



WPW and Preexcitation Syndromes

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Abstract

Wolff–Parkinson–White syndrome is a disorder characterized by presence of an accessory pathway which predisposes patients to tachyarrhythmias and sudden death. Among patients with WPW syndrome, atrioventricular reentrant tachycardia (AVRT) is the most common arrhythmia, accounting for 95% of re-entrant tachycardias. It has been estimated that one-third of patients with WPW syndrome have atrial fibrillation (AF). AF is a potentially life-threatening arrhythmia. If an accessory pathway has a short anterograde refractory period, then rapid repetitive conduction to the ventricles during AF can result in a rapid ventricular response with subsequent degeneration to ventricular fibrillation (VF). The accessory pathway may be located anywhere along the atrioventricular valve. Most of the patients are young and do not have structural heart disease hence it is important to risk stratify these patients so as to prevent the sudden death. Management of asymptomatic patients with WPW syndrome has always remained controversial. Catheter ablation of accessory pathways has become an established mode of therapy for symptomatic patients and asymptomatic patients employed in high-risk professions. ©

INTRODUCTION

Wolff–Parkinson–White syndrome has attracted cardiologists' attention not only because of its clinical importance but also because of the opportunity it provides to learn about electrical conduction in the heart.¹ The diagnosis of WPW syndrome is reserved for patients who have both pre-excitation and tachyarrhythmias. Historically, the possibility of the existence of atrioventricular accessory pathways was first raised by Stanley Kent² in 1913. In 1930, Wolff, Parkinson, and White reported on 11 young patients with paroxysms of tachycardia or atrial fibrillation that had a functional bundle branch block and an abnormally short PR interval on electrocardiograms recorded during sinus rhythm.¹ In 1933, Holzmann and Scherf³ reported that the mechanism in Wolff–Parkinson–White syndrome consisted of an acceleration of passage of the impulse from the atria to the ventricles and not a block, as had been proposed by Wolff, Parkinson, and White. In 1944, Ohnell⁴ introduced the term "preexcitation" to the medical literature, and along with Wood *et al.*,⁵ confirmed the presence of accessory pathways by histologic studies. Among patients with WPW syndrome, atrioventricular reentrant tachycardia (AVRT) is the most common arrhythmia, accounting for 95% of re-entrant tachycardias. Atrial fibrillation (AF) is a potentially life-threatening arrhythmia in patients with WPW syndrome as it can degenerate to ventricular fibrillation (VF).

Pathophysiology

The anomaly in WPW syndrome is accessory connections between the atrium and ventricle. This accessory connection which is also called bypass tract may be atriofascicular, fasciculoventricular, intranodal, or nodoventricular, the most common being atrioventricular (AV) pathway otherwise known as a Kent bundle. Conduction through a Kent bundle can be anterograde, retrograde, or both. Accessory pathways that are capable of only retrograde conduction are referred to as 'concealed', whereas those capable of anterograde conduction are 'manifest', demonstrating pre-excitation on a standard ECG. Manifest accessory pathways usually conduct in both anterograde and retrograde directions.⁶

Most patients with the Wolff–Parkinson–White syndrome have otherwise normal hearts, but some have concomitant congenital heart disease. Approximately 10 percent of patients with Ebstein's anomaly have the Wolff–Parkinson–White syndrome^{6,7} (Fig. 1). Other congenital heart diseases associated with the syndrome include atrial and

ventricular septal defects, coronary-sinus diverticula, and corrected transposition of the great vessels.⁷ Thus, the Wolff–Parkinson–White syndrome is an embryonic defect in which processes that electrically insulate the atria from the ventricles go awry.

Frequency

Delta waves detectable on an ECG have been reported to be present in 0.15% to 0.25% of the general population.⁶ A higher prevalence of 0.55% has been reported in first-degree relatives of patients with accessory pathways. Wolff–Parkinson–White syndrome is more commonly diagnosed in men than in women, although this sex difference is not observed in children. Among those with the Wolff–Parkinson–White syndrome, 3.4 percent have first-degree relatives with preexcitation.⁸ The familial form is usually inherited as a mendelian autosomal dominant trait.⁷⁻¹¹

Classification

Accessory pathways can be classified on the basis of their location along the mitral or tricuspid annulus. Current nomenclature for the atrioventricular (AV) junctions derives from a surgically distorted view, placing the valvar rings and the triangle of Koch in a single plane with antero-posterior and right-left lateral coordinates. Although this nomenclature has served its purpose for the description and treatment of arrhythmias dependent on accessory pathways it is less than satisfactory for the description of atrial and ventricular mapping. To correct these deficiencies, a consensus document has been

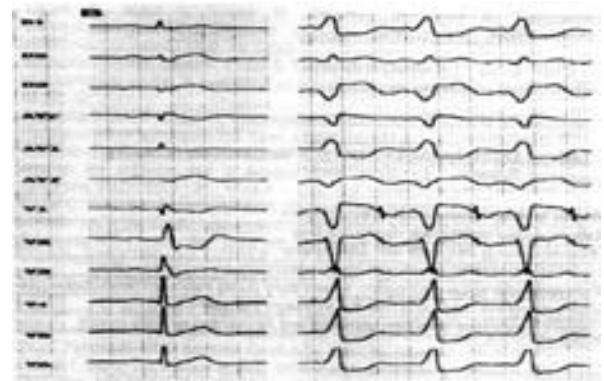


Fig. 1 : Atrioventricular pathway in Ebstein's disease: baseline ECG without preexcitation and disclosing RBBB with normal PR interval. During atrial pacing manifest preexcitation with LBBB, QRS 160 msec wide with a slurred initial r wave in V1.

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prepared by experts from the Working Group of Arrhythmias of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology.¹² It proposes a new anatomically sound nomenclature that will be applicable to all chambers of the heart the same has been shown in Fig. 2.

VARIANTS

A few clinical variants of accessory pathway are worth noting.

Concealed Accessory Pathways

Defined as pathways that are capable of conduction only in the retrograde (VA) direction at rates similar or greater than the sinus rate. The concealed accessory pathways are noted in between 15% to 42% of patients with accessory pathway.¹³ Approximately one third of AVRTs are due to concealed accessory pathways. The clinical presentation of patients who have a concealed accessory pathway is similar to the classic presentation of WPW syndrome with the exception that rapid preexcited responses are not observed during AF. Concealed pathways are more frequently localized to the left free wall (64%), and less frequently in Septal (31%) and right free wall locations.^{6,13}

Decremental Accessory pathways

The electrophysiologic properties of accessory pathways are similar to working myocardium. Few accessory pathways may exhibit progressive delay in conduction in response to increased rate of pacing. Decremental conduction can be seen in approximately 7% of the patients with WPW syndrome.⁶

Permanent Junctional Reciprocating Tachycardia

The permanent form of junctional reciprocating tachycardia (PJRT) is an infrequent circus movement tachycardia, originally described by Gallavardin subsequently characterized by Gallagher *et al*¹⁴ who coined the term PJRT. The accessory pathway has decremental properties and is located most frequently in the posteroseptal region. The tachycardia is incessant or nearly so and is found in all age subgroups but more so in children and young adults. The ECG shows P waves inverted in leads II, III and aVF. The RP interval is considerably longer than the PR. Tachycardia terminating either spontaneously or by vagal maneuvers ends with a QRS complex suggesting the occurrence of a block in the retrograde limb of the reentrant circuit. Onset of tachycardia after a subsequent pause always requires a preceding normal sinus beat, providing an important ECG distinction between PJRT and atrial tachycardia.

Atriofascicular “Nodoventricular Mahaim” Accessory Pathways

Mahaim originally described muscle fibres that provided direct anatomic continuity between the AV- node and the right ventricular myocardium, while HJJ Wellens subsequently described its electrophysiological properties.^{15,16}

The “nodoventricular pathway” is associated with a rather constant set of clinical, ECG, and electrophysiologic features as given in Table

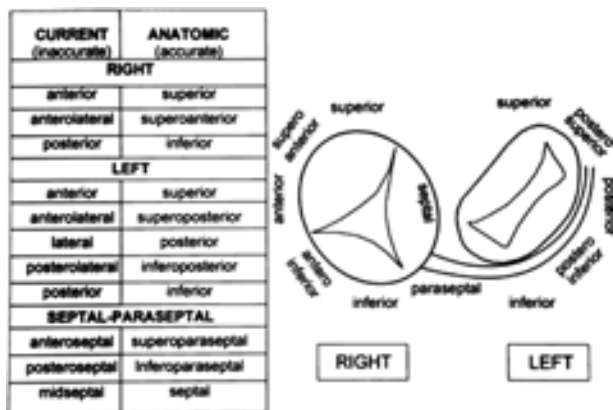


Fig. 2 : Schematic representation of AV junctions in left anterior oblique view along with important differences in the anatomically correct nomenclature from the presently accepted nomenclature.

1.The resting ECG is usually normal, although variable degrees of pre-excitation may be present. The preexcitation becomes evident during incremental atrial pacing, atrial extrastimuli or preexcited tachycardia, and resembles LBBB (Fig. 3), usually with a leftward axis. The most commonly documented tachycardia is a preexcited tachycardia with a retrograde atrial activation sequence compatible with conduction over the AV node.

LOCALIZATION OF THE ACCESSORY PATHWAY

The main electrocardiographic features of preexcitation are a short PR interval (<0.12 seconds), a prolonged QRS complex (>0.12 seconds), and a slurred, slow rising onset of the QRS complex that is known as the delta wave.

Localization of the accessory pathway is generally of value only when considering catheter ablation. The pathway localization or the degree of preexcitation otherwise does not predict the clinical course. Various algorithms (Chern – En Chiang’s, Fitzpatrick’s and Xie’s algorithms) have been used for predicting accessory pathway location using different electrographic criteria.¹³ An algorithm developed by Arruda *et al*¹⁷ utilizing the surface ECG has an overall sensitivity of 90% and specificity of 99%. Accessory pathway can be localised using following steps

Step 1: If the delta wave in lead I is negative or isoelectric or the R wave is greater in amplitude than the S wave in V1 a left free wall accessory pathway is present. If these criteria are fulfilled then lead aVF is examined. If the delta wave in lead aVF is positive, a left lateral, anterolateral accessory pathway is identified. If the delta wave in lead aVF is isoelectric or negative then the accessory pathway is located at the left posterior or posterolateral region.

Step 2: lead II is examined. A negative delta wave in lead II identifies the subepicardial posteroseptal accessory pathway. If the delta wave in lead II is isoelectric or positive, proceed to step 3.

Step 3: lead V1 is examined. A negative or isoelectric delta wave in lead Vi identifies a septal accessory pathway. If these criteria are fulfilled, lead aVf is examined. If the delta wave is negative, an

Table 1 : Electrophysiological features of nodoventricular accessory pathway

1. Minimal to absent preexcitation in sinus rhythm
2. Rate dependent anterograde conduction time
3. LBBB morphology frequently with leftward axis
4. Preferential preexcitation with right atrial versus coronary sinus stimulation
5. Right ventricular apical electrogram, usually early during maximum preexcitation (pre-delta)
6. Absent retrograde conduction over the accessory pathway
7. Frequent coexistence of multiple pathways and Atrioventricular node reentry

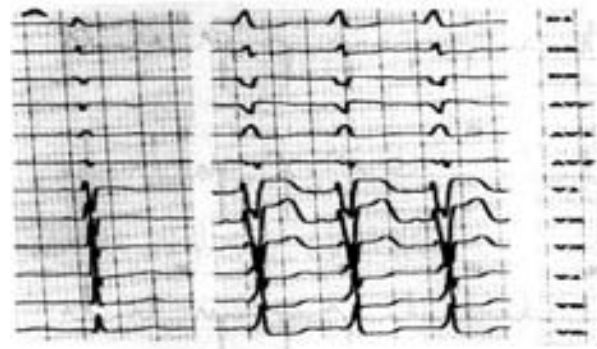


Fig. 3 : Atriofascicular pathway: baseline ECG discloses minimal preexcitation with a 0.12 s PR interval. During atrial pacing LBBB is noted with wide QRS.

accessory pathway is identified, which is located at the posteroseptal tricuspid annulus (Fig. 4). If the delta wave is isoelectric in lead aVF, the accessory pathway may be located to either the posteroseptal tricuspid annulus or the posteroseptal mitral annulus. A positive delta wave in aVF identifies a pathway located within the anteroseptal/right anterior paraseptal or midseptal tricuspid annulus regions (Fig. 5).

If the delta wave in V1 is positive after having excluded patients with a left free-wall accessory pathway in Step 1), a right free wall accessory AV pathway is identified. Proceed to Step 4.

Step 4: In patients with a right free –wall accessory pathways, examine aVF. A positive delta wave in aVF identifies a right anterior/ anterolateral accessory pathway. If the delta wave in aVF is isoelectric or negative, examine lead II. A positive delta wave in lead II identifies a right lateral accessory pathway (Fig. 6), and an isoelectric delta wave in lead II identifies a right posterior/posterolateral pathway.

The predictive accuracy of all these algorithms is significantly reduced in the presence of multiple pathways. Coexistent anomalies such as Acute MI or LVH may alter the QRS morphology.

Sudden death in WPW syndrome

The incidence of sudden cardiac death in patients with the WPW syndrome has been estimated to range from 0.15% to 0.39% over 3- to 10-year follow-up.⁶ It is unusual for cardiac arrest to be the first symptomatic manifestation of WPW syndrome. Risk factors identified for sudden death include, a shortest pre-excited R-R interval less than 250ms during spontaneous or induced AF, history of symptomatic tachycardia, multiple accessory pathways, Ebstein's anomaly and familial WPW syndrome. Fig. 7 shows a patient of WPW syndrome with AF. Findings suggestive of a low likelihood of sudden death include preexcitation that is intermittent, the ability to produce anterograde conduction block with drugs such as procainamide, and the disappearance of preexcitation during exercise. Hence it is important to risk stratify the patients with WPW syndrome.

Risk Stratification

All patients with WPW syndrome need to undergo risk stratification in view of the risk of sudden death. This can be done



Fig. 4 : Wolff-Parkinson-White syndrome in a patient having a posteroseptal pathway.

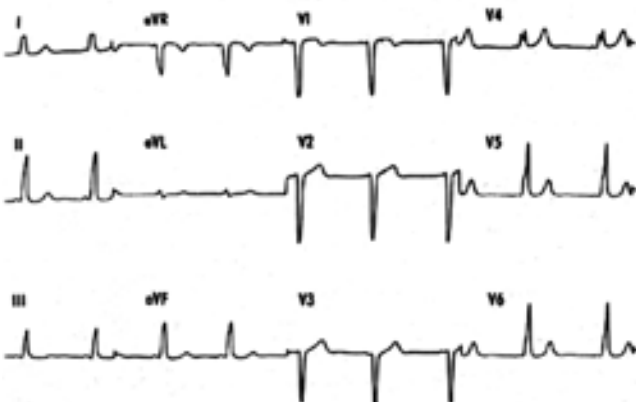


Fig. 5 : Wolff-Parkinson-White syndrome in a patient having a Right anteroseptal pathway.

using invasive and non-invasive means to assess the anterograde refractory period of the accessory pathway, a surrogate marker for the rate of conduction over the pathway during atrial fibrillation.

Non- invasive

ECG marker of low risk is the presence of intermittent WPW syndrome (Fig. 8), while septal location of accessory pathway has been thought to increase the risk of ventricular fibrillation.⁶ Sudden disappearance of pre-excitation during exercise (Fig. 9) indicates a long anterograde refractory period (RP) of the AP and is a marker of low risk.¹⁸ Catecholamine infusion results in shortening of the anterograde refractory period of the accessory pathway.¹⁹ When the RP of the AP is reached, as manifested by sudden block in the AP, one knows that the patient is not at risk for AF even during sympathetic stimulation. The loss of pre-excitation after administration of the antiarrhythmic drug has also been used to indicate a low-risk subgroup. When during sinus rhythm the intravenous injection of ajmaline (1 mg/kg body weight given in 3 minutes)²⁰ or procainamide (10 mg/kg body weight over a 5-minute period)²¹ results in complete block of the AP, a long anterograde RP (>270 ms) of pathway is likely. Noninvasive tests are considered inferior to invasive electrophysiological assessment for risk of sudden cardiac death.

INVASIVE

Electrophysiological testing (EPT) is usually recommended for symptomatic patients to elucidate the pathophysiological basis of their arrhythmias and for asymptomatic individuals with high-risk occupations.²² The positive predictive value of EPT has been considered too low to justify its routine use in asymptomatic patients. Because of the rarity of arrhythmic events reported among asymptomatic subjects, the negative predictive value of EPT has been considered excellent. Patients might be studied by transesophageal route^{23,24} or intracardiac route. The first route is indicated in asymptomatic patients while the second in symptomatic patients where the catheter ablation of the accessory pathway can also be performed.

The presence of an accessory AV connection with anterograde

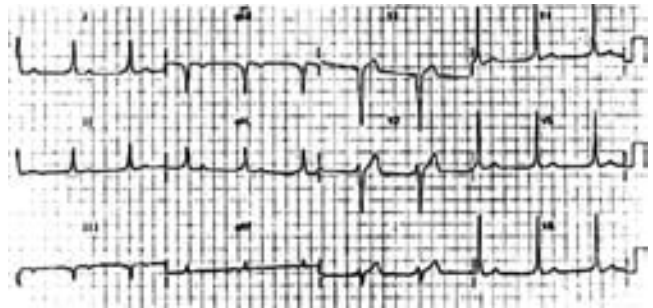


Fig. 6 : Wolff-Parkinson-White syndrome in a patient having a Right accessory pathway.

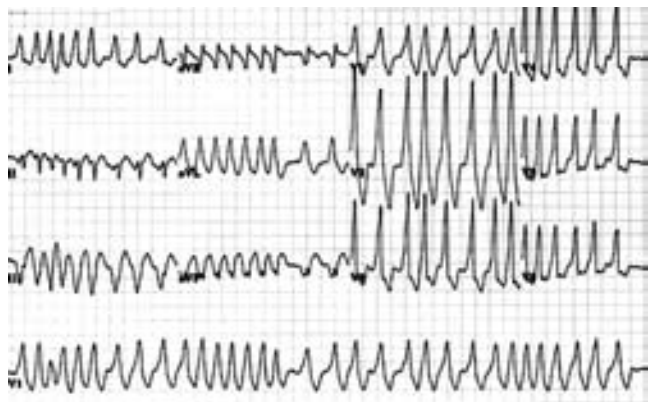


Fig. 7 : Bizarre wide QRS tachycardia "irregularly irregular", indicative of atrial fibrillation with a fast ventricular response in a patient with accessory pathway.

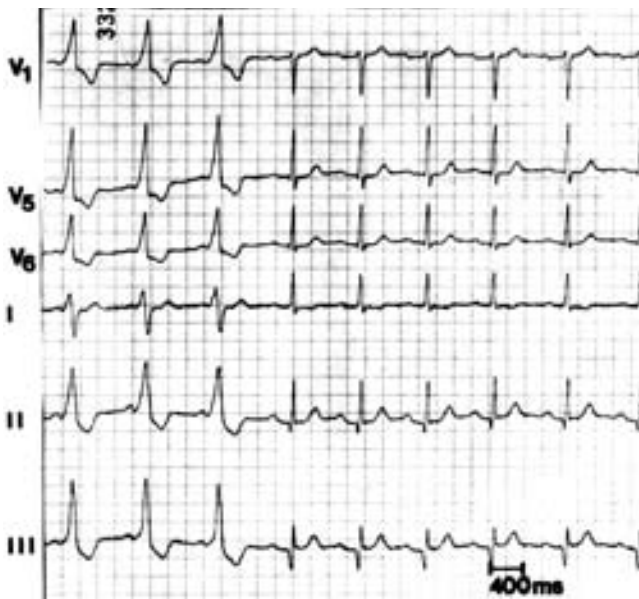


Fig. 8 : Intermittent WPW syndrome signifying long refractory period of accessory pathway.

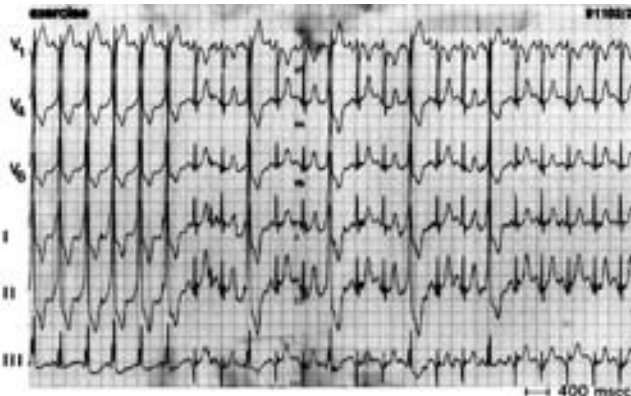


Fig. 9 : ECG during TMT showing disappearance of the conduction over accessory pathway.

conduction is confirmed during electrophysiologic study by the following criteria:

1. During incremental rapid atrial pacing or atrial stimulation with progressively premature extrastimuli, the QRS widens and the HV interval shortens, while the His- bundle depolarization moves into the QRS complex.
2. The stimulus to the onset of the delta wave generally remains constant, although some accessory pathways exhibit rate-dependent prolongation of conduction time.

Several measurements are obtained during electrophysiological evaluation to assess the risk of a potentially lethal arrhythmia. Electrophysiological evaluation is performed using Incremental atrial pacing and atrial extra stimuli is performed to determine the accessory pathway refractory period.^{6,13,25}

Antidromic tachycardia is a rare finding (5%), and seems more frequent in patients at risk of rapid arrhythmias. Orthodromic tachycardia is rarely induced in asymptomatic patients (< 10%),^{6,13} but represents the most frequent tachycardia of symptomatic patients complaining tachycardia and palpitations (90 %). Atrial fibrillation is induced in 95 % of those with documented atrial fibrillation while only in 27-41% of those without documented atrial fibrillation earlier.¹³ The induction of atrial fibrillation is rarely noted in children younger than 10 years.²⁶

Following parameters on EPS are considered significant

- Sustained atrial fibrillation or reciprocating tachycardia is defined as a tachycardia that is longer than 1 minute.^{22,27}

- Conduction over the accessory pathway is evaluated by the measurement of the shortest atrial cycle length at which there is 1 to 1 conduction over the accessory pathway.
- Risk of sudden death is high when sustained atrial fibrillation is induced and the shortest RR interval between preexcited beats is < 250 ms in the control state in adults, < 220 ms in children²² or < 200 ms during isoproterenol infusion

Indications of Electrophysiological Studies in WPW

Indications for systematic electrophysiological evaluation include:

- 1) Sudden deaths have the peculiarity to occur during exercise,²⁸ hence all competitive athletes with WPW syndrome should be studied.
- 2) Patient with high responsibility profession such as professional pilot (plane, truck, bus, train)
- 3) The indications in children are more controversial, the conduction in accessory pathway and normal AV conduction system are more rapid, probably without a clinical significance. The indications should be liberal in children who are competitive athletes and in all children above the age of 10 years.²⁸
- 4) In elderly, the propensity for atrial fibrillation increases hence the risk of occurrence of a potentially severe arrhythmia in an asymptomatic WPW patient should be not underestimated.²⁹

ACUTE TREATMENT

Treatment of AF associated with WPW is necessarily different than for a patient with a normal heart.³⁰ The basic treatment principle in WPW AF is to prolong the anterograde refractory period of the accessory pathway relative to the AV node. This slows the rate of impulse transmission through the accessory pathway and, thus, the ventricular rate.

- If AF were treated in the conventional manner by drugs that prolong the refractory period of the AV node (e.g. calcium channel blockers, beta-blockers, digoxin), the transmission through the accessory pathway would increase, with a corresponding increase in ventricular rate. This could have disastrous consequences, possibly causing the arrhythmia to deteriorate into V F.
- Procainamide (17 mg/kg IV infusion, not to exceed 50 mg/min) blocks the accessory pathway, but it has the added effect of increasing transmission through the AV node. Thus, although procainamide may control the AF rate through the accessory pathway, it may create a potentially dangerous conventional AF that may require treatment with other medications.
- Prompt cardioversion of patients with WPW and AF is recommended and is always the treatment of choice in unstable patients.

Treatment of tachycardia associated with WPW is similar to treating PSVT. Focus on breaking the cyclical transmission of impulses. This is best accomplished by temporarily prolonging the refractory period of the AV node with drugs such as adenosine.³¹

- In a stable patient, adenosine (6 mg rapid IV push; if unsuccessful, 12 mg rapid IV push) should be the first-line treatment in any regular tachycardia, regardless of whether the complex is wide or narrow.
- Once the circus movement is broken, the patient usually converts to sinus rhythm. Note that whether the QRS complex is regular or irregular distinguishes circus movement tachycardia (CMTs) from AF on ECG.
 - If the QRS complex is regular, the arrhythmia can be treated safely with adenosine .
 - If the QRS complex is irregular, the arrhythmia is likely AF. In this case, cardioversion, is the treatment choice.

Adenosine should be used with caution because it may produce AF with a rapid ventricular rate in pre-excited tachycardias. Ibutilide, procainamide, or flecainide, which are capable of slowing the conduction through the pathway, are preferred.

Long-term pharmacologic therapy

There have been no controlled trials of drug prophylaxis involving patients with AVRT. The drugs available to treat AVRT include any drug that alters either conduction through the AV node (e.g., calcium-channel blockers, beta blockers, digoxin) or a drug that alters conduction through the atrium, ventricle, or accessory pathway (e.g., class Ia, Ic, or III antiarrhythmic agents). Despite the absence of data from clinical trials, chronic oral beta-blocker therapy may be used for treatment of patients with WPW syndrome, particularly if their accessory pathway has been demonstrated during electrophysiological testing to be incapable of rapid anterograde conduction.^{6,32}

Following drugs have been used for long-term prophylaxis in patients of WPW syndrome with tachyarrhythmias.^{6,13}

- I. Flecainide. Treatment with flecainide increases the time to first symptomatic event and time to subsequent events. Oral administration of flecainide (200 to 300mg/d) resulted in an inability to induce sustained tachycardia. The addition of a beta-blocker results in greater efficacy, with more than 90% of patients achieving abolition of symptomatic tachycardia.
- II. Amiodarone is not superior to class Ic antiarrhythmic agents. Well-recognized organ toxicity and the high rate of discontinuation of this drug, makes it unpopular drug for treatment of patients with accessory pathways. Exceptions are for patients with structural heart disease who are not thought to be candidates for catheter ablation.
- III. Verapamil and diltiazem should not be used as the sole therapy for patients with accessory pathways that might be capable of rapid conduction during AF.

CATHETER ABLATION

Radiofrequency catheter ablation has become the treatment of choice for patients with symptomatic tachyarrhythmias.³³ Target sites for ablation of accessory pathways are identified by early ventricular activation relative to the delta wave onset (for manifest accessory pathways), by the earliest atrial activation in the retrograde direction (for any accessory pathway that conducts retrogradely), and/or by the presence of a high frequency electrogram consistent with an accessory pathway potential. For most free-wall accessory pathways, complete bidirectional block can be achieved with a conventional 4 mm-tip ablation catheter, using a power setting of 50 W and a temperature setting of 60 C. If the conduction block is transient, permanent accessory pathway block may be easier to achieve with an 8 mm-tip ablation catheter or with an irrigated-tip ablation catheter.^{6,13,33}

Accessory pathways located in the free wall of the left ventricle can be mapped and ablated using a retrograde aortic or transeptal approach. The overall success rates with both approaches have been similar. Accessory pathways posteroseptal in location are most often ablatable using a right-sided approach with delivery of radiofrequency energy along the posteroseptal aspect of the tricuspid annulus. Those located on the left side of the posterior septum, are ablatable using a transeptal or retrograde aortic approach. The accessory pathways along the right free wall can be approached from the inferior or superior vena cava. Anteroseptal or mid-septal pathways may be challenging to ablate because of their proximity to the atrioventricular junction. Cryothermal ablation is preferred to radiofrequency ablation as it carries minimum risk of atrioventricular block. Between 5 and 17% of posteroseptal and left posterior accessory pathways have been reported to be epicardial and ablatable only at the orifice of a venous branch within coronary sinus, or within a coronary sinus diverticulum. Rarely, a transcatheter pericardial approach is required to ablate epicardial atrioventricular accessory pathways that are posteroseptal or right-sided.

The initial efficacy of catheter ablation of accessory pathways is approximately 95% in most series.^{6,13,33} After an initially successful procedure, resolution of the inflammation or edema associated with the initial injury allows recurrence of accessory pathway conduction in approximately 5% of patients. Accessory pathways that recur can usually be successfully ablated during a second session.

Complications associated with catheter ablation of accessory pathways result from radiation exposure, vascular access (e.g., hematomas, deep venous thrombosis, arterial perforation,

arteriovenous fistula, pneumothorax), catheter manipulation (e.g., valvular damage, microemboli, perforation of the coronary sinus or myocardial wall, coronary artery dissection, thrombosis), or delivery of RF energy (e.g., AV block, myocardial perforation, coronary artery spasm or occlusion, transient ischemic attacks, or cerebrovascular accidents).^{6,36} The procedure-related mortality reported for catheter ablation of accessory pathways ranges from 0% to 0.2%.³⁶

Management of patients with asymptomatic accessory pathways

The appropriate strategy for persons with asymptomatic Wolff-Parkinson-White patterns on the electrocardiogram has been controversial. Although ventricular fibrillation leading to sudden death may be the first manifestation of the Wolff-Parkinson-White syndrome, it is rare. In at least five population-based studies^{34,35} in which more than 600 asymptomatic patients were followed for 5 to 20 years, only two sudden deaths overall were recorded.

One-third of asymptomatic individuals younger than 40 years of age when pre-excitation was identified eventually developed symptoms, whereas no patients in whom pre-excitation was first uncovered after the age of 40 years developed symptoms. Patients with asymptomatic pre-excitation should be encouraged to seek medical expertise whenever arrhythmia-related symptoms occur. Most patients with asymptomatic pre-excitation have a good prognosis. The positive predictive value of invasive electrophysiological testing is considered to be too low to justify routine use in asymptomatic patients.²⁵ The potential value of electrophysiological testing in identifying high-risk patients who may benefit from catheter ablation must be balanced against the approximately 2% risk of a major complication associated with catheter ablation. The most important factor in predicting outcome in patients with WPW syndrome was the inducibility of AVRT or AF during the baseline electrophysiological study. The presence of multiple accessory pathways was also identified as a predictor of future arrhythmic events.³⁶

SUMMARY OF MANAGEMENT

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

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