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## ■ Original Article

# The relationship between symptoms and QRS duration in patients with idiopathic ventricular premature complex

## *İdyopatik ventriküler prematür kompleksli hastalarda semptomlar ile QRS zamanı arasındaki ilişki*

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### Abstract

**Aim:** Premature ventricular complexes are one of the most common arrhythmias and, when not treated, can cause serious complications such as dilated cardiomyopathy and ventricular tachycardia. In our study, we investigated the relationship between QRS duration and symptoms in patients with idiopathic premature ventricles complex (IPVC).

**Material and Methods:** This is a multicenter, cross-sectional study involving 242 consecutive patients with more than 1,000 idiopathic PVC and normal QRS duration in 24-hour Holter follow-up who attended cardiology clinics in 18 different centers between January 2019 and May 2019. The relationship between the QRS durations was investigated by dividing the patients into 2 groups as symptomatic (n: 128) and asymptomatic (n: 114).

**Result:** The average age of 242 patients was  $51 \pm 13$  and 52.4% (127) of them were male patients. In the symptomatic IPVC group, sinus QRS duration, PVC QRS duration, coupling interval, and prematurity index were statistically significantly higher than the asymptomatic IPVC group. In the multivariate logistic regression analysis, a significant relationship was found between the sinus QRS duration (odds ratio (OR) = 1.3, 95% confidence interval (CI) = 1.01-1.05, p = 0.002) and symptoms in patients with IPVC. In the ROC analysis performed to show the power of sinus QRS duration in predicting symptoms in patients with IPVC, Area Under Curve (AUC) value was found as = 0.547 95% CI: 0.454-0.640, p = 0.320 (Figure 1).

**Conclusion:** In patients with IPVC; The prolonged sinus QRS duration was found to be superior to other parameters in patients being symptomatic.

**Keywords:** Idiopathic premature ventricular complex; coupling interval; QRS time

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## ÖZ

**Amaç:** Prematüre ventriküler kompleksler (PVC' ler) en sık karşılaşılan aritmilerden biridir ve tedavi edilmediğinde dilate kardiyomyopati, ventriküler taşikardi gibi ciddi komplikasyonlara neden olmaktadır. Çalışmamızda İdiyopatik premature ventriküler kompleksi (IPVC) olan hastalarda QRS süresi ile semptom arasındaki ilişkiyi araştırdık.

**Gereç ve yöntem:** Ocak 2019 ile Mayıs 2019 tarihleri arasında on dokuz farklı merkezde kardiyoloji kliniklerine başvuran 24 saatlik holter izleminde 1.000'den fazla idiyopatik PVC'si ve normal QRS süresi olan 242 ardışık hastanın dahil edildiği çok merkezli, kesitsel bir çalışmadır. Hastaların semptomlarına göre semptomatik (n: 128) ve asemptomatik (n:114) olarak 2 gruba ayrılarak QRS süreleri arasındaki ilişki araştırıldı.

**Bulgular:** 242 hastanın yaş ortalaması  $51 \pm 13$ 'ü ve %52,4 (127)'ü erkek cinsiyetteki hastalardan oluşmaktaydı. Semptomatik IPVC grubunda asemptomatik IPVC grubuna göre sinüs QRS süresi, PVC QRS süresi, coupling intervali ve prematürite indexi istatistiksel anlamlılıkla daha yüksekti. Yapılan multivariete lojistik regresyon analizinde IPVC'li hastalarda sinüs QRS süresi ile (odds ratio (OR) = 1.3, 95% confidence interval (CI) = 1.01-1.05, p=0.002) semptom arasında anlamlı ilişki saptandı. IPVC'li hastalarda sinüs QRS süresinin semptomları öngörmedeki gücünü göstermek için yapılan ROC analizinde Area Under Curve (AUC) değeri = 0,547 %95 GA: 0.454-0.640, p = 0.320 olarak saptandı (Şekil 1).

**Sonuç:** IPVC'li hastalarda; uzamış sinüs QRS süresi olması hastaların semptomatik olmasında diğer parametrelerden daha üstün saptanmıştır.

**Anahtar kelimeler:** İdiyopatik premature ventriküler kompleks, coupling interval, QRS time

## Introduction

Idiopathic premature ventricular complexes (IPVC); It is one of the most common arrhythmias, which is monomorphic ventricular beats originating mostly from the right or left ventricular outflow tract regions in patients without structural heart disease [1]. When IPVC are not treated, they can cause left ventricular dysfunction, dilated cardiomyopathy, ventricular tachycardia, and sudden cardiac arrest. IPVC is symptomatic or asymptomatic, and when treated, it has been shown to cause a significant improvement in quality of life [2], preservation, or even improvement of left ventricular function [3].

Information about patients with IPVC being symptomatic is limited and was associated with origin location, the number of PVCs, and the time of coupling interval (CI) [4]. Since the patients being symptomatic will cause them to be treated, detection of this group of patients will protect them from undesirable side effects of idiopathic PVCs. Therefore, we aimed to investigate the relationship between QRS durations and symptoms in patients with IPVC.

## Material and Methods

This multicenter cross-sectional study involved more than 1,000 consecutive patients with PVC at 24-hour Holter follow-up admitted to cardiology clinics from January 2019 to May 2019 at

eighteen different centers. Exclusion criteria: patients with sinus QRS duration > 120 ms, less than 24 hours and/or inconclusive Holter recording, ischemic in etiology before or during admission, coronary artery disease (CAD), atrial fibrillation, permanent cardiac pacemaker, constrictive, hypertrophic, diabetic, patients with or suspected arrhythmogenic cardiomyopathy, continuous ventricular tachycardia (VT), a history of cardiac arrest, sick sinus syndrome, second or third-degree AV block, genetic cardiac channelopathies, myocarditis, pericardial disease, thyroid disorders, electrolyte disorders, anemia, moderate to severe valvular heart disease chronic pulmonary disease, pulmonary embolism or pulmonary hypertension. After exclusion criteria, 242 patients were included in the study. The patients were divided into two groups according to the presence of symptoms. In Holter ECG examination, the time to occurrence of symptoms and the presence of PVC were compared. As a symptom; Complaints of palpitations, syncope, near syncope, and dizziness were accepted. Antiarrhythmic drug use, use of  $\beta$ -blocker for at least 1 month, calcium channel blocker, amiodarone, or propafenone was defined as active. The study was conducted after local ethics committee approval. Informed consent of each subject were obtained. The study protocol is in accordance with the Declaration of Helsinki.

### Electrocardiographic evaluation

PVCs were defined as premature beats originating from the ventricular focus with a wide QRS complex and abnormally shaped (QRS duration > 120 ms and QRS and T wave morphology different from the normal beat). QRS time and PVC QRS time; It was measured manually on a 12-lead surface ECG with a premature QRS complex. Early ventricular complex coupling interval; was calculated as the time from the beginning of the R wave of the previous sinus beat to the onset of PVC. In Holter recordings, the premature index (PI) is calculated, which is defined as the ratio of the mean CI of the dominant PVC morphology and the CI of the first isolated PVC to the RR interval of the sinus loop just before the isolated PVC [5]. The anatomical region of PVC was determined using 12-lead electrocardiographic criteria [6]. ECG interpretations were made by an electrophysiologist unaware of other clinical data.

### Holter ECG evaluation

24-hour Holter follow-up was done with 12 channels. 24-hour Holter monitoring was repeated, with the recording time less than 80% of the target time or those with heavy artifacts. PVC load was evaluated as daily PVC number and percentage. Total number of PVC; It was determined by dividing the total number of PVCs by the total number of beats recorded on the 24-hour Holter ECG. The difference in PVC load between day and night was defined as Circadian variability. PVCs with at least three different morphologies were defined as Polymorphic PVC. Having PVC without a fully compensatory pause was defined as Interpolation.

### Echocardiographic evaluation

A 16-segment model was used according to the American Echocardiographic Society guidelines [7]. Left ventricular ejection fraction (LVEF) was calculated using the modified Simpson's method. LV function was evaluated echocardiographically according to LV systolic and diastolic diameters. Systolic and diastolic volumes were evaluated according to the latest American Society of Echocardiography quantification guidelines.

### Statistical analysis

SPSS 17.0 (SPSS Inc. Chicago, IL, USA) program was used for the recording and statistical analysis of the data. Distribution characteristics of the data were made using the Kolmogorov-Smirnov test. Normally distributed data were given as mean  $\pm$  standard deviation, and non-normally distributed data were given as median (interquartile range). Comparison of continuous values between the two groups was carried out using the

independent sample T-test. The analysis of data that were not normally distributed among the groups was performed using the Mann-Whitney-U test. Analysis of categorical variables was performed using the Chi-Square test or Fisher Exact test. Multivariate logistic regression analysis was used to determine the relationship between QRS durations and symptoms in patients with IPVC using variables that were found to be significant in the univariate analysis. ROC analyzes were used to determine the strength of the sinus QRS duration to show symptoms in patients with IPVC. Predictive validities were measured as the area under the ROC curves (c statistics), and comparisons of statistics were performed by De long's test.  $p < 0.05$  was considered significant in all statistical analysis results.

### Results

242 patients with IPVC were included in our study. The average age of the patients was  $51 \pm 13$  and 52.4% (127) of them were male gender patients. The patients were divided into 2 groups as symptomatic and asymptomatic according to the presence of symptoms associated with IPVC. 52% of the patients included in our study were symptomatic ( $n = 128$ ) and 48% asymptomatic ( $n = 114$ ) (Table 1). The basal demographic, clinical, and laboratory characteristics of the patients included in our study are shown in Table 1. There was no significant relationship between age, gender, drug use, PVC number, and percentage of all patients included in the study ( $p > 0.05$ ) (Table 1). The sinus QRS duration was statistically significantly higher in the symptomatic IPVC group compared to the asymptomatic IPVC group. (89 (80/100) vs 80 (80/90));  $p = 0.002$ ). In the symptomatic IPVC group, compared to the asymptomatic IPVC group, PVC QRS duration, coupling interval time, and prematurity index were statistically significantly higher (Table 1).

In the univariate logistic regression analysis performed to determine the parameters that may be associated with symptoms in idiopathic PVC patients; Sinus QRS duration, PVC QRS duration, CI duration, and prematurity index were found to be associated with the symptom. In the multivariate logistic regression analysis performed to determine the predictors of the symptom in patients with idiopathic PVC, a significant relationship was found between the sinus QRS duration (odds ratio (OR) = 1.3, 95% confidence interval (CI) = 1.01-1.05,  $p = 0.002$ ) and the presence of symptoms (Table 2). In the ROC analysis performed to show the power of sinus QRS duration in predicting symptoms in patients with IPVC, Area Under Curve (AUC) value was found as = 0.547 95% CI: 0.454-0.640,  $p = 0.320$  (Figure 1).

**Table 1:** Basic Demographic, Clinical and Laboratory findings of the study patients

	Symptoms (-) (n: 116)	Symptoms (+) (n: 126)	p value
Age (years)	51 (38 / 63)	50 (37 / 61)	0,29
Male gender (n (%))	67 (n %57,7)	60 (n %47,6)	0,11
Hypertension (n (%))	35 (n %30,2)	47 (n %37,3)	0,24
Diabetes mellitus (n (%))	21 (n %18,1)	15 (n %11,9)	0,17
Body mass index	25 (23 / 28)	26 (23,9 / 28)	0,69
Smoking (n (%))	31 (n %26,7)	31 (n %24,4)	0,70
Ejection Fraction (%)	60 (55 / 65)	60 (55 / 65)	0,92
Use of beta blockers	55 (n %47,4)	70 (n %55,6)	0,25
Use of calcium blood blockers	16 (n %13,8)	12 (n %9,5)	0,30
Ablation story	4 (n %3,4)	8 (n %6,3)	0,29
Mean heart rate	78 (70 / 84)	75 (68 / 82)	0,13
QT sinus (msec)	417 (397 / 440)	420 (390 / 430)	0,37
QTC sinus (msec)	400 (366 / 410)	395 (384 / 410)	0,29
Sinus QRS (msec)	80 (80 / 90)	89 (80 / 100)	0,002
PVC QRS (msec)	130 (120 / 140)	135 (130 / 140)	0,055
Compensatory pause	83 (n %71,6)	97 (n %77)	0,33
Compensatory pause time (msec)	995 (605 / 1100)	1000 (702 / 1200)	0,158
PVC coupling interval	460 (401 / 511)	490 (440 / 520)	0,007
Premature Index	11,8 (10,6 / 12,9)	12,3 (10,9 / 13,4)	0,037
PVC number	11692 (4164 / 20454)	7888 (3399 / 17039)	0,16
PVC percentage	11,2 (4,7 / 19)	8,25 (4 / 17,1)	0,13
Multifocal PVC	17 (n %14,7)	18 (n %14,3)	0,93
Circadian variability PVC	19 (n %16,4)	23 (n %18,3)	0,7
PVC origin (RVOT)	49 (n %42,2)	65 (n %51,6)	0,23

NOTE: Data are expressed as mean ± SD for normally distributed data or count (percentage) for categorical variables; PVC = Premature Ventricular Complex

**Table 2:** Univariate and multivariate logistic regression analysis for symptoms in patients with IPVC

Variable	Univariate			Multivariate		
	Unadjusted OR	95 % CI	p value	Adjusted OR	95% CI	p value
Age	0,99	0,97-1,00	0.23			
Gender (male / female)	1,5	0,90-2,49	0.11			
Sinus QRS	1,3	1,01-1,05	0.002	1,03	1,009-1,054	0.006
PVC QRS	1,02	1,00-1,05	0,046			
PVC coupling interval	1,00	1,00-1,01	0,005			
Prematurity index	1,2	1,01-1,42	0,033			

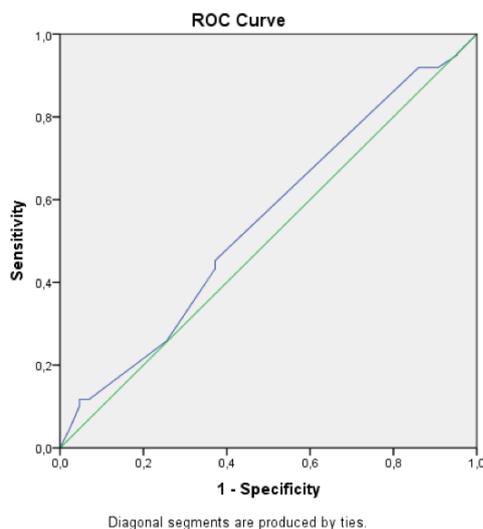
CI=confidence interval; OR=odds ratio; PVC = Premature Ventricular Complex

## Discussion

To the best of our knowledge, this study is the first study evaluating the sinus QRS duration and the symptoms in patients with IPVC. In our study; We found that the sinus QRS duration was higher in patients with symptomatic IPVC than patients with asymptomatic IPVC (p = 0.002).

When IPVC are not treated, they can cause left ventricular dysfunction, dilated cardiomyopathy, ventricular tachycardia, and sudden cardiac arrest. IPVC is symptomatic or asymptomatic, and when treated, it has been shown to cause a significant improvement in quality of life [2], preservation, or even improvement of left ventricular function [3]. Also, it has been reported

that PVC-induced cardiomyopathy is observed again in patients with PVC recurrence after catheter ablation [8]. PVC can be detected in up to 70% of healthy and young adults with Holter recordings [9]. The majority of patients with IPVC who receive treatment consist of patients who are admitted to the hospital with any symptoms. The differences in symptoms associated with PVC are due to hemodynamic changes. Other factors such as PVC burden and myocardial status, PVC origin, and CI can cause different hemodynamic effects on the heart [4]. In our study, no statistically significant difference was found between the two groups in ejection fraction and PVC origin (Table 1).



**Figure 1.** Comparison of receiver operating characteristic (ROC) curve of sinus QRS duration in predicting symptom in patients with IPVC

In previous studies, regardless of LV function, a PVC CI ratio > 50% was found to be associated with the presence of symptoms [4]. The shorter CI time would show itself with a stronger pulse, as it would provide longer LV filling for the next pulse. In our study, CI and prematurity index were found to be statistically significantly higher in symptomatic patients compared to asymptomatic patients (CI  $p = 0.007$ , PI  $p = 0.037$ ). The high number and load of PVC is also associated with the symptom. In our study, although the PVC load and the number of PVC were higher in asymptomatic patients, there was no statistically significant difference between the two groups.

The QRS complex reflects the time and speed of myocardial depolarization, which is associated with the LV structure rather than function. [10-16]. Although the severity of mechanical desynchronization is associated with the progressive expansion (> 120 ms) of the QRS complex [17,18] in many studies, it has been proven that there is mechanical desynchroniza-

tion in some patients with narrow QRS (<120 ms). This was explained by the detection of mechanical desynchronization with tissue doppler ECHO [19-22].

In our study, it was found that the prolonged sinus QRS duration in patients with IPVC with normal QRS periods without structural heart disease was associated with the symptom in patients. We thought that this situation could lead to the occurrence of symptoms by causing an increase in stroke volume as a result of increased QRS duration and myocardial coordination disorder or greater isovolumetric contraction.

## Conclusion

The presence of symptoms in patients with IPVC ensures their treatment. However, the relationship between patients with IPVC and QRS duration has not been investigated. Our study is the first study to reveal a relationship between the QRS duration and the symptom in patients with IPVC, and it has shown that there is a statistically significant relationship between the prolonged sinus QRS duration and the symptom. Considering that the symptoms may have more in patients with IPVC with prolonged sinus QRS duration, we think that more care should be taken to prevent possible complications.

## Declaration of conflict of interest

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