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P-wave terminal force in lead V1 is a predictive indicator for the diagnosis of tuberculous constrictive pericarditis

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ABSTRACT

Objectives: The purpose of this study is to explore the value of P-wave terminal force in lead V1 (PTFV1) in the clinical diagnosis of tuberculous constrictive pericarditis (TCP).
Methods: A total of 53 patients with TCP and 64 patients with tuberculous exudative pericarditis were enrolled in this retrospective study. The demographic and clinical characteristics were collected, including gender, age, the course of disease and New York Heart Association (NYHA) classification. Besides, echocardiography data also were obtained, including left atrial diameter, left ventricular end-diastolic diameter and left ventricular ejection fraction. In addition, the parameters of electrocardiogram (ECG) were obtained, such as heart rate, the time from the corrected ORS wave origin to T-wave terminal, atrial fibrillation, right bundle branch block, atrial premature beat, and PTFV1 value.
Results: No significant differences were found in age, gender, the course of disease, echocardiography results, ECG parameters (in addition to PTFV1) between patients with TCP and patients with tuberculous exudative pericarditis. The percentage of patients located in NYHA class IV in the patients with TCP was significantly higher than those of patients with tuberculous exudative pericarditis ($p = 0.041$). Moreover, the incidence rate of abnormal PTFV1 ($\leq$ -0.04 mm·s) was obviously higher in patients with TCP than those of patients with tuberculous exudative pericarditis (64.2% vs 9.4%, $p < 0.001$).
Conclusions: Abnormal PTFV1 ($\leq$ -0.04 mm·s) is associated with TCP, and PTFV1 may be a potential novel diagnostic indicator for TCP diagnosis.

Introduction

Tuberculous pericarditis is a rare clinical syndrome in tuberculosis patients, including constrictive pericarditis and exudative pericarditis.[1,2] Generally, there are high morbidity and mortality for patients with tuberculous pericarditis.[1,2] Tuberculous constrictive pericarditis occurs secondary to exudative pericarditis, and is usually induced by *Mycobacterium tuberculosis*.[3] Tuberculous constrictive pericarditis is characterized by thickening, adhesion, fibrosis and calcification of the pericardium, which can damage the diastolic function and lead to a poor blood circulation.[3] Currently, chest *x*-ray, computer tomography (CT) and echocardiography examination are the main diagnostic methods for tuberculous constrictive pericarditis diagnosis.[4,5] However, some patients without the thickening and calcification of pericardium also show severe physiopathologic changes of constrictive pericarditis, which cannot be diagnosed according to the echocardiography examination.[4] Therefore, it is essential to explore more supplementary examinations and diagnostic indicators for the diagnosis of tuberculous constrictive pericarditis.

Electrocardiogram (ECG) is the most common examination to record cardiac electrical activity produced by each cardiac cycle.[6] ECG parameters, including heart rate, the time from the corrected ORS wave origin to T-wave terminal (QTc), ST-segment change and T-wave change, can be used to reflect cardiac dysfunctions, such as arrhythmia, cardiac hypertrophy and myocardial infarction (MI).[6,7] In addition, Morris et al. first introduced the P-wave terminal force (PTF) in lead V1 (PTFV1) measured by 12-lead ECG that can reflect the severity of the cardiac diseases.[8] However, few studies have investigated the diagnostic value of ECG parameters in tuberculous constrictive pericarditis diagnosis.

In the retrospective study, we recruited patients with tuberculous constrictive pericarditis and patients with tuberculous exudative pericarditis, then the baseline characteristics of demography, echocardiography results and ECG parameters were compared. The aim of this study was to explore the relationships of ECG parameters and

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tuberculous constrictive pericarditis. And the PTFV1 diagnostic value in the clinical diagnosis of tuberculous constrictive pericarditis was also investigated.

Methods

Patients

This retrospective study was approved by the Ethics Committee of Zhejiang TCM and Western medicine integrated hospital. A total of 53 patients with tuberculous constrictive pericarditis (27 males and 26 females; aged 36–82 years) and 64 patients with tuberculous exudative pericarditis (28 males and 36 females; aged 35–84 years) during the period from November 2013 to June 2016 at Zhejiang TCM and Western medicine integrated hospital were enrolled in this study. The tuberculous constrictive pericarditis and tuberculous exudative pericarditis were diagnosed and confirmed according to tuberculin test, T.SPOT-TB test, CT and echocardiography examination, and microbiological confirmation. Here, the microbiological confirmation mainly included smear and culture confirmation of pericardial effusion. Patients were enrolled in the tuberculous constrictive pericarditis group if they fulfilled all the following criteria: (1) with the enlargement of atrium, the broadening of postcava and hepatic vein through echocardiography examination; (2) with the chronic systemic circulation congestion and low cardiac output; (3) with the significant pericardial thickening or calcification through x-ray and CT examination; (4) with a $\leq$ 5 mmHg (1 mmHg = 0.133 kPa) of end-diastolic difference between the left and right ventricle; (5) with a $>$ 12 cmH2O of central venous pressure; (6) with granulomatous inflammation and caseating necrosis through pathological diagnosis. Patients with cirrhosis, pulmonary heart disease, valvulopathy, coronary heart disease, and restrictive cardiomyopathy were excluded. In addition, patients presented the classical pericarditic symptom were included in the tuberculous exudative pericarditis group if they met all the following criteria: (1) found the *Mycobacterium tuberculosis* through the smear or culture confirmation of pericardial effusion; or (2) with a $>$ 40 U/l of adenosine isoenzyme (ADA) level; (3) found the tuberculosis lesions in other positions; (4) with a $>$ 250 ml of pericardial exudate through x-ray; (5) with an increased heart shadow, and a disappeared normal outline of the cardiac margin; (6) with a fluid sonolucent area through echocardiography examination. Patients with rheumatic pericarditis, purulent pericarditis, nonspecific pericarditis, coronary heart disease, pulmonary heart disease, and cardiac tamponade were excluded. The demographic and clinical characteristics were recorded, including gender, age, the course of disease and New York Heart Association (NYHA) classification. Echocardiography examination was conducted using the Philips iU 33 Doppler ultrasonographic instrument (Philips Healthcare, Andover, MA, USA). Echocardiography data were also obtained, including left atrial diameter (LAD), left ventricular end-diastolic dimension (LVEDD) and left ventricular ejection fraction (LVEF).

ECG measurement

All patients received a standard 12-lead at rest ECG examination in supine position. The 12-lead ECG data were recorded by the trained ECGs doctors at double amplitude (20 mm/mV) and paper speed (50 mm/s) PTFV1 was measured and calculated as following: (1) five continuous PTFs in the sinus rhythm were selected and measured; (2) PTFV1 value was recorded as 0 if P-wave showed in a vertical state; (3) the intersection of horizontal line derived from initial point of the P-wave and descending line of the P-wave was marked when P-wave presented in the positive and negative terminal deflection, then the vertical diameter and the horizontal spacing between the intersection and terminal point of the P-wave were recorded as the amplitude and duration of the negative terminal deflection of the P-wave, respectively; (4) mean amplitude (mm) and duration (s) were calculated based on five continuous amplitudes and durations of the negative terminal deflection of the P-wave; (5) product of the mean amplitude (mm) and duration (s) was recorded as PTFV1 (mm·s) value. The PTFV1 abnormality was defined as PTFV1 value ≤ -0.04 mm·s according to previously described.[9] Additionally, the ECG parameters were recorded such as heart rate, and the presence or absence of bundle branch block or arrhythmia, which included atrial fibrillation, right bundle branch block (RBBB), atrial premature beat, ventricular premature beat, low voltage, ST-segment change and T-wave change.

Statistical analysis

SPSS 16.0 software (IBM Corporation, New York, USA) was applied to analyze all the data. Continuous variables were analyzed utilizing the normality test. Here, continuous variables with normal distribution were expressed as the mean $\pm$ standard deviation (SD) and analyzed by the t test, while data with abnormal distribution were analyzed using Wilcoxon rank sum test. Classification variables were represented as percentage (%), and then analyzed by chi-square test. In the current study, p value $<$ 0.05 were considered as statistically significant.

Results

Patient characteristics

The demographic and clinical characteristics of patients with tuberculous constrictive pericarditis and patients with tuberculous exudative pericarditis were presented in Table 1. There were no significant differences in age, gender and the course of disease between patients with tuberculous constrictive pericarditis and patients with tuberculous exudative pericarditis. For the NYHA classifications, the percentage of patients with tuberculous constrictive pericarditis in NYHA class II, III, and IV were respectively 22.6% (12/53), 56.6% (30/53), and 17.0% (9/53). Analogously, the percentage of patients with tuberculous exudative pericarditis in NYHA class II, III, and IV were respectively 37.5% (24/64), 32.8% (21/64), and 3.1% (2/64). These results showed a significant difference in different NYHA classifications between patients with tuberculous constrictive pericarditis and patients with tuberculous exudative pericarditis (p = 0.041, Table 1). The results of echocardiography examination revealed that there were similar LAD, LVEDD and LVEF between patients with

Table 1
The clinical and demographic characteristics of patients with tuberculous constrictive pericarditis and patients with tuberculous exudative pericarditis

Characteristics	Tuberculous constrictive pericarditis (n = 53)	Tuberculous exudative pericarditis (n = 64)	P values
Age (year)	61.52 ± 8.81	63.20 ± 11.21	0.438
Gender (male/female)	27/26	28/36	0.257
The course of disease (month)	18.62 ± 14.35	15.42 ± 10.73	0.106
NYHA classifications (%)			0.041
II	22.6% (12/53)	37.5% (24/64)	
III	56.6% (30/53)	32.8% (21/64)	
IV	17.0% (9/53)	3.1% (2/64)	
Echocardiography data			
LAD (mm)	43.56 ± 13.42	42.03 ± 12.35	0.224
LVEDD (mm)	47.21 ± 7.95	49.35 ± 8.67	0.193
LVEF	0.49 ± 0.12	0.51 ± 0.11	0.152

NYHA, New York Heart Association; LAD, left atrial diameter; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction.

Table 2
Electrocardiograph parameters of patients with tuberculous constrictive pericarditis and patients with tuberculous exudative pericarditis

Characteristics	Tuberculous constrictive pericarditis ($n = 53$)	Tuberculous exudative pericarditis ($n = 64$)	*P* values
Heart rate (beat/min)	89.38 ± 33.21	87.53 ± 31.70	0.209
Bundle branch block and arrhythmia (%)			
Atrial fibrillation	13.2% (7/53)	7.8% (5/64)	0.276
RBBB	13.2% (7/53)	12.5% (8/64)	0.728
Atrial premature beat	15.1% (8/53)	7.8% (5/64)	0.212
Ventricular premature beat	11.3% (6/53)	12.5% (8/64)	0.845
PTFV1 ≤ −0.04 mm·s (%)	64.2% (34/53)	9.4% (6/64)	< 0.001
QTc (ms)	401.36 ± 39.24	407.35 ± 40.13	0.324
Low voltage (%)	43.4% (23/53)	42.2% (27/64)	0.895
ST-segment change (%)	67.9% (36/53)	59.4% (38/64)	0.340
T-wave change (%)	20.8% (11/53)	20.3% (13/64)	0.708

RBBB, right bundle branch block; PTFV1, P terminal force in lead V1; QTc corrected QT.

tuberculous constrictive pericarditis and patients with tuberculous exudative pericarditis (Table 1).

Comparison of ECG parameters

ECG parameters were compared between patients with tuberculous constrictive pericarditis and patients with tuberculous exudative pericarditis (Table 2). No significant differences were found in heart rate (89.38 ± 33.21 vs 87.53 ± 31.70 beat/min) and QTc (401.36 ± 39.24 vs 407.35 ± 40.13) ($p > 0.05$). Moreover, there were no significant differences in the incidence rates of atrial fibrillation (13.2% vs 7.8%), RBBB (13.2% vs 12.5%), atrial premature beat (15.1% vs 7.8%), ventricular premature beat (11.3% vs 12.5%), low voltage (43.4% vs 42.2%), ST-segment change (67.9% vs 59.4%) and T-wave change (20.8% vs 20.3%) between patients with tuberculous constrictive pericarditis and patients with tuberculous exudative pericarditis (Table 2, p > 0.05). Compared with patients with tuberculous exudative pericarditis, the incidence rate of abnormal PTFV1 (≤ −0.04 mm·s) was obviously increased in patients with tuberculous constrictive pericarditis (64.2% vs 9.4%, $p < 0.001$, Table 2). Furthermore, a receiver operating characteristic curve (ROC) analysis was performed to investigate the diagnostic performance of PTFV1 for tuberculous constrictive pericarditis. As shown in Fig. 1, the area under the ROC curve was 0.78, and the optimal cut-off value was 0.02. The sensitivity, specificity, positive predictive value, and negative expected value were respectively 64.2%, 90.6%, 85%, and 75.3%.

Typical cases

A 68-year-old male patient has been diagnosed with tuberculous constrictive pericarditis for two years. ECG image was illustrated in Fig. 2A, which presented sinus tachycardia, the change of ST-T and abnormal PTFV1. Similarly, a 60-year-old male patient has also been diagnosed with tuberculous constrictive pericarditis for one and half year. Notably, sinus rhythm, T-wave change and abnormal PTFV1 were observed in his ECG image (Fig. 2B).

Discussion

In the present study, our results presented that the percentage of patients located in NYHA class IV in the patients with tuberculous constrictive pericarditis was significantly higher than those of patients with tuberculous exudative pericarditis. The similar results of echocardiography examination could be observed in patients with tuberculous constrictive pericarditis and patients with tuberculous exudative pericarditis, including LAD, LVEDD and LVEF. Moreover, no

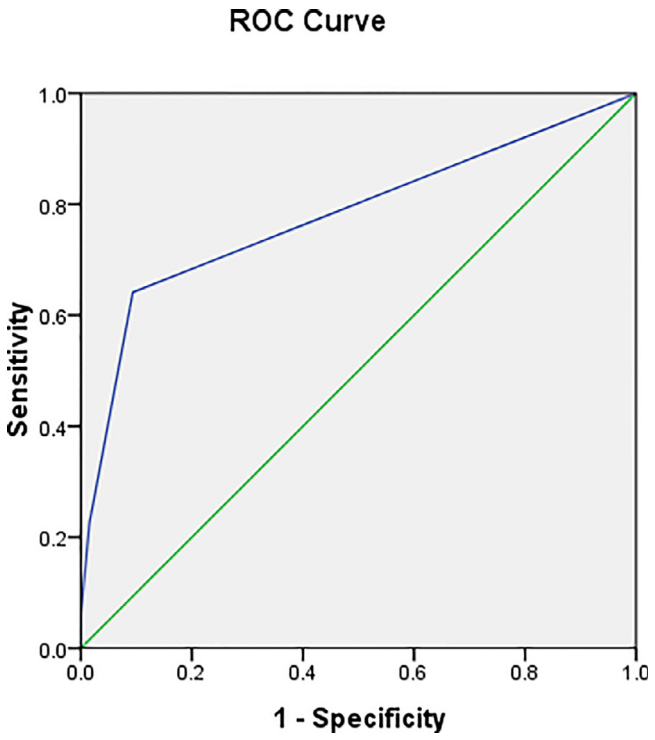

Fig. 1. ROC analysis for the PTFV1 value. ROC, receiver operating characteristic; PTFV1, P-wave terminal force in lead V1.

obvious differences were found in ECG parameters such as heart rate, the incidence rates of atrial fibrillation, RBBB, atrial premature beat, ventricular premature beat, low voltage, ST-segment change and T-wave change between patients with tuberculous constrictive pericarditis and patients with tuberculous exudative pericarditis. Furthermore, the incidence rate of abnormal PTFV1 (≤ −0.04 mm·s) in patients with tuberculous constrictive pericarditis was remarkably higher than those of patients with tuberculous exudative pericarditis.

PTFV1 had been regarded as a specific indicator to reflect left atrial structural abnormalities, and was related to the diastolic function of left ventricular.[10] In an early study, normal reference value of PTFV1 is defined as 0.03 mm·s, and about 7% of abnormal PTFV1 is apparently appeared in healthy middle-aged men.[11] Recently, PTFV1 ≤ −0.04 mm·s is considered as abnormal PTFV1.[12] Consequently, the present study selected −0.04 mm·s as the normal reference value of PTFV1. Generally, the abnormality of PTFV1 could be explained as the following two mechanisms: (1) the left atrial time depolarization and left atrial depolarization vector would be increased when left atrial load increase, hypertrophy, ischemia and fibrosis; (2) right atrial load increase and hypertrophy as well as prolonged interatrial bundle conduction interval could induce increased amplitudes and broadened durations of the negative terminal deflection of the P-wave. Previous studies indicated that abnormal PTFV1 was associated with left ventricular diastolic dysfunction, atrial fibrillation, stroke, congestive heart failure and mortality.[10,13–17] Abnormal PTFV1 could also predict the risk of adverse cardiovascular events.[18] In addition, PTFV1 was proved to be related to the pulmonary emphysema.[19] These above findings all revealed that PTFV1 has a clinical diagnostic value in some diseases. However, studies about PTFV1 diagnostic value in tuberculous constrictive pericarditis are sparse. Intriguingly, the present study showed that abnormal PTFV1 occurred in 64.2% of patients with tuberculous constrictive pericarditis, while only 9.4% of patients with tuberculous exudative pericarditis presented abnormal PTFV1. These results might be

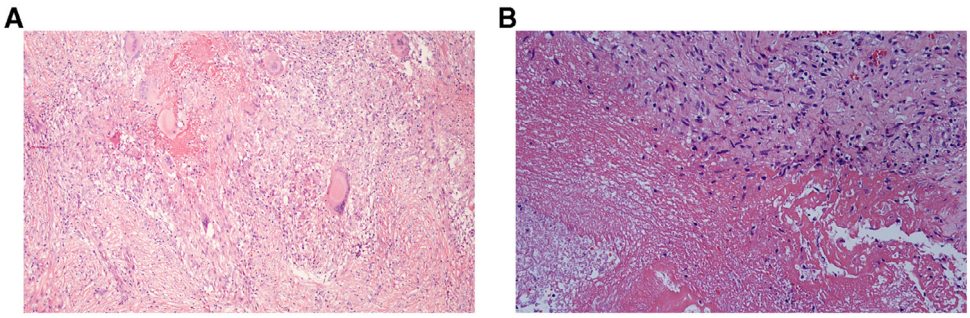

Fig. 2. Electrocardiograph images of a 68-year-old male patient with tuberculous constrictive pericarditis for two years (A) and a 60-year-old male patient with tuberculous constrictive pericarditis for one and half year (B).

explained that the thickening, adhesion, fibrosis and calcification of the pericardium resulted in the poor blood circulation, and then left and right atrial load increased, which eventually led to the PTFV1 abnormality. In addition, NYHA classification could reflect the damaged degree of the cardiac function.[20] Here, our results presented that the percentage of patients located in NYHA class IV was significantly higher in the patients with tuberculous constrictive pericarditis than those of patients with tuberculous exudative pericarditis. The result could partly explain the increased incidence rate of abnormal PTFV1. Altogether, these results indicated a close association of abnormal PTFV1 and tuberculous constrictive pericarditis. The PTFV1 abnormality examined by ECG might be served as an important auxiliary diagnostic indicator for the clinical diagnosis of tuberculous constrictive pericarditis, which could remedy the limitation of x-ray, CT and echocardiography examination in the tuberculous constrictive pericarditis diagnosis. Briefly, PTFV1 abnormality has a crucial diagnostic value in the clinical diagnosis of tuberculous constrictive pericarditis.

However, there are some limitations in our study. Firstly, this is a retrospective study with the small sample size, and the results of this study should be confirmed by more prospective studies with larger sample size confirm. Secondly, this study could not confirm that whether abnormal PTFV1 is a predictive indicator for the development of tuberculous exudative pericarditis from tuberculous constrictive pericarditis. Also, this question will be investigated in the future.

In summary, our results indicate that abnormal PTFV1 (≤ -0.04 mm·s) is associated with tuberculous constrictive pericarditis, and PTFV1 may be a potential diagnostic index for the diagnosis of tuberculous constrictive pericarditis.

Competing interests

All authors declare that they have no competing interest to state.

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Supplementary data

Supplementary data related to this article can be found at doi:10.1016/j.hrtlng.2018.09.007.

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