

Are children with mitral valve prolapse more anxious?

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ABSTRACT

- Background** : Mitral valve prolapse (MVP) is a common valvular disease in children. Symptoms in children with MVP are not explained by the severity of mitral regurgitation alone. Hence, we sought to correlate symptom status with the incidence of anxiety disorder in this population.
- Materials and Methods** : Groups were as follows: (a) MVP; $n = 115$; mean age: 13.5 ± 3.06 years and (b) control; $n = 53$; mean age: 15.1 ± 13.2 . The Screen for Child Anxiety-Related Emotional Disorders (SCAREDs) scale was filled by all participants. The SCARED scores of 25 and above determined a warning for anxiety disorders.
- Results** : The mean SCARED scale values of MVP and control groups were 29.2 ± 13.08 and 24.9 ± 14.17 , respectively ($P = 0.065$). Although the SCARED score was higher among the MVP patients, no significant difference was found between the groups in terms of the mean SCARED score, or the number of participants with a score of 25 or more. While girls with MVP had higher anxiety scores compared to boys with the disorder, there was no difference with respect to SCARED scores in children with MVP and the general population when analyzed separately by gender. Moreover, the SCARED scale score was significantly higher in symptomatic MVP patients than in asymptomatic cases.
- Conclusion** : Children with MVP did not have higher anxiety scores compared to those without the syndrome. However, MVP patients with higher anxiety scores may benefit from a psychiatric assessment since higher scores correlate with symptoms.
- Keywords** : Anxiety, children, mitral valve prolapse

INTRODUCTION

Mitral valve prolapse (MVP) is defined as the displacement by more than 2 mm of one or both of the mitral valve leaflets toward the left atrium during left ventricular systole. Its prevalence was reported as 2.4% in echocardiographic studies.^[1] In addition to echocardiographic findings, if symptoms such as chest pain, palpitations, dyspnea, and syncope are present, it is named MVP syndrome.^[2] Some patients with MVP

may have symptoms that cannot be explained by the severity of mitral valve regurgitation alone. There is diminished vagal activity and increased sympathetic tone in symptomatic children with MVP.^[3]

It can be difficult to distinguish whether the complaints are specific to MVP or a sign of an underlying anxiety disorder. An attempt has been made to find the answer to this question in studies, most of which investigated adult

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cases. However, the association between MVP and anxiety is still controversial. In adult studies, symptomatic MVP has only been associated with anxiety disorder.^[4-6] However, there are also studies supporting that MVP does not contribute to an increase in anxiety levels.^[7-10] Furthermore, it is important to determine whether there is mitral regurgitation (MR) with MVP because it has been shown that posttraumatic stress disorder associated with anxiety and depression is more common in patients with organic-MR than in normal controls and simple MVP.^[11]

Most studies investigating the association between MVP and anxiety disorder have been conducted in adults. Herein, we aimed to explore whether MVP or MVP-related symptoms and MR are linked to higher levels of anxiety in children.

MATERIALS AND METHODS

Study population

Children with MVP aged 8–18 years, diagnosed in our hospital between 2018 and 2021 were included in the study. The questionnaire was administered prospectively, for MVP-identified patients at their regular examination date.

Inclusion criteria included children older than 8 years old and having MVP. Those with additional congenital heart disease (except patent foramen ovale), arrhythmic cardiomyopathy, genetic diseases such as Marfan syndrome, Loeys-Dietz syndrome, and rheumatic heart disease were excluded. The control group included age- and gender-matched children among those with an innocent murmur. The participants were taken to a quiet room to answer the questions independently without any inducement.

The groups were as follows: (a) MVP: $n = 115$; mean age: 13.5 ± 3.06 years; 80 (69.6%) were girls and (b) control: $n = 53$; mean age: 15.1 ± 13.2 years; 33 (62.3%) were girls. Medical records were used to gather information relating to demographics and symptom status.

The participants were assessed by the researcher using The Screen for Child Anxiety-Related Emotional Disorders (SCARED) scale. The SCARED scale was developed by Birmaher *et al.*^[12] to screen for anxiety disorders in childhood. The SCARED has a parent and child form, and a Turkish validity and reliability study was completed by Çakmakçı^[13] in 2004. Since then, it has been successfully used in at least five studies of Turkish children.^[14-18] The SCARED scale consists of 41 items in total and scores of 25 and above indicate a warning for anxiety disorders. However, it should be taken into account that SCARED is only a screening scale, and there is no consensus between parent and child agreement in reporting internalizing symptoms (depression and anxiety). Therefore,

administration for both the parent and the child is recommended for further workup.^[12]

Echocardiographic evaluation

Comprehensive Doppler echocardiography was performed using Philips IE33 color ultrasound systems (Philips, Bothell, Seattle, WA, USA) with S8-3, S5-1 sector array transducers. The probes had a frequency of 3–8 MHz and 1–5 MHz, respectively.

Echocardiographic evaluation was performed for both symptomatic and asymptomatic cases based on referrals from the first outpatient clinic due to various indicators such as innocent murmur, cardiac disorder history in the family, or sports participation screening.

Through the echocardiography, displacement of the mitral valve into the left atrium, mitral valve thickness, the presence and degree of mitral valve regurgitation, and tricuspid valve annular velocity were recorded. MVP was defined as the displacement by >2 mm of the margin of one or more mitral valve leaflets beyond the annular plane during systole in the parasternal long-axis view.^[2] MVP patients were divided into two groups according to valve thickness. They were defined as classic and nonclassic MVPs (mitral valve thickness >5 mm and <5 mm, respectively).^[19] Concerning that, 32.2% (37) of cases had classic and 67.8% (78) had nonclassic MVP in the current study.

The degree of MR was assessed as the ratio of the maximal regurgitant jet area to the area of the left atrium in the parasternal and apical long-axis and apical four-chamber views. MR degree is classified as none-trace, mild, moderate, and severe based on ratios of $>0\%$ – 10% , $>10\%$ – 20% , $>20\%$ – 40% , and $>40\%$, respectively.^[20]

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) version 19 (IBM Inc. Chicago, IL, USA) was used to analyze the data. As the data were not normally distributed, the Mann-Whitney *U*-test was used for the comparison of numerical data. The Chi-square test or Fisher's exact test was used for the analysis of categorical data. An exact test was used for the analysis of categorical data with more than 2×2 cells. As descriptive statistics, the mean, standard deviation of continuous variables, and percentages of discontinuous variables were specified. The statistical significance limit was accepted as $P < 0.05$.

RESULTS

We found that 65.2% of MVP patients were symptomatic with one or more symptoms including palpitation, chest pain, chronic fatigue, syncope, dyspnea, and others related to orthostatic hypotension such as dizziness and lightheadedness when standing up suddenly. The rest of the patients were asymptomatic. Chest pain and palpitation

were the two most common symptoms. Symptomatology of the MVP patients is shown in Figure 1 (note that some patients have more than one symptom).

The degrees of mitral valve regurgitation of the patients were none, trivial-mild, and moderate-severe, 28 (27.3%), 69 (60%), and 18 (15.7%), respectively.

Characteristics of the MVP patients and control groups are given in Table 1. Accordingly, although the number of patients with a SCARED scale score of 25 and above was higher in the MVP group, no statistically significant difference was found between the groups. Similarly, there was a higher mean SCARED scale score in MVP patients, but it was not statistically significant.

The anxiety level and symptomatic status of MVP patients were compared according to gender. The incidence of symptoms was not statistically different in both sexes. However, among those with symptomatic MVP, the incidence of palpitations and dyspnea was higher in girls. The frequency of palpitation in boys and girls was 25.7% and 41.3%, respectively ($P = 0.11$), and the frequency of dyspnea in boys and girls was 2.9% and 15%, respectively ($P = 0.050$). The mean of the SCARED scale score and the number of patients with a score of 25 and above were found to be significantly higher in girls with MVP than in boys [Figure 2]. SCARED scale scores 25 and above were as follows: 55 (87.3%) girls and 25 (48.1%) boys ($P = 0.001$). Furthermore, when the control group was compared by gender, we also observed a statistically higher anxiety score in girls than boys ($P = 0.002$).

In addition, MVP and control groups were compared by gender. There was no difference between girls with MVP and healthy girls in terms of either the mean anxiety score or the number of people with an anxiety score above 25. Similarly, there was no difference between boys with MVP and healthy boys in terms of either the mean anxiety score or the number of people with an anxiety score above 25.

SCARED scale score was significantly higher in MVP patients who had one or more symptoms than in asymptomatic cases ($P = 0.001$) [Figure 3]. Those who had palpitation and dyspnea had significantly higher levels of anxiety score values. Table 2 shows the comparison of the anxiety scores of those with and without symptoms.

Table 1: The characteristics of the participants

	MVP (n=115)	Control (n=53)	P
Age, mean±SD	13.5±3.06	15.1±13.2	0.414
Gender, n (%)			
Girl	80 (69.6)	33 (62.3)	0.349
Boy	35 (30.4)	20 (37.7)	
BMI, mean±SD	18.75±3.46	19.48±4.08	0.272
SCARED Scale score ≥25, n (%)	63 (54.7)	22 (41.5)	0.076
The mean of SCARED Scale values	29.2±13.08	24.9±14.01	0.065

MVP: Mitral valve prolapse, SCARED: Screen for child anxiety-related emotional disorders, BMI: Body mass index, SD: Standard deviation

SCARED scale scores of 25 or higher were found in 61.3% of symptomatic patients ($P = 0.053$). We also compared the anxiety score values of MVP patients by gender, according to symptomatic and asymptomatic cases. Among symptomatic MVP patients, girls had higher levels of anxiety scores than boys ($P = 0.0001$). However, in the asymptomatic MVP patients, no significant difference was found according to gender ($P = 0.024$).

In this study, no significant difference was found in anxiety scores according to either MVP type or severity of

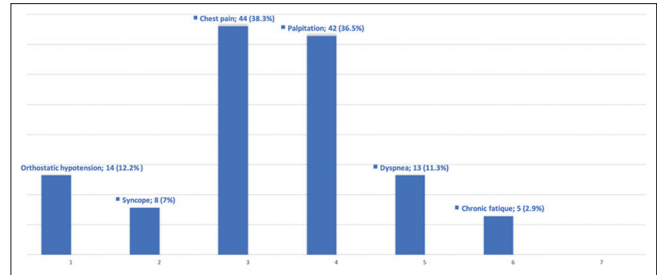


Figure 1: Symptomatology of the mitral valve prolapse patients (note that some patients have more than one symptom)

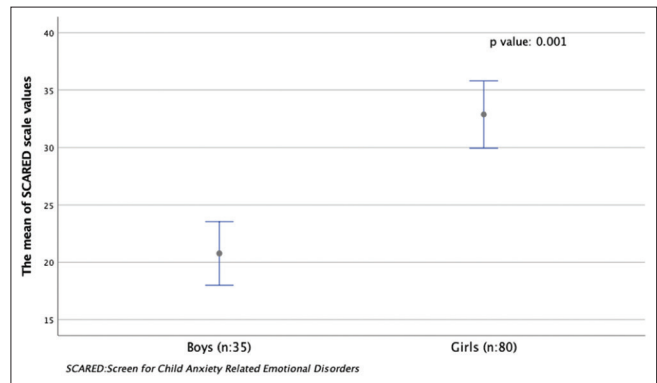


Figure 2: The mean of Screen for Child Anxiety-Related Emotional Disorder scale values according to gender in the Error Bar (bars represent the standard deviation of the mean). SCARED: Screen for Child Anxiety-related Emotional Disorders

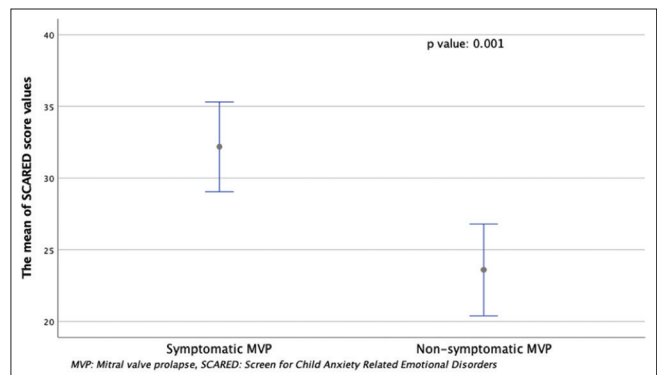


Figure 3: The mean of Screen for Child Anxiety-related Emotional Disorder scale values in symptomatic and nonsymptomatic mitral valve prolapse in the Error Bar (bars represent the standard deviation of the mean). MVP: Mitral valve prolapse, SCARED: Screen for Child Anxiety-related Emotional Disorders

mitral valve regurgitation [Figures 4 and 5]. There were no differences between symptomatic and asymptomatic MVP patients in terms of the degree of MR severity. When the MR degree was analyzed according to gender, there was a difference between boys and girls in terms of those with no MR and those with moderate-severe MR ($P = 0.040$). In other words, while the rate of no MR was 37.1% in boys, this rate was only 18.8% in girls, and while moderate-severe MR was 5.7% in boys, this rate was 20% in girls. However, the rate of mild MR was similar between genders. In summary, the frequency of MR and moderate-severe MR was higher in girls.

In addition, the groups were analyzed separately to determine if there was a difference between age and anxiety score values. Accordingly, no correlation was found between age and anxiety scores either in the MVP group or healthy children ($P = 0.226$ and $P = 0.586$, respectively).

DISCUSSION

Children with MVP seem to be more excited, nervous, and worried as can be noticed during the examination.

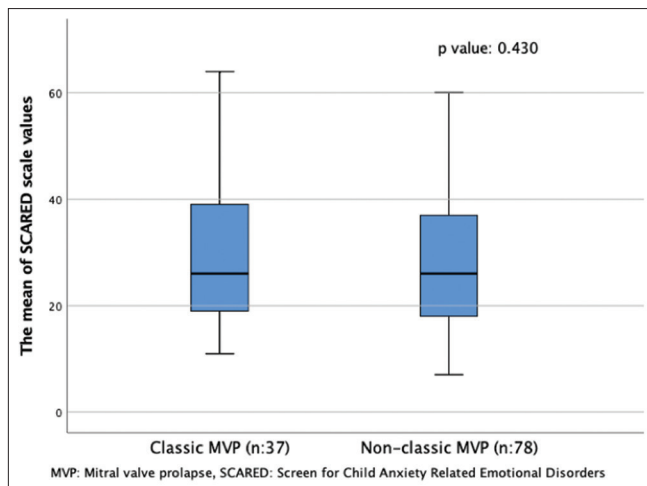


Figure 4: The mean of Screen for Child Anxiety-related Emotional Disorder scale values according to mitral valve prolapse types in the box plot (the black center line denotes the median value (50th percentile), whereas the blue box contains the 25th to 75th percentiles of the dataset. The black whiskers mark the 5th and 95th percentiles). MVP: Mitral valve prolapse, SCARED: Screen for Child Anxiety-related Emotional Disorders

Although there are some symptoms described in MVP syndrome, it is unclear whether symptoms reported by children with MVP syndrome are related to an underlying psycho-emotional disorder.

Some studies suggest that abnormal autonomic regulation causes symptomatic subjects. This occurs with elevated circulating concentrations of catecholamines and enhanced β -receptor affinity. Dysregulation of neurotransmitters, especially serotonin, may initiate changes in valve microstructure.^[21-23] In addition, sympathetically mediated cardiovascular overactivity was reported in adolescent MVP patients.^[24] Interestingly, according to another study, neurotransmitters such as catecholamines and serotonin influence the behavior of heart valve cells. Therefore, dysregulation of these mechanisms, prominently serotonin, may initiate changes to the valve microstructure associated with heart valve disease.^[25] Briefly, neurotransmitters are suggested to be linked to both symptoms and valvular disease.

Studies investigating the association between MVP and anxiety are limited in children. Arfken *et al.*^[10] in a study in 1990 found the frequency of MVP to be 4.3% among 813 pediatric patients aged 9–14 years, and they concluded that anxiety scores in these children were not higher than in healthy children. In the same year, MVP

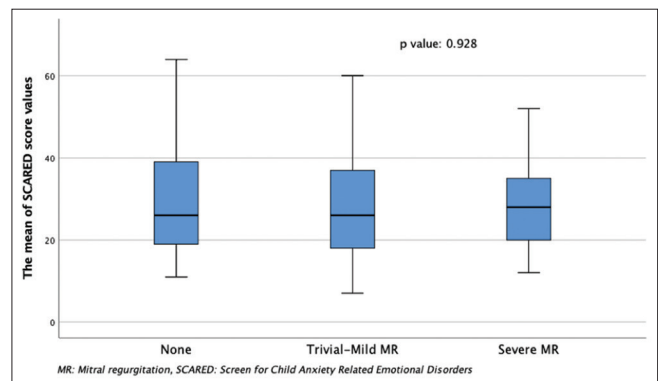


Figure 5: The mean of Screen for Child Anxiety-related Emotional Disorder scale values according to the severity of mitral regurgitation in the Box Plot (The black center line denotes the median value (50th percentile), whereas the blue box contains the 25th to 75th percentiles of the dataset. The black whiskers mark the 5th and 95th percentiles). MR: mitral regurgitation, SCARED: Screen for Child Anxiety-related Emotional Disorders

Table 2: The comparison of the anxiety scores of those with and without symptoms

	Orthostatic hypotension		Syncope		Chest pain		Palpitation		Dyspnea		Chronic fatigue	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
<i>n</i>	14	101	8	107	44	71	42	73	13	102	5	110
The mean of the AS	32.1	28.7	36.6	28.6	30.7	28.2	33.9	26.5	37.0	28.2	42.0	28.6
SD of the AS	13.4	13.0	15.4	12.8	13.8	12.6	14.8	11.2	16.0	12.3	15.1	12.7
<i>t</i>	0.878		1.428		0.963		2.811		1.919		1.940	
<i>df</i>	16.590		7.740		84.794		68.260		13.875		4.261	
<i>P</i>	0.393		0.192		0.338		0.003		0.046		0.120	

AS: Anxiety score, SD: Standard deviation

was detected in two of six children whose first panic attack was between 5 and 11 years of age and diagnosed with early-onset panic attacks. The authors concluded that MVP may be associated with panic disorder in children as adults.^[25] One year later, Stavrakaki *et al.* detected MVP in a 9-year-old boy diagnosed with anxiety and depression, and he noticed a regression in symptoms after propranolol treatment.^[26] In 1999, Toren *et al.* compared 52 children diagnosed with panic and anxiety disorder with normal children. They demonstrated that none of the patients had MVP, whereas one child in the control group did. Therefore, they concluded that there was no association between MVP and anxiety.^[27]

As we mentioned in the introduction part of our article, there are mostly adult studies on this subject in the years that followed. In a study conducted by Dubey *et al.*^[4] in 2016, the association between MVP and anxiety was investigated according to age. The authors found that there is a stronger association between anxiety and MVP in the younger than the older age group except for children aged 0–9 years old. In another adult study, Orhan *et al.*^[5] found that the anxiety scores of patients with MVP syndrome were higher than those of the anatomical MVP and control groups. However, the number of patients in this study was small. In a more recent study, Esfehni *et al.*^[6] added fluoxetine to the propranolol treatment in MVP patients because they assumed that MVP was accompanied by anxiety. Hence, they decided that the treatment of anxiety may reduce the symptoms of MVP. Nevertheless, the dual combination was found neither effective in improving echocardiographic changes nor in reducing the symptoms of MVP and anxiety. In Bayer's study,^[7] 216 patients with MVP were compared with 65 patients without MVP in terms of psycho-emotional status (symptoms of anxiety, depression, and posttraumatic stress), health-related quality of life, and perceived disease severity. They concluded that MVP was not independently associated with psycho-emotional status or health-related quality of life. However, psycho-emotional state and health-related quality of life are related to the patient's perception of the severity of mitral valve disease rather than the presence of MVP. In another study published in a journal dedicated to psychiatry, the incidence of MVP was investigated among patients diagnosed with social anxiety disorder and panic disorder, and no increased incidence was found compared to the control group.^[8]

Although not statistically significant, it is noteworthy that our MVP patients had high anxiety scores. What is more, we found that the levels of anxiety in children with MVP syndrome were significantly higher than in those with asymptomatic (anatomical) MVP. These children seem to have developed anxiety because of the symptoms related to MVP, not because of MVP itself. This could be related to the way they perceived the disease or to their hyperadrenergic

state. We think that it may be beneficial for children with high anxiety scores to be evaluated by a psychiatrist.

In this study, we found higher anxiety scores in girls with MVP compared to boys with MVP. It may be related to the fact that symptoms such as palpitation and dyspnea were relatively more common in girls. However, when the children with MVP and healthy subjects were compared separately by gender, no significant difference was found in terms of anxiety scores. Thus, this finding strongly supports the idea that higher anxiety scores in girls may be due to the higher prevalence of affective disorders in the female gender in general, rather than MVP.^[28]

In the current study, we could not demonstrate a significant difference in SCARED scale scores according to MR severity. However, in a study by Bayer-Topilsky *et al.*,^[11] posttraumatic stress disorder linked to anxiety is much more prevalent in patients with organic moderate or severe MR than simple MVP. Still, the severity of MR does not determine the presence of posttraumatic stress disorder. We had a small number of patients with moderate-severe MR in our population. Therefore, we may not have been able to show a significant difference according to the degree of MR.

Limitations

The number of participants was restricted to 53 participants. Our study could have benefited from a higher number of participants in the control group. In addition, it could have been better if the parent form of the SCARED scale was also used.

CONCLUSIONS

Children with MVP did not have higher anxiety scores as compared to age- and gender-matched controls. Symptomatic children with MVP are more anxious than asymptomatic children. In addition, girls had higher anxiety scores than boys among MVP patients. Children with refractory symptoms may benefit from further psychiatric evaluation and counseling.

The authors confirm their contribution to the paper as follows

Study conception and design: Meryem Beyazal; data collection: Meryem Beyazal, İlker Ufuk Sayıcı; analysis and interpretation of results: Meryem Beyazal, Supervision: Utku Arman Örün. All authors read and approved the final manuscript.

Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2013.

This study was approved by the TUEK department (Decision date: June 09, 2022 and decision number: 2022/5).

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Nil.

Conflicts of interest

There are no conflicts of interest.

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