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Ventricular Extrasystole in Children: Single-Center Experience

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What is already known on this topic?

- *It has been reported in many studies that ventricular extrasystole (VES) spontaneously improved over time in the majority of children. It was emphasized that only left ventricular origin VES could regress, and it was claimed that right VESs would not change at follow-up.*

What this study adds on this topic?

- *Ventricular extrasystole (VES) in children generally has a good prognosis; most of them are asymptomatic, and the rates of spontaneous regression over time are quite high, regardless of the origin. Medical treatment may not be necessary to reduce the frequency of VES.*

ABSTRACT

Objective: Ventricular extrasystole is one of the most common rhythm disorders in children, and almost all of them are characterized by normal cardiac functions without structural cardiac abnormalities. The aim of this study was to assess the clinical course of ventricular extrasystole in children who did not have cardiac structural abnormalities.

Materials and Methods: This retrospective study analyzed 24-hour rhythm Holter recordings performed in our clinic in children. Patients diagnosed with isolated ventricular extrasystole in Holter records and without structural heart disease on echocardiography were included in the evaluation.

Results: A total of 20 160 Holter results were evaluated in the study, and 226 patients (male; 66%) met the criteria. The mean follow-up time was 8.7 ± 3.2 years. While 81.8% of the patients were asymptomatic, the most common symptom was palpitation and 5 patients had syncope. Of the patients, 72 (31.8%) received medical therapy. Beta-blockers were the most often prescribed medication. Cardiomyopathy did not develop in any of the patients during the follow-up period. A partial reduction in the frequency of ventricular extrasystole was observed in 42% of the patients, while complete recovery was observed in 22%.

Conclusion: Ventricular extrasystole in children generally has a good prognosis; most of them are asymptomatic, and the rates of spontaneous regression over time are quite high, regardless of the origin.

Keywords: Ventricular extrasystole, children, follow-up

INTRODUCTION

Ventricular extrasystole (VES) is one of the most common rhythm disorders in children. In addition to the fact that it is often asymptomatic, almost all of them are characterized by normal cardiac functions without structural cardiac abnormalities.[1-5] Ventricular extrasystoles are observed in 15% of infants/children and 35% of adolescents without underlying heart disease.[6] It has been shown that the frequency of VES above 10% in adult patients is associated with ventricular dysfunction.[7] Additionally, patients with frequent isolated VES had a higher incidence of non-sustained and sustained ventricular tachycardia (VT) and the prognosis has been shown to be worse in these patients.[8] Although there are studies on long-term results in VESs, the majority of them have shown that this arrhythmia is benign, and spontaneous regression has been reported in most of them.[9-11] However, some studies have also shown that VES may have a worse prognosis in children.[12]

There is no single, well-defined strategy for the diagnosis, treatment, and management of VES in children. The purpose of this study was to assess the clinical course of VES in children who did not have cardiac structural abnormalities and to evaluate the effectiveness of medical treatment.

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MATERIALS AND METHODS

This retrospective study analyzed 24-hour rhythm Holter recordings performed in our clinic in children aged 6 months to 18 years between December 2010 and May 2022. Patients diagnosed with isolated VES in Holter records and without structural heart disease on echocardiography were included in the evaluation. This study was approved by the institutional research ethics board of Bursa Uludağ University and consent was waived (approval number; 2022-16/56).

Exclusion criteria included the following: those with congenital heart disease, a history of cardiopulmonary bypass, clinical or genetic cardiomyopathy (muscular dystrophies, aortopathies, etc.), ion channelopathy, coronary anomaly, and who had previously received chemotherapy. Patients with a history of sinus node dysfunction, supraventricular tachycardia, heart block, or cardiomyopathy or channelopathy in the family were also excluded from the study. Patients diagnosed with VES-related cardiomyopathy were included in the study. All patients' demographic information, clinical characteristics, and first and final Holter exams were assessed.

Electrocardiography

In the supine posture, when the patients were at rest, the GE MAC2000® equipment was used to record a 12-channel electrocardiography (ECG). Heart rate, QRS axis, PR interval, and QTc interval were evaluated in ECG. If there was VES, it was noted whether the VES originated from the right ventricle (left bundle branch block pattern) or left ventricle (right bundle branch block).

Echocardiography

Transthoracic echocardiography (t-ECHO) using Philips Affiniti 50® and Philips Affiniti 70® in the supine or left decubitus position on standard sections in accordance with the guidelines.[13-15] Shortening fraction (SF), left ventricular end-diastolic diameter (LVEDD) *z*-score, and mitral valve insufficiency were identified in the patients' t-ECHO assessment during the initial Holter test. The t-ECHO findings during the last Holter examination were also recorded.

Holter Monitoring

In all patients, Holter examination was performed after ECG evaluation and was evaluated by 2 pediatric cardiologists (FU and OMB). The minimum, maximum, and average heart rates were collected over the course of a 24-hour period while using the DMS® device for rhythm Holter monitoring. The percentage of VES was calculated by dividing the number of VES in a day by the number of QRS complex and multiplying by 100. The number of bigeminy, trigeminy, and couplet VES was noted. Ventricular tachycardia was defined as sustained VT if ≥30 seconds, and non-sustained VT if <30 seconds. As a result of Holter, patients were divided into 2 groups—group 1: VES frequency <10%; group 2: VES frequency ≥10%. The presence of non-sustained VT or couplet VES did not affect group categorization.

Exercise Test

Patients of the proper age and height had an exercise test and the cycling ergometer. The seat is adjusted according to the height of the child. Preliminary preparations were made by allowing the children to pedal for 3 minutes without power loading, and then the work rate was increased to 15 Watt/min for those with a height of 130-150 cm, and 20 Watt/min for those with a height of ≥150 cm.

Pedaling frequencies were adjusted to range from 60 to 80 per minute. Despite all the effort, the moment when the pedal frequency fell below 60 for 20 seconds was determined as the maximum effort time. Rhythm monitoring was performed with a 12-channel ECG throughout the test.

If done, cardiac MRI results and electrophysiological results (EPS) were evaluated.

In the study, a decrease in the percentage of VES below <5% was defined as partial recovery, while the absence of VES in the last Holter was defined as complete recovery.

Statistical Analysis

The data obtained from the research were analyzed with IBM Statistical Package for Social Sciences (SPSS) version 22.0 (IBM corp., Armonk, NY, USA). In the analysis of the data, "descriptive statistics, mean, and compliance of the data with the normal distribution were determined by kurtosis and skewness coefficients, Shapiro–Wilk, and Kolmogorov–Smirnov tests. Continuous variables with normal distribution were expressed by the means ± SD (range) and categorical variables were stated as frequencies (numbers with percentages) in descriptive analysis. The chi-square test was used to compare the nominal data. The "Student's *t*-test" was used to compare 2 normally distributed independent groups. The Mann–Whitney *U*-test was used to compare 2 independent groups that did not show normal distribution. Related categorical variables were compared by the McNemar test. The significance level was accepted as $P < .05$.

RESULTS

A total of 20 160 Holter results were evaluated in the study; 226 patients (male, 66%) met the criteria and VES ≥10% was seen in 136 of them. The mean follow-up time was 8.7 ± 3.2 years, whereas the average age was 11.9 ± 3.9 years old. While 81.8% of the patients were asymptomatic, the most common symptom was palpitation and 5 patients had syncope.

Electrocardiography

While 41.5% of the children included in the study had left bundle branch block pattern, 31.8% had right bundle branch block pattern, and VES morphology could not be evaluated in 26%. The inferior axis was seen in 89.3% of patients with left bundle branch block pattern, and VES with superior axis was seen in 9%.

Echocardiography and Exercise Test

Four patients had VES-induced cardiomyopathy. Three of these patients had LVEDD *z*-score greater than +2 while SF was measured as 22% in 1 of them. While the number of VES did not decrease in 5 of 114 patients who underwent exercise testing, unifocal VES increased with exertion only in 3 of them.

Holter Monitoring

All patients experienced unifocal VES, only 3 patients had sustained VT, 24 patients had non-sustained VT, and 46 patients

had couplet VES. The mean percentage of VES was found to be 8.2 ± 5.5.

Of the patients, 72 (31.8%) received medical therapy. Beta-blockers were the most often prescribed medication, followed by calcium channel blockers and propafenone. A total of 4 patients underwent EPS. Ventricular tachycardia could not be induced in any of these patients, and ablation was successfully performed in 2 of them with a focus on the right ventricular outflow tract. The demographic characteristics of the patients are shown in Table 1.

In the study, no significant difference was found between group 1 and group 2 according to the presence of symptoms, cardiac functions, LVEDDs, and presence of VT and couplets, while anti-arrhythmic drug use was significantly higher in group 2 (Table 2).

Follow-up

Cardiomyopathy did not develop in any of the patients during the follow-up period. Likewise, no increase in the frequency of VT was observed in Holter examinations and cardiac death was not observed in any patient. A partial reduction in the frequency of VES was observed in 42% of the patients, while complete recovery was observed in 22%. There was no significant difference between the groups in terms of a decrease in VES frequency (Figure 1).

Table 1. Characteristics of the Patients Included in the Study

Characteristics		**n (%)**
Mean age (years)	11.9 ± 3.9	
Mean follow-up duration (years)	8.7 ± 3.7	
Symptoms		
Asymptomatic		185 (81.8)
Palpitation		32 (14.5)
Chest pain		4 (1.7)
Syncope		5 (2.2)
VES features		
Mean percentage	8.2 ± 5.5	
Couplets		26 (11.5)
Non-sustained VT		24 (10.6)
Sustained VT		3 (1.3)
VES percentage ≥10%		136 (60.1)
VES morphology		
LBBB inferior axis		84 (37.1)
LBBB superior axis		10 (4.4)
RBBB		72 (31.8)
Unknown		60 (26.5)
VES induced cardiomyopathy		4 (1.7)
Exercise test response		114 (50.4)
Decreased VES		106 (92.9)
Not-changed VES		5 (4.3)
Increased VES		3 (2.6)
Medical therapy		
Beta-blockers		48 (21.2)
Calcium channel blockers		16 (7)
Propafenone		5 (2.2)
Sotalol		2 (0.8)
Amiodarone		1 (0.4)
None		154 (68.1)

LBBB, left bundle branch block; RBBB, right bundle branch block; VES, ventricular extrasystole; VT, ventricular tachycardia.

Table 2. Comparison of Ventricular Extrasystole Frequency and Sociodemographic Characteristics of Patients

	Group 1 (n = 90)	**Group 2 (n = 136)**	***P***
Age (years)	11.3 ± 3.1	12.2 ± 4.1	NS
Male	42	62	NS
Symptom presence	16	25	NS
Follow-up duration (years)	7.9 ± 2.9	8.9 ± 3.9	NS
Non-sustained VT	10	14	NS
Sustained VT	1	2	NS
Couplet	11	15	NS
Anti-arrhythmic medication	10	62	**<.001**
Initial t-EKO findings			
SF (%)	33.4 ± 10.4	32.8 ± 11.2	NS
LVEDD *z*-score	−0.6 ± 0.1	−0.7 ± 0.1	NS
MVR presence	12	19	NS
Last t-ECHO findings			
SF	34.2 ± 11.4	35.4 ± 12.2	NS
LVEDD *z*-score	0.1 ± 0.4	−0.2 ± 0.3	NS
MVR presence	11	19	NS
No change VES with exercise test	3	5	NS
Improvement of VES frequency			
Complete	16	34	NS
Partial	38	57	NS

LVEDD, left ventricular end-diastolic diameter; MVR, mitral valve regurgitation; NS, nonsignificant; SF, shortening fraction; t-ECHO, transthoracic echocardiography; VES, ventricular extrasystole; VT, ventricular tachycardia.

At the end of the follow-up, the percentage of VES decreased from 20.2% (9.2-24.2) to 12.3% (5.3-15.2) in the treated group, while it decreased from 10.9% (5.3-19.2) to 6.2% (1.3-11.2) in the untreated group (P = .46). There was no significant difference between the decrease in VES percentages and the origin of VES (Table 3).

In our study, the incidence of VES-induced cardiomyopathy was found to be quite low (1.7%). The clinical features of the patients that had cardiomyopathy are shown in Table 4.

DISCUSSION

Ventricular extrasystoles are one of the most common rhythm disorders in children and its prevalence varies with age. While the incidence of isolated VES in newborns is 20%, this rate decreases to 10% in the school-age period. Although isolated VES can be seen in 20%-30% of adolescents, the incidence of frequent VES is less than 5% in this age group.[16-20] In spite of the fact that asymptomatic VES is typically thought to be benign in children, cardiac dysfunction may develop as a result of dyssynchrony in some patients, particularly those who experience frequent VES. Data on this subject in children are scarce, and it is not clear at what frequency and under which conditions cardiomyopathy will develop.[21-23] In this study, the clinical features, ECG, Holter, first and last t-ECHO findings, and long-term

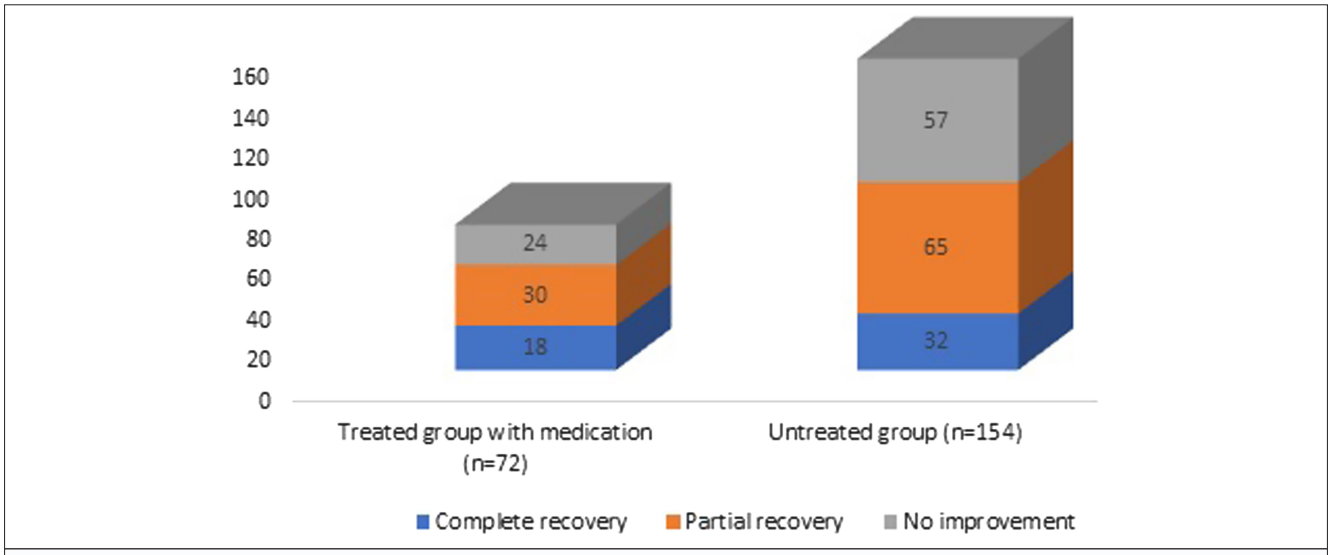

Figure 1. Ventricular extrasystole improvement rates between those who received medical treatment and those who did not in the follow-up of the patients. (*P* = .52)

follow-up results of 226 pediatric patients diagnosed with VES were evaluated.

In our study, male dominance (66%) was present and the mean age at diagnosis was 11.9, and these findings are consistent with other studies.[24-27] Furthermore 81.8% of our patients were asymptomatic. In a study, it was reported that less than 5% of patients had symptoms.[24]

Table 3. Ventricular Extrasystole Frequency Among Treated and Untreated Patients, as well as by VES Origin at Follow-Up Period

	VES (Initial) (%)	VES (Last) (%)	*P*
Treated group with medication	20.2 (9.2-24.2)	12.3 (5.3-15.2)	.46
Untreated group	10.9 (5.3-19.2)	6.2 (1.3-11.2)	
VES origin			
Left ventricle	18.1 (8.1-22.3)	11.3 (5.1-13.2)	.22
Right ventricle	13.2 (7.1-19.8)	8.5 (3.2-13.2)	

VES, ventricular extrasystole.

If VES ≥10% in 24 hours, it is considered to be frequent and it is known that this group of patients should be followed closely for cardiomyopathy. There were many studies demonstrating that this type of VES-related cardiomyopathy in children is reversible.[28-30] However, there was no comprehensive study that determined the risk factors for the development of VES-induced cardiomyopathy. In studies conducted with adult patients, the incidence of development of cardiomyopathy was found to be low in patients with frequent VES. In a study by Hasdemir et al.[30] the incidence of cardiomyopathy was found to be 6.8% in the 6-year follow-up of 249 patients. In another study by Niwano et al.[31] 239 patients with frequent VES were followed up for 5 years and it was shown that none of them developed cardiomyopathy.[32] Risk factors for VES-induced cardiomyopathy have been defined in adult patients.[33-35] These risk factors were male gender, being asymptomatic, and a high percentage of VES. It has also been shown that the risk of VES-induced cardiomyopathy was very low in people who had VES less than 20%-30% of the time.[34,35] In our study, the incidence of VES-induced cardiomyopathy was found to be quite low (1.7%),

Table 4. Clinical Characteristics of 4 Patients with Cardiomyopathy Associated with Ventricular Extrasystole

	Patient 1	Patient 2	Patient 3	Patient 4
Age (years)	9	15	16	14
Symptom	–	Palpitation	–	–
LVEDD (*z*-score)	3.2	2.9	1.9	2.2
LVSF (%)	31	34	22	36
VES with exercise test	Not changed	Decreased	Decreased	Decreased
VES frequency (%)	16.1	13.2	23.2	11.2
VES origin	RV	RV	RV	LV
Sustained VT	–	–	–	–
Non-sustained VT	–	+	+	–
Treatment	Beta-blocker	Ablation	Ablation	Beta-blocker
Follow-up duration (years)	2.3	2.1	4	1.2
CMP resolved	No	Yes	Yes	Yes

CMP, cardiomyopathy; LV, left ventricle; LVEDD, left ventricular end-diastolic diameter; LVSF, left ventricular shortening fraction; RV, right ventricle; VES, ventricular extrasystole; VT, ventricular tachycardia.

which was consistent with the literature. There was no significant difference between the percentage of VES and the risk of developing cardiomyopathy.

It has been reported in many studies that VES spontaneously improved over time in the majority of children.[1,24,36-39] Therefore, routine medical treatment to reduce the frequency of arrhythmias was not recommended. Catheter ablation as first-line treatment is recommended for symptomatic idiopathic VT/ Premature Ventricular Contraction (PVC)s from the Right Ventricular Outflow Tachcardia (RVOT) or the left fascicles in 2022 ESC guideline and ablation is not recommended as a first-line therapy in asymptomatic children and with normal left ventricle size or normal systolic functions.[40] In our study, there was a partial decrease in the frequency of VES in 42% of the children, and complete recovery was observed in 22% While most of the patients were not treated in our study, no significant difference was found between the treated and untreated groups in terms of improvement rates of VESs. For this reason, it was thought that medical treatment may not be necessary to reduce the frequency of VES.

Studies have shown that the origin of VES is often from the right ventricle.[41] It is not clear whether the reason for the frequency of VES originating from the right ventricle is related to the greater regression of VES originating from the left ventricle. In the study of Beaufort-Krol et al.[26] it was emphasized that only left ventricular origin VES could regress, and it was claimed that right ventricular VESs would not change at follow-up. In our study, 56.6% of the patients with known VES origin were in the right ventricle, consistent with the literature, but in our patient group, no significant difference was found in terms of regression and origin of VES in the long-term follow-up.

The limitations of this study were as follows: it was a retrospective study and it was not possible to determine the course of children in adulthood period whose do not improve with treatment.

CONCLUSION

Ventricular extrasystole in children generally has a good prognosis, most of them are asymptomatic, and the rates of spontaneous regression over time are quite high, regardless of the origin. Medical treatment may not be necessary to reduce the frequency of VES. Since it is not known exactly which patient will develop cardiomyopathy, these patients should be followed up in terms of cardiac functions at regular intervals.

Ethics Committee Approval: This study was approved by Ethics Committee of Bursa Uludağ University (Approval No: 2022-16/56).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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