Med. J. Cairo Univ., Vol. 90, No. 4, June: 1149-1154, 2022
www.medicaljournalofcairouniversity.net

Risk of Vasovagal Syncope and Cardiac Arrhythmias in Children with Mitral Valve Prolapse

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Abstract

Background: Mitral valve prolapse occurs when one or both mitral valve leaflets enter the left atrium during left ventricular systole (MVP). Mitral valve prolapse is a leaflet problem. It might be primary or secondary. Presyncope and syncope in individuals with mitral valve prolapse are caused by postural, cardiac, and autonomic dysfunction (MVP).

Aim of Study: The aim of this study was to determine the arrhythmia incidence and to assess the risk of vasovagal syncope in patients with MVP who had no history of syncope or near-syncope.

Patients and Methods: This study prospectively studied 50 patients, who were diagnosed as MVP, according to the echocardiographic criteria of Nascimento et al., **[9]** between April 2020 and December 2021 at Al-Hussein Hospital Al-Azhar University, Departments of Pediatric and Cardiology. 50 age- and sex-matched healthy children were also studied as a control group.

Results: There was no significant difference between study groups regarding age and sex. There was a significant difference regarding murmurs or orthostatic hypotension between the study groups. There was no significant difference between the study groups regarding Palpitation, Chest pain and drowsiness. There was a significant difference regarding incidence of Ventricular Extrasystole. There was no statistically significant difference with respect to mean QTc which was 0.39±4.5 in MVP and 0.39±5.2 in the control group (p>0.05).

Conclusion: Arrhythmia and syncope frequency was found to be higher in children with MVP than in the normal population. The risk of vasovagal syncope indicated by a positive tilt test was found to be increased in children with MVP. Therefore, patients and families must be informed about the conditions that may predispose to vasovagal syncope and caution should be recommended in these patients.

Key Words: *Vasovagal syncope – Cardiac Arrhythmias – Children – Mitral valve prolapse.*

Introduction

PROLAPSE of either one or both mitral valve leaflets into the left atrium during left ventricular systole is known as mitral valve prolapse (MVP). Mitral valve prolapse is a leaflet condition that affects the mitral valve. It may be classified as either main or secondary. The vast majority of cases are classified as primary MVP, and the cause of these instances is still unknown **[1,2]**.

MVP is seen in between 0.3 to 21 percent of children and young people who are otherwise healthy. It has been noted that it typically affects both males and females in equal measure **[3]**.

The great majority of people with MVP do not show any signs or symptoms **[4]** . On physical examination, there are typically no abnormalities to be found. Palpitations, atypical chest pain, dyspnea without orthopnea, decreased exercise tolerance, fatigue, syncope or near-syncope, signs of postural orthostatic syndrome, anxiety, and panic attacks are some of the most common symptoms and complaints associated with MVP, according to the American Heart Association **[5,6]**.

Patients typically complain of palpitations when they first arrive. Premature ventricular or atrial beats are shown to be the most common cause of these palpitations in the majority of instances. Patients with MVP have been observed to experience a variety of arrhythmias **[7]**.

Patients with MVP are most often found with paroxysmal supraventricular tachycardia, which is the most prevalent kind of arrhythmia. In individuals with MVP, arrhythmias are prevalent, as previously indicated; consequently, early detection and treatment are critical. Additionally, syncope and near-syncope occur at a higher rate than in the general population **[8]**.

The purpose of this study was to determine the arrhythmia incidence and to assess the risk of

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vasovagal syncope in patients with MVP who had no history of syncope or near-syncope.

Material and Methods

We prospectively studied 50 patients, who were diagnosed as MVP, according to the echocardiographic criteria of Nascimento et al., [9] between April 2020 and December 2021 at Al-Hussein Hospital Al-Azhar University, Departments of Pediatric and Cardiology. 50 age- and sex-matched healthy children were also studied as a control group.

All the children involved in this study were examined by a pediatrician. The symptoms of the patients were recorded on admission. For each child, telecardiography, 12-lead ECG, echocardiography, Holter monitoring, exercise test and head up tilt test were performed. Twelve-lead electrocardiograms were recorded with a three-channel electrocardiographic recorder at a paper speed of 25 millimeters per second.

All the electrocardiograms were analyzed by two different observers. The QT interval was measured from the first deflection of the QRS complex to the point of T wave offset, defined by return of terminal T wave to the isoelectric T-P interval baseline. In the presence of a U wave interrupting the T wave, the terminal portion of the visible T wave was extrapolated to the T-P interval baseline to define the point of T-wave offset. Three consecutive cycles in each of the 12 leads were measured and mean QT interval was calculated.

At least nine leads in which the QT interval could be measured were required for QT dispersion calculation. QT dispersion was defined as the difference between the minimal and maximal QT intervals.

Each QT interval was corrected for heart rate according to Bazett's formula [QTc equals to QT over (R-R) 1/2] and then QTc dispersion was calculated. Echocardiograms were performed for both groups with 2-D guided M-mode echocardiography using transducer frequencies appropriate for body size. Measurements were performed according to the American Society of Echocardiography recommendations.

MVP was assessed using the criteria which Nascimento et al., [9] suggested. In two-dimensional echocardiography, motion of one or both of the mitral leaflets from the annular plane to a posterosuperior direction in the parasternal long view or in any position for the posterior leaflet were defined as MVP. Also, in M-mode echocardiography a prolapse or posterior displacement of the mitral leaflet to greater than 3mm in late systole and a holosystolic posterior movement was defined as MVP.

All of the echocardiograms were recorded on a video cassette and then evaluated by another pediatric cardiologist for MVP again. For each child, a 24-hour Holter recording using a Holter was performed. Holter recordings were analyzed with respect to ventricular arrhythmias according to Lown's criteria. Each child involved in the study underwent a treadmill exercise test following the “modified Bruce protocol” and a head-up tilt test.

All tilt tests were performed in the early afternoon after at least a 4-hour fasting, preceded by a light breakfast. A vasodepressor response was defined as a decrease in systolic blood pressure to <80mmHg (or 20mmHg decrease) without a heart rate decrease during symptoms. A cardioinhibitory response was defined as an abrupt decrease in heart rate by >20% without any antecedent decrease in systolic blood pressure. A mixed response was defined as a concurrent decrease in systolic blood pressure <80mmHg and a decrease in heart rate by >20% as compared with averaged values measured 3 minutes before the onset of symptoms.

When a vasodepressor, cardioinhibitory or mixed response developed, the patient was returned to the supine position, the test was ended and it was considered as positive. If the patient had no symptoms during the test, the patient returned to the supine position after 50 minutes and the test was considered as negative. A positive tilt test result was defined as vasodepressor, cardioinhibitory or mixed response.

Written informed consent was obtained from all parents and all children aged 12 or older. The study was approved by the Ethical Committee of the Cairo University.

Statistical analysis:

IBM-SPSS version 24 was used for data analysis (May, 2016). Kristall-Wallis and Wilcoxon's tests, as well as Spearman's correlation and logistic regression analysis, were used to determine statistical significance. Based on the type of data it contained, each variable was analyzed (parametric or not). We considered results statistically significant if the p-values were less than 0.05 (five percent).

Results

Table (1): Basal Characteristics.

	Patients		Control		*p*-value
	N	%	N	%	
Age	11 (3.5)		11.5 (4.2)		<0.05 **[2]**
Sex:					
Male	28	56	27	45	<0.05 **[1]**
Female	22	44	23	46	

[1] Chi square test. *p*<0.05 Statistically Significant.
[2] t-Test. *p*>0.05 Statistically Insignificant.

There was no significant difference between study groups regarding age and sex.

Table (2): Presenting symptoms in MVP and control groups.

	Patients		Control		*p*-value
	N	%	N	%	
Murmur	11	22	23	46	<0.05 **[1]**
Palpitation	4	8	2	4	>0.05 **[1]**
Exercise intolerance	0	0	4	8	–
Chest pain	23	46	17	34	>0.05 **[1]**
Panic attack	1	2	0	0	
Orthostatic hypotension	9	18	2	4	<0.05 **[1]**
Drowsiness	2	4	2	4	>0.05 **[1]**
Total	50	100	50	100	

[1] Chi square test. *p*<0.05 Statistically Significant.
p>0.05 Statistically Insignificant.

There was a significant difference regarding murmurs or orthostatic hypotension between the study groups. There was no significant difference between the study groups regarding Palpitation, Chest pain and drowsiness.

Table (3): Ventricular Extrasystole and Arrhythmia in MVP and control groups.

	Patients		Control		*p*-value
	N	%	N	%	
Ventricular Extrasystole	10	20	2	4	<0.05
Arrhythmia	10	20	0	–	–

There was a significant difference regarding incidence of Ventricular Extrasystole. Arrhythmia was recognized in 10 (20%) of patients.

Table (4): Physical examination findings in MVP and control groups

	Patients		Control		*p*-value
	N	%	N	%	
Normal	22	44	12	24	<0.05 **[1]**
Click (Mid-systolic)	1	2	0	0	–
Specific murmur & click	3	6	0	0	–
Non-Specific murmur	21	42	38	76	<0.05 **[1]**
Gull Sound Murmur	3	6	0	0	–
Total	50	100	50	100	

[1] Chi square test. *p*<0.05 Statistically Significant.
p>0.05 Statistically Insignificant.

There was a significant difference between the two groups in physical examination findings regarding normal findings and Non-Specific murmur.

Table (5): ECG examination.

	Patients	Control	*p*-value
Mean QTc	4.5 (0.39)	5.2 (0.39)	>0.05 **[2]**
Mean QTc Dispersion	50 (3.7)	35 (3.5)	<0.05 **[2]**

[2] *t*-test. *p*<0.05 Statistically Significant.
p>0.05 Statistically Insignificant.

The mean QTc dispersions were 50±3.7 in the MVP and 35±3.5 in the control group, i.e. a statistically significant difference between the two groups ($p<0.05$). However, there was no statistically significant difference with respect to mean QTc which was 0.39±4.5 in MVP and 0.39±5.2 in the control group ($p>0.05$).

Table (6): Tilt test results in MVP and control groups.

	Tilt positive		Tilt negative		*p*-value
	N	%	N	%	
Patients	15	30	35	70	<0.001 **[1]**
Control	2	4	48	96	
Total	17		83		

[1] Chi square test. *p*<0.05 Statistically Significant.
p>0.05 Statistically Insignificant.

There was a statistically significant difference between patient and control groups with respect to tilt test positivity 6 (40%) of Tilt positive patients were recognized with Cardioinhibitory response and 2 (13.33%) of Tilt positive patients were recognized with vasodepressor response. Mixed response was recognized in both groups tilt positive patients as 7 (46.67%) in patients group and 2 (100%) in control group.

Table (7): Cardiac response in tilt positive subjects.

	Patients Tilt positive (N=15)		Control Tilt negative (N=2)		Total
	N	%	N	%	
Cardioinhibitory response	6	40			6
Vasodepressor response	2	13.3			2
Mixed response	7	46.67	2	100	9

Discussion

MVP incidence in childhood is 5% and most cases are idiopathic. Most patients are asymptomatic. Clinical findings can rarely be seen before adult age. In our study, the most common presenting symptom of the children was chest pain (45%). Nonetheless, palpitations were the most common presenting symptom in the majority of the other studies **[10,11]**.

Our results were similar to those of Ghandi et al., **[12]** who also reported chest pain as the most common presenting symptom in MVP. Mid-systolic click and/or late systolic murmur are characteristic for MVP on physical examination. Ohara et al., reported a mid-systolic click incidence of 23.1% in their 109 patients with MVP. Naçar et al., reported that mid-systolic click and gull sound were found in 23.6% and 3.6% of 147 children with MVP, respectively. In our study, the most common physical examination finding was a non-specific murmur (42%). Also, Cetinkaya et al., reported a close incidence of both mid-systolic click incidence (2.7%) and non-specific murmur (43.2%).

Previous studies reported that the ECG was usually normal in patients with MVP **[14]** we also found no abnormalities in the ECGs of our patients. QTc prolongation may be seen in the ECG of the patients with MVP. Previous studies reported that the QTc interval was normal, but observed a prolonged QT dispersion among patients with MVP; they suggested that QT dispersion might be a significant marker depicting patients at high risk for developing severe ventricular arrhythmia and sudden death **[15]**.

In our study, mean QT dispersion in the MVP group was significantly longer than in the control group ($p<0.05$). Also similar findings were reported by İmamogˇlu & Erogˇlu **[16]** regarding electrocardiogram findings of the patients with primary mitral valve prolapse and the control group. Similar to our study they reported that thirty four (81 %) of 42 patients with a diagnosis of primary MVP were female and eight (19%) were male. The mean age of the patients were 13.9±3.3 years ranging between 6.5 years and 18 years. In the control group, 25 (78.1%) of 32 healthy children were female and seven (21.9%) were male. The mean age were 14.6±3.1 years ranging between 6.3 years and 18 years. No significant difference was found between the groups in terms of age and gender ($p>0.05$ and $p>0.05$).

Although the prognosis of MVP in children is good, syncope associated with cardiac arrhythmias and sudden death have also been reported **[17,18]**. Studies evaluating the association between MVP and arrhythmias in children are limited. These studies reported that atrial arrhythmias, supraventricular tachycardia and severe ventricular arrhythmias could be found in patients with MVP although clinical findings were not associated with arrhythmias.

In our study, Arrhythmia was found in 10 (20%) of patients and there was significant difference between two groups regarding ventricular extra systole. Similar to our findings Cetinkaya et al., study, arrhythmias were found in 7 of 37 children (18.9%) with MVP. All of the patients had normal ECGs and treadmill exercise tests. These arrhythmias were found by 24-hour ambulatory Holter monitoring. Ventricular extrasystoles were the most common arrhythmia and there was no correlation between clinical symptoms and rhythm disorders. Also, they reported that arrhythmias in children with MVP were not correlated with physical examination findings, standard ECG results and clinical symptoms; our results are in agreement with their findings.

In agreement with our study results regarding Cardiac response in tilt positive subjects, Cetinkaya et al., reported that five patients (42%) had a cardioinhibitory response, one patient (8%) had a vasodepressor response and six (50%) had a mixed response. One patient in the control group had also a mixed response.

Although our patients did not have any history of syncope, the tilt test was found positive in 30% of the children who had MVP. This rate was found to be statistically significantly different when compared with the control group. This result may suggest that vasovagal mechanisms may play an important role in the development of syncope in patients with MVP. It also suggests the increased probability of the development of vasovagal syncope in these patients under particular conditions such as dehydration.

As a result, arrhythmia and syncope frequency was found to be higher in children with MVP than in the normal population. The risk of vasovagal syncope is increased in children with MVP. Patient and families must be informed about the conditions that may predispose to vasovagal syncope and protective cautions such as avoiding prolonged periods of standing and dehydration should be applied in these patients.

Conclusion:

Arrhythmia and syncope frequency was found to be higher in children with MVP than in the normal population. The risk of vasovagal syncope indicated by a positive tilt test was found to be increased in children with MVP. Therefore, patients and families must be informed about the conditions that may predispose to vasovagal syncope and caution should be recommended in these patients.

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خطر الإغماء الوعائى المتأثر بالعصب الحائر وعدم انتظام ضربات القلب لدى الأطفال المصابين بارتجاع الصمام التاجى

موضوع البحث : يحدث تدلى الصمام التاجى عند ما تدخل إحد شرفات الصمام التاجى أو كلتاهما إلى الأذين الأيسر أثناء انقباض البطين الأيسر. يعُد تدلى الصمام التاجى مشكلة فى الشرفات. قد يكون أساسياً أو ثانوياً. يحدث الغشيان والإغماء فى الأفراد الذين يعانون من تدلى الصمام التاجى بسبب الخلل الوظيفى لعضلة القلب، والجهاز العصبى اللاإرادى.

الهدف : كان الغرض من هذه الدراسة هو تحديد حدوث عدم انتظام ضربات القلب وتقييم مخاطر الإغماء الوعائى المتأثر بالعصب الحائر فى المرضى الذين يعانون من تدلى الصمام التاجى الذين ليس لديهم تاريخ من الإغماء أو الإغماء القريب.

طرق الدراسة : درسنا مستقبلياً ٥٠ مريضاً، تم تشخيصهم على أنهم لديهم تدلى الصمام التاجى، وفقاً لمعايير تخطيط صدى القلب الخاصة بنا سكميتو وزملائه بين أبريل ٢٠٢٠ وديسمبر ٢٠٢١ فى مستشفى الحسين بجامعة الأزهر، أقسام طب الأطفال وأمراض القلب. كما تمت دراسة ٥٠ طفلاً يتمتعون بصحة جيدة من العمر والجنس كمجموعة ضابطة.

النتائج : لا توجد فروق ذات دلالة إحصائية بين مجموعات الدرسة فيما يتعلق بالعمر والجنس. كان هناك فرق كبير فيما يتعلق بالنفخات أو انخفاض ضغط الدم الانتصابى بين مجموعات الدراسة. لم يكن هناك فرق ذو دلالة إحصائية بين مجموعات الدراسة فيما يتعلق بالخفقان وآلام الصدر والنعاس. كان هناك فرق كبير فيما يتعلق بحدوث انقباض البطينى. لم يكن هناك فرق ذو دلالة إحصائية فيما يتعلق بمتوسط فترة QTc والذى كان ٠.٣٩±٤٠٥ فى مجموعة الحالات و ٠.٣٩±٥٠٢ فى المجموعة الضابطة ($p>0.05$).

الخلاصة : تم العثور على عدم انتظام ضربات القلب وتواتر الإغماء لتكون أعلى فى الأطفال الذين يعانون من تدلى الصمام التاجى مقارنة بالمجموعة الضابطة. وجد أن خطر الإصابة بالإغماء الوعائى المتأثر بالعصب الحائر المشار إليه باختبار الميل الإيجابى يزداد عند الأطفال المصابين بتدلى الصمام التاجى. لذلك، يجب إبلاغ المرضى وأسرهم عن الظروف التى قد تؤهب للإغماء الوعائى المبهم ويجب توخى الحذر عند هؤلاء المرضى.