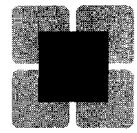

Long-term status and survival in Wolff-Parkinson-White syndrome

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■ In a long-term follow-up study of 103 patients who had Wolff-Parkinson-White syndrome, four died suddenly; two men had previously experienced paroxysmal atrial fibrillation and two women, both elderly, had paroxysmal tachyarrhythmias, one documented as atrial paroxysmal tachycardia on one occasion. Sixty-six (64%) of the patients had histories of paroxysmal tachyarrhythmias. Of 88 survivors, 10 of the 35 (29%) who did not have a history of arrhythmias on entry developed tachyarrhythmias, and 20 of 33 (38%) who did have symptomatic arrhythmias on entry had no symptoms at last follow-up. Thirteen (15%) of the survivors had frequent attacks of symptomatic arrhythmias.

□INDEX TERM: WOLFF-PARKINSON-WHITE SYNDROME □CLEVE CLIN J MED 1989; 56:601–606

REFERRAL BIAS is a problem in clinical studies of any disease. If effective treatment becomes available, referral patterns tend to change. Selection of patients who had Wolff-Parkinson-White syndrome (WPW) diagnosed during a period in which effective medical and surgical treatment was not available might more nearly represent the spectrum of the condition than a group selected in recent years.

MATERIALS AND METHODS

Between January 1, 1962, and June 30, 1970, a total of 103 patients at The Cleveland Clinic Foundation had electrocardiograms (ECG) that were diagnosed as WPW; their records were reviewed. ECG recording was done with high-fidelity photographic machines (Sanborn Twin Beam). All had delta waves, but for this study, only those whose QRS duration exceeded 0.10 seconds were included. Clinical data were recorded independently of survival information. The intent was to have a 10-year minimum follow-up for all survivors; this was accomplished from the standpoint of survival, though specific information on symptomatic status could not be determined for a few survivors. The mean duration of follow-up was 145 months (12 years, 1 month). The patient, patient's family, or referring physician was contacted by letter or telephone, and hospital records or death certificates were obtained when needed. Survival was calculated by the actuarial method.[1]

RESULTS

There were 72 males (mean age, 38.2 years) and 31 females (mean age, 38.1 years) in the study group. Two were less than one year old, three were between seven and 11 years old, and seven were teenagers. Thirteen, 28, 28, 16, and 6 were in the third, fourth, fifth, sixth, and seventh decades, respectively. The oldest patient

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TABLE 1
FREQUENCY OF ATTACKS OF TACHYCARDIA

Interval	No. of patients
Unknown	6
1–3 total	11
>3 mo–12 mo	15
>1 mo–3 mo	13
<1 mo	7
<1 wk	5
Daily	3
Irregular	6

Unknown = not stated or patient unable to estimate; *1–3 total* = total number of attacks recalled by patient.
Thirty-seven patients denied having had attacks.

TABLE 2
DOCUMENTED ARRHYTHMIAS

Arrhythmia	No. of patients
Atrial premature contraction	2
Atrial paroxysmal tachycardia	5
only	3
with ventricular premature contraction	1
with flutter	1
Atrial fibrillation	6*
Junctional rhythm	1
Mobitz II	1
Ventricular premature contraction	9
Ventricular tachycardia	1
TOTAL	25

*One additional patient with history of atrial fibrillation

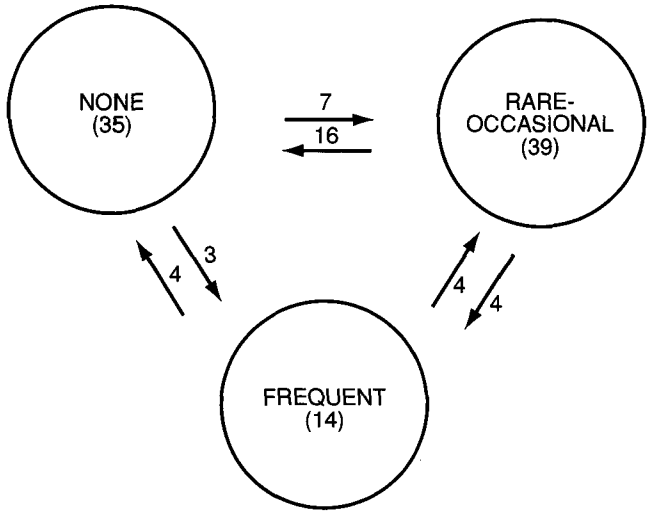

FIGURE 1. Frequency of symptomatic paroxysmal arrhythmias in 88 survivors whose status was known at both entry and follow-up. *Rare-occasional* means the attacks were less than once monthly. *Frequent* attacks were once monthly or more. The number in parentheses indicates the frequency of arrhythmia on entry. Numbers adjacent to arrows represent the patients whose frequency of attacks changed between baseline and follow-up.

was age 72 when ECG was performed. *Table 1* shows the frequency of attacks of arrhythmia by estimation of the patient, and *Table 2* shows the type of arrhythmias. The maximum duration of attacks was less than five minutes for 8 patients, five to 15 minutes for 9, more than 15 minutes to an hour for 13, and more than an hour for 22. Fourteen patients did not state the duration, and two were unable to estimate the duration. The ages by decades at onset of paroxysmal arrhythmia for 66 patients were first decade, 6 patients; second, 14; third, 18; fourth, 8; fifth, 7; sixth, 3; and seventh, 1. The age was not stated or recalled by the patient in eight cases. The mean age at onset was 27 years.

The chief complaint was related to paroxysmal tachycardia in 36 patients, dyspnea or chest pain in 36, and was noncardiac in 29. Two patients had no complaints, and one was referred after discovery of a murmur.

Type A configuration of the ECG was noted in 39 patients, type B in 60, and one had both types A and B according to various ECG records. Three could not be classified because of transient ECG appearance. ECG evidence of WPW was transient during recording of 13 patients, absent in some ECG records of 20 patients, and seven of these 20 patients had transient evidence of WPW both during recording and in serial records. The QRS duration was at least 0.12 seconds in 79 patients and of lesser duration in 24. Wide Q waves were present in aVL in 20 patients, in aVF in 23, and V_6 in two, both of whom had similar Q waves in aVL.

Paroxysmal arrhythmia had been experienced by 22 of 39 patients (56%) with type A WPW, and 41 of 60 patients (68%) with type B ($P>.05$). Frequent attacks of paroxysmal arrhythmia (more than one per week) were associated with type A configuration in two patients and type B in six. Seven of these eight had QRS durations of at least 0.12 seconds; the eighth was less than that. These differences were not statistically significant. Four of the five patients who had documented atrial fibrillation had type B configuration (NS).

Organic heart disease was found in 21 patients. Four had congenital cardiovascular disease (diverticulum of the left ventricle, mild aortic stenosis, double aortic arch, and coarctation of the aorta, respectively). Four patients had valvular disease, 11 had coronary disease

TABLE 3
PATIENT CHARACTERISTICS IN UNEXPLAINED SUDDEN DEATHS

Characteristic	Patient 1	2	3	4
Age at diagnosis	28	44	60	67
Age at death	32	56	70	78
Sex	M	M	F	F
Interval between attacks	<12 mo	<3 mo	<1 mo	Irregular
Duration of attacks (max.)	>1 hr	>1 hr	15 min	<1 min
Documented arrhythmias	Atrial fibrillation	Atrial fibrillation	Atrial paroxysmal tachycardia; ventricular premature contraction	None
Circumstances of death	Dead in bed	Instantaneous	Sudden, unwitnessed	Sudden, unwitnessed
Remarks	"Arrest" once, probably ventricular fibrillation		Hypertension	Hypertensive heart disease; angina

(clinically or as shown arteriographically), and 2 had both valvular and coronary disease. One patient had essential hypertension without apparent heart disease.

Cardiac catheterization was done in 28 patients. Indications for catheterization were pain or dyspnea in 22 patients, suspected congenital anomaly in four, and a previous diagnoses of heart disease based on an abnormal stress test in one and alleged cardiac enlargement in the other. Six of the 28 patients had coronary narrowing, but it was mild in two. In one, an ergonovine test resulted in severe narrowing. One each had diverticulum of the left ventricle, mild aortic stenosis, and double aortic arch. Nineteen patients had normal catheterization results.

Figure 1 shows the frequency of attacks of arrhythmia as reported on entry and on follow-up for the 88 survivors whose status could be determined. Ten patients noted arrhythmia after the original diagnosis of WPW, but in 20, attacks ceased.

Four patients underwent cardiac operations (three for coronary disease and one for mitral valvular disease). Thirteen patients died; five deaths were noncardiac, two died of coronary artery disease (one postoperatively), one died of cardiomyopathy, and one died after operation for combined aortic valvular and coronary disease. The remaining four patients (two men and two women) died instantaneously or were found dead (*Table 3*). The two males were known to have continued to have attacks of arrhythmia after the original diagnosis. These two men were among the six patients who had documented atrial fibrillation (one additional patient had a history of atrial fibrillation).

Mortality was higher in patients who had documented atrial fibrillation compared with those who had other documented arrhythmias; the difference was not statistically significant, although numbers of patients were small. The difference in mortality of those who had histories of atrial fibrillation compared with those who had histories of other arrhythmias is significant ($P<.01$). History of atrial fibrillation influences survival adversely compared with no history ($P<.001$) of atrial fibrillation.

All four patients who died had experienced paroxysmal tachyarrhythmias. Three of the four who died suddenly had type B WPW and one had type A. Both men

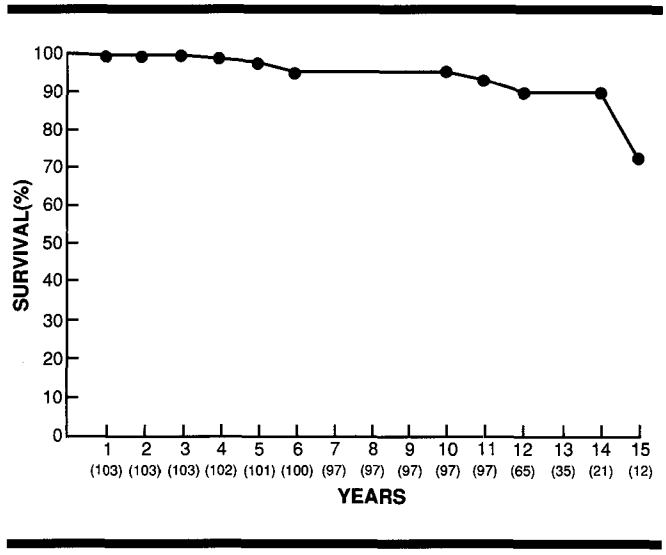

FIGURE 2. Actuarial survival curve for 103 patients. The numbers in parentheses indicate the patients alive on entry to respective years. Only one patient entered the 18th year, and that patient died.

had type B. One of the men had a minimum R-R interval of 0.36 seconds during atrial fibrillation, and the other had a 0.24-second interval. *Figure 2* shows an actuarial survival curve for 103 patients. Deaths occurred at 1, 44, 52, 62, 63, 67, 122, 131, 138, 143, 171, 178, and 211 months.

DISCUSSION

Long-term survival of 50 patients with WPW studied by Orinius[1] was similar to that of the general population of Sweden, after correction for age and sex. Only one patient died during an arrhythmic episode—a 32-year-old woman diagnosed as having myocarditis.

Mortensen et al[2] studied a large group of patients with WPW, and Flensted-Jensen[3] restudied 45 of these patients and added two more. All 47 were followed until death or a minimum period of 22 years. Nineteen died between one and 37 years after ECG-based diagnosis. The age at death ranged from 28 to 86 years. Mortality was significantly higher ($P<.05$) in the group compared to expected mortality in the Danish general population matched for age, sex, and year. Difference in survival was more striking in patients less than 50 years old in comparison with expected mortality ($P=.005$). Two of the six younger patients died accidentally. Two had myocardial disease (myocarditis and biventricular hypertrophy at autopsy). One died suddenly during an episode of atrial fibrillation, with a ventricular rate of 240 beats per minute. The other patient had a 2:1 atrioventricular block and syncope associated with familial cardiomyopathy. The latter patient had episodes of pronounced sinus bradycardia. Both of the remaining deaths occurred in patients who had only occasional but very prolonged episodes of paroxysmal supraventricular tachycardia; terminal attacks lasted eight hours and several weeks, respectively. Postmortem examination was done in neither case. Three of the six deaths were due to tachyarrhythmias, and a fourth patient may have died due to sinus arrest. Deaths in patients at least 50 years old were not thought to be related to arrhythmia except for two (aged 80 and 85) whose deaths were recorded as being due to "paresis cordis." One had heart failure but no history of paroxysmal arrhythmia, and the other had experienced paroxysmal tachycardia, but the circumstances at death were not known. These two patients were excluded from survival analysis for statistical reasons.

This study indicated that those with WPW died due to prolonged paroxysmal tachycardia as well as atrial fibrillation. Survival was affected for patients in the younger age group. No sudden deaths occurred due to prolonged arrhythmic episodes. Only one sudden death involved a young person. Both men who died had paroxysmal atrial fibrillation. The two elderly women could have died because of attacks of arrhythmia. Paroxysmal atrial fibrillation is encountered with increasing frequency as age advances.

Berkman and Lamble[4] reported survival of 128 military men with WPW who were followed five to 28 years; 48% were followed for more than 20 years. Paroxysmal tachycardia was documented in 17 at the time of the original diagnosis of WPW and was documented later in two additional men. Three of the 128 men died, two accidentally and one under unknown circumstances. Military service is an automatic selection process biased toward asymptomatic or minimally symptomatic individuals. The report, however, indicated that the prognosis was good for the patient population studied.

Sherf and Neufeld[5] collected and summarized reports of 717 cases of WPW, including 215 of their own patients. The subjects were followed incompletely in many instances; the follow-up period varied from 0 to 28 years. Death was ascribed to paroxysmal arrhythmias in nine (1.25%) and to questionable causes in seven cases; another had tetralogy of Fallot. Three other deaths (0.4%) were sudden. This review shows a lower incidence of death due to arrhythmias or sudden death than the report of Flensted-Jensen or our study.

Gallagher et al[6] studied 163 patients with WPW and followed 73 of those who were treated medically. The duration of follow-up was not indicated. There were six deaths, five of which were attributed to cardiac causes. One patient died after administration of digoxin during her only arrhythmic episode (atrial fibrillation). The other four died suddenly; two had paroxysmal atrial fibrillation, one had reciprocating tachycardia with a rate of 300 beats per minute, and one had a previously resected coarctation of the aorta and prosthetic aortic valve.

Curry and Krikler[7] reported one sudden death in 10 patients who had both WPW and atrial fibrillation. They pointed out the possible selection of patients as a result of death in the first attack of atrial fibrillation.

Long-term follow-up studies of infants and children with WPW have been reported by Giardina et al[8] and Mantakas et al[9] with groups of 62 and 20 patients, respectively. Three died of tachyarrhythmias; all had tetralogy of Fallot. Two deaths occurred postoperatively. All others survived, except for some deaths ascribed to associated congenital heart disease without arrhythmia terminally.

Though systematic follow-up studies of large groups of patients with WPW have been few, the risk of the condition has long been recognized. Sudden deaths have been reported since Wilson's warning in 1938; one of his patients died during an attack of paroxysmal arrhythmia.[10] Soon afterwards, Öhnell[11] gave a detailed account of a woman who was known to have had paroxysmal atrial fibrillation associated with WPW. Death was sudden in this patient, and later, another of his patients died during paroxysmal tachycardia.[12] Kimball and Burch[13] collected six reported cases and added two of their own in 1947. Sherf and Neufeld[5] reported 43 cardiac deaths of patients with WPW (29 sudden deaths and 14 deaths due to congestive failure or shock). Organic heart disease had been diagnosed in some of these patients. Gallagher et al,[6] Dreifus et al,[14,15] and Klein et al[16] have stressed atrial fibrillation as a cause of morbidity and mortality. They have demonstrated that ventricular fibrillation is relatively frequent in those who have paroxysmal atrial fibrillation. Because of their interest in the problems presented by WPW, it is possible that they have a larger percentage of referral patients who have atrial fibrillation than would be characteristic of many institutions. Dreifus et al[14] have also reported sinus bradycardia and sinus arrest in some patients with WPW and believed these were due to disease in the sinus node. Camm et al[17] reported a patient who had syncope associated with WPW; sinus pauses as long as 2.5 seconds were noted during a 24-hour recording. Atrial fibrillation was induced electrically and ventricular asystolic periods lasting as long as 11 seconds were recorded.

Klein et al[16] studied 31 patients with WPW who had had one or more attacks of ventricular fibrillation. Six had a cause for ventricular fibrillation independent of WPW. All of the 25 other patients had paroxysmal atrial fibrillation with rapid ventricular response. The combination of reciprocating tachycardia and atrial fibrillation at various times in the same patient was particularly prevalent (56%) in patients who experienced ventricular fibrillation. Six received digitalis for treatment of atrial fibrillation within 10 hours of the onset of ventricular fibrillation. Two children and one adolescent had ventricular fibrillation as the initial symptomatic arrhythmia. All but one patient had WPW as shown on ECG taken during sinus rhythm. The minimum R-R interval during atrial fibrillation was shorter than in a control group without previous ventricular fibrillation. Multiple anomalous pathways predisposed to ventricular fibrillation.

Cardiac death of those with WPW, when not due to associated cardiac disease, is usually caused by ventricular fibrillation; this arrhythmia is most likely to be encountered in patients who have had atrial fibrillation, especially if the patient has also had attacks of reciprocating tachycardia. Rapid ventricular rates during atrial fibrillation and multiple accessory pathways increase the predisposition to ventricular fibrillation. Digoxin may predispose to ventricular fibrillation occasionally in those who have rapid ventricular rates. Ventricular fibrillation may be the initial symptomatic arrhythmia rarely, perhaps only in children and adolescents. It is likely that some deaths are due to ventricular asystole and a small number succumb to prolonged attacks of supraventricular paroxysmal tachycardia. In general, the cardiac prognosis is excellent for those who have no associated cardiac disease, no paroxysmal tachycardia, only paroxysmal supraventricular tachycardia, relatively slow ventricular rates during attacks of atrial fibrillation, single anomalous pathways, and transient WPW during sinus rhythm.

Orinius[1] re-examined 31 long-term survivors of WPW who had experienced paroxysmal arrhythmias. The attacks decreased in frequency in 17, increased in 5, and 4 noted no change; 5 were uncertain or the information was not available. Eleven who did not have paroxysmal arrhythmias at the time of original diagnosis developed attacks subsequently. These findings do not differ greatly from our study.

Flensted-Jensen[3] found that surviving patients reporting an increase or decrease in frequency of attacks were about equal in number. Both Giardina et al[8] and Mantakas et al[9] reported disappearance of arrhythmias with time in most infants and children with paroxysmal arrhythmias.

The natural history of WPW syndrome cannot be defined because of the introduction of surgical division of accessory bundles for certain subsets known to be at high risk. Documentation of clinical status over long periods, Holter recordings, and electrophysiologic testing should define more precisely subsets susceptible to frequent or serious cardiac arrhythmias. It appears that cardiac death is rare in patients who have had no arrhythmia or uncomplicated supraventricular paroxysmal tachycardia. However, ventricular fibrillation may occur with the first symptomatic arrhythmic episode, at least in children and adolescents. Because atrial fibrillation is an age-related arrhythmia, it is possible that older patients could die during a first attack.

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