

Evaluation of Premature Ventricular Contractions in Children with Structurally Normal Hearts: A Single-Center Study

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ABSTRACT

Aim: Premature ventricular contractions are a prevalent arrhythmia in children, with the majority of cases exhibiting normal cardiac function and no anatomical abnormalities. The objective of this study was to assess the clinical course of premature ventricular contractions in children who do not have any structural heart abnormalities.

Materials and Methods: In this study, 60 patients younger than 18 years of age who were diagnosed with premature ventricular contractions in our clinic and who did not have any structural cardiac abnormalities on echocardiography were included. Demographic data, 12-channel standard resting electrocardiography, 24-hour Holter electrocardiography monitoring, and the exercise test records of the patients were retrospectively analyzed from their follow-up files.

Results: This study assessed 60 patients diagnosed with premature ventricular contraction, of whom 55% were male. Out of the total number of patients, 28 (46.7%) were asymptomatic, while the most often reported symptom was palpitations. Additionally, it was stated that five children had syncope. Medical treatment was given to 40 patients (66.7%). Beta-blockers (52.2%) were the most commonly prescribed drugs. Malignant arrhythmia or sudden cardiac death did not occur in any of the patients throughout the follow-up period. According to all patients' follow-up Holter electrocardiography results, a 61.6% decrease in premature ventricular contraction rates was observed. Complete recovery was observed in 16.7% of the patients.

Conclusion: Premature ventricular contractions in children generally have a good prognosis. Most cases are asymptomatic, and regardless of the origin, spontaneous regression rates over time are quite substantial. Determining the origin may help predict the prognosis.

Keywords: Premature ventricular contractions, ventricular arrhythmia, children

Introduction

One of the most prevalent rhythm problems in children is premature ventricular contractions (PVCs). PVCs are usually asymptomatic in children and are diagnosed incidentally due to electrocardiography (ECG) evaluations

performed for different purposes. Nearly all these cases have normal cardiac functioning and lack any structural cardiac abnormalities (1-3). PVCs are detected in 15% of babies and children and 35% of adolescents who do not have any pre-existing cardiac conditions (4).

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PVCs with a structurally normal heart in children are thought to be benign, although some studies have suggested adverse outcomes (1,5,6). Evidence from studies on the long-term consequences of PVCs shows that this arrhythmia is usually benign, and spontaneous regression is observed in the majority of cases (7). Therefore, it is not recommended to pursue routine medical therapy to reduce the frequency of PVCs (6).

However, some studies have shown that PVCs, which are common in pediatric patients, may cause cardiomyopathy during follow-up, which may worsen the prognosis (5). Evidence indicates that the frequency of PVCs exceeding 10% in adult patients is linked to ventricular dysfunction (8).

PVCs are an abnormal heart rhythm frequently seen in children. However, patients with frequent PVCs, even if isolated, are more likely to develop ventricular tachycardia (VT). It has been shown that the prognosis of PVCs with accompanying VT is worse (9). Currently, there is no universally accepted and clearly defined method for diagnosing, treating, and managing PVCs in children. This study aimed to determine the clinical progression of PVCs in children without any underlying cardiac structural abnormalities and assess the necessity and effectiveness of medical treatment.

Materials and Methods

Study Population

This retrospective study was conducted at the pediatric cardiology outpatient clinics of a tertiary referral hospital in Turkey. Sixty children younger than 18 years of age who were diagnosed with PVCs after incidental detection in the Well-Child Care Outpatient Clinics or who were symptomatic and diagnosed with PVCs as a result of investigations performed in the General Pediatric Outpatient Clinics were included in this study.

Exclusion Criteria

This study did not include pediatric patients with structural heart disease, a history of heart surgery, malignant ventricular arrhythmia, a history of stimulant drug use, any underlying chronic disease, or a family history of major arrhythmia. Moreover, newborns were also excluded from this study. Only the files of those patients diagnosed with PVCs and with complete data in their files were evaluated.

Definitions

PVCs are the early appearance of an abnormal QRS complex (typically duration ≥120 ms, the corresponding

T-wave is wide and in the opposite direction of the major QRS deviation, not preceded by a P-wave) (8). The diagnosis of PVCs is based on the recommendations of the European Paediatric and Congenital Cardiology Guidelines (8). The ventricle (right/left) where the PVCs originated was evaluated by looking at the heart rate, axis, and development of the right and left bundle branch block on 12-channel resting ECG. Only the first ECG recording of all patients was examined at the time of diagnosis.

A 24-hour Holter ECG was conducted utilizing a six-channel Holter ECG device (DMS 300-7 HolterReader; DMS, Stateline, NV, USA). The Holter ECG recordings were analyzed using the CardioScan 12.0 software developed by DM Software Inc. The percentage of total QRS complex and PVCs percentages, monomorphic, polyform, and VT percentages, and whether they have a single focal (unifocal/multifocal), were assessed according to the 24-hour Holter ECG monitoring data. Frequent PVCs were defined as the occurrence of PVCs in more than 10% (8). This study considered a reduction in the proportion of PVCs to <5% as indicative of partial recovery, and the absence of PVCs in the most recent Holter ECG was considered a complete recovery (10).

During the exercise test, the patient's rhythm was monitored at regular intervals with a 12-channel ECG while walking on a treadmill whose incline and speed increased for certain periods. The decrease or disappearance of PVCs in the ECG performed at rest or during exercise was considered positive.

Study Design

The examination comprised patients who were diagnosed with isolated PVCs in their Holter ECG recordings and did not have any structural cardiac abnormalities as determined by echocardiography (ECHO). All patient demographic information, admission symptoms, ECG, exercise test, Holter ECG monitorings (first and final), ECHO findings, medical treatments applied, responses to treatment, and follow-up periods were obtained from the patient files. Two ECGs and two Holter ECG recordings were evaluated for each patient, one at diagnosis and one during follow-up.

Ethical Consideration

Approval for this study was obtained from the Clinical Research Ethics Committee of Ege University Faculty of Medicine (approval no.: 16-4.1/9, date: 09.08.2016).

Statistical Analysis

Statistical analyses were performed with SPSS 25.0 software (IBM Corp., Armonk, NY, USA). The data's descriptive statistics mean, and compliance with the normal distribution were determined by kurtosis and skewness coefficients, Shapiro-Wilk, and Kolmogorov-Smirnov tests in the data analysis. In descriptive analysis, continuous data with normal distributions were expressed as mean ± standard deviation (SD) (range) and categorical variables as frequencies (numbers with percentages). The chi-square test was performed to compare the nominal data. Student's t-test was utilized to compare two normally distributed independent groups. The Kruskal-Wallis test was used to compare non-normally distributed parameters and ordinal variables. At the same time, the Mann-Whitney U test with Bonferroni correction was employed for group comparisons. Pearson's correlation test was used to assess univariate correlations between the patients' clinical follow-up data and, if available, response to medical treatment, prognosis, and different potential influencing factors. Statistical significance was defined as p<0.05 for all tests.

Results

A total of 60 patients (55% were male) with PVCs were evaluated in this study. The patients' median age was 10.75 [minimum (min.): 6 maximum (max.): 15] years. While 28 (46.7%) of the patients were asymptomatic, palpitations were the most prevalent symptom, and 5 of the children suffered syncope. Before the diagnosis of arrhythmia, no patients were using any drug therapy which could have a proarrhythmic effect. Table I shows the participants' demographic and clinical information at the time of diagnosis.

While 56.7% of the children in the research had a left bundle branch block pattern (right ventricle origin), 43.3% of the children had a right bundle branch block pattern (left ventricle origin) (Table I). The PVCs morphology of all of the patients were monomorphic. The presence of the inferior axis was observed in 90.2% of those patients exhibiting a left bundle branch block pattern, while a superior axis was observed in 8.6% of the patients.

The echocardiographic evaluations of all of the patients at diagnosis were normal, and no structural heart disease or cardiomyopathy was detected. There was a decrease in the number of PVCs in 33 out of 60 patients who underwent exercise testing, and the test result was positive. However, only 5 (15.6%) of the symptomatic children increased their PVCs with exercise.

Ninety-five percent of the patients experienced unifocal PVCs. When those patients with right and left-origin PVCs were compared, no significant difference was found between the PVCs percentages (p=0.21) (Table II). Only

Table I. Demographic characteristics and ECG, holter ECG, exercise test data and medical treatment conditions of the patients included in the study at the time of diagnosis

Characteristics	
Median age (minmax.), (year)	10.75 (6-15)
Gender, n (%) Male Female	33 (55) 27 (45)
Median follow-up duration (minmax.), (month)	18 (3-120)
Symptomatic patients, n (%)	32 (53.3)
Palpitation	13 (21.7)
Chest pain	10 (16.7)
Syncope	5 (8.3)
Fatigue	3 (5)
Presyncope	1 (1.7)
Asymptomatic patients, n (%)	28 (46.7)
Echocardiography findings at diagnosis, n (%) Normal Pathologic	100 (100) 0 (0)
PVCs features at diagnosis	
Mean PVCs percentage	8.7±6.4
Patients with VT, n (%)	18 (10.8)
Mean VT percentage	2.11±1.5
PVCs morphology Monomorphic	60 (100)
PVCs focal [n (%)] Unifocal Multifocal	57 (95) 3 (5)
PVCs origin	
LBBB, n (%) Inferior axis Superior axis	34 (56.7) 31 (90.2) 3 (8.8)
RBBB, n (%)	36 (43.3)
Exercise test response at diagnosis, n (%)	
Decreased PVCs	33 (55)
Not changed/Increased PVCs	27 (45)
Medical treatment, n (%)	
Medically treated patients Beta-blockers Propafenone	40 (66.7) 21 (52.2) 19 (47.5)
Untreated patients, n (%)	20 (33.3)
LBBB: Left bundle branch block, RBBB: Right bundle bra	nch block, PVC

LBBB: Left bundle branch block, RBBB: Right bundle branch block, PVCs: Premature ventricular contractions, VT: Ventricular tachycardia, min.-max.: Minimum-maximum

18 patients had VT. The mean percentage of PVCs was $8.7\pm6.4\%$, and the mean VT percentage was $2.11\pm1.5\%$ (Table I). The incidence of VT was higher in those cases with PVCs of right origin at the time of diagnosis than in those cases of left origin (p=0.046) (Table II).

The median follow-up period was 18 (min.: 3, max.: 120) months. After follow-up, none of the patients observed a rise in the occurrence of VT, experienced malignant arrhythmia or sudden cardiac death.

At the end of the follow-up, frequent PVCs were observed in 21.6% of the patients. 31.7% of the patients had a partial reduction in the frequency of PVCs, while 16.7% had a

complete recovery. It was observed that those patients with right-origin PVCs had higher rates of spontaneous complete recovery during follow-up than those patients with left-origin PVCs. However, this difference was not statistically significant (p=0.49) (Table II). Moreover, in the follow-up, it was observed that the PVCs percentages decreased more in those patients with positive exercise tests compared to the baseline (p=0.586).

Medical treatment was given to 40 patients (66.7%) with a mean duration of 19.45 (SD=13.6) months. Betablockers (52.2%) were the most commonly prescribed drugs, followed by propafenone (47.5%). While 35% of

Table II. Comparison of demographic data, clinical findings, treatment, and follow-up data of patients with PVCs originating from the right and left ventricles

	PVCs with right ventricle origin (n/%)	PVCs with left ventricle origin (n/%)	p value
Number of patients	34/56.7	26/43.3	NS
Gender Male Female	19/11.4 15/9	14/8.4 12/7.2	NS
Percentage of symptomatic patients (%)	19/58.8	13/50	0.36
Exercise test positivity (%)	14/41.17	19/73.07	0.014
Mean percentage of PVCs at diagnosis (minmax.)	11.12 (1.26-36)	6.77 (0.9-17.9)	0.21
Number of patients with VT at the time of diagnosis	15/44.1	3/11.5	0.046
Untreated patients (%)	9/26.4	11/42.3	0.39
Treated patients (%)	24/73.85	16/57.9	
Beta-blocker (%)	10/44	11/66.6	
Propafenone (%)	14/56	5/33.3	
Frequent PVCs (>10% PVCs) at follow-up	9/26.4	4/15.3	0.568
Improvement of PVCs in follow-up			
Complete (%)	5/14.7	5/19.2	0.49
Partial (%)	9/26.4	10/38.46	
No improvement (%)	20/58.8	11/42.3	

Table III. PVCs frequency, PVCs origin among treated and untreated patients with antiarrhythmic medication at follow-up period, exercise test positivity situation

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	Treated group	Untreated group	p value
Mean percentage of PVCs at the time of diagnosis (%)	19.2 (8.9-23.8)	17.7 (7.9-18.6)	0.007
Mean percentage of PVCs at last follow-up (%)	11.1 (5.2-19.5)	7.2 (3.9-12.5)	
PVCs origin Left ventricle Right ventricle	6.77 (0.9-17.9) 11.12 (1.26-36)	4.06 (0.9-10.9) 5.4 (1.06-15.6)	0.49
Exercise test positivity	19.3 (6.9-22.4)	11.6 (4.1-18.5)	0.586
PVCs: Premature ventricular contractions			

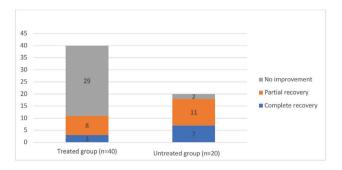


Figure 1. PVCs improvement rates between those who received medical treatment and those who did not in the follow-up of the patient (p=0.07)

PVCs: Premature ventricular contractions

patients who did not receive any medical treatment during follow-up had complete recovery, only 7.52% of those patients who received treatment had complete recovery. Thus, it was determined that antiarrhythmic treatment did not affect the course of the disease (p=0.007) (Figure 1, Table III). Among those patients receiving treatment, while no complete improvement in PVCs was observed in those patients using beta blockers, there was a complete clinical response in 15.7% of those using propafenone. In our study, propafenone was found to have a more successful clinical response than other medical treatments (p=0.033). When the origin of the PVCs was examined, it was seen that the spontaneous recovery rates of patients with PVCs originating from the right ventricle were higher than those of PVCs originating from the left ventricle. However, no significant difference was found (p=0.289).

No regression was observed in PVCs in any of the Holter ECG records of those patients with VT accompanying PVCs at the time of diagnosis, and these VT rates were found to be higher (p=0.0001). Four patients (6.7%) resistant to medical treatment were referred to a suitable center for electrophysiological studies.

Check-up ECHO could not be performed on any patient during the follow-up period. Therefore, the development of PVCs-induced cardiomyopathy could not be evaluated.

Discussion

PVCs are prevalent cardiac arrhythmias in children, and their prevalence varies with age. Although asymptomatic PVCs are generally considered harmless in children, cardiac dysfunction can occur in certain patients, especially those with frequent PVCs (8,10,11). There is limited data on this topic in children, and it is unclear when and under what conditions cardiomyopathy will develop (10-15).

The clinical characteristics, ECG, ECHO, exercise test, first and last Holter ECG, and long-term follow-up results of 60 pediatric patients diagnosed with PVCs were investigated in this study.

Male dominance (55%) was found in our study, and the median age at diagnosis was 10.75 years, which is similar to previous investigations (5,7,16). In the literature, the majority of pediatric patients with PVCs are asymptomatic. One study stated that the symptom prevalence was less than 5% (16). Similar to existing studies, the majority of patients in our study were asymptomatic at the time of diagnosis.

It has been found in many studies that most children's PVCs resolved on their own over time (6,11,17,18). For this reason, it is not advised to undergo regular medical therapy to decrease the occurrence of PVCs (19). In our study, 31.7% of the children experienced a partial improvement in the incidence of PVCs, while 16.7% showed complete resolution. There was no critical link between the decrease in PVCs rates and where the PVCs originated. In our study, some of the patients received medical treatment. Contrary to the literature, although medical treatment was initiated at a high rate to treat PVCs, there was no significant difference in the healing rates of PVCs between the groups that were given and those that were not given medical treatment (17). Hence, it can be concluded that medical treatment might be unnecessary when trying to mitigate the occurrence of PVCs.

Beta-blockers are the most commonly used antiarrhythmic drugs to reduce PVCs according to the literature (19). While no complete improvement in PVCs was observed in any of the patients using beta blockers in our study, a complete clinical response was achieved in 15.7% of those using propafenone. In our study, unlike the information in the current literature, it was determined that propafenone had a more successful clinical response than other medical treatments.

PVCs often originate from the right ventricle (20). This may be related to the higher rate of spontaneous regression of PVCs originating from the left ventricle. However, current literature is not sufficient to explain this relationship. A recent study to support this emphasized that only PVCs originating from the left ventricle showed regression, while PVCs originating from the right ventricle remained unchanged throughout the follow-up period (13). In the only study in the literature investigating the relationship between the disappearance of PVCs during follow-up and the ventricle from which they originate, it was reported

that PVCs originating from the left ventricle showed a spontaneous decrease and disappearance in the follow-up (21). Similar to the literature, 56.7% of the cases in our study were in the right ventricle. When the source of the PVCs was examined, it was seen that the spontaneous recovery rates of those patients with PVCs originating from the right ventricle were higher than those with PVCs originating from the left ventricle. This was contrary to current literature, but no statistically significant difference was found.

In addition to the absence of structural heart disease, the absence of a family history of arrhythmia and the reduction of PVCs with exercise have been evaluated as good prognoses in many studies (6,18,22). One study showed that another good predictor of prognosis was a decrease in PVCs in children with exercise (18). In our study, the exercise test positivity rate was high (55%) at the time of diagnosis. Additionally, those patients with a positive exercise test at the time of diagnosis had higher rates of complete recovery when PVCs percentages were evaluated at follow-up. This result we obtained supports the idea that exercise test positivity is an indicator of good prognosis.

Additionally, it is known that the detection of VT during diagnosis negatively affects the prognosis of PVCs (22,23). Supporting this information, no regression was observed in PVCs in any of the check-up Holter ECGs of our patients with VT accompanying PVCs at the time of diagnosis, and their VT rates were found to be higher compared to those without VT at baseline (23).

PVCs are classified as frequent if they are ≥10% in 24 hours, and it is well known that this group of patients should be constantly monitored for the development of cardiomyopathy. There are well-defined risk factors (being male, being asymptomatic, and having frequent PVCs formation) for the development of PVC-induced cardiomyopathy in adults (24-26). However, there has been no large-scale study which looked into the factors which might make children more likely to develop PVC-induced cardiomyopathy.

Many studies in the literature argue that as the frequency of PVCs increases in adults, the rate of cardiomyopathy increases and vice versa (24-26). Despite this, some current studies argue that there is no relationship between the frequency of PVCs and the development of cardiomyopathy (27,28). In none of our patients during follow-up, malignant arrhythmia or sudden cardiac death were observed. However, we could not detect the prevalence of PVC-induced cardiomyopathy as check-up ECHO evaluation was not performed.

Study Limitations

The primary constraint of this study was its retrospective design and small sample size. The patients' evaluation, testing, follow-up frequency, and treatment decisions were heterogeneous; thus, there is likely some selection bias in the data. Also, as left ventricular dysfunction was not assessed in our patients using follow-up echocardiography, we could not evaluate the link between the origin of PVCs and the risk of cardiomyopathy.

Conclusion

There are few studies on the clinical course of PVCs in the pediatric age group. PVCs, frequently encountered in childhood clinical practice and diagnosed incidentally, show a good prognosis in those children without structural heart disease. The majority of individuals are asymptomatic, and the rate of spontaneous regression is exceedingly high, regardless of the underlying cause. There may be no need for medical treatment to reduce the frequency of PVCs. As a result, in light of this study's findings, since it is impossible to precisely determine which patient may develop cardiomyopathy, the heart functions of all patients should be monitored at regular intervals with Holter ECG and ECHO. The results of this study offer valuable data for planning comprehensive studies with a standardized protocol for the evaluation, risk stratification, and followup of PVCs in children, including a larger group of patients from different age groups, preferably with prospective longterm follow-up.

Ethics

Ethics Committee Approval: Approval for this study was obtained from the Clinical Research Ethics Committee of Ege University Faculty of Medicine (approval no.: 16-4.1/9, date: 09.08.2016).

Informed Consent: Retrospective study.

Authorship Contributions

Concept: E.L., Design: M.T., E.L., Data Collection or Processing: M.T., E.L., Analysis or Interpretation: M.T., E.L., Literature Search: M.T., E.L., Writing: M.T., E.L.

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