represent one therapeutic option for management of accessory pathway mediated-arrhythmias, but they have been increasingly replaced by catheter ablation. Antiarrhythmic drugs that primarily modify conduction through the AV node include digoxin, verapamil, beta blockers, adenosine, and diltiazem. Antiarrhythmic drugs that depress conduction across the accessory pathway include class I drugs, such as procainamide, disopyramide, propafenone, and flecainide, as well class III antiarrhythmic drugs, such as ibutilide, sotalol, and amiodarone.

a. Prophylactic Pharmacologic Therapy

There have been no controlled trials of drug prophylaxis involving patients with AVRT; however, a number of small, nonrandomized trials have been performed (each involving fewer than 50 patients), and they have reported the safety and efficacy of drug therapy for maintenance of sinus rhythm in patients with supraventricular arrhythmias. A subset of the patients in these studies had AVRT as their underlying arrhythmia. Available data do not allow a comparison of the efficacy of these drugs relative to one another. The drugs available to treat AVRT include any drug that alters either conduction through the AV node (eg, nondihydropyridine calcium-channel blockers, beta blockers, digoxin) or a drug that alters conduction through the atrium, ventricle, or acces-

sory pathway (eg, class Ia, Ic, or III antiarrhythmic agents). The available data are outlined below. Of note is that no studies have examined the efficacy of chronic oral beta blockers in the treatment of AVRT and/or WPW syndrome. The absence of studies specifically examining the role of beta-blocker therapy in the treatment of WPW syndrome likely reflects the fact that catheter ablation is the therapy of choice for these patients. Despite the absence of data from clinical trials, chronic oral beta-blocker therapy may be used for treatment of patients with WPW syndrome, particularly if their accessory pathway has been demonstrated during electrophysiological testing to be incapable of rapid anterograde conduction.

PROPAFENONE. The largest published study that reported the efficacy of propafenone in adult patients involved 11 individuals. Propafenone resulted in anterograde conduction block in the accessory pathway in 4 of 9 patients and retrograde block in 3 of 11 patients. Atrioventricular re-entry tachycardia was rendered noninducible in 6 of 11 patients. During 9 plus or minus 6 months of follow-up, none of the 10 patients discharged on a combination of propafenone and a beta blocker experienced a recurrence. No major side effects were reported (265). Other small trials have evaluated the efficacy of propafenone in the treatment of AVRT in children (266-269). The largest of these involved 41 children. Chronic administration of propafenone was effective in 69%. Side effects occurred in 25% of these patients (248).

FLECAINIDE. A number of studies have examined the acute and long-term efficacy of oral and IV flecainide in the treatment of patients with AVRT. The largest of these studies involved 20 patients with AVRT (270). The oral administration of flecainide (200 to 300 mg/day) resulted in an inability to induce sustained tachycardia in 17 of these 20 patients. The electrophysiological effects of flecainide were partially reversed by administration of isoproterenol. During 15 plus or minus 7 months of follow-up on oral flecainide treatment, 3 patients developed a recurrence of tachycardia. Other studies have reported similar findings (271-276). The addition of a beta blocker results in greater efficacy, with greater than 90% of patients achieving abolition of symptomatic tachycardia (270,277). In addition to studies that specifically focused on patients with a known AVRT, several randomized trials have evaluated the efficacy of flecainide in the treatment of patients with PSVT of undetermined tachycardia mechanism. One study enrolled 34 patients with PSVT in a double-blinded, placebo-controlled trial with an 8-week crossover trial design (205). Flecainide was shown to be superior to placebo; 8 of the 34 patients had a recurrence during flecainide therapy, compared with 29 of 34 patients having a recurrence on placebo (205). Treatment with flecainide also increases the time to first symptomatic event and time to subsequent events.

SOTALOL. The efficacy of oral sotalol in the prevention of AVRT has been reported in a single study (278), which involved 17 patients with an accessory pathway. Fourteen of 15 patients with inducible sustained tachycardia during electrophysiological testing continued to have inducible tachycardia after administration of IV sotalol. Thirteen of the 16 patients who were discharged taking oral sotalol were free of symptomatic recurrences during a median of 36 months of follow-up (278).

AMIODARONE. Several studies have evaluated the efficacy of amiodarone in the treatment of patients with accessory pathway-mediated tachycardias (279-282). However, these studies do not demonstrate that amiodarone is superior to class Ic antiarrhythmic agents or sotalol. As a result of these findings, combined with the well-recognized organ toxicity associated with amiodarone and the high rate of discontinuation of this drug, amiodarone generally is not warranted for treatment of patients with accessory pathways. Exceptions are for patients with structural heart disease who are not thought to be candidates for catheter ablation.

VERAPAMIL. The efficacy of verapamil in the prevention of AVRT has been reported in a single study, which involved seven patients (283). Four of the 17 patients continued to have inducible AVRT during electrophysiological testing despite treatment with oral verapamil. Adequate follow-up data in these patients were not provided. Intravenous verapamil can precipitate hemodynamic deterioration during AF. Verapamil and diltiazem should not be used as the sole therapy for patients with accessory pathways that might be capable of rapid conduction during AF. This concern also applies to digoxin, which also should not be used in this situation.

OTHER DRUGS. No studies have been performed to determine the short- or long-term efficacy of procainamide or quinidine in the treatment of AVRT.

b. Single-Dose Oral Therapy (Pill-in-the-Pocket)

Some patients with infrequent episodes of tachycardia may be managed with the single-dose, "pill-in-the-pocket" approach: taking an antiarrhythmic drug only at the onset of a tachycardia episode (211). This approach to treatment is reserved for patients without pre-excitation and with uncommon and hemodynamically tolerated tachycardia. A recent study reported that 94% of induced PSVT episodes were terminated in the electrophysiology laboratory within 32 minutes plus or minus 22 minutes by administration of a combination of diltiazem (120 mg) plus propranolol (80 mg) (211). This treatment was successful in terminating PSVT within 2 hours during outpatient follow-up in 81% of patients. Another finding of this study was that flecainide, when given as a single dose for acute termination of PSVT, was significantly less effective than the combination of diltiazem and propranolol.

4. Catheter Ablation

Catheter ablation of accessory pathways is performed in conjunction with a diagnostic electrophysiological test. The purposes of the electrophysiological test are to confirm the presence of an accessory pathway, determine its conduction characteristics, and define its role in the patient's clinical arrhyth-

mia. Once the arrhythmia is localized, ablation is performed using a steerable ablation catheter. There have been no prospective, randomized clinical trials that have evaluated the safety and efficacy of catheter ablation of accessory pathways; however, the results of catheter ablation of accessory pathways have been reported in a large number of single-center trials (284-288), one multicenter trial (225), and several prospective registries (222,289,290). The initial efficacy of catheter ablation of accessory pathways is approximately 95% in most series (225,284-288). The success rate for catheter ablation of left free-wall accessory pathways is slightly higher than for catheter ablation of accessory pathways in other locations. After an initially successful procedure, resolution of the inflammation or edema associated with the initial injury allows recurrence of accessory pathway conduction in approximately 5% of patients. Accessory pathways that recur can usually be successfully ablated during a second session.

Complications associated with catheter ablation of accessory pathways result from radiation exposure, vascular access (eg, hematomas, deep venous thrombosis, arterial perforation, arteriovenous fistula, pneumothorax), catheter manipulation (eg, valvular damage, microemboli, perforation of the coronary sinus or myocardial wall, coronary artery dissection, thrombosis), or delivery of RF energy (eg, AV block, myocardial perforation, coronary artery spasm or occlusion, transient ischemic attacks, cerebrovascular accidents [284]) (222,225,285-290). The procedure-related mortality reported for catheter ablation of accessory pathways ranges from 0 to 0.2% (222,225,284-290). The voluntary Multicentre European Radiofrequency Survey (MERFS) reported data from 2222 patients who underwent catheter ablation of an accessory pathway (290). The overall complication rate was 4.4%, including 3 deaths (0.13%). The 1995 NASPE survey of 5427 patients who underwent catheter ablation of an accessory pathway reported a total of 99 (1.82%) significant complications, including 4 procedure-related deaths (0.08%) (289). Among the 500 patients who underwent catheter ablation of an accessory pathway as part of a prospective, multicenter clinical trial, there was 1 death (0.2%). This patient died of dissection of the left main coronary artery during an attempt at catheter ablation of a left free-wall accessory pathway (225). The most common major complications are complete AV block and cardiac tamponade. The incidence of inadvertent complete AV block ranges from 0.17 to 1.0%. Most occur in the setting of attempted ablation of septal accessory pathways located close to the AV junction. The frequency of cardiac tamponade varies between 0.13 and 1.1%.

5. Management of Patients With Asymptomatic Accessory Pathways

An ECG pattern of pre-excitation is occasionally encountered in a subject who has no symptoms of arrhythmia. The role of electrophysiological testing and catheter ablation in asymptomatic patients with pre-excitation is controversial. One-third of asymptomatic individuals younger than 40 years of age when pre-excitation was identified eventually developed symptoms, whereas no patients in whom pre-excitation was first uncovered after the age of 40 years developed symptoms (253). Most patients with asymptomatic pre-excitation have a good prognosis; cardiac arrest is rarely the first manifestation of the disease (258). Prior studies have reported that approximately 20% of asymptomatic patients will demonstrate a rapid ventricular rate during AF induced during electrophysiological testing (257,291). However, during follow-up, very few patients developed symptomatic arrhythmias, and none of these individuals experienced a cardiac arrest (257,291). The positive predictive value of invasive electrophysiological testing is considered to be too low to justify routine use in asymptomatic patients (89,258,292). The decision to ablate pathways in individuals with high-risk occupations, such as school bus drivers, pilots, and scuba divers (292), is made on the basis of individual clinical considerations (89). These recommendations are likely to remain unchanged despite the results of a study that identified the results of electrophysiological testing as an important predictor of arrhythmic events in patients with asymptomatic pre-excitation (293). This study reported the follow-up of 212 patients with asymptomatic pre-excitation, all of whom underwent a baseline electrophysiological study. After 38 plus or minus 16 months of follow-up, 33 patients became symptomatic, and 3 of these patients experienced VF (resulting in death in 1 patient). The most important factor in predicting outcome was the inducibility of AVRT or AF during the baseline electrophysiological study. The presence of multiple accessory pathways was also identified as a predictor of future arrhythmic events. Of the 115 noninducible patients, only 3.4% developed a symptomatic supraventricular arrhythmia during follow-up. In contrast, 62% of the 47 inducible patients developed a symptomatic arrhythmia during follow-up (including the 3 patients who experienced VF).

Patients with asymptomatic pre-excitation should be encouraged to seek medical expertise whenever arrhythmia-related symptoms occur. The potential value of electrophysiological testing in identifying high-risk patients who may benefit from catheter ablation must be balanced against the approximately 2% risk of a major complication associated with catheter ablation.

6. Summary of Management

In general, patients who have WPW syndrome (pre-excitation and symptoms), and particularly those with hemodynamic instability during their arrhythmia, should undergo catheter ablation as first-line therapy. Patients who experience uncommon, minimally symptomatic episodes of SVT who do not have evidence of pre-excitation can be treated with a variety of approaches. These patients with concealed accessory pathways can be managed as patients with AVNRT. Patient preference is always an important consideration. Catheter ablation has sufficient efficacy and low risk to be used for symptomatic patients, either as initial therapy or for patients experiencing side effects or arrhythmia recurrence during drug therapy.

Recommendations for Long-Term Therapy of Accessory Pathway–Mediated Arrhythmias

Arrhythmia	Recommendation	Class	Level of Evidence	References
WPW syndrome (pre-excitation and symptomatic arrhythmias), well tolerated	Catheter ablation	I	B	(89,222,265,285)
	Flecainide, propafenone	IIa	C	(205,265-277)
	Sotalol, amiodarone, beta blockers	IIa	C	(278-282)
	Verapamil, diltiazem, digoxin	III	C	(283)
WPW syndrome (with AF and rapid-conduction or poorly tolerated AVRT)	Catheter ablation	I	B	(222,225, 284-290)
AVRT, poorly tolerated (no pre-excitation)	Catheter ablation	I	B	(222,225,284-290)
	Flecainide, propafenone	IIa	C	(205,265-277)
	Sotalol, amiodarone	IIa	C	(278-282)
	Beta blockers	IIb	C	(283)
	Verapamil, diltiazem, digoxin	III	C	(283)
Single or infrequent AVRT episode(s) (no pre-excitation)	None	I	C	
	Vagal maneuvers	I	B	
	’Pill-in-the-pocket”—verapamil, diltiazem, beta blockers	I	B	(211,212)
	Catheter ablation	IIa	B	(222,225,284-290)
	Sotalol, amiodarone	IIb	B	(278-282)
	Flecainide, propafenone	IIb	C	(205,265-277,283)
	Digoxin	III	C	
Pre-excitation, asymptomatic	None	I	C	
	Catheter ablation	IIa	B	(222,225,284-290)

The order in which treatment recommendations appear in this table within each class of recommendation does not necessarily reflect a preferred sequence of administration. Please refer to text for details. For pertinent drug dosing information, please refer to the ACC/AHA/ESC Guidelines on the Management of Patients With Atrial Fibrillation.

AF indicates atrial fibrillation; AVRT, atrioventricular reciprocating tachycardia; WPW, Wolff-Parkinson-White.

E. Focal Atrial Tachycardias

1. Definition and Clinical Presentation

Focal ATs are characterized by regular atrial activation from atrial areas with centrifugal spread (294). Focal ATs are usually manifest by atrial rates between 100 to 250 bpm and rarely at 300 bpm. Neither the sinus nor the AV node plays a role in the initiation or perpetuation of the tachycardia.

Nonsustained AT is frequently found on Holter recordings and seldom associated with symptoms. Sustained focal ATs are relatively rare; they are diagnosed in about 10 to 15% of patients referred for catheter ablation of SVT (295,296). The prevalence of focal AT has been calculated to be 0.34% in asymptomatic patients versus 0.46% in symptomatic patients (297). Focal ATs account for 10 to 23% of SVTs in children with normal hearts and a much higher percentage in children with congenital heart disease (298-302).

The outlook of patients with focal AT is usually benign with the exception of incessant forms, which may lead to tachycardia-induced cardiomyopathy (303). In adults, focal AT can occur in the absence of cardiac disease, but it is often associated with underlying cardiac abnormalities (184,186, 295,304-309). Atrial tachycardia, usually with AV block, may be produced by digitalis excess. This arrhythmia may be exacerbated by hypokalemia. Focal ATs may present as either paroxysmal or permanent tachycardias.

2. Diagnosis

In ATs, the P waves generally occur in the second half of the tachycardia cycle (see Section I–B). Therefore, in ATs, the P wave is frequently obscured by the T wave of the preceding QRS complex (Fig. 11). The PR interval is directly influenced by the tachycardia rate. The presence of AV block during tachycardia excludes AVRT and makes AVNRT very unlikely. During ATs, an isoelectric baseline is usually present between P waves, and it is used to distinguish AT from typical or atypical flutter (ie, saw-toothed or sinusoidal P-wave morphologies) (Figs. 12 and 13). However, in the presence of rapid rates and/or atrial conduction disturbances, P waves can be very wide without an isoelectric baseline, thus mimicking atrial flutter (294). It should also be emphasized that an ECG pattern of AT with discrete P waves and isoelectric baselines does not rule out macro–re-entrant tachy-

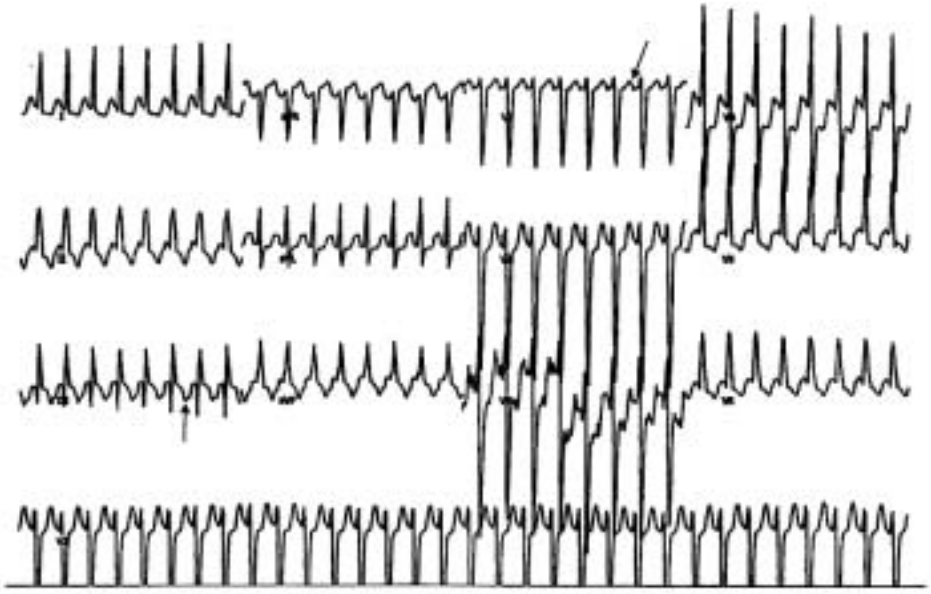

Figure 11. Focal atrial tachycardia showing a long RP interval relationship. The P wave in AT usually occurs in the latter part of the tachycardia cycle (arrows) but can appear earlier, depending on the rate and status of AV-nodal conduction. AT indicates atrial tachycardia; AV, atrioventricular.

cardia, especially if complex structural heart disease is present and/or there has been surgery for congenital heart disease. The diagnosis of AT can be established with certainty only by an electrophysiological study, including mapping and entrainment.

Although definite localization of the source of AT requires intracardiac mapping, the P-wave morphology on the 12-lead surface ECG is different from sinus rhythm and may be useful for the determination of the site of origin of the focal AT (310). A positive or biphasic P-wave morphology in surface lead aVL and a negative or biphasic P wave in lead V1 favors a right atrial origin. A negative P wave in leads I or aVL, or a positive P wave in lead V1, favors a left atrial origin. In addition, negative P waves in the inferior leads are suggestive of a caudal origin, whereas a positive P wave in those leads suggests a cranial origin (310). Of interest, the P waves during sinus rhythm may be similar to those originating from the high crista terminalis or right superior pulmonary vein (311). The latter site will, however, often show a positive P wave in lead V1; hence, a change in P-wave polarity from sinus rhythm should arouse suspicion of a right superior pulmonary vein (PV) site. Multilead body surface potential mapping can be used to help localize the tachycardia site of origin (312).

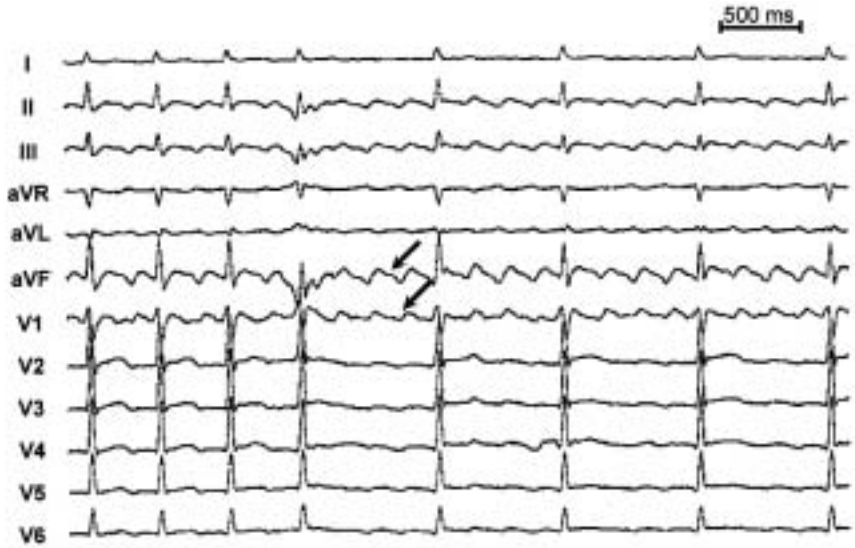

Figure 12. 12-Lead ECG from a patient with counterclockwise cavotricuspid isthmus-dependent flutter. Note that the flutter waves in the inferior leads are predominantly negative (arrow), whereas the flutter waves in lead V1 are positive (arrow). ECG indicates electrocardiogram; ms, milliseconds.

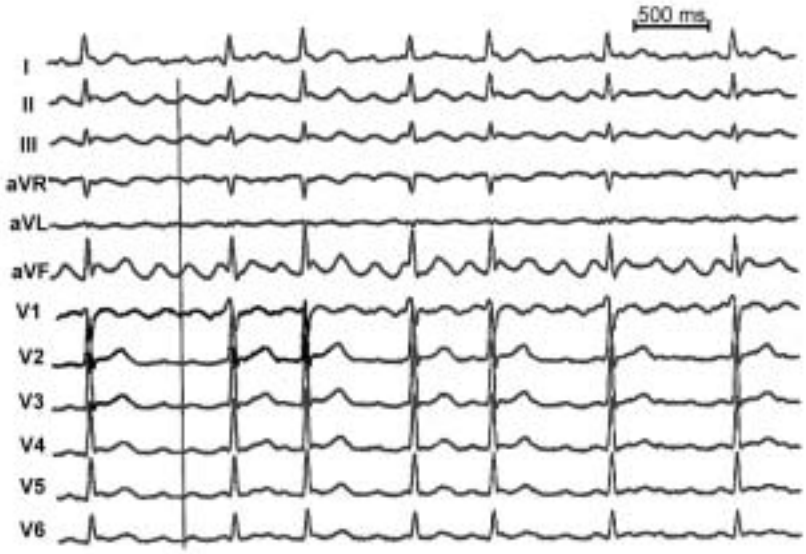

Figure 13. 12-Lead ECG from a patient with clockwise cavotricuspid isthmus-dependent flutter. Note that the flutter waves are positive in the inferior leads and predominantly negative double waves in lead V1. ECG indicates electrocardiogram; ms, milliseconds.

3. Site of Origin and Mechanisms

Focal ATs are not randomly distributed but rather tend to cluster over certain anatomical zones. The majority of right-sided ATs originate along the crista terminalis from the SA node to the AV node (313,314), but other right atrial sites include the atrial septum, atrial appendages, Koch's triangle, and the tricuspid annulus (314-321). Conversely, several venous structures have been demonstrated to have atrial myocardial extensions that may contain a tachycardia focus, such as SVC or coronary sinus ATs (322-325). In the left atrium, foci are often found in the pulmonary veins, in the atrial septum, or on the mitral annulus (326); in many cases, they are generators for AF.

Focal ATs are characterized by radial spread of activation from a focus, with endocardial activation not extending through the entire atrial cycle. The mechanism of focal discharge is difficult to ascertain by clinical methods. Available information suggests that focal activity can be caused by abnormal or enhanced automaticity, triggered activity (due to delayed afterdepolarization), or micro–re-entry (306,327, 328). Automatic ATs could arise from atrial foci in which spontaneous phase 4 depolarization occurs in cells with normal or abnormal resting membrane potentials. The progressive increase in atrial rate with tachycardia onset (ie, "warm-up") and/or progressive decrease before tachycardia termination (ie, "cool- down") are suggestive of an automatic mechanism (329). Typical automatic ATs may arise spontaneously or increase their rate of discharge in response to adrenergic stimulation. However, inducibility of re-entrant and triggered ATs is also enhanced by catecholamines (306,327-331). Automatic ATs tend to be incessant, especially in children, whereas those attributed to triggered activity may be either incessant or paroxysmal (305,327-331).

a. Drug-Induced Atrial Tachycardia

The drug most commonly associated with induction of focal AT is digitalis. This drug-induced AT is usually characterized by development of AT with AV block; hence, the ventricular rate is not excessively rapid. Serum digoxin levels are helpful for diagnoses. Treatment consists of discontinuing the digitalis. In cases of persistent advanced AV block, digitalis-binding agents may be considered (332).

4. Treatment

The efficacy of antiarrhythmic drugs is poorly defined because the clinical definition of focal ATs is often not very rigorous. No large studies have been conducted to assess the effect of pharmacologic treatment on patients with focal ATs, but both paroxysmal and incessant ATs are reported to be difficult to treat medically.

a. Acute Treatment

On rare occasions, ATs may be terminated with vagal maneuvers. A significant proportion of ATs will terminate with administration of adenosine. Adenosine-sensitive ATs are usually focal in origin (306,315,316,333,334). Persistence of the tachycardia with AV block is also a common response to adenosine. In addition, ATs that are responsive to IV verapamil or beta blockers have been reported. It is conceivable that the mechanism of AT in these patients relates either to micro–re-entry, involving tissue with slow conduction, or to triggered activity. Class Ia or class Ic drugs may suppress automaticity or prolong action-potential duration and, hence, may be effective for some patients with AT (335).

For patients with automatic AT, atrial pacing (or adenosine) may result in transient postpacing slowing but no tachycardia termination. Similarly, DC cardioversion seldom terminates

automatic ATs, but DC cardioversion may be successful for those in whom the tachycardia mechanism is micro–re-entry or triggered automaticity. An attempt at DC cardioversion should, therefore, be considered for patients with drug-resistant arrhythmia.

The usual acute therapy for AT consists of IV beta blockers or calcium-channel blockers for either termination, which is rare (336,337), or to achieve rate control through AV block, which is often difficult to achieve. Direct suppression of the tachycardia focus may be achieved by use of IV class Ia and Ic (338,339) or class III (340) (eg, sotalol, amiodarone) (209,336,341) agents. Intravenous class Ia or Ic agents may be taken by patients without cardiac failure, whereas IV amiodarone is preferred for those with poor ventricular function (303,342).

b. Long-Term Pharmacologic Therapy

The available studies pertaining to long-term pharmacologic therapy are observational, and there are problems in discerning whether the tachycardias were carefully differentiated from other mechanisms (ie, AVRT or AVNRT) or from other forms of AT. Review of the available data supports a recommendation for initial therapy with calcium-channel blockers or beta blockers because these agents may prove to be effec-

Recommendations for Treatment of Focal Atrial Tachycardias*

Clinical Situation	Recommendation	Class	Level of Evidence	References
Acute treatment†				
A. Conversion				
Hemodynamically unstable patient	DC cardioversion	I	B	
Hemodynamically stable patient	Adenosine	IIa	C	(333,334)
	Beta blockers	IIa	C	(337,351)
	Verapamil, diltiazem	IIa	C	(295,339)
	Procainamide	IIa	C	
	Flecainide, propafenone	IIa	C	(335,336, 338,339)
	Amiodarone, sotalol	IIa	C	(209,303,336, 340-342)
B. Rate regulation (in absence of digitalis therapy)	Beta blockers	I	C	(337,351)
	Verapamil, diltiazem	I	C	(306)
	Digoxin	IIb	C	
Prophylactic therapy				
Recurrent symptomatic AT	Catheter ablation	I	B	(346)
	Beta blockers, calcium-channel blockers	I	C	
	Disopyramide‡	IIa	C	(342)
	Flecainide, propafenone‡	IIa	C	(335,336,339, 343,344)
	Sotalol, amiodarone	IIa	C	(209,303, 340,342)
Asymptomatic or symptomatic incessant ATs	Catheter ablation	I	B	
Nonsustained and asymptomatic	No therapy	I	C	
	Catheter ablation	III	C	

The order in which treatment recommendations appear in this table within each class of recommendation does not necessarily reflect a preferred sequence of administration. Please refer to text for details. For pertinent drug dosing information, please refer to the ACC/AHA/ESC Guidelines on the Management of Patients With Atrial Fibrillation.

*Excluded are patients with MAT in whom beta blockers and sotalol are often contraindicated due to pulmonary disease.

†All listed drugs for acute treatment are taken intravenously.

‡Flecainide, propafenone, and disopyramide should not be used unless they are combined with an AV-nodal–blocking agent.

AT indicates atrial tachycardia; DC, direct current; MAT, multifocal atrial tachycardia.

tive and have minimal side effects. If these drugs are unsuccessful, then class Ia (342), class Ic (flecainide [335,336,339, 343, 344)], propafenone [209,336]) in combination with an AV-nodal–blocking agent, or class III agents (sotalol and amiodarone) may be tried because they may prove to be effective. The potential benefit should be balanced with the potential risks of proarrhythmia and toxicity. Because ATs commonly occur in older patients and in the context of structural heart disease, class Ic agents should be used only after coronary artery disease is excluded.

c. Catheter Ablation

Several mapping techniques have been described to search for a possible ablation site for focal ATs. Regardless of whether the arrhythmia is due to abnormal automaticity, triggering, or micro–re-entry, focal AT is ablated by targeting the site of origin of the AT. Electrograms at such sites are often fractionated and prolonged, and the activation time is generally 30 to 100 ms before the onset of the P wave (184,186,304,305,307-309,345). High-density mapping techniques using an electroanatomical map can facilitate successful ablation.

Pooled data from 514 patients (346) who underwent catheter ablation for focal AT (301) showed an 86% success rate, with a recurrence rate of 8% (184,186,304,305,307-309,313,345,347-350). In these series, left atrial origins accounted for 18% of ATs, and 10% of patients had multiple foci. The incidence of significant complications is low (1 to 2%) in experienced centers but includes cardiac perforation, damage to the right and left phrenic nerves, and sinus node dysfunction. Ablation of AT from the atrial septum or Koch's triangle may produce AV block.

For patients with drug-refractory AT or incessant AT, especially when tachycardia-induced cardiomyopathy has developed, the best therapy is catheter ablation of the focus.

5. Multifocal Atrial Tachycardia

The diagnosis of MAT is made on the basis of finding an irregular tachycardia characterized by three or more different P-wave morphologies at different rates (352). The rhythm is always irregular and frequently confused with AF, but the rate is usually not excessively rapid (352). This arrhythmia is most commonly associated with underlying pulmonary disease but may result from metabolic or electrolyte derangements. It is seldom caused by digitalis excess. There is seldom success using antiarrhythmic agents, but a modicum of success has been reported using calcium-channel blockers (353). Beta blockers are usually contraindicated because of the presence of severe underlying pulmonary disease (354). Therapy is instead directed at correction of pulmonary disease and/or electrolyte abnormalities. Chronic therapy often requires use of calcium-channel blockers, as there is no role for DC cardioversion, antiarrhythmic drugs, or ablation (355).

F. Macro–Re-entrant Atrial Tachycardia

1. Isthmus-Dependent Atrial Flutter

Atrial flutter is characterized by an organized atrial rhythm with a rate typically between 250 and 350 bpm. Electrophysiological studies have shown that this simple ECG definition includes tachycardias using a variety of re-entry circuits. The re-entry circuits often occupy large areas of the atrium and are referred to as "macro-re-entrant." The classic type of atrial flutter (ie, typical flutter) is dependent on the cavotricuspid isthmus (CTI). The precise type of flutter and, in particular, dependence on a defined isthmus (see below) is an important consideration for catheter ablation but does not alter the initial approach to management.

a. Definitions of Cavotricuspid Isthmus-Dependent Flutter Circuits

Isthmus-dependent flutter refers to circuits in which the arrhythmia involves the CTI. The most common patterns include a tachycardia showing a counterclockwise rotation (ie, left anterior oblique view) around the tricuspid valve (294). A less common pattern involves clockwise rotation around the tricuspid annulus (ie, reverse typical flutter) (356). Counterclockwise atrial flutter is characterized electrocardiographically by dominant negative flutter waves in the inferior leads and a positive flutter deflection in lead V1 with transition to a negative deflection in lead V6 at rates of 250 to 350 bpm (Fig. 12). Clockwise isthmus-dependent flutter shows the opposite pattern (ie, positive flutter waves in the inferior leads and wide, negative flutter waves in lead V1 (357), transitioning to positive waves in lead V6) (Fig. 13). Patients may at times show unusual ECG patterns; hence, confirmation of isthmus involvement can only be made by entrainment pacing of the CTI during electrophysiological studies (358).

b. Other CTI-Dependent Flutter Circuits

Isthmus-dependent flutter may also occur as double-wave or lower-loop re-entry. Double-wave re-entry is defined as a circuit in which two flutter waves simultaneously occupy the usual flutter pathway (359). This arrhythmia is transient, usually terminating within three to six complexes but may, on rare occasions, deteriorate into AF (359). Lower-loop re-entry is defined as a flutter circuit in which the re-entry wavefront circulates around the inferior vena cava due to conduction across the crista terminalis (360-362). The resultant circuit may produce unusual surface ECG patterns, but these arrhythmias are still dependent on CTI conduction and, hence, are amenable to ablation of the isthmus.

c. Pathophysiology and Treatment Rationale

Cavotricuspid isthmus-dependent flutter is caused by a macro-re-entrant right atrial circuit around the tricuspid annulus. This circuit contains a propagating wavefront and an excitable gap. The crista terminalis or sinus venosa (ie, area between superior and inferior cava) is thought to be the

functional posterior barrier, whereas the tricuspid annulus forms the anterior barrier (363). Bursts of rapid transitional atrial rhythms or AF allow for formation of functional conduction block along the crista terminalis (or sinus venosa), encouraging impulses to circulate parallel to the tricuspid ring (364). General mechanisms discussed previously (see Section III) apply to flutter circuits. For example, class Ia drugs have been shown to decrease conduction velocity and prolong refractoriness in the flutter circuit; overall, these drugs tend to shorten the excitable gap (52,53). Class Ic drugs depress conduction and can slow flutter (52). In contrast, class III drugs (ie, ibutilide, dofetilide, and amiodarone) prolong refractoriness and may terminate flutter because the circulating wavefront encounters tissue that is refractory (53,365). Rapid, atrial overdrive pacing can terminate the arrhythmia when capturing stimuli penetrate the circuit early enough to produce block in both directions (ie, antidromic and orthodromic) in the circuit (366). In addition, the efficacy of pacing can be enhanced by antiarrhythmic drug therapy that facilitates penetration of the circuit by pacing impulses. Direct current cardioversion is a very effective mode of therapy because of rapid homogeneous depolarization of the entire atrium. The practical implications of these findings are discussed in the appropriate therapy sections.

d. Clinical Presentation

Patients with atrial flutter commonly present with acute symptoms of palpitations, dyspnea, fatigue, or chest pain. In contrast, this arrhythmia may also present with more insidious symptoms or conditions, such as exercise-induced fatigue, worsening heart failure, or pulmonary disease.

Atrial flutter occurs in approximately 25 to 35% of patients with AF (367) and may be associated with more intense symptoms owing to more rapid ventricular rates. In most instances, patients with atrial flutter present with a two-to-one AV-conduction pattern. The flutter rate is approximately 300 per minute with a ventricular response of 150 bpm. (Flutter with varying AV block can result in a grossly irregular rhythm.) In exceptional circumstances, one-to-one AV conduction may occur in patients during exercise or in those with rapid AV-nodal conduction and may be associated with life-threatening symptoms. Class Ic drugs may, by slowing the atrial rate, also cause one-to-one AV conduction and should, therefore, be combined with AV-nodal–blocking agents. Patients with accessory AV pathways capable of rapid conduction also present with rapid ventricular rate and life-threatening symptoms (368). Patients with impaired cardiac function, in whom the coordinated contribution of atrial function and regular rate are hemodynamically important, can experience hemodynamic deterioration with the development of atrial flutter even if the ventricular rate is not excessively rapid. Atrial flutter, if untreated and accompanied by an excessive ventricular rate, may also by itself promote cardiomyopathy. Hemodynamic deterioration due to atrial flutter is a problem late after repair of congenital heart disease, particularly after Senning or Fontan operations (369-374). In these patients, flutter is associated with a worse hemodynamic profile and is a marker for worse prognosis (375).

e. Acute Treatment

Acute therapy for patients with atrial flutter depends on clinical presentation. If the patient presents with acute hemodynamic collapse or CHF, then emergent DC-synchronized shock is indicated (Fig. 14). Atrial flutter can most often be successfully reverted to sinus rhythm with energies less than 50 joules using monophasic shocks and with less energy using biphasic shocks. In most instances, patients present with two-to-one or higher grades of AV block and are hemodynamically stable. In this situation, the clinician may elect to use AV-nodal–blocking drugs for rate control. Adequate rate control, albeit commonly difficult to achieve, is especially important if conversion to sinus rhythm is deferred. Atrial overdrive pacing, either through the transesophageal route or with atrial electrodes, if present, should be considered as an option for conversion to sinus rhythm. For those with atrial flutter of more than 48 hours in duration, anticoagulant therapy is deemed important prior to any mode of cardioversion (see below). Moreover, if acute chemical cardioversion is planned, then rate control is desirable because antiarrhythmic drugs, such as class Ic agents, may slow the flutter rate and cause a paradoxical increase in the ventricular response owing to decreased concealed conduction into the AV node.

In approximately 60% of patients, atrial flutter occurs as part of an acute disease process, such as exacerbation of pulmonary disease, postoperative cardiac or pulmonary surgery, or during acute myocardial infarction. If the patient survives the underlying disease process, then chronic therapy for the arrhythmia is usually not required after sinus rhythm is restored. In summary, acute treatment of atrial flutter might include the initial use of electrical pacing, DC or chemical cardioversion, or AV-nodal–blocking agents. The anticipated effects of these modalities are detailed below.

ATRIOVENTRICULAR-NODAL–BLOCKING AGENTS. Available randomized, controlled trials of AV-nodal–blocking agents include patients with AF and atrial flutter. It is often difficult to isolate the data for atrial flutter patients alone, and the general impression is that rate control may be especially difficult to achieve in patients with atrial flutter.

Two randomized, placebo-controlled, double-blinded trials assessed use of IV diltiazem for rate control in patients with AF or atrial flutter (376,377). Both studies showed rapid reductions in heart rate, but this drug was less effective for rate control in patients with atrial flutter compared with AF. Hypotension was the chief adverse effect for the group as a whole, occurring in approximately 10% of patients. A prospective, randomized, open-labeled trial compared IV diltiazem with IV digoxin (378) for rate control. Rate control was usually achieved within 30 minutes with IV diltiazem compared to more than 4 hours with IV digoxin.

Intravenous verapamil is also efficacious in slowing the ventricular rate (91,379). One prospective, randomized, double-blinded, crossover trial compared the safety and efficacy of IV diltiazem and IV verapamil for patients with either AF (7 patients) or atrial flutter (10 patients) and decreased ejection fraction (380). In this relatively small sample, both drugs

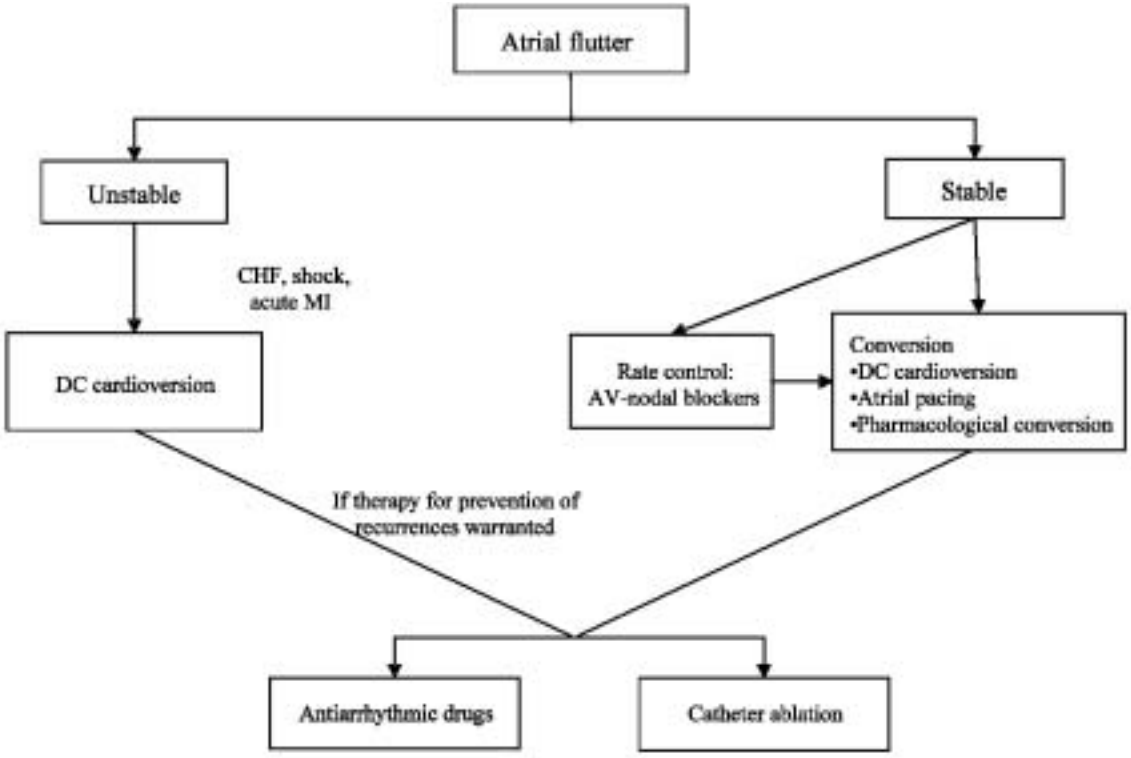

Figure 14. Management of atrial flutter depending on hemodynamic stability. Attempts to electively revert atrial flutter to sinus rhythm should be preceded and followed by anticoagulant precautions, as per AF. AF indicates atrial fibrillation; AV, atrioventricular; CHF, congestive heart failure; DC, direct current; MI, myocardial infarction.

had comparable efficacy in terms of rate control and effect on systolic function. However, the incidence of symptomatic hypotension was significantly higher for those initially randomized to IV verapamil.

Although IV verapamil appears to be as effective as IV diltiazem for rate control, small observational studies suggest that IV verapamil may be more likely to adversely affect systolic function or blood pressure (380,381).

The decrease in heart rate achieved with calcium-channel blockers is similar to that observed for IV beta blockers (379). A randomized, open-labeled study comparing IV digoxin to IV amiodarone showed the superiority of IV amiodarone for more rapid achievement of rate control (382). However, IV amiodarone appears to be less effective than IV calcium-channel or beta blockers because adequate rate control (ie, fewer than100 bpm) was not achieved for 6 hours. In addition, IV calcium-channel blockers, beta blockers, or amiodarone are seldom associated with conversion of atrial flutter to sinus rhythm.

ACUTE INTRAVENOUS DRUGS FOR PHARMACOLOGIC CONVERSION. A number of drugs have been shown to be effective in conversion of atrial flutter to sinus rhythm.

INTRAVENOUS IBUTILIDE. Placebo-controlled IV ibutilide trials show an efficacy rate of 38 to 76% for conversion of atrial flutter to sinus rhythm (383,384). In these studies, conversion rates of atrial flutter were not related to duration of the arrhythmia. For patients who responded to ibutilide, the mean time to conversion was 30 minutes. The incidence of sustained polymorphic VT for the group as a whole was 1.2 to 1.7%; for nonsustained VT (not requiring DC cardioversion), the incidence was 1.8 to 6.7% (383,384). Randomized, double-blinded studies comparing IV ibutilide and IV procainamide are available (385,386). In the largest study available (385), the efficacy of IV ibutilide was significantly greater than that of IV procainamide for patients with atrial flutter-13 out of 17 patients (76%) versus 3 out of 22 (14%). One patient treated with ibutilide developed polymorphic VT, while 7 of those treated with procainamide developed hypotension. Intravenous ibutilide should not be taken by patients with severe structural cardiac diseases or prolonged QT interval, or in those with underlying sinus node disease.

INTRAVENOUS CLASS IC DRUGS. Several single-blinded, randomized, controlled trials comparing IV flecainide with either IV propafenone or IV verapamil have shown relatively poor efficacy for acute conversion (387,388). In one study (388), only 13% of patients converted after IV flecainide administration; 40% responded to propafenone (not statistically significant); and only 5% reverted with verapamil. Similar results were found in one additional randomized study comparing IV flecainide with propafenone (387). Adverse effects included QRS widening, dizziness, and paresthesias.

INTRAVENOUS SOTALOL. A randomized trial of IV sotalol versus placebo for patients with SVT included only a limited number of patients with atrial flutter (389). The conversion rate varied from 20 to 40% depending on the sotalol dose but was not different from placebo. Adverse effects included

hypotension and dyspnea. A large double-blinded, randomized trial involving 308 patients compared IV sotalol with IV ibutilide for conversion of patients with AF or atrial flutter to sinus rhythm (390). High-dose (2 mg) ibutilide was more effective than sotalol (1.5 mg/kg) in conversion of patients with atrial flutter (70 vs. 19%) to sinus rhythm.

A review of the existing literature for IV antiarrhythmic drugs taken by patients with atrial flutter suggests that dofetilide or ibutilide are more effective than sotalol or class I agents but are associated with a significant incidence of torsades de pointes (1.5 to 3%). Controlled trials have demonstrated the greater efficacy of IV class III agents (eg, dofetilide, ibutilide) compared to IV amiodarone or class Ia (eg, procainamide) or class Ic agents (eg, flecainide, propafenone) (95). Neither IV AV-nodal–blocking agents nor amiodarone appears to be effective for arrhythmia conversion, but they may be effective in rate control.

ACUTE NONPHARMACOLOGIC THERAPY. *EXTERNAL DIRECT CURRENT CARDIOVERSION*. The success rate for external DC cardioversion for patients with flutter is between 95 and 100% (391). Conversion can commonly be achieved with relatively small amounts of energy (ie, 5 to 50 joules), especially when biphasic wave forms are used, but higher-energy initial shocks are warranted for emergent cardioversion of patients with hemodynamic embarrassment. Direct current cardioversion is the procedure of choice when rapid termination of flutter is required.

ATRIAL OVERDRIVE PACING. The use and efficacy of rapid atrial pacing to terminate atrial flutter has been long established (366,392-394), and a comprehensive review showed a cumulative success rate of 82% (range 55 to 100%) (395). Overdrive pacing is particularly useful in atrial flutter after cardiac surgery, as these patients frequently have epicardial atrial pacing wires. A number of studies have demonstrated the efficacy of transesophageal pacing (396-400). In addition, it has been clearly shown that use of antiarrhythmic drugs, including procainamide (398), ibutilide (401), and propafenone (399,402), may facilitate conversion of atrial flutter by pacing because they facilitate impulse penetration of the flutter circuit and reduce the risk of provoking AF (396). Moreover, high-frequency atrial pacing (403) or overdrive pacing with atrial extrastimuli (404) have been shown to be effective in cases in which atrial overdrive alone is not effective, an option available in most modern pacemaker technologies. It is important to recognize that atrial overdrive pacing may result in the induction of sustained AF. In addition, periods of AF may precede conversion to sinus rhythm.

f. Chronic Pharmacologic Treatment

CLASS I DRUGS. It is difficult to evaluate long-term antiarrhythmic therapy for patients with atrial flutter because most studies combine patients with AF and atrial flutter without specifying the results for each arrhythmia. Review of the flecainide database showed the long-term efficacy of this drug to be 50% for patients with atrial flutter, but results were available for only 36 patients (95). Randomized, prospective long-term trials comparing flecainide and quinidine are available (405) for patients with AF or atrial flutter. No mention is made of patients with atrial flutter as a distinct group, but the incidence of adverse side effects for the group as a whole was significantly higher with quinidine compared with flecainide. Beta blockers or calcium-channel blockers should always be used in conjunction with class Ic agents for treatment of patients with atrial flutter because the class Ic drugs may slow the flutter rate and encourage one-to-one AV conduction.

CLASS III DRUGS. The efficacy of oral dofetilide has been assessed in several randomized, placebo-controlled trials (406,407). At the highest dose of dofetilide tested (500 mcg twice per day), maintenance of sinus rhythm more than or equal to 350 days occurred in 73% of patients with atrial flutter compared to 40% of patients with AF. Contraindications for dofetilide include a creatinine clearance less than 20, hypokalemia, hypomagnesemia, and prolonged QT at baseline. Other randomized dose-titration studies have been reported (408) (ie, sotalol), but, unfortunately, results for the atrial flutter patients are not distinguished from those with AF.

g. Role of Anticoagulant Therapy for Patients With Atrial Flutter

The role of anticoagulant therapy for patients with AF is determined on the basis of a number of prospective, randomized trials. Such trials are not available for patients with atrial flutter. It was initially thought, on the basis of observational studies, that the risk of embolization during cardioversion for atrial flutter was negligible (409-411). However, observational studies have shown a significant risk of embolization for these patients, ranging from 1.7 to 7% (412-415).

In addition, a number of studies (416-418) have shown that the incidence of atrial echo-dense material or clot varies from 0 to 34% in nonanticoagulated patients with atrial flutter. The incidence of echo-dense material or clot increases with atrial flutter duration longer than or equal to 48 hours. Another area of concern is the finding of atrial stunning after conversion of atrial flutter, which appears to persist for several weeks (419,420). In several studies, risk factors for development of embolic events were similar to those described for AF (413,415).

In a collective review of the risk of embolization after DC cardioversion for atrial flutter, the risk of embolism for inadequately anticoagulated patients was 2.2% and was significantly lower than that reported for patients with AF (5 to 7%) (413-415). Although randomized, controlled trials of thromboembolic prophylaxis for atrial flutter are not available, it is our consensus that the guidelines for anticoagulation for patients with AF should be extended to those with atrial flutter (359,421). Cardioversion-electrical, chemical, or by ablation-should thus be considered only if the patient is anticoagulated (international normalized ratio [INR] equals 2 to 3), the arrhythmia is less than 48 hours in duration, or transesophageal echocardiography (TEE) shows no atrial clots.

Negative TEE should be followed by anticoagulation, as by itself it is not protective against thromboembolism.

h. Catheter Ablation of the Cavotricuspid Isthmus for Isthmus-Dependent Flutter

A technique for placing lesions between the tricuspid annulus and the inferior vena cava to block the atrial flutter circuit and cure patients with atrial flutter is available (422,423). Initially, success was deemed present when ablation simply terminated the arrhythmia, but stopping energy delivery after initial flutter termination was subsequently found to be associated with high incidence of atrial flutter recurrence (367). Using more stringent criteria to prove the existence of bidirectional conduction block in the CTI results in better chronic success rates (90 to 100%) (424-426). One prospective, randomized study compared chronic oral antiarrhythmic therapy (in 61 patients with atrial flutter) to RF ablation (427). After a mean follow-up of 21 plus or minus 11 months, only 36% of patients treated with drugs compared to 80% of those treated with catheter ablation remained in sinus rhythm. In addition, 63% of patients in the drug-treatment group required one or more hospitalizations, compared to 22% for those treated with ablation. Quality of life was significantly improved in those treated with ablation.

A number of studies have documented that patients with AF who are treated with propafenone, flecainide, or amiodarone have a 15 to 20% risk of developing atrial flutter (428-430). Prospective trials have shown that, if atrial flutter becomes the dominant rhythm, then ablation of the CTI and continued use of the antiarrhythmic drug result in decreased incidence of atrial flutter and facilitate the pharmacologic management of AF (431,432). The incidence of AF after successful ablation of the CTI flutter circuit varies, depending on the presence of AF before ablation. For patients with a history of only atrial flutter, the occurrence of AF over a follow-up of 18 plus or minus 14 months was only 8%. In contrast, for those with a history (follow-up of 20 plus or minus 14 months) of both AF and predominant atrial flutter, the recurrent rate of AF was 38%; whereas AF recurred in 86% of those in whom AF predominated prior to ablation. It appears that the best results of catheter ablation are achieved in patients who have sole or predominant atrial flutter. It is conceivable that chronic atrial flutter results in remodeling of the atrial function and structure that predisposes to AF.

i. Treatment of Atrial Flutter in Special Circumstances

Atrial arrhythmias are commonly observed after cardiac surgery. Atrial fibrillation is the most common arrhythmia, occurring in 20 to 50% of patients depending on the nature of the surgery (ie, higher incidence with mitral valve surgery) (433). Likewise, atrial flutter also occurs after cardiac surgery. Pathogenetic factors that may be involved in develop-

Recommendations for Acute Management of Atrial Flutter

Clinical Status/ Proposed Therapy	Recommendation*	Class	Level of Evidence	References
Poorly tolerated				
•Conversion	DC cardioversion	I	C	
•Rate control	Beta blockers	IIa	C	
	Verapamil, diltiazem	IIa	C	
	Digitalis†	IIb	C	
	Amiodarone	IIb	C	
Stable flutter				
•Conversion	Atrial or transesophageal pacing	I	A	(396-400)
	DC cardioversion	I	C	(391)
	Ibutilide‡	IIa	A	(383,384)
	Flecainide§	IIb	A	(387,388)
	Propafenone§	IIb	A	(387,388)
	Sotalol	IIb	C	(389,390)
	Procainamide§	IIb	A	(385)
	Amiodarone	IIb	C	(95,382)
•Rate control	Diltiazem, verapamil	I	A	(91,377-379)
	Beta blockers	I	C	(379)
	Digitalis†	IIb	C	(378)
	Amiodarone	IIb	C	(382)

The order in which treatment recommendations appear in this table within each class of recommendation does not necessarily reflect a preferred sequence of administration. Please refer to text for details. For pertinent drug dosing information, please refer to the ACC/AHA/ESC Guidelines on the Management of Patients With Atrial Fibrillation.

Cardioversion should be considered only if the patient is anticoagulated (INR equals 2 to 3), the arrhythmia is less than 48 hours in duration, or the TEE shows no atrial clots.

*All listed drugs are taken intravenously.

†Digitalis may be especially useful for rate control in patients with heart failure.

‡Ibutilide should not be used in patients with reduced LV function.

§Flecainide, propafenone, and procainamide should not be used unless they are combined with an AV-nodal–blocking agent.

AV indicates atrioventricular; DC, direct current; INR, international normalized ratio; LV, left ventricular; TEE, transesophageal echocardiography.

ment of postoperative flutter include pericarditis, a change in autonomic tone, or atrial ischemia (433,434). Because atrial electrodes are usually left in place after cardiac surgery, atrial overdrive pacing for conversion to sinus rhythm is often a useful therapeutic technique to restore sinus rhythm. If this approach fails, then a number of antiarrhythmic drugs have been utilized, and a number of prospective, randomized, controlled trials have been published using a variety of agents (435-439). Unfortunately, in these studies, patients with atrial flutter are not distinguished from those with AF. One randomized, placebo-controlled, drug-titration trial used IV ibutilide for 101 postoperative patients with atrial flutter (440). The conversion rate for atrial flutter was 78% (44% for those with AF) and usually occurred within 90 minutes of the infusion. Polymorphic VT was observed in 1.8% of the patients and typically occurred within several minutes of the ibutilide infusion. Intravenous dofetilide has also been reported to be effective for patients with postoperative AF or atrial flutter (441).

Atrial flutter may occur in patients with a variety of comorbid conditions. These include chronic lung disease, acute pneumonia, after pulmonary surgery, or as a complication of acute myocardial infarction. Rate control may be achieved with either AV-nodal blockers or IV amiodarone (442). If the arrhythmia is associated with severe CHF or hypotension, then urgent DC cardioversion is appropriate.

2. Non–Cavotricuspid Isthmus-Dependent Atrial Flutter

Atrial flutter caused by macro–re-entry circuits that do not use the CTI are less common than CTI-dependent atrial flutter. Most are related to an atrial scar that creates conduction block and a central obstacle for re-entry. Prior cardiac surgery involving the atrium, such as repair of congenital heart disease, mitral valve surgery, or the atrial maze procedure, is a common cause. The resulting arrhythmias are referred to as "lesion-related macro–re-entrant ATs" (186,294,443-447). Atrial mapping often reveals extensive low-voltage areas involving portions of the atrium distant from the location of the incision, possibly indicating extensive atrial injury or infarction (444). In patients who have not had prior cardiac surgery, abnormal areas with low-amplitude electrical activity are often present, a finding consistent with the presence of scar tissue of unclear cause (448).

Although CTI-dependent flutter is the most common underlying mechanism in these circumstances, it often coexists with incisional macro-re-entrant ATs, resulting in multiple re-entry circuits. Simultaneous circulation of wavefronts through two loops of two potential circuits can create complex, figure-of-eight types of re-entry (443,449).

The appearance of the flutter waves on ECG usually differs from CTI-dependent flutter but can resemble typical patterns (see Figs. 12 and 13) (294). In some cases, discrete P waves are difficult to identify, possibly because of extensive atrial

Recommendations for Long-Term Management of Atrial Flutter

Clinical Status/ Proposed Therapy	Recommendation	Class	Level of Evidence	References
First episode and well-tolerated atrial flutter	Cardioversion alone	I	B	(391)
	Catheter ablation*	IIa	B	(427)
Recurrent and well-tolerated atrial flutter	Catheter ablation*	I	B	(424-426)
	Dofetilide	IIa	C	(406,407)
	Amiodarone, sotalol, flecainide,†‡ quinidine,†‡ propafenone,†‡ procainamide,†‡ disopyramide†‡	IIb	C	(95,405,408)
Poorly tolerated atrial flutter	Catheter ablation*	I	B	(424-426)
Atrial flutter appearing after use of class Ic agents or amiodarone for treatment of AF	Catheter ablation*	I	B	(431,432)
	Stop current drug and use another	IIa	C	
Symptomatic non–CTI-dependent flutter after failed antiarrhythmic drug therapy	Catheter ablation*	IIa	B	(450-452)

The order in which treatment recommendations appear in this table within each class of recommendation does not necessarily reflect a preferred sequence of administration. Please refer to text for details. For pertinent drug dosing information, please refer to the ACC/AHA/ESC Guidelines on the Management of Patients With Atrial Fibrillation.

*Catheter ablation of the AV junction and insertion of a pacemaker should be considered if catheter ablative cure is not possible and the patient fails drug therapy.

†These drugs should not be taken by patients with significant structural cardiac disease. Use of anticoagulants is identical to that described for patients with AF (459).

‡Flecainide, propafenone, procainamide, quinidine, and disopyramide should not be used unless they are combined with an AV-nodal–blocking agent.

AF indicates atrial fibrillation; AV, atrioventricular; CTI, cavotricuspid isthmus.

scar. Definitive diagnosis requires intracardiac mapping. These arrhythmias are often recognized when CTI-dependent atrial flutter is anticipated but catheter mapping demonstrates a non–CTI-dependent mechanism.

a. Catheter Ablation and Mapping of Non–Cavotricuspid Isthmus-Dependent Flutter

Ablation of non–CTI-dependent flutter can be substantially more difficult than for CTI-dependent flutter. When this type of atrial flutter is suspected, such as in patients with congenital heart disease who have had surgery, referral to an experienced center should be considered. Cavotricuspid isthmus-dependent flutter is common in patients with prior atrial surgery, and both CTI- and non–CTI-dependent macro–re-entry circuits often coexist in a single patient (443,450-454). When multiple potential re-entry circuits are present, the rhythm may switch back and forth among different circuits, complicating attempts to identify an appropriate target for ablation. The presence of non–CTI-dependent flutter may not be clear until ablation in the CTI fails to abolish atrial flutter.

Successful ablation is dependent on identifying a critical portion of the re-entry circuit where it can be interrupted with either one or a line of RF applications. Mapping and ablation are facilitated by the use of specialized systems that allow creation of three-dimensional reconstructions of the atria with plots of the atrial activation sequence in tachycardia and the location of regions of scar or conduction block. For patients who have had prior surgery, the surgical operative report is often helpful in suggesting the location of possible re-entry circuits around atrial incisions.

Surgical incisions in the right atrium for repair of atrial septal defects (ASDs) are probably the most common cause of lesion-related re-entry in adults (294,443,444,447,448, 450-456). The incision is often placed in the lateral right atrium; the re-entry wavefront circulates around the incision. A line of ablation lesions extending from the inferior margin of the scar to the inferior vena cava, or from the superior margin of the scar to the SVC, can interrupt the circuit, but it can also be difficult to complete. Some tachycardias use a narrow channel of conduction between regions of dense scar in the lateral right atrium that can be targeted for ablation.

In six series including 134 patients (predominantly young adults with various types of surgically corrected congenital heart disease), ablation abolished arrhythmia recurrences in 50 to 88% of patients during average follow-up periods of up to 2 years (444,446,450-452). Complications of diaphragmatic paralysis caused by phrenic nerve injury and thromboembolism after conversion from atrial flutter have occurred.

Macro–re-entry circuits occur in the left atrium but are much less common than right atrial circuits (294,454, 457,458). Ablation can be effective, but the number of patients studied is small and the efficacy and adverse effects of ablation are not yet well defined (457).

VI. SPECIAL CIRCUMSTANCES

A. Pregnancy

Premature atrial beats are observed in approximately 50% of patients during pregnancy, but they are generally benign and well tolerated (460). Although sustained arrhythmias are relatively rare (2 to 3 per 1000), in those who have supraventricular arrhythmias, symptomatic exacerbation of paroxysmal SVT occurs during pregnancy in approximately 20% (461). Moreover, because the number of patients who have congenital heart diseases and are reaching reproductive age is increasing, more patients with SVT are to be anticipated. The major concern during treatment of SVT during pregnancy is the potential for adverse effects on the fetus, as all commonly used antiarrhythmic drugs cross the placental barrier to some extent. Although the first 8 weeks after conception is the period associated with the greatest teratogenic risk, other adverse effects may occur with drug exposure later in pregnancy. The major concern with taking antiarrhythmic drugs during the second and third trimesters is the adverse effect on fetal growth and development as well as the risk of proarrhythmia. Several of the physiological changes that occur during pregnancy, such as increased cardiac output and blood volume, decreased serum protein concentration, alterations in gastric secretion and motility, and hormonal stimulation of liver enzymes, can affect absorption, bioavailability, and elimination of many drugs. More careful monitoring of the patient and dose adjustments are, therefore, necessary because the above-mentioned changes vary in magnitude during different stages of pregnancy (462).

As with many other drugs used in pregnancy, use of certain antiarrhythmic agents has crept into common practice because of an absence of reported ill effects, rather than as a result of controlled studies. All antiarrhythmic drugs should be regarded as potentially toxic to the fetus and should be avoided if possible, especially during the first trimester. The U.S. Food and Drug Administration (FDA) drug classification is outlined in Table 4. All currently available antiarrhythmic drugs that are used for SVT are categorized as class C drugs, except for sotalol (a class B agent) and for atenolol and amiodarone (class D agents).

In patients with mild symptoms and structurally normal hearts, no treatment other than reassurance should be provided. Antiarrhythmic drug therapy should be used only if symptoms are intolerable or if the tachycardia causes hemodynamic compromise.

Catheter ablation should be recommended in women with symptomatic tachyarrhythmias before they contemplate pregnancy. Because of the potential problem of recurring tachyarrhythmias during pregnancy, the policy of withdrawing antiarrhythmic drugs and resuming them later can be recommended only as an alternative in selected cases. A large-scale clinical experience with catheter ablation procedures performed during pregnancy will never be reported, although fetal radiation dose and risk from the procedures have been calculated (463). Catheter ablation is the procedure of choice

Table 4. Definitions of U.S. FDA Classification (Use in Pregnancy Setting

FDA Classification	Definition
Category A	Controlled studies show no risk. Adequate well-controlled studies in pregnant women have failed to demonstrate risk to the fetus.
Category B	No evidence of risk in humans. Either animal studies show risk, but human studies do not, or, if no adequate human studies have been done, animal findings are negative.
Category C	Risk cannot be ruled out. Human studies are lacking, and animal studies are either positive for fetal risk or are lacking as well. However, potential benefits may justify the potential risk
Category D	Positive evidence of risk. Investigational or postmarketing data show risk to the fetus. Nevertheless, potential benefits of the drug may be acceptable when they outweigh the potential risk.
Category X	Contraindicated in pregnancy. Studies in animals or humans, or investigational or postmarketing report, have shown fetal risk that clearly outweighs any possible benefits to the patients.

FDA indicates Food and Drug Administration.

for drug refractory, poorly tolerated SVT. If needed, it should be performed in the second trimester.

1. Acute Conversion of Atrioventricular Node–Dependent Tachycardias

Intravenous adenosine is the drug of choice if vagal maneuvers fail to terminate an episode of PSVT. This drug has been used safely in pregnant women, although most of the reports of adenosine administration were in the second and third trimesters (462,464).

If adenosine fails, then IV propranolol or metoprolol are recommended. Intravenous administration of verapamil may be associated with a greater risk of maternal hypotension and subsequent fetal hypoperfusion.

Available data suggest that DC cardioversion is safe in all phases of pregnancy and can be used when necessary (465).

2. Prophylactic Antiarrhythmic Drug Therapy

If prophylactic drug therapy is needed, then digoxin or a beta-blocking agent (ie, propranolol or metoprolol) is the first-line agent. The experience with digoxin is extensive, and it is considered one of the safest antiarrhythmic drugs to take during pregnancy (462); however, its efficacy for arrhythmia treatment or prophylaxis has never been demonstrated. Propranolol and metoprolol are generally considered to be safe but are best avoided in the first trimester. Rare cases of adverse effects on the fetus, including bradycardia, hypoglycemia, premature labor, and metabolic abnormalities, have been reported but may be secondary to fetal dis-

Recommendations for Treatment Strategies for Supraventricular Tachycardia During Pregnancy

Treatment Strategy	Recommendation	Classification	Level of Evidence
Acute conversion of PSVT	Vagal maneuver	I	C
	Adenosine	I	C
	DC cardioversion	I	C
	Metoprolol, propranolol	IIa	C
	Verapamil	IIb	C
Prophylactic therapy	Digoxin	I	C
	Metoprolol*	I	B
	Propranolol*	IIa	B
	Sotalol,* flecainide†	IIa	C
	Procainamide	IIb	B
	Quinidine, propafenone,† verapamil	IIb	C
	Catheter ablation	IIb	C
	Atenolol‡	III	B
	Amiodarone	III	C

The order in which treatment recommendations appear in this table within each class of recommendation does not necessarily reflect a preferred sequence of administration. Please refer to text for details. For pertinent drug dosing information, please refer to the ACC/AHA/ESC Guidelines on the Management of Patients With Atrial Fibrillation.

*Beta-blocking agents should not be taken in the first trimester, if possible.

†Consider AV-nodal–blocking agents in conjunction with flecainide and propafenone for certain tachycardias (see Section V).

‡Atenolol is categorized in class C (drug classification for use during pregnancy) by legal authorities in some European countries.

AV indicates atrioventricular; DC, direct current; PSVT, paroxysmal supraventricular tachycardia.

tress in high-risk pregnancies. Prospective, randomized studies have failed to demonstrate a higher incidence of these complications with beta-blocking agents as compared to placebo (466,467). The potential for intrauterine growth retardation has been reported with propranolol and has raised concerns, especially when it is taken in the first trimester (462). Later studies reported growth retardation in babies receiving atenolol in the first trimester and a higher prevalence of preterm delivery (468,469). Atenolol is, therefore, classified as a category D agent by the FDA. In view of these results, beta blockers should be avoided during the first trimester, if possible. Beta blockers with selective B_1 properties are theoretically preferable because they may interfere less with peripheral vasodilatation and uterine relaxation.

If the above-mentioned drugs fail, then sotalol may be considered. Although sotalol has been used successfully during pregnancy for other indications, the experience is limited; so, caution is still advised (470). The reported experience with flecainide is also limited, but it appears to be relatively safe during pregnancy (471). The experience with propafenone is even more limited, although no adverse effects to the fetus have been reported when it is taken during the third trimester (472). Quinidine is considered to be relatively well tolerated, although isolated cases of adverse effects, such as fetal thrombocytopenia and eighth-nerve toxicity, have been reported (462). Procainamide is considered to be well tolerated and appears to be relatively safe for short-term therapy (473). The use of amiodarone, a category D agent, in pregnancy should be restricted to arrhythmias that are resistant to other drugs or are life threatening (474).

It should be emphasized that these recommendations rely mainly on observational data; the cited references are, therefore, not all inclusive.

B. Supraventricular Tachycardias in Adult Patients With Congenital Heart Disease

1. Introduction

An increasing number of patients with congenital heart disease are surviving to adulthood. Supraventricular arrhythmias are an important cause of morbidity and, in some of these patients, mortality. In patients who have not had operative repair of their malformation, AF and atrial flutter are the most common arrhythmias. Increased atrial filling pressures may contribute to the cause of AF or atrial flutter. Surgical repairs that place incisions in the atria predispose to incision-related atrial flutter late after surgery. There is currently interest in devising surgical procedures to avoid later development of atrial flutter. In addition, some patients may be candidates for percutaneous device closure of ASDs.

Many patients warrant referral to an experienced specialist. The new development of atrial arrhythmias can be an indication of deteriorating hemodynamic function, which in some cases warrants specific investigation and occasionally operative treatment. An SVT itself dramatically impairs hemodynamic performance in some patients. Coexistent sinus node dysfunction is common after surgical repair of many of these conditions and can be further aggravated by antiarrhythmic therapy, requiring pacemaker implantation to allow management of the supraventricular arrhythmia. Cardiac malformations often increase the difficulty of pacemaker implantation and catheter ablation procedures. The presence of intracardiac shunts creates a risk of systemic embolism from clots that may form on pacing leads even though they are in the right-sided (ie, systemic venous) cardiac chambers.

2. Specific Disorders

a. Atrial Septal Defect

Atrial fibrillation or atrial flutter occurs in approximately 20% of adults who have an unrepaired ASD (475,476). Atrial fibrillation, rather than atrial flutter, predominates in the majority; incidence increases with patient age. Surgical or percutaneous closure of ASDs associated with pulmonary blood flow/systemic blood flow (Qp/Qs) greater than 1.5 and or symptoms before the age of 40 years may reduce atrial arrhythmias but has little effect after the age of 40 years (475-477).

Gatzoulis and coworkers retrospectively reviewed 218 adults who had surgical closure of an isolated ASD (475). Sustained atrial flutter or AF was present in 19% of patients prior to surgery, 5% had atrial flutter, 2.8% had AF and flutter, and 11% had AF. During a mean follow-up of 3.8 years, 60% of patients with preoperative AF or atrial flutter continued to have arrhythmias, and new AF or atrial flutter developed in 2.3% of patients. All of the patients with persistent arrhythmias and those who developed new atrial arrhythmias were older than 40 years of age at the time of repair. None of the 106 patients younger than 40 years of age at the time of surgery had late atrial arrhythmias during this follow-up period ($P = 0.008$).

Attie and coworkers randomized 521 adults older than 40 years of age who had isolated secundum or sinus venosus ASDs with a Qp/Qs greater than 1.7 and pulmonary artery systolic pressure less than 70 mm Hg to surgical closure versus medical therapy (476). Prior to randomization, 21% of patients had a history of AF or atrial flutter managed with rate control and anticoagulation, and 5% had a history of other types of SVT. During a median follow-up of 7.3 years, new atrial flutter or AF developed in 7.4% of patients in the surgical group and 8.7% of patients in the medical group. Cerebral embolic events occurred in 2.1% of patients. The risk was not different between the surgical and medically treated patients.

Management of atrial flutter is the same as described in Section V–F. In patients who have not had surgical repair, atrial flutter is likely to be dependent on conduction through the CTI and susceptible to catheter ablation. If closure of the ASD is not warranted by hemodynamic criteria, then catheter ablation of the atrial flutter is preferable to surgical closure of the septal defect, which is unlikely to abolish the atrial flutter. If closure of the septal defect is warranted in a patient with atrial flutter, then electrophysiological study with catheter ablation prior to surgery may still be considered or ablation of the atrial flutter isthmus may be performed during surgery in a center with experience in arrhythmia surgery.

In patients with prior surgical repair, both CTI-dependent and non–CTI-dependent (so-called "incisional" or scar) atrial flutter occur and can coexist in a single patient (294,443,444,447,448,450,452-456,478). Management is as discussed above. If catheter ablation is warranted, then the possibility that the flutter will have a non-CTI-dependent mechanism should be considered. Ablation may be best performed in an experienced center with advanced, three-dimensional mapping equipment for defining non–CTI-dependent arrhythmias.

b. Transposition of the Great Vessels

Patients surviving to adulthood have generally had restoration of circulation by either an arterial switch procedure or rerouting of venous return. Atrial arrhythmias are uncommon late after arterial switch procedures (373). The Mustard and Senning repairs reroute systemic venous blood to the morphologic LV that is connected to the pulmonary artery, and they reroute the pulmonary venous blood to the morphologic right ventricle that is connected to the aorta. The atrial surgery is extensive, and sinus node dysfunction is common (369,479,480). Of 478 patients who survived the perioperative period after Mustard repair in a study reported by Gelatt and coworkers, atrial flutter subsequently occurred in 14%, and ectopic AT occurred in 1% (3 patients) (369). The actuarial rate of atrial flutter at 20 years after repair was 24%. An even greater incidence of atrial arrhythmias was observed in earlier series (481).

Loss of coordinated atrial activity and acceleration of rate can produce severe symptoms and hemodynamic compromise. Development of atrial arrhythmias is also associated with impaired ventricular function (372,482). For these reasons, development of atrial arrhythmias has been associated with an increased risk of death and sudden death in some, but not all, studies (369,480).

Acute management of rapid SVT is as discussed above (see Sections IV and V). These arrhythmias tend to be recurrent, and attempts to maintain sinus rhythm are usually warranted due to the hemodynamic compromise produced by the arrhythmia. Associated ventricular dysfunction and risk of sudden death and sinus node dysfunction can complicate selection of antiarrhythmic drug therapy. Referral to a specialist with experience in the care of these patients is usually warranted. Catheter ablation of the lesion related to the atrial flutter can be effective but is more difficult than for patients without structural heart disease and should be attempted only at experienced centers (478). In particular, access to the pulmonary venous atrium is usually required for ablation, which may be approached either in a retrograde or a transseptal fashion.

c. Tetralogy of Fallot

Atrial incisions are commonly made at the time of repair, predisposing to the late development of incision-related atrial flutter (371,374,483,484). During 35 years of follow-up after repair, 10% of patients developed atrial flutter, 11% developed sustained VT, and 8% died suddenly (484).

The sinus rhythm ECG shows RBBB in the vast majority of patients, such that SVTs are conducted with RBBB aberrancy. Ventricular tachycardia arises due to re-entry in the region of the right ventricular outflow tract or infundibular septum. Although most of these VTs have a QRS configuration resembling LBBB, the VT QRS resembles RBBB in approximately one-quarter of patients (485). An RBBB configuration of the tachycardia is not, therefore, a reliable guide for distinguishing a VT from an SVT. Atrial flutter precipitates hemodynamic compromise in some patients. Acute management is dictated by hemodynamic stability (see Section IV–B). Establishment of the correct diagnosis is critical to guide further management. Electrophysiological testing may be required, and referral to a specialist is advised.
Atrial flutter can be CTI dependent or incision related (444,478). Development of atrial flutter can be an indication of worsening ventricular function and tricuspid regurgitation (351,371,484,486). Hemodynamic reassessment of the repair and consideration for revision are sometimes warranted. Chronic management is as discussed above.

d. Ebstein's Anomaly of the Tricuspid Valve

In Ebstein's anomaly, the attachment of the septal and inferior leaflets of the tricuspid valve is displaced downward into the right ventricle. Patent foramen ovale or ostium secundum ASD are present in more than half of patients. Accessory AV and atriofascicular pathways occur in up to 25% of patients and are more often right sided and multiple than in patients without the disorder (487-490). In addition to AVRT, AF, atrial flutter, and ectopic AT can occur. Finally, Ebstein's anomaly is also often present in patients with congenitally corrected transposition of the great vessels (ie, ventricular inversion), in which the left-sided (ie, systemic) AV valve is morphologically a tricuspid valve.

Right bundle-branch block is usually present and, in the presence of a right-sided accessory pathway, ventricular preexcitation can mask the ECG evidence of RBBB. Thus, patients may present with orthodromic AVRT with RBBB aberrancy and, after termination of the arrhythmia, there may be evidence of a right-sided accessory pathway causing preexcitation during sinus rhythm. Left bundle-branch block-configuration tachycardias can be due to antidromic AVRT or conduction over a bystander accessory pathway during, for example, AT, AVRT, or atrial flutter.

The malformation can be mild, producing no symptoms. Alternatively, tricuspid regurgitation and a large ASD can cause cyanosis and hemodynamic compromise that may be exacerbated by arrhythmias. Depending on the severity of the malformation and the arrhythmia, SVTs can produce cyanosis and severe symptoms or death. Sudden death can also occur as a consequence of rapid repetitive conduction to the ventricles during AF or atrial flutter when an accessory pathway is present (490).

When hemodynamic consequences of the malformation warrant operative correction and supraventricular arrhythmias are present, arrhythmia management should be coordinated with the surgical team (491,492). Preoperative electro-

Recommendations for Treatment of Supraventricular Tachycardias in Adults With Congenital Heart Disease

Condition	Recommendation	Class	Level of Evidence	References
Failed antiarrhythmic drugs and symptomatic:				
•Repaired ASD	Catheter ablation in an experienced center	I	C	(186,444,447, 452,455,478)
•Mustard or Senning repair of transposition of the great vessels:	Catheter ablation in an experienced center	I	C	(447,452, 455,478)
Unrepaired asymptomatic ASD not hemodynamically significant	Closure of the ASD for treatment of the arrhythmia	III	C	(476,477)
Unrepaired hemodynamically significant ASD with atrial flutter*	Closure of the ASD combined with ablation of the flutter isthmus	I	C	
PSVT and Ebstein's anomaly with hemodynamic indications forsurgical repair	Surgical ablation of accessory pathways at the time of operative repair of the malformation at an experienced center	I	C	(491,492)

*Conversion and antiarrhythmic drug therapy initial management as described for atrial flutter (see Section V–F).

ASD indicates atrial septal defect; PSVT, paroxysmal supraventricular tachycardia.

physiological evaluation is often warranted. Failure to address potential accessory pathways can lead to recurrent arrhythmias and instability in the perioperative period. Catheter ablation prior to surgery is, therefore, recommended. Surgical division of accessory pathways may be considered as an option for selected patients in centers with experience.

In general, management of accessory pathways in Ebstein's anomaly is as discussed in Section V–D. However, the associated malformation and common coexistence of multiple accessory pathways increase the difficulty of mapping and ablation. Of 65 patients reported in the Pediatric Radiofrequency Ablation Registry, acute success rates ranged from 75 to 89%, depending on pathway location (septal vs. free wall); late recurrences occurred in up to 32% of patients (493).

e. Fontan Repairs

The Fontan procedure and its modifications are used to direct systemic venous blood into the pulmonary artery for patients with single-ventricle physiology, including tricuspid atresia or single LV with pulmonary stenosis. The venous return, from the superior and inferior vena cava or right atrium, is directed to the pulmonary circulation without the benefit of assistance from right ventricular contraction. Incision-related atrial flutter or AF occurred in up to 57% of patients, depending on the particular type of repair (494,495). Atrial arrhythmias can cause rapid hemodynamic deterioration and are associated with more heart failure. Acute management is as discussed for atrial flutter above. Referral to a specialist is advised. Catheter ablation can be effective but is often difficult due to multiple circuits and should be attempted only at experienced centers. In addition to the low success rate of catheter ablation in the Fontan atriopulmonary connection, there is a high rate of recurrence after initially successful ablation procedures, limiting the usefulness of this approach (478).

C. Drug-Drug and Drug-Metabolic Interactions

The general tenets of the use of antiarrhythmic agents in supraventricular arrhythmias have been extensively outlined in the previously published ACC/AHA/ESC Guidelines for the Management of Patients With Atrial Fibrillation (1). In Tables 2 through 4 of these guidelines (1), the Vaughan-Williams Classification scheme of antiarrhythmic drugs, typical doses of drugs used to maintain sinus rhythm, and types of proarrhythmic side effects are summarized.

The vulnerable parameter (496) or target of therapy depends on the type of arrhythmia and the goals of treatment (ie, conversion of the arrhythmia, maintenance of sinus rhythm, suppression of triggers, or ventricular rate control).

A major concern accompanying the use of antiarrhythmic drugs, particularly when treating an arrhythmia that is not life threatening, such as SVT, is the occurrence of ventricular proarrhythmia (eg, torsade de pointes). A number of clinical factors increase the risk of proarrhythmia, including age, gender, fluid and electrolyte abnormalities, the presence of underlying heart disease, abnormalities of drug clearance, polypharmacy and drug-drug interactions. Drug-induced slowing of the rate of atrial flutter with the production of one-to-one conduction to the ventricle represents a potentially life-threatening form of proarrhythmia unique to the treatment of SVT. This phenomenon has been observed with drugs with class Ic and Ia action, particularly flecainide

(497). Concomitant administration of AV-nodal–blocking agents, such as a beta blocker, will reduce the likelihood of this form of proarrhythmia. Most antiarrhythmic drugs with class I and class III action, except for propafenone, can be started in an outpatient, provided the patient has no structural heart disease or other concomitant diseases and is taking no other drugs that may affect the metabolism of the particular drug.

The removal of antiarrhythmic drugs from the systemic circulation typically depends on hepatic metabolism, renal excretion, or both. Patients with kidney or liver disease are at increased risk of drug toxicity, including proarrhythmia. Amiodarone is hepatically metabolized and, therefore, should be avoided in patients with significant hepatic dysfunction. In situations in which the SVT is readily treated by nonpharmacologic interventions, this is generally the preferred approach in patients with serious liver or kidney disease.

Kidney disease increases not only the incidence of cardiac arrhythmias but also the risk associated with their treatment. Patients with renal failure are at increased risk for cardiac morbidity and mortality; estimates suggest that half of the deaths in patients with renal failure result from concomitant cardiac disease (498).

Antiarrhythmic drug use is complicated in patients with renal disease for a number of reasons. In the case of drugs cleared by the kidneys, the incidence of toxicity may be unacceptably high, as in the case of sotalol or dofetilide. Furthermore, patients with kidney disease commonly have a myocardial substrate that renders them susceptible to proarrhythmic side effects of antiarrhythmic drugs (498-512). An example is hypertension and LV hypertrophy that accompany renal failure and are associated with abnormal ventricular (513) and atrial (514) repolarization. Patients with renal failure and ventricular hypertrophy also exhibit conduction abnormalities that seem to correlate with the degree of fibrosis (515-517). Finally, fluid and electrolyte shifts characteristic of dialysis are likely to act as triggers in susceptible hearts (500-508,510,511,518,519).

Perhaps the most consistent attribute of antiarrhythmic drugs is their narrow therapeutic window. For this reason and because most patients taking an antiarrhythmic drug are also receiving other drug therapy, drug interactions are prominent and clinically significant. Modification of the action of one drug by another may occur as a result of pharmacokinetic and/or pharmacodynamic interactions. Pharmacokinetic interactions occur when one drug influences the absorption, distribution, or metabolism and elimination of another drug (eg, the increase in serum dofetilide concentration produced by verapamil). Pharmacodynamic interactions result when a drug blunts or exaggerates the effect of another drug without altering its serum concentration, as might occur when a sodium-channel–blocking drug (eg, mexiletine) is added to drugs that have class III action (520). Numerous examples of both types of interactions involving antiarrhythmic agents have been described.

One of the most prominent pharmacokinetic interactions is the interference of one drug's metabolism with another. Such interactions are most likely to be clinically significant when a drug is eliminated predominantly via a single pathway. The cytochrome P450 system plays a prominent role in antiarrhythmic drug metabolism (Table 5) (521). The table accurately suggests that the most important cytochrome P450 isoenzyme is 3A4 (CYP3A4), at least in terms of the number of drugs that are metabolized by this enzyme system (522). CYP3A4 has no known clinically important polymorphisms and is widely distributed in the liver, intestine and other parts of the gut and kidney (523). This isoenzyme is responsible for presystemic metabolism and, therefore, the first-pass effect exhibited by a number of oral agents metabolized by this pathway. Several notorious examples of adverse interactions resulting in torsades de pointes of compounds metabolized by CYP3A4 have been described, including the combination of terfenadine or cisapride with ketoconazole.

The CYP2D6 isoform is important in the metabolism of beta blockers and antiarrhythmic agents with class Ic action (522). The enzyme is expressed primarily in the liver and exhibits clinically important polymorphisms (524). Approximately 7% of Caucasians and African-Americans, but not Asians, are "poor" metabolizers (525). The important clinical consequence in treatment of cardiovascular disease is the exaggerated effect of beta blockers in patients who exhibit poor metabolism. Similarly, patients treated with CYP2D6 inhibitors, such as quinidine, especially if they are poor metabolizers, may have profound bradycardia from a low dose of beta blockers. Side effects related to the beta-blocking action of propafenone are more common in poor metabolizers (524).

P-glycoprotein is the most widely studied drug-transport molecule. It is structurally related to the family of proteins known as the ABC- or ATP-binding cassette family and actively transports substrates, including drugs, across cell membranes (526). It is expressed in the gut lumen, hepatocytes lining bile canniculi, and endothelial cells in the blood-brain barrier. Inhibition of P-glycoprotein is not clinically important for the elimination of most drugs because many have other pathways for elimination. An exception is digoxin, which does not undergo extensive P450 isoenzyme metabolism. Instead, its bioavailability is limited by P-glycoprotein–mediated re-excretion into the gut lumen (and possibly other transporters in the kidney and liver) (527). Many structurally unrelated drugs may increase digitalis concentrations by inhibition of P-glycoprotein.

D. Quality-of-Life and Cost Considerations

Improvement of quality of life is usually the major therapeutic goal of treatment for SVT. Although it was reported early that catheter ablation improves quality of life (528,529) and is cost effective compared with other strategies (530), these studies were observational rather than randomized (528,530) or were limited to more symptomatic patients on stable antiarrhythmic medical therapy (529). A later study compared the effect on quality of life between catheter ablation

Table 5. Antiarrhythmic Drug Metabolism

	CYP3A4	CYP2D6	P-glycoprotein
Substrates	Amiodarone Quinidine Lidocaine Mexiletine Cyclosporine Sildenafil Any calcium-channel blocker Any statin Any HIV PrInh	Propafenone Flecainide Propranolol Metoprolol Timolol	Digoxin Many antineoplastic drugs
Inhibitors	Amiodarone Verapamil Cyclosporine Erythromycin Clarithromycin Ketoconazole Itraconazole Ritonavir Grapefruit juice	Quinidine Propafenone Fluoxetine TCA Erythromycin Ketaconazole Itraconazole	Amiodarone Quinidine Verapamil Cyclosporine
Inducers	Rifampin Ddiphenylhydantoin Phenobarbital		

HIV indicates human immunodeficiency virus; PrInh, protease inhibitor; TCA, tricyclic antidepressant.

Modified from Roden DM. Antiarrhythmic drugs: from mechanisms to clinical practice. Heart 2000;84:339-46.

and pharmacologic therapy as an initial strategy for patients with SVTs (531). Both treatments improved quality of life and decreased frequency of disease-specific symptoms, but ablation improved quality of life in more general health categories and resulted in complete amelioration of symptoms in more patients (74 vs. 33%) than did medication. Potential long-term costs were similar for medication and ablation (531). Among patients who had monthly episodes of SVT, RF ablation was, however, the more effective and less expensive therapy compared with long-term drug therapy (532). Another prospective study compared the long-term effects on health outcome of catheter ablation and medical therapy as an initial treatment for patients with newly documented PSVT, excluding those with drug-refractory symptoms referred specifically for ablation (533). At 5-year follow-up, patients who received ablation had improved quality-of-life scores and a reduction in disease-specific symptoms when compared with patients who continued to take medical therapy. More patients reported complete elimination of symptoms with ablation therapy (70%) than did those taking medical therapy (43%). Over 5 years, the average cumulative cost for patients in the medical therapy group was statistically significantly lower than in patients initially treated with ablation therapy: $6249 plus or minus $1421 per patient versus $7507 plus or minus $1098 per patient (533). It was concluded that patient preference remains the critical determinant in choosing a particular treatment in cases of mildly to moderately symptomatic PSVT (533).

Baseline quality-of-life scores appear to be lower for patients with atrial flutter and AF than for those with other arrhythmias who are undergoing RF ablation (528). Several studies have described improvement in symptoms and quality of life after catheter ablation of atrial flutter (427,534-537). Ablation of atrial flutter resulted in an improvement in quality of life as well as reductions in symptom-frequency scores and symptom-severity scores compared with preablation values (536). There was a reduction in the number of patients visiting accident and emergency departments, requiring cardioversion, or being admitted to a hospital for a rhythm problem. Patients with atrial flutter and concomitant AF before ablation and those with atrial flutter alone both derived significant benefit from atrial flutter ablation (536). Others reported that patients who had atrial flutter associated with AF before ablation had less improvement than those without AF (535). Moreover, in a prospective, randomized comparison of antiarrhythmic therapy versus first-line RF ablation in patients with atrial flutter, the sense of well-being and function in daily life improved after ablation but did not change significantly in patients treated with drugs (427). Ablation was associated with a better success rate and effect on quality of life, a lower occurrence of AF, and a lower need for rehospitalization at follow-up (427).

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APPENDIX 1: ABBREVIATIONS

ACC	=	American College of Cardiology
ACCF	=	American College of Cardiology Foundation
ACLS	=	Advanced Cardiovascular Life Support
AF	=	atrial fibrillation
AHA	=	American Heart Association
AHCPR	=	Agency for Healthcare Policy Research
AP	=	accessory pathway
ASD	=	atrial septal defect
AT	=	atrial tachycardia
AV	=	atrioventricular
AVNRT	=	atrioventricular nodal reciprocating tachycardia
AVRT	=	atrioventricular reciprocating tachycardia
BBB	=	bundle-branch block
bpm	=	beats per minute
CCS	=	clinical classification software
CHF	=	congestive heart failure
CPG	=	Committee for Practice Guidelines (of the European Society of Cardiology)
CTI	=	cavotricuspid isthmus
DAD	=	delayed afterdepolarization
DC	=	direct current
ECG	=	electrocardiogram; electrocardiographic
ESC	=	European Society of Cardiology
FDA	=	Food and Drug Administration
HCFA	=	Health Care Financing Administration (since renamed the Centers for Medicare and Medicaid Services, or CMS)
HCUP-3	=	Healthcare Cost and Utilization Project
HIV	=	human immunodeficiency virus
INR	=	international normalized ratio
IV	=	intravenous
LBBB	=	left bundle-branch block
LV	=	left ventricle; left ventricular
MAST	=	military antishock trousers
MAT	=	multifocal atrial tachycardia
MEDPAR	=	U.S. Medicare Provider Analysis and Review
MERFS	=	Multicentre European Radiofrequency Survey
MESA	=	Marshfield (Wisconsin, U.S.A.) Epidemiologic Study Area
ms	=	milliseconds
NASPE	=	North American Society of Pacing and Electrophysiology-Heart Rhythm Society
P wave	=	ECG inscription of atrial electrical activity
PJRT	=	permanent form of junctional reciprocating tachycardia
POTS	=	postural orthostatic tachycardia syndrome
PrInh	=	protease inhibitor
PSVT	=	paroxysmal supraventricular tachycardia
PVs	=	pulmonary vein
Qp/Qs	=	pulmonary blood flow/systemic blood flow
QR	=	ventricular activation with an initial large negative followed by a smaller positive deflection on ECG
QRS	=	ventricular activation on ECG
QS	=	ventricular activation with a negative deflection on ECG
QT	=	time interval measured from the start of the QRS deflection to the end of the T wave
R wave	=	ventricular activation
RBBB	=	right bundle-branch block
RF	=	radiofrequency
RR	=	relative risk
RS	=	ventricular activation with an initial positive deflection followed by negative deflection on ECG

SA	=	sinoatrial	TCA	=	tricyclic antidepressant
SVA	=	supraventricular arrhythmia	TEE	=	transesophageal echocardiography
SVC	=	superior vena cava	VF	=	ventricular fibrillation
SVT	=	supraventricular tachycardia	VT	=	ventricular tachycardia
T wave	=	ventricular repolarization	WPW	=	Wolff-Parkinson-White syndrome

APPENDIX 2: EXTERNAL PEER REVIEWERS FOR THE ACC/AHA/ESC GUIDELINES FOR THE MANAGEMENT OF PATIENTS WITH SUPRAVENTRICULAR ARRHYTHMIAS

Reviewer Name*	Review Category and Affiliation
Stephen L. Winters, MD, FACC	Official Reviewer – ACC (Board of Governors)
Marian C. Limacher, MD, FACC, FAHA	Official Reviewer – ACC (Board of Trustees)
Michael H. Crawford, MD, FACC, FAHA	Official Reviewer – AHA
Kenneth A. Ellenbogen, MD, FACC, FAHA	Official Reviewer – AHA
Silvia G. Priori, MD, PhD, FESC	Official Reviewer – ESC
Panogiostis Vardas, MD, PhD, FACC, FESC	Official Reviewer – ESC
Valentin Fuster, MD, PhD, FACC, FAHA, FESC	Official Reviewer – ACC/AHA Task Force on Practice Guidelines
Jamie B. Conti, MD, FACC	Organizational Reviewer – NASPE–Heart Rhythm Society
Jeffrey L. Anderson, MD, FACC, FAHA	Content Reviewer – ACC/AHA Task Force on Practice Guidelines
Maria Angeles Alonso Garcia, MD, FESC	Content Reviewer – ESC Committee for Practice Guidelines
Elliott M. Antman, MD, FACC, FAHA	Content Reviewer – ACC/AHA Task Force on Practice Guidelines
Gust H. Bardy, MD, FACC	Content Reviewer – AHA ECG/Arrhythmias Committee
Kathleen Blake, MD, FACC, FAHA	Content Reviewer – AHA ECG/Arrhythmias Committee
Jean-Jacques Blanc, MD, PhD, FESC	Content Reviewer – ESC Committee for Practice Guidelines
Mitchell I. Cohen, MD, FACC	Content Reviewer – AHA ECG/Arrhythmias Committee
Francisco G. Cosio, MD, FACC, FESC	Content Reviewer – ESC Working Group on Arrhythmias
Anne B. Curtis, MD, FACC	Content Reviewer – ACCF Electrophysiology Committee
John E. Deanfield, MD, FESC	Content Reviewer – ESC Task Force on Grown-Up Congenital Heart Disease
Jaap Willem Deckers, MD, PhD, FESC	Content Reviewer – ESC Committee for Practice Guidelines
Leonard S. Dreifus, MD, MACC	Content Reviewer – ACCF Electrophysiology Committee
Ann Marie Dubin, MD, FACC	Content Reviewer – AHA ECG/Arrhythmias Committee
N.A. Mark Estes, III, MD, FACC, FAHA	Content Reviewer – AHA ECG/Arrhythmias Committee
Fiorenzo Gaita, MD	Content Reviewer – ESC Working Group Arrhythmias
Leonard I. Ganz, MD, FACC	Content Reviewer – ACCF Electrophysiology Committee
Gabriel Gregoratos, MD, FACC, FAHA	Content Reviewer – ACC/AHA Task Force on Practice Guidelines
Joachim Hebe, MD	Content Reviewer – ESC Working Group on Grown-Up Congenital Heart Disease
Ray E. Hershberger, MD, FACC	Content Reviewer – AHA ECG/Arrhythmias Committee
Sharon Ann Hunt, MD, FACC, FAHA	Content Reviewer – ACC/AHA Task Force on Practice Guidelines
Pamela E. Karasik, MD, FACC	Content Reviewer – ACCF Electrophysiology Committee
Peter R. Kowey, MD, FACC, FAHA	Content Reviewer – ACCF Electrophysiology Committee
Bertil Lindahl, MD	Content Reviewer – ESC Committee for Practice Guidelines
Gianfranco Mazzotta, MD, FESC	Content Reviewer – ESC Committee for Practice Guidelines
Gregory F. Michaud, MD, FACC	Content Reviewer – ACCF Electrophysiology Committee
João Carlos Araujo Morais, MD, FESC	Content Reviewer – ESC Committee for Practice Guidelines
Koonlawee Nadamanee, MD	Content Reviewer – AHA ECG/Arrhythmias Committee
Celia Oakley, MD, FACC, FESC	Content Reviewer – ESC Task Force on Cardiovascular Disease During Pregnancy
Jeffrey E. Olgin, MD, FACC	Content Reviewer – ACCF Electrophysiology Committee
Ali Oto, MD, FACC, FESC	Content Reviewer – ESC Working Group on Arrhythmias
Richard L. Page, MD, FACC	Content Reviewer – AHA ECG/Arrhythmias Committee
Richard O. Russell, Jr., MD, FACC, FAHA	Content Reviewer – ACC/AHA Task Force on Practice Guidelines
Hue-Teh Shih, MD, FACC, FAHA	Content Reviewer – ACCF Board of Governors
Ruey Jen Sung, MD, FACC, FAHA	Content Reviewer – ACCF Electrophysiology Committee
Stuart E. Trenholme, MD, FACC	Content Reviewer – ACCF Board of Governors
George F. Van Hare, MD, FACC	Content Reviewer – Individual Review
Hein J.J. Wellens, MD, FACC, FAHA, FESC	Content Reviewer – ESC Working Group on Arrhythmias

*Names are listed in alphabetical order within each category of review.

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