Gender Differences in Clinical and Electrophysiological Characteristics of Patients with Wolff-Parkinson-White Syndrome: Assiut University Heart Hospital Experience

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Abstract:

Background: Wolf-Parkinson-white (WPW) syndrome is a form of ventricular preexcitation syndrome where the ventricle is preexcited by one or more accessory pathways (AP). Patients with WPW syndrome are at risk for the development of preexcited atrial fibrillation, ventricular fibrillation, and sudden cardiac arrest.

Objectives: Our purpose was to investigate and obtain insight into the possible relation between the patient's gender and the clinical and electrophysiological characteristics, and to look for possible differences between males and females regarding the duration between the first attack of tachypalpitation and referral for ablation.

Patients and Methods: Our study included 73 patients who underwent successful catheter ablation for a manifest AP. A detailed history was obtained, including (age, first tachycardia attack, and associated symptoms). An electrophysiological study and ablation of the accessory pathway were done. Electrophysiological parameters, including antegrade effective refractory period (AERP) and retrograde effective refractory period of the accessory pathway (RERP), were determined, and the site of successful ablation of the AP was recorded.

Results: Twenty-six patients (35%) were females, and 47 patients (64%) were males (AP is almost twice as common in males as in females). The mean age of females versus males at the time of ablation was (34.73 ± 9.64) VS (31.87 ± 13.06). Females were referred to ablation later than males, as seen from the time passed since 1st attack of tachypalpitation till the ablation procedure (50.69 ± 36.07 months) for females versus (31.83 ± 23.55 months) for males, P=0.033.

Conclusions: Female patients' diagnosis and referral to catheter ablation are delayed compared to equally affected male patients, with a longer duration passing from the first episode of tachypalpitation till the ablation procedure.

There are gender differences in sites of APs; females more commonly had right-sided APs.

Keywords: Accessory pathway, gender differences, WPW.

Introduction:

Wolf-Parkinson-White (WPW) syndrome is a form of ventricular preexcitation syndrome where one or more accessory pathways (AP) connect the atria and the ventricles, bypassing the normal AV conducting system and resulting in premature ventricular depolarization (1).

Most of these APs lack the decremental property of conduction that is present in the normal AV conducting system, putting patients with this syndrome at risk for developing malignant arrhythmia or even sudden cardiac death (2, 3).

There are conflicting reports about the sex distribution of patients with WPW syndrome. For instance, WPW is thought to be determined by the autosomal dominant form of inheritance (4), and epidemiological studies have not shown a male preponderance of pre-excitation in infants (5, 6). However, in the adult population, males are twice as likely as females to have pre-excitation, resulting in the characteristic ECG pattern of WPW syndrome (short PR interval, Delta wave, and wide QRS complex) being seen more often in men (7). In adult patients with symptomatic WPW referred for electrophysiological testing, a male preponderance has also been noted. It is unclear what factors underlie the differences in the sex distribution among WPW patients (8).

Patients and Methods

Study Population

Seventy-three patients with WPW syndrome were referred for management of tachycardia and underwent electrophysiological study and catheter ablation of manifest AP. Patients with structural or congenital heart disease, previous failed ablation, or multiple APs were excluded from the study.

Ethical Considerations

The study protocol was approved by the ethical review committee of the Faculty of Medicine, Assiut University, with approval number (IRB 17100758). This study complies with the Declaration of Helsinki. Informed consent was obtained from all patients, clarifying all study steps.

Method

Seventy-three patients with WPW syndrome who underwent successful ablation of a single AP in Assuit University Heart Hospital were subjected to detailed history taking, including age, symptoms, frequency, time from first attack to referral for the ablation, and an ECG was obtained. All patients underwent a standard electrophysiological study to determine AP antegrade effective refractory period (AERP) and retrograde effective refractory period (RERP), arrhythmia induction, and ablation of AP.

Statistical Analysis

SPSS (Statistical Package for the Social Sciences) for Windows version 24 (IBM and Armonk, New York) was used to verify, code, and analyze the data. Descriptive statistics were expressed as Means, standard deviations, medians, interquartile ranges (IQR), frequency, and percentages. The normality of continuous variables was tested using the appropriate Kolmogorov–Smirnov /Shapiro–Wilk test. A significant p-value was considered when it was <0.05.

Results

Seventy-three patients were enrolled in our study; 47 were males (64.3%), and 26 were females (35.6%). The mean age of male patients was (31.87 ± 13.06) versus (34.73 ± 9.64) for female patients. Dyspnea was the most commonly reported symptom with tachypalpitation by female patients, reported by 46.2% of them versus 23.4% of male patients, P= 0.045. Female patients had a longer duration passing from the 1st attack of

tachycardia till referral for catheter ablation, with a mean of (50.69 ± 36.07 months) versus (31.83 ± 23.55 months) for male patients.

P =0.033. Both groups had almost the same frequency of tachypalpitation attacks in the last month before ablation **(Table 1)**

Electrophysiological Differences

Females had a higher baseline heart rate than males (83.58 ± 15.05 beat/min) versus (75.72 ± 13.84 beat /min), *P* = 0.027 (**Table 2).**

EP study:

Both males and females had the same risk regarding APAERP (242.80 ± 36.77 VS 245.77 ± 38.07 msec), *P* = 0.760, and APEERP (238.30 ± 36.97 VS 234.23 ± 30.09 msec), *P* = 0.633.

Regarding the type of induced tachycardia, preexcited AF occurred more frequently in males (31.9% of males had preexcited AF versus 7.7% of females, *P* = 0.019) (**Table 2**).

Site of ablation:

The successful ablation sites of APs are shown in **Table 3)**. The most common site of AP was the posteroseptal tricuspid annulus (PSTA) (30.1% of patients), followed by the left lateral site (LL) (24.6% of cases). There were no gender differences regarding the site of AP except for the right posterior and posterolateral sites, which were all females, *P* = 0.043 (**Table 3).**

Table 1: Clinical differences between males and females

Characteristic	**Male**, N = 47	**Female**, N = 26	**p-value**^
Age	31.87 ± 13.06	34.73 ± 9.64	0.185
Symptoms			
Palpitation	47 (100%)	25 (96%)	0.356
Dyspnea	11 (23%)	12 (46%)	**0.045***
Syncope	2 (4%)	4 (15%)	0.178
Presyncope	2 (4%)	1 (4%)	0.999
Chest pain	9 (19%)	2 (8%)	0.308
Dizziness	10 (21%)	5 (19%)	0.836
Onset of 1st attack (months)	31.83 ± 23.55	50.69 ± 36.07	**0.034***
Frequency in the last month	3.74 ± 3.23	3.04 ± 1.66	0.806

Table 2: Electrophysiological differences between males and females

Characteristic	**Male**, N = 47	**Female**, N = 26	**p-value**^
Baseline HR	75.72±13.84	83.58 ± 15.05	**0.027***
Refractory periods			
AERP	242.80±36.77	245.77 ± 38.07	0.760
RERP	238.30±36.97	234.23 ± 30.09	0.622
Type of induced tachycardia			
Orthodromic AVRT	33 (70%)	19 (73%)	0.796
Preexcited AF	15 (31.9%)	2 (7.7%)	**0.019***
Antidromic AVRT	0 (0%)	2 (8%)	0.124
None	5 (11%)	5 (19%)	0.314

HR= heart rate, **AERP**=antegrade effective refractory period, **RERP**=retrograde effective refractory period, **AVRT**= atrioventricular reentrant tachycardia, **AF**= atrial fibrillation.

Table 3: Sites of AP in males and females

Ablation site	**Male (n= 47)**		**Female (n= 26)**		**p-value**^
	No.	**%**	**No.**	**%**	
LAL	2	4.3%	1	3.8%	1.000
LL	14	29.8%	4	15.4%	0.172
LP	6	12.8%	2	7.7%	0.703
LPL	3	6.4%	0	0.0%	0.548
PSMA	1	2.1%	3	11.5%	0.126
RP	0	0.0%	3	11.5%	0.043*
RPL	0	0.0%	2	7.7%	0.124
RL	2	4.3%	0	0.0%	0.535
PSTA	14	29.8%	8	30.8%	0.930
CS	3	6.4%	1	3.8%	1.000
NH	2	4.3%	2	7.7%	0.613

CS=coronary sinus, **LAL**=left antrolateral, **LL**= left lateral **LP**=left posterior, **LPL**=left posterolateral, **NH**= nodohisian, **PSMA**= posteroseptal mitral annulus, **PSTA**=posteroseptal tricuspid annulus, **RL**=right lateral, **RP**=right posterior , **RPL**=right posterolateral

Discussion:

In our study, 64.4% were males, and 35.6% were females; such adult male predominance was also observed in many previous studies (5, 7-10); male predominance was also noted in sporadic forms but not in cases with familial forms of the syndrome(11, 12). Such predominance was reported in multiple previous studies (13-17). Whether this male predominance has a genetic, developmental, hormonal, or structural basis is unknown.

The mean age of female patients was three years older than that of male patients;

such a difference is usually due to delayed referral

of female patients to ablation procedures, and this was also shown with the longer duration
since they first experienced palpitation till referral time. Previous studies demonstrated that females experience tachycardia at younger ages than males. Such observation was justified by the ability of females to accurately recoil remote episodes or have a heightened perception of tachycardia-related symptoms(18). This is consistent with our results despite our study's higher mean age of females, as our female patients reported first episodes of tachycardia sooner than male patients. Delayed referral of female patients for catheter ablation is because female patients usually have their symptoms attributed to panic attacks, anxiety, or stress, delaying their diagnosis and management; such an observation was also confirmed in other observational studies (19). This observation may explain such male predominance in adult patients with WPW syndrome and its absence in children(5).

There were no substantial differences in intraprocedural characteristics between males and females except for male predominance regarding the induction of preexcited AF (20); such observation translates into a higher risk despite having almost the same APAERP and APREP(21). Because sudden death is usually a consequence of atrial fibrillation with rapid conduction across AP, resulting in ventricular fibrillation, males are at higher risk for such catastrophic events (22, 23). Although preexcited AF is more common in males, female patients are also at risk for sudden death as APERP is < 250 m (234.23±30.09).

Regarding the site of AP: Patients with RP and RPS APs were all females; such observation was also noted in previous studies (24). Previous studies have shown that patients with a right-sided AP had a lower inducibility of AVRT and a relatively long RERP over the AP. This allowed only relatively late PVCs to be conducted

retrogradely over the AP to the atria, which might explain the lower rate of inducibility of AF in these patients, translating into a relatively lower risk of AP (12, 25). It's unknown whether there is a genetic, developmental, hormonal, or structural basis for the relation between the AP site and the gender of the patient.

Conclusions:

Female patients' diagnosis and referral to catheter ablation were delayed compared to equally affected male patients, with a longer duration passing from the first episode of tachypalpitation till the ablation procedure.

There are gender differences in sites of APs; females more commonly have right-sided APs.

Limitations: The small sample size.

List of abbreviations

AP: accessory pathway

APAERP: accessory pathway antegrade effective refractory period

APRERP: accessory pathway retrograde effective refractory period

AV: atrioventricular

ECG: electrocardiograme

RP: right posterior

RPS: right paraseptal.

Conflict of interest: The authors declare that they have no competing interests.

Authors' contributions:

MAFA participated in the work's design, performed the statistical analysis, interpreted the findings, and completed the work's final formatting. HY participated in patient recruitment and clinical assessment, data gathering, and manuscript writing. SA made significant revisions to the work and helped

with its idea, design, findings, and data interpretation. AAK contributed to the design of the work, established the results and interpretation of data, and substantially revised the work. AAY established the results

and data interpretation, helped with the work's conception and design, and made significant revisions. AA has contributed to the study conception, format, and design, revised the collected data, and substantially revised the work. All authors have read, revised, and approved the final manuscript.

Funding: No Funding.

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