SUDDEN CARDIAC DEATH IN THE WOLFF-PARKINSON-WHITE SYNDROME

W S Teo, G J Klein, R Yee

ABSTRACT

Sudden death in the Wolff-Parkinson-White syndrome is an uncommon event but strikes in otherwise healthy children or young adults, often without much warning. They tend to occur in symptomatic but have also been reported in asymptomatic individuals. Several studies have been done profiling the sudden death survivor in the Wolff-Parkinson-White syndrome. In general, they tend to be symptomatic, have a short RR interval between preexcited beats during atrial fibrillation, have multiple pathways and may be associated with familial occurrence and Ebstein's anomaly. Several noninvasive investigations can help to assess the risk for sudden death, but the gold standard remains the use of electrophysiological testing. The management of patients with documented ventricular fibrillation or resuscitation from sudden death is unquestionably ablation of the accessory pathway but for the asymptomatic patients, it is still controversial whether they should be routinely studied by electrophysiological studies.

Keywords: Wolff-Parkinson-White syndrome, Sudden cardiac death, Electrophysiological studies

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INTRODUCTION

Sudden death in the Wolff-Parkinson-White (WPW) syndrome is rare but tragic as it mainly occurs in young and otherwise healthy children and adults with no evidence of underlying heart disease. This occurs mainly in symptomatic patients but have been rarely reported in previously asymptomatic patients. Efforts have thus been made to understand the mechanisms of arrhythmias in the WPW syndrome with electrophysiological studies to allow better assessment of the risk involved and help plan in its management.

The estimated prevalence of WPW varies from 0.1 to 3 per 1000[1-3]. The true prevalence of WPW is difficult to determine as routine electrocardiograms are not done in the general population. Subtle and intermittent preexcitation adds to the problem, as they may be missed on routine electrocardiographic screening. In view of its rarity in the general population, it is not surprising that studies of the incidence of sudden death in children and young adults[4-10] suggest that sudden death from WPW is rare. However a significant number of case reports [11-24] and long term follow up studies[2,25-30] of patients with preexcitation on the surface electrocardiogram suggest that the incidence of sudden death varies from 0% to 4% and has been estimated to occur in the order of 1 per 100 patients years of follow up[31]. With the availability of surgical and catheter ablation of the accessory pathways with minimal morbidity and mortality, this has meant patients who are at risk can be cured and the risk of sudden death extinguished.

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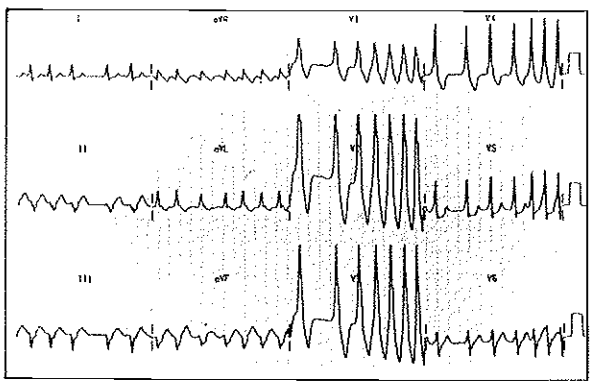
Mechanism Of Sudden Death In WPW

Sudden death in the majority of patients with WPW is believed to occur secondary to rapid conduction over the accessory pathway during atrial fibrillation. The rapidity of conduction over the accessory pathway is determined by several factors including the properties of the accessory pathway, ventricular refractoriness and the properties of the atrioventricular nodal pathway[32,33]. Concealed conduction into the accessory pathway [34] and conduction over the atrioventricular node have been postulated to be important as it has been suggested that rather than a short refractory period of the accessory pathway alone, it is lack of concealed conduction, that allows the ventricles to reach very high ventricular rates and at times to fibrillate[35]. In those patients in whom the accessory pathway can conduct rapidly and produce very fast ventricular rates (Fig 1), ventricular fibrillation (VF) can result and is the main mechanism for the sudden death in these patients[14,20]. This mechanism is believed to be contributory even in patients with underlying heart diseases eg hypertrophic cardiomyopathy[36]. Other causes for sudden death are rare and is related to underlying heart disease such as coronary artery disease and long QT syndrome[20,37].

Fig 1 - 12 Lead electrocardiogram showing rapid preexcited atrial fibrillation



Profile Of The Patient With Sudden Cardiac Death

In the Duke study[20], comparing patients who had a history of VF related to preexcitation with those without, there was a higher prevalence of both reentrant tachycardia and atrial fibrillation and multiple accessory pathways. The shortest RR

interval (SRR) between preexcited beats during atrial fibrillation was less in the group with VF (mean SRR, 180 vs 240 ms, $P < 0.0001$) as was the average R-R interval (mean average R-R, 269 vs 340 ms, $P < 0.0001$). Similarly, in the European study[38], where 26 patients with WPW and spontaneous VF were studied, it was shown that the antegrade conduction properties of the accessory pathway were a major determinant of the occurrence of VF. Other markers of risk for VF were the type of previous documented supraventricular tachycardia, documentation of more than one supraventricular tachycardia and presence of 2 or more accessory pathways. VF was the first spontaneous manifestation of the disease in 27% of the patients in this series.

Thus the profile of the patients with sudden death includes:

(i) *Symptomatic*

The majority of the patients who had history of VF were symptomatic[14,20,38]. However several case reports and follow up studies[10,16,20-22,38] suggest that some patients may present with sudden cardiac death as the first presentation of the WPW.

(ii) *Shortest RR interval between preexcited beats during atrial fibrillation < 250ms*

The major studies[20,38] found that with rare exceptions, patients with a history of VF have been found during baseline electrophysiological studies to have a SRR between preexcited beats during atrial fibrillation < 250 msec.

(iii) *Short antegrade effective refractory period (ERP) of the accessory pathway*

A long antegrade ERP of the accessory pathway (> 270 ms) makes it unlikely that fast ventricular rates during atrial fibrillation will occur. In the Duke study[20] all patients in the VF group had ERPs < 350 ms.

(iv) *Multiple accessory pathways*

An increased risk has been described in the studies from Duke[20] and the European study[38]. It has been estimated that the odds ratio for VF is increased by almost 3 times in those patients with multiple accessory pathways[39].

(v) *Familial WPW*

A recent study from Duke[3] on familial WPW suggested that there was an increased incidence of VF and sudden death. Whether this increased incidence is due to the familial occurrence of the WPW or due to the commonly associated multiple pathways, which by itself had been shown to be associated with sudden death, is uncertain.

(vi) *Ebstein's anomaly*

Patients with Ebstein's anomaly have a reported higher incidence of sudden cardiac death[40]. This may however be related to the more frequent occurrence of multiple accessory pathways and the higher incidence of spontaneous atrial flutter-fibrillation. Also the myocardium especially the right ventricle may be abnormal and more predisposed to ventricular arrhythmias.

ASSESSMENT FOR RISK OF SUDDEN DEATH

Who should be assessed?

All symptomatic patients with preexcitation pattern on the electrocardiogram should be evaluated for risk of sudden death. Wellens[41] believes that even asymptomatic patients should be evaluated, to identify those at risk of sudden death. Certain categories of asymptomatic patients such as athletes or those engaged actively in sports, airline pilots or those who operate mass transportation vehicles[42] should routinely be evaluated.

What to assess?

At present, the reference method for determination of the risk of sudden death is the deliberate induction of atrial fibrillation during invasive electrophysiological studies or by transesophageal pacing, and measuring the SRR between preexcited beats. Klein[20] found that the SRR between preexcited beats during atrial fibrillation and not the antegrade ERP of the accessory pathway correlated best with a history of VF, and the correlation of antegrade ERP of the accessory pathway and SRR between preexcited beats during atrial fibrillation remains controversial. Initial studies[30,43] in small groups of patients showed there was a close correlation between the ERP of the accessory pathway and the SRR during atrial fibrillation, and thus advocated using the antegrade ERP of the accessory pathway as an indirect guide to ventricular rates during atrial fibrillation. Two studies[20,44] reported a significant but poor correlation between these 2 variables while another[45] found no correlation between the antegrade ERP of the accessory pathway and SRR between preexcited beats during atrial fibrillation. Sharma et al[46] observed that the deviations between SRR and ERP were dependent on the initial SRR. The SRR was overestimated by the ERP when the SRR was short and underestimated when the SRR was long. Others have also noted that the refractory period of the accessory pathway failed to predict the ventricular rate during atrial fibrillation[47]. There are several theoretical reasons for the poor reliability of the antegrade ERP of the accessory pathway as a guide to SRR between preexcited beats during atrial fibrillation. These may include electrophysiologic and anatomic determinants of accessory pathway, antegrade and retrograde concealed conduction into accessory pathway and ventricular refractoriness. Furthermore during atrial fibrillation, rapid ventricular rates and changes in autonomic tone and sympathetic stimulation may affect conduction and refractoriness of the accessory pathway[44].

NONINVASIVE TESTS

As it will be impossible to do invasive test in all patients with preexcitation, various noninvasive tests have been advocated to attempt to estimate the risk. These include the electrocardiogram, 24 hour Holter monitoring, exercise stress test and pharmacologic test with antiarrhythmic drugs. In those patients in whom the noninvasive test suggest a short refractory period for the accessory pathway, invasive electrophysiological studies should then be performed. These noninvasive tests, however, correlate better with the antegrade ERP of the accessory pathway rather than the SRR during atrial fibrillation and patients, assessed noninvasively to have a long antegrade ERP, may still have rapid, hemodynamically unstable arrhythmias.

Electrocardiogram

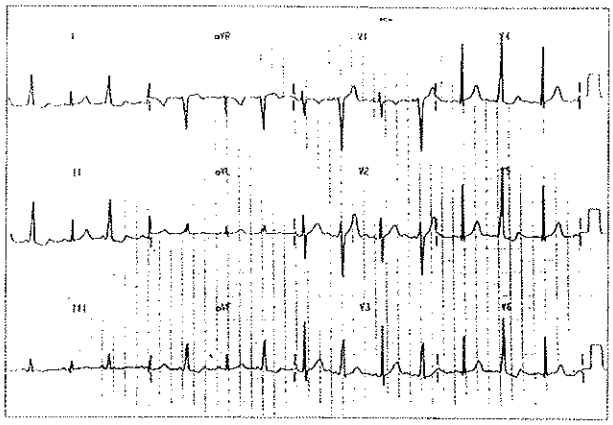
The electrocardiogram at rest or as monitored by ambulatory monitoring may demonstrate intermittent preexcitation or atrial fibrillation. Intermittent preexcitation (Fig 2) was found to suggest a long antegrade refractory period and a fairly reliable predictor of a slower ventricular response (SRR > 250 ms) during atrial fibrillation[48]. However as reported by Critelli et al[49] there were false positives. In the study by Klein[48], 4 out of the 26 patients had an SRR < 250 ms. This was attributed to pseudonormalization with apparent loss of delta wave and subtle preexcitation being still present. Another possibility was that multiple accessory pathways could interplay and cancel out the delta wave in some leads. Finally, the possibility of the influence of sympathetic tone on the accessory pathways in some patients may result in a rapid ventricular response during atrial fibrillation. The normalized QRS should be preceded by a P wave since it may be due to a His extrasystole. Also normalization of the QRS immediately after a ventricular ectopic may be due to concealed retrograde conduction into the accessory pathway and thus prevent antegrade conduction over the accessory pathway for the next beat[50].

Spontaneous atrial fibrillation

When documented,this is the best noninvasive test as the ab-

sence of ventricular preexcitation during spontaneous atrial fibrillation confirms that the antegrade refractory period of the accessory pathway is long and the patient is thus not at risk for sudden death. In those with ventricular preexcitation, the SRR interval between preexcited beats during atrial fibrillation can be measured and the risk estimated.

Fig 2 - Intermittent loss of the delta wave on the 12 lead ECG



Exercise Stress Test

Sudden and complete disappearance of preexcitation during exercise (Fig 3) points to along antegrade ERP for the accessory pathway[51,53] but false positive tests have been reported[54,55]. In order to detect loss of preexcitation, special attention should be paid to the electrocardiogram after exercise as well, where in the case of exercise induced block in the accessory pathway a sudden marked change in the electrocardiogram takes place on resumption of atrioventricular conduction over the accessory pathway. In patients with subtle preexcitation (Fig 4) at rest it can be very difficult to see the loss of preexcitation with exercise and may falsely give the impression of antegrade block in the accessory pathway. The preexcitation may also be inapparent because sympathetic stimulation during exercise will speed up atrioventricular nodal conduction and therefore diminish the degree of preexcitation seen on the electrocardiogram. Since the PR interval may shorten with exercise, a gradual diminution of preexcitation during exercise not accompanied be PR prolongation cannot be considered to represent loss of preexcitation. Multiple leads must be examined since preexcitation may appear to be lost in some leads while clearly still present in other leads.

Pharmacologic Tests

Wellens noted that the magnitude of the increase in the refractory period after intravenous class I antiarrhythmic drugs is related to the initial ERP of the accessory pathway; being relatively small if the ERP is < 270 ms and relatively great if the ERP > 270 ms and initially proposed the ajmaline[56] and

Fig 3A - Loss of preexcitation with exercise. Shows the electrocardiogram at rest with an obvious delta wave

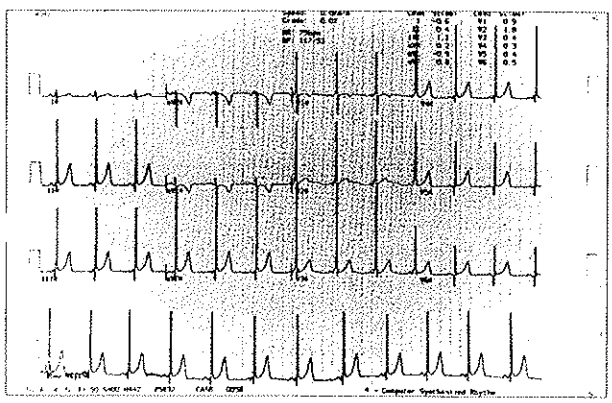


Fig 3B - Loss of preexcitation with exercise. During treadmill stress test, the delta wave is abruptly lost and associated with prolongation of the PR interval

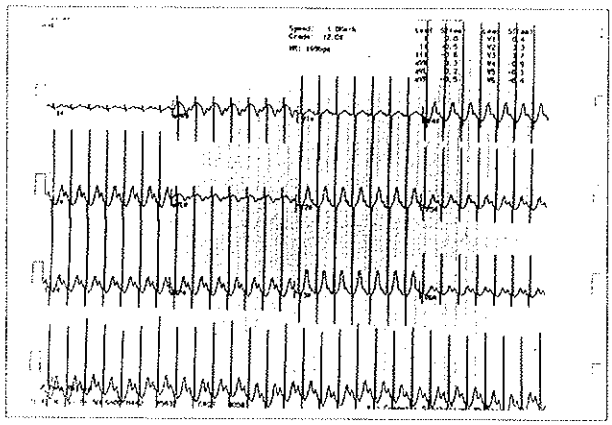


Fig 3C - Loss of preexcitation with exercise. Delta waves are seen again during recovery

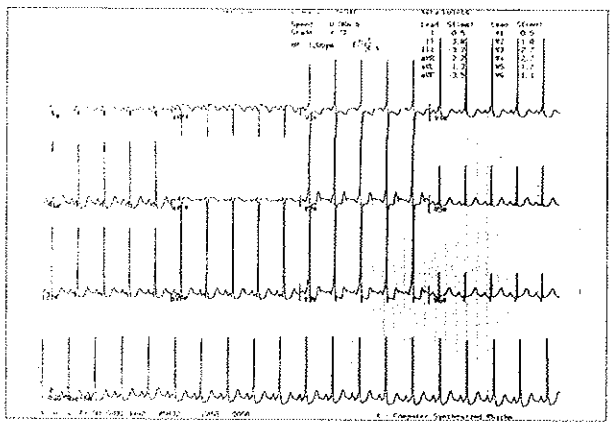
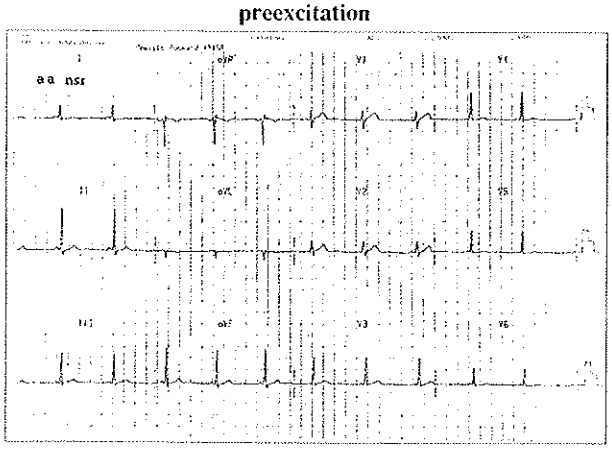


Fig 4 -12 Lead electrocardiogram showing subtle preexcitation



subsequently the procainamide[57] infusion tests. Other drugs which have been used include disopyramide[54], propafenone[58] and flecainide[59]. Failure to produce complete block in the accessory pathway by intravenous ajmaline (1 mg/kg body weight given over 3 mins or procainamide 10 mg/kg body weight over 5 mins) strongly suggest a short antegrade ERP of the accessory pathway (< 270 msec). Drug induced abolition of resting preexcitation has been thought to preclude the development of dangerously high ventricular rates during atrial fibrillation. Such tests however have limitations and cases have been reported where the preexcitation was abolished by ajmaline but during electrophysiological study the ventricular rate during atrial fibrillation was < 200 ms[60]. Other disadvantages of

these tests include reports of mortality[61] and significant adverse reactions eg bradycardia and hypotension with procainamide may occur and complete heart block transiently with ajmaline. Another problem is that patients with minimal preexcitation on the surface electrocardiogram may be impossible to evaluate. Abrupt loss of preexcitation may be easier to judge in the patient with greater degree of preexcitation.

Esophageal Pacing

Another less invasive test proposed is the use of esophageal pacing to disclose the refractory period of the accessory pathway and the SRR during the atrial fibrillation[50,62]. This technique may be valuable when other noninvasive tests are equivocal and is especially useful in children. Esophageal pacing could be used to identify risk and also for assessing response to drug therapy. Atrial pacing via the esophagus is also easier, cheaper, and less traumatic, and for many patients will provide most, if not all, the necessary information.

INVASIVE TESTS

The additional costs and specialized equipment and personnel involved makes it less available. The invasive test involves a complete electrophysiological study[42]. It gives an assessment of the functional properties of the accessory pathway and is able to determine the SRR during atrial fibrillation. These help in the decision for medical or ablative therapy by surgery or catheter ablation. Invasive tests are also required for accurate localization prior to ablative therapy.

Sensitivity, Specificity and predictive value of the tests for assessment of risk of sudden death

In general the tests for assessment of risk for sudden death have good sensitivity and negative predictive values in identifying patients at risk (based on criteria of SRR < 250 ms) but low specificity and positive predictive value[54,58]. The SRR between preexcited beats during atrial fibrillation, was the most accurate variable in the prediction of sudden death with a positive predictive value of 19%. Its value however lies more in its negative predictive value than its positive predictive value and specificity for sudden death[54]. In a study of asymptomatic WPW patients[30], 17% of asymptomatic patients with the WPW pattern were found to have a similar ventricular response (SRR ≤ 250 msec) during a baseline electrophysiological study. A more recent study of asymptomatic patients[63] found that 31% of asymptomatic patients had an SRR between preexcited beats during atrial fibrillation ≤ 250 ms. No patient died suddenly during a median follow up of 4.3 years. Thus the number of patients at risk for VF according to this criterion is much greater than the very few in this group who die.

MANAGEMENT

Patients With Documented Ventricular Fibrillation Or Resuscitated From Sudden Cardiac Death

There is no question that patients who have documented VF or resuscitation from sudden death should be treated by ablation of the accessory pathway either by surgery or catheter ablation. Drugs that can suppress the conduction properties of the accessory pathway may also be used. However drugs are usually not useful in these group of patients who almost invariably have a short effective refractory period of the accessory pathway and a short effective refractory period of the accessory pathway and a short SRR between preexcited beats during atrial fibrillation[20]. This is because it has been shown that the magnitude of increase in the refractory period of the accessory pathway after drugs is related to its initial length[64]. Also in those in whom it appears that the use of drug therapy is useful, there have been reports of reversal of the drug effect by adrenaline at doses which are equivalent to that present with exercise[65].

Feasibility Of Primary Prophylaxis In Symptomatic Patients

The patients may be separated into those with documented preexcited atrial fibrillation and those with symptomatic tachycardia only.

a. *Patients with documented preexcited atrial fibrillation and a rapid ventricular response (SRR during atrial fibrillation < 250 ms)*

   These patients have been shown to have a higher incidence of atrial vulnerability and sustained atrial fibrillation at electrophysiological studies[66]. As they have a potentially life threatening arrhythmia, primary prophylaxis with ablation by either surgery or catheter ablation is probably preferred. This approach has also been demonstrated to be safe and successful in children[24]. Medical therapy demonstrated to be effective by electrophysiological studies may also be an acceptable alternative.

b. *Patients with symptomatic tachycardia but no history of spontaneous atrial fibrillation, and an inducible SRR during atrial fibrillation < 250 ms*

   These patients have a lower risk as compared with the above category as they have not demonstrated spontaneous atrial vulnerability. The probability of atrial fibrillation developing in this group of patients is unknown but have been documented[67,68]. Arguments may be made to treat them with ablative therapy prophylactically especially if the risk of such therapy is minimal, as some of these patients have been shown to develop atrial fibrillation later in life. In one study[69] with a follow-up period of over 2 years, 29% of patients who initially presented with paroxysmal supraventricular tachycardia only, developed atrial fibrillation. Ablative therapy have been shown to decrease the incidence of atrial fibrillation in patients with WPW syndrome[70].

Primary Prophylaxis In Asymptomatic Patients?

The most difficult problem is in asymptomatic patients with an SRR < 250 ms during induced atrial fibrillation. The risk of sudden death in asymptomatic patients is extremely low although sporadic case reports attest to its occurrence in this of patients. Small prospective studies of asymptomatic patients[30,63] with the WPW pattern have failed to show an increased risk for sudden death. Thus currently there is not enough data to give firm recommendations. In certain categories of patients however, such as airline pilots or professional athletes, prophylactic ablative therapy may be considered.

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