

## Original Article

# Cardiac characteristics in the premature ventricular contraction patients with or without ventricular tachycardia

Yafen Su<sup>1\*</sup>, Meng Xia<sup>2,3\*</sup>, Junxian Cao<sup>2</sup>, Qianping Gao<sup>2</sup>

<sup>1</sup>Ambulatory Electrocardiogram Room, The First Affiliated Hospital of Harbin Medical University, China; <sup>2</sup>Unit of Cardiology, The First Affiliated Hospital of Harbin Medical University, China; <sup>3</sup>Unit of Cardiology, Liaoyang Central Hospital, China. \*Equal contributors.

Received August 21, 2017; Accepted March 22, 2018; Epub June 15, 2018; Published June 30, 2018

**Abstract:** Background/Aims: Frequent (sustained) premature ventricular contractions (PVCs) lead to ventricular tachycardia (VT), which triggers ventricular fibrillation and sudden cardiac death. The cardiac characteristics and risk prediction in frequent/sustained PVC patients with or without VT have been still in need of investigation. Methods: The data from patients with frequent PVCs via 24 h ambulatory electrocardiogram (ECG) monitor were collected at the Department of Cardiology in the First Affiliated Hospital of Harbin Medical University from January 1, 2012 to August 31, 2015. Total 342 patients were grouped into VT group (n=136) and Non-VT group (n=206) based on the presence or absence of VT. Cardiac functional examination and blood tests were carried out on the second day of admission. Independent risk factors related to the occurrence of VT were identified. The receiver operating characteristic (ROC) curves was established to evaluate the accuracy of the risk factors and VT. Results: The baseline characteristics were similar between the two groups. The blood potassium, extensive PVC burden, left ventricular ejection fraction (LVEF), PVC couplets, and alcohol consumption were associated with the occurrence of VT. Of them, the occurrence of PVC couplets was an independent high risk factor for the development of VT in the patients with frequent PVCs. Based on the weight of these risk factors for the occurrence of VT, a simple scoring method for VT prediction was set up in this study. The area under curve (AUC) for receiver operating characteristic (ROC) curves of the new scores resulted from the scoring method was 0.8874, indicating a valuable predictor for VT occurrence. Conclusion: The PVC couplets is an independent high risk factor for the development of VT in the patients with frequent PVCs.

**Keywords:** Sudden cardiac death, ventricular tachycardia, premature ventricular contractions, left ventricular ejection fraction, electrocardiogram

## Introduction

The premature ventricular contractions (PVCs) are early depolarization of the myocardium caused by an electrical impulse or ectopic rhythm from any part of the ventricles, including the ventricular septum, before the sinoatrial impulse has reached the ventricles. According to the frequency of ventricular premature beats (VPB), PVCs can be divided into sporadic and frequent [1]. Sporadic PVCs are, also called functional premature beats, defined as less than 6 pulses/min, which can occur in healthy people; while frequent PVCs, defined as more than 6 pulses/min, can occur in patients with

structural cardiopathy such as coronary artery disease (CAD), aortic stenosis, cardiomyopathy and electrolyte problem. The electrical events of the heart detected with the ECG allow the PVC to be easily distinguished from a normal heart beat. PVCs can be observed in both healthy people and patients with or without structural cardiopathy [2, 3]. Frequent PVCs, also called sustained PVCs, is a risk factor that leads to ventricular tachycardia.

Ventricular tachycardia (VT) is the myocardial arrhythmias under His bundle branch and myocardial conduction fiber. Wellens [4] defined VT as more than 100 beats/min, and three or more

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**Table 1.** Basic characteristics and medical history of the two groups (n (%))

Parameter	VT (n=136)	Non-VT (n=206)	P
Ages (years), mean $\pm$ SD	58.10 $\pm$ 13.50	56.44 $\pm$ 15.17	0.300
Male	70 (51.47)	83 (40.29)	0.042
Smoking	44 (32.35)	56 (27.18)	0.304
Drinking alcohol	38 (27.94)	32 (15.53)	0.005
CAD	54 (39.71)	94 (45.63)	0.279
OMI	11 (8.09)	7 (3.40)	0.057
Hypertension	45 (33.09)	83 (40.29)	0.178
Diabetes	20 (14.71)	24 (11.65)	0.409
DCM	48 (35.29)	11 (5.34)	< 0.001
Alcoholic cardiomyopathy	5 (3.68)	0 (0.00)	0.021
ICM	18 (13.24)	6 (2.91)	< 0.001
Valvular heart disease	4 (2.94)	4 (1.94)	0.816
HCM	1 (0.74)	0 (0.00)	0.398
Tachycardiomyopathy	1 (0.74)	0 (0.00)	0.398

VT: ventricular tachycardia, CAD: coronary artery disease, OMI: old myocardial infarction, DCM: Dilated Cardiomyopathy, ICM: ischemic cardiomyopathy, HCM: hypertrophic cardiomyopathy.

consecutive spontaneous PVCs. Six or more rapid ventricular beats (frequency > 100/min) are considered as persistent VT (longer than 30 seconds), while less than 6 beats as non-persistent VT (episodes less than 30 seconds). Persistent VT is very dangerous, as it can trigger ventricular fibrillation and sudden cardiac death.

Although clinical and electrophysiological studies have featured the different initiation patterns of VT [5, 6], studies on the cardiac characteristics in the PVC patients with or without VT have not been reported. Therefore, this study was designed to explore the predictors for the PVC patients who may develop into VT, and an evaluating method based on the weights of these predictors on VT. Due to a higher morbidity of cardiac diseases in the northeastern part of China, where there have been a longer winter and the unhealthy diet, all patients in the current study were from one hospital in Harbin, a representative city in the northeast of China.

### Patients and methods

#### Patients

This was a retrospective study. The medical records were collected from 342 patients with frequent PVCs detected via 24 h ambulatory ECG monitoring at Department of Cardiology in

First Affiliated Hospital of Harbin Medical University from January 1, 2012 to August 31, 2015. Inclusion criteria for the study were: 1) with a more than 30-beat of ventricular premature per hour; 2) the frequency of PVCs ranged from 746 to 47083 per 24 h. Exclusion criteria were: 1) pulmonary heart disease, severe dysfunction of kidney and liver, rheumatic disease, and tumor; 2) receiving the treatment with digitalis, quinidine and tricyclic antidepressant. The 342 patients were assigned into VT group (136) and non-VT group (206) based on the presence or absence of VT. The study was approved by the Ethical Committee of Institutional Hospital Board at the First Affiliated Hospital of Harbin Medical University.

#### Information collection

The baseline information was collected at admission, including gender, age, blood pressure, and heart rate. Medical history included hypertension, coronary artery disease (CAD), dilated cardiomyopathy (DCM), ischemic cardiomyopathy (ICM), smoking and drinking (alcohol). Heart function examination and blood tests were carried out on the second day of hospitalization. Measurements of LVEF, left ventricular end-diastolic diameter (LVEDD), inter-ventricular septal thickness (IVST) and left ventricular posterior wall thickness (LVPWT) were conducted by a cardiology specialist through Vivid Echocardiogram. The left ventricular muscle mass (LVM) was calculated according to the Devereux formula. Ambulatory monitoring was initiated in the afternoon following the hospitalization. An electrocardiogram specialist was responsible for recoding and analyzing the 24 h ambulatory ECG monitoring results. The total heart beats, frequency of PVCs, PVC burden, PVC couplets, polymorphic and multifocal PVCs, and VT were recorded.

#### Statistical analysis

Normally distributed variables were compared with Student's *t*-test, while non-normally distributed variables were compared with Wilcoxon two sample test. Qualitative data were compared by  $\chi^2$  test. The receiver operating characteristic (ROC) curves were drawn with the proc

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**Table 2.** Comparison of laboratory blood examination in the two groups (mean  $\pm$  SD)

Parameter	VT group (n=136)	Non-VT group (n=206)	P
Glucose (mmol/L)	5.80 $\pm$ 2.28	5.30 $\pm$ 1.13	0.373
Cholesterol (mmol/L)	4.40 $\pm$ 1.13	4.69 $\pm$ 1.01	0.016
TG (mmol/L)	1.50 $\pm$ 1.02	1.58 $\pm$ 0.83	0.044
LDL (mmol/L)	3.01 $\pm$ 0.93	3.18 $\pm$ 0.89	0.065
K <sup>+</sup> (mmol/L)	4.21 $\pm$ 0.44	4.05 $\pm$ 0.38	0.001
Mg <sup>2+</sup> (mmol/L)	0.85 $\pm$ 0.08	0.87 $\pm$ 0.09	0.076
Ca <sup>2+</sup> (mmol/L)	2.30 $\pm$ 0.14	2.31 $\pm$ 0.16	0.093
TNI (ng/mL)	0.10 $\pm$ 0.81	0.01 $\pm$ 0.08	< 0.001
CKMB (u/L)	14.39 $\pm$ 13.25	11.71 $\pm$ 10.20	0.032
Fibrinogen (g/L)	2.71 $\pm$ 0.76	2.68 $\pm$ 0.70	0.626
UA (umol/L)	361.8 $\pm$ 143.2	308.7 $\pm$ 87.94	0.003

VT: ventricular tachycardia, TG: triglyceride, LDL: low density lipoproteins, TNI: troponin I, CKMB: creatine kinase-MB, UA: uric acid.

**Table 3.** Cardiac parameters by Doppler echocardiography and ambulatory electrocardiogram (mean  $\pm$  SD)

Parameter	VT (n=136)	Non-VT (n=206)	P
VPCs (beats/24 h)	11628 $\pm$ 9227	8440 $\pm$ 8520	< 0.001
Heart rates (beats/24 h)	98662 $\pm$ 15947	104732 $\pm$ 64126	0.156
LVPWT (mm)	9.13 $\pm$ 1.04	9.17 $\pm$ 1.05	0.797
IVST (mm)	9.35 $\pm$ 1.33	9.26 $\pm$ 1.23	0.714
LVEDD (mm)	59.00 $\pm$ 12.07	49.16 $\pm$ 6.67	< 0.001
LVEF	47.29 $\pm$ 16.24	61.29 $\pm$ 11.07	< 0.001
LVM (g)	277.49 $\pm$ 99.42	201.37 $\pm$ 59.34	< 0.001
QT interval (ms)	408.42 $\pm$ 60.34	396.65 $\pm$ 49.88	0.020
QTc (ms)	460.71 $\pm$ 49.90	448.73 $\pm$ 47.22	0.002
PVCcouplets, n (%)	132 (97.06)	88 (42.72)	< 0.001
Multifocal PVCs, n (%)	19 (13.97)	5 (2.43)	< 0.001
Polymorphic PVCs, n (%)	35 (25.93)	11 (5.34)	< 0.001
PVC burden (%)	11.99 $\pm$ 9.5	8.33 $\pm$ 8.07	< 0.001

VT: ventricular tachycardia, PVCs: premature ventricular contractions; LVPWT: left ventricular posterior wall thickness, IVST: interventricular septal thickness, LVEDD: left ventricular end-diastolic diameter, LVEF: left ventricular ejection fraction, LVM: left ventricular muscle mass, QTc: Corrected QT Interval.

logistic program in the SAS9.3 statistic software to visualize the performance of risk factors versus the dependent variable (VT). With the same software, specificity and sensitivity of each independent variables (risk factors) were also obtained and an optimal cut-point value was obtained by the Youden Index with maximum potential effectiveness. The Mann-Whitney U test was used for analysis of the area under the ROC curves. Multiple stepwise logistic regression analysis was utilized to identify independent factors related to the occurrence of VT. All statistical analysis was carried out

with SAS 9.3 software and the statistical significance was set at  $P < 0.05$  for two-tailed tests.

### Results

#### Comparisons of baseline characteristics and blood test results

Of the 342 enrolled patients, 130 patients (38.0%) had no structural heart diseases, while 212 (62.0%) did, including CAD, DCM, ICM, hypertension and valvular heart disease. The baseline characteristics of the patients were shown in **Table 1**. No significant differences in age, smoking history, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were observed between the two groups. However, the ratios of patients with DCM (35.29% vs 5.34%), ICM (13.24% vs 2.91%), alcohol drinking history (27.94% vs 15.53%), and gender (male/female ratio) (51.47% vs 40.29%) were significantly higher in VT group than that in non-VT group ( $P < 0.05$ ).

The results of laboratory blood test were shown in **Table 2**. There were significant differences in blood cholesterol (4.40  $\pm$  1.13 vs 4.69  $\pm$  1.01), triglyceride (1.50  $\pm$  1.02 vs 1.58  $\pm$  0.83), potassium (4.21  $\pm$  0.44 vs 4.05  $\pm$  0.38), troponin I (0.10  $\pm$  0.81 vs 0.01  $\pm$  0.08), creatine kinase-MB (14.39  $\pm$  13.25 vs 11.71  $\pm$  10.20), and uric acid (361.8  $\pm$  143.2 vs 308.7  $\pm$  87.94) between the two groups ( $P < 0.05$ ), but there were no sig-

nificant differences in blood glucose (5.80  $\pm$  2.28 vs 5.30  $\pm$  1.13), low density lipoproteins (3.01  $\pm$  0.93 vs 3.18  $\pm$  0.89), magnesium (0.85  $\pm$  0.08 vs 0.87  $\pm$  0.09), calcium (2.30  $\pm$  0.14 vs 2.31  $\pm$  0.16), and fibrinogen (2.71  $\pm$  0.76 vs 2.68  $\pm$  0.70) between the two groups ( $P > 0.05$ ).

#### Cardiac characteristics monitored with Doppler echocardiography and ambulatory electrocardiogram

Cardiac function and ventricular arrhythmia characteristics were shown in **Table 3**. There

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**Table 4.** Risk factor prediction for patients with or without ventricular tachycardia by multivariate logistic regression analysis

Model	Parameter (Independent variables)	Model parameter	SD of parameter	OR	95% CI of OR lower limits	95% CI of OR upper limits	P
Model	Constant term	-2.7289	1.7038				
	K <sup>+</sup> (unit=0.1)	0.0886	0.0372	1.093	1.016	1.175	0.017
	PVC Burden	0.0673	0.0181	1.070	1.032	1.108	< 0.001
	LVEF	-0.0508	0.0105	0.950	0.931	0.970	< 0.001
	PVC Couplets	1.7629	0.2758	33.984	11.526	100.199	< 0.001
	Alcohol	0.4034	0.2004	2.241	1.021	4.915	0.044

Note: The model was obtained by stepwise logistic regression. Occurrence of ventricular tachycardia was used as the dependent variable. The variables with P value less than 0.1 by the single factor analysis in **Tables 1-3** were used as the independent variables. The fitting of this model was tested using the Hosmer and Lemeshow goodness test,  $P=0.652$ .

**Table 5.** Comprehensive scoring system

Number	Index	Points
1	K <sup>+</sup>	0 point: $K < 4.225$ 1 point: $4.225 \leq K < 4.37$ 2 points: $4.37 \leq K$
2	PVC Burden	0 point: Load of PVCs < 3.0% 1 point: $3.0\% \leq \text{Load of PVCs} < 7.56\%$ 2 points: $7.56\% \leq \text{Load of PVCs} < 15.0\%$ 3 points: $15.0\% \leq \text{Load of PVCs}$
3	LVEF	0 point: $68\% \leq \text{LVEF}$ 1 point: $60\% \leq \text{Load of PVCs} < 68\%$ 2 points: $50.5\% \leq \text{Load of PVCs} < 60\%$ 3 points: Load of PVCs < 50.5%
4	PVC Couplets	0 point: No 5 points: Yes
5	Alcohol	0 point: No 1 point: Yes

were significant differences in LVEDD ( $59.00 \pm 12.07$  vs  $49.16 \pm 6.67$ ), LVEF ( $47.29 \pm 16.24$  vs  $61.29 \pm 11.07$ ), LVM ( $277.49 \pm 99.42$  vs  $201.37 \pm 59.34$ ), QT interval ( $408.42 \pm 60.34$  vs  $396.65 \pm 49.88$ ), QTC ( $460.71 \pm 49.90$  vs  $448.73 \pm 47.22$ ), PVC couplets (97.06% vs 42.72%), multifocal PVCs (13.97% vs 2.43%), polymorphic PVCs (25.93% vs 5.34%), PVC burden ( $11.99 \pm 9.5$  vs  $8.33 \pm 8.07$ ), and total PVCs ( $11628 \pm 9227$  vs  $8440 \pm 8520$ ) between the two groups ( $P < 0.05$ ), but there were no differences in total heart rates ( $98662 \pm 15947$  vs  $104732 \pm 64126$ ), LVPWT, QI interval, and IVST between the two groups ( $P > 0.05$ ).

### Predicting factors of VT

As shown in **Table 4**, through multiple stepwise logistic regression analysis, 5 independent fac-

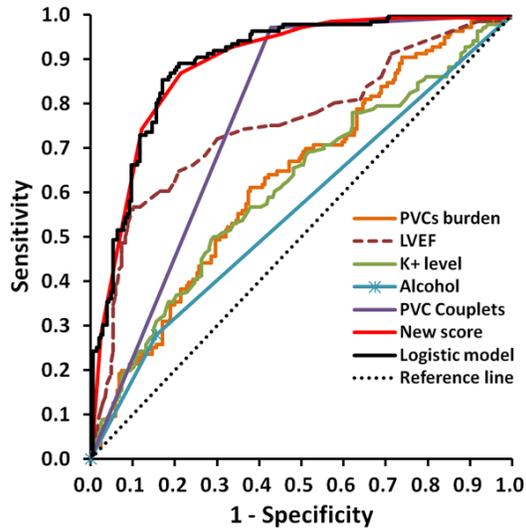
tors that significantly associated with the occurrence of VT were identified. Of the 5 risk factors, PVC couplet with odds ratio (OR) of 33.98 seemed to be the factor with highest risk for the development of VT. The rest 4 risk factors were alcohol consumption (OR 2.24), blood potassium (OR 1.09), PVCs burden (OR 1.07), and LVEF (OR 0.950).

Based on the weight of these 5 risk factors to the development of VT, a scoring system for predicting VT was established by creating the Receiver Operating Characteristic (ROC) curves (**Table 5**). The weight of risk factor was determined based on their scoring in the logistic regression analysis, with necessary ranges for variables requiring more than two intervals. As shown in **Table 5**, weight of PVC couplets was 5 points while the rest factors

were 3 points or less, and sum of the 5-factor-weight created a comprehensive scoring system. The new scores, which were derived from the summed weight of the 5 risk factors, were tested as a new variable against the 5 factors for the purpose of accuracy testing. The predicting accuracy of the scoring system and the 5 independent variables were shown through ROC curves in the **Figure 1**, which demonstrated that our scoring system was more accurate, and further supported the aforementioned correlation of the 5 risk factors with the development of VT in the patients.

As shown in **Table 6**, the area under the curve (AUC) value of PVC couplets (AUC=0.772) was surpassed only by that of new scores (AUC=0.887), indicating higher accuracy of our scoring system, and the relevance of other factors

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**Figure 1.** ROC curves of independent variables, new score and logistic regression model. AUC (95% CI) for PVC Burden 0.6298 (0.5700, 0.6896), LVEF 0.7519 (0.6966, 0.8072), K<sup>+</sup> level 0.6117 (0.5498, 0.6735), PVC Couplets 0.7717 (0.7350, 0.8084), Alcohol 0.5620 (0.5168, 0.6073), New score 0.8874 (0.8521, 0.9226), Logistic model 0.8932 (0.8593, 0.9270).

in the prediction of VT occurrence. Furthermore, the AUC value of the comprehensive scores lies within the realm of accuracy for clinically useful models (0.7-0.9), and approaches that of a significantly accurate predictive model.

### Discussion

The patients with frequent or sustained PVCs often suffer from structural cardiac diseases such as hypertension, and CAD. The structural cardiac diseases are common risk factors for VT occurrence. While the univariate analysis showed that the morbidity of ICM and DCM was significantly different between the two groups, there was no correlation between the arrest of VT and the baseline diseases such as CHD, hypertension, ICM and DCM by the multivariate analyses. These findings are different from the report of a previous published study in 2016 [7]. Severe hypokalemia can aggravate ventricular arrhythmia tendency and increase the risk of adverse events [8]. Although there was significant difference of serum potassium concentration between the two groups in our study, all those concentrations were within a normal range of serum potassium.

Heart failure is an end-point of various cardiac diseases and is associated with significant

mortality. Arrhythmia disorders contribute to the development of heart failure. Frequent PVCs are associated with the presence or subsequent development of left ventricular dilatation and dysfunction [9, 10]. Recurrent ventricular arrhythmias are responsible for significant mortality and morbidity in patients with heart failure secondary to reduced ejection fraction [11]. In the current study, the univariate analysis showed that there were significant differences in the LVEDD, LVM and LVEF between the two groups. However, only LVEF reduction ( $\leq 45\%$ ) was an independent risk factor for the development of VT.

Multiform PVCs are associated with an adverse prognosis in the general population [12]. Patients with PVC couplets are more prone to the development of VT than with single PVC [13]. A higher PVC burden ( $> 26\%/day$ ) is associated with left ventricular dysfunction in patients without structural cardiac diseases [14, 15]. While univariate regression analysis showed that PVC couplets, multifocal PVCs and polymorphic PVCs might be the predictors of VT, multivariate analysis showed that only PVC couplets was an independent predictor for the development of VT, but not multifocal PVCs or polymorphic PVCs. In addition, the current study indicated that PVC burden was also an independent predictor for the development of VT. The results of multivariate analysis further indicated that depressed LVEF, extensive PVC burden and PVC couplets were the risk factors for the development of VT, and that PVC couplets was the factor with highest risk (highest OR) for VT occurrence.

Despite the very high correlation of PVC couplets with VT, a comprehensive scoring system derived from the statistical analysis in the current study showed higher predictive accuracy. Our results confirmed that a model encompassing multivariate contributing and related to VT provided the most clinically relevant standard for VT prediction.

There were limitations of this study. First, the small sample size might reduce the efficacy of multiple logistic regression analysis. Second, it was a retrospective study, in which there might be a case selection bias. Third, the grouping of patients was based on presence or absence of VT, which might lead to the group heterogeneous and affect the analysis results.

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**Table 6.** The prediction value of independent variables and new scores in logistic regression model

Parameter	AUC for ROC	SD of AUC	95% CI of AUC limits		P*	Cutoff value	Sensitivity	Specificity	Youden index
			Lower	Upper					
Model	0.8932 <sup>a</sup>	0.0172	0.8593	0.9270	0.606	-	-	-	-
PVC Burden	0.6298 <sup>a</sup>	0.0305	0.5700	0.6896	< 0.001	7.56	0.61	0.621	0.231
LVEF	0.7519 <sup>a</sup>	0.0282	0.6966	0.8072	< 0.001	50.5	0.898	0.566	0.464
K <sup>+</sup> level	0.6117 <sup>a</sup>	0.0315	0.5498	0.6735	< 0.001	4.225	0.5	0.709	0.209
PVC Couplets	0.7717 <sup>a</sup>	0.0187	0.7350	0.8084	< 0.001	-	-	-	-
Alcohol	0.5620 <sup>a</sup>	0.0231	0.5168	0.6073	< 0.001	-	-	-	-
New scores	0.8874 <sup>a</sup>	0.0180	0.8521	0.9226		8.5	0.868	0.786	0.654

\*AUC compared with new scores  $P < 0.05$ ; a: Compared with 0.5,  $P < 0.05$ .

### Conclusion

PVC couplets is the only highest risk factor for the development of VT in the patients with frequent PVCs. The model encompassing multiple variables contributing and related to VT can provide the most clinically relevant standard for VT prediction.

### Acknowledgements

This work was supported by the National Natural Science Foundation of China (813013-43) and National Natural Science Foundation of China (81700352).

### Disclosure of conflict of interest

None.

**Address correspondence to:** Qianping Gao, Unit of Cardiology, The First Affiliated Hospital of Harbin Medical University, 23 Youzheng Street, Nangang District, Harbin 150001, China. Tel: +861379600-0952; E-mail: 2604843564@qq.com

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