ORIGINAL RESEARCH

Clinical Characteristics of Patients with Arrhythmias of the Idiopathic Outflow Tract Ventricular: Age, Gender, Comorbidities, Laboratory Test Results, and Echocardiographic Parameters

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ABSTRACT

Context • Idiopathic ventricular arrhythmias (IVAs) are a spectrum of ventricular arrhythmia (VA) without structural heart disease (SHD), that includes premature ventricular contractions (PVCs) and ventricular tachycardia (VT). The clinical characteristics of patients with PVCs or VT remain unclear, including distribution of the origin of arrhythmias, age and gender differences, comorbidities, laboratory tests, and electrocardiographic parameters.

Objective • The study intended to compare the clinical characteristics of the right ventricular outflow tract (RVOT)- and left ventricular outflow tract (LVOT)-VT of a large group of consecutive patients, to investigate the distribution of the origin of the arrhythmias, age and gender differences, comorbidities, laboratory-examination results, and echocardiographic parameters.

Methods • The research team designed a retrospective study to collect data on the above-mentioned variables.

Setting • The study occurred at the Second Hospital of Hebei Medical University in Shijiazhuang, China.

Participants • Participants were 774 patients with symptomatic ventricular arrhythmias, 328 males and 446 females with the mean age of 48.6 ± 15.7 years, who underwent catheter ablation between January 2015 and January 2019. Participants were divided into the right ventricular outflow tract (RVOT) group and left ventricular outflow tract (LVOT) group, according to the different origins of their arrhythmias, with 428 participants in the RVOT group and 180 in the LVOT group.

Outcome Measures • The research team collected and analyzed the data for the original sites of the IVAs; ages; genders; comorbidities; laboratory examinations, including routine blood tests, liver function, kidney function, blood lipid and potassium; and echocardiographic parameters.

Results • Among the 774 participants, 76 had experienced VTs and 698 PVCs. The original site of IVAs was 2.38 times more likely to be in the RVOT than the LVOT, with the ratio for RVOT/LVOT = 2.38. IVAs usually occurred in participants between 50 and 70 years old and exhibited a decreasing incidence after 70 years of age. IVAs derived from the His bundle were more common in older participants, with a mean age of 60.4 ± 10.4 years, while IVAs derived from the fascicular were more common in younger patients, with a mean age of 36.08 ± 16.01 years. Compared with the LVOT group, the RVOT group was younger, 51.91 ± 14.65 years vs 46.95 ± 14.95 years, respectively ($P < .001$). PVCs in the RVOT group were more common in women, with the ratio of females/males = 2.10, and no gender difference existed in the overall incidence of IVAs in the LVOT group ($P > .05$). The most common cardiovascular comorbidities of outflow tract ventricular arrhythmias (OTVAs) were hypertension, coronary heart disease, and hyperlipidemia, while the most common noncardiovascular comorbidities were diabetes, ischemic stroke, and thyroid disease. The red-blood-cell counts, hemoglobin, creatinine, and gamma-glutamyl transpeptidase (GGT) of the LVOT group were higher than those from the RVOT, with $P = .008$, $P = .009$, $P = .001$, and $P < .001$, respectively. The left atrial diameter (LAD), left ventricular end-diastolic diameter (LVEDD), interventricular septal thickness (IVS), and left ventricular posterior wall thickness (LVPWT) in the LVOT group were larger than those in the RVOT group ($P < .001$), while the LVOT group's left ventricular ejection fraction (LVEF%) was lower than that of the RVOT group.

Conclusions • The outflow tract served as the major original site of IVAs, and significant differences existed between participants in the LVOT and RVOT groups in age; gender; comorbidities; results of laboratory examinations, including red-blood-cell counts, hemoglobin, creatinine, and GGT; and echocardiographic parameters, including LVEF%, LAD, LVEDD, IVS, and LVPWT. (*Altern Ther Health Med.* 2022;28(6):88-95)

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Idiopathic ventricular arrhythmias (IVAs) are a spectrum of ventricular arrhythmia (VA) without structural heart disease (SHD), that contain premature ventricular contractions (PVCs) and ventricular tachycardia (VT). IVAs are a common type of arrhythmia seen in medical clinics, for which the ventricular outflow tract is the most common site of origin.[1,2]

Idiopathic outflow tract VAs (OTVAs) manifest clinically in three forms: (1) paroxysmal, sustained monomorphic ventricular tachycardia (SMVT); (2) repetitive nonsustained ventricular tachycardia (NSVT); and (3) PVCs.[3] The clinical characteristics of patients with PVCs or VT remain unclear, including distribution of the origin of the arrhythmias, age and gender differences, comorbidities, laboratory tests, and electrocardiographic parameters.

Despite clinical differences among patients with the three subtypes of OTVAs, subsets of patients from each group have shown a similar electrophysiological profile in some studies, suggesting a common underlying cellular mechanism.[4-6] One previous study found that those patients showed a unique arrhythmogenic substrate and electropharmacologic profile; their VT was adrenergically mediated and sensitive to perturbations that lowered the intracellular calcium.[7] A few studies published to date have shown that incidence as well as age distribution differed by gender among idiopathic VT patients.[8,9]

Gender differences in the prevalence of IVAs have been reported in several studies. A literature review of 748 patients with IVAs included 387 female participants (52%).[4] In that study, right ventricular outflow tract (RVOT)-VAs occurred twice as frequently in females than in males, with a M/F ratio = 0.49, and left ventricular outflow tract (LVOT)-VAs occurred slightly more frequently in males than in females, with a M/F ratio = 1.38. Verapamil-sensitive intra-fascicular left ventricle-VT was three times more frequent in males than in females, with a M/F ratio = 3.37.

Many electrocardiogram (ECG) parameters have been shown to have gender-specific differences. Two studies found that females were inclined to have a higher mean for the resting heart rate; a corrected QT (QTc) interval prolongation; and a lower QRS voltage, which could be associated with gender differences in the incidence of different kinds of arrhythmias.[10,11] Some studies examining Torsades de Pointes found that females usually exhibited a more significant correlation with arrhythmias, accompanied by congenital or acquired long QT syndrome,[10,12] whereas males more frequently had atrioventricular block, atrial fibrillation, supraventricular tachycardia, Wolff-Parkinson-White syndrome, ventricular fibrillation, or cardiac attack.[11] Few studies had analyzed gender differences in different kinds of IVAs.[9,13]

Marchlinski et al found that initiation of RVOT-PVCs or -VT showed obvious gender discrepancies in the specific condition; females owed the initiation to established states of hormonal flux.[14] Moreover, recent animal studies have indicated that estrogen levels and current densities of potassium (K+) have a close correlation with ventricular repolarization. Saito et al found that estrogen can downregulate the transcription of Kv4.3 and Kv1.5, which is one of the mechanisms underlying gender differences in mouse ventricular repolarization.[15]

Gender exerts significant influences on the epidemiology, pathophysiology, and clinical presentation of many cardiac rhythm disorders. Santangeli et al found gender-related differences in the outcomes of invasive electrophysiological procedures.[16] Some researchers found that catheter ablation of supraventricular arrhythmias was equally effective regardless of gender. The outcomes of catheter ablation for atrial fibrillation in women has been reported to be worse than for men[12,17] which may be explained by a later referral to receive the procedure. Of note, with regard to atrial flutter and VAs, no gender differences in the outcomes of catheter-ablation procedures have been reported.[16,18]

Few studies have occurred on gender-related differences in the outcomes of VT ablation in the setting of SHD. The International VT Ablation Center Collaborative Group compared the outcomes for women and men with SHD.[18] This large multicenter observational study showed that women, compared to men, were younger, had a lower prevalence of medical comorbidities, a higher left ventricular ejection fraction (LVEF) and fewer VT storm episodes, were less likely to have an implantable cardioverter defibrillator (ICD) and previous shocks, and were less likely to be treated with antiarrhythmic drugs (AADs). The study also found that women had higher rates of VT recurrence at a one-year follow-up after ablation than men, at 30.5% and 25.3%, respectively ($P = .03$), and that women and men with non-ischemic dilated cardiomyopathy (NIDCM) had similar rates of VT recurrence, at 29.9% and 28.6%, respectively ($P = .55$). However, women with ischemic cardiomyopathy were more likely to have a recurrence than men with ischemic cardiomyopathy, at 31.7% and 22.8%, respectively ($P = .02$).

Thyroid dysfunction has been reported to have a close relationship with arrhythmia,[15] and hyperthyroidism has been found to be a crucial cause of atria and VAs.[19] Purtell et al found that thyroid hormones can change cardiac excitability and thus disturb myocardial electrical stability and that increased excitability can be linked to elicited activity leading to a PVC.[20]

Chojnowski et al found that hypothyroidism can also be associated with some kinds of arrythmias.[21] That study found that bradycardia, low QRS voltage, prolonged QT, and flattening or inverting T waves were all typical ECG features

in hypothyroidism. Those researchers found that severe hypothyroidism and a decreased triiodothyronine concentration in cardiac cells can worsen cardiac contractility, decrease heart rate, and retard stimuli conduction in the myocardium, which may explain the bradycardia and prolonged QT interval, followed by life-threatening arrhythmias, such as torsades de pointes (TdP)-type tachycardia.

Two other studies found that patients with both overt and subclinical thyroid dysfunctions had ECG parameters that showed significant changes in heart rate, QTc duration, P-wave duration, PR interval, and low voltage, and these were less prominent in the older patients compared with younger patients.[22]

To date, no systematic study has occurred that has examined the clinical characteristics of patients with idiopathic OTVAs that have been classified according to their origins in the RVOT and LVOT. The current study intended to compare the clinical characteristics of the RVOT- and LVOT-VT of a large group of consecutive patients, to investigate the distribution of the origin of the arrhythmias, age and gender differences, comorbidities, laboratory-examination results, and echocardiographic parameters.

METHODS

Participants

The research team retrospectively collected data from 774 consecutive patients with symptomatic ventricular arrhythmias, 328 males and 446 females with the mean age of 48.5 ± 15.7 years, who underwent mapping and ablation of idiopathic PVCs or VT. They were patients at the Second Hospital of Hebei Medical University between January 2015 and January 2019. In general, VT and PVCs are considered idiopathic when the patient has a normal baseline ECG and no evidence of SHD.

Potential participants were included in the study if: (1) they had frequent PVCs or VT that were confirmed by an ECG or by 24-hour ambulatory (Holter) monitoring; (2) they had received a chest X-ray, transthoracic echocardiography, and related laboratory examinations; (3) they had PVCs or VT symptoms, including palpitations, a feeling of cardiac arrest, chest tightness, chest pain, and syncope; (4) they had symptomatic VAs, and 24-hour ambulatory (Holter) monitoring had suggested that they experienced frequent premature ventricular beats, more than 10 000 in 24 hours; (5) they were refractory to medical therapy or couldn't tolerate antiarrhythmic drugs; and (6) they had an indication for radiofrequency ablation (RFA) and had no contraindications.

Patients who were unable to cooperate with clinical treatment and follow-up were excluded.The study was approved by the ethics committee of the Second Hospital of Hebei Medical University (2021-P052). Written informed consent was obtained from each patient.

Procedures

Groups. Patients were divided into the RVOT group or the LVOT group according to the different origin of their arrhythmias, with 428 participants in the RVOT group and 180 participants in the LVOT group.

Electrophysiological Study and Catheter Ablation. All procedures were conducted by cardiologists qualified for interventional surgery. A fluoroscopy and 3D-mapping system, either the Carto 3 (Biosense Webster, Diamond Bar, CA, USA) or the Ensite NavX (St. Jude Medical, St Paul, MN, USA) were used. When a patient's ECG showed an image of a left bundle branch block (LBBB), the medical practitioners inserted a 6F, two-mm-tip quadripolar catheter (Supreme, St. Jude Medical) that was positioned at the His bundle region and an irrigated ablation catheter with a 7.5F, 3.5-mm-tip (Navistar, Biosense) was inserted into the RVOT via the right femoral vein for mapping.

All participants received activation mapping to figure out the earliest site of ventricular activation in clinical or induced VT or PVC. If participants had frequent VT or PVCs, they underwent electroanatomic mapping. Ablation was performed if the target site had an earliest local activation time prior to Q/R/S wave (QRS) onset during the VT or PVCs and had a tremendous match during the pace mapping, with >11/12 leads.[10]

Further mapping was conducted for the LVOT group and the great cardiac vein and anterior interventricular vein (GCV-AIVV) with obscure suitable ablation sites or unsuccessful ablation in RVOT.

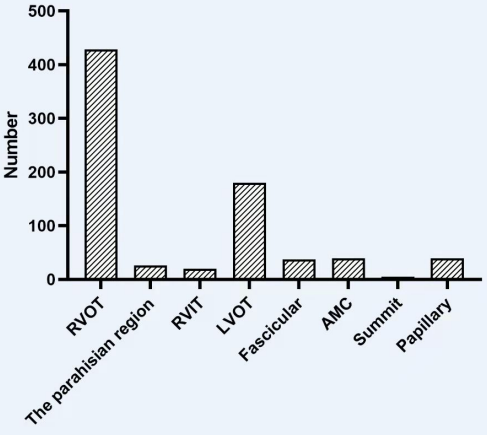
When ventricular activity first became discernible over the aortic valve, the anatomical relationship between the coronary artery and aorta and the ablation catheter's location was evaluated by performing selective angiography. Radiofrequency power was titrated to 30W and 50W in coronary artery and aorta, respectively, aiming to decrease the impedance by 5-10 W, and temperature was carefully limited to be under 41° C. Radiofrequency delivery would be prolonged for 30 seconds to one minute if the VTs or PVCs exhibited an increasing or decreasing incidence in the first 10 seconds of application.[23,24]

The endpoint of the catheter ablation was the elimination and noninducibility of VT or PVCs during an isoproterenol infusion (2-4 μg/min) and burst pacing from the right ventricle, to a cycle length as short as 240 milliseconds.[13] The success of the acute procedural ablation was defined as the absence of spontaneous or induced clinical PVCs or VT at 30 min after the last radiofrequency energy application.

Follow-up. Follow-up of patients after the procedure included clinic visits with 12-lead ECGs and 24-hour ambulatory (Holter) monitoring, and telephone calls to all participants and their referring physicians. All patients who reported symptoms were given a 24-hour Holter monitoring or events monitor to document the cause of the symptoms.

Outcome Measures. The main outcomes were collected by reviewing the medical records of patients, including clinical characteristics, laboratory examination results, and echocardiographic parameters as well as surgery data by doctors who did not participate in the treatment.

Figure 1. Most Common Site of Idiopathic Ventricular Arrhythmias (IVAs). The outflow tract was the most common site (78.6%), and the incidence of them in the RVOT was 2.38 times higher than that of the LVOT, with the ratio of RVOT/LVOT = 2.38.



Abbreviations: AMC, aortomitral continuity; LVOT, left ventricular outflow tract; RVIT, right ventricular inflow tract; RVOT, right ventricular outflow tract.

Table 1. The Onset Ages for Different Sites of IVAs

Site of IVAs' Origins	Onset Age (y)
ROVT	46.96 ± 14.95
Parahisian region	60.38 ± 10.41
RVIT	44.00 ± 22.15
LVOT	51.91 ± 14.65
Fascicular	36.08 ± 16.01
AMC	56.49 ± 12.60
Summit	52.20 ± 15.87
Papillary	48.38 ± 18.85

Abbreviations: AMC, aortomitral continuity; IVA, idiopathic ventricular arrhythmias; LVOT, left ventricular outflow tract; RVOT, right ventricular outflow tract; RVIT, right ventricular inflow tract.

Outcome Measures

Sites of Origin of IVAs. The study collected data regarding the sites of origin of participants' IVAs, to include aortomitral continuity (AMC), fascicular, left ventricular outflow tract (LVOT), His bundle, papillary, right ventricular outflow tract (RVOT), right ventricular inflow tract (RVIT), and summit.

Clinical Characteristics. The study collected data regarding participants' ages, genders, and comorbidities, including coronary heart disease, hypertension, hyperlipidemia, diabetes, ischemic stroke, and thyroid disease.

Laboratory Examination. The study collected data regarding participants' red-blood-cell count (men–4.7 to 6.1 million cells per microlitre (cells/mcL) women–4.2 to 5.4 million cells/mcL), white-blood-cell count (4000 and 11000/microliters), hemoglobin (13.0 g/dL-16.0 g/dL, total cholesterol (125 to 200 mg/dL), creatinine (0.6–1.3 mg/dL), gamma-glutamyl transpeptidase (GGT, 5 to 40 U/L), and potassium (K, Between 3.5 and 5.0).

Echocardiographic Parameters. The study collected data regarding participants' interventricular septal (IVS, 0.6-1.1 cm) thickness in mm; left atrial diameter (LAD) in mm, left ventricular end-diastolic diameter (LVEDD) in mm, left ventricular ejection fraction (LVEF) as the EF% (55% to 70%.), and left ventricular posterior wall thickness (LVPWT, 0.6-1.1 cm) in mm.

Statistical Analysis

The SPSS 25.0 software (SPSS, Chicago, IL, USA) was used to perform statistical analysis. Continuous variables are expressed as means ± standard deviations (SDs), and the comparisons between continuous data were performed using Student's *t* test. Comparisons of categorical data were performed using a Chi-square test with a Yates' correction or Fisher's exact test. A $P < .05$ was considered to be statistically significant.

RESULTS

Participants' Characteristics

Of the 774 participants, 76 had experienced VTs and 698 PVCs; 608 had outflow tract ventricular tachycardia (OTVTs), and all manifested PVCs clinically. The research team performed a preliminary statistical analysis of the origins and population characteristics of IVAs for the 774 participants, and the ventricular outflow tract (78.6%) was the most common site of origin of IVAs (Figure 1).

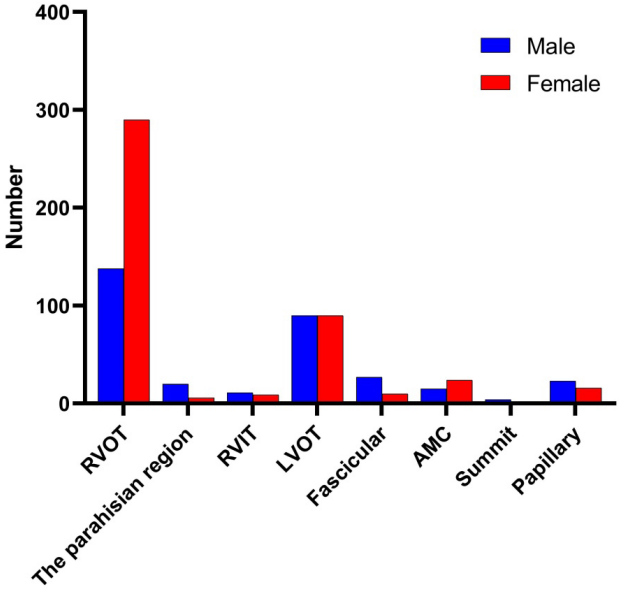
In terms of the age distribution of PVCs at different sites (Table 1), PVCs derived from the His bundle were more common in older participants, with a mean age of 60.38 ± 10.41 years, than in younger participants, while IVAs from the fascicular were more common in younger participants, with a mean age of 36.08 ± 16.01 years, than in older participants.

The incidence of RVOT was 2.38 times higher than that of LVOT, with the ratio of RVOT/LVOT = 2.38. In the RVOT group, the most common site of PVCs was the anterior septum, at 34.8%, and the most common site in the LVOT group was the left sinus, at 46.1% (data not shown). Furthermore, participants with IVAs from different sites showed differences in age and gender (Figure 2). PVCs of the outflow tract usually occurred in participants between 50 and 69 years old (Figure 3). IVAs decreased significantly after participants turned 70 years of age.

Differences Between RVOT and LVOT

Outflow tract PVCs usually occurred in participants between 50 and 70 years of age and exhibited a decreasing incidence after 70 years of age. In participants under 70 years of age, the prevalence of PVCs in the RVOT group gradually increased with age.

Figure 2. Participants With IVAs at Different Sites Showed Differences in Gender. PVCs of the RVOT and AMC original were more common for female participants than for male participants, while the other sites were more common for males than for females.



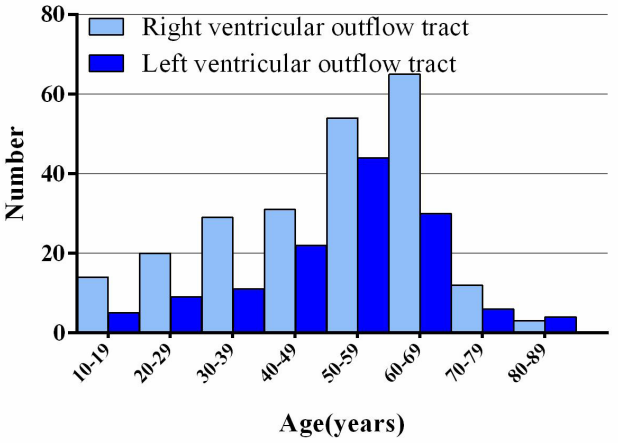
Abbreviations: RVOT, right ventricular outflow tract; RVIT, right ventricular inflow tract; LVOT, left ventricular outflow tract; AMC, aortomitral continuity; VAs, idiopathic ventricular arrhythmias; PVC, premature ventricular contractions.

Age and gender differences. Compared with the LVOT group, participants with PVCs from RVOT were significantly younger, with $P < .001$ (Table 2). The mean onset age of PVCs in the RVOT and LVOT groups was 46.95 ± 14.95 and 51.91 ± 14.65 years old, respectively. PVCs in the RVOT group were more common among women, with the ratio of females/males = 2.10, with $P < .001$, while this tendency was reversed after participants reached 70 years of age (Figure 4). In females under 60 years old, the incidence of PVCs in the RVOT group increased gradually with age.

PVCs in the LVOT group showed no significant differences by gender, with p>0.05 (Figure 5). However, among participants with PVCs in the LVOT group, females had a lower onset age than males, at 50-59 and 60-69 years old, respectively. In addition, females with PVCs in the LVOT group had two peaks of onset age, at 30-39 and 50-59. In those two phases, females had a higher incidence of PVCs than males, while that tendency was reversed in the older age groups, indicating a potential correlation between female PVCs in the LVOT group and estrogen.

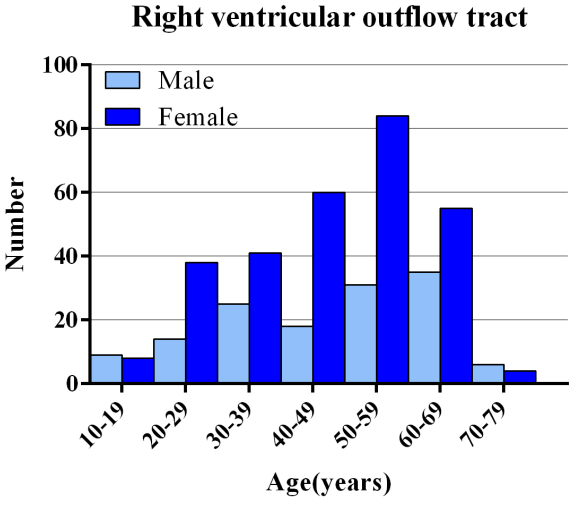
Comorbidities. The most common cardiovascular comorbidities were coronary heart disease, hypertension, and hyperlipidemia, while the most common noncardiovascular comorbidities were diabetes, ischemic

Figure 3. Outflow Tract PVCs. These usually occurred in participants who were between 50 and 70 years old and exhibited a significantly decreasing incidence after 70 years of age. In participants under 70 years old, the incidence of PVCs in the RVOT gradually increased with age. Compared with LVOTs, participants with PVCs in the RVOT were younger. The mean onset ages of PVCs in the RVOT and LVOT were 46.96 ± 14.95 and 51.91 ± 14.65 years old, respectively (Table 1).



Abbreviations: LVOT, left ventricular outflow tract; PVC, premature ventricular contractions; RVOT, right ventricular outflow tract

Figure 4. PVCs in RVOTs. These were more common in women, with the ratio of females/males = 2.10, while this tendency reversed after participants turned 70 years of age. In female participants under 60, the incidence of PVCs in the RVOT increased gradually with age.



Abbreviations: PVC, premature ventricular contractions; RVOT, right ventricular outflow tract.

Table 2. Differences in Age, Gender, Comorbidities, Laboratory Examination, and Echocardiographic Parameters between RVOT and LVOT. $P < .05$ was statistically significant. Data with a normal distribution are expressed as means ± standard deviations (SDs); otherwise data are expressed as expressed as numbers and percentages or medians and upper and lower quartiles.

Variable	RVOT Mean ± SD	LVOT Mean ± SD	Total Mean ± SD	*P* value
Onset Age, y	46.96 ± 14.95	51.91 ± 14.65	48.42±15.02	<0.001
Variable	**RVOT n (%)**	**LVOT n (%)**	**Total n (%)**	***P* value**
Gender				
Male	138 (32.2)	90 (50.0)	228 (37.5)	<.001[a]
Female	290 (67.8)	90 (50.0)	380 (62.5)	
Coronary heart disease				
Yes	82 (19.2)	52 (28.9)	134 (22.0)	.008[b]
No	346 (80.8)	128 (71.1)	474 (78.0)	
Hypertension				
Yes	142 (33.2)	90 (50.0)	232 (38.2)	<.001[c]
No	286 (66.8)	90 (50.0)	376 (61.8)	
Hyperlipidemia				
Yes	79 (18.5)	45 (25.0)	124 (20.4)	.068
No	349 (81.5)	135 (75.0)	484 (79.6)	
Diabetes				
Yes	36 (8.4)	18 (10.0)	54 (8.9)	.530
No	392 (91.6)	162 (90.0)	554 (91.1)	
Ischemic stroke				
Yes	24 (5.6)	14 (7.8)	38 (6.3)	.313
No	404 (94.4)	166 (92.2)	570 (93.8)	
Thyroid disease				
Yes	27 (6.3)	10 (5.6)	37 (6.1)	.723
No	401 (93.7)	170 (94.4)	571 (93.9)	
Variable	**RVOT Median (Upper, Lower Quartile)**	**LVOT Median (Upper, Lower Quartile)**	**Total Median (Upper, Lower Quartile)**	***P* value**
Red-blood-cell count	4.44 (4.16, 4.77)	4.61 (4.26, 4.90)	4.48 (4.19, 4.83)	.008[c]
White-blood-cell count	6.10 (5.10, 7.40)	6.40 (5.35, 7.30)	6.20 (5.20, 7.40)	.395
Hemoglobin	135.0 (126.0, 143.0)	138.0 (128.0, 146.0)	135.0 (126.0, 144.0)	.009[c]
Total cholesterol	4.07 (3.57, 4.75)	4.32 (3.73, 4.91)	4.13 (3.61, 4.80)	.063
Creatinine	61.3 (53.1, 70.4)	66.0 (55.1, 75.0)	62.0 (54.0, 71.8)	.001[c]
GGT	16.0 (11.0, 24.0)	19.0 (13.0, 29.1)	17.0 (12.0, 26.0)	<.001[c]
K^+	4.03 (3.82, 4.26)	4.01 (3.76, 4.26)	4.03 (3.81, 4.26)	.355
LVEF, EF%	62.06 (61.47, 63.73)	61.86 (60.63, 63.46)	61.97 (60.99, 63.64)	.001[d]
LAD, mm	33.0 (30.0, 35.0)	34.0 (31.0, 37.0)	33.0 (30.0, 36.0)	<.001[c]
LVEDD, mm	47.0 (45.0, 49.0)	49.0 (46.0, 53.0)	48.0 (45.0, 50.0)	<.001[c]
IVS, mm	9.0 (8.0, 10.0)	10.0 (9.0, 10.0)	9.0 (8.0, 10.0)	<.001[c]
LVPWT, mm	9.0 (8.0, 10.0)	10.0 (9.0, 10.0)	9.0 (8.0, 10.0)	<.001[c]

[a] $P < .001$, showing that the RVOT group was significantly younger than the LVOT group.
[b] $P < .001$, showing that PVCs in the RVOT group were significantly more common among women than in men.
[c] $P < .05$, showing that the measurements were significantly higher in the LVOT group than in the RVOT group.
[d] $P = .001$, showing that the measurements were significantly lower in the LVOT group than in the RVOT group.

Abbreviations: GGT, gamma-glutamyl transpeptidase; IVS, interventricular septal thickness; K, potassium; LAD, left atrial diameter; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVOT, left ventricular outflow tract; LVPWT, left ventricular posterior wall thickness; RVOT, right ventricular outflow tract.

stroke, and thyroid disease. Compared with the RVOT group's, the rate of comorbidities, except for thyroid diseases, in the LVOT group was higher than that of the RVOT group, and the prevalence rates for coronary heart disease ($P = .008$) and hypertension ($P < .001$) were significantly higher than those of the RVOT group. However, more participants in the RVOT group had thyroid disease than those in the LVOT group.

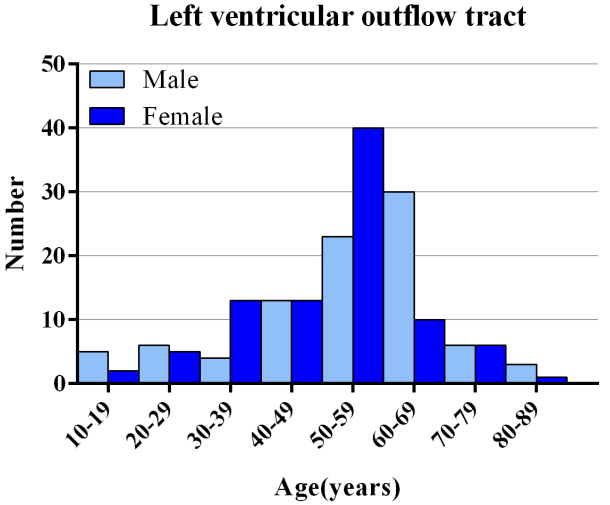
Laboratory Examination

The red-blood-cell count, hemoglobin, creatinine, and GGT of participants with PVCs in the LVOT group were higher than those of the RVOT group—with $P = .008$, $P = .009$, $P = .001$, and $P < .001$, respectively—which may be related to the gender dominance of females in the RVOT group. However, the reference values for red-blood-cell count, hemoglobin, and creatinine for normal females are lower than those for males.

Echocardiographic Parameters

The left atrial diameter (LAD), left ventricular end-diastolic diameter (LVEDD), interventricular septal thickness (IVS), and left ventricular posterior wall thickness (LVPWT) in the LVOT group were larger than those in the RVOT group ($P < .001$), while the left ventricular ejection fraction (LVEF%) in the LVOT group was lower than that in the RVOT group ($P = .001$).

Figure 5. PVCs in LVOT. These PVCs showed no differences in gender; however, among the population with PVCs in the LVOT, female participants had a lower Onset Age than males, at 50-59 vs 60-69 years old, respectively. In addition, female participants with PVCs in the LVOT had two peaks of Onset Age, 30-39 and 50-59. In those two phases, females had a higher incidence than that of males.



Abbreviations: LVOT, left ventricular outflow tract; PVC, premature ventricular contractions; RVOT, right ventricular outflow tract.

DISCUSSION

The current study also found that the incidence of arrhythmias in the LVOT group gradually increased with age, which was consistent with the results of Tanaka et al'sstudy.[9] The incidence of such arrhythmias decreased significantly in participants over 70 years old, which was different from the age characteristics of participants with atrial fibrillation in Koshiyama eta al's study, which was increased with age.[24]

Gender differences in clinical manifestations, electrophysiological properties, and treatment of IVAs have been an area of research in the last years. Consistent to other studies,[11-15] the current study found gender differences in the prevalence of IVAs.

Women in the RVOT group had more frequent PVCs than those in the LVOT group Gender-related differences in the autonomic nervous system, hormonal status and/or arrhythmogenic characteristics of the substrate may explain these differences.

The current study demonstrated that differences of gender-specific and age distribution existed between the RVOT and LVOT group. PVCs in the RVOT group were more common in females, 67.8% in females and 32.2% in males. Compared with the LVOT group, the RVOT group has a significant female predominance. However, no gender differences existed for the LVOT group, and the overall incidence was the same for females and males, 50% for females and 50% for males, but the incidence was higher in females than in males between the ages of 30-39 years old and 50-59 years old. These results suggested that estrogen might be correlated to the occurrence of outflow tract VT, as other studies have found[14,15]. However, the pathophysiological basis of this gender disparity in human should be further investigated.

As supported by the findings of other studies showing the effects of thyroid disease,[24,25] the current study found that the prevalence of thyroid disease in the RVOT group was higher than that of the LVOT group.[25] Compared with the LVOT group, the ROVT group was younger and had a higher mortality rate from thyroid dysfunction.

The current study has some limitations. First, the study included patients who underwent RFA in the cardiology department of the research team's hospital from January 2015 to January 2019 (not recently), and those patients under 10 years old weren't included. Therefore, the results have a certain bias and fail to explain the onset-age characteristics of VT in the whole-age range. Second, as far as the included females were concerned, the research didn't analyze their estrogen levels and menstruation and the relationship between the onset age of the first PVCs and estrogen levels. Third, except for participants with VT who had undergone radiofrequency ablation (RFA) in the research team's hospital in the prior 4 years, a small number of patients had surgical indications but refused surgery due to economic factors, and they weren't included in the current study, which may have a

certain impact on its results. Finally, the relationship between sex hormones, thyroid hormones, neuroendocrine levels, and PVCs in the outflow tract and its internal mechanism needs to be further clarified.

CONCLUSIONS

The current study found that age and gender-related differences existed for different sites of origins for PVCs and VTs. A significant difference in the age of onset, gender, comorbidities and echocardiographic parameters existed between the RVOT and LVOT groups. The above results can enable clinicians to have a further profound and comprehensive understanding of the population characteristics of patients with outflow tract VT.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

REFERENCES

1. Liang JJ, Han Y, Frankel DS. Ablation of outflow tract ventricular tachycardia. *Curr Treat Options Cardiovasc Med*. 2015;17(2):363. doi:10.1007/s11936-014-0363-9
2. Xiong Y, Zhu H. Electrocardiographic characteristics of idiopathic ventricular arrhythmias based on anatomy. *Ann Noninvasive Electrocardiol*. 2020;25(6):e12782. doi:10.1111/anec.12782
3. Yarlagadda RK, Iwai S, Stein KM, et al. Reversal of cardiomyopathy in patients with repetitive monomorphic ventricular ectopy originating from the right ventricular outflow tract. *Circulation*. 2005;112(8):1092-1097. doi:10.1161/CIRCULATIONAHA.105.546432
4. Yamada T, Doppalapudi H, Maddox WR, McElderry HT, Plumb VJ, Kay GN. Prevalence and Electrocardiographic and Electrophysiological Characteristics of Idiopathic Ventricular Arrhythmias Originating From Intramural Foci in the Left Ventricular Outflow Tract. *Circ Arrhythm Electrophysiol*. 2016;9(9):e004079. doi:10.1161/CIRCEP.116.004079
5. Yamada T. Twelve-lead electrocardiographic localization of idiopathic premature ventricular contraction origins. *J Cardiovasc Electrophysiol*. 2019;30(11):2603-2617. doi:10.1111/jce.14152
6. Li S, Wang Z, Shan Z, et al. Surface electrocardiography characteristics and radiofrequency catheter ablation of idiopathic ventricular arrhythmias originating from the left infero-septal papillary muscles: differences from those originating from the left posterior fascicle. *Europace*. 2018;20(6):1028-1034. doi:10.1093/europace/eux071
7. Kim RJ, Iwai S, Markowitz SM, Shah BK, Stein KM, Lerman BB. Clinical and electrophysiological spectrum of idiopathic ventricular outflow tract arrhythmias. *J Am Coll Cardiol*. 2007;49(20):2035-2043. doi:10.1016/j.jacc.2007.01.085
8. Yang SG, Mlček M, Kittnar O. Gender differences in electrophysiological characteristics of idiopathic ventricular tachycardia originating from right ventricular outflow tract. *Physiol Res*. 2014;63(suppl 4):S451-S458. doi:10.33549/physiolres.932920
9. Tanaka Y, Tada H, Ito S, et al. Gender and age differences in candidates for radiofrequency catheter ablation of idiopathic ventricular arrhythmias. *Circ J*. 2011;75(7):1585-1591. doi:10.1253/circj.CJ-10-0941
10. Nakagawa M, Takahashi N, Nobe S, et al. Gender differences in various types of idiopathic ventricular tachycardia. *J Cardiovasc Electrophysiol*. 2002;13(7):633-638. doi:10.1046/j.1540-8167.2002.00633.x
11. Bernal O, Moro C. [Cardiac arrhythmias in women]. *Rev Esp Cardiol*. 2006;59(6):609-618. doi:10.1157/13089748
12. Nakagawa M, Sekine Y, Ono M, et al. Gender differences in the effect of auditory stimuli on ventricular repolarization in healthy subjects. *J Cardiovasc Electrophysiol*. 2009;20(6):653-657. doi:10.1111/j.1540-8167.2008.01401.x
13. Peng J, Ruan FH, Yang RH, et al. [Clinical features of idiopathic ventricular tachycardia of various types and their radiofrequency ablation therapy]. Nan Fang Yi Ke Da Xue Xue Bao 2006; 26(8): 1152-3, 62.
14. Marchlinski FE, Deely MP, Zado ES. Sex-specific triggers for right ventricular outflow tract tachycardia. *Am Heart J*. 2000;139(6):1009-1013. doi:10.1067/mhj.2000.106164
15. Saito T, Ciobotaru A, Bopassa JC, Toro L, Stefani E, Eghbali M. Estrogen contributes to gender differences in mouse ventricular repolarization. *Circ Res*. 2009;105(4):343-352. doi:10.1161/CIRCRESAHA.108.190041
16. Santangeli P, di Biase L, Pelargonio G, Natale A. Outcome of invasive electrophysiological procedures and gender: are males and females the same? *J Cardiovasc Electrophysiol*. 2011;22(5):605-612. doi:10.1111/j.1540-8167.2010.01920.x
17. Mukai Y. Sex Differences in Atrial Fibrillation. *Circ J*. 2022;CJ-21-1072. doi:10.1253/circj.CJ-21-1072
18. Frankel DS, Tung R, Santangeli P, et al. Sex and Catheter Ablation for Ventricular Tachycardia: An International Ventricular Tachycardia Ablation Center Collaborative Group Study. *JAMA Cardiol*. 2016;1(8):938-944. doi:10.1001/jamacardio.2016.2361
19. Kannan L, Kotus-Bart J, Amanullah A. Prevalence of Cardiac Arrhythmias in Hypothyroid and Euthyroid Patients. *Horm Metab Res*. 2017;49(6):430-433. doi:10.1055/s-0043-105275
20. Purtell K, Roepke TK, Abbott GW. Cardiac arrhythmia and thyroid dysfunction: a novel genetic link. *Int J Biochem Cell Biol*. 2010;42(11):1767-1770. doi:10.1016/j.biocel.2010.07.013
21. Chojnowski K, Bielec A, Czarkowski M, Dmowska-Chalaba J, Kochanowski J, Wasowska A. Repeated ventricular. *Cardiol J*. 2007;14(2):198-201.
22. Tayal B, Graff C, Selmer C, et al. Thyroid dysfunction and electrocardiographic changes in subjects without arrhythmias: a cross-sectional study of primary healthcare subjects from Copenhagen. *BMJ Open*. 2019;9(6):e023854. doi:10.1136/bmjopen-2018-023854
23. Yoshida N, Yamada T, McElderry HT, et al. A novel electrocardiographic criterion for differentiating a left from right ventricular outflow tract tachycardia origin: the V2S/V3R index. *J Cardiovasc Electrophysiol*. 2014;25(7):747-753. doi:10.1111/jce.12392
24. Koshiyama M, Tamaki K, Ohsawa M. Age-specific incidence rates of atrial fibrillation and risk factors for the future development of atrial fibrillation in the Japanese general population. *J Cardiol*. 2021;77(1):88-92. doi:10.1016/j.jjcc.2020.07.022
25. Akın A, Unal E, Yıldırım R, Ture M, Balık H, Haspolat YK. Evaluation of QT dispersion and Tp-e interval in children with subclinical hypothyroidism. *Pacing Clin Electrophysiol*. 2018;41(4):372-375. doi:10.1111/pace.13286