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ORIGINAL RESEARCH

Sex-Specific Analysis of the Relationship Between Ventricular Premature Contractions Frequency Distribution and Heart Rate: A Cross-Sectional Study in Chinese Adults

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Objective: To investigate the correlation between premature ventricular contraction (PVC) frequency and heart rate (HR) in Chinese adults, with an emphasis on sex-specific differences in clinical characteristics.

Patients and Methods: This retrospective study analyzed 24-hour Holter monitoring data from 478 inpatients at the First People's Hospital of Yibin between January 2021 and December 2022. The inclusion criteria were age ≥18 years, ≥20 hours of Holter recording, frequent PVCs (≥ 500 PVCs), and complete clinical profiles. Patients were stratified into three groups on the basis of the hourly correlation between PVC counts and HR: fast heart rate-related PVC (F-HR-PVC), slow heart rate-related PVC (S-HR-PVC), and independent heart rate-related PVC (I-HR-PVC). Heart rate variability (HRV) indices were assessed to evaluate autonomic nervous system activity.

Results: Among the 478 patients, 267 were males and 211 were females with a mean age of 65.7±13.0 years. The mean PVC burden was 5.7±7.0%, and the mean left ventricular ejection fraction (LVEF) was 59.1±8.7%. In males, the F-HR-PVC group was most common (45.3%), while in females, the I-HR-PVC group was most prevalent (50.2%). Despite these observed differences, a chi-square test did not reveal statistically significant differences in the distribution of VPC profiles between sexes (P=0.167). Analysis of clinical characteristics and Holter indices across sex groups showed significant differences in males, particularly in age, maximum heart rate, and minimum heart rate ($P < 0.05$). In females, significant intergroup differences were observed in VPC burden ($P < 0.05$).

Conclusion: Although no significant sex differences were observed in the correlation between PVC frequency and HR, the study suggests a potential gender influence on VPC characteristics. These findings may inform future research and have implications for the development of sex-specific diagnostic and therapeutic strategies for PVCs.

Keywords: premature ventricular contractions, autonomic nervous system, Holter monitoring, heart rate variability

Introduction

Premature ventricular contractions (PVCs) are cardiac arrhythmias that occur frequently in individuals, irrespective of the presence of structural heart disease, and are notably prevalent among subjects undergoing long-term ambulatory monitoring.[1] An increased frequency of PVCs can present with a spectrum of symptoms, including palpitations, shortness of breath, atypical chest pain, and syncope.[2] Moreover, PVCs have been associated with serious conditions such as dilated cardiomyopathy, left ventricular dysfunction, and heart failure,[3–5] thereby posing considerable challenges to public health.

In clinical practice, the diurnal pattern of PVC occurrence varies significantly among individuals, potentially related to the activity of the autonomic nervous system (ANS).[6] Some patients exhibit an increase in PVC frequency during

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the day, with activities, exercise, or stress that accelerate heart rate (HR) due to sympathetic nervous system excitement. However, other patients show the opposite pattern, with PVCs predominantly occurring at night or during rest and being less frequent during the day or with activity. A third group of patients seems to have PVC frequency distributions unrelated to any discernible diurnal rhythm or HR changes. These varying patterns suggest that the association between PVCs and HR may involve more complex autonomic neural control mechanisms.[7]

Gender differences play a significant role in the clinical presentation and therapeutic response of cardiovascular diseases.[8] Studies have shown that there are marked differences in cardiac structure, function, and the impact of the ANS between males and females, which could influence the occurrence and development of PVCs.[9,10] However, the specific nature of these gender-specific differences and their implications for PVC management remain underexplored, particularly within the adult Chinese population.

Therefore, this study aimed to investigate the correlation between PVC frequency distribution and HR in Chinese adults, with a specific focus on sex-specific clinical characteristics. We hypothesize that there may be significant sex differences in the correlation between PVC frequency and HR, which could have implications for the development of sex-specific diagnostic and therapeutic strategies for PVCs.

Materials and Methods

Study Design and Participants

This study included inpatients who underwent 24-hour Holter monitoring at the First People's Hospital of Yibin between January 2021 and December 2022. The inclusion criteria were as follows: (1) age 18 years or older; (2) a minimum of 20 hours of Holter recording; (3) a diagnosis of frequent PVCs, defined as 500 or more PVCs; and (4) availability of complete clinical profiles (including age, sex, ejection fraction, and coexisting conditions such as hypertension, coronary heart disease, heart failure, diabetes, and dyslipidemia). Patients with congenital heart disease were excluded from the study to ensure that the results were not confounded by the presence of structural heart abnormalities that could significantly affect PVC frequency and distribution. Only data from the initial Holter monitoring session were included in the analysis for patients who underwent multiple sessions. The study protocol was approved by the Medical Ethics Committee of the First People's Hospital of Yibin.

Holter Electrocardiogram Analysis

The 24-hour Holter recordings were analyzed via MARS software (GE Medical Systems). The PVC burden was defined as the percentage of PVCs relative to the total QRS complexes on a 24-hour Holter. As depicted in Figure 1, the participants in our study were stratified into three groups on the basis of the hourly correlation between PVC counts and HR, as determined by Holter ECG analysis. Specifically, a positive correlation, indicating an increase in PVCs with an elevated HR (assessed via Pearson's correlation with a significance level of $P < 0.05$), was classified into the fast heart rate-related PVC (F-HR-PVC) group. Conversely, a negative correlation, suggesting a greater incidence of PVCs with

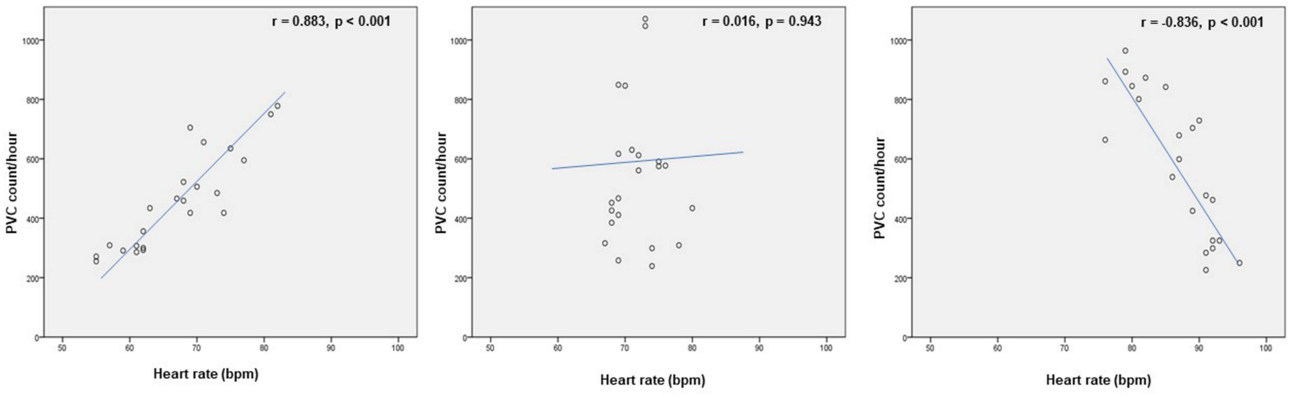

Figure 1 Correlation between ventricular premature contractions (PVCs) and heart rate in different patient groups.

a decreased HR (also significant at $P < 0.05$), was associated with the slow heart rate-related PVC (S-HR-PVC) group. Individuals with no significant correlation between PVC counts and HR were assigned to the independent heart rate-related PVC (I-HR-PVC) group.

Heart Rate Variability Analysis

In this study, we evaluated the activity of the cardiac autonomic nervous system by analyzing heart rate variability (HRV). The time-domain indices of HRV included the standard deviation of all normal sinus RR intervals (SDNN), the standard deviation of the average NN intervals for all 5-minute segments (SDANN), the root mean square of the successive differences in RR intervals (RMSSD), and the proportion of RR interval pairs differing by more than 50 milliseconds (PNN50). The frequency-domain indices included low-frequency (LF) power, high-frequency (HF) power, and the ratio of LF to HF. Furthermore, we calculated the total power (TP), which reflects the overall level of the HRV. These metrics were automatically computed via MARS software (GE Medical Systems) to represent the response of the heart to autonomic modulation. Prior to HRV analysis, essential preprocessing of the ECG data was conducted to ensure precise outcomes.

Statistical Analysis

All the statistical analyses were conducted via SPSS software, version 22.0 (Chicago, USA). Data normality was assessed via the Kolmogorov–Smirnov test. The quantitative data are presented as the means ± standard deviations, with group comparisons performed via one-way ANOVA. Post hoc analyses for multiple group comparisons were conducted via the least significant difference (LSD) method or Dunnett's T3 method, contingent upon the outcome of the homogeneity of variance test. Nonnormally distributed data are represented by median values and were compared via the Mann–Whitney *U*-test. Categorical data are expressed as frequencies and were analyzed via the chi-square test. The Pearson correlation test was used to assess the presence and strength of a linear correlation between the 24-hour-Holter hourly mean HR and the corresponding PVC frequencies. Patients were subsequently classified into the F-HR-PVC, the S-HR-PVC, or the I-HR-PVC groups if a positive ($P < 0.05$), a negative ($P < 0.05$) or a lack of correlation ($P = NS$) was found. A significance level of $p < 0.05$ was set for all the statistical tests.

Results

In this study, we analyzed 24-hour Holter monitoring data from 478 patients, including 267 males and 211 females with a mean age of 65.7±13.0 years. The prevalence of hypertension was 55.6%, coronary heart disease was 57.3%, diabetes was 29.3%, dyslipidemia was 20.5%, and heart failure was 19.7%. The mean PVC burden was 5.7±7.0%, and the mean left ventricular ejection fraction (LVEF) was 59.1±8.7% (Table 1).

Table 1 Clinical Characteristics and 24-Hour Holter Monitoring Data by Sex

	All patients (n=478)	**Males (n=267)**	**Females (n=211)**	**P value**
Clinical Characteristics				
Age (years)	65.7±13.0	65.8±13.8	65.5±12.0	0.805
Hypertension [n (%)]	266 (55.6)	143 (53.6)	123 (58.3)	0.346
CAD [n (%)]	274 (57.3)	150 (56.3)	124 (58.8)	0.635
Diabetes [n (%)]	140 (29.3)	81 (30.3)	59 (28.0)	0.642
Dyslipidemia [n (%)]	98 (20.5)	46 (17.2)	52 (24.6)	0.060
Heart failure [n (%)]	94 (19.7)	60 (22.5)	34 (16.1)	0.105
Smoking [n (%)]	175 (36.6)	151 (56.6)	24 (11.4)	<0.001
LVEF (%)	59.1±8.7	58.4±8.9	60.0±8.4	0.042

(*Continued*)

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Table 1 (Continued).

	All patients (n=478)	Males (n=267)	Females (n=211)	P value
Holter Data				
PVC burden (%)	5.7±7.0	6.0±7.4	5.2±6.5	0.217
Mean HR (bpm)	74.2±10.0	74.4±10.0	73.9±10.0	0.579
Max mean HR (bpm)	108.2±18.1	108.0±17.2	108.6±19.1	0.725
Min mean HR (bpm)	54.0±9.1	53.9±9.1	54.2±9.1	0.697
SDNN (ms)	136.4±45.7	137.0±45.1	135.6±46.5	0.740
SDANN (ms)	109.6±50.7	110.8±54.5	108.1±45.5	0.562
RMSSD (ms)	96.3±54.9	96.2±54.6	96.5±55.3	0.948
PNN50 (ms)	17.5±15.6	18.2±16.0	16.7±15.2	0.295
LF (ms^2)	821.5±842.5	822.4±851.5	820.3±833.0	0.979
HF (ms^2)	1166.3±1302.0	1180.2±1356.3	1148.7±1232.8	0.793
LF/HF	0.8±0.4	0.8±0.5	0.8±0.3	0.179
TP (ms^2)	9270.7±7859.8	9673.3±9262.5	8761.2±5584.2	0.184

Abbreviations: CAD, coronary artery disease; LVEF, left ventricular ejection fraction; PVC, premature ventricular contraction; HR, heart rate; SDNN, Standard Deviation of NN Intervals; SDANN, Standard deviation of 5-min average NN intervals; RMSSD, Root Mean Square of the Successive Differences; PNN50, percent of NN50 in the total number NN interval; LF, low frequency; HF, high Frequency; TP, total power.

Clinical Characteristics and Holter Data Stratified by Sex

Table 1 details the clinical characteristics and Holter monitoring data, stratified by sex. A significant difference was observed in smoking prevalence, with males having a higher rate (56.6%) compared to females (11.4%, $P < 0.001$). No significant sex differences were noted in age, hypertension, coronary heart disease, diabetes, or dyslipidemia. Males had a slightly lower LVEF ($P = 0.042$), while other Holter-derived electrocardiographic indices did not show significant sex differences.

Sex Differences in VPC Frequency Distribution and Heart Rate Correlation

The distribution of VPC profiles among male and female patients is presented in Table 2 and Table 3 and Figure 2. In males, the F-HR-PVC profile was the most common, with 121 cases (45.3%), followed by I-HR-PVC with 111 cases (41.6%), and S-HR-PVC with 35 cases (13.1%). Among females, the I-HR-PVC profile was most prevalent, comprising

Table 2 Comparison of Clinical Characteristics and Holter Data Among Male Groups

Total Males (n=267)	F-HR-PVC (n=121)	I-HR-PVC (n=111)	S-HR-PVC (n=35)	P value
Clinical Characteristics				
Age (years)	65.7±13.7	68.6±13.0	57.1±13.3[ab]	<0.001
Hypertension [n (%)]	63 (52.1)	63 (56.8)	17 (48.6)	0.633
CAD [n (%)]	60 (49.6)	71 (64.0)	19 (54.3)	0.085
Diabetes [n (%)]	32 (26.4)	37 (33.3)	12 (34.3)	0.450
Dyslipidemia [n (%)]	20 (16.5)	17 (15.3)	9 (25.7)	0.351
Heart failure [n (%)]	20 (16.5)	33 (29.7)	7 (20.0)	0.052
Smoking [n (%)]	65 (53.7)	65 (58.5)	21 (60.0)	0.688
LVEF (%)	59.3±8.0	57.7±9.5	57.9±9.7	0.387

(*Continued*)

Table 2 (Continued).

Total Males (n=267)	F-HR-PVC (n=121)	I-HR-PVC (n=111)	S-HR-PVC (n=35)	P value
Holter Data				
PVC/HR correlation coef	0.67±0.13	0.09±0.22[a]	−0.61±0.15[ab]	<0.001
PVC burden (%)	6.8±8.3	5.5±7.0	4.9±4.6	0.261
Mean HR (bpm)	73.0±10.2	75.1±9.8	77.0±9.4	0.076
Max mean HR (bpm)	106.3±18.5	107.4±15.6	115.6±15.9[ab]	0.017
Min mean HR (bpm)	52.1±8.5	55.7±9.5a	54.3±8.6	0.009
SDNN (ms)	140.8±48.8	131.7±42.6	140.7±38.8	0.269
SDANN (ms)	113.2±49.0	107.7±64.0	112.0±38.0	0.736
RMSSD (ms)	98.0±59.0	96.3±53.5	89.3±41.8	0.710
PNN50 (ms)	18.4±16.7	18.4±16.6	16.4±10.9	0.800
LF (ms^2)	894.2±1005.0	782.0±713.6	702.3±649.0	0.407
HF (ms^2)	1154.2±1299.2	1239.8±1542.8	1080.8±841.6	0.801
LF/HF	0.9±0.7	0.8±0.3	0.8±0.3	0.204
TP (ms^2)	10,485.7±11,795.7	8349.5±5168.6	11,063.0±9145.5	0.136

Notes: [a]P < 0.05 when compared with F-HR-PVC group; [b]P < 0.05 when compared with I-HR-PVC group. Abbreviations are as in Table 1.

Table 3 Comparison of Clinical Characteristics and Holter Data Among Female Groups

Total Females (n=211)	F-HR-PVC (n=82)	I-HR-PVC (n=106)	S-HR-PVC (n=23)	P value
Clinical Characteristics				
Age (years)	66.1±11.3	65.8±11.2	62.2±17.2	0.361
Hypertension [n (%)]	52 (63.4)	60 (56.6)	11 (47.8)	0.360
CAD [n (%)]	48 (58.5)	66 (62.3)	10 (43.5)	0.252
Diabetes [n (%)]	27 (32.9)	27 (25.5)	5 (21.7)	0.412
Dyslipidemia [n (%)]	22 (26.8)	27 (25.5)	3 (13.0)	0.384
Heart failure [n (%)]	14 (17.1)	17 (16.0)	3 (13.0)	0.835
Smoking [n (%)]	8 (9.8)	13 (12.3)	3 (13.0)	0.897
LVEF (%)	60.7.3±7.8	59.4±9.2	60.4±6.5	0.553
Holter Data				
PVC/HR correlation coef	0.67±0.14	0.02±0.38[a]	−0.63±0.15[ab]	<0.001
PVC burden (%)	6.7±7.3	4.4±3.9[a]	3.9±6.3[a]	0.031
Mean HR (bpm)	73.0±9.4	74.4±10.5	74.5±9.4	0.602
Max mean HR (bpm)	109.7±19.6	107.6±19.1	109.2±18.5	0.756
Min mean HR (bpm)	52.6±8.4	55.4±9.8	54.4±7.4	0.123
SDNN (ms)	141.4±44.0	130.9±49.4	136.6±40.1	0.313
SDANN (ms)	113.6±46.0	103.3±46.0	110.3±40.9	0.305
RMSSD (ms)	99.7±60.0	95.2±53.4	90.8±47.0	0.754
PNN50 (ms)	17.9±16.6	15.9±13.8	16.0±16.2	0.652
LF (ms^2)	871.7±842.3	784.4±863.1	802.8±663.1	0.773
HF (ms^2)	1181.5±1240.2	1144.7±1306.7	1050.1±825.2	0.903
LF/HF	0.8±0.3	0.7±0.2	0.8±0.3	0.065
TP (ms^2)	9406.4±5438.6	8177.8±5844.6	9149.1±4730.1	0.308

Notes: [a]P < 0.05 when compared with F-HR-PVC group; [b]P < 0.05 when compared with I-HR-PVC group. Abbreviations are as in Table 1.

106 cases (50.2%), followed by F-HR-PVC with 82 cases (38.9%), and S-HR-PVC with 23 cases (10.9%). Although the chi-square test did not reveal statistically significant differences in the distribution of VPC profiles between sexes (P=0.167), these findings suggest a potential gender influence on VPC characteristics.

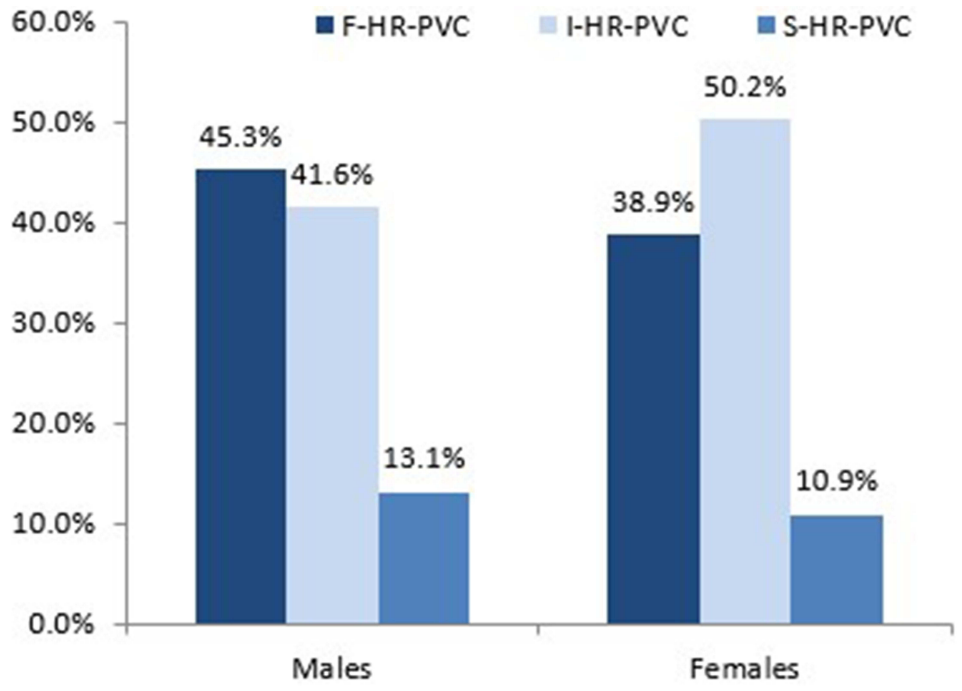

Figure 2 Distribution of ventricular premature contractions (PVCs) correlation groups by sex.

Sex-Specific Clinical Characteristics, Holter Indices, and VPC Frequency Distribution Correlations

Further analysis of clinical characteristics and Holter indices across sex groups showed significant differences in males, particularly in age, maximum heart rate, and minimum heart rate ($P < 0.05$). Post hoc comparisons indicated that the S-HR-PVC group was significantly younger and had a higher maximum heart rate than the F-HR-PVC and I-HR-PVC groups ($P < 0.05$). The I-HR-PVC group also had a significantly lower minimum heart rate than the F-HR-PVC group. In females, significant intergroup differences were observed in VPC burden ($P < 0.05$), with the F-HR-PVC group exhibiting a higher VPC load compared to the I-HR-PVC and S-HR-PVC groups.

Heart rate variability (HRV) indices, indicative of autonomic nervous system (ANS) activity, were also analyzed. While some differences in HRV indices were noted between sexes, they were not statistically significant, suggesting a limited impact of sex on VPC frequency and distribution patterns.

Discussion

This study provides an in-depth analysis of the correlation between the frequency distribution of PVCs and heart rate in an adult Chinese population, with a particular emphasis on sex-specific clinical characteristics. 45.3% of males were categorized as F-HR-PVC, indicating a positive correlation between PVC frequency and heart rate, whereas 50.2% of females were categorized as I-HR-PVC, indicating no significant correlation with heart rate. Although the chi-square test indicated no statistical significance (P=0.167), these findings suggest a potential gender influence on PVC patterns. This underscores the value of considering sex in the analysis of PVC distribution relative to heart rate.

Expanding on the pioneering work of Winkle et al,[11] who initially characterized the clinical classification of PVC frequency distribution and its association with heart rate, and further elaborating on the work of Pitzalis et al.[12] In the present study, we employed a methodology akin to that of David et al,[13] utilizing 24-hour Holter monitoring to assess heart rate variability and identify three distinct patterns of PVCs. Our findings indicate that among males, PVCs with a positive correlation to heart rate (F-HR-PVC) constitute a significant proportion, reaching 45.3%, aligning with the general trend observed by David et al, where F-HR-PVC was noted in nearly half of the cases. However, our study did not yield statistically significant differences in this distribution, suggesting that while there may be a trend, it does not

apply universally across our entire patient cohort. In contrast, within our study, females were more likely to be categorized under the independent heart rate-related PVCs (I-HR-PVC) group, accounting for 50.2% of cases, a finding that contrasts with the results from David et al, where the prevalence of I-HR-PVC was lower. Additionally, PVCs with a negative correlation to heart rate (S-HR-PVC) were consistently the least common in both genders, with 13.1% in males and 10.9% in females, a result that echoes the findings of David et al, indicating that S-HR-PVC is the least prevalent pattern in both sexes. These observations highlight the potential sex-related differences in the distribution of PVC patterns, despite the lack of statistical significance. This may point to the underlying role of sex in the distribution of PVC patterns and underscores the importance of considering sex differences in clinical practice. Our findings underscore the necessity of incorporating sex as a factor in the management of PVCs and suggest potential directions for future research to explore how sex influences PVC patterns and their clinical implications.

Our observations suggest that the etiology of PVCs may involve more complex mechanisms of autonomic neural control. The autonomic nervous system, with its sympathetic and parasympathetic components, plays an essential role in the initiation, perpetuation, and cessation of ventricular arrhythmias.[14,15] The considerable variability in the diurnal pattern of PVCs among different patients may be related to the imbalance between the sympathetic and parasympathetic tones, which exhibit significant sex variations. The higher prevalence of F-HR-PVCs in males could be associated with increased sympathetic activity. This is supported by evidence that elevated catecholamine levels can lead to accelerated heart rates and enhanced myocardial contractility, potentially disrupting cardiac repolarization and increasing PVC occurrence.[16,17] Conversely, the prevalence of I-HR-PVCs in females might be linked to hormonal fluctuations, such as sex hormones including estrogens and progesterone, which significantly influence cardiac structure and function, and are posited to modulate the function of cardiac ion channels.[18,19] These sex-specific cardiac characteristics may account for the observed prevalence of I-HR-PVCs in females.

These findings have profound implications for therapeutic strategies for treating PVCs, which may differ between the sexes. The high incidence of F-HR-PVCs in males might necessitate interventions targeting sympathetic modulation, whereas the predominance of I-HR-PVCs in females might require strategies considering hormonal management and sex-specific electrophysiological characteristics. For example, beta-blockers could be considered for patients with F-HR-PVCs,[20] whereas their use in S-HR-PVC patients (typically young, healthy women) might be avoided owing to the potential paradoxical adverse effects on the PVC burden,[13,21] For I-HR-PVC patients, given the neutral effect of beta-blockers, alternative medical treatments or catheter ablation might be considered earlier when PVC suppression is needed,[22] Such tailored therapeutic approaches could enhance treatment efficacy, minimize adverse effects, and improve patients' quality of life.

In addition to conventional Western medicine, traditional Chinese medicine (TCM) also has potential in the management of PVCs.[23] Recent clinical studies suggest that TCMs, such as Shensong Yangxin capsules, can reduce the occurrence of PVCs and may improve cardiac function by modulating the activity of the ANS and the function of cardiac ion channels.[24–27] The multicomponent nature of TCM may offer a multitarget therapeutic mechanism. However, further research is needed to determine the efficacy of these remedies for different categories of PVCs, indicating a significant scope for future research.

This study has several limitations. First, as a single-center retrospective analysis, the robustness of prospective, randomized controlled trials may be lacking. Second, while the study included some clinical data for comparison, critical data such as the use of antiarrhythmic medications were absent. Third, potential measurement errors or unquantifiable factors in the electrocardiographic data could have influenced the accuracy of the results.

Conclusion

In conclusion, although no significant sex differences were observed in the correlation between PVC frequency and HR, the study suggests a potential gender influence on VPC characteristics. These findings may inform future research and have implications for the development of sex-specific diagnostic and therapeutic strategies for PVCs.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Approval

Ethical approval for this study was obtained from the Ethics Review Committee of Yibin First People's Hospital (Approval No. 2023-70) and was conducted in accordance with the guidelines laid down in the Declaration of Helsinki in 2013. The Ethics Review Committee of Yibin First People's Hospital approved this study and waived the need for consent to participate because of this study's retrospective, non-interventional design, and because patient data confidentiality and privacy were maintained.

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Disclosure

The authors declare that they have no competing interests.

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