Original Paper

Evaluation of Early Repolarization Pattern in Children with Mitral Valve Prolapse

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ABSTRACT: Background: Patients with mitral valve prolapse (MVP) may be prone to ventricular arrhythmias and sudden cardiac death and presence early repolarization pattern (ERP) in electrocardiography may be predict for ventricle arrhythmia. This study aimed to evaluation ERP in Children with MVP. Methods: In a cross-sectional study, we enrolled ERP in 70 MVP children with 70 age-and sex-matched healthy individuals. After echocardiography procedure for confirmation MVP, standard 12-lead electrocardiography recordings with sweeping rate of 25mm/s and an amplitude of 10mV/cm, and two cardiologists assessed who were blinded to the both groups. Result: We detected ERP in 17.14% of MVP patient's and seen in 8 case (11.43%) in control group, (P=0.23). the ERP occurred in MVP patient's mild, moderate and severe 4, 6 and 2 cases, (P=0.29). The ERP found in patients with and without chest pain 13 and 7, respectively (P=0.46) and, in patients with and without palpitations 15 and 5 cases, respectively (P=0.24). The ERP occurred 1.6 time more in patient with MVP in comparing with individual without MVP. The ERP occurred more frequently in among patients with moderate MVP in comparing with severe and mild. Chest pain and palpitation occurred more frequently in among patients with severe MVP. Conclusion: The prevalence of ERP in children with MVP has been at a higher-level incidence, especially among patients with complaining from chest pain. We suggested that children with MVP are in need of follow up considering the occurrence of arrhythmias.

KEYWORDS: Arrhythmia, Children, Electrocardiogram, Early Repolarization, Mitral Valve Prolapse, Sudden Cardiac Death.

Introduction

Mitral valve prolapse (MVP) which is considered as the most common abnormality of the cardiac valve, is defined as coving back of mitral valve into the left atrium during systole phase [1].

Although MVP is known as a benign abnormality, there is evidence of deteriorating MVP to ventricular arrhythmia and sudden cardiac death (SCD) [2].

The accurate mechanism of developing to ventricular arrhythmia is still unclear but abnormalities of the autonomic nervous system along with mechanical triggering of mitral valve can be the causes of ventricular arrhythmias [3].

Indeed, different studies showed source of atrial [4] and ventricular arrhythmias [5,6] and some degrees of autonomic dysfunction [7] as in patients with mitral regurgitation and MVP [8,9].

Other studies showed different heart rates, ST-segment depression and P-wave dispersion in patients with MVP [10,11].

ECG features of early repolarization include the presence of J-point elevation ≥1mm in ≥2 contiguous inferior and/or lateral leads of a standard 12-lead ECG. The presence of early repolarization pattern (ERP) divided based on the figure (slurred vs. notched) and location of ER (lateral, inferior, or inferior-lateral). And also divided based on high-risk ECG features of ERP (i.e., horizontal/descendent pattern, inferior or inferior-lateral location or J-waves ≥2mm) [12].

Recent studies have showed that early repolarization pattern is associated with an increased risk of idiopathic ventricular fibrillation and cardiac sudden death [13].

The aim of our study was to evaluate early repolarization pattern comparison between MVP patients and a control group of individuals by using electrocardiogram (ECG).

Materials and Methods

Study Population

The study was performed after obtaining informed parental consent and approving of the proposal in the Ethic Committee of university Medical Sciences. In a cross-sectional study, we enrolled 70 patients with MVP pattern and

70 healthy subjects, age-and sex-matched children as a control group, who referred between September 2019 and August 2020.

Electrocardiographic and echocardiographic procedures were performed on all patients.

We obtained the main information of patients such as gender, age, past medical history and clinical presentation from the admission records.

The exclusion criteria were as follow: history or echocardiographic evidence of rheumatic heart disease; additional congenital heart disease; Marfan's syndrome; arrhythmia; ventricular dysfunction; or any medication that could affect ECG parameters.

Echocardiography

Two echocardiographic experts who performed echocardiography with the utilization of 3 and 5 MHz transducers were blinded to the patients.

Our echocardiographic indexes for MVP diagnosis were based on mitral valve displacement 2mm or more above the mitral annulus in the long-axis view which can be parasternal or apical three chambers.

We obtained the degree of mitral regurgitation using guideline's recommendations [14].

Figure 1 shows the MVP and normal mitral valve echocardiography in long axis view in the subjects in our study.
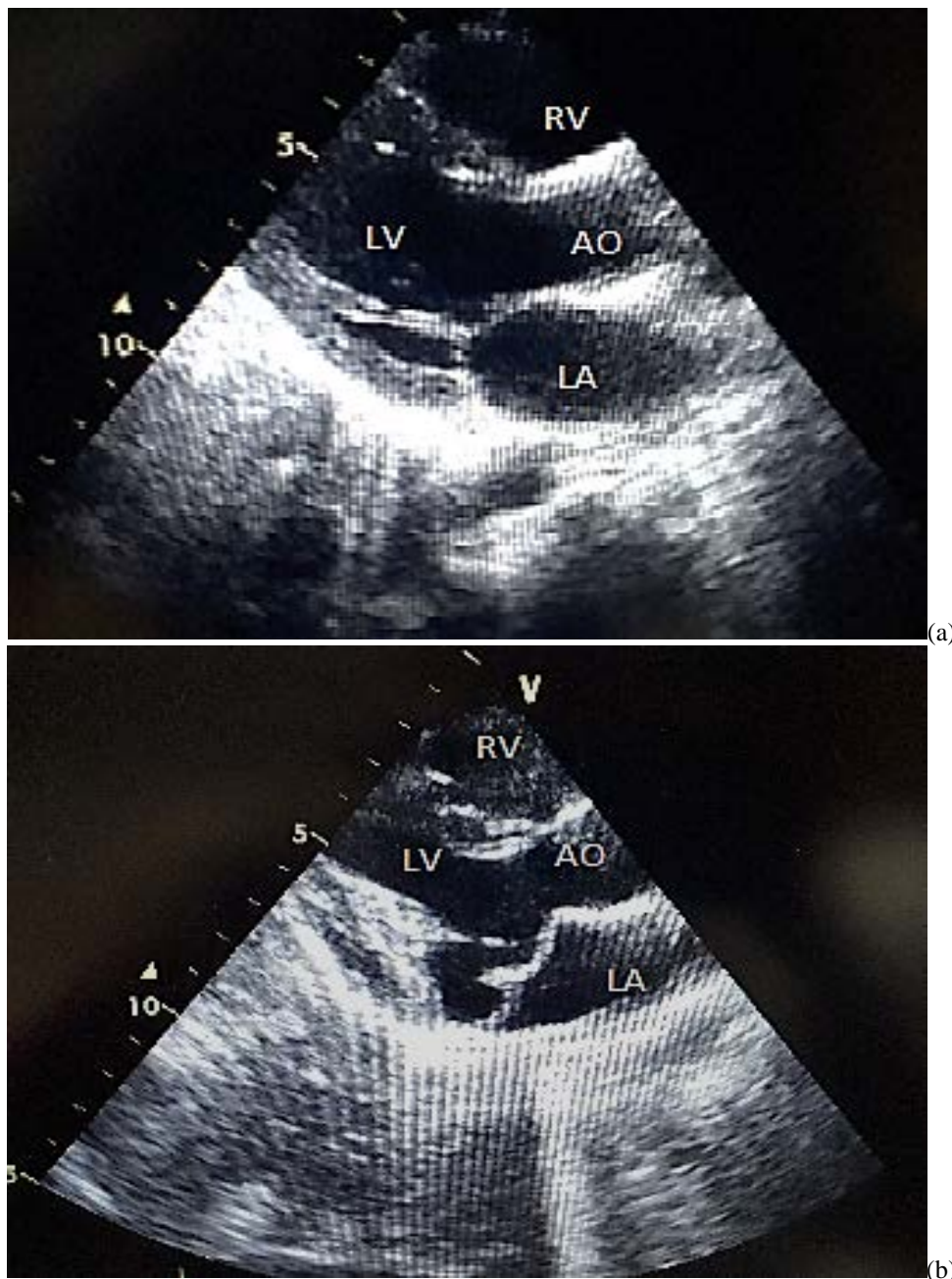

(a)

(b)

Figure 1 (a,b). Two-dimensional echocardiographic long axis parasternal view of mitral valve prolapses (a) and normal mitral valve (b). LV: left ventricle, LA: left atrium, RV: right ventricle, Ao: aorta.

ECG

After echocardiography procedure, standard 12-lead ECG recordings with a sweeping rate of 25mm/s and an amplitude of 10mV/cm while in the supine position were made.

Two cardiologists who detect sign of ERP on ECG were also blinded to the both groups.

Figure 2 shows three ECG from the control group and children with MVP as patients in our study.
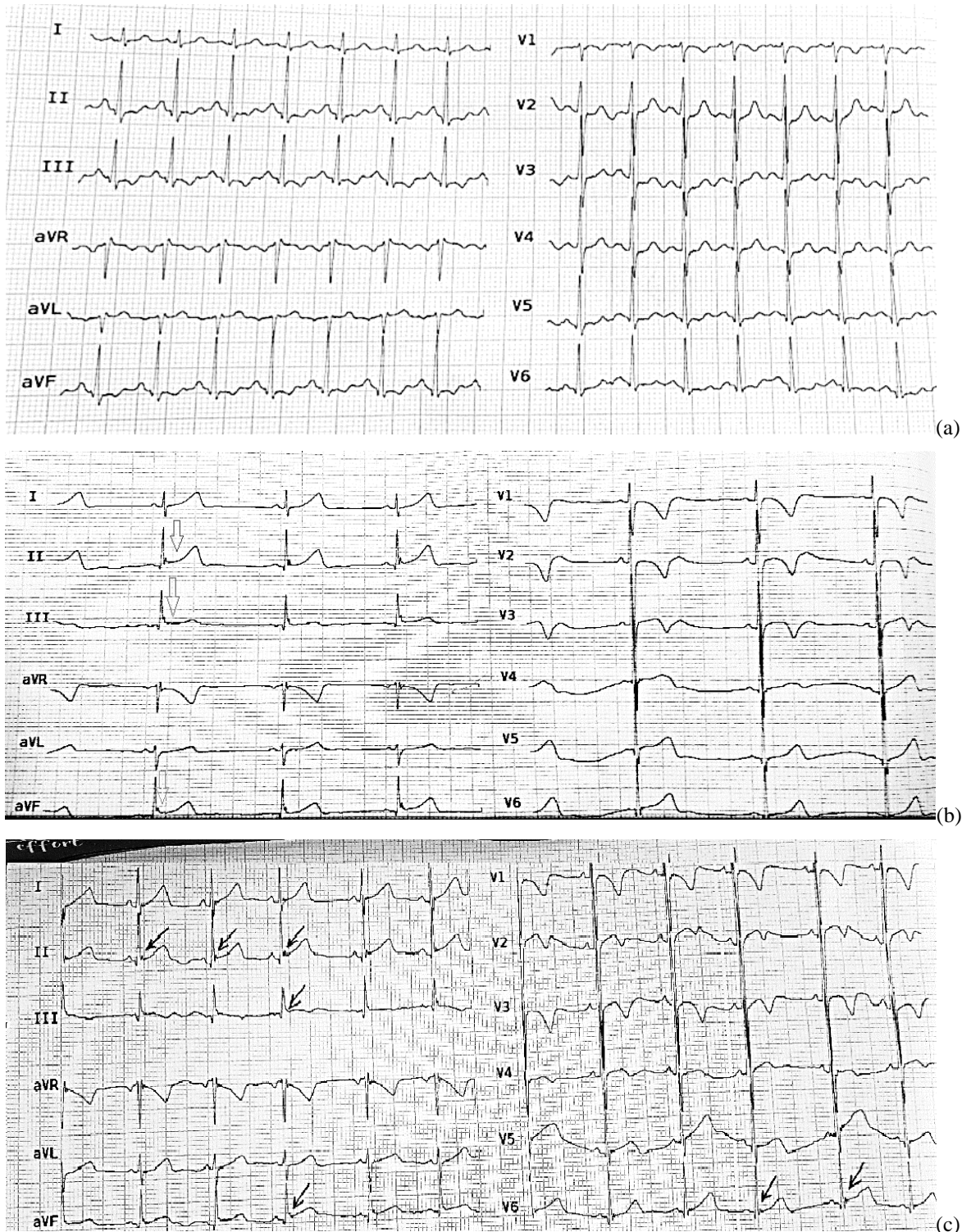
(a)

(b)

(c)

Figure 2. The ECG patterns of in normal group and children with MVP. (a); the 12 lead ECG patterns of in child without MVP. (b,c); the ECG patterns of early repolarization in child with MVP. The ECG recording of patient shows a predominant early repolarization pattern in the inferior leads a 17-year-old male athlete a 14-year-old female. Notch in descending arm of QRS and J-point in lead II, III, aVF and V5, V6.

Statistical Methods

Numerical variables are presented as mean±SD (standard deviation), and frequencies and percentages were measured to present the categorical variables.

For comparison of categorical variables were used chi-square and Fisher's exact tests, while independent samples t-test was applied for continuous variables.

For the statistical analysis, the statistical software SPSS version 17.0 for windows (SPSS Inc., Chicago, IL, USA) was used.

A *p* value≤0.05 was considered statistically different.

Results

In all 140 subjects, the ERP occurred in 6 males and 14 females.

The ERP in persons with and without MVP were 12 and 8, respectively (P=0.23).

In MVP patient's ERP occurred in 12 cases in location inferior (7 cases) and lateral leads (5 cases) and in the group without MVP occurred in 8 cases in lateral leads, and nobody there were not high-risk subtype ERP (P=0.23).

The ERP occurred in MVP patients mild, moderate and severe 4, 6 and 2 cases, respectively (P=0.29).

The ERP found in patients with and without chest pain 13 and 7, respectively (P=0.46).

Also, the ERP occurred in patients with palpitations 15 cases and in the group without palpitations 5 cases (P=0.24).

The demographic variables in children with and without MVP showed that the mean of weight, BSA and BMI in patients with MVP and without MVP were significantly higher than mean in patients without MVP.

There was no significant statistical difference between two groups in height, systolic and diastolic blood pressure (Table 1).

The results in table 2 showed the association between MVP and ERP, chest pain, and heart rate.

Based on these results, there was no significant difference between two groups in what it regards chest pain and heart rate (Table 2).

However, the univariate and multivariate OR between MVP and other variables showed that the ERP had occurred 1.6 time more frequent in patients with MVP if compared with individuals without MVP (Table 3).

Table 1. Demographic variables in subjects with and without MVP.

Variables	MVP		P-value[*]
	Without (n=70)	with (n=70)	
Age			
Mean±SD	11.52±2.92	11.9±2.87	0.225
Min/Max	7/17	7/17	
Gender			
Female/male	42/28	48/22	0.290
Weight			
Mean±SD	39.08±12.55	43.5±13.36	0.022
Min/Max	18/60	12.5/77	
Height			
Mean±SD	144.01±15.58	146.34±14.9	0.183
Min/Max	118/167	110/182	
BMI			
Mean±SD	18.32±3.46	19.73±2.99	0.005
Min/Max	12.9/31.5	10.3/26.7	
SBP			
Mean±SD	95.78±5.42	95.42±5.34	0.652
Min/Max	90/105	90/105	
DBP			
Mean±SD	67.85±4.04	68.5±3.93	0.171
Min/Max	60/75	60/75	
BSA			
Mean±SD	1.22±0.29	1.32±0.27	0.024
Min/Max	0.28/1.66	0.61/1.92	

*P-value calculated by independent t-test and Chi2 test at 95% CI.

MVP: mitral valve prolapse, BMI: body mass index, BSA: body surface area, SBP: systolic blood pressure, DBP: diastolic blood pressure

Table 2. Association between MVP and ERP, chest pain, and heart rate.

Variables	MVP		P-value[*]
	No (n=70)	Yes (n=70)	
ERP			
No	62 (88.57)	58 (82.86)	0.334
Yes	8 (11.43)	12 (17.14)	
Chest pain			
No	24 (34.29)	30 (42.86)	0.298
Yes	46 (65.71)	40 (57.14)	
Heart rate			
No	20 (28.57)	28 (40.0)	0.154
Yes	50 (71.43)	42 (60.0)	

*P-value calculated by Chi2 test at 95% CI

MVP: mitral valve prolapse, ERP: effective refractory period

Table 3. The Univariate and multivariate OR between MVP and other variables.

Variables	Crude OR (95% CI)					
	ERP	P-value	**Chest pain**	P-value	**Heart rate**	P-value
MVP						
No	Ref	0.337	Ref	0.298	Ref	0.156
Yes	1.60 (0.61-4.20)		0.69 (0.35-1.37)		0.60 (0.29-1.21)	
	Adjusted* OR (95% CI)					
MVP						
No	Ref	0.590	Ref	0.270	Ref	0.298
Yes	1.32 (0.47-3.68)		0.66 (0.32-1.37)		0.67 (0.32-1.41)	

*Adjust for age, gender, BMI, SBP, and DBP

Also, according to the results of the univariate and multivariate OR between MVP severity and other variables, resulted that the ERP had occurred more frequently among patients with moderate MVP in comparison with severe and mild cases.

But chest pain and palpitation occurred more frequently among patients with severe MVP (Figures 1 and 3, Table 4).
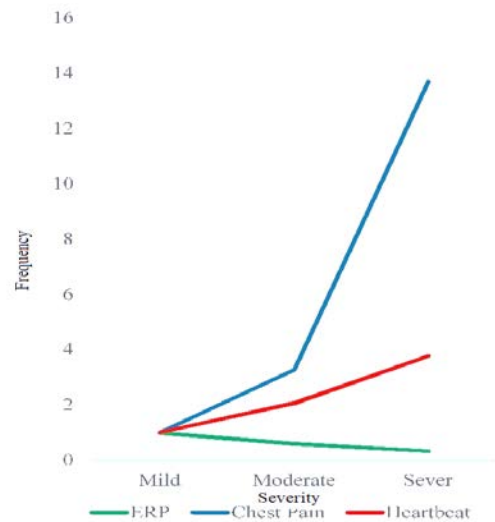

Figure 3. Chest pain and heart beat among patients with MVP occurred more frequently than in cases with ERP.

Table 4. The Univariate and multivariate OR between MVP severity and other variables.

Variables	Crude OR (95% CI)					
	ERP	P-value	**Chest pain**	P-value	**Heart rate**	P-value
MVP						
Mild	Ref		Ref		Ref	
Moderate	0.74 (0.2-2.7)	0.653	2.80 (0.94-8.26)	0.062	2.14 (0.73-6.21)	0.160
Sever	0.42 (0.04-4.26)	0.467	14 (1.47-133.2)	0.022	4.2 (0.7-24.9)	0.114
	Adjusted* OR (95% CI)					
MVP						
Mild	Ref		Ref		Ref	
Moderate	0.60 (0.14-2.48)	0.487	3.27 (1-10.68)	0.049	2.07 (0.65-6.56)	0.213
Sever	0.34 (0.02-4.23)	0.409	13.7 (1.3-144.5)	0.029	3.78 (0.55-25.9)	0.176

*Adjust for age, gender, BMI, SBP, and DBP

Discussion

Symptoms of MVP are often silent in many patients; however, palpitation, anxiety, chest pain, dizziness and ECG changes can be seen in some patients with mitral valve prolapse [5,15,16], that defined such as MVP syndrome.

In some adult people, Mitral valve prolapse can lead to ventricular arrhythmias.

On transthoracic echocardiogram (TTE), more symmetric leaflet prolapse is highly associated with ventricular arrhythmia in patients suffering from mitral valve prolapse.

Furthermore, papillary muscle positive late gadolinium enhancement (LGE) on cardiac magnetic resonance imaging (CMR) and female gender can be a leading point to the occurrence of ventricular arrhythmias [17].

Isolated ventricular premature complexes inducing delay after depolarization can be a major cause of ventricular tachycardia (VT) in patient with mitral valve prolapse [18].

Mitral valve prolapse (MVP) can eventually lead to sudden cardiac death.

Ventricular fibrillation (VF) is stimulated by premature ventricular contractions (PVCs) of papillary muscles which can initiate PVC-mediated cardiomyopathy.

Eliminating PVC is highly associated with catheter ablation [19].

In the absence of structural heart disease, the early repolarization pattern in the electrocardiogram (ECG) and ventricular fibrillation can highly describe the definition of early repolarization syndrome.

Early repolarization of inferior leads can be responsible for increasing cardiovascular.

However, based on the research accomplished by Ricardo Stein et al, ER was lost after 10 years emphasizing the fact that the loss of ER is highly depends on heart rate's changes and other aging related factors but not higher occurrence of cardiovascular events [20].

Early repolarization pattern (ERP) can be associated with arrhythmia and sudden cardiac death (SCD).

Ahmed Tageldien Abdellah et al studied 124 individuals (6.7%) with ERP. 24 patients were excluded due to their structural abnormalities. 80% of individuals were less than 50 years old (60% of patients were male).

Early repolarization of inferolateral, antero-lateral, inferior and global were 50%, 38%, 10% and 2%, respectively.

ERP group had lower BMI than control group (25.3 vs 30 kg/m2, P value<0.001) with higher metabolic equivalents (METS) achievement on stress ECG.

Only 4% of ER individuals were detected with horizontal/descending ST slope on their ECG; however, 8% had ST elevation ≥ 2ms. There were neither reports of arrhythmia nor sudden cardiac death (SCD) during their 1-year follow up in both groups [21].

MVP which is considered as the most common abnormality of heart valve, is highly associated with arrhythmia and sudden cardiac death.

ECG features of early repolarization include notch in descending arm QRS and/or J-point or ST segment elevation [22].

Incidence rate of sudden cardiac death in MVP patients is twice higher than of general population.

Some studies showed that ventricular arrhythmia can be seen in patients with MVP with the absence of mitral regurgitation (MR) [6].

Although the exact mechanism of ventricular arrhythmias and sudden cardiac death in MVP is still unclear, there were some innovative ideas including tension in papillary muscles, thickened and prolapsed leaflets, and inferonasal left ventricle wall with endocardial lesions to explain the mechanism [23].

Increased autonomic tone along with increased catecholaminergic activity has been described, to explain the mechanism of ventricular arrhythmias and repolarization state in patients with MVP [23].

Researchers showed the incidence of ventricular arrhythmias in MVP patients by using 12-lead electrocardiogram [24].

Early repolarization has higher incidence among young populations with MVP showing the symptoms of chest pain and anxiety which can be more effective due to high prevalence of MVP and high occurrence of the ECG changes.

It looks that prolapse pf leaflet onto the left atrium with traction of papillary muscle is highly useful in defining the mechanism of ER in MVP patients.

Also, impaired autonomic function is correlated with arrhythmias, syncope and hemodynamic changes in MVP syndrome [15,25].

There is yet no exact explanation for the sudden death of these patients.

The role of vascular malformation and its effect on the cardiac chambers has been proposed to describe sudden death in MVP [26].

Also, increased corrected QT dispersion and length of anterior mitral valve leaflet can highly be associated with ventricular arrhythmias in MVP [27].

Furthermore, based on previous studies, ER is the most common signs in positive familial history of cardiac sudden death, unexplained syncope or survival after idiopathic ventricular fibrillation (VF) [26].

In our study, we excluded patients with such findings; however, we could determine signs of ERP in our patients.

We showed that early repolarization is the most common findings in patients suffering from MVP which can be used as a lead for determining MVP syndrome.

Reaching higher specificity and sensitivity of these findings and relationship with these findings and different symptoms, signs, we suggest studies with larger scales as well as finding the relationship between the incidence of early repolarization and ventricular and supraventricular arrhythmias.

Because of the occurrence of arrhythmias and sudden cardiac death, follow up of children with MVP is necessary.

Despite the initial sample size including 140 subjects for screening, our ERP patients had low-risk clinical manifestations, i.e., no syncope, no history of aborted SCD, and rare family history of SCD with low-risk ECG criteria for malignant ERP.

Altogether, these signs and symptoms may have led to absence of SCD or arrhythmia at follow-up.

We believe that follow up should be proposed to evaluate symptoms and arrhythmias.

Asymptomatic patients have better prognosis.

We recommend initial 24-holter monitoring for atrial and ventricular arrhythmias along with yearly echocardiographic examination to evaluate the progression of the disease.

To prevent ventricular arrhythmias and sudden cardiac death, close follow ups for patients with palpitations, chest pain, tachycardia, syncope or moderate to severe mitral regurgitation is necessary.

Limitation

Our study has limitations that must be considered. The first, we did not perform 24-holter monitoring in our study.

The second, our study is a single-center, prospective study without follow-up period for ventricular arrhythmias.

Eventually, we suggest that to do a Large prospective study to demonstrate correlations among these parameters and arrhythmic events.

Conclusion

In conclusion, based on the cases discussed in this study, our results showed that, the prevalence of early repolarization in patients with mitral valve prolapse has been at a higher level.

Therefore, because of life expectancy, children with MVP are in need of follow up considering the occurrence of arrhythmias.

Acknowledgments

Conflict of interests

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