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EHRA POSITION PAPER

European Heart Rhythm Association (EHRA) consensus document on the management of supraventricular arrhythmias, endorsed by Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), and Sociedad Latinoamericana de Estimulación Cardiaca y Electrofisiologia (SOLAECE)

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Abbreviations

AAD:	antiarrhythmic drugs
ACHD:	adult congenital heart disease
AF:	atrial fibrillation
AFL:	atrial flutter
ANP:	atrial natriuretic peptide
AP:	accessory pathway
ASD:	atrial septal defect
AV:	atrioventricular
AVN:	atrioventricular node
AVNRT:	atrioventricular nodal reentrant tachycardia
AVRT:	atrioventricular reentrant tachycardia
AT:	atrial tachycardia
BBB:	bundle branch block
bpm:	beats per minute
CI:	confidence interval
CL:	cycle length
CTI:	cavo-tricuspid isthmus
DC:	direct current
ECG:	electrocardiogram
EPS:	electrophysiology study
ERP:	effective refractory period
HPS:	His-Purkinje system
HR:	heart rate
IV:	intravenous
IVC:	inferior vena cava
LA:	left atrium
LBBB:	left bundle branch block
LV:	left ventricle
MESA:	Marshfield (Wisconsin) Epidemiologic Study Area
MRT:	macroreentrant tachycardia
ms:	milliseconds
PJRT:	permanent junctional reciprocating tachycardia
POTS:	postural orthostatic tachycardia syndrome
PPI:	post-pacing interval
QALY:	quality-adjusted life years
QoL:	quality of life
RA:	right atrium
RBBB:	right bundle branch block
RCT:	randomized controlled trials
RF:	radiofrequency
RV:	right ventricle
s:	seconds
SR:	sinus rhythm
SVC:	superior vena cava
SVT:	supraventricular tachycardia
VA:	ventricular arrhythmia
WPW:	Wolff–Parkinson–White

Preamble/definitions

Supraventricular arrhythmias are common, and patients are often symptomatic requiring management with drug therapies and electrophysiological procedures. The European Society of Cardiology published management guidelines for supraventricular tachycardias (SVT) in 2003,[1] and corresponding US guidelines have also been published, the most recent being in 2015.[2]

There is a need to provide expert recommendations for professionals participating in the care of patients presenting with SVT. In addition, several associated conditions where SVTs may co-exist need to be explained in more detail. To address this topic, a Task Force was convened by the European Heart Rhythm Association (EHRA) with representation from the Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), and Sociedad Latinoamericana de Estimulación Cardiaca y Electrofisiologia (SOLAECE), with the remit to comprehensively review the published evidence available, and to publish a joint consensus document on the management of SVT patients, with up-to-date consensus recommendations for clinical practice.

This document summarizes current developments in the field, with focus on new advances since the last ESC guidelines, and provides general recommendations for the management of SVT patients based on the principles of evidence-based medicine.

Evidence review

Members of the Task Force were asked to perform a detailed 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 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 prepared by the Task Force with representation from EHRA, HRS, APHRS, and SOLAECE. The document was peer-reviewed by official external reviewers representing EHRA, HRS, APHRS, and SOLAECE.

Consensus statements are evidence-based, and derived primarily from published data. Current systems of ranking level of evidence are becoming complicated in a way that their practical utility might be compromised.[3] We have, therefore, opted for an easier and, perhaps, more user-friendly system of ranking that should allow physicians to easily assess current status of evidence and consequent guidance (*Table 1*). Thus, a green heart indicates a recommended/indicated treatment or procedure and is based on at least one randomized trial, or is supported by strong observational

Table 1 Scientific rationale of recommendations

Scientific evidence that a treatment or procedure is beneficial and effective. Requires at least one randomized trial, or is supported by strong observational evidence and authors' consensus.	Recommended/ indicated	
General agreement and/or scientific evidence favour the usefulness/ efficacy of a treatment or procedure. May be supported by randomized trials that are, however, based on small number of patients to allow a green heart recommendation.	May be used or recommended	
Scientific evidence or general agreement not to use or recommend a treatment or procedure.	Should NOT be used or recommended	

This categorization for our consensus document should not be considered as being directly similar to that used for official society guideline recommendations which apply a classification (I–III) and level of evidence (A, B, and C) to recommendations.

Table 2 Conventional classification of supraventricular tachycardias

- Atrial tachycardias
  - Sinus tachycardia
    - Physiological sinus tachycardia
    - Inappropriate sinus tachycardia
    - Sinus node reentrant tachycardia
  - Atrial tachycardia
    - Focal atrial tachycardia
    - Multifocal atrial tachycardia
    - Macro-reentrant tachycardia
      - Cavotricuspid isthmus-dependent, counter-clockwise or clockwise (typical atrial flutter)
      - Non cavotricuspid isthmus–dependent, mitral isthmus-dependent, and other atypical left or right atrial flutters
- Atrioventricular junctional tachycardias
  - Atrioventricular nodal reentrant tachycardia
    - Typical
    - Atypical
  - Non-reentrant junctional tachycardia
    - Non-paroxysmal junctional tachycardia
    - Focal junctional tachycardia
    - Other non-reentrant variants
- Atrioventricular tachycardias
  - Atrioventricular reentrant tachycardia
    - Orthodromic
    - Antidromic (with retrograde conduction through the AV node or, rarely, through another pathway)

evidence that it is beneficial and effective. A yellow heart indicates that general agreement and/or scientific evidence favour the usefulness/efficacy of a treatment or procedure. May be supported by randomized trials that are, however, based on small number of patients to allow a green heart recommendation. Treatment strategies for which there has been scientific evidence that they are potentially harmful and should not be used are indicated by a red heart. European Heart Rhythm Association grading of consensus statements does not have separate definitions of Level of Evidence. The categorization used should not be considered as being directly similar to that used for official society guideline recommendations which apply a classification (I–III) and level of evidence (A, B, and C) to recommendations.

Overall, this is a consensus document that includes evidence and expert opinions from several countries. The pharmacologic and non-pharmacologic antiarrhythmic approaches discussed may, therefore, include drugs that do not have the approval of governmental regulatory agencies in all countries.

Relationships with industry and other conflicts

It is EHRA/ESC policy to sponsor position papers and guidelines without commercial support, and all members volunteered their time. Thus, all members of the writing group as well as reviewers have disclosed any potential conflict of interest in detail, at the end of this document.

Definitions and classification

The term supraventricular literally indicates tachycardias (atrial and/or ventricular rates >100 bpm at rest), the mechanism of which involves tissue from the His bundle or above.[1,2] Traditionally, SVT has been used to describe all kinds of tachycardias apart from ventricular tachycardias and atrial fibrillation (AF) and has, therefore, included tachycardias such as atrioventricular reentry due to accessory connections that is not, in essence, a supraventricular rhythm (*Table 2*). The term narrow-QRS tachycardia indicates those with a QRS duration ≤120 ms. A wide-QRS tachycardia refers to one with a QRS duration >120 ms (*Table 3*). In clinical practice, SVT may present as narrow- or wide-QRS tachycardias, and most of them usually, although not invariably, manifest as regular rhythms. This position paper does not cover atrial fibrillation, which is the subject of a separate clinical guideline, as well as various consensus documents.

Epidemiology

Supraventricular arrhythmias are relatively common, but rarely life threatening. However, precise description of the epidemiology of SVT is difficult as there is often poor distinction between AF, atrial flutter (AFL) and other supraventricular arrhythmias. In contrast to the extensive epidemiology on AF, specific focus on SVT population epidemiology is sparse.

In a 3.5% sample of medical records in the Marshfield (Wisconsin) Epidemiologic Study Area (MESA) the prevalence of paroxysmal SVT was 2.25/1000 persons, and the incidence was 35/100 000 person-years.[4] Based on these old data, it was estimated that there are ~89 000 new cases per year, and 570 000 patients with paroxysmal SVT in the USA.

The precipitants of SVT can be related to age, sex, and associated comorbidities. Thus, in the general population appear to be two

Table 3 Differential diagnosis of narrow and wide QRS tachycardias

Narrow QRS (≤120 ms) tachycardias
Regular
Physiological sinus tachycardia
Inappropriate sinus tachycardia
Sinus nodal reentrant tachycardia
Focal atrial tachycardia
Atrial flutter
Atrial fibrillation with very fast ventricular response
Atrioventricular nodal reentrant tachycardia
Non-paroxysmal or focal junctional tachycardia
Orthodromic atrioventricular reentrant tachycardia
Idiopathic ventricular tachycardia (especially high septal VT)
Irregular
Atrial fibrillation
Atrial focal tachycardia or atrial flutter with varying AV block
Multifocal atrial tachycardia
Wide QRS (>120 ms) tachycardias
Regular
Antidromic atrioventricular reentrant tachycardia
Any regular atrial or junctional reentrant tachycardias with:
aberration/bundle branch block
pre-excitation/bystander accessory pathway
Ventricular tachycardia/flutter
Irregular
Atrial fibrillation or atrial tachycardia with varying block conducted with aberration
Antidromic atrioventricular reentrant tachycardia with a variable VA conduction
Pre-excited AF
Polymorphic VT
Torsade de pointes
Ventricular fibrillation

distinct subsets of patients with paroxysmal SVT: those with other cardiovascular disease and those with lone paroxysmal SVT. In MESA, other cardiovascular disease was present in 90% of males, and 48% of females. Overall, females had 2-fold greater relative risk (RR) of paroxysmal SVT compared with males. Compared with patients with other cardiovascular disease, those with lone paroxysmal SVT were younger (mean 37 vs. 69 years), had a faster paroxysmal SVT heart rate (mean 186 vs. 155 beats/min) and were more likely to have their condition first documented in the emergency room (69% vs. 30%). The onset of symptoms occurred during the childbearing years in 58% of females with lone paroxysmal SVT, vs. 9% of females with other cardiovascular disease. Older individuals (age >65 years) had >5-fold risk of developing paroxysmal SVT compared to younger subjects.[4] Data from specialized centres reporting on paroxysmal SVT patients referred for electrophysiology procedures, indicate that patients tend to be younger, have similar age distribution, and lower prevalence of cardiovascular comorbidities.[5–7]

The prevalence of SVT mediated by an accessory pathway decreases with age. For example, manifest pre-excitation or WPW pattern on ECG tracings in the general population is 0.1% to 0.3%. However, not all patients with manifest ventricular pre-excitation develop paroxysmal SVT.[6,8] In female, middle-aged or older persons, atrioventricular nodal reentrant tachycardia (AVNRT) is more common. In younger subjects (e.g. adolescents), the prevalence may be more balanced between atrioventricular reentrant tachycardia (AVRT) and AVNRT. Porter *et al.* described 1754 patients undergoing catheter ablation, where AVNRT was the most common (56%) aetiology, followed by AVRT 27%, and atrial tachycardia (AT) 17%.[9] The proportion of AVRT decreased with age, whereas the proportion of AVNRT and AT increased. Most patients with AVRT were male (55%), in contrast to patients with AVNRT and AT who were predominantly female (70% and 62%, respectively). Recently, in the first Latin American registry on catheter ablation including 15 099 procedures from 120 centres in 13 participating countries, AVRT was the group of arrhythmias most frequently ablated (31%), followed by AVNRT (29%), typical AFL (14%), and AF (11%).[10]

Limited population data on other supraventricular arrhythmias (apart from AF) are available. For AFL, one report from MESA of 181 new cases of AFL estimated an overall incidence of 88/100 000 person-years.[11] Incidence rates ranged from 5/100 000 in those <50 years old to 587/100 000 in subjects older than 80 years. Atrial flutter was 2.5-fold more common in men, 3.5-fold more common in subjects with heart failure, and 1.9-fold more common in subjects with chronic obstructive pulmonary disease. Only 3 subjects (1.7%) were labelled as having 'lone AFL'. In MESA, AFL had an incidence of 0.09% and 58% of the patients also had AF. These data translate to 200 000 new cases of AFL in the USA annually, the arrhythmia being more common in men, the elderly and individuals with pre-existing heart failure or chronic obstructive lung disease.

Clinical presentation

The clinical presentation of SVT usually reflects several factors such as heart rate which can be quite variable depending on age, blood pressure during the arrhythmia and resultant organ perfusion, associated comorbidities, and the individual patient symptom threshold (*Table 4*). Some patients with paroxysmal arrhythmias may be asymptomatic (or minimally symptomatic) at time of evaluation. Other patients can present with a variety of symptoms, even, rarely,

Table 4 Most common symptoms during sustained SVT

Common	Uncommon	Rare
Chest discomfort or pressure	Chest pain	Asymptomatic
Dyspnoea	Diaphoresis	Tachycardiomyopathy
Lightheadedness, dizziness, or presyncope	Nausea	Sudden death with WPW syndrome
Palpitations	Syncope	
Polyuria		

imitating panic disorders.[12] Thus, SVT may have a heterogeneous clinical presentation, most often occurring in the absence of heart disease in younger individuals ('lone SVT'). A careful clinical history should include description of the arrhythmia pattern in terms of number of episodes, duration, frequency, mode of onset, and possible triggers. Irregular palpitations may be associated with premature depolarizations, AF, or multifocal atrial tachycardia. Paroxysmal AF is often asymptomatic whilst paroxysmal SVT is usually symptomatic,[13] although symptoms may be minimal and, on certain occasions, prolonged asymptomatic episodes may lead to a tachycardiomyopathy.[14]

Gradual increase in heart rate is suggestive of focal atrial tachycardia or sinus node (physiological or inappropriate) tachycardia. Typically, these forms of SVT have shorter duration but episodes may occur frequently (often daily or weekly episodes). If the SVT symptoms are suggestive of regular and paroxysmal palpitations with a sudden onset and termination, these most commonly result from AVRT or AVNRT; sinus node reentry is less common. Episodes of AVNRT or AVRT typically are longer but less frequent (weekly or monthly) compared to AT. Usually the symptoms are abrupt or rapid in onset, but may vary depending on the specific arrhythmia. Patients with underlying cardiovascular comorbidities such as ischaemic heart disease, cardiomyopathy or valvular heart disease (with or without heart failure), are more likely to present with breathlessness or chest discomfort/pain, particularly at fast heart rates, such as $>$150 bpm.

Termination by vagal manoeuvres further suggests a re-entrant tachycardia involving atrioventricular (AV) nodal tissue (e.g. AVNRT, AVRT). Polyuria may be a symptom supportive of a sustained supraventricular arrhythmia, related to the release of atrial natriuretic peptide in response to increased atrial pressures. This is most pronounced in AVNRT.[15] Breathlessness may be related to a tachycardia-mediated cardiomyopathy if the untreated SVT persists for weeks to months with a fast ventricular response, leading to dilation and impaired left ventricular function.[14] Syncope may be present in up to 20% of patients presenting with a narrow QRS complex tachycardia.[16] In most instances, the heart rate is not so rapid as to impair ventricular function and cardiac output. A SVT with a very rapid ventricular rate (e.g. $>$250 bpm) might be seen in persons with an accessory pathway or 1:1 conducting atrial flutter leading to reduced cardiac output and syncope. A presentation with syncope may also suggest concomitant structural abnormalities, for example, valvular aortic stenosis, hypertrophic cardiomyopathy, etc. Thus, the presence of associated cardiac disease should be part of the initial patient evaluation, and an echocardiogram is recommended. Physical examination during tachycardia usually does not lead to a definitive diagnosis, but it may provide significant clues toward the diagnosis of associated heart disease or heart failure.

Differential diagnosis of tachycardias

Narrow QRS ($\leq$120 ms) tachycardias

Narrow QRS complexes are due to rapid activation of the ventricles via the His-Purkinje system, which suggests that the origin of the arrhythmia is above or within the His bundle. However, early activation of the His bundle can also occur in high septal ventricular tachycardias thus resulting in narrow QRS complexes. A classification of narrow QRS tachycardias is shown in *Table 3*.

12-lead ECG in sinus rhythm

In the absence of ECG recorded during the tachycardia, an ECG in SR may provide clues for the diagnosis of SVT and should be scrutinized for any abnormality. Baseline intra-atrial conduction delay is a finding which suggests atrial reentry, but does not rule out other SVTs.

The presence of pre-excitation in a patient with a history of regular paroxysmal palpitations is strongly suggestive of AVRT, while irregular palpitations are suggestive of AF. The absence of apparent pre-excitation does not rule out the diagnosis of AVRT, since it may be due to a more common concealed accessory pathway (AP) that conducts only retrogradely.

12-lead ECG during tachycardia

An ECG taken during tachycardia is of key importance for the proper diagnosis of SVT, although it may fail to lead to a specific diagnosis.[17] It is easily obtained in most cases, but not always available in patients with very short or infrequent periods of palpitations. *Figure 1* demonstrates the circuits and 12-lead ECGs of different types of SVT.

Initiation and termination of the tachycardia

Sudden prolongation of the PR interval occurs in typical AVNRT after an atrial ectopic beat. An atrial tachycardia (AT) may also be initiated by an atrial ectopic beat, but is not dependent on marked PR prolongation. Automatic ATs are characterized by gradual acceleration (warm-up phenomenon), and then deceleration (cool down). Premature atrial or ventricular beats may trigger AVRT. Premature ventricular beats are a common trigger of atypical AVNRT, but rarely induce typical AVNRT, and only exceptionally AT.

Regularity of tachycardia cycle length

The regularity of the RR interval should be assessed (*Figure 2*). Irregular tachycardias may represent focal or multifocal AT, AF and AFL with varying AV conduction. Patterns of irregularity can sometimes be found, such as in AFL or in the case of Wenckebach phenomena. Irregular arrhythmias, such as multifocal AT, typically display variable P wave morphologies, and varying PP, RR, and PR intervals. Atrial flutter can have fixed AV conduction and present as a regular tachycardia, and even AF can be almost regular when very fast. The QRS regularity provides some information with respect to the tachycardia mechanism, but has significant limitations due to varying AV conduction and due to the fact that the ventricles may not be part of the arrhythmia circuit. Multifocal ATs are very rare but irregular ATs are not. When they manifest as very dynamic arrhythmias and even start and stop frequently, they are usually due to focal mechanisms. Incessant tachycardias may also be the so-called permanent junctional reciprocating tachycardia, and, rarely, atypical AVNRT (see the sections 'atrioventricular junctional tachycardias' and 'atrioventricular reentrant tachycardias'). Reentrant tachycardias, whether micro- or macro-reentries, are never irregular. If the irregularity does not exceed 15% of the CL, a reentry is possible, while above this threshold, a focal arrhythmia is much more likely.[18]

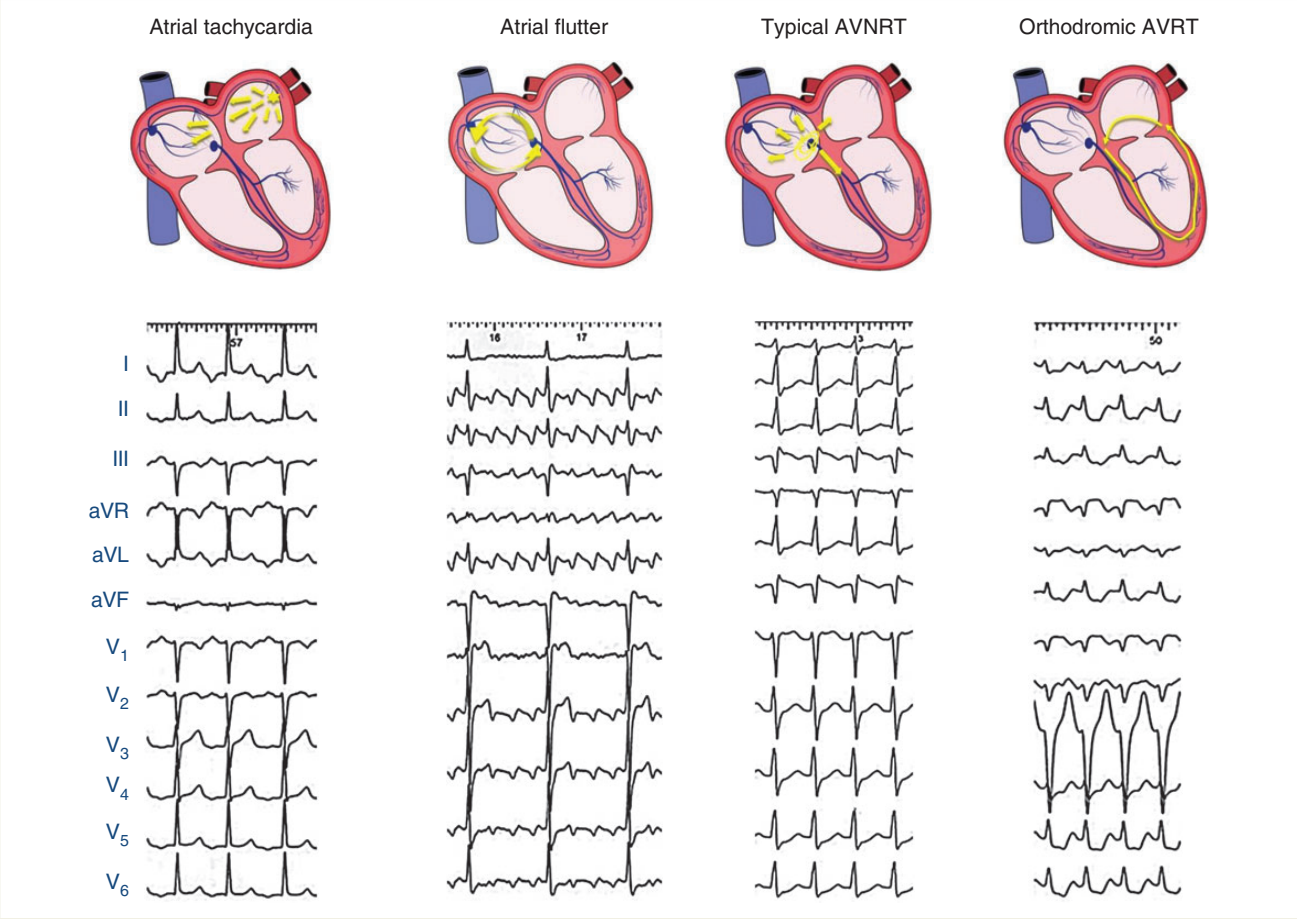


Figure 1 Tachycardia circuit and typical 12-lead ECGs in different types of narrow-QRS SVT. AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; AP, accessory pathway.

A change in ventricular CL preceded by the change in the atrial CL is seen in AT or atypical AVNRT. A change in ventricular CL preceding the change in subsequent atrial CL favours typical AVNRT or AVRT.[19] A fixed VA interval in the presence of variable RR intervals excludes AT. QRS alternans is a rare phenomenon in slow SVTs and suggests AVRT as the likely diagnosis. However, this is a common finding in any fast SVT.

P/QRS relationship

According to their P/QRS relationships, SVTs are classified as having short or long RP intervals. A very short RP interval (<70 ms) rules out AVRT and indicates typical AVNRT or, less commonly AT, as the most likely diagnosis. The 70 ms cut-off interval is based on VA intervals that have been examined in electrophysiology studies. An cut-off interval of 90 ms has been shown to be useful for surface ECG measurements and can be used if P waves are visible,[20] but data on actual RP measurement during various types of SVT are scarce.

Short RP SVTs are those with RP intervals shorter than half the tachycardia RR interval, whereas long RP SVTs display RP > PR (*Figure 2*). Rarely, recording of U waves during typical AVNRT may simulate a long RP tachycardia.[21]

P waves similar to those in normal sinus rhythm suggest appropriate or inappropriate sinus nodal tachycardia, sinus nodal reentrant tachycardia, or AT arising close to the sinus node. P waves different from those in sinus rhythm and conducted with a PR interval equal to or longer than the PR in sinus rhythm are typically seen in AT. In this case, the morphology of the P wave can also provide clues as to the location of the AT focus. In AT, the QRS can be regular or irregular, and the conduction to the ventricles fast (1:1) or slow, (3 or 4:1). The possibility of AFL with 2:1 conduction should also be considered if the ventricular rate during SVT is ~150 bpm, since the atrial activity is usually 300 bpm. In the presence of antiarrhythmic medication, lower atrial rates may also result in lower ventricular rates. The diagnosis may be established by considering the atrial activity. The P waves are usually well seen (in absence of fast conduction to the ventricles) and are monomorphic and regular.

In case of relatively delayed retrograde conduction that allows the identification of retrograde P waves, a pseudo-R deflection in lead V1 and a pseudo S wave in the inferior leads are more common in typical AVNRT rather than in AVRT due to an accessory pathway or atrial tachycardia.[22,23] These criteria are specific (91–100%) but modestly sensitive (58–14%).[22] A difference of RP intervals in lead V1 and III >20 ms is also indicative of AVNRT rather than AVRT due

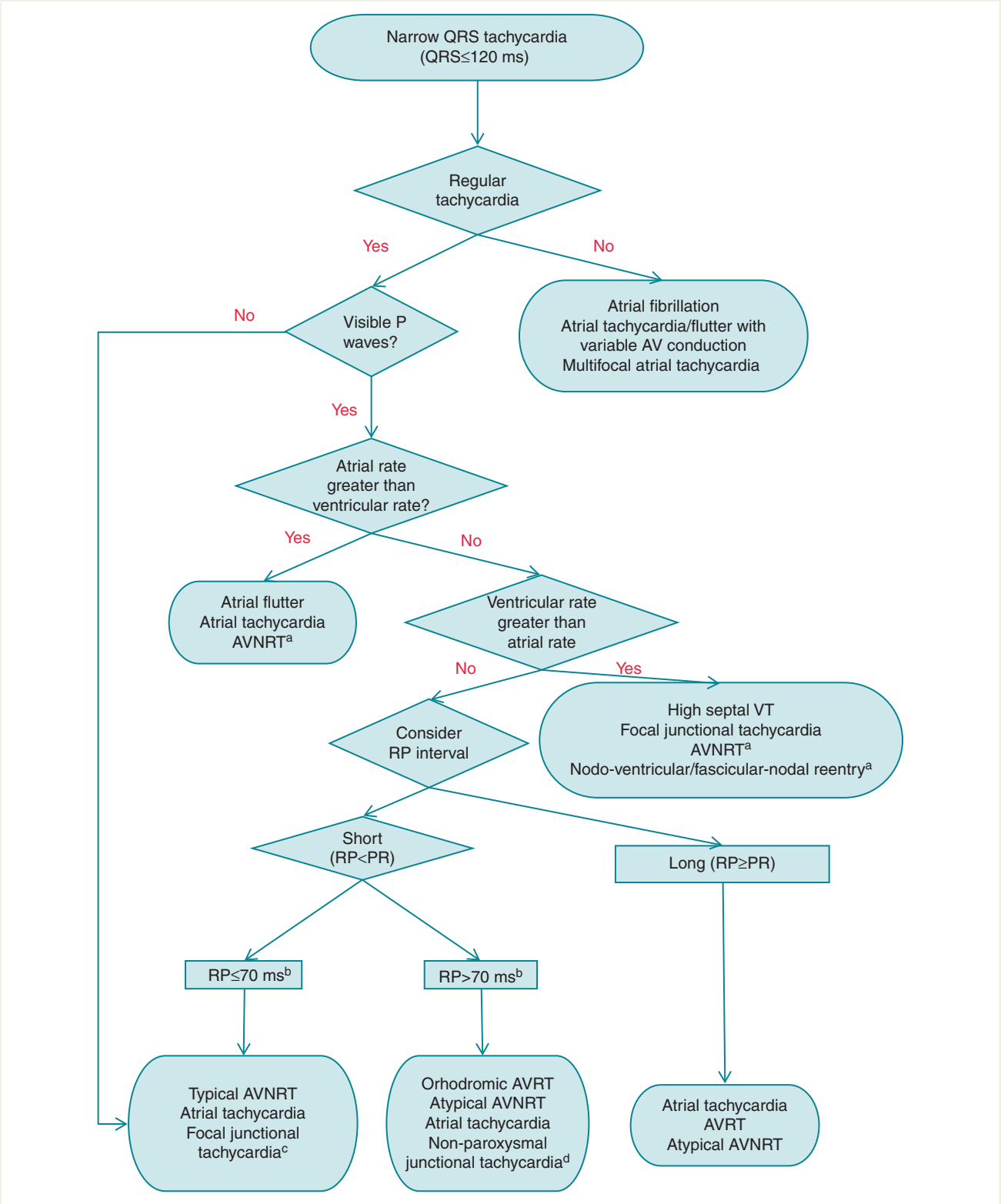


Figure 2 Differential diagnosis of narrow QRS tachycardia. [a]Rare causes. [b]Arbitrary number based on the VA interval for which data exist. An interval of 90 ms may also be used for surface ECG measurements if P waves are visible. [c]It may also present with AV dissociation. [d]It may also present with a short RP. AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; AP, accessory pathway.

to a posteroseptal pathway.[23] The presence of a QRS notch in lead aVL has also been found as a reliable criterion suggesting AVNRT,[24] while a pseudo-R in aVR was shown to have higher sensitivity and specificity than a pseudo-R in V1.[25] However, in all of these studies, cases of atrial tachycardia or atypical AVNRT were limited or entirely absent. Thus, electrocardiographic criteria may provide clues suggestive of typical, slow-fast AVNRT, but are of limited value for appropriate differential diagnosis.

AV block or dissociation during narrow-QRS tachycardia is not often seen, but it rules out AVRT, as both atria and ventricles are parts of the circuit. The development of bundle branch block (BBB) during SVT may also be helpful in the diagnosis of AVRT. Bundle branch block ipsilateral to the AP can result in CL prolongation due to VA prolongation, as the ventricular arm of the circuit is prolonged by conduction through the interventricular septum from the conducting His bundle branch.

Table 5 Possible responses of narrow-QRS tachycardias to vagal manoeuvres

1. Slowing of AVN conduction and AVN block. Atrial electrical activity can thus be unmasked, revealing P waves or underlying atrial flutter or atrial fibrillation waves.
2. Temporary decrease in the atrial rate of automatic tachycardias (AT or sinus tachycardia).
3. Tachycardia termination. This can happen by interrupting the reentry circuit in AVNRT and AVRT by acting on the AVN that is part of the circuit. More rarely, ATs due to triggered activity can slow down and terminate.
4. No effect is observed in some cases.

Vagal manoeuvres and adenosine

Vagal manoeuvres, such as carotid sinus massage or adenosine injection, may be of great help in clinical diagnosis, particularly whenever the ECG during tachycardia is unclear. Possible responses to vagal manoeuvres are shown in *Table 5*.

Figure 3 shows the different type of response to adenosine. Termination of the arrhythmia with a P wave after the last QRS complex is very unlikely in AT, and most common in AVRT and typical AVNRT. Termination with a QRS complex is often seen in AT, and possibly in atypical AVNRT, and AVRT. Fascicular VTs, in particular, are verapamil but not adenosine-sensitive. Most VTs, as opposed to SVTs, do not respond to carotid sinus massage, although a narrow-QRS VT originating from the left bundle branch, and terminated with carotid sinus massage has been reported.[26]

Electrophysiology study

Several electrophysiology techniques and manoeuvres can be employed in the electrophysiology laboratory for differential diagnosis of regular, narrow-QRS tachycardias. A summary is presented in

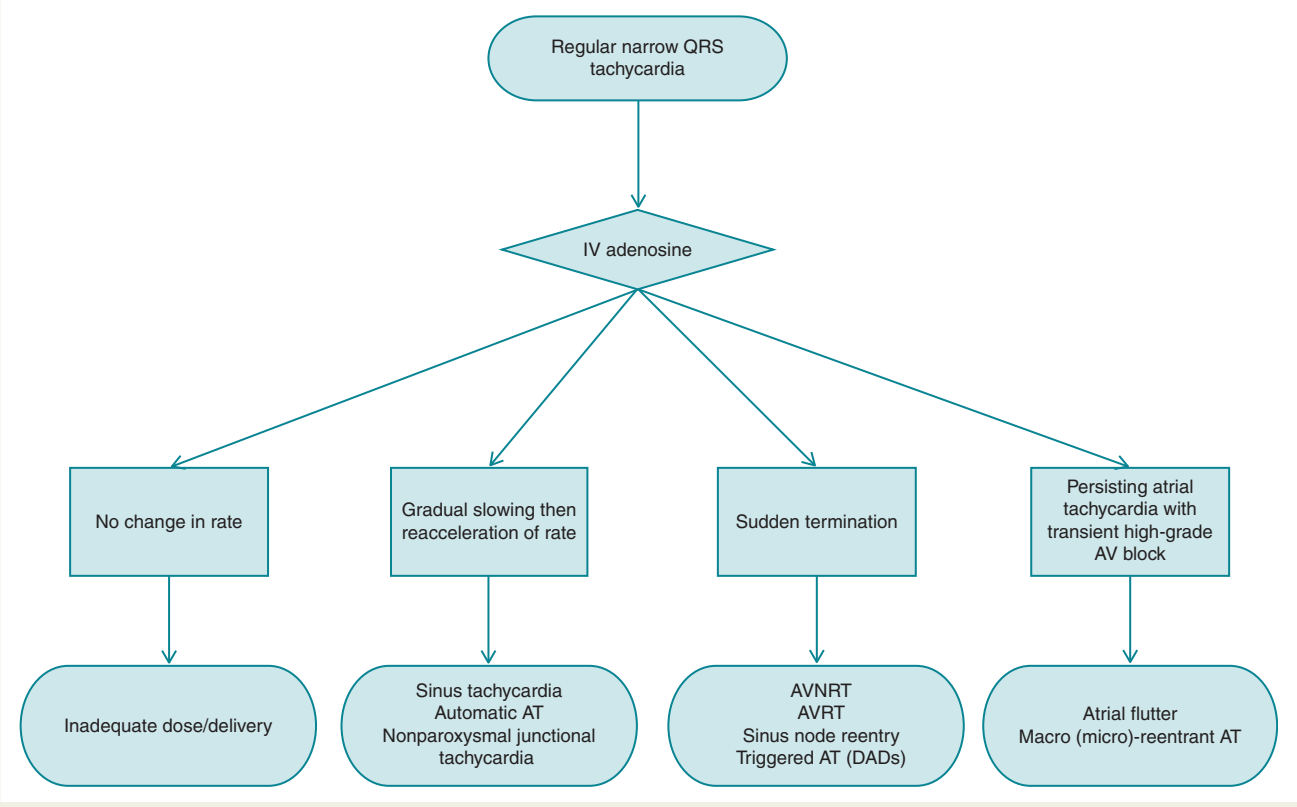


Figure 3 Responses of narrow complex tachycardias to adenosine. AVNRT, atrioventricular nodal reciprocating tachycardia; AVRT, atrioventricular reciprocating tachycardia; AT, atrial tachycardia; AV, atrioventricular; IV, intravenous; DAD, delayed afterdepolarization; VT, ventricular tachycardia.

Table 6 Electrophysiology techniques for the differential diagnosis of narrow-QRS tachycardias

V pacing in SR	V pacing during tachycardia	A pacing in SR	A pacing during tachycardia
VA ratios during V pacing[27,28]	His-synchronous extra-stimuli[29]	Comparison of AH during pacing and tachycardia[30]	
Ventriculoatrial index[31]	Overdrive pacing – AAV/AAHV response[32] – With and without stable fusion (entrainment)[33] – Entrainment with SA-VA and cPPI-TCL intervals[34–37] – Differential entrainment or cessation[38]		
ΔHA during V pacing and tachycardia[39]	*Pre-excitation index*[40]		*Differential entrainment*[41]
VHA pattern[42]	*Entrainment* – *Anterograde His capture*[43] – *Progressive fusion during or after the transition zone*[44,45] – *ΔHA during entrainment and tachycardia*[46] – *Para-Hisian entrainment*[47–49]		
Parahisian pacing[50]			
Induction of retrograde RBBB[51]			
SA_{init}-VA and $cPPI_{init}$-TCL intervals during induction of tachycardia[52]			

Procedures with text in italics are classified as cumbersome, while those shown in normal text are easily applicable.
A, atrial; H, His; cPPI, corrected postpacing interval; RBBB, right bundle branch block; SA, stimulus to atrium interval; SR, sinus rhythm; TCL, tachycardia cycle length; V, ventricular; VA, ventriculo-atrial.
Modified from Katritsis and Josephson.[17]

Table 6, but a detailed discussion is beyond the scope of this paper.[17,27–52]

Wide-QRS (>120 ms) tachycardias

Wide-QRS tachycardias can be ventricular tachycardias, and supraventricular tachycardias conducting with bundle-branch block aberration, or over an accessory pathway, with a reported proportion of 80%, 15% and 5%, respectively (*Figure 4*).[53] Functional right bundle branch block (RBBB) occurs more frequently than functional left bundle branch block (LBBB) because of the longer refractoriness of the former. Bundle branch block can occur with any SVT. A rate-related BBB can develop also during orthodromic AVRT, and tachycardia rate may slow if the BBB is ipsilateral to the accessory pathway location. An accessory pathway may participate in the circuit (antidromic AVRT), or be a by-stander during atrial tachycardia, AFL, AF, and AVNRT. SVT with widening of QRS interval can be also induced by drug or electrolyte disturbances. Pacemaker-related endless loop tachycardia and artefacts that mimic VT can lead to misdiagnosis of a wide-QRS tachycardia.

Differential diagnosis should always be considered in the context of the underlying disease, with conditions such as myocardial infarction, congestive heart failure, and recent angina pectoris favouring VT.[53] Antiarrhythmic drug therapy is also important. Class Ic and Ia drugs cause use-dependent slowing of conduction, and class III drugs prolong refractoriness at His-Purkinje tissue more than in the ventricular myocardium.[54,55] They can both result in atypical BBB morphologies during SVT that mimics VT.

12-lead ECG in sinus rhythm

Comparison of the QRS morphology during normal sinus rhythm and wide-QRS tachycardia is helpful, and the presence of contralateral BBB in wide-QRS tachycardia and sinus rhythm strongly favours VT. However, identical QRS morphology during normal sinus rhythm and wide-QRS tachycardia, although strongly suggestive of SVT, can also occur in bundle branch reentrant and high septal VTs.

12-lead ECG during tachycardia

Atrioventricular dissociation

AV dissociation is one of the most important ECG criteria for the diagnosis of VT. The relation between atrial and ventricular events is 1:1 or greater (more atrial than ventricular beats) in most cases of SVT (*Figure 2*). Although ventriculo-atrial conduction can be found in up to 50% of patients with VT and a 1:1 relation is possible, most of VTs have a relation less than 1:1 (more QRS complexes than P waves).

AV dissociation is characterized by atrial activity that is completely independent of ventricular activity. This phenomenon can be documented on the ECG as P waves dissociated from the ventricular rhythm due to *fusion or capture beats* (*Figure 5*). Atrioventricular dissociation may be difficult to recognize because P waves are often hidden by wide QRS and T waves during a wide-QRS tachycardia.

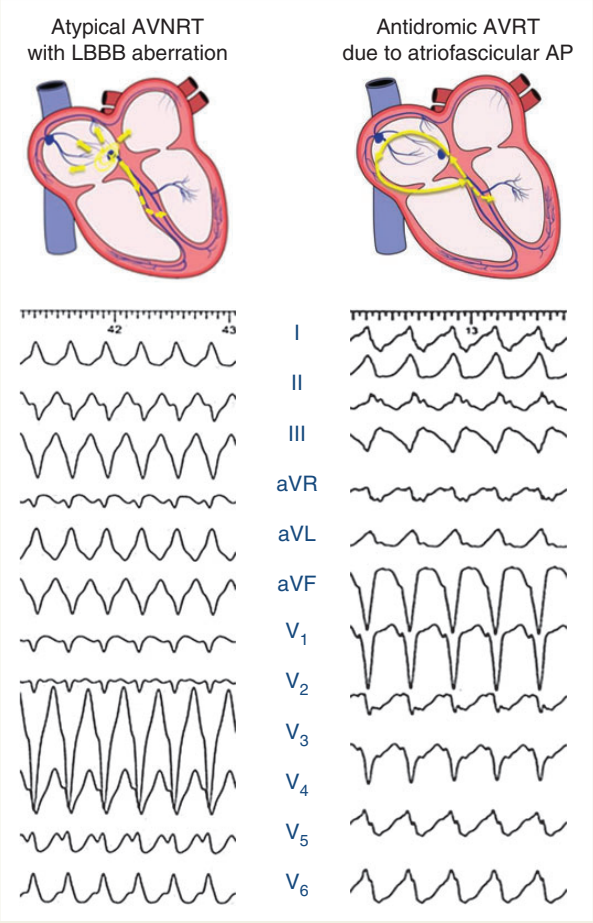


Figure 4 Tachycardia circuit and typical 12-lead ECGs in different types of wide-QRS SVT. Antidromic AVRT due to an atriofascicular pathway usually produces a horizontal or superior QRS axis, but normal axis may also occur, depending on the way of insertion into the right bundle and fusion over the left anterior fascicle. AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; AP, accessory pathway; LBBB, left bundle branch reentry.

P waves are usually more prominent in inferior leads, and modified chest lead placement (Lewis lead).[53]

QRS duration

A QRS duration >140 ms with RBBB or >160 ms with LBBB pattern suggests VT. These criteria are not helpful for differentiating VT from SVT in specific settings such as pre-excited SVT or when class Ic or class Ia antiarrhythmic drugs are administered.

QRS axis

In SVT patients with aberration pattern, the QRS axis is confined between -60° and $+120^{\circ}$. Therefore, wide-QRS tachycardias with a QRS axis outside this range are likely to be VT. In particular, extreme left axis deviation (axis from -90° to $\pm 180^{\circ}$) strongly suggests VT both in the presence of RBBB and LBBB patterns.[56] Thus, predominantly negative QRS complexes in leads I, II, and III are a useful criterion for identifying VT.

Concordant negativity

The coincidence of all positive or negative ('concordant') QRS complexes in all precordial leads is suggestive of VT. While positive concordance may occur during antidromic SVT using a left posterior or left lateral accessory pathway a negative concordance is nearly always VT.[53] This pattern suggests VT with a specificity of more than 90%, but this criterion has low sensitivity being present in <20% of all VTs.

Right bundle branch block morphology

Lead V_1: The right bundle branch does not contribute greatly to the initial part of the normal QRS; thus, when blocked, the first part of the QRS is substantially unchanged. This leads to typical patterns of RBBB aberrancy that include rSR′, rSr′, or rR′ in lead V_1. On the contrary, a monophasic R, Rsr′, biphasic qR complex, or broad R (more than 40 milliseconds) in lead V_1 favours VT. Additionally, a double-peaked R wave in lead V_1 favours VT if the left peak is taller than the right peak (the so-called rabbit ear sign). A taller right rabbit ear characterizes the RBBB aberrancy but does not exclude VT.[57]

Lead V_6: A small amount of normal right ventricular voltage is directed away from V_6. Because this is a small vector in RBBB aberrancy, the R:S ratio is >1. In VT, all of the RV voltage, and some of the left, is directed away from V_6, leading to an R:S ratio <1 (rS, QS patterns). A RBBB morphology with a R:S ratio in V_6 of less than 1 is seen rarely in SVT with aberrancy, mainly when the patient has a left axis deviation during sinus rhythm.[56]

Left bundle branch block morphology

Lead V_1: The presence of broad R wave, slurred or notched down stroke of the S wave, and delayed nadir of S wave are strong predictors of VT.[58]

Lead V_6: In true LBBB, no Q wave is present in the lateral precordial leads. Therefore, the presence of any Q or QS wave in lead V6 favours VT.[56]

The morphology criteria are not fulfilled in any lead in 4% of SVTs and 6% of VTs, and in a third of cases when one lead (V_1 or V_6) favours one diagnosis, the other one favours the opposite diagnosis (VT in one lead and SVT the other one and vice versa).[59]

Algorithms for differential diagnosis

RS interval in precordial leads

The absence of RS complex in precordial leads (only R and S complexes are seen on ECG) is only found in VTs (*Figure 6*). An RS complex is found in all SVTs and in 74% of VTs. The longest interval from the onset of the R wave to the deepest part of the S wave longer than 100 ms, irrespective of the morphology of the tachycardia, is not observed in any SVT with aberrant conduction. About half of the VTs have an RS interval of 100 ms or less and the other half have an RS interval of more than 100 ms. The Brugada *et al.* algorithm, when all 4 steps are applied, has a sensitivity and specificity of 98.7% and 96.5%, respectively.[59]

QRS complex in aVR lead

During sinus rhythm and SVT, the wavefront of depolarization proceeds in a direction away from lead aVR, yielding a negative QRS

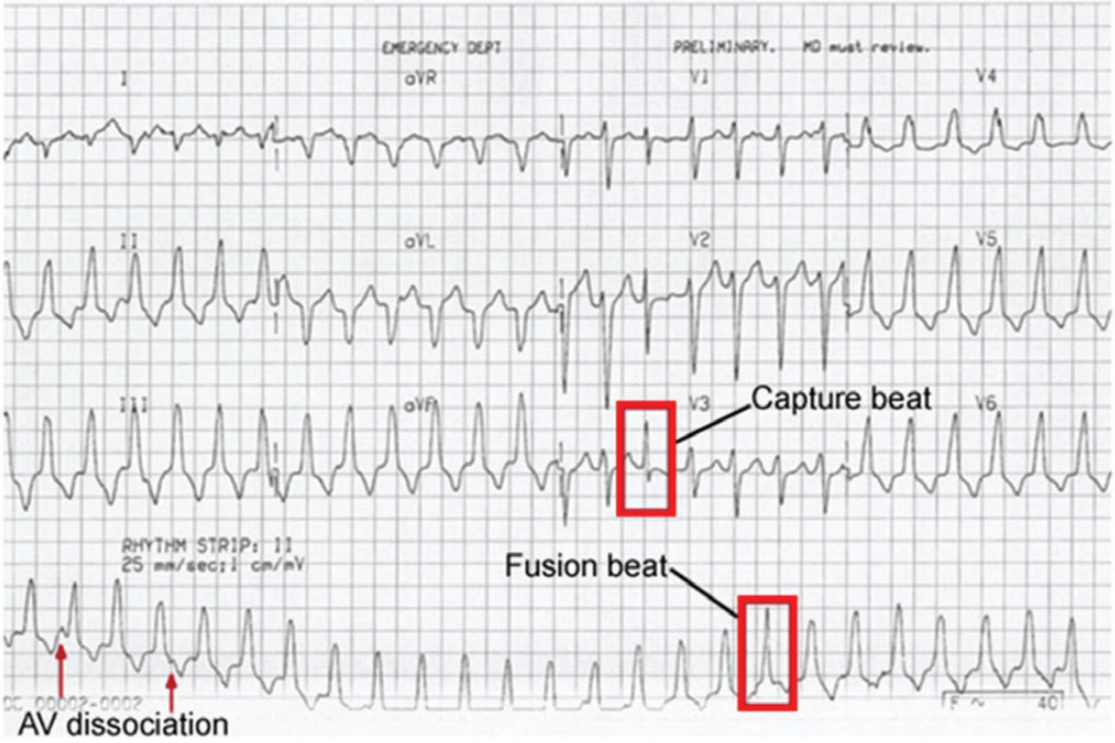


Figure 5 12 lead ECG showing AV dissociation, capture and fusion beat during ventricular tachycardia.

complex in lead aVR with few exceptions (e.g. inferior MI). On the contrary, the presence of an initial R wave (Rs complex) in aVR suggests VT (*Figure 7*). Additional criteria in cases not showing an initial R wave in aVR are shown in *Figure 7*. The Vereckei *et al.* algorithm has a 91.5% overall accuracy in the diagnosis of VTs.[60]

R-wave peak time at lead II ≥50 ms

This criterion has the potential advantage that lead II is a lead easy to obtain and it almost always is present on ECG rhythm strips recorded in different settings (e.g. ECG monitoring in emergency rooms and intensive care units). The R-wave peak time (RWPT) at lead II ≥50 ms, independent of whether the complex is positive or negative, has been reported to have a sensitivity of 93%, and a specificity of 99%, for identifying VT (*Figure 8*),[61] but these results were not verified in the first large external application of this criterion.[62]

All these criteria have limitations. Conditions like bundle branch reentrant tachycardia, fascicular VT, VT with exit site close to the His-Purkinje system, and wide-QRS tachycardia occurring during antiarrhythmic drug treatment are difficult to diagnose by using mentioned morphological criteria. Differentiation between VT and antidromic AVRT is virtually impossible for the very fact that the QRS morphology in antidromic AVRT is similar to that of a VT with its origin at the insertion of the accessory pathway in the ventricular myocardium. There has been one report on the analysis of 267 wide-QRS tachycardias, consisting of VT and antidromic AVRT. The derived criteria were found to offer sensitivity of 75% and specificity of 100%,[63] but this algorithm has not been validated in other studies.

Vagal manoeuvres and adenosine

SVT conducted with aberrancy or antidromic AVRT respond to vagal manoeuvres and adenosine as described in narrow-QRS tachycardia. Most VTs, as previously discussed, do not respond to carotid sinus massage.

Acute management in the absence of an established diagnosis

Many patients with SVT are seen for the first time in the emergency room with ongoing tachycardia, and acute treatment is necessary without an established diagnosis. For adequate management, rapid clinical orientation is needed for efficient and safe treatment. This should include: (i) information about the patient's age and gender; (ii) evaluation of the patient's vigilance and hemodynamic status; (iii) ruling out of acute and life-threatening conditions (e.g. unstable angina due to an acute coronary syndrome, acute pulmonary embolism, aortic dissection, stroke); (iv) evaluation for known and previously diagnosed cardiovascular disease, (v) evaluation of first episode of SVT or recurrence; (vi) previous acute therapies/management in case of recurrence; (vii) duration of the ongoing episode. However, even if this information is

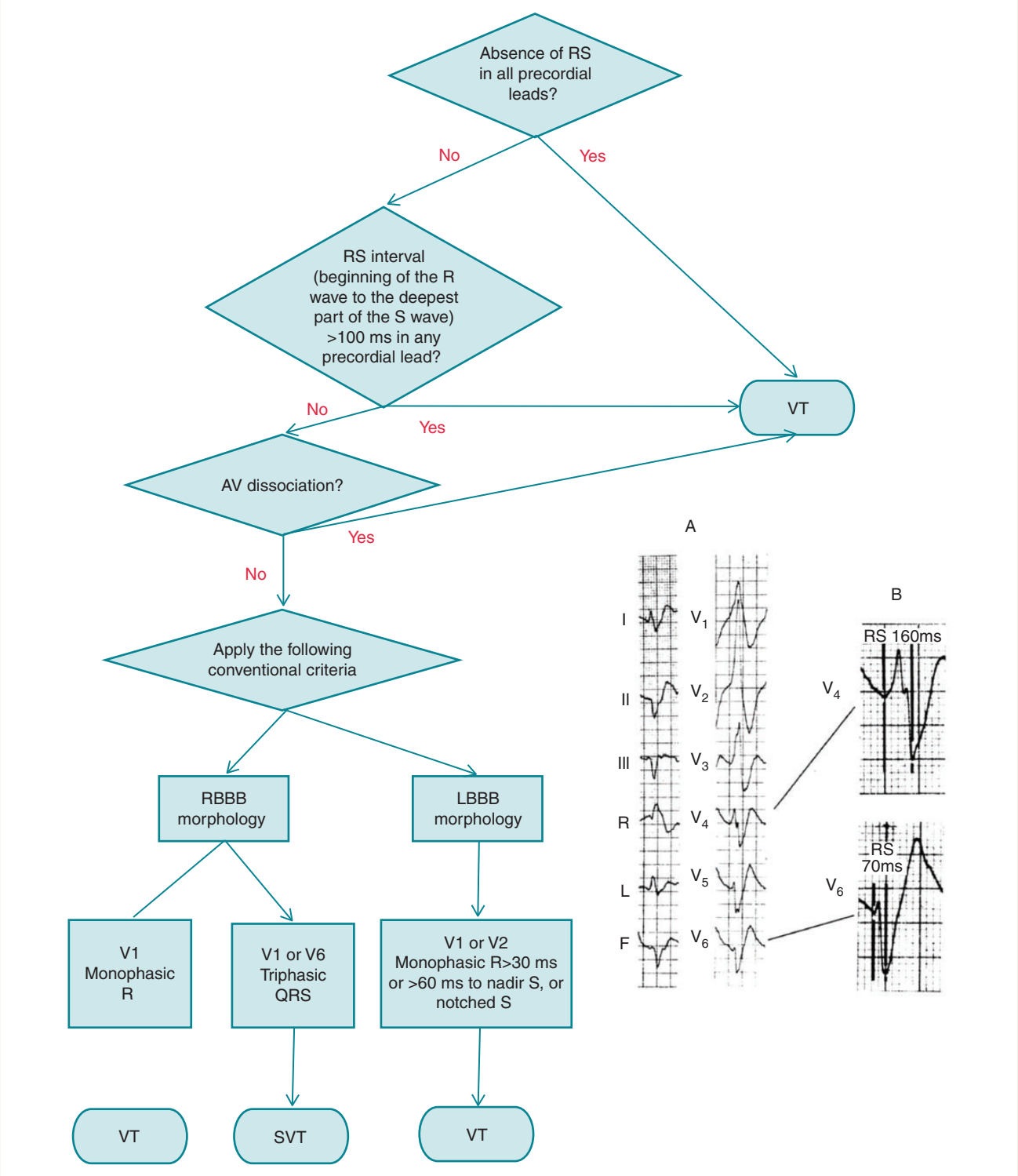
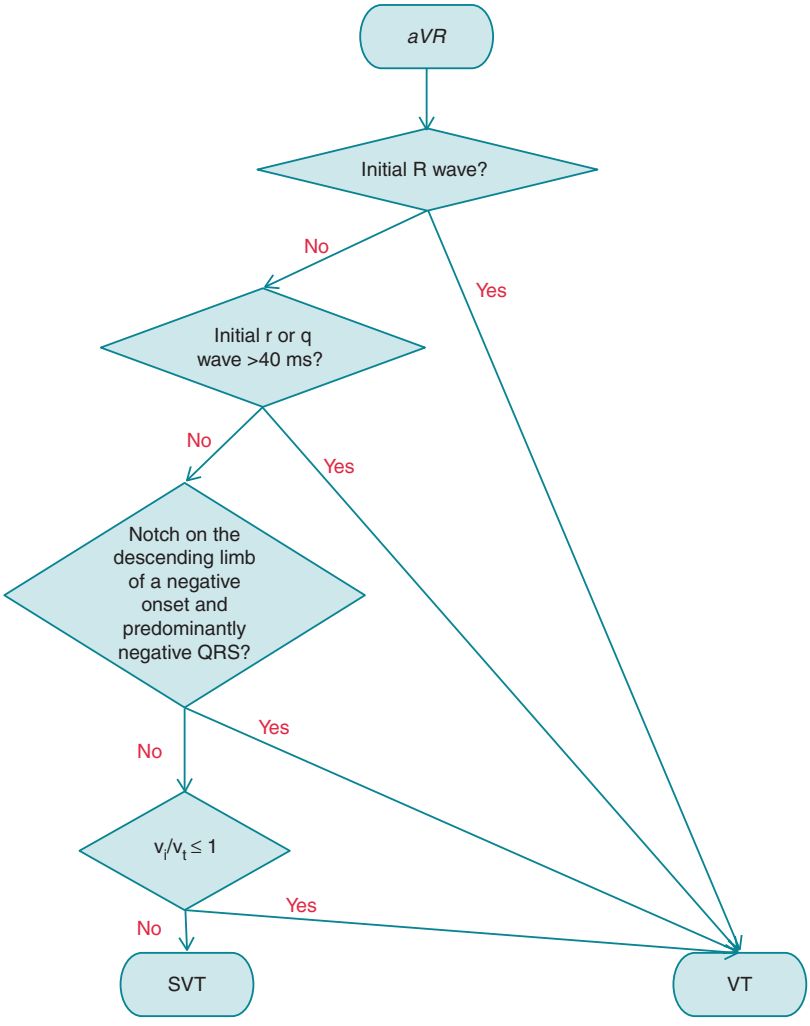


Figure 6 Flowchart for differential diagnosis of wide QRS tachycardia using the Brugada *et al.* algorithm. The RS interval (enlarged in the right panel) measures 160 ms in lead V, and 70 ms in lead V6. Thus, the longest RS interval is more than 100 ms and diagnostic of ventricular tachycardia. From Brugada *et al.*[59]

available, a definitive diagnosis of the tachycardia may be difficult or impossible, and acute treatment needs to be performed in the absence of an established diagnosis.

Before treatment is attempted, documentation of the tachycardia with a 12-lead-ECG is mandatory, as this is the basis for the acute management but also for long-term treatment.



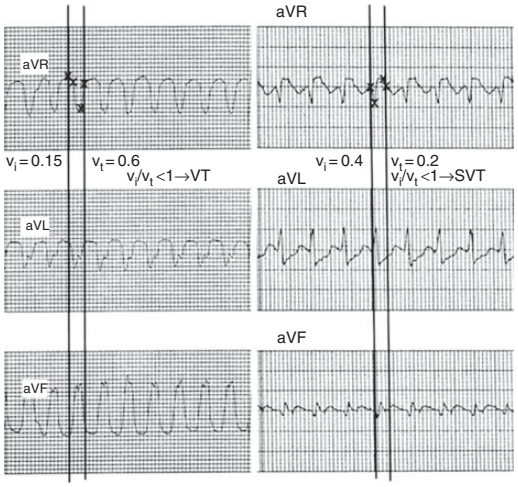


Figure 7 Flowchart for differential diagnosis of wide QRS tachycardia using the Vereckei *et al.* algorithm. In the lower panel, the crossing points of the *vertical lines* with the QRS contour in lead aVR show the onset and end of the QRS complex in lead aVR. The crossing points and initial and terminal 40 ms of the chosen QRS complex are marked by *small crosses*. v_i/v_t is the ventricular activation velocity ratio by measuring the vertical excursion in mV recorded on the ECG during the initial (vi) and terminal (vt) 40 ms of the QRS complex. Left: During the initial 40 ms of the QRS, the impulse travelled vertically 0.15 mV; therefore, vi = 0.15. During the terminal 40 ms of the QRS, the impulse travelled vertically 0.6 mV; therefore, vt = 0.6. Thus, vi/vt < 1 yields a diagnosis of VT. Right: vi = 0.4 and vt = 0.2, determined the same way as in the left panel; thus, vi/vt > 1 suggests a diagnosis of SVT. From Vereckei *et al.*[60]

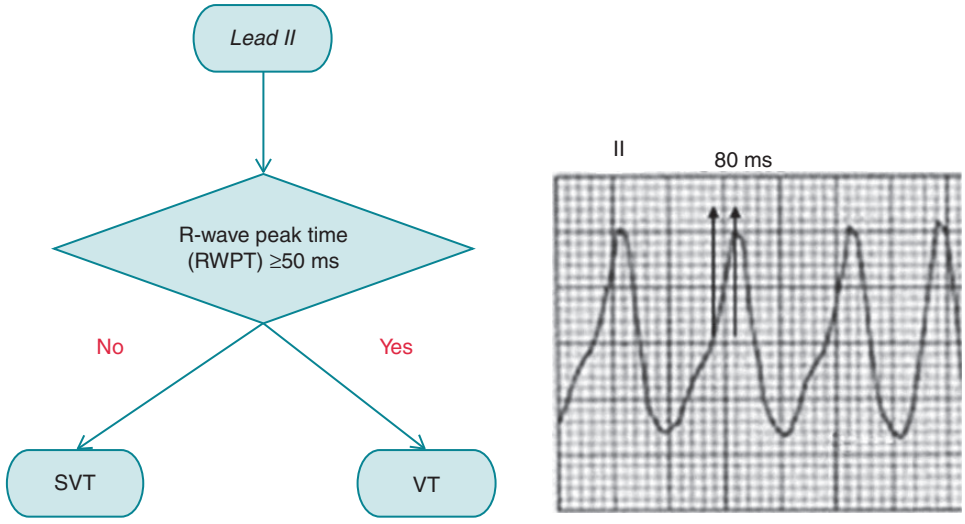


Figure 8 Measurement of the R-wave peak time (RWPT) in lead II. R-wave peak time (RWPT) measured from the isoelectric line to the point of first change in polarity, was >50 ms (80 ms). From Pava *et al.*[61]

Tachycardia termination before 12-lead-ECG documentation may only be acceptable in rare situations with acute hemodynamic collapse. In these cases, at least a minimal rhythm documentation with monitor strips is mandatory. In cases of tachycardia with a QRS complex ≥120 ms, the differential diagnosis should include (i) SVT with BBB/aberrant conduction, (ii) VT, and (iii) antidromic AVRT. This is important, since administration of calcium antagonists (verapamil/diltiazem) in cases of VT or pre-excitation may lead to severe hemodynamic compromise. If the specific diagnosis of a wide QRS-complex tachycardia cannot be made despite careful evaluation, then the patient should be treated for VT. The most effective and rapid means of terminating any haemodynamically unstable narrow or wide QRS-complex tachycardia is direct current (DC) synchronized cardioversion.[64,65]

Acute management of patients with haemodynamically stable and regular tachycardia is outlined in *Figure 9* and *Table 7*.

Acute management of narrow QRS tachycardia

In regular narrow QRS-complex tachycardia, vagal manoeuvres (i.e. Valsalva, and facial immersion in cold water) should be initiated to terminate the arrhythmia or to modify AV conduction. Effectiveness of vagal manoeuvres in terminating SVT has been reported as between 19.4–54%,[66–68] with higher success rates in the supine position.[69] The Valsalva manoeuver has generally been shown to be most effective in adults, having a superior effect on SVT termination compared to carotid sinus massage. Caution is advised when considering carotid sinus massage in older patients. It should be always unilateral, as there is a risk of carotid atheroembolism and stroke even in the absence of an audible bruit. Duration of the manoeuvre should be 15–20 s; two attempts seem to be reasonable. The practice of applying pressure on the eyeball has been abandoned.

If vagal manoeuvres fail, then intravenous (IV) antiarrhythmic drugs should be administered for arrhythmia termination in hemodynamically stable patients. Adenosine, 6–18 mg IV bolus (or adenosine triphosphate [ATP]) is the drug of first choice.[70–73] If contraindicated or not effective, non-dihydropyridine calcium-channel antagonists (verapamil or diltiazem) or short acting beta blocker (esmolol) should be used for acute tachycardia termination (*Figure 9* and *Table 7*).[70,71,74–79] The advantages of adenosine relative to IV calcium channel are its rapid onset, the short half-life, and the avoidance of hypotension.[71] Intravenous adenosine is, therefore, the preferred agent except for patients with severe asthma or angina pectoris. Rapid intravenous injection of adenosine may result in unpleasant but transient side effects (flush, bronchospasm, shortness of breath, temporary AV block). Thus, patients should be informed about such side effects before injection. Patients treated with theophylline may require higher doses of adenosine and adenosine effects are potentiated by dipyridamole. In addition, higher rates of heart block may be seen when adenosine is concomitantly administered with carbamazepine. Adenosine may also induce AF (1% to 15%), which is usually transient but may be particularly problematic in patients with ventricular pre-excitation. Longer-acting agents (e.g. IV calcium-channel blockers or beta blockers, i.e. verapamil/diltiazem or metoprolol) are of value, particularly for patients with frequent atrial premature beats or ventricular premature beats, which may trigger early recurrence of SVT. Caution is needed with concomitant use of IV calcium-channel blockers and, perhaps, beta blockers, because of possible potentiation of hypotensive and/or bradycardic effects. An ECG should be recorded during vagal manoeuvres or drug administration since the response may aid in the diagnosis even if the arrhythmia does not terminate. Direct

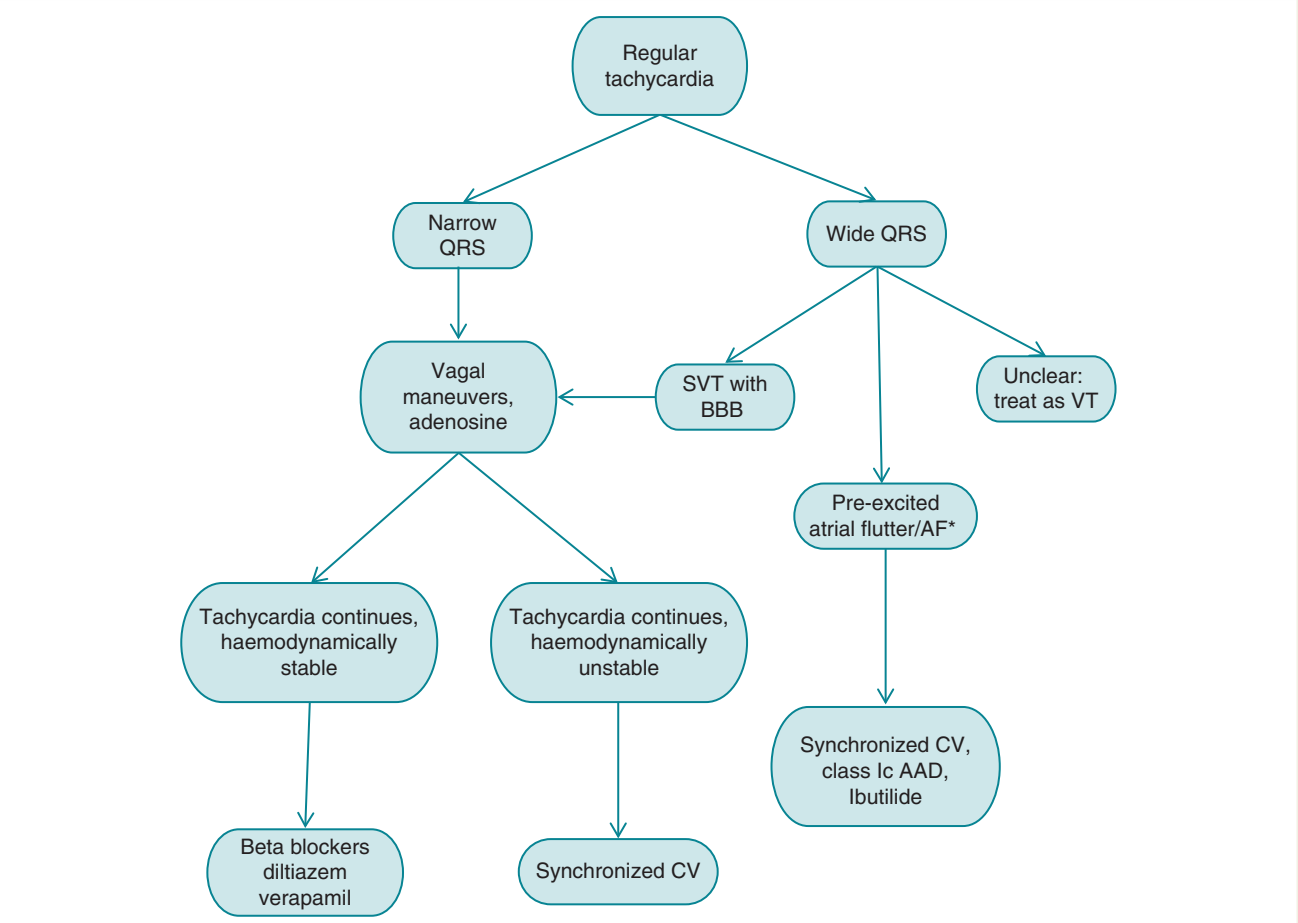


Figure 9 Acute treatment of regular tachycardia. *Pre-excited AF at fast rates may simulate a regular tachycardia. CV indicates electrical cardioversion.

Table 7 Acute management of SVT without established diagnosis

Recommendation	Reference	
Haemodynamically unstable SVT		
Synchronized electrical cardioversion is recommended.[a]	64,65	
Haemodynamically stable SVT		
Vagal manoeuvres, preferably in the supine position, or adenosine are recommended.	66–73	
IV diltiazem or verapamil may be considered.	70,71,74–76	
IV beta blockers may be considered.	74,77,78	

[a]Recommendation supported by strong observational evidence and authors' consensus but no specific RCT.

current cardioversion is first choice in patients who are hemodynamically compromised (*Table 7*). No randomized trials have been conducted comparing DC with IV drugs for conversion in this situation. Although amiodarone has been found effective for conversion of SVTs to sinus rhythm in many but mostly very small and non-randomized trials, it should not be used as a first-line agent.[80]

Acute management of wide QRS tachycardia

Immediate DC cardioversion is the treatment of choice for hemodynamically unstable tachycardias.[81] If the tachycardia is hemodynamically stable, a 12-lead ECG should be recorded and carefully analysed. If the tachycardia is definitely supraventricular, then management is as described for narrow QRS tachycardias (*Figure 9*). Treatment of stable wide QRS-complex tachycardia that is possibly VT is described in relevant guidelines.[81] For termination of an irregular wide QRS-complex tachycardia (i.e. pre-excited AF), DC cardioversion is recommended. If the patient is hemodynamically stable, pharmacologic conversion using IV ibutilide or flecainide is appropriate.[82,83] IV amiodarone and procainamide may also be used. Adenosine may also be helpful by means of allowing a diagnosis or interrupting an adenosine-sensitive VT, but caution is needed in case of pre-excited AF.[84]

Atrial tachycardias

Sinus tachycardias

Physiological sinus tachycardia

Physiological sinus tachycardia denotes appropriate increase in the sinus rate >100 bpm in response to identifiable underlying causes that can have an influence upon the sinus node, and increase the sinus rate. The triggers of this tachycardia can be physiological or secondary to other medical conditions, drugs or recreational agents (*Table 8*). The 12-lead ECG shows a P-wave morphology typical of normal sinus rhythm.

Physiological sinus tachycardia is managed by identifying and eliminating or treating the cause (*Table 9*). As interim measure, beta-blockers, diltiazem, or verapamil can be useful in very symptomatic cases.

Inappropriate sinus tachycardia

Inappropriate sinus tachycardia is a fast sinus rhythm (>100 bpm) at rest or minimal activity that is out of proportion with the level of physical, emotional, pathological, or pharmacologic stress. The syndrome of inappropriate sinus tachycardia is also defined as a sinus rate >100 bpm at rest (with a mean 24-h heart rate >90 bpm not due to primary causes), and is associated with distressing symptoms of palpitations.[93] The underlying mechanism of inappropriate sinus tachycardia remains poorly understood and is likely to be multifactorial.[94] The tachycardia tends to be persistent and most of the affected patients are young and female, but this disorder is not limited to that population.[95] Despite limited information about the long-term consequences of inappropriate sinus tachycardia the prognosis is generally considered benign,[95] and the arrhythmia has been very rarely associated with tachycardia-induced cardiomyopathy in patients with long-standing inappropriate sinus tachycardia.[96,97]

Diagnosis

Patients with inappropriate sinus tachycardia have a wide spectrum of clinical presentations ranging from asymptomatic or minimally symptomatic tachycardia noted during a routine physical examination to incapacitating symptoms. Palpitations are the predominant symptom at presentation but patients may also report dyspnoea, exercise intolerance, dizziness, lightheadedness, and presyncope.

The diagnosis of inappropriate sinus tachycardia is a diagnosis of exclusion, and a thorough medical history and physical examination should be performed to rule out primary underlying causes of sinus tachycardia (*Table 8*). A differential diagnosis with postural orthostatic tachycardia syndrome (POTS) must be considered. A detailed discussion of POTS is beyond the scope of this document. However, it must be highlighted that as opposed to inappropriate sinus tachycardia, in POTS the tachycardia occurs gradually moving from supine to upright position in the absence of orthostatic hypotension.[93]

Blood testing should be routinely considered including complete blood count, fasting blood glucose and thyroid function screen.

The standard 12-lead ECG should be routinely performed to document the tachycardia. The characteristic findings are a heart rate (HR) at rest >100 bpm with P-wave morphology and axis similar to that observed during normal sinus rhythm.

24-h Holter monitoring is also required and useful to determine the mean HR, fluctuation according to activity, and correlation of symptoms to rate. The 24-h Holter monitoring characteristically demonstrates a mean HR >90 bpm with an exaggerated HR response >100 bpm during the waking hours.[95]

Treadmill exercise might be also useful to document the exaggerated HR or blood pressure response to minimal exercise.

A transthoracic echocardiogram should be performed to exclude any significant structural heart disease.

An electrophysiology study is generally not useful for making the diagnosis and should not be routinely performed. This study could be considered in selected cases when the mechanism of the

Table 8 Causes of physiological sinus tachycardia

Physiological causes	Emotion, physical exercise, pain
Pathological causes	Anxiety, panic attack, anaemia, fever, dehydration Infection, malignancies, hyperthyroidism, hypoglycaemia, phaeochromocytoma, Cushing's disease, diabetes mellitus with evidence of autonomic dysfunction, pulmonary emboli, myocardial infarction, pericarditis, aortic or mitral regurgitation, shock, congestive heart failure
Drugs	Epinephrine, norepinephrine, dopamine, dobutamine, atropine, β2-adrenergic receptor agonists (salbutamol), methylxanthines, doxorubicin, daunorubicin, β-blocker withdrawal
Recreational agents	Caffeine, tobacco, alcohol
Illicit drugs	Amphetamines, cannabis, cocaine, lysergic acid (LSD), psilocybin

Table 9 Therapy of sinus tachycardia

Recommendation	Reference
Inappropriate sinus tachycardia	
Therapy is recommended mainly to control symptoms. Ivabradine is recommended for symptomatic patients.	85,86
Beta-blockers and non-dihydropyridine calcium channel blockers are frequently ineffective or not tolerated at required doses. Therefore, may be considered as second- and third-line therapy, respectively.	86,87
Catheter ablation should not be routinely considered in patients with inappropriate sinus tachycardia. This treatment must be restricted to the most symptomatic patients after the failure of other therapy and measures.	88–90
Sinus nodal reentrant tachycardia	
Catheter ablation may be used in patients with symptomatic sinus nodal reentrant tachycardia.	91
Oral beta blockers, diltiazem, or verapamil may be used in patients with symptomatic sinus nodal reentrant tachycardia.	86,92

documented tachycardia is uncertain, or when other SVTs sinus node reentrant tachycardia and focal atrial tachycardias are suspected. The electrophysiological properties of inappropriate sinus tachycardia are: (i) the HR changes gradually at onset and termination of the tachycardia; (ii) programmed atrial stimulation and atrial burst pacing do not initiate and/or terminate the tachycardia; and (iii) the intracardiac atrial activation sequence shows a craniocaudal pattern (iv) shifts in the earliest site of activation along the crista terminalis in response to changes in the tachycardia rate.

Therapy

Lifestyle interventions such as exercise training, volume expansion, and avoidance of cardiac stimulants have been suggested before drug treatment.

Chronic pharmacological therapy. Medical management remains the mainstay of therapy and ivabradine, a selective If current blocker that directly slows the HR without influence on intraventricular conduction, contractility, or haemodynamics, has been found safe and effective in multiple small trials (*Table 9*).[85,86] In a double-blind, randomized, placebo-controlled trial with a crossover design on 21 patients, 75% of inappropriate sinus tachycardia-related symptoms were eliminated in the ivabradine cohort, with nearly 50% of patients experiencing prompt and complete resolution of all symptoms in a short-term follow-up.[85] This treatment has been also associated with an increased tolerance of physical exercise. In a more recent study of 20 patients, ivabradine had a similar effect on resting heart rate as metoprolol but was more effective in relieving symptoms during exercise or daily activity, and was better tolerated.[86] Thus, ivabradine has shown particular benefit in patients with inappropriate sinus tachycardia and should be considered the preferred choice for the treatment. Beta-blockers and non-dihydropyridine calcium channel blockers have been used in inappropriate sinus tachycardia patients for several years, but often have been ineffective or needed at doses high enough to cause intolerable side effects like hypotension and bradycardia.[87] Therefore, they should be considered as second- and third-line therapy, respectively.

Catheter ablation. Catheter ablation has been proposed as a therapeutic option in symptomatic patients with inappropriate sinus tachycardia refractory to other treatments.[88,89] The current approach consists in sinus node modification, achieved by multiple endocardial ablation of the cranial part of the sinus node starting from superior portions of the crista terminalis to eliminate faster sinus rates while trying to preserve chronotropic competence. The endpoint of the procedure is an abrupt and sustained slowing of the sinus rate at baseline and during isoproterenol infusion, with inferior shift of the site of earliest atrial activation down the crista terminalis. On the ECG, a transition is observed to a superiorly directed P-wave morphology with negative P-wave in lead III. This approach has limited efficacy, with a very modest long-term clinical success ranging from 23 to 83%. Anecdotal evidence on epicardial ablation targeting the site with the earliest activation during inappropriate sinus tachycardia have been described to increase the success rate of the procedure after failed endocardial approach, but the safety and efficacy of this approach need to be proved in larger trials. Complications of sinus node modification may occur in up to 14% of cases, and include cardiac tamponade, SVC syndrome, diaphragmatic paralysis due to phrenic nerve palsy, and sinus node dysfunction with the need for permanent pacing.[88–90] The limited and disappointing evidence, resulting from small observational studies, suggest that catheter ablation should not be considered as part of the routine management of patients with IST. At present, this treatment must be restricted to the most symptomatic patients after failure of other therapy and measures.

Sinus node reentrant tachycardia

Sinus node reentrant tachycardia arises from a reentry circuit involving the sinus node and, as opposed to IST, is characterized by paroxysmal episodes of tachycardia. This uncommon arrhythmia may be associated with paroxysmal symptoms of palpitation, dizziness and syncope. On the ECG the polarity and configuration of the P waves are similar to the configuration of sinus P waves.

Diagnosis

The diagnosis of sinus node reentrant tachycardia can be confirmed with an electrophysiology study. This is indicated in patients with frequent or poorly tolerated episodes of tachycardia that are not adequately responding to drug therapy, and in those in whom the exact nature of the tachycardia is uncertain and electrophysiology study would aid appropriate therapy. The following criteria need to be considered for diagnosis: (i) sinus node reentrant tachycardia is easily and reproducibly induced with programmed atrial stimulation differently from inappropriate sinus tachycardia; (ii) the heart rate can shift suddenly at initiation of sinus node reentrant tachycardia, as opposed to the gradual increase of the inappropriate sinus tachycardia rate; (iii) earliest activation is localized to the area of sinus node in the region of superior crista terminalis as happens with sinus rhythm; (iv) demonstration of the arrhythmia mechanism independent of the AV node conduction; (v) pacing manoeuvres such as entrainment can confirm the reentry mechanism; (vi) the tachycardia can be acutely terminated by vagal manoeuvres, adenosine, atrial pacing and premature atrial stimulation.[92]

Therapy

Medical treatment is empirical, and no drugs have been studied in controlled trials. Verapamil, digoxin, and amiodarone have demonstrated variable success while beta-blockers are often ineffective, and the potential benefit of ivabradine is likely to be minimal.[92,98] Sinus node reentrant tachycardia may be effectively and safely treated with catheter ablation targeting the site of earliest atrial activation with respect to the P wave. This treatment has been shown to be feasible with a good long-term outcome (*Table 9*).[91]

Focal atrial tachycardias

Definition

Atrial tachycardia (AT) is defined as an organized atrial rhythm ranging from 100 to 250 or even 300 bpm. The ventricular rate varies, depending on AVN conduction. In asymptomatic young people the prevalence of focal AT has been reported to be as low as 0.34%, with an increased prevalence of 0.46% in symptomatic patients.[99] Most studies reported no gender impact on prevalence.[7]

Tachycardia mechanism

The three putative mechanisms of focal AT are automaticity, triggered activity, and microreentry. The often progressive increase in atrial rate at tachycardia onset (warm-up) and/or progressive decrease before tachycardia termination (cool-down) is suggestive of an automatic mechanism. Automatic ATs tend to be incessant,

especially in children, whereas those attributed to triggered activity may be either incessant or paroxysmal.

Establishing a mechanistic diagnosis of focal AT is beyond the reach of clinical EP studies, and has no practical implications, since the ablation strategy, irrespective of the mechanism, is targeting the site of earliest activation. However, distinguishing macro-reentries from focal ATs is important for the ablation strategy. In centrifugal arrhythmias, (such as focal AT and localized reentry) the activation originates from a source and spreads centrifugally to the rest of the atria, while in macro-reentries, it follows a large path around a central obstacle and reenters.[18] To distinguish between focal and reentrant AT, an EP study with activation and entrainment mapping is needed (*Figure 10*). Reproducible initiation, termination, and entrainment of the tachycardia are arguments for a reentrant mechanism. Atrial overdrive pacing can be used to localize the focus of these tachycardias, since the PPI increases with increasing distance from the source.[100] Focal AT may arise from any site in both atria, but crista terminalis, tricuspid and mitral valve annulus, and within the thoracic veins joining to the atria, are sites of predilection.[101]

Clinical presentation

Symptoms may include palpitations, shortness of breath, chest pain, discomfort and rarely syncope or pre-syncope. The arrhythmia is rarely incessant but the episodes may be sustained. Dynamic forms with frequent interruptions and re-initiations are typical of a focal mechanism, whereas micro- or macro-reentries are stable. When three or more focal ATs coexist, they result in a multifocal atrial tachycardia (MAT) characterized by an irregular and polymorphic aspect easily confused with AF. This condition is usually associated with advanced pulmonary diseases. AT is considered a benign condition, but cases of tachycardiomyopathy have been described.[102]

Diagnosis

12-lead ECG during tachycardia

P wave identification is critical. Depending on the AV conduction and AT rate, the P waves may be hidden in the QRS or T waves. The diagnosis is obvious when the ventricular rate is low with clearly more P waves than QRS. The P waves are monomorphic with stable cycle length, which helps ruling out organized AF. Adenosine injection can help by terminating focal AT or by slowing the ventricular rate.[103] Usually, adenosine has no impact on macro-reentries, although termination has been rarely reported. A discrete P wave with an intervening isoelectric interval suggests a focal AT. However, distinguishing focal from macro-reentrant arrhythmias on surface ECG is not easy. The presence of an isoelectric line does not rule out a macro-reentry, particularly in presence of significant heart disease or previous extensive ablation procedure. The value of the ECG in localizing the origin of the arrhythmia is also limited in this context. In normal heart and in absence of previous ablation, the usual ECG localization rules apply.[101] A negative P wave in lead I and aVL suggests a left atrial origin and, therefore, the need for a left atrial access for catheter ablation. V_1 is negative when the arrhythmia source or exit is in the lateral RA, while septal RA and LA show biphasic or positive P waves. Negative P waves in inferior leads suggest a caudal origin, whereas positive P waves in those leads favour a superior location. Body surface mapping has been shown

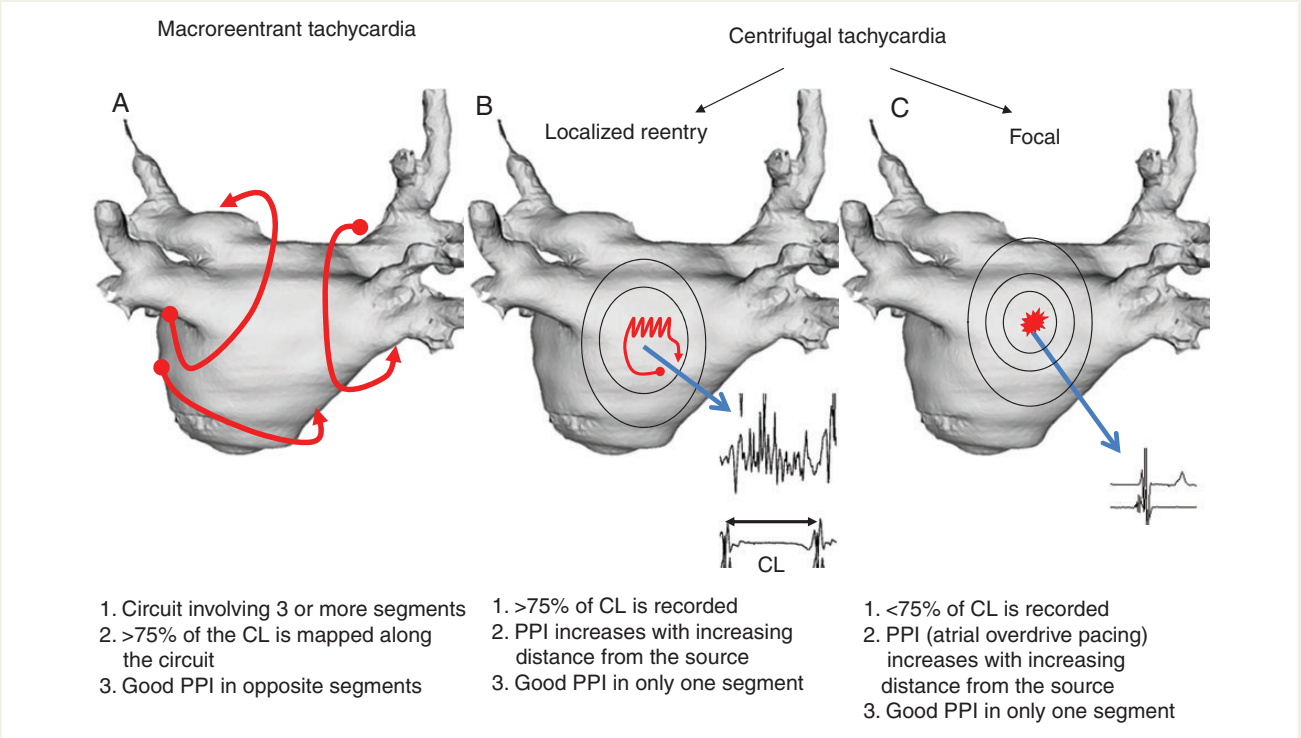


Figure 10 Different mechanisms of atrial tachycardias.
In localized reentry fractionation is present and accounts for a significant part of the cycle lengthy (CL), while in truly focal AT the electrogram at the earliest site is much narrower, with sometimes a preceding sharp activity.

accurate in localizing focal ATs, and this is particularly interesting in case of rare or difficult to induce arrhythmia.[104]

Therapy

AT may be drug- or hypokalaemia-induced. Typically, digitalis can be associated with focal AT with slow ventricular response due to its action on AV node; it should then be discontinued. I_C drugs may prolong the QRS duration, due to rate dependent blockage of the Na channel, thus mimicking VT. The efficacy of antiarrhythmic drugs (AAD) on ATs is not very well defined, but it is probably better in focal ATs than reentrant ones.

Acute therapy

It could be initiated with beta blockers or calcium-channel blockers (*Table 10*). They may terminate focal ATs and or/have a positive effect on slowing the ventricular rate even if this is usually hard to achieve. Intravenous adenosine has been shown to terminate AT, particularly when there is a focal origin, but the tachycardia may continue with AV block.[103,105] Class Ia, Ic, and III drugs may work as well, by prolonging the action potential or suppressing automaticity.[107,108,110]

Direct current (DC) cardioversion is usually effective in acutely terminating the tachycardia, irrespective of the mechanism. However, reentry is very sensitive to DC shocks and energy as low as 50 J may terminate it, which is a striking difference when compared with AF. If the arrhythmia has been documented to be very dynamic, with frequent initiations and terminations, DC cardioversion is not appropriate.

Table 10 Therapy of focal atrial tachycardia

Recommendation	Reference	
Acute therapy		
Synchronised DC cardioversion is recommended for hemodynamically unstable patients[a]	65	♥
Adenosine may be used in terminating a non-reentrant AT or diagnosing the tachycardia mechanism.	103,105	♥
IV beta blockers or verapamil or diltiazem may be used for pharmacologic cardioversion or rate control.	70,76,106	♥
IV flecainide or propafenone may be used for pharmacologic cardioversion in the absence of structural or ischaemic heart disease.	107,108	♥
IV amiodarone may be used for pharmacologic cardioversion or rate control.	80,109	♥
IV ibutilide may be used for pharmacologic cardioversion of micro-reentrant AT.	110	♥
Chronic therapy		
Catheter ablation is recommended, especially for incessant AT.[b]	111,112	♥
Beta blockers or verapamil or diltiazem may be considered.	113,114	♥
Flecainide or propafenone in the absence of structural or ischaemic heart disease may be considered.	107,108,115	♥

[a]Randomized data exist only for post-AF ablation AT.
[b]Recommendations supported by strong observational evidence and authors' consensus but no specific RCT.

Table 11 Therapy of multifocal atrial tachycardia

Metoprolol is recommended in the absence of pulmonary disease.	106,117	♥
Verapamil or diltiazem may be considered in the presence of pulmonary disease.	106	♥

Chronic pharmacological therapy

Again, studies are limited and probably not accurate enough to draw firm conclusions (*Table 10*). Beta blockers and calcium-channel blockers may be effective and there is a low risk of side effects.[113,114] Class Ia, Ic, and III drugs may be effective if first-line therapy has failed, but Ia and Ic agents should be ideally combined associated with AV node blocking agents.[107–109,115,116] In patients with ischaemic heart disease or heart failure, only class III drugs will be used. Multifocal atrial tachycardia is not a good indication for catheter ablation, and metoprolol has been found superior to verapamil, but should be used with caution as pulmonary disease is frequent in MAT (*Table 11*).[106,117]

Catheter ablation

Distinguishing macro-reentries from focal ATs is the key for the ablation strategy (*Figure 10*). Macroreentries can easily be mapped with or without a mapping system. Three circuits (cavotricuspid isthmus in the RA, perimitral or roof dependent in the LA) are responsible for more than 90% of macroreentries.[18] They will show opposite activation on opposite segments. For example, a clockwise perimitral circuit will show a septal to lateral activation of the anterior LA and a lateral to septal activation of the posterior LA (or coronary sinus). Activation and entrainment mapping are complementary. A macroreentry is the unique mechanism in which return cycles are good (within 20 ms) at opposite segments. Ablation of macroreentry requires a complete line of block, usually deployed at the narrowest isthmus, and this can be very challenging, particularly at mitral isthmus. Localized reentries are small reentrant circuits, with a diameter that is less than 2–3 cm.[118] They are localized in one segment of the atrium and depend on a very slow conduction area showing a very long duration and fragmented signal which usually encompass more than half the cycle length and are the target for ablation.[119] As in most focal ATs, the PPI following entrainment or overdrive pacing increases with increasing distance from the circuit and this is very helpful to progressively get closer to the circuit.

Catheter ablation is reported to have a 75–100% success rate,[111,120] and has been shown superior to antiarrhythmic drugs in a randomized study in the context of AF ablation.[112]

Macro-reentrant atrial tachycardias

Cavo-tricuspid isthmus-dependent atrial flutter (typical atrial flutter, anticlockwise or clockwise)

Definition

Typical atrial flutter (AFL) refers to a very reproducible ECG pattern with regular, predominantly negative atrial deflections in the

inferior leads ('saw tooth pattern') at rates 240–350/min, that is a due to an anatomically determined macro-reentrant tachycardia (MRT) based in the RA.[121] This pattern has been called *common AFL*, but the term *typical AFL* is preferred as it includes reentry in counter clockwise and clockwise directions in the circuit (*Figure 11*). Advances in electrophysiologic mapping have obscured the once traditional separation between atrial tachycardia and AFL on the bases of ECG patterns. Atrial rate above or below 240 bpm and the presence or absence of an isoelectric baseline between atrial deflections, that were the diagnostic clues, do not discriminate focal (centrifugal activation) from MRT mechanisms, since activation in slow conduction tracts associated with areas of diseased myocardium, may not be recorded in the ECG.[121]

Tachycardia mechanism

Atrial mapping studies have identified the mechanism of *typical AFL* as a macroreentrant circuit contained in the right atrium (RA) with passive activation of the left atrium (*Figure 11*).[122] The reentry mechanism is supported by a line of conduction block in the posterior RA, extending from the IVC toward the SVC, most often related to anisotropic conduction at the crista terminalis,[123] although other structures of the posterior RA may also play a role.[124] The superior turning point for the activation is variable, depending on the presence or absence of transverse conduction across the posterior RA wall and crista terminalis. If complete block is present, the superior turning point is the atrial roof, between the superior vena cava (SVC) and the tricuspid ring, but in other cases the turning point may be at different levels of the postero-lateral wall,

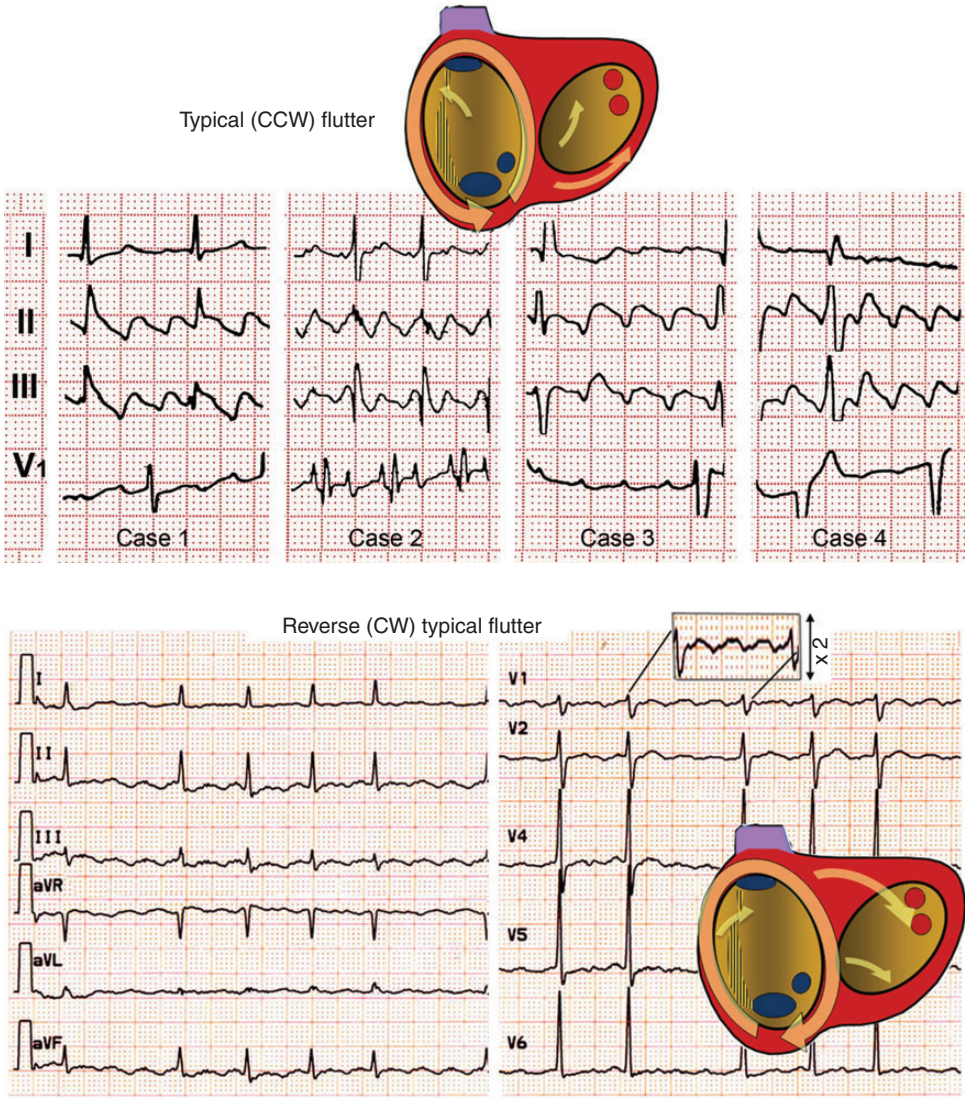


Figure 11 Upper panel: ECG patterns in typical, counterclockwise AFl proven by mapping and entrainment. Note the variation in AFl wave polarity in V1 being positive, biphasic, while the 'saw tooth' pattern is present in all cases. Lower panel: ECG pattern in reverse (*clockwise*) typical AFl. Note continuous undulation in II, III and aVF giving the impression of positive deflections. V1 shows negative bimodal waves ('W') better seen in the tracing amplified at double gain.

Table 12 Therapy of atrial flutter/ macro-reentrant tachycardia

Recommendation	Reference	
Acute therapy		
Synchronised DC cardioversion is recommended for haemodynamically unstable patients with AFL/MRT[a]	131,132	
IV anticoagulation may be considered in case emergency cardioversion is necessary. Anticoagulation should be continued for 4 weeks after sinus rhythm is established.	133,134	
Intravenous beta blockers, diltiazem, or verapamil are recommended for acute rate control in patients with AFL who are hemodynamically stable.	135–137	
IV ibutilide or dofetilide, under close monitoring due to proarrhythmic risk, are recommended to cardiovert AFL.	138–142	
Amiodarone may be considered to control ventricular rate in the acute setting.	143,144	
Atrial overdrive pacing (via oesophagus or endocardial) may be considered for conversion of AFL/MRT.	145–148	
Oral dofetilide may be considered to cardiovert AFL in non-urgent situations but only in hospitalized patients since there is a proarrhythmic risk.	149	
Class Ic antiarrhythmic drugs should not be used in the absence of AV blocking agents because of the risk of slowing atrial rate, and leading to 1:1 AV conduction.	150,151	
Chronic therapy		
One-time or repeated cardioversion associated with AAD are recommended as a long-term alternative for patients with infrequent AFL recurrences or refusing ablation.	152,153	
In patients with recurrent or poorly tolerated typical AFL, CTI ablation is recommended for preventing recurrences with a low incidence of complications.	153,154	
In patients with depressed LV systolic function, ablation may be considered to revert dysfunction due to tachycardiomyopathy, and prevent recurrences.	155,156	
Atypical AFL/MRT appearing early (3–6 months) after AF ablation may be initially treated by cardioversion and AAD, as it may not recur in the long term.	157,158	
In patients with recurrent atypical or multiple ECG AFL patterns, catheter ablation may be considered after documentation of mechanism.	159–164	
Given the high incidence of AF after CTI ablation for typical AFL, correction of 'AF risk factors' may be considered after ablation.	165–167	
Oral anticoagulation may be considered for patients with episodes of atrial flutter.	133,134,168–170	
Stroke prevention is recommended with the same indications as in AF amongst patients with typical FL and associated episodes of AF.[a] • 'Low risk' AFL patients, defined as CHA_2DS_2-VASc 0 in males or 1 in females, do not need antithrombotic therapy. • Effective stroke prevention in patients with CHA_2DS_2-VASc score ≥ 1, is oral anticoagulation, whether with well controlled vitamin K antagonist (VKA) with a time in therapeutic range $>70\%$, or with a non-VKA oral anticoagulant (NOAC, either dabigatran, rivaroxaban, apixaban or edoxaban). • Bleeding risk should be assessed using the HAS-BLED score. Patients at high risk (score >3) should be identified for more regular review and follow-up, and the reversible bleeding risk factors addressed. A high HAS-BLED score is not a reason to withhold anticoagulation.	133,134	

[a]Recommendations supported by strong observational evidence and authors' consensus but no specific RCT.

across the crista terminalis.[125–127] In either case, the myocardium between the tricuspid ring and the inferior vena cava (IVC) orifice is the necessary link conducting activation between the low anterior and low septal RA (*Figure 11*). This relatively narrow passage is known as the *cavo-tricuspid isthmus* (CTI) and has become the preferred target for ablation directed to interruption of the circuit. The diameter of the circuit, necessary to sustain reentry is dependent on the presence of the area or line of block in the posterior RA, which is in keeping with an increased thickness,[128,129] and the increased capacity to block transverse conduction at the crista terminalis.[123,130] In about 90% of *typical AFL* cases, activation courses supero-inferiorly in the anterior and lateral RA and infero-superiorly in the septal RA. Conduction through the CTI is anterior to posterior in what is often called *counterclockwise AFL* (*Figure 11*). In the minority of cases activation turns in the opposite (*clockwise*) direction, i.e. supero-inferior in the septal wall and infero-superior in the antero-lateral wall, with the same lines of block in the posterior RA, and the same obligatory passage through the CTI, now in posterior to anterior direction.[125,126] The ECG shows rounded or bimodal positive deflections in the inferior leads and in V_1 a very characteristic bimodal negative wave in the shape of a W (*Figure 11*). This *clockwise AFL* is considered also *typical* (*reverse typical AFL*). Right atrium reentry dependent on the CTI, as in typical AFL, is a frequent mechanism of tachycardia even in patients with previous ablation or surgery (*Table 12*). In these cases with scar-related areas of block the ECG pattern may not

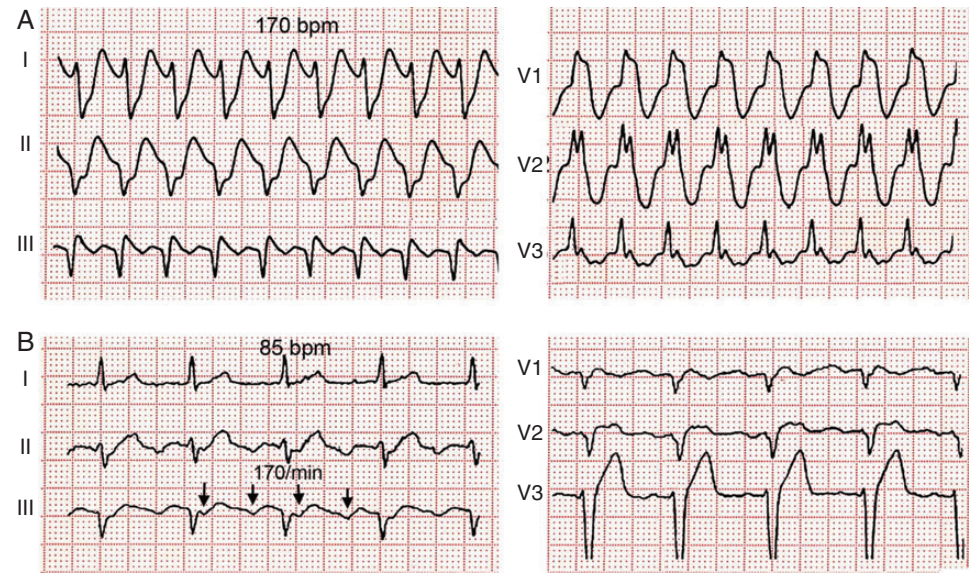


Figure 12 (*A*) FL with 1:1 AV conduction at 170 bpm and a wide QRS complex with right bundle branch block and superior axis in a patient treated with flecainide for paroxysmal AF. In (*B*) 2:1 AV block allows recognition of a very slow but typical AFl pattern and the QRS is narrow, indicating that the wide QRS was due to functional bifascicular block at high rate, under flecainide.

be typical,[159,160] and, conversely, a typical AFL ECG may be produced by atypical MRT even due to LA circuits.[171]

Clinical presentation

Male sex is more prevalent in AFL (≈80%) than AF.[11] AFL is seen in clinical conditions very much alike those seen in AF, including old age, hypertension, diabetes, chronic obstructive lung disease, excessive alcohol consumption[172] and high intensity sports practice.[173] Initial presentation of AFL is often alternating with AF.[174] About 50% of patients with AFL as the only arrhythmia initially, will develop AF in a 8-year follow-up. This figure is not far from the proportion of patients developing AF in long-term follow-up after CTI ablation for typical AFL.[175] Typical AFL may be paroxysmal or persistent. Its clinical presentation will depend in large part on the ventricular rate, which tends to be rapid in the majority of cases.

An ECG pattern with regular, predominantly negative atrial deflections in inferior leads ('saw-tooth pattern') at rates 240–350/min indicates CTI-dependent AFL if there is no prior history of surgery or ablation.[121,176] If there is a history of surgical atriotomy or atrial ablation AFL/MRT other than CTI-dependent AFL should be considered, even in the face of a typical 'saw-tooth' ECG pattern. Multiple circuits are possible, including CTI-dependent AFL which still is the most common type even in these situations.[11,159,160] One-to-one AV conduction is rare and there is usually a degree of AV block, most often 2:1 with regular ventricular rates typically 130–160/min. This may precipitate hypotension, angina, heart failure, syncope or a feeling of palpitation. Atrial flutter can also be asymptomatic, even in the presence of rapid ventricular rate. Heart failure due to tachycardiomyopathy is a not an uncommon presentation of AFL when the arrhythmia is not symptomatic and sustained for weeks or months.[155,156] RA dilatation is present in AFL, but it can be reversible after AFL interruption by CTI ablation. Atrial flutter rarely presents with 1:1 conduction with very fast and regular ventricular rate, in the absence or previous AAD treatment. In this case, however, the ECG pattern may be impossible to recognize until a higher degree of AV block is attained by vagal manoeuvres or drugs. Atrioventricular block may be variable in AFL, leading to an irregular ventricular rate, despite the regular atrial rate. Diagnosis can be established by examining the atrial activity, and if this is not clear due to superposition of QRS and T waves, vagal manoeuvres or intravenous adenosine may help by inducing AV block (see Therapy). In patients treated with AADs for AF, AFL may appear with a slow atrial rate (≤200/min) with 1:1 AV conduction. This occurs typically in patients treated with class Ic or Ia agents. The Na^+ channel blocking effect of class Ia and Ic drugs may slow atrial rate and lead to 1:1 AV conduction at rates ≤200/min, often with QRS widening that mimics ventricular tachycardia (*Figure 12*).[150]

Systemic embolism occurs in AFL about 30% as frequently as in AF,[168–170] a difference that disappears when AFL is associated with AF episodes. Spontaneous echo contrast and LA appendage stunning have been reported in patients undergoing cardioversion of AFL, suggesting a high embolic risk in this situation.[133,134]

Therapy

Acute therapy. In some cases presenting with 2:1 AV block the diagnosis of AFL may not be obvious on the ECG. In these cases intravenous adenosine may increase the degree of AV block and reveal the typical ECG pattern. However, adenosine can produce a rebound increase of AV conduction to 1:1, and may also precipitate AF.[177,178] Thus, it should be used only if deemed necessary for diagnosis, and resuscitation equipment is readily available.

Rate control should be the first step in very symptomatic patients with rapid ventricular rate (*Table 12*). This is a particularly difficult goal in AFL and even the combination of AV node blocking drugs (digoxin, β blockers, calcium channel blockers)[135–137] may fail, making cardioversion to sinus rhythm necessary. Dofetilide and ibutilide, pure class III AADs, are very effective for interrupting AFL in intravenous administration, while Class Ia and Ic drugs have little or no effect.[138–142,149] Class Ic antiarrhythmic drugs should not be used in the absence of AV blocking agents because of the risk of slowing atrial rate, and leading to 1:1 AV conduction.[150,151] Amiodarone may not be very effective acutely to reestablish sinus rhythm, but it does help control ventricular rate if it is too fast.[143,144] Cases with haemodynamic compromise and hypotension are dealt with by synchronized electrical cardioversion.[131,132]

Cardioversion. In patients with AFL lasting >48 h the risk of thromboembolism would appear high at the time of cardioversion to sinus rhythm, either by DC shock, atrial stimulation or CTI ablation,[133,134] and anticoagulation is recommended as in AF. Electrical cardioversion is more successful in maintaining sinus rhythm in patients with new-onset AFL than in patients with new-onset AF,[174] but with the use of antiarrhythmic drugs, the poor results of rhythm control strategies in AF may also apply to AFL.[152,153] Transthoracic electrical cardioversion is the quickest and most effective method to recover sinus rhythm. This can be performed very effectively and very rapidly, under sedation, with very low energies (≤-50 J-biphasic) in an emergency setting. Alternatively, AFL interruption can be achieved in a large percentage of cases by atrial pacing at rates above the AFL rate, through a transvenous catheter. This technique has the advantage of avoiding deep sedation or anaesthesia, as pacing is painless. Using high output stimulation this technique can also be applied through the oesophagus.[145–148] In patients with implanted AAI or DDD pacemakers, atrial pacing at rates above AFL rate is often possible by programming the device.

If AFL has been present for >48 h, the risk of thromboembolism is higher, no matter the technique used for cardioversion, unless trans-oesophageal echocardiography has ruled out intra-atrial thrombi. This may not be feasible if hemodynamic instability demands immediate cardioversion, and in such a case, anticoagulation with unfractionated heparin should be instituted. Once sinus rhythm is re-established, anticoagulation should be continued for a minimum of 4 weeks, or indefinitely if the patient has risk factors.

Catheter ablation. Two randomized studies have shown the superiority of catheter ablation over AAD in terms of AFL recurrence, quality of life, repeat hospitalization and AAD side effects.[153,154] The full thickness of the CTI must be ablated along a line reaching from the TV to the IVC.[179,180] Complete, persistent, bidirectional CTI block is the procedure endpoint, and, if attained, recurrence of the arrhythmia is seen in <10% of cases.[181,182] Complications of CTI ablation are infrequent, and usually limited to the vascular access, although a 0.17% in-hospital mortality has been reported.[161] Inappropriate extension of ablation to the septal RA can result in AV block,[183,184] while damage to the right coronary artery is rare.[185] Hemopericardium and tamponade may occur if very high power RF is applied, and if tissue 'steam pop' occurs.[186]

Typical AFL recurrence is rare after successful CTI ablation, and repeat ablation can be effective if it occurs. However, post-ablation prognosis is affected by the incidence of AF that can be 30–50% in the long term (5–8 years).[175] AF is more likely in patients having had AF episodes before ablation and in those with a dilated LA.[187] In patients with AFL appearing during AAD treatment of AF CTI ablation may help stabilize sinus rhythm while maintaining the AAD.[188] It may also allow continued use of flecainide or propafenone, if they are effective against AF, without the risk of slow AFL with 1:1 AV conduction. Correction of AF risk factors should be attempted to prevent the incidence of AF after AFL ablation.[165–167]

Chronic pharmacological therapy. A first and only well tolerated episode of AFL can be followed with or without AAD prophylactic therapy, but the recurrence rate may be up to 90%.[189] Class Ic agents should be combined with beta blockers to avoid slow FAL rates with 1:1 AV conduction in case of recurrence. Amiodarone, dronedarone and sotalol may be preferable in this respect but the risk of side effects and/or proarrhythmia should be considered. Dofetilide is moderately effective in cardioverting AF or AFL to SR, and significantly effective in maintaining SR but in-hospital initiation and dosage adjustment based on QTc and renal function are necessary to minimize a small but not negligible proarrhythmic risk.[149]

Anticoagulation. There is no direct evidence of the risk vs. benefit ratio of chronic anticoagulation in patients with AFL, as no specific randomized trials in AFL per se have been conducted. In patients with episodes of both AF and AFL the embolic risk appears the same as in AF and the same indications for chronic anticoagulation should be considered, in the presence of stroke risk factors. In patients with AFL and no documented episodes of AF the question is unsettled, particularly after successful CTI ablation.

In the AFL patient population, anticoagulation should be recommended according to established thromboembolic risk and bleeding criteria such as the CHA_2DS_2-VASc, and HAS-BLED scores, respectively. Low risk AFL patients, defined as CHA_2DS_2-VASc 0 in males or 1 in females, do not need antithrombotic therapy. A high HAS-BLED score (>3) is not a reason to withhold anticoagulation but should identify those patients potentially at risk of bleeding, for more careful review and follow-up, as well as correction of reversible bleeding risk factors (e.g. labile INRs, uncontrolled blood pressure, excess alcohol or NSAID use, etc.).

Non-cavo-tricuspid isthmus-dependent macroreentrant tachycardia and other atypical atrial flutters

Definition

The term atypical AFL or MRT is applied to reentrant rhythms not dependent on the CTI and the crista terminalis, no matter what the ECG pattern. However it can also be used to refer to CTI-dependent atrial reentry not fitting the typical AFL ECG.[190] Atypical AFL/MRT can occur with cycle lengths as long as 400 ms. In some cases more than one ECG pattern can be recorded, suggesting multiple tachycardia mechanisms, especially in the presence of structural heart disease, advanced intra-atrial conduction disturbance, surgical atriotomy, or after catheter ablation for AF.[191–193] Atypical, surgery-related AFL/MRT often occurs years after the procedure, suggesting that an atrial remodelling process may be necessary to make reentry stable around the surgical obstacle. Atypical AFL/MRT may also occur after AAD treatment of AF.[151] The ECG pattern is difficult to relate to the mechanism, since slow conduction segments in reentry pathways may produce isoelectric lines and the atrial waves may reflect activation outside the circuit.[171] MRT may coexist with focal (centrifugal) mechanisms and only EPS

including activation and entrainment mapping, supported by computer assisted navigation systems can guide ablation therapy.

Atypical right atrial flutter/macroreentrant tachycardia

Several atypical MRT circuits have been described in the RA (*Figure 13*). There is no argument about the atypical nature of circuits that are not dependent of the CTI, but the so called *'lower loop'* circuit could be considered a variation of typical AFL in which the activation crosses the posterior RA and TC at a lower level than usual, and the ECG tends to show a typical AFL pattern.[125] MRT circuits may turn around the SVC and the upper portions of the crista terminalis (*'upper loop'*) or around a lateral RA surgical scar or a septal patch.[159,194] In some cases without prior surgery a low voltage non-excitable area is present in the lateral RA, a common feature of atypical MRT of the LA. The nature of these low voltage areas is not known, but they are thought to be fibrotic areas of the atrial myocardium. In patients with complex congenital heart disease undergoing the Mustard, Senning, or Fontan procedures, complex suture lines and large areas of myocardial damage create multiple substrates while in many cases the CTI is still a critical isthmus in the reentry circuit, with a difficult access for ablation.[195,196] MRT based on surgical atriotomies is often associated with typical AFL, either as double loop (*'figure of 8'*) circuits or presenting more than one tachycardia pattern on the ECG.

Atypical left atrial flutter/macroreentrant tachycardia

Atypical AFL/MRT of the LA is generally supported by abnormal, non-excitable areas of myocardium, sometimes due to surgical or ablation scars and others of unknown origin. These non-excitable areas may form mixed obstacles by attaching to anatomical obstacles, such as the mitral valve or the pulmonary veins.[118,159,162,191,192] Peri-mitral or roof-dependent MRT may occur in 4–20% of AF ablation cases, being higher with linear or fractionated electrogram ablation techniques.[119,197,198] The ECG pattern of interatrial (Bachmann) block has been associated with a high incidence of MRT, that could be related to low-voltage non-excitable areas in the LA.[199] The superior transseptal surgical approach to mitral valve repair or replacement is more arrhythmogenic than direct posterior LA atriotomy, leading to the appearance of MRT circuits involving both atria, and that are difficult to eliminate by ablation.[160,200] After AF 'maze' surgery, MRT may depend on breaks of the surgical ablation lines that can be localized by endocardial mapping allowing interruption of the MRT by localized ablation at these sites.[201,202] CTI dependent MRT is very common in all kinds of postoperative cases. In post-AF ablation AFL, more than one tachycardia mechanisms often coexist, both MRT and focal,[157,203] making sometimes difficult to identify the circuits' structures, particularly when entrainment manoeuvres result in changes in activation. During ablation the usual endpoint is absence of inducible tachycardia, however, this

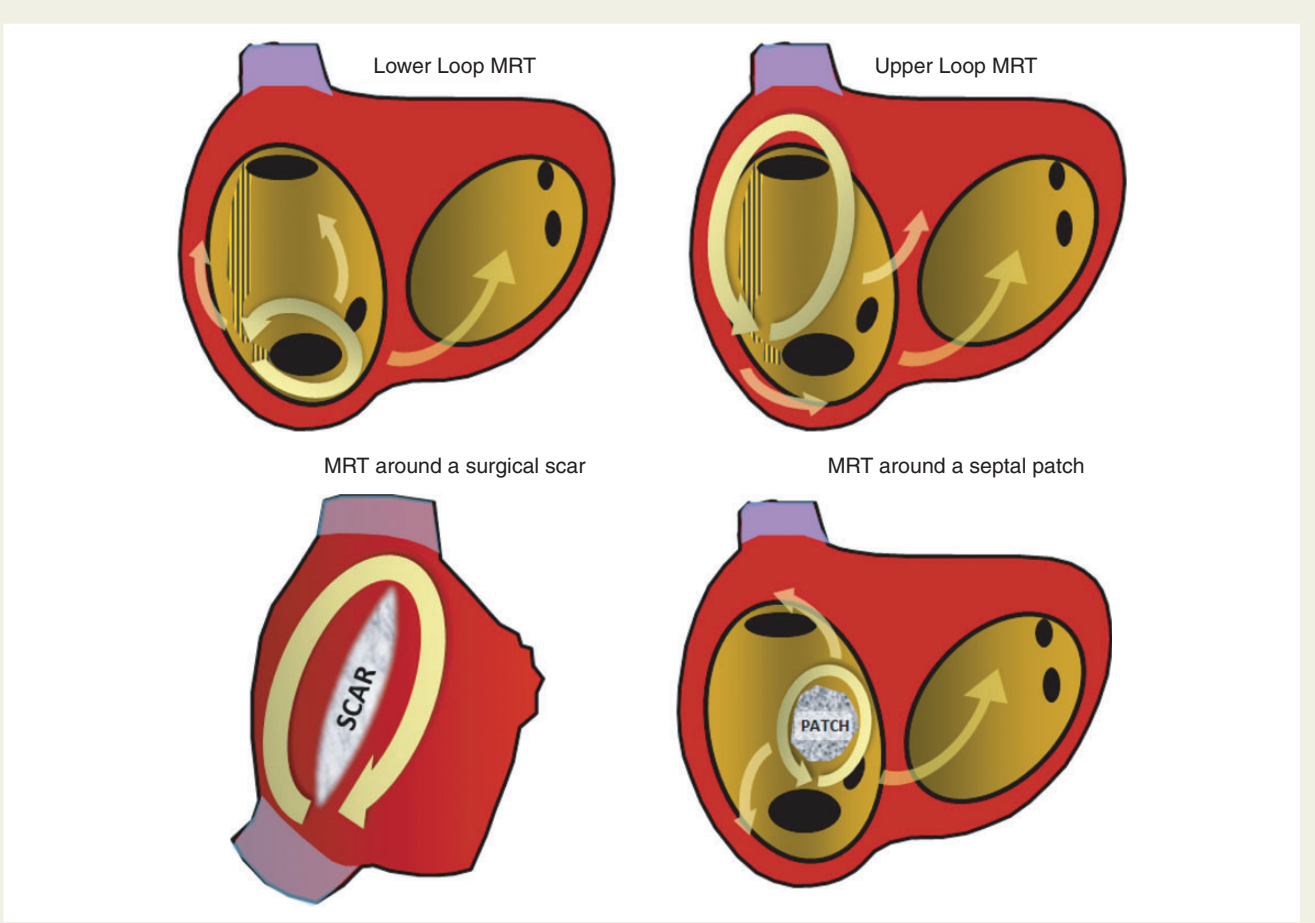


Figure 13 Schematic representation of four types of atypical macro-reentrant tachycardias in the right atrium.

may not be necessary. Tachycardia inducibility at the end of the procedure is not predictive of the long-term occurrence of MRT, and most of tachycardias appearing in the initial 6–8 weeks of follow-up disappear under AAD.[158,193] This would suggest that some kind of remodelling or maturation process may be necessary before a MRT tachycardia circuit becomes stable, and that a new ablation procedure early after AF ablation should not be indicated, unless tachycardia does not respond to antiarrhythmic drugs. When MRT is diagnosed and treated under the effect of AAD, continuation of the AAD may be necessary after interruption of the MRT circuit by ablation.[162]

Therapy of atypical flutter/macroreentrant tachycardia

Management of the acute episode does not differ from that of typical AFL. Long-term indications for AAD do not differ with that of typical AFL, but the often complex associated heart disease should be always taken into consideration. There is very little evidence regarding indications for anticoagulation in patients with atypical FL/MRT of the RA, but the associated heart disease could make embolic risk higher, making anticoagulation, as proposed above, a reasonable alternative. When atypical AFL/MRT is poorly tolerated and is not controlled with antiarrhythmic drugs, catheter ablation should be considered. Ablation of these atypical MRT circuits usually consists of a line cutting fully across the activation path, creating a line of block between two fixed obstacles such as end of scar to IVC. In cases of scar MRT of the RA submitted to ablation, ablation of the CTI may be useful to stabilize reentry to the scar-related circuit. Atypical AFL/MRT ablation can be very challenging and has a lower success rate and a higher recurrence rate than CTI ablation.[163,164,204–206] MRT circuits located in the septal LA are particularly challenging.

Prevention of macroreentrant tachycardia at catheter ablation for atrial fibrillation

Extensive left atrial ablation beyond pulmonary vein isolation has been proposed for patients with persistent AF. This entails additional linear lesions along the roof of the left atrium connecting the superior aspects of the left and right upper pulmonary vein isolation lesions, along the region between the mitral annulus and the left inferior pulmonary vein (mitral isthmus) and the intervenous ridge, or ablation of complex fractionated electrograms. However, these techniques carry a potentially increased risk of macroreentrant or focal iatrogenic atrial tachycardias,[197,207] and their value is rather not established in patients with paroxysmal or persistent AF.[208–210]

Prevention of macroreentrant tachycardia at cardiac surgery

Large atriotomies should be taken to an electrical obstacle whenever possible, in order to avoid creating new reentry circuits. The superior septal approach to the left atrium should be avoided. In patients with previously documented typical AFL, undergoing cardiac surgery, CTI ablation could be performed during the procedure. The cause of MRT after biatrial surgical ablation of atrial fibrillation has been shown to be gaps with conduction across a surgical lesion, most of which were found towards the annular end of the mitral or tricuspid isthmus incision.[211]

The incidence of atrial arrhythmias in the early postoperative period (days) after coronary artery by-pass surgery, is 20–30%.[212] This high incidence has been related to inflammatory changes in the atrial myocardium,[213] not unlike the experimental pericarditis animal models, and it may be prevented by anti-inflammatory corticosteroid or colchicine treatment.[214]

Type II atrial flutter

Type II AFL is defined as a rapid, regular atrial tachycardia, generally induced by rapid pacing of typical AFL, and that cannot be interrupted by rapid pacing but is often self-terminating by returning to the baseline AFL pattern. Type II AFL is likely related to the functional reentrant rhythms induced by rapid pacing under acetylcholine in the dog, and in most cases is probably a laboratory, pacing-induced artefact of little clinical significance.

Atrioventricular junctional tachycardias

Atrioventricular nodal reentrant tachycardia

Definition

AVNRT denotes reentry in the area of the AV node, but the exact circuit still remains elusive.

Tachycardia mechanism

The concept of longitudinally dissociated dual AV nodal pathways that conduct around a central obstacle with proximal and distal connections can provide explanations for many aspects of the electrophysiological behaviour of these tachycardias. However, the 'fast' pathway has not been demonstrated histologically, and the exact circuit responsible for the reentrant tachycardia is unknown. Several attempts to provide a reasonable hypothesis in the context of the anisotropic properties of the transitional tissue around the AV node, have appeared.[215–217] The AV node is a three-dimensional structure with greater variability in the space constant of tissue, and poor gap junction connectivity due to differential expression of connexin isoforms, conditions that provide an explanation of dual conduction and nodal reentrant arrhythmogenesis.[218,219] It has also been shown that the sinus venosus myocardium contributes to the nodal extensions or transitional cells of the AV node.[220] Thus, multiple sources of cells that participate in the AV node may play a role in its heterogeneity, and form the substrate underlying AV nodal reentrant tachycardia. Regarding the slow pathway, there has now been considerable histologic and electrophysiologic evidence that the right and left inferior extensions of the human AV node and the atrio-nodal inputs they facilitate may provide its anatomic substrate.[29,221] Thus, comprehensive models of the tachycardia circuit for all forms of atrioventricular nodal reentrant tachycardia based on the concept of atrio-nodal inputs in an anisotropic environment, have been proposed.[222]

Clinical presentation

Onset of AVNRT seems to occur bimodally over time. In many patients attacks indeed manifest early in life, whereas in a substantial proportion of patients AVNRT starts only in the 4th or 5th decade.[223] Occasionally, certain events such as physical exercise, emotional upset, indigestion or alcohol consumption precipitate attacks.

Polyuria, probably indicating increased ANP levels, may be present during or after a prolonged attack. Atrioventricular nodal reentrant tachycardia may result in AF that usually, although not invariably, is eliminated following catheter ablation of AVNRT.[224] Half of patients with minimal symptoms and short-lived, infrequent episodes of tachycardia may become asymptomatic within the next 13 years.[225] In female patients, the rare possibility of concealed Brugada syndrome should be considered.[226]

Diagnosis

12-lead ECG during tachycardia

Typically, AVNRT is a narrow-complex tachycardia, i.e. QRS duration less than 120 ms, unless aberrant conduction, which is usually of the RBBB type, or a previous conduction defect exists.

In the *typical form* of AVNRT (also called slow-fast AVNRT), retrograde P waves are constantly related to the QRS and in the majority of cases are indiscernible or very close to the QRS complex. Thus P waves are either masked by the QRS complex or seen as a small terminal P′ wave that is not present during sinus rhythm.

In the *atypical form* of AVNRT, P waves are clearly visible before the QRS, i.e. RP > PR, denoting a long RP tachycardia, and are negative or shallow in leads II, III, aVF and V_6 but positive in V_1. Other causes of long RP tachycardia are presented in *Figure 2*. Tachycardia-related ST depression, RR interval variation as well as QRS alternans (although more common in AVRT) may be seen. Specific, although modestly sensitive, ECG criteria for AVNRT, as opposed to AT and AVRT, are a pseudo R deflection in lead V_1 and a pseudo S wave in the inferior leads, a notch in lead aVL, and a pseudo R in aVR.[17] Although AV dissociation is usually not seen, it can occur since neither the atria or the ventricles are necessary for the reentry circuit. If the tachycardia is initiated by atrial ectopic beats, the initial (ectopic) P wave usually differs from the subsequent (retrograde) P waves.

Electrophysiologic classification

The recognition of the fact that AVNRT may present with atypical retrograde atrial activation has made diagnosis of the arrhythmia as well as classification attempts more complicated.[227] Heterogeneity of both fast and slow conduction patterns has been well described, and all forms of AVNRT may display anterior, posterior and middle or even left atrial retrograde activation patterns.[228]

Typical AVNRT: In the slow-fast form of AVNRT the onset of atrial activation appears prior, at the onset or just after the QRS complex thus maintaining an atrial-His/His-atrial ratio AH/HA >1. The VA interval measured from the onset of ventricular activation on surface ECG to the earliest deflection of the atrial activation in the His bundle electrogram is ≤60 ms. Although, typically, the earliest retrograde atrial activation is being recorded at the His bundle electrogram, careful mapping studies have demonstrated that posterior or even left septal fast pathways may occur in up to 7.6% in patients with typical AVNRT.[229–231] There has also been evidence that were left septal His recordings routinely performed in patients with AVNRT, the proportion of left-sided retrograde fast pathways might be considerably higher than previously reported.[230]

Atypical AVNRT: Atypical AVNRT is seen in ~6% of all AVNRT cases,[221] and in some patients it may co-exist with the typical form.[232] It is traditionally classified as fast-slow or slow-slow, but criteria used for the differentiation of the two types are not unanimously accepted.[227] In the so-called 'fast-slow' form of AVNRT retrograde atrial electrograms begin well after ventricular activation with an AH/HA ratio <1, indicating that retrograde conduction is slower than antegrade conduction. The AH interval is less than 185–200 ms. The VA interval measured from the onset of ventricular activation on surface ECG to the earliest deflection of the atrial activation in the His bundle electrogram is >60 ms. Earliest retrograde atrial activation is traditionally reported at the base of the triangle of Koch, near the coronary sinus ostium. Detailed mapping of retrograde atrial activation in large series of patients, however, has produced variable results with eccentric atrial activation at the lower septum or even the distal coronary sinus.[231,233,234] In the 'slow-slow' form, the AH/HA ratio is >1, and the AH interval >200 ms, but the VA interval is >60 ms, suggesting that two slow pathways are utilized for both anterograde and retrograde activation. Earliest retrograde atrial activation is usually at the coronary sinus ostium, but variants of left-sided atrial retrograde activation have also been published.[235,236] The distinction between 'fast-slow' and 'slow-slow' forms is of no practical significance and certain cases of atypical AVNRT cannot be classified according to described criteria.[227] There is also evidence that the 'fast' pathway during slow-fast AVNRT is not identical to 'fast' component of the so-called fast-slow AVNRT.[232] AVNRT, therefore, can be classified as typical or atypical according to the HA interval or, when a His bundle electrogram is not reliably recorded, according to the VA interval measured on the His bundle recording electrode (*Table 13*).

Upper and lower common pathways

Lower and, especially, upper common pathway represent concepts the mechanism and relevance of which remain speculative. The existence of an upper common pathway can now be rather easily refuted by subsequent evidence indicating that multiple atrial breakthroughs are extremely common, and retrograde activation often changes in timing and/or activation without significant alteration in tachycardia cycle, thus negating the notion of a simplistic focal atrial exit site.[237] The perinodal transitional tissue is the route to the atrium, and in this context it may be considered as a common pathway of tissue but not a discrete site. The concept of a lower common pathway has been used to explained phenomena of AV block during AVNRT. However, the methodology for the

Table 13 Classification of AVNRT types

	HA	VA (His)	AH/HA
Typical AVNRT	≤70 ms	≤60 ms	>1
Atypical AVNRT	>70 ms	>60 ms	Variable

The distinction is for categorization only, and not relevant for mechanism or therapy. Atypical AVNRT has been traditionally classified as fast-slow (HA > 70 ms, VA > 60, AH/HA < 1, and AH < 200 ms) or slow-slow (HA > 70 ms, VA > 60 ms, AH/HA > 1, and AH > 200 ms). Not all of these criteria are always met and atypical AVNRT may not be sub-classified accordingly.
AH: atrial to His interval, HA: His to atrium interval, VA: interval measured from the onset of ventricular activation on surface ECG to the earliest deflection of the atrial activation on the His bundle electrogram.
From Katritsis and Josephson.[227]

identification and measurement of a lower common pathway depends on several assumptions that may not be valid,[238] and attempts at identifying and 'measuring' such a pathway are of no practical significance.

Therapy

Acute

Most data on the effectiveness of vagal manoeuvres for acute termination of tachycardia are derived from mixed populations of SVT, but it seems that they are less successful in AVNRT than in AVRT, and standing Valsalva produces similar results with carotid sinus massage (steady pressure over the right, or left, carotid sinus for 5–10 s in the absence of a bruit), and the diving reflex (facial immersion in cold water), offering a <20% conversion rate (*Table 14*).[66–68] A modified Valsalva manoeuvre with leg elevation and supine positioning at the end of the strain is more effective (up to 43% conversion) and safe.[69] In acute episodes of AVNRT that do not respond to Valsalva manoeuvres, intravenous adenosine (bolus of 6 or 12 mg) is the treatment of choice with a success rate up to 96%.[70–73] IV verapamil (0.075–1.5 mg/kg) or diltiazem (0.15–0.45 mg/kg) are also effective but are associated with a risk of hypotension.[70,71,74–76,79] These drugs should be avoided in patients with haemodynamic instability, or a suspicion of VT, or pre-excited AF. Intravenous beta blockers such as metoprolol (2–15 mg) or esmolol (0.5 mg/Kg), are more effective in reducing the tachycardia rate than in terminating it.[74,77,78] IV amiodarone (5 g/kg over 10 min) is also effective.[240] Alternatively, a single dose of oral diltiazem (120 mg) and a beta blocker (i.e. propranolol 80 mg) may convert up to 94% of patients.[241,242] A single dose of oral flecainide (3 mg/kg) is effective in 60–90% of patients.[242,252] Rarely, when vagal manoeuvres and adenosine cannot terminate the tachycardia and hypotension ensues, synchronized direct-current cardioversion is indicated.[239]

Table 14 Therapy of AVNRT

Recommendation	Reference	
Acute therapy		
Valsalva manoeuvre, preferably in the supine position, is recommended.	66–69	
IV adenosine is recommended.	70–73	
Synchronized direct-current cardioversion is recommended for haemodynamically unstable patients in whom adenosine fails to terminate the tachycardia.[a]	239	
IV verapamil or diltiazem may be considered in the absence of hypotension or suspicion of VT or pre-excited AF.	70,71,74–76,79	
IV beta blockers (metoprolol or esmolol) may be considered.	74,77,78	
IV amiodarone may be considered.	240	
Single oral dose of diltiazem and propranolol may be considered.	241,242	
Chronic Therapy		
Catheter ablation for slow pathway modification is recommended in symptomatic patients or in patients with an ICD.	243–247	
Diltiazem or verapamil may be considered.	248–251	
Beta blockers may be considered.	242,250	
No therapy for minimally symptomatic patients with infrequent, short-lived episodes of tachycardia.	225	

[a]Recommendation supported by strong observational evidence and authors' consensus but no specific RCT.

Catheter ablation

A recently published RCT that compared catheter ablation as first-line treatment with antiarrhythmic drugs, demonstrated significant benefits in arrhythmia related hospitalizations.[243] Furthermore, catheter ablation for SVT in general and AVNRT in particular, is the current treatment of choice in symptomatic patients, by substantially improving QoL,[244–246,253–257] and reducing costs.[247,258,259] Slow pathway ablation or modification is effective in both typical and atypical AVNRT. Usually, a combined anatomical and mapping approach is employed with ablation lesions delivered at the inferior or mid part of the triangle of Koch either from the right or the left septal side.[260,261] This approach offers a success rate of 95%, is associated with a risk of 0.5–1% AV block and has an ~4% recurrence rate.[244,253,257] Inappropriate sinus tachycardia may occur but it is usually transient and not frequent following slow pathway ablation.[262] There is no procedure-related mortality in most published studies,[244,253,257] although in the Latin American Catheter Ablation Registry there was one death (corresponding to 0.02% mortality) following tamponade.[10] AV block may be preventable by avoiding an anterior approach and targeting only the anatomical area of the slow pathway either from the left or right septal side, avoiding the coronary sinus ostium, and terminating the energy delivery with the onset of a fast junctional rhythm that is not conducted to the atria.[261,263–265] Slow pathway modification is successful regardless of the patient's age, and advanced age is not a contraindication for slow pathway ablation.[253,266,267] The pre-existence of first-degree heart block carries a higher risk for late AV block and avoidance of extensive slow pathway ablation, i.e. to achieve an antegrade effective refractory period longer than the cycle length of AVNRT, is preferable in this setting.[268] Cryoablation may carry a lower risk of AV block, but this mode of therapy is associated with a significantly higher recurrence rate.[269,270] Its favourable safety profile and higher long-term success rate in younger ages make it especially attractive in children.[271] AVNRT is a cause of inappropriate shocks in patients with ICDs, and in the case of frequent episodes catheter ablation is clearly indicated.[272]

Chronic pharmacological therapy

Patients with minimal symptoms and short-lived, infrequent episodes of tachycardia can be followed-up without the need for ablation or long-term pharmacological therapy. Approximately half of them may become asymptomatic within the next 13 years.[225]

Chronic administration of antiarrhythmic drugs decreases the frequency and the duration of AVNRT, but has a variable success in abolishing tachycardia episodes, ranging from 13 to 82%, and up

to 20% of patients may discontinue therapy. Verapamil has been mainly studied,[248–251] but diltiazem has similar effects on the AV node.[273,274] Beta blockers and digoxin are also probably of value but data are limited.[250] Long-term therapy with a combination of diltiazem and propranolol can also be tried provided the effect on the AV node is being monitored.[242] Flecainide and propafenone are effective,[275–277] probably more than verapamil,[278] but they are potentially proarrhythmic, and cases of ventricular tachycardia during prophylactic therapy of SVT have been reported both by the Propafenone PSVT and the FAPIS groups.[275,276] Co-administration of a beta blocker may prevent proarrhythmic effects.[279] Flecainide and propafenone are contraindicated in patients with ischaemic or structural heart disease. Sotalol[280] and dofetilide[281] have been found effective but potential proarrhythmia due to QT prolongation make these agents less attractive for long-term therapy. Amiodarone is also effective, but its long-term use is prohibited by its complications. In view of the excellent success rate and minimal risk of catheter ablation in symptomatic cases, the value of long-term antiaarhythmic drug therapy seems very limited.

Non-paroxysmal junctional tachycardia

Non-paroxysmal junctional tachycardia was frequently diagnosed in the past as a junctional rhythm of gradual onset and termination with a rate between 70 to 130 beats/min, and was considered a typical example of digitalis-induced delayed after-depolarizations and triggered activity in the AV node. The RP interval during tachycardia is variable. Myocardial ischaemia, hypokalaemia, COPD, and myocarditis are also associated conditions.

Focal junctional tachycardia

Focal junctional tachycardia or junctional ectopic tachycardia is an uncommon arrhythmia that arises from abnormal automaticity at the AV node or proximal His bundle. The rare form of verapamil-sensitive atrial tachycardia is due to reentry in the atrial tissue close to the atrioventricular node, but not the atrioventricular nodal conducting system.[282] Focal junctional tachycardia in children may be seen as a congenital arrhythmia or, more often, early after infant open heart surgery.[283,284] Congenital junctional tachycardia carries a considerable mortality exceeding 30%.[283] Junctional tachycardia can also be seen in adult patients with a structurally normal heart,[285,286] or during acute myocardial infarction.[287,288] The usual electrocardiographic finding is a narrow QRS tachycardia with short RP interval or AV dissociation. Occasionally the tachycardia might be irregular thus resembling atrial fibrillation. Intravenous propranolol with or without procainamide,[286] verapamil or procainamide,[289] and flecainide[290] may be used for acute therapy, but data are scarce (*Table 15*). For chronic therapy, propranolol,[286] or in the absence of ischaemic or structural heart disease flecainide,[291] and propafenone,[292] may be tried. In children with congenital junctional tachycardia, amiodarone alone or with propafenone or ivabradine appears effective.[283,294–296] Selective catheter ablation at the site of the earliest retrograde atrial activation is feasible but carries a lower success rate and higher AV block risk compared to AVNRT.[285] Cryoablation is probably safer.[293]

Table 15 Therapy of focal junctional tachycardia

Recommendation	Reference	
Acute therapy		
IV propranolol with or without procainamide, verapamil or flecainide may be considered for acute therapy.	286,289,290	
Chronic therapy		
Beta blockers and in the absence of ischaemic or structural heart disease flecainide or propafenone, may be considered for chronic therapy.	286,291,292	
Catheter ablation may be considered but at a risk of AV block.	285,293	

Other non-reentrant variants

Non-reentrant atrioventricular nodal tachycardia caused by simultaneous multiple nodal pathway conduction is an uncommon mechanism of AV nodal tachycardia, and has been associated with repetitive retrograde concealment or 'linking' phenomena.[297–299] These are expressed in the form of ventricular pauses with consistent AV relationship after the pause. These extremely rare tachycardias respond to slow pathway ablation.

Atrioventricular reentrant tachycardias

Wolff–Parkinson–White syndrome and atrioventricular reentrant tachycardia

Definition

This group consists of macro-reentrant tachycardias with an anatomically defined circuit that includes two different pathways: the normal conduction system (atrioventricular node and His-Purkinje system), and an atrioventricular bypass pathway (accessory pathway-AP). Due to differences in refractoriness and conduction time between these pathways, a properly timed premature atrial or ventricular contraction can initiate reentry.

APs are strands of working myocardial cells that bypass the normal conduction system (AVN-HPS), and are able to connect atrial and ventricular myocardium. These atrioventricular connections are generally due to incomplete embryological development of the AV annuli, without separation between the atria and ventricles. Accessory pathways can be classified on the basis of their location along the mitral or tricuspid annulus. Their distribution in these regions is heterogeneous: 46–60% of APs originate from the left free wall, 25% from the posteroseptal wall, and 13–21% from the right free wall. Several ECG algorithms can be used for the localization of APs.[300–302]

APs present typical electrophysiological features that differ from AV nodal conduction. They exhibit fast, non-decremental conduction properties ('all-or none conduction'), similar to that of working myocardial cells. Moreover, although the majority of APs conduct both anterogradely and retrogradely (~60%), some of them are able of

propagating impulses in only one direction. Those that conduct in the anterograde direction only are uncommon (<5%), whereas those that conduct in the retrograde direction only are more frequent (17–37%).[303] When the AP is able to conduct anterogradely, ventricular pre-excitation is usually evident at rest during sinus rhythm, and the AP is referred to as 'manifest'. When AVBPs are able of only retrograde conduction they are referred to as 'concealed'.

Wolff–Parkinson–White (WPW) syndrome refers to the presence of an AP resulting in a delta wave and pre-excited ECG during sinus rhythm, in association with recurrent tachyarrhythmias. The AP connects the atrium to the ventricle along the mitral or tricuspid annulus, and a typical ECG pattern with the following features is present: (i) short PR interval (<120 ms); (ii) slurred upstroke of the QRS ('delta wave') (iii) wide QRS (>120 ms). In the general population, the prevalence of WPW pattern on surface ECG is from 0.15% to 0.25%,[304] increasing to 0.55% among first-degree relatives of affected patients.[305] The WPW pattern on the ECG can be intermittent, and can even permanently disappear (in up to 40% of patients) over time. Furthermore several degrees of pre-excitation can be possible due to variable degrees of fusion from conduction to the ventricle over the AVN-HPS vs. the AP. In some cases, pre-excitation may not be present on the standard resting surface ECG, especially with APs located in the left lateral area, and may only become apparent by atrial stimulation during an EPS.

Atrioventricular reentrant tachycardias are the most common (80%) tachycardias associated with WPW syndrome. According to the direction of conduction along the AVN-HPS, two possible mechanisms of reentry are possible, and are classified as orthodromic and antidromic AVRT.

Orthodromic atrioventricular reentrant tachycardia

Orthodromic AVRT accounts for ~95% of AVRTs, and 35% of all sustained paroxysmal SVTs. The re-entrant impulse conducts from the atrium to the ventricle through the AVN-HPS that is the anterograde limb of the reentrant circuit, whereas the AVBP conducts from the ventricle to the atrium, and serves as the retrograde limb of the reentrant circuit. Orthodromic AVRT tends to be a rapid tachycardia, with frequencies ranging from 150 to more than 250 bpm. During tachycardia the following ECG features can be present: (i) RP interval constant and ≤half of the tachycardia cycle length; (ii) narrow QRS and not pre-excited; (iii) functional bundle branch block usually associated with an accessory pathway ipsilateral to the blocked bundle, especially in young patients (<40 years); and (iv) ST segment depression.

Antidromic atrioventricular reentrant tachycardia

Antidromic AVRT occurs in approximately 5% of patients with WPW syndrome. The re-entrant impulse travels from the atrium to the ventricle through the AVBP with anterograde conduction, meanwhile retrograde conduction occurs over the AV node or another accessory pathway, usually located in a contralateral position to ensure longer travel distances, thus allowing for sufficient recovery of refractoriness of the respective elements of the reentrant circuit. Up to 50–75% of patients with spontaneous antidromic AVRT have multiple AP (manifest or concealed), which could act or not as the retrograde limb during the AVRT. Antidromic AVRT has the following ECG features: (i) RP interval ≥half of the tachycardia cycle length (P wave may be difficult to be identified, because it is usually inscribed within the ST-T segment); (ii) wide QRS complex (fully pre-excited).

Other pre-excited tachycardias

In the context of AT, atrial flutter, AF or AVNRT, a pre-excited tachycardia can occur with the accessory pathway acting as a bystander. Paroxysmal atrial fibrillation (AF) has been found in 50% of patients with WPW, and is the presenting arrhythmia in 20%. Atrial fibrillation with fast ventricular response is a potentially life-threatening arrhythmia in patients with WPW syndrome due to degeneration in VF.[306,307] In early studies, identified predictors of ventricular fibrillation in patients with WPW syndrome were R-R interval during spontaneous or induced AF < 180 ms, history of symptomatic tachycardia and inducibility of AVRT, and multiple accessory pathways.308, 309 For a detailed discussion see "The asymptomatic patient with ventricular preexcitation".[308,309]

Therapy

Acute therapy

Non-invasive approaches for orthodromic AVRT with vagal manoeuvres, including Valsalva and carotid sinus massage, could represent the first-line treatment with a success rate of approximately 50% (*Table 16*).[66–68] In the emergency room adenosine IV bolus can terminate AVRT.[71,72] However it should be used with caution because of potential induction of fast AF.[178] AF with fast ventricular conduction could also induce VF, therefore electrical cardioversion should always be available. Haemodynamically unstable patients should be treated with synchronized cardioversion if vagal manoeuvres or adenosine are ineffective or not feasible. During orthodromic and antidromic AVRT, drug therapy could be directed at one of the components of the circuit, the AV node (beta blockers, diltiazem, verapamil),[77,312,313] or the accessory pathway (ibutilide, procainamide, propafenone or flecainide).[83,310,311] In case of antidromic AVRT with multiple bypass tracts, one acting as the anterograde limb and one as the retrograde, drugs acting on the AVN are ineffective.

In the case of irregular pre-excited tachycardia (usually AF with antegrade conduction over the accessory pathway) and haemodynamic instability, electrical cardioversion is the acute treatment of choice. In AF, antiarrhythmic drugs as ibutilide, procainamide, propafenone or flecainide, which act mainly to prevent fast conduction through the pathway, are preferable, even if they do not restore sinus rhythm.[83,310,311] Calcium antagonists (verapamil/diltiazem), beta blockers, and intravenous digoxin are contraindicated in this situation.[314,315] In case of pre-excited AF, amiodarone may not be as a safe as previously thought.[316–319]

Catheter ablation

The treatment of choice for patients with a manifest accessory pathway on the ECG or who have been resuscitated from cardiac arrest is catheter ablation. For other patients with symptomatic AVRT, therapeutic decisions should be balanced between the overall risks and benefits of the invasive nature of ablation vs. long-term commitment to pharmacological therapy. In the past decade, radiofrequency catheter ablation has become firmly established as first-line therapy of paroxysmal SVT.[320–322] Accumulated experience and newer techniques have significantly improved ablation efficacy while minimizing peri-procedural complications and

Table 16 Therapy of AVRT due to manifest or concealed accessory pathways

Recommendation	Reference	
Acute therapy		
Vagal manoeuvres (Valsalva and carotid sinus massage), preferably in the supine position, are recommended as the first-line approach to achieve SVT termination. However, reversion rates range from 45.9 to 54.3%.	66–69	
Adenosine is recommended for conversion to sinus rhythm but should be used with caution because it may precipitate AF with a rapid ventricular rate and even ventricular fibrillation.	71,72,178	
Synchronized DC shock is recommended in haemodynamically unstable patients with AVRT if vagal manoeuvres or adenosine are ineffective or not feasible[a]	64	
IV ibutilide, procainamide, propafenone or flecainide in antidromic AVRT may be considered.	83,310,311	
IV beta blockers, diltiazem, verapamil in orthodromic AVRT may be considered.	77,312,313	
IV digoxin, beta blockers, diltiazem, verapamil and, possibly, amiodarone are potentially harmful in patients with pre-excited AF.	314–319	
Chronic therapy		
Catheter ablation of the accessory pathway is recommended in patients with symptomatic AVRT and/or pre-excited AF.[a]	320–322	
Catheter ablation of concealed accessory pathways may be considered in symptomatic patients with frequent episodes of AVRT	244–247	
Oral flecainide or propafenone, preferably in combination with a beta blocker, may be considered in patients with AVRT and/or pre-excited AF, and without structural or ischaemic heart disease.	275–277,279,323,324	
Oral beta blockers, diltiazem, or verapamil may be considered for chronic management of AVRT if no pre-excitation sign on resting ECG are present.	248–251	
Oral amiodarone may be considered only among patient in whom other AADs are ineffective or contraindicated, and catheter ablation is not an option.	325,326	

[a]Recommendation supported by strong observational evidence and authors' consensus but no specific RCT.

procedure times (*Table 16*). Patients with episodes of SVT are commonly referred early for catheter ablation before extended trials of drug therapy. When weighing the risks and benefits of these two options, an up-dated knowledge of current risks of catheter-based procedures is of critical importance. The 2015 ACC/AHA/HRS Guideline for the Management of Adult Patients With Supraventricular Tachycardia report major complication rates after radiofrequency catheter ablation of 3.0% and 2.8% for AVNRT and AVRT, respectively.[2] Although these rates are higher than most experienced electrophysiologists have in daily practice, in the latest meta-analysis AVRT still carried a mortality rate of 0.1% after radiofrequency ablation, whereas there was no procedural-related mortality for AFL or AVNRT.[244] In the recently published Latin American Catheter Ablation Registry there was one death (0.08% mortality) following ablation of a right accessory pathway.[10]

Chronic pharmacological therapy

Class Ic antiarrhythmic drugs which act mainly on accessory pathway, in combination with beta blockers, may be used in patients with pre-excitation and symptomatic antidromic AVRT who are not candidates for ablation, and in whom structural or ischaemic heart disease has been excluded. Small trials have reported the safety and efficacy of this drug therapy in the context of WPW syndrome,[323,324] but no randomized trials in this setting have been performed. Amiodarone should be used only in symptomatic patients who did not respond to other antiarrhythmic drugs, and in whom catheter ablation is not an option.[325,326]

Concealed and other accessory pathways

Concealed accessory pathways

Concealed accessory pathways are defined as connections between the atria and ventricles that are capable of retrograde conduction only. The true prevalence is unknown because they are not expressed on the surface rest ECG but only during AVRT, and can be identified among those symptomatic patients that undergo EP testing. Moreover, no gender predilection was found and these pathways tend to occur more frequently in younger patients than in those with AVNRT; however significant overlap exists.[303] Concealed pathways are more frequently localized along the left free wall (64%), and less frequently at septal (31%) and right free wall locations.[327]

The electrocardiogram is normal (no delta wave) during sinus rhythm without any evidence of pre-excitation, but the patient is prone to paroxysmal SVT. Conduction into the ventricles is normal during AF because the accessory pathway does not conduct in that direction. The commonest tachycardia in patients with concealed accessory pathways is orthodromic AVRT, with a reentrant circuit using the AV node and His Purkinje system in the anterograde direction, followed by conduction through the ventricle, retrograde conduction over the concealed accessory pathway, and completion of the circuit by conduction through the atrium back into the AV node. Permanent Junctional Reciprocating Tachycardia (PJRT) represents a rare form of atrioventricular reciprocating tachycardia using a concealed accessory pathway, usually located in the posteroseptal region, with retrograde decremental conduction properties.[328] This unusual tachycardia that was originally described by P. Coumel, has deeply inverted retrograde P waves in leads II, III, and aVF, with a long RP interval due to the location and decremental conduction properties of the accessory pathway. The incessant nature of PJRT may result in tachycardia-induced cardiomyopathy that usually resolves after successful treatment by radiofrequency catheter ablation.[328] Catheter ablation is recommended in significantly symptomatic patients (*Table 15*).

Mahaim fibres

Several other pathways have been postulated to result in cardiac pre-excitation. Mahaim fibers are nodoventricular (as initially described) or atriofascicular (more often) decrementally conducting connections between the right atrium or the AV node and the right ventricle in or close to the right bundle branch.[329–332] They usually contain accessory nodal tissue, and connect the atrium to the fascicles by crossing the lateral aspect of the tricuspid annulus, but posteroseptal locations can also be found.[333] Mahaim conduction is usually antegrade only, but concealed fibres have also been described.[332] In clinical practice, the usual criteria for the presence of Mahaim fibre conduction are: (i) baseline normal QRS or manifest pre-excitation with left bundle branch block morphology; (ii) programmed atrial pacing leading to manifest pre-excitation and increase in AV interval along with shortening of HV interval at shorter pacing cycle lengths; (iii) right bundle electrogram preceding His bundle activation during antegrade pre-excitation and SVT. Mapping of the accessory fibers identifies the proximal and distal insertion of the fibers, and, usually, a pathway potential, for successful ablation (*Table 15*).[329,331]

The asymptomatic patient with ventricular pre-excitation

Natural history of asymptomatic pre-excitation

Patients with WPW syndrome have an increased risk of sudden cardiac death (SCD) presumably approaching to 4% over a lifetime.[334] In a large retrospective series of 690 WPW patients, 15 (2.2%) had aborted sudden death, and in 8 of them (>50%) VF was the first clinical manifestation of the syndrome.[335] For many decades the exact risk of sudden death in asymptomatic ventricular pre-excitation has remained unknown, because the majority of prior reports were retrospective, with small number of patients and/or with short follow-up periods, predominantly in older subjects.[306,309,336–338] In the last years, prospective large electrophysiology-guided studies with extensive follow-up periods from Italy have provided additional data to better define the natural history of ventricular pre-excitation and predictors of outcome.[322,339–342] In an 8-year prospective registry of 550 initially asymptomatic subjects, ventricular fibrillation developed in 2.4% and malignant arrhythmias in 8.7%, primarily in patients with accessory pathway anterograde refractory period <240 ms and AV re-entrant tachycardia initiating AF. Benign arrhythmias including AVRT and AF developed in 15.6%, while 21.6% of older patients (median age, 42 years) lost ventricular pre-excitation remaining asymptomatic.[322]

Risk stratification

Several randomized and observational studies indicate that in the asymptomatic WPW population risk stratification using an invasive electrophysiological testing may be beneficial (*Table 17*).[322,336,337,339,341,343] Asymptomatic patients who developed VF had short accessory pathway anterograde ERP less than 200–220 ms, and a shorter pre-excited RR interval during AF (SPERRI) less than 200–230 ms.[339,341] In an 8-year prospective study on 2169 symptomatic or asymptomatic WPW patients, electrophysiologic testing revealed that patients who developed VF, showed more inducible pre-excited sustained AF triggered by AV reciprocating tachycardia (73.3% vs. 44.9%), and shorter median accessory pathway ERP (220 vs. 240 ms) than subjects not experiencing ventricular arrhythmias.[322] A posteroseptal location of accessory pathways was found in almost all patients with VF, whereas the rate of multiple accessory pathways was similar in patients with or without VF, as reported by other investigators.[335] Of note, the Kaplan–Meier estimates showed that initially asymptomatic individuals were more likely to experience VF than the symptomatic individuals.[322] Multivariable analysis showed that only shorter accessory pathway ERP and AVRT triggering AF were associated with VF or malignant arrhythmias.[322] Analysis of time-dependent receiver operating curves for the prediction of VF showed an optimal accessory pathway ERP cut-off point at 240 ms,[322] which confirms the key role of a very short effective refractory period of the accessory pathway to facilitate degeneration of AF into VF.[306,322,335,337–342] In a recent review, data from observational studies on 833 patients who did not undergo ablation showed that up to 9% of patients developed malignant arrhythmias, and up to 2% developed VF during follow-up.[344] Thus, available large data support the usefulness of electrophysiologic testing to identify those asymptomatic WPW patients at high risk of ventricular fibrillation to prevent sudden death, which in many cases can be the first clinical manifestation of the syndrome (*Table 17*).[339–342] In some cases, patients can be readily identified as having an accessory pathway that has a long refractory period, and therefore are a very low risk of sudden death, when they demonstrate intermittent loss of pre-excitation during sinus rhythm.

Table 17 Management of asymptomatic pre-excitation

Recommendation	Reference	
Electrophysiologic testing may be considered for risk stratification in subjects with asymptomatic ventricular pre-excitation.	322,339–345	♥
Catheter ablation of accessory pathways may be considered in asymptomatic patients with accessory pathways with antegrade refractory period <240 ms, inducible atrioventricular reentrant tachycardia triggering pre-excited atrial fibrillation, and multiple accessory pathways.[a]	322,343,345	♥
Observation without treatment may be reasonable in asymptomatic WPW patients who are considered to be at low risk following electrophysiology study or due to intermittent pre-excitation.	322,341	♥
Screening programmes may be considered for risk stratification of asymptomatic subjects with pre-excited ECG.	322,341	♥

[a]Recommendation supported by two randomized trials based on small numbers of patients.

Catheter ablation in the asymptomatic patient with pre-excited ECG

The benefit of catheter ablation in asymptomatic ventricular pre-excitation represents a controversial issue. Recently, large observational prospective studies and two randomized clinical trials have provided accumulating evidence on the benefit of catheter ablation

to prevent malignant arrhythmias and ventricular fibrillation in high-risk asymptomatic WPW subjects without major complications.[322,339,343,345] In the first randomized trial, patients 35 years old or younger in whom arrhythmias were reproducibly induced were randomly assigned to radiofrequency catheter ablation of accessory pathways (37 patients) or no treatment (35 patients). Two patients in the ablation group (5%) and 21 in the control group (60%) had arrhythmic events within the next 9–60 months. The 5-year Kaplan–Meier estimates of the incidence of arrhythmic events were 7% among patients who underwent ablation, and 77% among the controls ($P < 0.001$ by the log-rank test); the risk reduction with ablation was 92% (relative risk, 0.08; 95% CI, 0.02 to 0.33; $P < 0.001$). Complications related to EP study developed in three patients (1%) (2 pneumothorax and 1 large femoral haematoma). An ablation-related complication (permanent RBBB) developed in 1 (3%) of 37 patients.[343] The second randomized study was conducted on asymptomatic children (age range, 5 to 12 years) with WPW syndrome and in whom AVRT or AF were reproducibly inducible. After randomization of 60 children, but before any ablation had been performed, the parents withdrew 13 of them from the study. Of the remaining children, 20 underwent prophylactic ablation and 27 had no treatment. During follow-up, 1 child in the ablation group (5%), and 12 in the control group (44%) had arrhythmic events. Two children in the control group had ventricular fibrillation, and one died suddenly. The cumulative rate of arrhythmic events was lower among children at high risk who underwent ablation than among those at high risk who did not. The reduction in risk associated with ablation remained significant after adjustment in a Cox regression analysis. In both ablation and control groups, the independent predictors of arrhythmic events were the absence of prophylactic ablation and the presence of multiple accessory pathways. Respiratory arrest and femoral vein thrombosis were seen in two patients, while ablation-related complications were seen in three patients (RBBB, transient AV block and pericardial effusion).[345] The number of high-risk patients needed to treat to prevent arrhythmic events in 1 high-risk patient has been reported to be 7.6 at 1 year, 2.3 at 2 years, and 1.8 at 4 years.[340] These results should be considered in the context of the relatively small number of randomized patients in the two studies, and the potential periprocedural or long-term complications (*Table 17*).[257,346,347] In a recent review, little evidence was found from randomized, controlled trials with regard to the best management of patients with asymptomatic pre-excitation.[344]

Supraventricular tachycardia in adult congenital heart disease

Supraventricular tachycardia in adult congenital heart disease

With the advent of modern diagnostic tools and successful surgical repairs, an increasing number of patients with congenital heart disease (CHD) survive to adulthood. The atrial incisions in childhood with subsequent myocardial scarring, however, result in the development of macroreentrant AT, and there is also an increased risk of pump failure, stroke and SCD.[348] These incisional-related AFL or intra-atrial re-entrant tachycardia (IART) are the most common type of SVT (75%) in adult congenital heart disease (ACHD) patients, and occur most frequently in patients with Ebstein anomaly, Tetralogy of Fallot, single-ventricle, Fontan procedures, transposition of the great arteries (TGA), and atrial septal defects.[349,350] Over 60% of these atrial reentry circuits involve the cavo-tricuspid isthmus.[349]

Even though the incidence of SCD is low (0.09% per year) in the CHD population, it is higher than in age-matched controls,[351] and related to arrhythmias in 14% of all deaths after initial repair.[352,353] Atrial tachycardias and impaired ventricular function are important and consistent risk factors for SCD in patients with CHD, of which corrected Tetralogy of Fallot, post-atrial switch operation Mustard or Senning, left heart obstructed lesions and univentricular hearts have the highest (2–9% per decade) risk of SCD.[352–354]

The management of ACHD patients is often complicated, not only because of the nature of their tachycardia, but also because the tachycardia may be a sign of worsening hemodynamic function which may require interventions as part of the arrhythmia management. The complex cardiac anatomy and haemodynamic changes require special precautions due to: (i) an increased risk for pro-arrhythmia when antiarrhythmic drugs are prescribed and (ii) the need for specialized expertise and sophisticated mapping systems when complex catheter ablation procedures are performed. As recommended for patients with AF, antithrombotic therapy is indicated in ACHD patients who have AT or AFL.[355,356]

Acute therapy

The recommendations for acute treatment of a regular SVT are shown in *Table 18*.

Chronic pharmacological therapy

The efficacy and safety of AADs in ACHD patients have not been evaluated in randomized clinical trials (*Table 19*). Beta-blocking agents may provide protection from rapid 1:1 AV conduction, and tachycardia-mediated hypotension, but their protective efficacy is uncertain. Independent predictors for appropriate ICD shocks in multicentre cohort study of patients with transposition of the great arteries with intra-atrial baffle repair were, among others, lack of beta-blockers (hazard ratio, 16.7; $P = 0.0301$).[367] Documented SVT preceded or coexisted with VT in 50% of patients with appropriate shocks. All AADs have an increased risk of proarrhythmia, and may exacerbate sinus node dysfunction as well as heart failure, and thus require in-hospital observation. Sinus node deterioration may require pacemaker implantation to allow for antiarrhythmic medication. Based on retrospective studies comparing AAD for prevention of SVT in CHD patients, only 45% of the patients were free from SVT after 2.5 years follow-up. Although Class III AADs such as sotalol and amiodarone were most effective, adverse effects were common (22%).[368] Class Ic drugs such as encainide and flecainide are also proarrhythmic and should not be used in ACHD patients.[370] In a recent Cochrane Database System Review of randomized trials regarding the safety of AAD as compared with controls in adult AF patients, all AADs but amiodarone, dronedarone and propafenone, were associated with an increased risk of pro-arrhythmia.[369] Quinidine, disopyramide, and sotalol, were also associated with increased all-cause

Table 18 Acute therapy of SVT in ACHD patients

Recommendation	Reference	
SVT haemodynamically unstable		
Electrical cardioversion is recommended (caution for sinus node dysfunction and impaired ventricular function with need for chronotropic or inotropic support).[a]	357	
IV adenosine for conversion may be considered (caution for sinus node dysfunction and impaired ventricular function with need for chronotropic or inotropic support).	103,105	
AVNRT/AVRT haemodynamically stable		
IV adenosine may be considered.	103,105	
Atrial overdrive pacing (via oesophagus or endocardial) may be considered.	145–148	
Atrial flutter/AT haemodynamically stable		
IV ibutilide for conversion of atrial flutter may be considered (caution for pro-arrhythmia in patients with impaired ventricular function).	358	
IV metoprolol (caution for hypotension) may be considered for conversion and rate control.	77,117	
Atrial overdrive pacing for conversion of atrial flutter (via oesophagus or endocardial) may be considered.	145–148	

[a]Recommendation supported by strong observational evidence and authors' consensus but no specific RCT.

Table 19 Chronic therapy of SVTs in ACHD patients

Recommendation	Reference	
Recurrent symptomatic SVT		
Haemodynamic evaluation of structural defect for potential repair may be considered as initial evaluation of SVT.	359,360	
Catheter ablation may be considered.	349,361–366	
Oral beta blockers may be considered for recurrent AT or atrial flutter.	367	
Amiodarone may be considered for prevention, if other medications and catheter ablation are ineffective or contraindicated.	368	
Antithrombotic therapy for AT or atrial flutter is the same as for patients with AF, since CHD patients with atrial tachycardias and atrial flutter probably have similar risks for thromboembolism as patients with AF.	355,356	
Oral sotalol should not be used related to increased risk for proarrhythmias and mortality.	369	
Flecainide should not be used in patients with ventricular dysfunction related to increased risk for proarrhythmia and mortality.	370	
Implantation of a pacemaker for atrial-based pacing to decrease recurrence of atrial tachycardia/flutter is not recommended.	371	
Planned surgical repair and symptomatic SVT		
Surgical ablation of AT, atrial flutter or accessory pathway may be considered.	372,373	
In patients planned for surgical repair of Ebstein's anomaly, preoperative electrophysiologic study may be considered as a routine test.	374,375	
In patients with SVT planned for surgical repair of Ebstein's anomaly, preoperative catheter ablation or intraoperative surgical ablation of accessory pathways, flutter or AT may be considered.	374–377	

mortality.[369] There is no reason to believe that these drugs would be safer to use in an ACHD population, and they can therefore not be recommended other than as a last resort therapy. Although amiodarone is less often associated with proarrhythmia, the severe side effects (thyroid and pulmonary disorders) limit its long-term use in these patients.[368]

Atrial-based pacing does not seem to prevent subsequent atrial arrhythmias according to multivariate analysis.[371]

Catheter and surgical ablation

Catheter ablation procedures for SVT are more complicated in ACHD patients related not only to the atrial flutter per se, but is challenged by limitations of venous access to the heart, fibrotic atrial tissue, multiple atrial reentrant circuits, and atrial baffles separating the coronary sinus and CTI from the systemic atrium. Special expertise and knowledge of complex tachyarrhythmias and scar-related ablation procedures is required. Patients should be referred to centres with extensive experience in complex incisional tachycardias and advanced mapping capability.

In Fontan and atrial switch patients, transcatheter ablation is limited by difficult access to the pulmonary venous atrium. In recent years, trans-baffle access has been described, and was successful in 96% of 74 attempted cases and does not seem to be associated with a higher incidence of adverse events.[361] Desaturation observed in some patients is of uncertain significance but warrants post-ablation monitoring and prospective study.[361,378] The acute success rates of catheter ablation procedures of SVT in ACHD patients ranges from 65 to 100%, with a higher recurrence rate, 20–60% within 2 years, than seen in other cohorts for routine SVT ablation.[362–364,379] Catheter ablation of AT or AFL are associated with lower success rates, 65% to 82%, as compared with those in the absence of CHD,[362,363,365] although higher success rates have been achieved with the advent of advanced mapping and ablation techniques.[366] Ablation of CTI-dependent flutter results in high acute success rates, 96%, depending on the type of anomaly although the recurrence rate after 45 ± 15 months follow-up is 18%.[380]

Arrhythmia surgery can be integrated into a surgical repair with high efficacy and without evidence of increased surgical morbidity.[372] For populations with Tetralogy of Fallot- double-outlet right ventricle, tricuspid valve repairs, and ASD, freedom from recurrent AT or AFL ranges between 73%–93% without anti-arrhythmic medications during medium-term follow-up of 2.5 to 10 years.

Specific disease states

Atrial septal defect

In patients without prior closure, the AFL is likely to be CTI-dependent and susceptible to catheter ablation. Closure of the ASD is unlikely to abolish the AFL and catheter ablation is therefore the recommended approach.[381] If the septal defect warrants closure, catheter ablation of the atrial flutter prior to closure should be considered. However, significant ASDs in adults can be closed even later in life with consequent improved morbidity and survival,[359] albeit new or recurrent ATs are frequent.[360] Therefore, in patients with significant ASD and tachyarrhythmias both catheter ablation of the AT and closure of the ASD should be performed. In patients with repaired ASD, both CTI-dependent and 'incisional' AFL can occur and coexist in the same patient.[349] Catheter ablation is associated with excellent results.[379] Long-term outcomes after secundum ASD closure using transcatheter closure and surgical closure are excellent without significant differences with regard to atrial arrhythmias (9.3%), survival, or thromboembolism.[382] Therefore, patients with unoperated significant ASD and arrhythmias should undergo ablation of the AT, as well as closure of the ASD. The choice of catheter vs. surgical approaches to therapy is determined by anatomic features of the ASD likely to be successfully addressed with a catheter approach. No randomized comparison trials of catheter vs. surgical closure of ASD combined with arrhythmia intervention have been reported. Surgical closure of large ASDs combined with arrhythmia surgery for AT or fibrillation can be safely performed, with 6.5% occurrence of AF reported during 2 years of follow-up.

Ebstein's anomaly

In Ebstein's anomaly, accessory pathways are frequent (15–30%) more often right sided and multiple than in other patients,[383] and other SVTs that can occur include AF, AFL and focal AT. The haemodynamic consequences of SVTs relate to the degree of the malformation, and can vary from mild variants without any symptoms to severe haemodynamic compromise and cyanosis in cases with tricuspid regurgitation and large ASD. Rapidly conducting AFL or pre-excited AF may result in SCD. Catheter ablation is challenging, and success rates are lower (78–89%) and recurrences higher (25–30%) than in other patients depending on pathway location. However, it is still recommended prior to surgery when the malformation warrant operative correction and supraventricular arrhythmias are present.[384] Surgical ablation of accessory pathways is successful in 92–100%.[385,386] Preoperative EPS has a high diagnostic and therapeutic yield and is recommended as a routine preoperative test for this population.[374] Patients who underwent repair of Ebstein anomaly and preoperative EP study with intraoperative ablation of arrhythmia substrate, in a small series, had a lower risk of SCD than patients without arrhythmia intervention.[375] Related to the complex anatomy and the more complex arrhythmias, ablation procedures should be performed by experienced physicians.[376,377]

Transposition of the great arteries (d-TGA) with post-atrial switch operation (Mustard or Senning)

Atrial flutter is common (14%–24%) as is sinus node dysfunction related to the extensive atrial surgery. Supraventricular tachycardias have been associated with increased risk of sudden death, and recurrences are common, and often associated with haemodynamic compromise. Maintenance of sinus rhythm is thus desirable. The selection of antiarrhythmic drugs is limited related to ventricular dysfunction and risk of pro-arrhythmia as well as sinus node dysfunction. Catheter ablation of IART and AVNRT in patients following Mustard or Senning operation for d-TGA has a high primary success rate albeit high 30% recurrence rates for IART but excellent long-term results after a second ablation.[364] Catheter ablation is a complex procedure and should be performed at experienced centres with access to sophisticated mapping systems.

Tetralogy of Fallot

Incisional related AFL is common (20%) as is sustained VT (11%) and risk of SCD (8%).[387,388] The atrial flutters are drug-refractory and/or severely symptomatic in more than half of the patients, and the CTI-dependent mechanism underlies approximately half of the sustained, symptomatic AFLs.[388] It was recently reported that the occurrence of arrhythmias was associated with higher mortality (15.6% vs. 8.6%, $P = 0.001$).[389] Right bundle branch block is present during sinus rhythm in the majority of patients, and may cause differential diagnostic difficulties requiring electrophysiology testing for a correct diagnosis.[390] AFL can indicate worsening ventricular function and haemodynamic evaluation of the repair is warranted. Surgery or catheter-based haemodynamic revision of the repair may result in complete or partial control of the arrhythmia.[391] Catheter ablation of AT is associated with a high procedural success rate during long-term follow-up in the vast majority of patients.[392]

Fontan repairs

The incidence of atrial arrhythmia is high despite more modern surgical approaches. Atrial flutter or AF can develop in up to 42% of patients, whereas the most common atrial tachyarrhythmia is an incision-related (incisional) atrial tachycardia (66%).[393] Atrial tachycardia can cause rapid haemodynamic deterioration resulting in heart failure. Catheter ablation can be effective, but it is often difficult due to multiple circuits and should be attempted only at experienced centres. Both Fontan and Mustard repairs have been associated with less successful ablation results as compared to other ACHD anomalies, related not only to the low success rate of catheter ablation (54% vs. 83% for other CHD) but also to a high recurrence rate (50% vs. 32%) after an initial successful ablation procedure.[363,365] A modified right atrial maze procedure vs. CTI ablation was associated with lower recurrence rates,[373] but selection of suitable patients is important.[394]

Supraventricular tachycardia in pregnancy

The exact incidence of PSVT during pregnancy is not well established, but seems to be relatively low.[395] Although often well tolerated, an increased incidence of SVT during pregnancy has been described,[396,397] as well as more pronounced symptoms during arrhythmia episodes than in the non-pregnant state.[398]

Physiological changes occurring during a normal pregnancy, such as an increased circulating blood volume, hormonal changes, alterations in autonomic tone and emotional changes have been postulated as possible mechanisms for arrhythmogenesis. A higher frequency of atrial and ventricular premature extra systoles may also serve as triggers of SVT episodes.[399]

Management of SVT in pregnant women is in many aspects similar to that of a non-pregnant patient. However, the wellbeing of the foetus and the effect on labour, delivery and lactation should be also addressed. The foetus may suffer from both the direct haemodynamic effect of the tachycardia as well as adverse effects from the treatment. Beyond the usual basic evaluation of the patient presenting with symptoms of sustained arrhythmia, special attention should be paid to symptoms or signs suggestive of heart failure, and if so an underlying or peripartum cardiomyopathy should be ruled out. Worsening factors, occurring more often during pregnancy, such as electrolytic imbalance, hyperthyroidism and anaemia should be evaluated, and if present, corrected.

Acute therapy of supraventricular tachycardia episodes

Management of SVT in pregnancy is a challenging, difficult situation, since the available data are mainly limited to observational studies and case reports.

Vagal manoeuvres are first-line treatment to terminate episodes. Overdrive pacing via the oesophagus is another non-pharmacological alternative. Adenosine has been used safely for termination of SVT in pregnant women,[400] and is the suggested drug of choice when vagal manoeuvres fail. Beta blockers intravenously are inferior to adenosine in converting episodes but can be used as a second choice.[401] Verapamil is associated with a higher degree of maternal hypotension and subsequent foetal hypoperfusion and is therefore considered a third-line agent (*Table 20*).[403]

Direct current cardioversion can be performed at all stages of pregnancy and is considered safe.[402] The current reaching the foetus is insignificant and furthermore the foetus has been shown to have a high fibrillation threshold. However, since transient foetal arrhythmias have been reported, foetal rhythm monitoring is recommended.[402,410] Direct current cardioversion should be performed in all forms of sustained tachycardia causing severe haemodynamic effects, and can be used as a second line option in well tolerated SVT where drug therapy fails.

Prophylactic pharmacological therapy

Prophylactic AADs should be used cautiously and only if symptoms are intolerable or if the tachycardia causes haemodynamic compromise (*Table 20*). According to the recently abandoned FDA classification system of drugs during pregnancy, the majority of AADs are classified as category C, meaning that risk cannot be ruled out for adverse effect on the foetus, and none of the AADs has been proven completely safe. The risk of teratogenic effects is highest during the organogenesis which takes place during the first 8–10 weeks of gestation. Hence, AADs should be avoided during this period. In the later stages of pregnancy, the main concerns with AAD are related to proarrhythmia in the mother and adverse effects on foetal growth and development, as well as effects on labour and hypotension and bradycardia in the newborn. The use of AAD is further complicated by changes in pharmacokinetics during different stages of the pregnancy. These includes changes in gastrointestinal absorption, an increased blood volume, a lower binding to proteins with an increased free fraction of drug, and an increased renal and hepatic elimination.[411] The lowest effective dose should be used and more careful monitoring of the patient with dose adjustments as required, is advised. Close collaboration between the cardiologist and an experienced obstetrician is essential.

Beta-blockers have been used extensively in pregnancy without evidence of teratogenicity, and are recommended as first-line treatment if prophylactic treatment is indicated. The main concern is related to intrauterine growth retardation.[404] Long-term use of atenolol has been associated with intrauterine growth retardation, especially when given in early pregnancy,[409] and is therefore not recommended. Metoprolol, propranolol or acebutolol, if available, are generally preferred but after the first trimester. Metoprolol or acebutolol may, based on their primary β1-selective properties,

Table 20 Recommendations for treatment of SVT during pregnancy

Recommendation	Reference	
Acute therapy		
DC cardioversion in patients with SVT causing haemodynamic instability[a]	402	
Vagal manoeuvres, preferably in the supine position, may be considered as first-line therapy.		
Adenosine may be considered if vagal manoeuvres fail.	400	
IV metoprolol or propranolol may be considered as a second line drug if adenosine is ineffective.	401	
IV verapamil may be considered if adenosine and beta blockers are ineffective or contraindicated.	403	
Chronic therapy		
No medical therapy may be considered in patients with tolerable symptoms.		
Metoprolol, propranolol, or acebutolol may be considered in highly symptomatic patients.[b]	401,404	
Verapamil may be reasonable in highly symptomatic patients when beta blockers are ineffective or contraindicated.[b]	405	
Sotalol and flecainide may be reasonable in highly symptomatic patient when beta blockers are ineffective or contraindicated.[b]	406,407	
Catheter ablation may be considered in highly symptomatic, drug refractory SVT after the first trimester.	408	
Atenolol is not recommended.	401,409	

[a]Recommendation supported by strong observational evidence and authors' consensus but no specific RCT.
[b]Drugs should be avoided during the first trimester if possible.

theoretically be of advantage in that they would be less likely to interfere with β_2-mediated uterine relaxation.[401] Among the calcium channel blockers the experience is greatest with verapamil which overall appear to be relatively safe.[405] Bradycardia in the foetus has however been reported and caution is advised.[406] For patients not responding to these agents, as well as for patients with pre-excitation, a Vaughan-William class I or III drugs may be considered. Although based on limited data flecainide and sotalol appear to be well tolerated and reasonably safe.[406] Additional support for safety has been gained from treatment of foetal arrhythmias.[407] The experience with propafenone and disopyramide is more limited and the latter has been associated with contractions of the uterus.[406] Procainamide has been used in pregnant women for acute treatment of pre-excited tachycardia but can cause lupus-like syndrome with long-term use. Detailed recommendations on the safe use of antiarrhythmic drugs during pregnancy and breastfeeding have been provided by the ESC 2011 guidelines on pregnancy.[412]

Catheter ablation

Catheter ablation has been performed in selected cases and has been reported effective with minimal maternal and foetal complications.[408] These data are however based on small case series with no long time follow-up of risk for the infant. If carried out, it is of the utmost importance that radiation exposure is kept to a minimum, which may be facilitated by the use of newer technologies such as non-fluoroscopic mapping systems and intracardiac echocardiography. In experienced hands, the use of 3-D Mapping Systems allows completely x-ray free ablation, thus obviating the foetal risk of radiation. The risk of intervention, including foetal radiation, a higher thrombogenicity and possible difficulties to intervene in case of cardiac tamponade, must be balanced against a prolonged use of AAD. Ablation should therefore mainly be restricted to cases with drug refractory, poorly tolerated SVT and avoided in the first trimester. Furthermore ablation in pregnant women should only be performed in high experienced centres. Catheter ablation can preferably be advised to patients with regular indications prior to a planned pregnancy.

Health economics

Interventional procedures are aimed at reducing symptoms, morbidity and, possibly, mortality related to arrhythmic events. As shown in cost of illness studies, many arrhythmic conditions induce substantial costs. Thus, effective treatments (interventional or pharmacological) may have a positive impact on disease-related hospitalizations, with a consequent favourable economic profile in terms of mid- or long-term cost-effectiveness.[413,414]

In the case of SVT most of the interest in economic analysis has been focused on ablation techniques. In view of the high efficacy of ablation in most SVTs, the initial (relatively substantial) cost of the procedure can be counterbalanced by the high effectiveness in the long-term, coupled with improved QoL. This results in attractive cost-effectiveness and cost-utility estimates in comparison with pharmacological treatment. Drug therapy is characterized by continuous diluted costs, variable patient adherence (sometimes very low), limited efficacy, and poor patient satisfaction in the long-term. The most important determinant of favourable cost-effectiveness of any treatment of SVT, and specifically of ablation procedures, is high efficacy, leading to avoidance of hospitalizations due to arrhythmia recurrences. It is worth emphasizing that one day of hospitalization has important costs, ranging from $476–835 in European countries to $4287 (on average) in the USA.[415]

With regard to the costs of radiofrequency catheter ablation procedures, variable data have been reported in literature (from $5000 to $16 000), varying not only according to setting and country but also according to consideration of actual costs or billed hospital charges.[258] Cheng *et al.* compared, in a Markov model, RF ablation vs. pharmacological treatment (continuous or only at the time of arrhythmia recurrence) in highly symptomatic adult patients with monthly recurrences of SVTs, excluding patients with WPW syndrome.[247] As shown in *Table 20*, RF ablation procedures resulted in substantial improvement of QoL and cost reduction at long term, with a highly favourable ('dominant') cost-utility profile. In a 5-year study performed in patients with mild-to-moderate symptomatic SVT, Goldberg *et al.* found that RF ablation when compared to pharmacological treatment was associated with a sustained improvement in QoL and a reduction in disease-specific symptoms, particularly in women and patients aged $<$50 years.[254] RF ablation was also found highly cost-effective ('dominant') in a comparative study vs. medical treatment of SVT of adult patients in Latin America (Guatemala) (*Table 21*).[416] In the same setting, a previous study on paediatric patients showed that in children and adolescents the mean cost of an ablation procedure was 4.9 times higher than that of medical/pharmacological treatment at a follow-up of around 1 year, but it was estimated to become equal to that of medical therapy after 5.1 years, and 3.4 times lower after 20 years.[417] Recently, many centres have successfully adopted the strategy of performing ablation procedures for SVT without overnight hospital stay, provided that the procedure was not complicated and the patient status was clinically stable. This strategy was analysed in a retrospective study of 1142 patients who underwent elective EP procedures with or without RF ablation for SVT. Avoidance of overnight stay, with an average cost of $450, resulted in important savings for the institution ($365 000), and this was coupled with a reassuring patient safety profile.[418]

In conclusion, a favourable cost-effectiveness profile has been demonstrated for ablation therapy in SVT patients with frequent arrhythmia recurrences. In patients with symptoms that can be controlled with medications, the upfront cost of ablation therapy is equalled, with time, by the cumulative cost of medical therapy, usually after a period of around 10 years.[258] The perspective of a curative treatment and patient preferences have expanded the indication of ablation therapy in SVT outside of the setting of drug refractory arrhythmic episodes, and ablation is currently proposed as a first-line treatment option in SVT patients.

Patient preferences

To date there is scant evidence to advocate patient values or preferences for particular treatment modalities for SVT since the patient's perspective has not been specifically explored in research studies in this patient group. The available evidence on patient's experiences

Table 21 Studies that evaluated costs and cost-effectiveness of ablation vs. pharmacological treatment of SVTs in different settings

Comparison and setting	Success rate	Cost	QALYs	Saving	Reference
RF ablation vs. medical treatment for adults with monthly episodes of SVT.	For RF ablation 95%	At lifetime $61 880 for RF ablation and $89 820 for pharmacological treatment	With RF ablation the incremental quality-adjusted life expectancy was 3.1 QALYs	RF ablation reduced lifetime medical expenditures by $27 900	[247]
RF ablation vs. medical treatment.	For RF ablation 83% in first procedure, 94% cumulative after second procedure	For RF ablation $5411	1.46 QALYs in favour of RF ablation vs. medical treatment	$7993 in favour of RF ablation vs. medical treatment	[416]

of SVT has recently been reviewed in a European Heart Rhythm Association (EHRA) position document.[419]

Patients with SVT may commonly experience symptoms such as dyspnoea, fatigue, palpitations, and pre-syncope/syncope, which vary in frequency, duration, and intensity.[1,2,16,420,421] This uncertain trajectory can provoke significant anxiety and fear in anticipation of when the next symptomatic episode will occur, leading to avoidance of situations or triggers of symptom-onset.[16,420–423] Consequently, patients with SVT may restrict their normal daily and leisure activities (social events, sports, and sexual relationships),[16,419] and may be unable to initiate or continue certain 'high-risk' occupations (flying, competitive athletics etc.)[1,2,419] or drive,[422,423] all of which can adversely affect a patient's QoL. Limitations to participation in social activities and driving are most frequently reported and appear to have the greatest negative impact on QoL.[419] One of the main goals of treatment for SVT is to reduce symptoms and improve QoL.[1,2,419]

Several studies have investigated patient-reported QoL,[2,245,246,254–256,258,424,425] and these may offer some insight into patient preferences for treatment where particular therapies result in improvements in QoL. Almost all of the studies examining QoL, measured with validated questionnaires, have been conducted in patients undergoing catheter ablation for SVT,[245,246,254–256,258,424,425] although often without a comparison group. Every study has demonstrated an improvement in self-reported QoL following ablation.[2,245,246,254–256,258,424,425] This is perhaps not surprising given that ablation often significantly reduces or eliminates symptoms. However, these studies are limited by their small sample sizes, in highly selected populations, with short follow-up periods, often lacking a suitable control group, and are frequently hampered by recall and responder bias. As a result the latest ACC/AHA/HRS guidelines for SVT do not make recommendations for ablation or medical therapy on the basis of their effect on patient-reported QoL.[2]

Patient education can help to facilitate greater patient participation in treatment decisions since informed choices about therapy requires patients to understand the natural trajectory of their condition, what the treatment options are and what they can offer, and the likely impact of these treatments on their symptoms and QoL. Advice and recommendations for key discussion points between physicians and patients with SVT have recently been outlined in another EHRA document.[419]

Areas for further research

With the advent of catheter ablation in the 1990s resulting in successful elimination of accessory pathways in symptomatic patients, AVRT nowadays represents less than 30% of all SVTs.[9] AVNRT that accounts for 50% of all cases is seen with the same frequency as before and the proliferation of AF ablation, will unavoidably result in more iatrogenic left AFLs. Moreover, the prolonged survival of ACHD patients is expected to impose a further challenge for the adult electrophysiologists who will have to deal with even more complex atrial macroreentrant tachycardias. Several and important advances in the field of anatomic and electrical mapping, as well as appreciation of scar tissue and transmurality of ablation lesions, should improve our efficiency in treating these patients.

The last decade has witnessed a rapid evolution of ablation equipment and electrode guiding systems that have resulted in more controllable and safer procedures. Robotic techniques and sophisticated anatomical navigation systems have been developed, and it is now possible to perform ablation without exposing the operator to radiation and ergonomically unfavourable positions.[426] New materials for electrodes and other equipment have allowed the concept of radiation-free EP laboratory with the use of MRI. The vision of a fully radiation-free, magnetic laboratory in the future is not science fiction any more.[427]

The revolution in computer technology offers not only improved mapping and electrode moving systems, but also enhances specific SVT classification schemes by fully automated algorithms that may greatly assist emergency departments, ambulances, and monitored patients.[428] Mathematical modelling and numerical analyses have also been employed in the investigation of the circuit of AVNRT.[221,232] It might be possible that further analysis of recorded ECGs using fast Fourier and Gaussian models might be able to provide useful diagnostic information about the nature of the tachycardia.

Last, but not least, the revolution in genetics has also affected SVTs. New data on the genetics of SVT continually appear since the identification of a missense mutation in the gene *PRKAG2*, that

encodes the regulatory γ-subunit of AMP-activated protein kinase, as a cause of familial Wolff–Parkinson–White syndrome.[429,430] The R302Q mutation in *PRKAG2* has been associated with Mahaim fibres.[431] A novel form of WPW syndrome is associated with microdeletion in the region of gene *BMP2*, that encodes the bone morphogenetic protein-2, a member of the transforming growth factor (*TGF-β*) gene superfamily, and affects the development of annulus fibrosus.[432] Whether this kind of genetic predisposition translates into a higher VF risk remains to be seen. Spontaneous AVNRT has also been identified as a potential first clinical manifestation of concealed Brugada syndrome, particularly in female patients.[226] It has been postulated that genetic variants that reduce the sodium current (I_{Na}) may predispose to expression of both phenotypes. Cellular electrophysiology is now being integrated into genetic analysis. Coupling whole exome sequencing with cellular electrophysiologic functional analysis may elucidate the underlying pathophysiologic mechanism responsible for certain phenotypes.[433] Recently, a familial form of inappropriate sinus tachycardia was shown to be associated with a gain-of-function mutation in the *HCN4* pacemaker channel (R524Q), conferring an increased sensitivity to the second messenger cAMP, which is a key mediator in sympathetic modulation.[434] These developments may have important implications for a more specific diagnosis, and personalized therapeutic approach in SVT.

SVTs are not only an everyday clinical problem, with AVNRT being the most common regular arrhythmias in the human, they also provide the background for proper training of future electrophysiologists by means of their well-defined circuits, in most cases, and predictable responses in the EP lab. In the era of computerized, video-game-style approaches that are now available for AF and VT ablation, this is very important for a rational, Aristotelian approach to the art of medicine.[435]

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