RESEARCH LETTER

**Demographic and Clinical Features of** **Sudden Cardiac Death in Pre-excitation and Wolff-Parkinson-White: Report of 19 Cases from a Large Pathology Registry.**

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The prevalence of the Wolff-Parkinson-White (WPW) ECG pattern is estimated between 0.1% and 0.3%1. The risk of malignant arrhythmias in asymptomatic individuals is low and ablation of the accessory pathway can abolish the risk of sudden cardiac death (SCD)2. Autopsy reports on sudden cardiac death (SCD) victims with a previously recognized WPW ECG pattern are anecdotal3. The aim of the study was to describe the clinical and pathological features of SCD cases victims with a pre-morbid diagnosis of WPW.

The Cardiac Risk in the Young (CRY) center for cardiac pathology at St. George’s University of London receives over 400 cases of SCD annually. We reviewed a database of 3684 consecutive cases of SCDs referred to our institute between 1994 and 2014 and identified a subgroup of 19 (0.5%) cases with a recognized WPW ECG pattern before death. Clinical information was obtained from referring coroners that were asked to complete a questionnaire inquiring about the demographics of the deceased, past medical history, family history, cardiac symptoms and circumstances of death. All subjects underwent detailed autopsy evaluation of the heart by an expert cardiac pathologist including histological analysis conducted The heart weight was recorded in grams and ventricular wall thickness and internal cavity dimensions were measured at mid-ventricular level excluding the papillary muscles and fat. A minimum of 10 blocks of tissue are taken for histological analysis as reported previously. Sections of myocardium were fixed in formalin, embedded in paraffin and stained with haematoxylin and eosin as well as elastic Van Gieson stain to highlight myocardial fibrosis. SCD was defined as a death within 12 hours of apparent wellbeing. Results are expressed as mean ± standard deviation (SD) for continuous variables or as number of cases and percentage for categorical variables.

The vast majority of patients were men (n=16, 84%) and white Europeans (n=17; 89%). The mean age at death was 31±15 years. Five cases (26%) were asymptomatic. Of the 14 symptomatic patients, 13 (68%) had reported palpitation, 1 (5%) experienced syncope and 2 had documented supraventricular tachycardia at hospital admission. Five individuals (26%) had a previous ablation, 4 of which were associated with successful resolution of the WPW pattern on the ECG. In the majority of cases (n=15; 79%) SCD occurred at rest. The mean heart weight was 408 ± 105 g. In 10 patients (53%) the autopsy also revealed a normal heart, 5 cases showed definitive cardiac pathology (4 cases of hypertrophic cardiomyopathy and 1 case of cardiac sarcoid), and 4 cases demonstrated autopsy findings of uncertain significance 2 cases of idiopathic left ventricular hypertrophy, 1 with idiopathic fibrosis, and 1 with an enlarged left ventricle). Of the 5 asymptomatic patients, the post-mortem revealed hypertrophic cardiomyopathy in 3 and a normal heart in 2 cases. Two out of the four patients with HCM showed myocardial fibrosis in the interventricular septum. All deaths attributed to HCM were characterized by left ventricular hypertrophy associated with myocyte disarray. None showed intracellular vacuolization characteristic of glycogen storage diseases associated with pre-excitation. None of the cases in this cohort showed significant valvular abnormalities. Among patients who underwent ablation, 3 showed a normal heart and 2 showed idiopathic left ventricular hypertrophy. Based on our pathologic series, the proportion of WPW cases with structural abnormalities at autopsy was similar to cases without the reported WPW ECG pattern (n=1870;51%).

In conclusion our findings suggest that (1) a proportion cases with the WPW ECG pattern may die suddenly in the absence of symptoms, (2) many die at rest, (3) deaths f may occur in the fourth decade and (4) substantial proportion of individuals have concomitant pathology that may contribute to atrial fibrillation. Previous prospective studies have showed that the presence of symptoms is not useful in the risk stratification of WPW patients2,4,5. In addition, accessory pathway ablation did not seem to eliminate the risk of SCD, since 5 of the SCD victims were subjected to an ablation procedure. This is possibly due to the presence of multiple pathways or of other co-existing substrates for fatal arrhythmias. Finally, pre-excitation was associated with additional structural abnormalities in almost 50% of cases, underscoring the importance of performing baseline echocardiography and possibly cardiovascular magnetic resonance in all individuals with WPW and suggesting that the combination of pre-excitation with additional cardiac pathology may render individuals at higher risk of SCD.

Our study has some limitations. Although all the clinical information relating to the deceased was gathered in a meticulous fashion, only a small percentage of the entire cohort in our SCD registry was investigated with an ECG, therefore the true prevalence of SCD from WPW cannot be ascertained from this study. Our data suggest that WPW causes death in asymptomatic individuals and deaths may occur following ablation however this study cannot ascertain the prevalence of fatal events in these circumstances because our information relied on secondary reports and we did not have adequate details about the electrophysiological studies, including the refractory period or the number of pathways respectively. Finally the cardiac autopsy did not include a standardized demonstration of accessory pathways at the histological assessment.

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**Table. Characteristics of the study population**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Age** | **Sex** | **Ethnicity** | **Symptoms and medical history** | **Circumstances of death** | **HW** | **MWT** | **LV fibrosis** | **RV fibrosis** | **PM diagnosis** |
| ASYMPTOMATIC | | | | | | | | | |
| 7 | M | White | Known WPW, | Unknown | 200 |  | No | No | Normal heart |
| 48 | M | White | Known WPW, | Died at rest | 526 | 20 | Yes | No | HCM, mild CAD, myocardial fibrosis |
| 50 | F | White | Known WPW, | Died during sleep | 384 | 18 | No | No | HCM |
| 26 | M | White | Known WPW, athlete, | Died during exertion | 510 | 20 | Yes | No | HCM, myocardial fibrosis |
| 18 | M | White | Known WPW, asymptomatic | Died at rest | 390 | 19 | No | No | Normal heart |
| SYMPTOMATIC | | | | | | | | | |
| 20 | M | Indian | Known WPW, palpitations, planned ablation, on flecainide | Died at rest | 237 | 9 | No | No | Normal heart |
| 26 | M | White | Recent diagnosis of WPW, palpitations, no medications | Died at rest | 361 | 16 | No | No | Normal heart |
| 20 | M | White | Known WPW, palpitations, symptom free for 11 years, recent palpitations, no medications | Died at rest | 444 | 14 | No | No | Normal heart |
| 20 | F | White | Known WPW, palpitations, no medications | Died at rest | 311 |  | No | No | Normal heart |
| 46 | M | Black | Known WPW, palpitations, currently under evaluation, FH of SD over the age of 60, on a beta-blocker | Died at rest | 474 | 16 | No | No | Cardiac sarcoid |
| 33 | M | White | Known WPW, palpitations, no medications | Died at rest | 532 | 21 | No | No | Enlarged left ventricle |
| 16 | M | White | Known WPW, palpitations, no meds | Died at rest | 366 | 25 | No | No | HCM |
| 36 | M | White | Known WPW, syncopal episode, meds unknown | Died at rest | 498 |  | Yes | No | Idiopathic fibrosis |
| 55 | F | White | Known WPW, palpitations, on betablocker | Died at rest | 385 | 13 | No | No | Normal heart |
| PREVIOUS ABLATION | | | | | | | | | |
| 28 | M | White | Known WPW, palpitations, previous attempted ablation | Died at sleep | 316 | 19 | No | No | Mild LVH, mild CAD |
| 27 | M | White | Known WPW, previous ablation | Died during exertion | 426 | 21 | No | No | Normal heart |
| 24 | M | White | Known WPW, previous ablation | Died at rest | 578 |  | No | No | ILVH |
| 65 | M | White | Known WPW, palpitations, previous ablation | Died at rest | 486 |  | No | No | Normal heart |
| 28 | M | White | Known WPW, palpitations, previous ablation | Died during sleep | 302 | 12 | No | No | Normal heart |

**Abbreviations: CAD : coronary artery disease ;** F: female, FH: family history, HCM: hypertrophic cardiomyopathy, HW: heart weight; ILVH: idiopathic left ventricular hypertrophy; LV: left ventricle; M: male; MWT: maximal wall thickness; PM: post-mortem, RV: right ventricle, SD: sudden death.