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P-Wave Dispersion in Patients with Constrictive Pericarditis of Non-Ischemic Etiology Including Tubercoulous and Non-Tuberculous Subjects: A Pilot Study

Gholam Reza Rezaian,[1,*] Masoud Pour Moghaddas,[2] Shahed Rezaian,[3] Lida Liaghat,[4] and Najaf Zare[5]

[1]Department of Cardiology, Shiraz University of Medical Sciences, Shiraz, IR Iran
[2]Department of Cardiology, Isfahan University of Medical Sciences, Isfahan, IR Iran
[3]Department of Radiology, Shiraz University of Medical Sciences, Shiraz, IR Iran
[4]Department of Internal Medicine, Isfahan University of Medical Sciences, Isfahan, IR Iran
[5]Department of Biostatistics, Shiraz University of Medical Sciences, Shiraz, IR Iran

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ABSTRACT

***Background*:** Although P-wave dispersion has proven to be a reliable electrocardiographic predictor of Atrial Fibrillation (AF) in many clinical settings, its significance in patients with Constrictive Pericarditis (CP) of non-ischemic origin is to be reported.
***Objectives*:** This study aimed to find out whether p-wave dispersion is prolonged in patients with documented CP of non-ischemic origin.
***Patients and Methods*:** This study was conducted on twenty patients with CP, 16 males and 4 females, with the mean age of 39.0 ± 20.5 years and 20 age- and sex-matched healthy subjects. All the Electrocardiograms (ECGs) were scanned and the P-wave parameters were measured electronically after × 400% magnification.
***Results*:** Our main finding was a significantly prolonged maximum P-wave duration (P = 0.018) and P-wave dispersion (P = 0.049) in the patients with CP compared to the control group. These parameters, however, did not have any correlation with the patients' age and disease duration.
***Conclusions*:** Since AF is common in patients with CP of any etiology and may have a negative impact on their outcome, detection of individuals susceptible to development of AF could be of great clinical value.

►*Implication for health policy/practice/research/medical education:*
AF is a common finding in patients with CP. The reason for this phenomenon is not quite clear. In addition, tuberculosis is endemic in our region and could be associated with CP. P-wave dispsersion can help distinguish susceptible subjects for the development of AF. We hope that the results of this study could open up a new horizon for research in this field.

1. Background

P-wave prolongation and increased p-wave dispersion (PWD) in 12-lead surface electrocardiogram (ECG) are well-known electrophysiological characteristics in patients with paroxysmal atrial fibrillation (AF). Although P-wave dispersion has proven to be a sensitive and specific ECG predictor of AF in various clinical settings (1-3), its significance in patients with constrictive pericarditis (CP) is to be reported.

*Corresponding author: Gholam Reza Rezaian, Department of Medicine (Cardiology), Nemazee Hospital, 71937-11351, Shiraz University of Medical Sciences, Shiraz, Iran, Tel: +98-711648-6508, Fax: +98-711648-6509, *E-mail:* grezaian@gmail.com

2. Objectives

Since AF is commonly encountered in patients with CP, this study aims to find out whether these p-wave parameters are really prolonged in patients with documented CP of non-ischemic origin and whether they have any correlation with the patients' age or disease duration. Because of the frequent association of PWD with coronary artery disease and myocardial ischemia (4, 5), patients with bypass graft surgery and CP were not included in this study.

3. Patients and Methods

The medical records of all the consecutive patients with

hemodynamically and surgically proven CP admitted to our university hospitals in Shiraz and Isfahan during 1975 - 2010 were reviewed. Patients were included in the study only if they were normotensive, had normal sinus rhythm on presentation, their P-wave parameters could be accurately measured in nine or more leads of the surface ECG, and had a completely normal or non-significant coronary artery disease in their coronary angiograms. Post Coronary Artery Bypass Graft (CABG) patients were excluded from the study. Overall, twenty patients with CP fulfilled the inclusion criteria and were enrolled into the research. In addition, 20 age- and sex-matched healthy individuals with no history of hypertension or ischemic heart disease and normal physical findings and ECGs were included in the study as the control group. Written informed consents for participation in the study were obtained from all the participants and the study protocol was approved by the local institutional research committee.

3.1. Twelve-Lead Surface ECG

All 12-lead ECGs were recorded at paper speed of 25 mm/s and gain of 10 mm/mV, with subjects in supine position. To improve the accuracy of the measurements, all ECGs were scanned through a Cannon scanner (at 300 dpi), saved as pictures in a personal computer, and analyzed electronically after × 400% magnification by Adobe Photoshop software.

The starting point of P-wave was considered as the positive deflection crossing the iso-electric line and the end-point was considered as the end of deflection crossing the iso-electric line. P-wave duration was measured from the onset to the offset of the P-wave. P-wave durations were measured for 3 consecutive P-waves in each of the 12 leads and the mean of the 3 measurements was considered as the P-wave duration of that lead. When the beginning or the end of the deflection could not be identified clearly, that lead was excluded. Once the P-wave durations were determined, the maximum and minimum P-wave durations were identified and P-wave dispersion, defined as the difference between the maximum and minimum P-wave durations, was calculated. It should be noted that the measurements were done by an independent expert physician who was kept blind to the subjects' clinical status.

3.2. Statistical Methods

Continuous variables (expressed as mean ± SD or median values) were compared by Mann Whitney test. Besides, Pearson's correlation (2-tailed) was used to determine the correlation between P-wave parameters and the patients' age and disease duration. All the data were analyzed using the SPSS statistical software, version 15 (SPSS Inc. Chicago ILL) and $P < 0.05$ was considered as statistically significant.

4. Results

The patients' disease duration ranged from 2 to 60 months with a mean ± SD of 26.1 ± 18.4 months and a median of 24 months. Moreover, nine patients (45%) had tuberculous pericarditis and 8 ones (40%) had idiopathic CP. Among the remaining 3 patients, 2 (10%) had postoperative CP following valve replacement and one (5%) had systemic lupus erythematosus.

4.1. Clinical and Paraclinical Findings

Exertional dyspnea, easy fatigue, and abdominal and lower extremity swelling were the most common symptoms. A mistaken diagnosis of liver cirrhosis was made in a 19-year-old female. Chest x-ray showed cardiomegaly in 6 patients and linear pericardial calcification in 3 subjects. Echocardiography was available in 10 patients and showed pericardial thickening in all the subjects, calcification in 3, and evidence of pericardial effusion in 5 patients. Besides, nine patients had biatrial enlargement and varying degrees of mitral and tricuspid valve regurgitation. Paradoxical septal motion was also noted in 3 subjects. Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) of chest were available in 3 patients, all showing the presence of thickened pericardial layers. It should be mentioned that all the patients had undergone simultaneous left and right ventricular catheterization, showing the characteristic equalization of diastolic pressures and the dip and plateau contour. Histopathological studies were also done on pericardial samples obtained at the time of surgery.

Baseline characteristics and P-wave parameters of the two groups have been presented in Tables 1 and 2, respectively. Although both maximum P-wave duration and P-wave

Table 1. The Baseline Characteristics of the 20 Patients with Constrictive Pericarditis and the 20 Age- and Sex-Matched Controls

Variables	Control Group (N = 20)	Patients with CP (N = 20)	P value
Age (years)	37.8 ± 20.1	39.0 ± 20.5	0.860
Age (median)	35.5	38	1.000
Male, n (%)	16 (80)	16 (80)	0.093
Heart rate (bpm)	83.7 ± 12.4	91.2 ± 11.0	
Heart rate (median)	85.5	95	

Abbreviations: CP, constrictive pericarditis; Mean ± SD, mean ± standard deviation; n, number; bpm, beats per minute

Table 2. P-wave Parameters in the 20 Patients with CP and the 20 Age- and Sex-Matched Controls

P-wave parameters	Controls (N = 20)		CP Patients (N = 20)		P value
	Range	Mean ± SD	Range	Mean ± SD	
Minimum P-wave duration (msec)	40 - 86	55.9 ± 12.0	44 - 82	60.4 ± 10.7	0.188
P-max (msec)	86 - 128	106.5 ± 12.7	88 - 156	120.3 ± 18.0	0.018
P-disp (msec)	32 - 80	50.4 ± 13.8	40 - 88	60.0 ± 15.0	0.049

Abbreviations: CP, constrictive pericarditis; Mean ± SD, Mean ± Standard Deviation; n, number; P-disp, P-wave dispersion; P-max, maximum P-wave duration; P-min, minimum P-wave duration

dispersion were significantly higher in the patients with CP compared to the control group, there was no significant correlation between these parameters and the patients' age or disease duration. The heart rate was also somewhat higher in the patients with CP than in the control group. However, no significant correlation was detected between heart rate and P-wave parameters.

5. Discussion

Our main finding was a significantly prolonged maximum P-wave duration (P = 0.018) and P-wave dispersion (P = 0.049) in the patients with CP in comparison to the control group. In order to avoid the impact of underlying myocardial ischemia on these parameters, patients with post-CABG surgery constriction were not included in this study. Also, none of our subjects had coronary artery disease in their coronary angiograms.

Abnormal atrial properties and mechanism for AF in CP have received little attention in spite of AF being common as a part of the natural history of this disease. In a recent series of 143 patients with surgically proven constriction, 22% had AF (6). AF is closely associated with some electrophysiological abnormalities of the atria, namely reduction in refractory period and conduction velocity and increase in the dispersion of the refractory period of the atrial muscle (7, 8). Constriction increases atrial filling pressures, reflecting both ventricular non- compliance and atrial constraint by the thickened pericardial shell. Atrial dilatation as well as underlying myocardial abnormalities, epicardial inflammation, and calcification could all contribute to development of atrial arrhythmias, especially AF, in these patients (9). Due to the compliance abnormalities of the right and left ventricles, the atria may dilate (9). In our series, nine out of the 10 patients with available echocardiograms had right and left atrial enlargement. Prolongation of atrial conduction time and heterogeneous propagation of sinus impulses in the atria can lead to development of AF. Tükek et al. showed that increased sympathetic activity was associated with a significant increase in P-wave dispersion (10). In addition, the influence of autonomic nervous system on development of AF has been well documented (11). Furthermore, increased sympathetic tone is common in patients with CP (12, 13). Anand et al. revealed greatly increased activity of the sympathetic nervous system indicated by high plasma concentrations of norepinephrine as well as by stimulation of the rennin-angiotensin-aldosterone system in untreated patients with CP (14). Therefore, other than mechanical, structural (15), and hemodynamic factors, enhanced autonomic tone can be a possible contributing factor to development of AF in patients with CP. AF can be associated with an increased risk of thrombo-embolic events and have a negative impact on the already reduced cardiac output in patients with CP, especially those who suffer from postoperative low-output syndrome, thus increasing the morbidity and mortality in these patients. Hence, detection of CP patients susceptible to development of AF is of great value. Prolongation of maximum P-wave duration and increase in P-wave dispersion could help detect such patients.

5.1. Limitation of the Study

The present work was limited by the small number of our CP patients whose cardiac rhythm was normal sinus rhythm and could be examined. Furthermore, a large number of our CP subjects had AF and, thus, could not be included in this investigation. Yet, it should be remembered that, nowadays, tuberculosis is getting rare and tuberculous pericarditis is even less frequent; therefore, having this number of subjects with documented tuberculous pericarditis could be interesting by itself.

Despite the limited number of patients, the study results revealed statistically significant differences between the two groups regarding maximum P-wave duration and P-wave dispersion. In addition, no significant correlation was found between the P-wave parameters and the patients' age or disease duration. This again could have been influenced by the small sample size and the wide range of age distribution and disease duration in our patients. Thus, larger studies are needed to further clarify these issues.

5.2. Conclusion

Since AF is common in patients with CP of any etiology and may have a negative impact on their outcome, detection of subjects susceptible to development of AF could be of great clinical value.

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Authors' Contribution

Gholam Reza Rezaian: Study conception and design, review of literature, patients and electrocardiographic gathering, Analysis and interpretation of data, drafting of manuscript, critical revision; Masoud Pour Moghaddas: Patients and electrocardiographic gathering, contribution in drafting of manuscript; Shahed Rezaian: Review of literature, patients and electrocardiographic gathering, Acquisition of data and measurement of p-wave durations and dispersions; Lida Liaghat: Review of literature, patients and electrocardiographic gathering, Acquisition of data and measurement of p-wave durations and dispersions; Najaf Zare: Statistical analysis, contribution in critical revision

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