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Original Article

Prevalence of P wave dispersion and interatrial block in patients with systolic heart failure and their relationship with functional status, hospitalization and one year mortality

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ABSTRACT

Background and objectives: P-wave dispersion (PWD) and Interatrial block (IAB) are common in heart failure (HF), and could be associated with adverse cardiac events. We aimed to assess the prevalence of PWD and IAB and their relationship with functional status, hospitalization and mortality rate in patients with systolic HF.

Methods: We enrolled 110 HF patients in sinus rhythm & LVEF <50%. Patients had undergone clinical evaluation, 6 min walking test (6MWT), 12-lead electrocardiography (ECG), 24-h Holter ECG & echocardiogram. Hospitalization and mortality rate were followed-up for one year. PWD was defined as the difference between maximum & minimum P-wave duration >40 ms. IAB was defined as maximum P duration >110 ms. Measurements were done by 2 blinded investigators using a caliber, a ruler and a magnifying lens.

Results: Mean age was 58.9 ± 9.7 years and 67.3% were males. Prevalence of PWD and IAB was 68.2% and 57.3%, respectively. Patients with PWD showed these features: 84% in NYHA class III or IV HF, 77.4% had LVEF <35%, 78.7% had paroxysmal Atrial Fibrillation (AF) and 89.4% couldn't complete >200 m (m) in 6MWT. Patients with PWD had more hospitalizations (72% vs 28.6%, P value <0.02) and higher 1-year mortality rate (20% vs 8.6%, P value <0.04) than patients without PWD. Likewise, patients with IAB had nearly similar clinical features, hospitalization and mortality as patients with PWD.

Conclusion: PWD and IAB are prevalent in patients with systolic HF and they are significantly associated with low LVEF, paroxysmal AF, poor functional capacity, hospitalization and mortality rate.

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1. Introduction

HF is a growing epidemic worldwide, associated with significant morbidity and mortality burden.¹ Several clinical and bedside parameters were investigated to suspect major cardiac events and mortality in HF, including PR interval and P-wave indices. In a recent published study, we reported that prolonged PR interval is associated with short term mortality in HF patients.²

However, there are conflicting data and uncertainty in literature regarding the association of prolonged PR interval with morbidity and mortality.^{3–5} A study conducted on 2541 deaths retrospec-

tively reported that the association between PR interval and mortality was dependent on the level of P-wave duration, not the PR segment ($P < 0.008$).³ Many other studies concluded that no increased mortality among individuals with prolonged PR interval (>200 ms), whereas it was the contribution of the P-wave duration that was associated with morbidity and mortality.^{4,5}

Prolongation of P-wave reflects inhomogeneous atrial depolarization in response to several electrical and structural remodeling.^{3–6} P-wave duration and PWD are influenced by the autonomic tone, which induces changes in the velocity of impulse propagation. Sympathetic activity has been well known to be elevated in patients with HF and was associated with PWD in patients with paroxysmal AF.^{7–10}

Despite the presence of recent publications addressing the issue of abnormal P-wave indices in the general population and in HF patients, their clinical consequences and correlation with morbidity and mortality haven't received significant scrutiny in literature.

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The aim of this study was to assess the prevalence of PWD and IAB in HF patients and its correlation with functional status of patients, hospitalization and mortality rate during one-year follow-up.

2. Methods

2.1. Study design

This was a single center, prospective observational study. It was approved by the faculty of medicine - Suez Canal university (FOMSCU) ethical review board.

2.2. Population and data collection

Initially, 125 consecutive HF patients in sinus rhythm were enrolled from March 2014 to July 2015. We included patients presented to the outpatient clinic of the cardiology department FOMSCU hospital with chronic HF, LVEF <50%, in NYHA FC II, III or ambulatory NYHA FC IV, who were stable and not hospitalized during the past 3 months. Patients were excluded if they were <18 years old, permanent AF, liver failure, cancer, renal failure or unable to provide informed consent. All patients have given written informed consent. Only 110 patients completed their follow-up, 5 patients had incomplete data and 10 patients had withdrawn from the study.

2.3. Study protocol

Patients evaluation included: medical history, physical examination, 6MWT, 12-lead ECG, echocardiography and 24-h Holter ECG. Patients were followed up for hospitalization frequency and mortality at the outpatient clinic and by telephone contact or hospital registry data until 1 year from enrollment.

All patients were medically managed according to our institutional guidelines. Blood samples were collected from patients at the time of admission for complete blood count, kidney and liver functions, and electrolytes. Ischemic etiology of HF was considered in patients with angiographically documented IHD, i.e. at least 75% obstruction of at least one coronary artery or 50% obstruction of the left main artery. Other criteria included history of myocardial infarction (MI) admission, evidence of regional wall motion abnormalities detected by echocardiography and the presence of ECG changes suggestive of MI.

2.4. Leads surface ECG

A 12-lead ECG was obtained from all patients in the supine position. All ECGs were recorded at a paper speed of 25 mm/s with 1 mV/cm standardization. The P-wave duration was measured manually by 2 investigators who were blinded to the patients' clinical status. Manual measurements with hand-held calipers performed by increasing the ECG rate to 50 mm/s with 20 mm/mV standardization, and use of magnifying lens and 0.5 mm scale precision ruler (BIOTRONIC).⁶ Then, all ECG strips were examined with automated calculations using Schiller MT-101.

The onset of the P-wave was defined as the junction between the isoelectric line and the beginning of the P-wave deflection. The offset of the P-wave was defined as the junction between the end of the P-wave and the isoelectric line. The maximum and minimum P-wave durations (P_{max} and P_{min}, respectively) were measured in all leads of the ECG. The PWD was defined as the difference between the P_{max} and P_{min}.⁴

2.5. Six minutes-walk test

The objective of this test is to walk as far as possible for 6 min. Distance walked was calculated, and any associated symptoms were reported. All vital signs and clinical evaluation were obtained.

2.6. Ambulatory 24-hours Holter ECG

All patients had undergone 24-h Holter at S.C.U hospital, using Schiller device. This test was done for risk stratification of HF, to assess HR variability and record arrhythmias.¹⁰

2.7. Statistical analysis

All data were gathered, calculated and statistically analyzed using the Statistical Package for the Social Sciences (SPSS) for Windows software, v.22.0. Quantitative variables were presented as mean \pm the standard deviation and qualitative variables as frequencies and percentages. Normally distributed data were analyzed using the Student t-test to compare means. The Chi-square test was used to analyze differences between qualitative variables. Multiple logistic regression analysis and Spearman correlation coefficient were used to estimate the correlations between the different variables and abnormal P-wave indices. P value of less than 0.05 was used as a cut off for statistical significance.

3. Results

3.1. Demographic and clinical data

Males constituted 67.3% of study population. The study participants age mean \pm SD was 58.9 \pm 9.7 years. The most common comorbidities were: IHD (53.6%), hypertension (26.3%) and diabetes (24.5%), while 52 patients (47.27%) were smokers. Many of the recruited HF patients had multiple co-morbidities. Most of the recruited patients were in NYHA III, IV (68.2%) [Table 1](#).

3.2. Echocardiographic, 6MWT and 24-hours Holter ECG findings

Echocardiographic screening revealed that the study participants had dilated LV& LA with low LVEF. The mean distance walked in the 6MWT was 162.41 m. The 24-h Holter revealed that the mean SDNN was 64.89 ms. Paroxysmal AF was prevalent in 57.3% of patients, other SVT were prevalent in 12.72% of patients. Non-sustained ventricular tachycardia (NSVT) was prevalent in 17.2%, sustained VT was found in 2 patients (1.81%) who gave a history of syncope [Table 2](#).

3.3. Prevalence of PWD and IAB

The prevalence of PWD is 68.2%, while IAB was prevalent in 57.3%. [Fig. 1](#) explains the different P-wave durations and PWD.

3.4. Hospitalizations and mortality rate during one-year follow-up

The mortality rate was 16.3% during one-year follow-up. Moreover, our patients had frequent hospitalizations during one-year follow-up. 58.2% of patients were hospitalized due to decompensated HF more than once, nearly 1/6th of these hospitalizations were more than 3 times ([Table 3](#)).

Table 1
Baseline demographic and clinical characteristics of HF patients.

Age (years)	
Mean ± SD	58.9 ± 9.7 years
Gender, N (%)	
Males	74 (67.3%)
Females	36 (32.7%)
BMI, Mean ± SD	27.2 ± 4.6
Active smokers, N (%)	52 (47.27%)
Co-morbidities, N (%)	
IHD	59 (53.6%)
Hypertension	29 (26.3%)
Diabetes mellitus	27 (24.5%)
Valvular heart disease	24 (21.8%)
Dilated cardiomyopathy	16 (14.5%)
CABG	14 (12.7%)
NYHA functional classification and BP	
NYHA II, N (%)	35 (31.8%)
NYHA III & IV, N (%)	75 (68.2%)
SBP (mmHg), Mean ± SD	118 ± 21
DBP (mmHg), Mean ± SD	68 ± 10
Cardiovascular drugs, N (%)	
Diuretics	99 (90%)
Beta blockers (bisoprolol, carvedilol, and nebivolol)	97 (88.2%)
ACEi or ARBs	93 (84.5%)
Aldosterone antagonists	81 (73.6%)
Digoxin	29 (26.4%)
Amiodarone	12 (10.9%)
Ivabradine	6 (5.45%)
Laboratory data, mean ± SD	
Serum creatinine, mg/dl	1.4 ± 0.5
Haemoglobin, g/dl	10.5 ± 2.4
ALT, IU/L	32 ± 11
AST, IU/L	34 ± 13
Serum Na, mEq/L	138 ± 9

BMI, body mass index; CABG, coronary artery bypass graft; NYHA, New York Heart Association; SPB, systolic blood pressure; DBP, diastolic blood pressure; ACEi, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; ALT, Alanine aminotransferase; and AST, Aspartate aminotransferase.

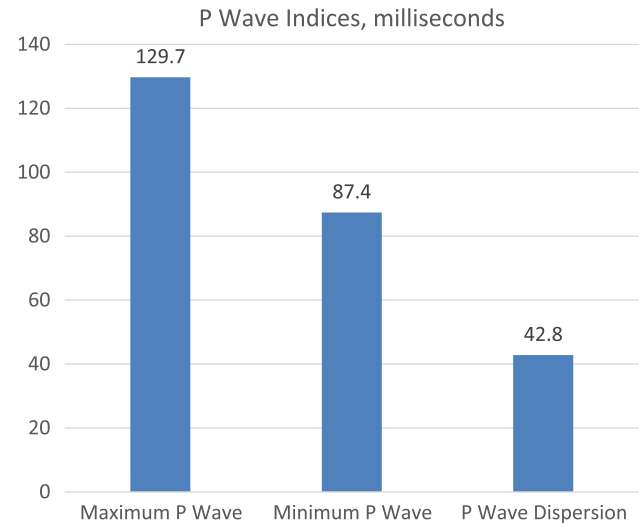
Table 2
Baseline echocardiography, 6MWT and 24-h Holter ECG findings of HF Patients.

<i>Echocardiographic parameters of patients</i>	
LVEF%, Mean ± SD	31.85 ± 9.79
LVEF <35%, N (%)	66 (60%)
LVESD, mm	53.47 ± 9.67
LVEDD, mm	64.57 ± 7.97
LA diameter, mm	47 ± 6.85
<i>6MWT, Mean ± SD</i>	
Distance, meter	162.41 ± 69.49
Resting heart rate, beats per minute	83.75 ± 10.68
Maximum heart rate, beats per minute	98.39 ± 34.65
Duration of 6MWT, minutes	4.25 ± 1.69
<i>24-h Holter ECG results</i>	
SDNN, ms, Mean ± SD	64.89 ± 30.65
SDNN <70 ms, N (%)	71 (64.5%)
<i>Arrhythmias, N (%)</i>	
Paroxysmal AF	63 (57.3%)
SVT	14 (12.72%)
NSVT	19 (17.2%)
Sustained VT	2 (1.81%)

LV left ventricular, EF ejection fraction, FS fractional shortening, ESD end systolic diameter, EDD end diastolic diameter, LA left atrium, SDNN mean of the SD of normal-to-normal R-R intervals.

3.5. Comparison of the study variables, hospitalization and mortality data of HF patients with and without abnormal P-wave indices (PWD and IAB)

HF patients with abnormal P-wave indices have worse NYHA class, more attacks of paroxysmal AF in Holter ECG, less LVEF, short

**Fig. 1.** P-wave indices in HF patients.**Table 3**
Hospitalization and mortality rate of HF patients during one-year follow-up.

<i>Hospitalization rate during one-year follow-up, N (%)</i>	
All Hospitalizations: 81 (73.6%)	
> 1 Hospitalization event: 64 (58.2%)	<ul style="list-style-type: none"> • Twice: 36 (32.7%) • Three times: 17 (15.5%) • 3 times: 11 (10%)
<i>Mortality during one-year follow-up, N (%)</i>	
	18 (16.3%)

Table 4
Comparison of the study variables, hospitalization and mortality data of HF patients with and without PWD.

	PWD		P value
	Yes, N (%) = 75, (68.2%)	No, N (%) = 35, (31.8%)	
<i>NYHA functional class</i>			
III & IV, N (%)	63 (84%)	12 (34.4%)	0.001
<i>24-h Holter ECG, N (%)</i>			
SDNN <70 ms	59 (78.7%)	12 (34.3%)	0.01
Paroxysmal AF, N (%)	59 (78.7%)	4 (11.4%)	0.01
<i>Echocardiography</i>			
LA diameter, mm	51 ± 5.96	42 ± 6.15	0.01
LVEF < 35%, N (%)	58 (77.4%)	8 (22.8%)	0.001
<i>6MWT, N (%)</i>			
Distance walked <200 m	67 (89.4%)	16 (45.7%)	0.01
<i>>1 Hospitalization/12 months, N (%)</i>			
	54 (72%)	10 (28.6%)	0.02
<i>Mortality during 12 months, N (%)</i>			
	15 (20%)	3 (8.6%)	0.04

NYHA New York heart association, SDNN mean of the standard deviation of normal to normal R-R intervals. LA left atrium, LV left ventricular, EF ejection fraction.

distance walked at 6MWT, more hospitalizations and mortality rates than HF patients who have normal P-wave indices. [Tables 4 and 5.](#)

3.6. Correlation between abnormal P-wave indices and different study variables, hospitalization and mortality

The presence of PWD and IAB is positively correlated with NYHA class, LA size, paroxysmal AF, hospitalization and mortality.

Table 5
Comparison of the study variables, hospitalization and mortality data of HF Patients with and without IAB.

Parameter	IAB		P value
	Yes, N (%) = 63 (57.3%)	No, N (%) = 47 (42.7%)	
<i>NYHA functional class</i>			
III, IV, N (%)	55 (87.3%)	20 (42.6%)	0.01
<i>24-h Holter ECG, N (%)</i>			
SDNN < 70 ms	48 (76.2%)	20 (42.6%)	0.01
Paroxysmal AF, N (%)	49 (77.8%)	13 (27.6%)	0.01
<i>Echocardiography</i>			
LA diameter, mm	52 ± 4.76	41 ± 7.35	0.01
LVEF < 35%, N (%)	50 (79.4%)	16 (31.9%)	0.01
<i>6MWT, N (%)</i>			
Distance walked <200 m	57 (90.5%)	26 (55.3%)	0.01
>1 Hospitalization/12 months, N (%)	39 (61.9%)	18 (38.3%)	0.019
<i>Mortality during 12 months, N (%)</i>			
	16 (25.3%)	2 (4.3%)	0.012

Refer to Table 4.

Table 6
Correlation between PWD and different study variables, hospitalization and mortality.

Parameters	r	P value
Age	-0.086	0.395
Gender	0.171	0.09
NYHA III/IV	0.481	0.001
Mortality rate	0.219	0.03
Hospitalization rate	0.282	0.01
<i>Echocardiography</i>		
LVEF	-0.576	0.001
LA Diameter	0.531	0.001
<i>6MWT</i>		
Distance	-0.365	0.01
<i>24-h Holter ECG</i>		
Paroxysmal AF	0.644	0.001

NYHA New York heart association, LV left ventricular, EF ejection fraction, LA left atrium, 6MWT Six minutes-walk test distance.

On the other side, it is negatively correlated with LVEF and distance walked in 6MWT Tables 6 & 7.

4. Discussion

In this work, we assessed the prevalence of PWD and IAB in patients with HF, and their association with echocardiographic, Holter ECG, functional capacity and one-year follow-up of hospitalization and mortality. Up to our knowledge, this is the first study in Egypt to address this topic in HF patients.

4.1. Prevalence of PWD and IAB

We observed a high prevalence of PWD (68.2%) and IAB (57.3%) in our HF cohort. We previously reported that prolonged PR interval was prevalent in 28.8% of HF patients, and in 51.7% of HF patients with short term mortality.²

The reported prevalence of IAB and PWD in HF patients is variable across studies. It was reported that PWD in HF patients was significantly higher than those of control subjects (47 vs. 38 ms, $P < 0.001$).⁹ The maximum P-wave duration was 126 ms, denoting IAB. They explained that LV dysfunction could lead to significant cardiac hemodynamic changes and altered LA electrical properties which result in high prevalence of PWD and IAB in such patients.⁹

Table 7
Correlation between IAB and different study variables, hospitalization and mortality.

Parameters	r	P value
Age	-0.141	0.161
Gender	0.142	0.159
NYHA III/IV	0.416	0.001
Mortality	0.252	0.012
Hospitalization	0.279	0.01
<i>Echocardiography</i>		
LVEF	-0.525	0.001
LA Diameter	0.486	0.001
<i>6MWT</i>		
Distance	-0.344	0.001
<i>24-h Holter ECG</i>		
Paroxysmal AF	0.428	0.001

Refer to Table 6.

Another study reported that the prevalence of PWD was 52.5% and IAB was 68.8% in HF cohort.¹¹ The highest reported prevalence of P-wave abnormalities was recorded by a study included 163 patients hospitalized for HF worsening. They reported that 81.6% of admitted HF patients had IAB.¹²

Similarly, it was reported that patients with low LVEF had PWD, and that the use of beta blockers improved HF and PWD.¹³ It was reported that IAB is common even in hospitalized patients regardless the etiology (41.1%), especially in patients >60 years.¹⁴

4.2. Demographic and clinical findings

Our study showed that the mean age of our cohort was 58.9 ± 9.7 years, more than half of them were males (67.3%), and IHD is the most common cause of HF (53.6%). This is consistent with the results of the Egyptian prospective HF study, where median age was 61 years, males constituted 67.9% of recruited patients and IHD prevalence was 67.6%.¹⁵

We think that the high prevalence of IHD could be responsible for the high prevalence of PWD and IAB among our cohort, as it was reported that PWD was associated with presence of IHD and was correlated with its severity as well.¹⁶ Several anatomic and hemodynamic modulations take place in LA due to IHD including: LA fibrosis, dilatation, overload, and increased LA pressure.^{10,17,18}

In the present study 47.27% were smokers; this is slightly less than the reported prevalence of smoking (61%) in the Egyptian HF study.¹⁵

Patients who were in NYHA III/IV constitute two-thirds of the recruited patients (68.2%) which is close to the Egyptian HF registry where NYHA III/IV HF constituted 61.6%. This might reflect poor compliance or adherence to medications and absence of device therapy in our cohort.¹⁵ This relatively NYHA class was reflected on the patients' functional capacity as the mean 6MWT distance was 162.41 m and most of patients didn't complete 200 m.

4.3. Echocardiographic findings

The echocardiographic data revealed dilated LV & LA dimensions, and impaired LVEF as most of our patients (82.72%) had HF with reduced EF (LVEF < 40%), and only few (17.28%) had HF with mid-range EF (LVEF 40–49%). Two Egyptian studies reported that less than one quarter of their recruited HF patients had LVEF >45%.^{15,19} We also reported in a recent study of hospitalized HF patients significantly dilated LV& LA dimensions, and impaired LVEF.² It was reported that HF patients with PWD had markedly dilated LV compared to the control group without PWD, P value <0.001.⁹

We reported that LA diameter was dilated in our cohort. Senen and co-workers reported that patients with HF had PWD due to significant LA anatomical and hemodynamic changes like LA dilatation and fibrosis influenced by HF. Furthermore, they reported that PWD was significantly positively associated with increased LA diameter.⁹

Another study reported that in patients with HF, the LA volume was independently associated with IAB and PWD.¹¹ Recently, it was reported that disturbed P-wave indices are associated with dilated LA size across different cardiovascular diseases, including IHD, HF and hypertension.⁶

Ariyarajah and co-workers reported that IAB was associated with several pathophysiologic derangements that result in LA electromechanical dysfunction. The degree of conduction delay and IAB is directly correlated with LA enlargement.²⁰

Cardiac resynchronization therapy (CRT) improves LVEF, LV size, atrial function and remodelling.²¹ In a study involving HF patients with CRT, maximum P-wave duration and PWD were decreased along with an improvement of LVEF and reduction in LA diameter.²²

4.4. Holter ECG findings

We reported from Holter ECG recording that SDNN was short in our HF cohort, 64.5% had SDNN <70 ms, which is a surrogate of autonomic dysfunction. Previous studies reported that SDNN was found to be an independent predictor of all-cause mortality in patients with HF.^{8,10}

Sympathetic activity has been well known to be elevated in patients with HF.^{8,10} P-wave duration and PWD have been reported to be influenced by the autonomic tone.⁷ It was reported that no significant diurnal variation of PWD in HF patients treated with optimal drug therapy, indicative of impaired sympathetic tone.⁷

We reported a high prevalence of SVT (70.02%): paroxysmal AF (57.3%) and other SVT (12.72%). A study investigated 97 HF patients with CRT, 38% had advanced IAB at baseline, over a mean follow-up of 32 months, AF was detected in 30%. The AF incidence was greater in patients with advanced IAB compared to those without it (62% vs 28%; P < 0.003).²³

We found only one study in the literature correlating PWD with hospital events in Egyptian patients with Acute Coronary Syndrome (ACS).²⁴ The study concluded that PWD couldn't predict AF or hospital complications in patients with ACS during 5 days follow-up. However, there are many caveats in this study: they included only 60 patients, subdivided them into 3 subgroups; no

data about LVEF and LV size; follow-up period was too short; and the mean PWD measured was 20 ms, too small number to draw any conclusions, as they explained.²⁴

Our results are comparable to a Chinese study which reported a high prevalence of SVT in HF (62%), 40.81% AF and 21.16% other SVT.²⁵ There is large variability of SVT and AF prevalence in HF; the Euro-HF survey of AF reported that up to 45% of patients with CHF could have AF.²⁶ Other studies reported that AF is common in 50% of HF patients,²⁷ and paroxysmal AF was reported in 36% of patients with HF.²⁸ The structural and neurohormonal changes in HF make the development and progression of AF much more likely. Patients with concomitant HF and AF have significantly worse prognosis.²⁹

We reported VT in 19.01% in our cohort of HF. A Chinese study reported the highest prevalence of PVCs in patients with HF (68.30%), while VT prevalence was 14.50%.²⁵ Another study enrolled 2205 HF patients in India reported that 58% of HF patients had arrhythmia: 15% bradyarrhythmia, 15% AF, 10% other SVT, and 4.5% VT.³⁰ On the other side, another study reported the highest prevalence of VT in HF patients, they detected VT and VF episodes in 199 HF patients with CRT-D as 25.8%, increased to 37.8% in patients with chronic kidney disease, P value <0.05.³¹

Overall, there are multiple factors contributing to the high prevalence of arrhythmia in HF patients compared to normal individuals, this include: dilated cardiac chambers, myocardial stretch, scarring, electrophysiological modulations, Ca handling dysregulation, neurohumoral and biochemical abnormalities.¹⁰

4.5. Hospitalizations and mortality

Our patients had frequent hospitalizations, 58.2% of patients were hospitalized due to HF more than once over one-year follow-up, nearly 1/6th of these hospitalizations were >3 times. This is similar to the findings of Hassanein and co-workers who reported that 54.3% of 1475 Egyptian HF patients had HF hospitalizations during 3 years follow-up.¹⁵

The one-year mortality of our cohort with HF was 16.3%. This is close to the Paradigm HF study which reported 18.4% mortality in HF patients¹ and the Euroheart survey reported long-term mortality of HF patients of 20.5%.³² Many factors could explain this mortality: many of enrolled patients were in NYHA FC III/IV, short distance walked at 6MWT, low mean LVEF, and prevalent cardiac arrhythmia in Holter ECG.

However, this is quite less than the previously reported short term mortality (24.16%) in HF patients in our previous work.² This could be explained by the nature of the enrolled HF patients who were admitted due to decompensated HF in an unstable condition, while this study enrolled more stable HF patients.

Alvarez and co-workers conducted a prospective study in 163 patients hospitalized for HF worsening. The incidence of 1-month MACE was significantly high in patients with IAB (44.8%) compared to patients without (6.7%). The study concluded that IAB in patients with worsening of HF was highly prevalent and represented independent predictor of MACE.¹²

4.6. Abnormal P-wave indices and functional status

Ninety percent (90%) of patients with PWD didn't walk more than 200 m in 6MWT and 84% were in NYHA FC III/IV; the same pattern applies to HF patients with IAB. This reflects marked functional limitations in HF with PWD and IAB. This could be explained by two factors, firstly, more than 2/3rd of our cohort were in NYHA FC III/IV HF and they were able to walk only a mean of 162.41 m in 6MWT. Secondly, presence of abnormal P-wave indices was associated with less LVEF (<35%) and more prevalent cardiac arrhythmia, which could contribute to this functional impairment.

These observations proved in our study by the significant positive correlation between presence of abnormal P-wave indices and NYHA class, paroxysmal AF reported in Holter ECG, and their negative correlation with LVEF and distance walked in 6MWT.

Alvarez and co-workers reported that elevated NTproBNP >1000 ng/L was more common in HF patients with IAB than in those without (P value <0.003). NYHA FC III/IV was more prevalent in HF with IAB compared to HF patients without, but this was not statistically significant. Both observations indicate worse status of patients with IAB.¹²

4.7. Abnormal P-wave Indices, Hospitalization and mortality

PWD and IAB reflect electromechanical atrial changes caused by variable cardiovascular and systemic diseases. Abnormal P-wave indices have been associated with HF, diastolic dysfunction, hypertension, obesity, and diabetes, which are all associated with increased mortality.^{4,10}

HF patients have abnormal atrial conduction manifested by unstable refractoriness, IAB and PWD. This might be due to widespread impairment in the cardiac conduction system.³³

IAB was associated with a 2-fold increased risk of AF and ischemic stroke, both cardiovascular conditions are associated with significant morbidity and mortality burden. Moreover, AF per se potentiates HF and boosts its morbidity and mortality.^{18,34}

We reported that HF patients with abnormal P-wave indices have more hospitalizations and mortality rates than HF patients who have normal P-wave indices. Hospitalization more than once/year was reported in nearly 3/4th of HF patients with PWD (72%) versus only 1/3rd (28.6%) of HF patients without PWD, P value <0.02. HF patients with IAB have more hospitalizations than those who haven't (61.9% vs. 28.3%, P value <0.02). Correlation analysis revealed that PWD and IAB were positively correlated with hospitalization ($r = 0.282$, P value <0.01) and ($r = 0.279$, P value <0.01), respectively.

This was reported by Alvarez-Garcia and co-workers,¹² who reported that hospital admissions per year were more common in patients with IAB compared to those without (P value <0.028). Moreover, they reported the 1-month MACE in 44.8% of HF patients with IAB. NTproBNP was significantly elevated (>1000 ng/L) in HF patients with IAB than in those without (P value <0.003). They concluded that IAB in patients with worsening of HF was highly prevalent and represented independent predictor of MACE leading to frequent hospitalizations.¹²

The reported one-year mortality in our study was 20% in HF patients with PWD versus 8.6% in those who haven't, P value <0.04. Likewise, HF patients with IAB have more than 5-fold increase in one-year mortality than who haven't, 25.3% vs. 4.3%, P value <0.012. Correlation analysis revealed that PWD and IAB were positively correlated with mortality ($r = 0.219$, P value <0.03) and ($r = 0.252$, P value <0.012), respectively.

The association of abnormal P-wave indices and mortality was reported in a large study conducted by Magnani and co-workers,⁴ enrolled 8561 subjects over a median 8.6-year follow-up. There were 679 cardiovascular deaths and 1559 all-cause mortality deaths. P-wave duration was significantly associated with cardiovascular mortality, P value <0.004 and all-cause mortality, P <0.05. This finding established that prolonged P-wave duration (IAB) carries an adverse association with mortality. When the study investigators excluded individuals with cardiovascular illness, P-wave duration was still associated with significant cardiovascular mortality. The study further reported that prolonged P-wave duration and IAB were associated with high mortality rate even in patients without prevalent cardiovascular disease.⁴

Another study reported the association of P-wave indices abnormalities and mortality, over 5.4 years follow-up, in 209

haemodialysis patients, a group of investigators reported 45.5% mortality rate associated with PWD. However, they assumed that this high mortality rate is affected by several confounders, including old age, high prevalence of DM, hypertension, IHD, cerebrovascular disease and arterial stiffness.³⁵

One of the explanations of increased mortality and hospitalization in HF patients with abnormal P-wave indices is disturbed autonomic tone. We reported in our HF cohort that SDNN was short (64.5% had SDNN <70 ms) which is a major surrogate of autonomic dysfunction. Short SDNN was found to be an independent predictor of all-cause mortality in patients with HF, regardless its etiology, with evidence of LV dysfunction.^{8,10}

5. Conclusion

Up to our knowledge, this is the first study in Egypt to assess the prevalence of PWD and IAB in patients with HF, and their association with functional capacity, echocardiographic findings, Holter ECG recording, hospitalization and mortality during one-year follow-up.

We reported a relatively high prevalence of PWD (68.2%) and IAB (57.3%) in our HF cohort. We found that PWD and IAB were associated with NYHA FC III/IV HF, short distance walked at 6MWT, dilated LV, paroxysmal AF, and VT. During one-year follow-up, PWD and IAB were associated with frequent hospitalizations and higher mortality rate. We think that adding these feasible and simple tools of ECG assessment to the clinical evaluation could significantly improve the prediction of cardiovascular morbidity and mortality in HF. Identifying high risky HF patients could recognize patients who should be carefully monitored and appropriately managed.

6. Study limitations

This study is a prospective, single center study with a limited number of consecutively recruited HF patients, who were followed-up only for 1 year. We didn't include HF patients with preserved ejection fraction. More large-scale, multicenter studies with longer follow-up are needed to validate our findings.

Conflicts of interest

No conflicts of interest.

Authorship declaration

All listed authors are in agreement with the manuscript.

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