Using the right drug: a treatment algorithm for regular supraventricular tachycardias

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Despite the recent advent of and the successful results from catheter ablation, pharmacological therapy is still used by most clinicians as the first line therapy in patients with regular supraventricular tachycardias. Before prescribing an antiarrhythmic agent, documentation of the arrhythmia using a 12-lead electrocardiogram (ECG) is necessary to identify the type of tachycardia. The ECG diagnosis is based on the presence and polarity of the P wave, the P to QRS relationship, the presence of QRS alternation and the effect of bundle branch block on tachycardia rate. Most regular supraventricular tachycardias use the atrioventricular node either passively, as in atrial tachycardias or flutter, or actively, as paroxysmal junctional tachycardias. The Sicilian Gambit approach attempted to introduce some rationale in the choice of an antiarrhythmic agent, taking into account tachycardia mechanism, by defining the critical components of the tachycardia and the vulnerable parameter, i.e. the component that may readily be affected by an appropriate antiarrhythmic agent. For this approach, an electrophysiological study is particularly useful. The most common regular paroxysmal supraventricular tachycardias include atrioventricular nodal re-entrant tachycardias and atrioventricular re-entrant tachycardias which use an overt or concealed accessory atrioventricular connection (Kent bundle) or atriofascicular connection (Mahaim). For acute termination of paroxysmal junctional tachycardia, intravenous adenosine is the drug of choice. For the prevention of the tachycardia attacks in atrioventricular nodal re-entrant tachycardia, the agents with a depressive effect on the antegrade slow pathway, such as calcium channel blockers or β-blockers, are likely to be effective. If they fail, sodium channel blockers (propafenone or flecainide) may be indicated. In tachycardias involving accessory connections, agents that affect fast channel dependent tissue (propafenone, flecainide, cibenzoline, disopyramide or hydroquinidine) are effective. Potassium current blockers, such as sotalol or amiodarone, represent an alternative therapy. In atrial tachycardias, the use of propafenone, flecainide or sotalol constitute a logical choice. In drug-resistant cases, amiodarone is the most potent agent. Radiofrequency ablation of the slow atrioventricular nodal pathway, of an accessory connection or of an atrial focus, is indicated in drug-resistant or drug-intolerant patients and is increasingly offered as an alternative therapy.

Introduction

Despite the fact that catheter ablation represents a major advance in the treatment of regular supraventricular tachycardias, pharmacological therapy is still used by most clinicians as a first line therapy in patients with supraventricular tachycardia. Pharmacological therapy may be indicated for acute termination of persistent (non-self-terminating) paroxysmal supraventricular tachycardia or for prevention of attack recurrences. Electrocardiographic documentation of supraventricular tachycardia is an essential step in the management as it represents an essential tool with which to categorize the type of supraventricular tachycardia and select the appropriate treatment.

Classification of regular supraventricular tachycardias

By definition, supraventricular tachycardias are defined as tachycardias originating above the bifurcation of the bundle of His. The latter include tachycardias which originate in the atrium and in the atrioventricular junction. As shown in Table 1, regular tachycardias of atrial origin include sinus tachycardia, appropriate or
Table 1  Classification of regular supraventricular tachycardias

<table>
<thead>
<tr>
<th>Atrium</th>
<th>Sinus tachycardia (appropriate)</th>
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<tr>
<td></td>
<td>'Inappropriate sinus tachycardia'</td>
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<tr>
<td></td>
<td>Sinoatrial re-entry</td>
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<td></td>
<td>Unifocal atrial tachycardia</td>
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<td></td>
<td>Multifocal atrial tachycardia</td>
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<tr>
<td></td>
<td>Atrial flutter</td>
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<tr>
<td>Atrioventricular junction</td>
<td>Atroventricular nodal re-entrant tachycardias (ANRT)</td>
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<tr>
<td></td>
<td>— Common</td>
</tr>
<tr>
<td></td>
<td>— Uncommon</td>
</tr>
<tr>
<td></td>
<td>— 'Slow-slow'</td>
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<tr>
<td>Atrioventricular re-entrant tachycardias (AVRT)</td>
<td>Kent (over or concealed)</td>
</tr>
<tr>
<td></td>
<td>— orthodromic</td>
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<tr>
<td></td>
<td>— antidromic</td>
</tr>
<tr>
<td></td>
<td>Atiofascicular (Mahaim fibre)</td>
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<td></td>
<td>Slow-conducting Kent bundle</td>
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‘inappropriate’, sinoatrial re-entry, ectopic atrial tachycardias (unifocal or multifocal) and atrial flutter. Paroxysmal atrioventricular junctional tachycardias account for the vast majority of patients with paroxysmal regular supraventricular tachycardias. As presented by Professor Camm in this issue, there are two main mechanisms for paroxysmal atrioventricular junctional tachycardias; (1) re-entry involving the atroventricular nodal area, the so-called atrioventricular nodal re-entrant tachycardias; (2) re-entry involving an accessory pathway, which constitutes the atrioventricular re-entrant tachycardias. The most common type uses an atrioventricular accessory pathway, the so-called Kent bundle bridging the atroventricular ring and connecting the atrium to the ventricle. The Kent bundle may be responsible for overt pre-excitation, the so-called Wolff–Parkinson–White syndrome. The Kent bundle may operate in some patients in the retrograde direction only (concealed pre-excitation). Another less common type of accessory pathway is a Mahaim fibre also called the nodofascicular pathway, or nodoventricular pathway. More recently, another type of pathway was found to be atiofascicular and related to a small atroventricular node-like structure connecting the atrium to the right bundle fascicle, as supported by recording of a Mahaim potential over the right tricuspid annulus. A permanent form of tachycardia, called permanent junctional reciprocating tachycardia, is related to a slow conducting Kent bundle, operating in the retrograde direction only.

Differential diagnosis of regular supraventricular tachycardias

Analysis of the 12-lead electrocardiogram allows the clinician to diagnose supraventricular tachycardia, as in the vast majority of patients a narrow (<0.12 s) QRS tachycardia is recorded. As pointed out by Wellens et al.[9], Akhtar et al.[10] and others[11-3] there are numerous clues which are helpful in defining the type of regular supraventricular tachycardia, i.e. the presence and polarity of the P wave, the location of the P wave in relation with the QRS complex, the presence of QRS alternation (in favour of atrioventricular re-entrant tachycardia) and the effect of bundle branch block on heart rate. The diagnosis may be difficult if P waves are not visible and the diagnosis of tachycardia mechanism may require an electrophysiological evaluation, particularly when the tracing in sinus rhythm does not show evidence of pre-excitation. Regular supraventricular tachycardia may present with wide (>0.12 s) QRS complex and the problem of differentiating supraventricular tachycardia from ventricular tachycardia may require endocavitary recordings[2-3]. It is important to emphasize that the vast majority of regular supraventricular tachycardias occur in patients without organic heart disease.

Management of regular supraventricular tachycardias

The management of supraventricular tachycardias includes no therapy when attacks are uncommon and self-terminating. When attacks are episodic, long-term pharmacological therapy and radiofrequency catheter ablation may be necessary. Long-term pharmacological therapy may be empirical or guided by electrophysiological study. An interesting approach has been recently proposed by the members of the Sicilian Gambit[6-8]. For this approach, electrophysiological study is particularly useful as it defines the critical components of the tachycardia and vulnerable parameters. The latter are
The components of an arrhythmogenic mechanism that is readily and safely manipulated by antiarrhythmic agents\(^a\), as seen in Figure 1. The electrophysiological study is useful to obtain ECG documentation of the tachycardia if hitherto unavailable, to define the mechanism, the critical components and vulnerable parameters and to evaluate the efficacy of the antiarrhythmic therapy selected.

There are some important principles which should be kept in mind: (1) electrocardiographic documentation is essential and may require Holter monitoring, event recording, exercise testing or/and electrophysiological study; (2) the tolerance of the arrhythmia should be evaluated; (3) the presence and nature of associated heart disease should be defined; (4) precipitating factors (such as electrolytes, hypoxia, ischaemia, drugs) should be looked for; (5) the type of supraventricular tachycardia should be clarified.

In the Sicilian Gambit approach, it is necessary to know the effect of antiarrhythmic agents on the different components of the circuit.

### Pharmacological treatment of regular supraventricular tachycardias

#### Inappropriate sinus node tachycardia

Recently, a rare arrhythmia has been recognized and defined as 'inappropriate' sinus node tachycardia. The P waves have the same configuration as the sinus P waves. This atrial tachycardia is characterized by an inappropriate and exaggerated acceleration of heart rate during physiological stresses\(^a\). The mechanism is still speculative and a number of possible hypotheses include an ectopic atrial focus located in the sinoatrial node area, a normal sinoatrial node with increased response to the sympathetic tone or failure to respond to vagal stimulation, or an intrinsic anomaly of the sinoatrial node. The appropriate therapy is the use of \(\beta\)-blockers. Some patients do not respond to \(\beta\)-blockers or the dose required is associated with intolerable side effects. Catheter ablation of such arrhythmia is under investigation and we were successful in treating one of these patients using radiofrequency ablation. The role of specific bradycardiac agents in this arrhythmia has not, to our knowledge, been studied before. Inappropriate sinus node tachycardia has also been observed following radiofrequency ablation of an accessory connection or an ectopic focus and may be related to reversible parasympathetic denervation.

#### Atrioventricular nodal tachycardia

This tachycardia (Fig. 2) in its 'common' form utilizes the slow pathway in the antegrade direction and the fast pathway in the retrograde direction. The common form

<table>
<thead>
<tr>
<th>I</th>
<th>aVR</th>
<th>V1</th>
<th>V4</th>
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<tr>
<td>II</td>
<td>aVL</td>
<td>V2</td>
<td>V7</td>
</tr>
<tr>
<td>III</td>
<td>aVF</td>
<td>V3</td>
<td>V6</td>
</tr>
</tbody>
</table>

Figure 2 Twelve-lead electrocardiogram of the common form of atrioventricular nodal re-entrant tachycardia. No P waves are seen as they fall on the QRS complexes.

represents approximately 90% of the patients with atrioventricular nodal re-entrant tachycardia\(^{16}\).

#### Acute termination of atrioventricular nodal re-entrant tachycardia

In a number of patients, the tachycardia attack terminates spontaneously or with vagal manoeuvres (e.g. Valsalva manoeuvre) that the patient has been taught to use. In persistent tachycardia attacks, particularly if they are poorly tolerated, the use of intravenous pharmacological therapy may be needed for termination of tachycardia. Adenosine or adenosine triphosphate which blocks the Ik (ATP), a potassium current, represents the drug of choice because of its effectiveness (it terminates more than 80% of episodes) and its short half-life\(^{12}\) (Fig. 4). The use of a short-acting \(\beta\)-blocker such as esmolol may also be a valuable option. Before adenosine was available, intravenous verapamil, a calcium channel blocker was the most commonly used agent. Intravenous diltiazem has also been found to be effective and safe in terminating atrioventricular nodal re-entrant tachycardia. All these agents affect the so-called slow atrioventricular nodal pathway. If the therapeutic choice is to affect the fast pathway, sodium channel blockers (Class IA or IC of Vaughan-Williams) or potassium channel blockers (i.e. amiodarone or sotalol) may be indicated. The fast pathway may have fast channel-dependent cells, whereas the slow pathway may have slow channel-dependent tissue. Despite the high success rate of sodium channel blockers in terminating supraventricular tachycardia\(^{12,13}\), the vulnerable parameter, which is the most likely to be affected or interrupted in atrioventricular nodal re-entrant tachycardia, is the slow pathway. Again, intravenous adenosine has become the drug of choice for acute termination of re-entrant paroxysmal supraventricular tachycardia.

#### Prevention of tachycardia attacks

The clinician must first evaluate the need for long-term pharmacological therapy. The slow pathway again is the vulnerable parameter, the 'weak link' of the circuit (Fig. 3). Therefore, agents with a depressant effect on the antegrade slow pathway, such as calcium channel
blockers (verapamil or diltiazem) or β-blockers (e.g. propranolol, metoprolol, nadolol) are likely to be effective in the prevention of recurrences. The agents with preferential depressant effects on the antegrade fast pathway (sodium channel blockers and potassium channel blockers) may be used alone or in combination with β-blockers. This is an important combination therapy to consider, as the effects of sodium channel blockers may be suppressed in situations with increased catecholamine levels such as exercise or emotion. The use of antiarrhythmic agents that affect fast channels may be associated with ventricular proarrhythmia. The incidence is probably low as most patients with regular supraventricular tachycardia have a normal heart. In patients with drug resistant or drug intolerant atrioventricular nodal re-entrant tachycardia, radiofrequency ablation of the slow pathway is a valuable option. It has, however, a 1% risk of producing high degree atrioventricular block requiring a permanent pacemaker.

Wolff–Parkinson–White syndrome

The arrhythmias associated with this syndrome are discussed in this issue. They include reciprocating or circus movement tachycardias and atrial arrhythmias. The better defined and the most common atrioventricular re-entrant tachycardia is the so-called orthodromic tachycardia (Fig. 5). The impulse traverses the normal atrioventricular node and His bundle in the antegrade direction resulting in narrow QRS complexes (in the absence of bundle branch block or aberration) and uses the accessory connection (Kent bundle) in the retrograde direction. If re-entry is associated with a short excitable gap, the vulnerable parameter may be the refractory period of the accessory connection. Therefore, in order to increase the refractory period, one should target the potassium current through agents such as amiodarone or sotalol. In contrast, if re-entry is associated with a long excitable gap, the vulnerable parameter may be conduction through a fast-conducting accessory pathway by using sodium channel blockers such as propafenone or flecainide. Such an approach requires an electrophysiological study.

As most patients in the Wolff–Parkinson–White are young, long-term therapy with pharmacological agents may be a problem and ablation of the accessory connection may be a valuable option, provided the risk-benefit ratio of ablation is adequately evaluated. A pre-excited QRS complex tachycardia, the so-called antidromic tachycardia is uncommon. It involves antegrade conduction through the accessory pathway and retrograde conduction through the normal pathway. The appropriate antiarrhythmic agent should be a sodium channel blocker such as propafenone or flecainide. These agents have been shown to be particularly effective in the management of atrioventricular re-entrant tachycardia. In patients with two accessory connections, the impulse may use one pathway in the antegrade direction and the other accessory pathway in the retrograde direction. Flutter with 1:1 conduction or 2:1 conduction over the accessory pathway may be observed. In some instances, atrioventricular nodal

Figure 3 Effects of commonly used antiarrhythmic agents on the slow and fast pathways in the common form of atrioventricular nodal re-entrant tachycardia. (From Akhtar et al. with permission.)

Ventricles

Figure 4 (a) Termination of atrioventricular nodal re-entrant tachycardia with adenosine. (b) Continuous tracing of lead 1. Note the short half-life of the drug by the effect on PR interval.
Treatment algorithm for supraventricular tachycardias

C31

aVR  aVL  V9
HI  aVF  V3  V6

Figure 5 Twelve-lead electrocardiogram of an orthodromic tachycardia in the Wolff-Parkinson-White syndrome.

aVR  aVL  V1  V4
II
III

Figure 6 Unifocal atrial tachycardia. Note that alternation is present in this tachycardia with a rate exceeding 200 beats min⁻¹.

Tachycardias related to Mahaim fibres

These tachycardias have a particular electrocardiographic presentation with left bundle branch block and left axis.

In most reported cases, these tachycardias involve the accessory pathway (an atrioventricular-like structure) in the antegrade direction and the right branch, the His bundle and atrioventricular node in the retrograde direction. However, there are some convincing cases of nodofascicular fibres used also in the retrograde direction during the tachycardia and responsible for a tachycardia with left bundle branch block configuration. The ECG in sinus rhythm shows the features of the Wolff-Parkinson-White syndrome. The electrophysiological study will demonstrate decremental conduction over the accessory pathway.

As the pathway behaves as an atrioventricular node-like structure it is likely that it contains slow-dependent tissue and the use of calcium blockers such as verapamil or diltiazem is logical. β-blockers may also be a valuable choice. Ablation of the accessory pathway offers an alternative therapy.

Permanent junctional reciprocating tachycardia

This tachycardia described by Coumel et al. was found to be related to a concealed accessory connection capable of decremental conduction. The tachycardia uses the atrioventricular node in the antegrade conduction and a slow conduction accessory connection in the retrograde direction. This tachycardia may be incessant (permanent) and becomes sustained in situations in which catecholamines are increased such as exercise or emotion. It should be treated as it may have a deleterious effect on cardiac function. The differential diagnosis includes atypical atrioventricular nodal tachycardia using the fast pathway in the antegrade direction and the slow pathway in the retrograde direction and atrial tachycardia arising from the lower part of the atrium near the orifice of the coronary sinus. Pharmacological therapy could target conduction either through the atrioventricular node, using calcium channel blockers or in the slow conducting accessory connection with sodium channel blockers (propafenone, flecainide). Amiodarone or sotalol may affect both limbs of the circuit. Ablation of the accessory connection may also be a valuable option.

Atrial tachycardias

Atrial tachycardias may be due to re-entry, abnormal automaticity or both mechanisms. Sinoatrial re-entry should be suspected if the P wave morphology during the tachycardia is similar to that during sinus rhythm and the tachycardia can be induced and terminated with one or two paced premature atrial beats. This diagnosis can only be made by electrophysiological study. Intra-atrial re-entry is also initiated and terminated with premature atrial stimulation but the P wave during the tachycardia is different from the P wave during sinus rhythm (Fig. 6). In tachycardia related to an ectopic focus, the morphology of the P wave during tachycardia is dependent on the site of origin. Some atrial tachycardias are catecholamine-sensitive and for them the use of β-blockers is appropriate. The first line drugs for atrial tachycardias are sodium channel blockers (propafenone, flecainide, disopyramide, hydroquinidine). Atrial tachycardias are often resistant to pharmacological therapy. In cases resistant to sodium channel blockers, amiodarone may be effective. Another choice
would be simply to control heart rate using calcium channel blockers or β-blockers and slow atrioventricular nodal conduction. Unifocal tachycardias may be cured by radiofrequency ablation[17]. Multifocal tachycardias are more difficult to ablate and pharmacological therapy (except for amiodarone) aimed at eliminating the arrhythmia is often ineffective. Control of heart rate is the second best choice.

Radiofrequency ablation of atrial tachycardia is effective in 50–70% of cases[17]. Recurrence, despite an initially successful ablation, is not uncommon. The literature on ablation of atrial tachycardias is limited and this option should be limited to experienced teams.

**Atrial flutter**

Pharmacological therapy is the first-line option in the prevention of recurrences. Sodium channel blockers such as flecainide, propafenone, disopyramide or hydroquinidine are the antiarrhythmic agents most likely to be effective. Sotalol or amiodarone are also valuable options. In drug refractory or drug intolerant patients, radiofrequency ablation should be considered. The technique is effective in 50–90% of reported series[18,19]. However experience is still limited and follow-up is too short to propose ablation as a first line therapy.

**Conclusion**

Pharmacological therapy remains the first line therapy used by most clinicians for patients with regular supraventricular tachycardia. The Sicilian Gambit should be used to select the antiarrhythmic agent (when indicated) most likely to be successful. This process takes into account the mechanism, the critical components and vulnerable parameter(s) of the arrhythmogenic substrate. Radiofrequency ablation with an ectopic focus, of a slow atrioventricular nodal pathway or of an accessory connection is increasingly offered as an alternative to regular supraventricular tachycardia.

**References**


