



Anterior Mitral Valve Prolapse Contributes to Mitral Regurgitation and Panic Disorder

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Objective: Mitral valve prolapse is affecting 2,4% of general population which shows similar prevalence, age and gender distribution and share common nonspecific symptoms with panic disorder. The aim of this prospective study is to investigate the contribution of the anterior mitral leaflet prolapse to mitral regurgitation and panic disorder.

Material and Methods: Ninety-six patients, who were finally diagnosed as having non-cardiac chest pain with anterior mitral valve prolapse during the evaluation of chest pain, palpitation and fatigue were assessed for panic disorder.

Results: From 96 patients with mitral valve prolapse (mean age 40±8 years), 46 (48%) had panic disorder and 32 (33%) had mitral regurgitation. Majority of the patients were female (53%). 48 % of the patients with panic disorder had mitral regurgitation. Among 32 patients with mitral regurgitation, 22 (69%) had panic disorder. The incidence of panic disorder in patients with mitral regurgitation was 69%. Among those with panic disorder, 48% had mitral regurgitation. There was a significant correlation between mitral regurgitation and panic disorder (p=0.004).

Conclusion: This study has demonstrated the possible contribution of the anterior mitral leaflet prolapse to mitral regurgitation and panic disorder. Panic disorder and mitral valve prolapse presents a co-morbidity, which deserves further clinical investigations.

Key Words: Mitral Valve Prolapse; Panic Disorder; Mitral Regurgitation.

Anterior Mitral Kapak Prolapsusu Mitral Yetersizlik ve Panik Bozukluğa Katkıda Bulunmaktadır

Amaç: Mitral kapak prolapsusu genel popülasyonun %2,4'ünü etkilemektedir. Panik bozuklukla benzer sıklık, yaş ve cinsiyet dağılımı göstermekte ve ortak nonspesifik semptomları paylaşmaktadır. Bu prospektif çalışmada anterior mitral kapak prolapsusunun mitral yetersizlik ve panik bozukluğa katkısının araştırılması amaçlanmaktadır.

Gereç ve Yöntemler: Göğüs ağrısı, çarpıntı ve halsizlik yakınması nedeniyle değerlendirilen ve sonuçta anterior mitral kapak prolapsusu ve non kardiyak göğüs ağrısı tanısı konulan 96 hasta panik bozukluk açısından araştırıldı.

Bulgular: Mitral kapak prolapsusu olan 96 hastadan (ortalama yaş 40±8) 46'sında (%48) panik bozukluk ve 32'sinde (%33) mitral yetersizlik saptandı. Hastaların çoğunluğu (%53) kadındı ve mitral yetersizlikli 32 hastanın 22'sinde (%69) panik bozukluk vardı. Panik bozukluk saptanan hastaların %48'inde mitral yetersizlik saptandı. Mitral yetersizlikle panik bozukluk arasında istatistiksel olarak önemli korelasyon saptandı (p=0,004).

Sonuç: Bu çalışmanın sonuçları anterior mitral kapak prolapsusunun mitral yetersizlik ve panik bozuklukla muhtemel birlikteliğini ortaya koymaktadır. Panik bozukluk ve mitral kapak prolapsusu birliktelik oluşturmakta ve bu durum daha geniş çaplı ileri çalışmalarla desteklenmelidir.

Anahtar Kelimeler: Mitral Kapak Prolapsusu; Panik Bozukluk; Mitral Yetersizliği.

Introduction

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Mitral valve prolapse (MVP) syndrome is one of the most prevalent cardiac valvular abnormalities, effecting 2,4% of general population. Recent studies have suggested an equal prevalence among males and females whereas earlier studies suggested a female preponderance with a ratio of up to 2 times.^{1,2} Most

frequently MVP occurs as a primary condition commonly associated with myxomatous proliferation of the mitral leaflets and its supporting apparatus resulting in redundancy, abnormality and prolapse of the valve leaflets.^{1,2} It has also been associated with many other conditions like hereditary connective tissue disorders (Marfan syndrome, Ehler-Danlos syndrome, osteogenesis imperfecta, pseudoxanthoma elasticum), hyperthyroidism, congenital thoracic deformities and congenital malformations (Ebstein anomaly, ostium secundum type atrial septal defect, Holt Oram syndrome). There is a hereditary form with autosomal dominant pattern, site on chromosomes 11, 13, 16³ Complications such as cardiac arrhythmias, sudden death, infective endocarditis, severe mitral regurgitation (with or without chordae tendinae rupture) and cerebral ischemic events can be seen¹

Panic disorder (PD) is a psychiatric disorder with somatoform symptoms similar to those of MVP including palpitation, tachycardia, chest pain, shortness of breath and fatigue. Diagnosis is made according to DSM-IV criteria. Panic disorder has been estimated to have 4% to 6% prevalence in the general population.¹ Predisposing factors include genetic contribution and gender specificity.^{4,5} Compared with males, females have almost twice the risk for developing panic disorder.⁶ Precipitating factors are; a family history of panic disorder, a personal history of anxiety, depression and cardiac symptoms.⁷⁻⁹ Liberthson et al had found that more than 30% of patients with panic disorders have been diagnosed with mitral valve prolapse (MVP).¹⁰ A possible relationship is believed to exist between these two disorders, although there are inconsistent findings for such an association among different researchers.¹¹ Some symptoms of MVP, such as chest compression and palpitation can evoke a panic attack. Hence, it is believed that panic disorder could be caused by MVP, or conversely, panic disorder may result in MV:^{12,13} The aim of this prospective study is to investigate the contribution of anterior mitral valve prolapse to mitral regurgitation (MR) and PD in patients presenting with non-cardiac chest pain, palpitation and fatigue.

Patients and Methods

Approval was first obtained from the institutional review board of Gülhane Military Medical Faculty. Written informed consent was collected from all participants after a detailed explanation of the purpose of the study. Ninety-six patients, who were evaluated for chest pain, palpitation and fatigue, and finally found to have non-cardiac chest pain with anterior MVP were enrolled in this study. They were assessed for panic disorder, which was defined according to the criteria of the American Psychiatric Association. The definition of the non-cardiac chest pain was described on practice

guidelines of chronic stable angina.¹⁴ Palpitation was described as any kind of feeling of heart pounding or irregular heart beating not necessarily documented. Any feeling of weakness or shortness of breath was accepted as fatigue. Patients with heart failure, cardiac rhythm disorder, cerebrovascular disease, coronary artery disease (CAD) and mitral regurgitation (MR) greater than mild degree were excluded from the study.

Echocardiographic studies were performed with a System Five instrument (GE Vingmed Sound, Horten, Norway) utilizing a phased array duplex 2.5 MHz transducer. Two-dimensional (2-D) echocardiographic images from four standard parasternal and apical windows were obtained. The measurements of systolic displacement of the mitral valves and the diastolic anterior mitral leaflet thickness were performed by three different cardiologists blind to the patient's psychiatric diagnosis at three different times. The interobserver and intraobserver reproducibility of the echocardiographic measurements were 70%. The mathematical average of these measurements was used for statistical analysis. Patients with superior displacement of any mitral leaflet with more than 2 mm during left ventricular systole and diastolic anterior mitral leaflet thickness of more than 5 mm (classic MVP) or less than 5 mm (non-classic MVP) were diagnosed as MVP. These patients were evaluated for panic disorder, which was defined according to the criteria of the American Psychiatric Association as at least three panic attacks within a 3-week period or one panic attack followed by fear of subsequent panic attacks for at least one month.^{1,15}

In statistical analysis, values of selected variables were summarized by standard descriptive statistics and expressed as mean \pm SD. Independent-Samples T test (Mann-Whitney U test when Levene test is significant) and chi-square test were used to compare continuous and categorical variables between groups, respectively. Statistical significance was defined by a p value < 0.05.

Results

From 96 patients with MVP (mean age 40 ± 8 years), 46 (48%) had panic disorder and of these 46 patients 32 (33%) had MR. Majority of the patients were female (53%). Among 32 patients with MR, 22 (69%) had PD. The distribution of the patients according to the gender, presence of MR and PD has been depicted on Table 1.

The incidence of PD in patients with MR was 69%. There was a significant correlation between MR and PD in chi-square test ($p=0.004$). The average displacement of the anterior leaflet was 4.3 ± 1.4 mm in the whole study population. In patients with and without MR, the displacement was 5.4 ± 1.3 and 3.8 ± 1.0 mm, respectively

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($p < 0.001$). In patients with and without PD, the displacement was 4.9 ± 1.5 and 3.8 ± 1.0 mm, respectively ($p < 0.001$).

Table 1. The distribution of the patients according to the gender, presence of MR and PD.

Gender		PD		Total	
		No	Yes		
F	MR	No	19	29	
		Yes	6	22	
	Total		25	26	51
M	MR	No	21	35	
		Yes	4	6	10
	Total		25	20	45
Total	MR	No	40	24	64
		Yes	10	22	32

MR: Mitral regurgitation, PD: Panic Disorder, F: Female, M: Male

Among the patients with PD, the leaflet displacement between those with ($n=22$) and without ($n=24$) MR was 5.8 ± 1.3 mm and 4.0 ± 1.2 mm, respectively ($p < 0.001$). Among the patients with MR, the leaflet displacement between those with ($n=22$) and without ($n=10$) PD was 5.8 ± 1.3 mm and 4.7 ± 1.2 mm, respectively ($p = 0.027$). The most significant difference was between the patients with both MR and PD ($n=22$), and those without MR and PD ($n=40$). In the former, the leaflet displacement was 5.8 ± 1.3 mm and in the latter it was 3.6 ± 0.9 mm ($p < 0.001$).

Discussion

In this study we demonstrated a possible contribution of the anterior mitral leaflet prolapse to MR and PD. The prevalence of PD in patients with MVP is 48% in our study which is quite higher than those reported in the literature. Previous studies have reported PD prevalence rates ranging from 0% to 16% among idiopathic mitral valve prolapse cases.^{1,11,16} Margraf et al, in their metaanalysis, found the mean prevalence of PD to be 8% among idiopathic mitral valve prolapse patients, 5% among cardiac control subjects, and 2% among normal controls.¹¹ This relatively high incidence of the PD (48%) and MR (33%) in patients with MVP in our study can be attributed to selection bias.¹⁰ Only the patients with symptoms of non-cardiac chest pain, palpitation and fatigue were included in the study. Additionally a premature echocardiographic examination might also contribute the high incidence of PD. Also echocardiographic MVP criteria variance strongly influences estimates of the prevalence of MVP among patients with PD.¹⁶

Anxiety disorders, especially PD shows a co-morbidity with MVP.^{1,15} MVP has been observed more frequently than expected among patients with panic attacks.¹⁷ Although there is a controversy regarding the co-morbidity of MVP with PD, our study has confirmed that there is a tendency towards the co-morbidity of MVP-PD with a relative increase of our study group of 45% comparing to that of control group and the contribution of anterior mitral leaflet prolapse to PD.^{10,12,18,22} Amelioration of MVP after treatment for PD was also reported in the literature, which PD was a somatic disease, in terms of the etiology of anxiety disorder.¹⁶ Panic disorder was also reported in the etiology of MVP with direct hemodynamic or indirect effects.²²

Although there are no clear pathophysiologic or biochemical explanatory mechanisms and no convincing evidences of cause-effect relationship regarding the anterior MVP to MR and PD, we conclude that the high rate of this co-occurrence is entirely predictable. Additionally, the absence of a unifying mechanism does not diminish the high rate of co-occurrence between these two conditions. Ischemia originating from the contraction of the tip of the papillary muscle attaching to the chordae tendinea, giving rise to papillary ischemia has been proposed as a possible cause of non-cardiac chest pain in patients with MVP, corresponding a typical myofascial pain of a somatic disorder.¹ High prevalence of PD in our patients can be explained by the patient bias, since the study population represents a highly selected cases presenting with non-cardiac chest pain, palpitation and fatigue.

Main limitations of our study were its small sample size and lack of a cardiac control group. Because of the lack of a cardiac control group, we made theoretical comparisons with epidemiological and clinical results from the literature, which is not an adequate procedure to make confident inferences.

In conclusion, anterior mitral leaflet prolapse contributes to MR and PD. Keeping the limitations of this study in mind, MVP could be considered as a cardiac disease with possible psychiatric consequences, such as panic disorder. Clinicians from other somatic fields and psychiatrists should be aware of the possibility of comorbidity of these two disorders, and investigate the presence of an other, which might be of benefit in treatment course and improving the quality of life. The co-morbidity of MVP and PD needs further clinical investigations, which utilizes echocardiography, molecular cardiology and biochemistry to find if there is a specific biologic marker for the detection of these disorders.

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