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ORIGINAL ARTICLE

Relationship Between Mmitral Valve Prolapse and Panic Disorder

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ABSTRACT

Aim: The present study assessed the relationship between mitral valve prolapse and panic disorder.

Methods: This prospective study included 45 patients with echocardiographic diagnosis of mitral valve prolapse (MVP) and an equal number of age and sex-matched patients with panic disorder. All subjects underwent evaluation by a cardiologist with echocardiography and psychiatric evaluation by a psychiatrist.

Results: Nine (20%) of the MVP patients had PD. Among the PD patients, 5 (16.67%) had asymptomatic MVP. These were significantly higher than in the general population. Abnormal body habitus occurred in 45.8% of patients. The association between thin body habitus and MVP was supported. Prolapse of AML only was associated with less severe symptoms.

Conclusion: The high prevalence of panic disorder in MVP patients and of MVP in panic disorder patients is consistent with earlier studies. Panic disorder associated with MVP is no different from uncomplicated panic disorder and responds as well to antidepressants.

KEYWORDS

• Comorbidity in cardiac disorders • Anxiety • Depression • Echocardiography • Prevalence • Psychopathology

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INTRODUCTION

Medical literature has connected panic disorder to mitral valve prolapse (MVP), indicating that those with MVP may be more likely to suffer from anxiety-related symptoms and panic episodes. The mitral valve malfunctions in MVP. Blood may leak backward into the left atrium, resulting in symptoms like dizziness, palpitations, chest pain, and shortness of breath. Conversely, panic disorder is a mental illness marked by abrupt and severe episodes of worry and terror, frequently accompanied by symptoms like perspiration, a racing heartbeat, and a sense of impending doom. Patients and healthcare professionals can benefit from knowing how these two illnesses are related. In the general adult population, the prevalence of MVP using echocardiographic criteria is 2.4%, and PD is 5.2%.[1-5]

Numerous studies indicated a higher prevalence of MVP in individuals with PD compared to the general population. A meta-analysis of 14 studies, including 1146 patients, revealed that MVP was found in 27.20% of the panic disorder patients and 9.21% of the healthy controls.[1] The precise reasons for this association remain uncertain; however, several theories propose that the autonomic nervous system may be a contributing factor. This autonomic nervous system may influence both the symptoms of MVP and the manifestations of panic attacks. In particular, dysregulation within this system could lead to heightened activity of the sympathetic nervous system, thereby producing symptoms such as palpitations and chest discomfort that are frequently observed in both MVP and panic disorder. The physical signs of MVP, including palpitations and chest pain, might be interpreted as indicators of a looming heart attack, potentially provoking a panic attack in vulnerable individuals. This can establish a feedback loop, where the physical signs of MVP enhance anxiety, which then intensifies the physical signs. This cycle can complicate the ability of individuals with MVP to distinguish between symptoms related to the heart and those related to anxiety, leading to an increased feeling of fear and panic. Furthermore, MVP symptoms often intensify during times of stress or anxiety, indicating that psychological stress could aggravate the physical effects of MVP.[1-5]

Interestingly, several studies have investigated genetic connections between MVP and anxiety disorders.[6] Both conditions seem to have an inherited aspect, with research showing a family tendency for MVP and a genetic inclination for anxiety disorders. This overlap may suggest that specific individuals are genetically inclined to experience both MVP and panic disorder. Furthermore, serotonin, a neurotransmitter that affects mood regulation, has been linked to both MVP and anxiety disorders. Discrepancies in serotonin levels are recognized to influence anxiety and panic symptoms, and some studies propose that serotonin imbalance could also play a role in MVP. However, further research is required to confirm this link. Several studies in developed countries have assessed the relationship between MVP and PD but have not been adequately studied in the Indian population. The paucity of Indian studies prompted us to undertake a study of MVP and panic disorder patients to ascertain the clinical profile and to determine the incidence of panic disorder in MVP and MVP in Panic disorder.

MATERIALS AND METHODS

This hospital-based cross-sectional study was carried out in a tertiary care hospital's Psychiatry and Cardiology departments. The protocol was submitted to and approved by the institutional ethical committee. Written informed consent was obtained from all the subjects.

Sample

Two study groups were recruited using purposive sampling per the inclusion and exclusion criteria. The first study group included 45 consecutive patients with an echocardiographic diagnosis of MVP. These patients had been referred to the cardiologist for evaluation of cardiac murmur and/or click. They were referred to the psychiatric outpatient department for this study. The second group included an equal number of age and sex-matched drug naïve patients who were referred to the psychiatry outpatient department of our hospital and received the diagnosis of panic disorder according to the ICD 10 Diagnostic Criteria for Research.[7] They were referred to the Cardiology outpatient department for this study. Patients with myocardial infarction, pheochromocytoma,

hyperthyroidism, epilepsy, psychosis, and substance use disorder (except nicotine and caffeine abuse and dependence) were not included in the study.

Procedure

The cardiologist and psychiatrist examined all subjects. The cardiologist performed the physical and cardiology examination while the psychiatrist carried out the psychiatric evaluation. The cardiologist was blind to the psychiatric diagnosis, while the psychiatrist was blind to the cardiology diagnosis. The patients were mainly studied for symptomatology, body habitus, auscultatory findings, and associated physical and psychiatric disorders. Patients were classified as either mild, moderate, or severely symptomatic, depending upon the severity of chest discomfort. Patients with vague chest discomfort and/or transient palpitations were classified as mildly symptomatic, those with definite chest pain and/or palpitations as moderate, and those with distressing chest pain and/or palpitations as severely symptomatic. To determine patients' body habitus, the height and weight of individual patients were expressed in the form of the Quetelets index (QI).

$$QI = \frac{\text{Body weight in Kgs}}{(\text{Height in meters})^2}$$

Typical values of QI range from 20 to 25.

All subjects underwent the following investigations: hemogram, urinalysis, blood sugar (fasting and post-prandial), lipid profile, blood urea, serum creatinine, radiological examination of the heart, standard 12 lead ECG, and two-dimensional (2D) echocardiography. The criteria for 2D echocardiography diagnosis of MVP were: (i) Marked systolic displacement of the mitral leaflet with coaptation point at/on the left atrial side of the annulus or (ii) Moderate systolic displacement of the leaflets with at least moderate MR, chordal rupture or annular dilation. ICD 10 Diagnostic Criteria for Research were followed to diagnose PD.

Statistical Analysis

The data was analyzed using the SPSS-23 (IBM, Armonk, USA). Frequency data was compared using the chi-square test or Fisher exact test as appropriate. Continuous data was compared using the Student's t-test.

RESULTS

Forty-five consecutive patients with MVP (forty men, five women) and an equal number of PD patients matched for age and sex were included in the study. The two groups were well-matched in age, pulse rate, resting blood pressure, and Quetlet's index (Table 1). Nine (20%) of the MVP patients had PD. Among the PD patients, 5 (16.67%) had asymptomatic MVP.

Table 1: Characteristics of panic disorder patients and idiopathic mitral valve prolapse patients

Variables	Mitral valve prolapse patients	Panic disorder patients	t-test (pdf)	P
Age (in years) Mean (±SD) Range	28.71 (±4.05) 20-34	28.51 (±4.15) 23-39	0.231 (88)	0.818 NS
Pulse Mean (±SD) Range	87.58 (±10.39) 64-104	90.27 (±9.09) 64- 106	-1.307 (88)	0.195 NS
Systolic blood pressure Mean (±SD) Range	124.18 (±14.67) 100-160	126.84 (±9.43) 110-150	-1.026 (88)	0.308 NS
Diastolic blood pressure Mean (±SD) Range	77.38 (±7.78) 68-104	79.51 (±9.74) 70-106	-1.148 (88)	0.254 NS
Quetlet's index Mean (±SD) Range	19.97 (±2.80) 13.51-25.08	20.15 (±1.62) 15.50-24.90	-0.321 (88)	0.749 NS

Symptomatology: Out of the 45 MVP patients in the study, 34 (75.6%) were symptomatic, while 11 (24.4%) patients were asymptomatic. All the PD patients were symptomatic (Table 2). Palpitations were paroxysmal, spontaneous, or precipitated by emotion or exertion, or spontaneous. Chest pain was atypical, varying widely in intensity, location, duration, and precipitating factors. The character of chest pain varied from prolonged retrosternal discomfort to dull, boring, and prolonged precordial pain without radiation. However, one patient with MVP had angina pectoris. The other significant physical symptoms, breathlessness and giddiness, were also of mild degree only.

Table 2: Symptomatology of Mitral Valve Prolapse (n=45) and panic disorder (n=45) patients

Symptom	Mitral Valve prolapse patients Number (%)	Panic disorder patients Number (%)	Chi-square/Fisher exact test value	P
Chest pain	32 (71.1%)	39 (86.97%)	3.27	0.07 NS
Palpitations	23 (51.1%)	42 (93.33%	17.95	.0002 S
Breathlessness	22 (48.9%)	34 (75.56%)	5.72	0.017 S
Anxiety	17 (37.8%)	45 (100%)	28.34	<0.05 S
Fatigue	17 (37.8%)	31 (68.89%)	7.54	0.006 S
Giddiness	14 (31.1%)	35 (77.78%)	17.92	0.0002 S
Tremors	13 (28.9%)	39 (86.67%)	28.47	<0.05 S
Hyperhidrosis	7 (15.6%)	15 (33.33%)	2.95	0.086 NS
Restlessness	6 (13.3%)	27 (60.00%)	19.14	0.00001 S
Syncope	6 (13.3%)	0 (0.0%)	0.026*	<0.05 S

***Fisher's exact test**

Auscultatory findings: Both systolic click and murmur over the mitral area were heard in 22 (48.9%) subjects. Isolated click and isolated murmur were present in 6 (13.33%) and 13 (28.89%) patients, respectively. In one patient with an isolated systolic click, the S2 was widely split and mobile. Two PD patients had systolic click and murmur, and two had isolated clicks over the mitral area.

Body habitus: Some form of abnormal body habitus was detected in 15 (33.33 %) patients and two patients with PD. Details are given in Table 3. The QI in MVP patients varied from 13.51 to 25.08, with a mean (± S.D.) of 19.97 (± 2.79). The QI in patients with PD varied from 15.50 to 24.90, with a mean (± S.D.) of 20.15 (± 1.62). Twenty-three (51.1%) patients with MVP and 26 (57.78%) patients with PD had QI below 20, indicating an association of the disorders with thin body habitus (Table 3).

Table 3: Marfanoid physical features observed in the Mitral Valve Prolapse (n=45) and panic disorder (n=45) patients

Marfanoid physical features	Mitral Valve prolapse patients Number (%)	Panic disorder patients Number (%)	Chi-square / Fisher exact test value	P
High arch palate	13 (28.89)	2 (4.44%)	8	0.004 S
Pes cavus	2 (4.44%)	0(0.0%)	0.494*	>0.05 NS
Marfans syndrome	2 (4.44%)	0 (0.0%)	0.494*	>0.05 NS
Ligament laxity	2 (4.44%)	0(0.0%)	0.494*	>0.05 NS
Flat feet	2 (4.44%)	0(0.0%)	0.494*	>0.05 NS
Pectus exacavatum	1 (2.2%)	0(0.0%)	1*	>0.05 NS
Scoliosis of thoracic spine	1 (2.2%)	0(0.0%)	1*	>0.05 NS
Polydactyly hand	1 (2.2%)	0(0.0%)	1*	>0.05 NS
High myopia	1 (2.2%)	0(0.0%)	1*	>0.05 NS

*Fisher's exact test

Comorbid disorders: Comorbid disorders in MVP and PD patients are shown in Table 4. None of the subjects had an associated organic heart disease except one MVP patient with congenital aortic stenosis.

Table 4: Comorbid disorders in subjects with mitral valve prolapse.

Psychiatric disorders	Mitral Valve prolapse patients Number (%)	Panic disorder patients Number (%)	Chi-square / Fisher exact test value	P
Panic disorders	9 (20%)	45 (100%)	<0.00001*	<0.05 S
Other anxiety disorders	3 (6.67%)	9 (20.00%)	2.40	0.121 NS
Depression	3 (6.67%)	5 (11.11%)	0.137	0.711 NS
ASPD	1 (2.2%)	0 (0.0%)	1*	>0.05 NS
Impotence	1 (2.2%)	0 (0.0%)	1*	>0.05 NS
Insomnia	1 (2.2%)	4 (8.89%)	0.847	0.357 NS
Physical disorders				
Mitral valve prolapse	45 (100%)	5 (16.67%)	<0.00001*	<0.05 S
Duodenal ulcer	2 (4.44%)	0 (0.0%)	0.494*	>0.05 NS
Pleural effusion	1 (2.2%)	0 (0.0%)	1*	>0.05 NS
Congenital aortic stenosis	1 (2.2%)	0 (0.0%)	1*	>0.05 NS
Hypertension	1 (2.2%)	1 (2.2%)	1*	>0.05 NS
NIDDM	1 (2.2%)	0 (0.0%)	1*	>0.05 NS

*Fisher's exact test

ECG changes: ECG changes were observed in 14 (31.11%) MVP patients. Of these, 7 (15.56%) had ST-T changes in inferior and/or lateral chest leads; 5 (11.11%) had premature ventricular beats; 1 (2.2%) patient each had cardiac arrhythmias, sinus tachycardia, early repolarization syndrome, LAHB, and LVH. In panic disorder patients, sinus arrhythmia and Tall T waves were seen in 2 patients each.

Echocardiography: on 2D echo, the prolapsing mitral valve leaflet was identified as AML only in 16 (35.56%); PML only in 5 (11.11%); both AML & PML in 24 (53.33%) patients. In panic disorders, patient 6 had prolapse of both AML and PML.

Radiology: Abnormalities were noted in the chest radiographs of 4 MVP patients and included one patient, each showing borderline cardiomegaly, materialization of the heart, cervical spondylosis, and pleural thickening. In patients with panic disorder, all chest radiographs were normal.

Treatment: Apart from 15 (33.33%) patients with panic/anxiety/depression who responded satisfactorily to psychiatric treatment, only 6 (13.33%) patients required treatment with propranolol for chest pain and/or palpitations. The remaining patients overcame their anxiety after an explanation of the benign nature of MVP, along with reassurance. Panic disorder patients were treated with antidepressants, anxiolytics, propranolol, and psychotherapy with good response.

DISCUSSION

The consensus among cardiologists is that despite the complications of MVP syndrome, it should not be forgotten that, on the whole, this is a benign condition and that the vast majority of patients with this syndrome remain asymptomatic for their entire lives and require, at most, observation every few years and reassurance.[8] In contrast, 34 (75.6%) subjects with MVP were symptomatic, while only 11 (24.4%) patients were asymptomatic in the present study. However, despite the presence of symptoms, only 21 (46.67%) of the patients required short-term symptomatic treatment, indicating that the remaining patients had probably become symptomatic as a result of the fear of having a serious heart disease. This fact highlights the importance of adequate explanation and reassurance being given to these patients who are prone to hypochondriacal fears. The prognosis of MVP patients is excellent. The majority of MVP patients remain entirely symptom-free. Only one per 100 patients developed serious complications, and 4 percent of patients died

during the 8 years. In contrast, one study reported a much more aggressive course in 833 patients with MVP, with a 19 percent mortality rate at 10 years and a 20 percent rate of MVP-related events, including heart failure, AF, cerebrovascular events, arterial thromboembolism, and endocarditis.[9,10] Obviously, some patient education is indeed indicated.

Beta-adrenergic blockers are helpful in the treatment of palpitations and chest discomfort. The high incidence of chest pain and palpitations in MVP patients observed in our study has also been reported earlier.[11] The cause of the chest pain in MVP remains obscure. It is improbable that only mechanical phenomena, such as the exaggerated movement of the leaflets, can explain it.[12] Hypotheses have been thought of; for example, the exaggerated traction of the leaflets over the papillary muscles could cause ischemia and pain;[13] the increased tension of the leaflet could deform the atrioventricular groove affecting the circumflex artery and producing ischemia. Nervous terminals in the overly tensioned leaflets could result in arrhythmia.[12] Myxoma degeneration is sometimes found in the valves of MVP patients.[14] It is common to find concomitant myxoma degeneration of other cardiac valves[12] Myocardiopathy and MVP make it easier to understand arrhythmia, pain, asynergy of contraction, and the electrocardiographic alterations found in MVP syndrome.[15]

The association of thin body habitus with MVP is well established and led to the speculation that it constituted a form of Marfan syndrome. However, there is no firm evidence to establish it. Lower body weight of MVP patients has also been attributed to hypercatabolic state, which may share a common etiology with other clinical facets of the disease. A linked embryologic mesenchymal dysplasia has been put forth to explain the high prevalence of thoracic skeletal abnormalities reported in MVP patients and the present study. Both the mitral valve and the thoracic bony cage undergo differentiation during the same period in intra-uterine life (35th – 42nd day), and any factor influencing the growth of one may also alter the development of the other.[16]

The high prevalence of panic disorder in MVP patients observed in the present study is consistent with earlier studies.[17] Panic disorder associated with MVP is no different from uncomplicated panic disorder and responds as well to antidepressants. However, beta-blockers may be very effective in the treatment of a panic disorder associated with MVP.[17,18,19]

LIMITATIONS

The sample size was modest and included patients from one centre only. The psychiatrist and cardiologist were not blind to the diagnosis, which might have caused some bias.

CONCLUSION

In conclusion, we can state that there is a high prevalence of MVP in panic disorder patients and panic disorder in patients with MVP. The connection between MVP and panic disorder is intricate and diverse, probably encompassing a mix of physiological, genetic, and psychological elements. The shared symptoms can generate a cycle of anxiety and physical unease that affects individuals' quality of life. Recognizing this relationship is crucial for delivering thorough care to those with MVP and panic disorder, enabling them to tackle both the physical and emotional dimensions of these issues.

Conflict of Interest: Nil

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