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Prevalence and heart rate variability characteristics of premature ventricular contractions detected by 24-hour Holter among outpatients with palpitations in China: a cross-sectional study

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ABSTRACT

Objective To analyse the prevalence and heart rate variability (HRV) characteristics of premature ventricular contraction (PVC) detected by 24-hour Holter among Chinese outpatients with palpitations.

Design A cross-sectional study.

Setting This study was conducted in a tertiary hospital.

Participants A total of 4754 outpatients who received 24-hour Holter for palpitations.

Main outcome measures Prevalence, HRV time-domain and frequency-domain analyses of 24-hour Holter, and echocardiographic parameters were assessed. Propensity score matching (PSM) was applied to balance baseline variables (age, gender) to decrease the bias between comparison groups.

Results The prevalence of PVC was 67.7% (3220/4754), and was higher in men than women (69.9% vs 66.0%, p=0.004); the prevalence of frequent PVCs (PVC burden≥5%) was 7.7% (368/4754). Older patients had the highest frequency of PVC among all patients. However, among 3220 patients with PVC, younger patients' PVC burden was much higher. Matched 1:1 by age and gender, the HRV time-domain parameters in patients with PVC were all lower than those in patients without PVC (all p<0.05); for the HRV frequency-domain parameters, the patients with frequent PVCs had a higher low frequency/high frequency (LF/HF) ratio (5.4 vs 2.8, p<0.001) than those with PVC burden less than 5%.

Conclusions The prevalence of PVC and frequent PVCs were 67.7% and 7.7%, respectively, detected by 24-hour Holter among Chinese outpatients with palpitations. Decreased HRV time-domain parameters suggested the occurrence of PVC, and increased LF/HF ratio represented the imbalance of autonomic nervous system in patients with frequent PVCs. Further studies are needed to understand the HRV indexes in PVC patients.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is a cross-sectional study with a large sample size.
⇒ The heart rate variability parameters were used to evaluate cardiac autonomic tone, reflecting the interplay of sympathetic and parasympathetic nervous systems.
⇒ Propensity score matching was applied to balance baseline variables (age, gender) to decrease the bias.
⇒ A single 24-hour Holter recording may not reflect the true premature ventricular contraction (PVC) burden because of the daily variability in PVC frequency.

INTRODUCTION

Premature ventricular contraction (PVC) is the most common type of ventricular arrhythmias. It has been reported that the prevalence of PVC is 1%–4% based on the detection of 12-lead electrocardiography (ECG) and 40%–75% based on the 24-hour to 48-hour Holter monitoring in the general population.[1 2] However, most of the data on the characteristics of PVC were obtained from the Western population. A recent cross-sectional study[3] of 517 Japanese men showed that 429 (83%) men had at least 1 PVC in 1 hour detected by 24-hour Holter. Hwang *et al*[4] also investigated the clinical characteristics and features of frequent idiopathic PVCs in 666 Korean participants. However, the frequency and characteristics of PVCs in the Chinese population have not yet been studied in large samples.

The autonomic nervous system is important in ventricular arrhythmias, including PVC and ventricular tachycardia.[5] Heart rate variability (HRV) is a non-invasive marker used to estimate the modulation of cardiac autonomic nerves, describing the oscillations between consecutive ECG R–R intervals. HRV is associated with age, circadian rhythm, exercise, respiratory rate, metabolic diseases and cardiovascular diseases.[6–8] It has been shown to be an independent predictor of

cardiovascular risk.[9 10] Tang *et al*[11] reported using short-term HRV indexes to diagnose of cardiovascular autonomic neuropathy with high sensitivity and specificity. Jørgensen *et al*[12] and Zhang *et al*[13] all demonstrated the important value of HRV in predicting ventricular tachyarrhythmias in patients with acute myocardial infarction.

Whereas, the association between HRV and PVC in the general population still remains controversial.[14 15] Chen *et al*[14] reported that the number of PVCs was not significantly correlated with HRV parameters in patients with mitral valve prolapse. A study conducted by Barutçu *et al*[15] showed that the number of PVCs was positively correlated with the low frequency/high frequency (LF/HF) ratio (one of the HRV parameters) in patients with frequent PVCs (more than 30 times in 1 hour). Therefore, the relationship between PVC and HRV in the general population needs to be explored in the large sample studies.

This study aimed to investigate the prevalence and clinical characteristics of PVC detected by 24-hour Holter monitoring among outpatients with palpitations in a single Chinese centre; and to analyse the relationship between PVC and HRV in these patients.

METHODS

Study design and participants

This cross-sectional and observational study included outpatients who underwent 24-hour Holter for palpitations in the First Affiliated Hospital of Nanjing Medical University between 1 January and 31 December in 2015. The exclusion criteria were: (1) patients aged<18 years old; (2) patients with short Holter recording duration (<20 hours); (3) patients with incomplete recorded parameters of 24-hour Holter. Only the data of the first 24-hour Holter was recorded if a patient received the 24-hour Holter several times.

24-HOUR HOLTER MONITORING

All participants underwent a 24-hour Holter ECG monitoring by using a validated three-channel device (Seer Light Dynamic ECG record system, GE Healthcare, USA). The parameters recorded by 24-hour Holter consisted of PVC, average heart rate and HRV indexes. The PVC was defined as an early ventricular depolarisation of ectopic excitatory foci of the ventricular muscles with a wide QRS complex (figure 1). The PVC burden was defined as the percentage of PVCs relative to the total QRS complexes on a 24-hour Holter. In the existing study, the frequent PVCs were considered to be >5% of PVC burden, which has been reported as the least resulting in cardiomyopathy.[16 17]

HRV analysis

The HRV data, including time-domain and frequency-domain parameters, were automatically calculated by the MARS software (GE Medical). The first step before HRV analysis was to determine and extract the consecutive ECG R–R interval time series. When processing the R–R interval time series for HRV analysis, it is necessary to consider aspects related to signal quality, the excerpt to be used and the presence of ectopic beats, arrhythmias and noise.[18] If non-stationary signals are identified, the trend should be validated and removed from the beat-to-beat data using filters or specific algorithms.[18] The HRV parameters were used to evaluate cardiac autonomic tone, reflecting the interplay of sympathetic and parasympathetic (vagal) nervous systems.

HRV time-domain analysis

The parameters of HRV time-domain analysis[19 20] included the SD of all NN intervals (SDNN), SD of average of NN intervals in all 5 min segments (SDANN), the square root of the mean of the sum of the squares of differences between adjacent NN intervals (rMSSD), and percent of NN50 in the total number NN interval (PNN50). NN50 was defined as the NN interval longer than 50 ms. The SDNN and SDANN, indexes of sympathetic activation, were negatively correlated with sympathetic activity, while the rMSSD and PNN50, indexes of parasympathetic activation, were positively correlated with parasympathetic activity.

HRV frequency-domain analysis

The HRV frequency-domain analysis[19 20] contained the following parameters: power in the LF ranging from 0.04 to 0.15 Hz, power in the HF ranging from 0.15 to 0.4 Hz and the LF/HF ratio. The HF component was used as an index of vagal activity, while the LF component represented a mixture of both vagal and sympathetic activity. The high LF/HF ratio represented the autonomic nervous system imbalance.

Transthoracic echocardiography

Transthoracic echocardiography (TTE) (Vivid E9, GE Healthcare, Chicago, USA) was performed to detect structural heart disease (SHD) according to the recommendations of the American Society of Echocardiography Committee.[21] The parameters included left ventricular end-diastolic diameter and left ventricular ejection fraction (LVEF). The LVEF was measured using the Simpson's method. A baseline LVEF<50% was considered to have LV systolic dysfunction.[21 22]

Statistical analysis

All statistical analyses were performed using IBM SPSS software (V.25.0). Continuous variables with a normal distribution were presented as mean±SD and were compared using the two-sample t-test. Non-normally distributed continuous variables were presented as median with IQR and were compared using the Mann-Whitney U test. Categorical variables were presented as frequency (percentage) and were analysed using the χ^2 test or Fisher's exact test. Propensity score matching (PSM) was used to select controls to minimise potential confounding bias. The propensity scores were constructed using the following variables: age and gender. We conducted a

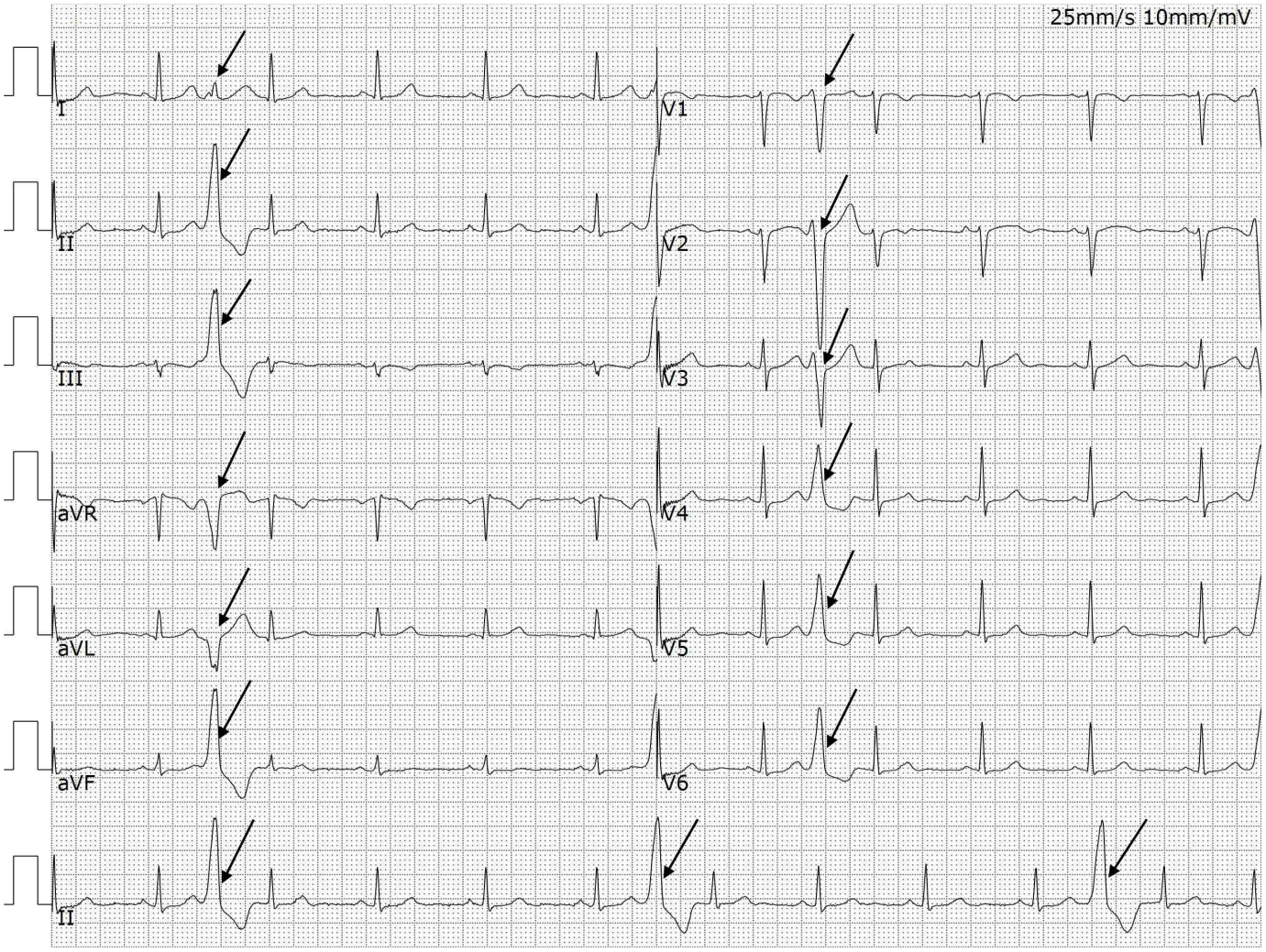

Figure 1 Example of premature ventricular contraction (PVC). The arrows show the morphology of PVC.

nearest-neighbour matching algorithm without replacement, using a calliper width of 0.02. Spearman's correlation analysis was performed to show the correlation between HRV parameters and clinical characteristics among patients with PVC. A two-tailed p value of <0.05 was considered statistically significant.

Patient and public involvement

Patients or the public were not involved in the design, conduct, reporting or dissemination plans of our research.

RESULTS

Prevalence and distribution of PVC in 4754 patients

A total of 4754 patients with palpitations were included. Mean age was 57.4±16.0 years old, and 44.4% of patients were male. The prevalence of PVC detected by 24-hour Holter monitoring among 4754 patients with palpitations is shown in figure 2. A total of 3220 (67.7%) patients had at least one PVC, with 2852 (60.0%) having PVC burden<5% and 368 (7.7%) having PVC burden≥5%.

Figures 3 and 4 depict the prevalence of PVC and frequent PVCs in 4754 patients regarding their gender and age group, respectively. The PVC prevalence was 67.7% higher in men than in women (69.9% vs 66.0%, p=0.004). It generally increased with age, ranging from

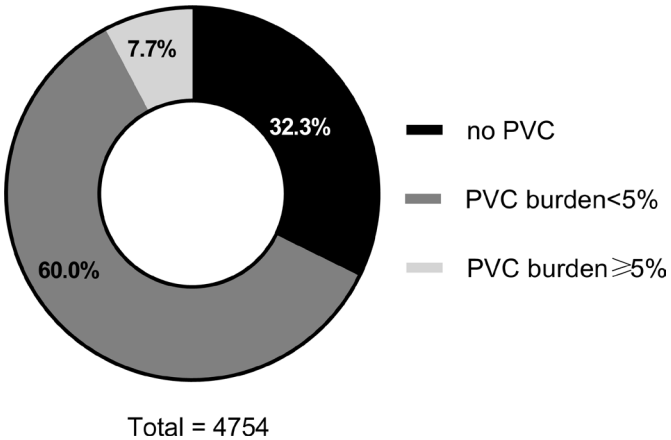

Figure 2 The prevalence of PVC detected by 24-hour Holter monitoring in 4754 patients with palpitations. A total of 3220 (67.7%) patients had at least 1 PVC, with 2852 (60.0%) having PVC burden<5% and 368 (7.7%) having PVC burden≥5%. PVC, premature ventricular contraction.

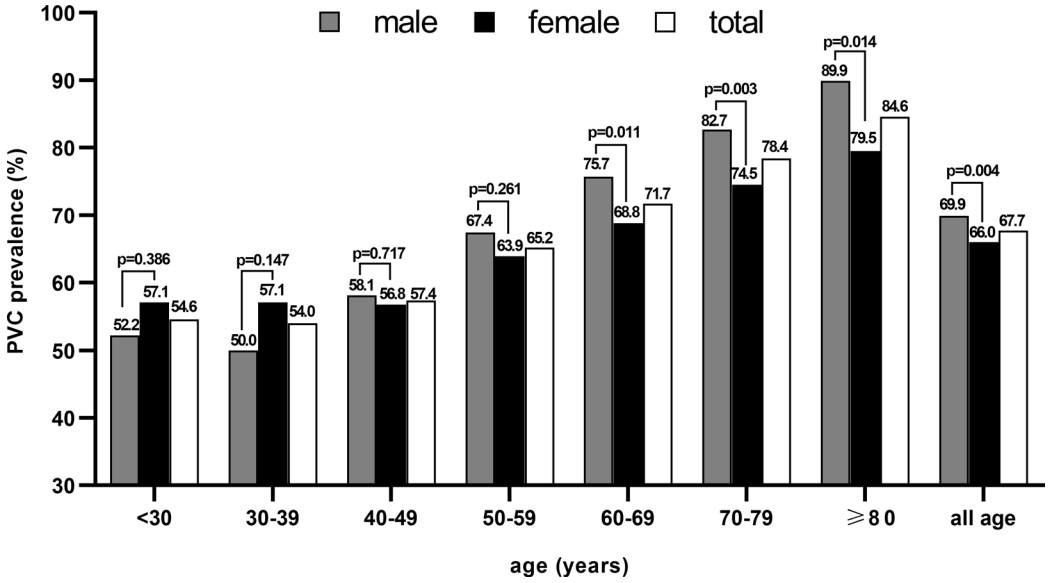

Figure 3 The prevalence of PVC detected by 24-hour Holter monitoring in 4754 patients of different gender and age groups. The PVC prevalence was 67.7% in men than in women (69.9% vs 66.0%, p=0.004). It generally increased with age, ranging from 54.0% (30–39 age group) to 84.6% (≥80 age group). PVC, premature ventricular contraction.

54.0% (30–39 age group) to 84.6% (≥80 age group). Interestingly, PVC prevalence was higher in men than in women in the >60 years of age group, while it was comparable in men and women in the <60 years of age group. The prevalence of frequent PVCs was 7.7%, with no significant difference between men and women (7.6% vs 7.8%, p=0.779).

Figure 5 shows the mean PVC burden in 3220 PVC patients of different ages. The PVC burden decreased as age increased, except for three very elderly patients with higher PVC burden (patient 1, woman, 89 years old, PVC burden 30.2%; patient 2, man, 88 years old, PVC burden 12.8%; patient 2, woman, 88 years old, PVC burden 16.6%).

Comparison of HRV parameters between patients with and without PVC

Table 1 compares of HRV parameters between patients with and without PVC before and after PSM based on age and gender. A total of 3220 (67.7%) patients had more than 1 PVC, while 1534 (32.3%) patients had no PVC during the 24-hour Holter. Totally, 3220 patients with PVC were older than those without PVC (59.6±15.6 vs 53.0±15.8, p<0.001), with a higher proportion of men (45.9% vs 41.5%, p=0.004). In addition, HRV time-domain and frequency-domain parameters in patients with PVC were significantly lower than those in patients without PVC (all p<0.05).

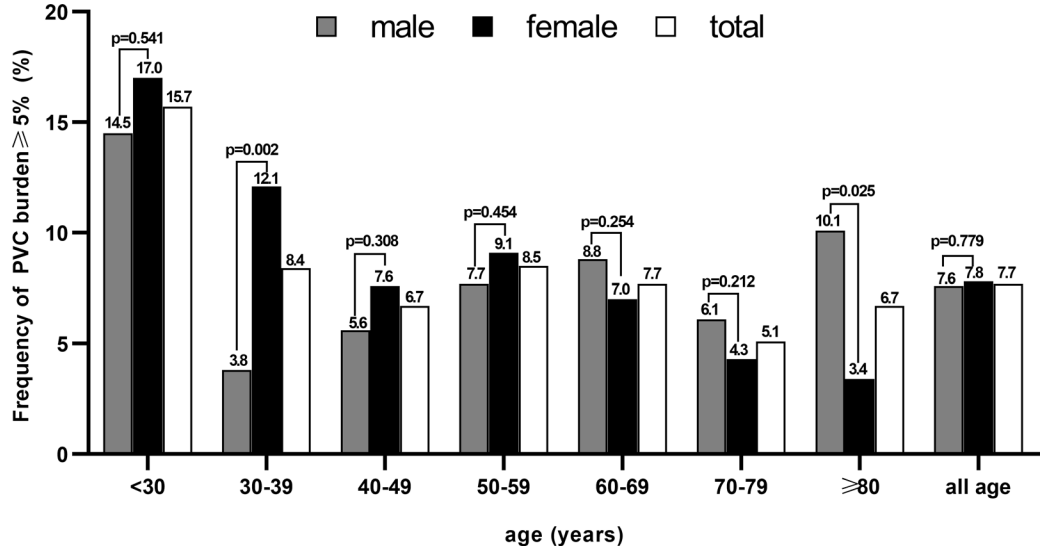

Figure 4 The frequency of frequent PVCs (PVC burden≥5%) based on 24-hour Holter monitoring in 4754 patients of different gender and age groups. The frequency of frequent PVCs (PVC burden≥5%) was 7.7%, with no significant difference between men and women (7.6% vs 7.8%, p=0.779). PVC, premature ventricular contraction.

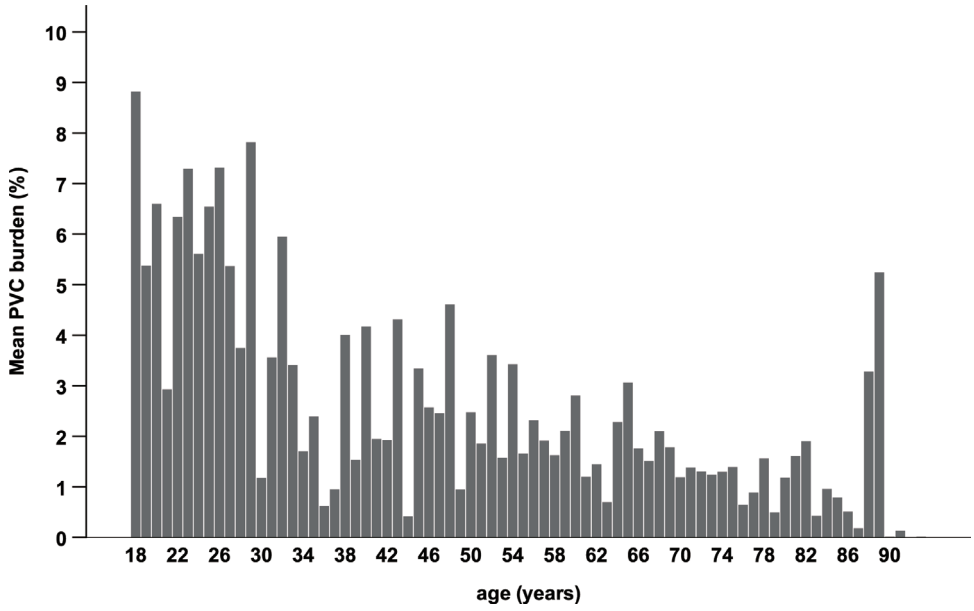

Figure 5 The mean PVC burden based on 24-hour Holter monitoring in 3220 patients with PVC. The PVC burden decreased as age increased, except for three very elderly patients with higher PVC burden. PVC, premature ventricular contraction.

Table 1 Comparison of HRV parameters between patients with and without PVC before and after 1:1 PSM based on age and gender

	Before PSM			After PSM		
	PVC≥1 N=3220	No PVC N=1534	P value	PVC≥1 N=1533	No PVC N=1533	P value
Age (years)	59.6±15.6	53.0±15.8	<0.001*	53.1±15.4	53.0±15.8	0.84
Male (%)	1477 (45.9)	636 (41.5)	0.004*	690 (45.0)	635 (41.4)	0.05
Average heart rate (bpm)	71.6±10.5	72.1±10.1	0.11	72.4±10.6	72.1±10.1	0.34
HRV time-domain parameters						
SDNN (ms)	124.1±57.8	133.2±46.6	<0.001*	128.4±52.6	133.2±46.7	0.007*
SDANN (ms)	110.3±50.0	119.9±43.0	<0.001*	114.6±48.9	119.9±43.0	0.001*
rMSSD (ms)	28.4±16.2	31.1±14.9	<0.001*	29.5±15.5	31.1±14.9	0.003*
pNN50 (%)	5.6 (1.7,13.0)	7.1 (2.9,14.2)	<0.001*	6.4 (2.3,14.0)	7.1 (2.9,14.2)	0.01*
HRV frequency-domain parameters						
LF (nu)	45.6 (10.2,249.8)	59.0 (12.8,289.1)	<0.001*	45.6 (11.7,287.8)	59.0 (12.9,289.4)	0.05
HF (nu)	21.5 (0.6,113.6)	28.2 (0.9,138.1)	<0.001*	21.5 (0.7,124.3)	28.2 (0.9,138.3)	0.007*
LF/HF	2.8 (1.6,12.0)	2.9 (1.7,13.7)	<0.001*	3.1 (1.8,12.3)	2.9 (1.7,13.7)	0.64
TTE parameters						
LVDd (mm)	47.7±5.0	46.7±4.2	<0.001*	48.0±5.2	46.7±4.2	<0.001*
LVEF (%)	64.1±5.8	65.3±3.8	<0.001*	64.0±6.2	65.3±3.8	<0.001*
LVEF<50% (%)	67 (3.3)	5 (0.6)	<0.001*	41 (4.3)	5 (0.6)	<0.001*

Values are expressed as either mean±SD, median (IQR) or number (percentage).
*P<0.05.
HF, high frequency; HRV, heart rate variability; LF, low frequency; LVDd, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; NN50, the NN interval longer than 50 ms; PNN50, percent of NN50 in the total number NN interval; PSM, propensity score matching; PVC, premature ventricular contraction; rMSSD, the square root of the mean of the sum of the squares of differences between adjacent NN intervals; SDANN, SD of average of NN intervals in all 5 min segments; SDNN, SD of all NN intervals; TEE, transthoracic echocardiography.

Table 2 Comparison of HRV parameters between patients with PVC burden≥5% and <5% before and after 1:1 PSM based on age and gender

	Before PSM			After PSM		
	PVC burden≥5% N=368	PVC burden<5% N=2852	P value	PVC burden≥5% N=368	PVC burden<5% N=368	P value
Age (years)	53.8±17.2	60.3±15.3	<0.001*	53.8±17.2	54.9±17.0	0.40
Male (%)	161 (43.8)	1316 (46.1)	0.39	161 (43.8)	175 (47.6)	0.30
Average heart rate (bpm)	72.8±9.3	71.4±10.6	0.02*	72.8±9.3	72.3±10.5	0.50
HRV time-domain parameters						
SDNN (ms)	134.1±60.4	122.8±57.3	<0.001*	134.1±60.4	130.1±51.2	0.33
SDANN (ms)	114.5±41.9	109.7±50.9	0.08	114.5±41.9	116.6±47.6	0.53
rMSSD (ms)	32.3±15.6	28.0±16.2	<0.001*	32.3±15.6	30.1±16.1	0.06
pNN50 (%)	7.5 (3.2,16.4)	5.3 (1.5,12.5)	<0.001*	7.5 (3.2,16.4)	6.3 (2.0,14.0)	0.05
HRV frequency-domain parameters						
LF (nu)	23.8 (8.2,267.0)	45.6 (10.5,249.8)	0.24	23.8 (8.2,267.0)	66.7 (13.3,274.5)	0.01*
HF (nu)	9.4 (0.7,89.9)	21.5 (0.6,116.0)	0.35	9.4 (0.7,89.9)	26.4 (0.8,127.3)	0.04*
LF/HF	5.4 (2.1,11.3)	2.6 (1.5,12.1)	<0.001*	5.4 (2.1,11.3)	2.8 (1.7,11.9)	<0.001*
TTE parameters						
LVDd (mm)	48.2±5.4	47.7±4.9	0.09	48.2±5.4	47.3±4.5	0.04*
LVEF (%)	63.4±6.8	64.2±5.6	0.03*	63.4±6.8	64.4±5.3	0.06
LVEF<50% (%)	14 (5.2)	56 (3.2)	0.11	14 (5.2)	6 (2.7)	0.17

Values are expressed as either mean±SD, median (IQR) or number (percentage).
*P<0.05.
HF, high frequency; HRV, heart rate variability; LF, low frequency; LVDd, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; NN50, the NN interval longer than 50 ms; PNN50, percent of NN50 in the total number NN interval; PSM, propensity score matching; PVC, premature ventricular contraction; rMSSD, the square root of the mean of the sum of the squares of differences between adjacent NN intervals; SDANN, SD of average of NN intervals in all 5 min segments; SDNN, SD of all NN intervals; TEE, transthoracic echocardiography.

After PSM, there were 1533 patients in each group. There were no significant gender and age distribution differences between the two groups. The HRV time-domain parameters in patients with PVC were lower than those in patients without PVC (all p<0.05). There were no significant differences in the frequency-domain parameters except HF. Compared with patients without PVC, HF was significantly decreased in patients with PVC (21.5 vs 28.2, p=0.007). We observed a significantly higher proportion of LVEF<50% in patients with PVC than in patients without PVC, either before or after PSM.

Comparison of HRV parameters between patients with PVC burden≥5% and <5%

Table 2 shows the clinical characteristics of patients with PVC burden≥5% and <5% before and after PSM. Among 3220 (67.7%) PVC patients, 368 (7.7%) had PVC burden≥5% and 2852 (60.0%) had PVC burden<5%. Patients with PVC burden≥5% were younger than those with PVC burden<5% (53.8±17.2 vs 60.3±15.3, p<0.001). The average heart rate was significantly higher in patients with PVC burden≥5% compared with those with PVC burden<5% (72.8±9.3 vs 71.4±10.6, p=0.02). The HRV time-domain parameters were significantly lower in patients with PVC burden≥5% (all p<0.05). For the HRV frequency-domain parameters, the LF and HF were comparable between the two groups, while the LF/HF in patients with a PVC burden of ≥5% was significantly higher than those with a PVC burden<5% (5.4 vs 2.6, p<0.001).

After PSM based on age and gender, no significant difference was observed in the average heart rate between the two groups. There were also no significant differences between the two groups in the HRV time-domain parameters, including SDNN, SDANN, rMSSD and pNN50, between the two groups. For the HRV frequency-domain parameters, the patients with PVC burden≥5% had lower LF (23.8 vs 66.7, p=0.01), lower HF (9.4 vs 26.4, p=0.04), but higher LF/HF ratio (5.4 vs 2.8, p<0.001) than those with PVC burden<5%. The proportions of LVEF<50% were both comparable between the two groups before and after PSM. Only 14 (5.2%) patients had LV systolic dysfunction (LVEF<50%) among patients with frequent PVCs

Table 3 demonstrates the correlation analyses between HRV parameters and clinical characteristics in patients with PVC. Each HRV time-domain and frequency-domain

Table 3 Correlation analyses between HRV parameters and clinical characteristics in patients with PVC (N=3220)

	Age (years)		PVC burden (%)	
	r	P value	r	P value
SDNN (ms)	−0.232	<0.001*	0.002	0.897
SDANN (ms)	−0.222	<0.001*	−0.022	0.208
rMSSD (ms)	−0.185	<0.001*	0.047	0.008*
pNN50 (%)	−0.209	<0.001*	0.041	0.019*
LF (nu)	−0.174	<0.001*	−0.061	0.001*
HF (nu)	−0.138	<0.001*	−0.062	<0.001*
LF/HF	−0.153	<0.001*	0.073	<0.001*

*P<0.05.
HF, high frequency; HRV, heart rate variability; LF, low frequency; NN50, the NN interval longer than 50 ms; PNN50, percent of NN50 in the total number NN interval; PVC, premature ventricular contraction; rMSSD, the square root of the mean of the sum of the squares of differences between adjacent NN intervals; SDANN, SD of average of NN intervals in all 5 min segments; SDNN, SD of all NN intervals.

parameter were weakly correlated with age (all r<0.3, p<0.001). The LF/HF ratio was weakly correlated with the PVC burden (r=0.073, p<0.001).

DISCUSSION

To the best of our knowledge, no data to date are available about the prevalence and clinical characteristics of PVC in a large number of Chinese patients. Previous studies on PVC were mostly limited by the small sample sizes of patients referred for PVC ablation. The main findings of the present study are: (1) the prevalence of PVC in our population was 67.7% and was higher in men; the prevalence of frequent PVCs was 7.7%; (2) the HRV time-domain parameters in PVC patients were significantly decreased compared with patients without PVC; (3) patients with frequent PVCs had higher LF/HF ratio, suggesting the autonomic nervous system imbalance; (4) among patients with frequent PVCs, only 14 (5.2%) patients had LV systolic dysfunction, reflecting that the LV systolic functions in these patients were mostly in a compensatory state.

Prevalence of PVC detected by 24-hour Holter

In this large population-based study, which included 4754 patients, we found that 3220 (67.7%) had at least one PVC during 24-hour Holter monitoring. The prevalence of PVC in our study is consistent with that of the prevalence of PVC in another study that included 2048 young and healthy adults from Liechtenstein's group (68.7%).[23] However, it was reported that the PVC prevalence was 6% using 2 min ECG recordings in the Atherosclerosis Risk in Communities study.[24] The detection rate of PVCs using 24-hour Holter monitoring is significantly higher than that using 12-lead ECG and 2 min ECG recordings. Therefore, the ACC and AHA expert consensus recommends the Holter analysis for patients with palpitations and dizziness as class I indications for further evaluation.[25]

Relationship between PVC and gender

Our data showed that men had a higher prevalence of PVC than women. Currently, there is still no conclusion about whether the prevalence of PVC is higher in men or women. A study[26] conducted in Japan, which included 5685 subjects, showed no significant difference in the prevalence of PVC between the genders. However, Sirichand *et al*[27] demonstrated that the incidence of symptomatic idiopathic PVC was greater in women. Therefore, the differences among these studies may be attributed to different study populations.

PVC and HRV time-domain parameters

HRV, a non-invasive marker used to estimate the cardiac autonomic function, describes the oscillations between consecutive ECG R–R intervals. High levels of HRV parameters are generally signs of efficient autonomic mechanisms in a healthy individual, while reduced HRV parameters often show an autonomic nervous system malfunction.[18] Various studies have shown that reduced HRV is associated with increased cardiovascular morbidity and mortality.[10] Low values of HRV parameters are a strong predictor of a low probability of survival in patients with heart failure, prior myocardial infarction or bypass surgeries.[28] In our study, between age-matched and gender-matched cohorts with or without PVC, HRV time-domain parameters were reduced in PVC patients as compared with those without PVC. We speculate that low values of HRV time-domain parameters could be a predictor of PVC occurrence, and individuals prone to have PVC could be easily screened by HRV time-domain parameters. Among four parameters of HRV time-domain analysis, it has been recognised that the SDNN and SDANN were negatively correlated with sympathetic activity, and the rMSSD and PNN50 were positively correlated with vagal activity. In the present study, patients with PVC had lower SDNN, SDANN, rMSSD and PNN50 than patients without PVC, illustrating that sympathetic activity was enhanced and vagal activity was reduced in PVC patients. This is the way beta-blockers treat PVC—by inhibiting sympathetic nerves. But beta-blockers may not have a therapeutic effect on various PVCs. Hamon *et al*[29] reported that only patients displaying a positive correlation between the heart rate and hourly PVC count (a fast-HR-dependent PVC profile) benefited from beta-blockers. However, Yu *et al*[30] reported that the number of night-time PVCs (a slow-HR-dependent PVC profile) was an independent predictor of decreased SDNN (β=−0.446, p=0.030) and increased LF/HF ratio (β=0.027, p=0.038), indicating the enhanced cardiac sympathetic activity as well. The result was contrary to the previous well accepted view that night-time PVCs coincides with vagal activity excitation. The relationship of the night-time PVCs and autonomic nerve system remains controversial and needs to be further explored. The analysis of Holter PVC diurnal

variability may provide incremental value to guide clinical PVC management.

PVC and HRV frequency-domain parameters

Frequency-domain parameters include LF, HF and the LF/HF ratio. It is widely recognised that HF denotes parasympathetic activity and the LF/HF ratio represents the autonomic nervous system balance. In the present study, we observed a lower HF but higher LF/HF ratio in patients with frequent PVCs, indicating the decreased excitability of the parasympathetic nerves and the imbalance of the sympathetic-parasympathetic nervous system.[31 32] However, the interpretation of the LF component is still controversial as some studies defined it as a marker of sympathetic modulation, while others reported it as a marker showing the comprehensive influence of sympathetic and vagal nervous systems.[30] In our study, the LF was lower in patients with frequent PVCs than in those with a PVC burden of <5%. However, Askin *et al*[32] reported that the LF in the group with frequent PVCs (>10 PVCs/hour) was significantly increased as compared with the group with occasional PVCs (5–10 PVCs/hour). The true meaning of LF in patients with PVC needs to be further investigated.

PVC burden and LV systolic function

Several studies have demonstrated that a high burden of PVCs is associated with the development of LV systolic dysfunction and heart failure.[33 34] Presently, no clear cut-off points delineate the PVC burden at which LV systolic dysfunction may develop. In the present study, patients with PVC had a higher proportion of LV systolic dysfunction compared with those without PVC, while patients with frequent PVC had a comparable proportion of LV systolic dysfunction than those with PVC burden<5%. The major reasons may be as follows: first, several studies have demonstrated an association between frequent PVCs and LV systolic dysfunction.[33 34] Whereas, those patients were mostly hospitalised for radiofrequency catheter ablation due to LV systolic dysfunction. In the present study, the cardiac functions of patients are mostly in a compensatory state because only a few patients (5.2%) developed LV systolic dysfunction (LVEF<50%). Therefore, we could not conclude the relationship between PVC burden and LV function in patients with preserved LVEF. Second, in patients with frequent PVCs, LV systolic dysfunction was also related to longer PVC coupling interval, greater PVC QRS width, presence of NSVT, and multiform PVC in addition to greater PVC burden.[35 36] These parameters were not included in the present study. Thirdly, as we did not exclude the patients with SHD in our population, a low PVC burden may contribute to LV systolic dysfunction in the patients with SHD.

Clinical implications

The clinical implications of our study are as follows: first, this cross-sectional study investigated the epidemiological data of PVCs detected by 24-hour Holter among Chinese outpatients with palpitations. It is feasible to detect PVC with 24-hour Holter in patients with palpitations. Patients with frequent PVCs should be treated with antiarrhythmic drugs or interventional therapy. Before starting treatment, it is necessary to perform echocardiography or cardiac MRI to detect SHD. Second, our study not only analysed the epidemiological data of PVC but also investigated the HRV characteristics of PVC. Decreased HRV time-domain parameters suggested the occurrence of PVC, and increased LF/HF ratio (HRV frequency-domain index) presented the imbalance of the autonomic nervous system in patients with frequent PVCs. Therefore, the PVC could be preliminarily estimated using HRV parameters in a simpler, non-invasive way.

Limitations

The limitations of our study should be acknowledged. First, this was a single-centre, cross-sectional and observational study with inherent limitations. The prevalence and characteristics may not be applicable to other ethnicities. Further, larger, multicenter and prospective studies are warranted to confirm our results. Second, a single 24-hour Holter recording may not reflect the true PVC burden. A longer duration than the common 24-hour monitoring period should be performed because of day-to-day variability in PVC frequency.[37] Third, the TTE was conducted to exclude SHDs. It may be necessary to perform MRI when there is a possibility of irreversible SHD. In addition, it is well known that HRV also relates to circadian rhythms, exercise, respiratory rate, metabolic diseases and cardiovascular diseases; however, these factors were not considered when the HRV indexes were compared between patients with and without PVC.

CONCLUSION

The prevalence of PVC and frequent PVCs detected by 24-hour Holter in Chinese outpatients with palpitations were 67.7% and 7.7%, respectively. Decreased HRV time-domain parameters suggested the occurrence of PVC, and increased LF/HF ratio represented the imbalance of the autonomic nervous system in patients with frequent PVCs. Further studies are needed to understand the HRV indexes in PVC patients.

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Contributors All authors approved the final version to be submitted for publication. XL contributed to the conception of the study. YD, WZ and YM were responsible for the data acquisition. YD wrote the manuscript. JL and PY contributed significantly to the data analyses. FZ, BY and KC checked the manuscript with constructive discussions. XL is responsible for all the study work as the guarantor.

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Ethics approval This study involves human participants. The study had been approved by the Ethics Committee of the First Hospital of Nanjing Medical University (approval no. 2011SR-014). Participants gave informed consent to participate in the study before taking part.

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