

# The prevalence and clinical characteristics of mitral valve prolapse in a large population-based epidemiologic study: the MELEN study

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**Abstract. – OBJECTIVE:** Mitral valve prolapse (MVP) is the most common cardiac valvular abnormality in industrialized countries. Its prevalence has been estimated to be between 2% to 4%. However, some studies found the prevalence of MVP less than 1% which is significantly lower than the prevalence reported in the Framingham Heart Study. The purpose of this study was to determine the prevalence, demographic, clinical and echocardiographic characteristics of MVP in a large population-based epidemiologic study.

**PATIENTS AND METHODS:** The final cohort included 2,228 participants. Data were obtained by a validated questionnaire, physical examination of the cardiovascular system, recording of a resting electrocardiogram, transthoracic echocardiographic examination.

**RESULTS:** The echocardiographic prevalence of MVP was 0.36%. Baseline demographic and clinical characteristics of patients were as follows; 12.5% had hypertension, 37.5% had depression, 12.5% had migraine, 12.5% had diabetes mellitus, 12.5% had diastolic dysfunction, 25% had multinodular goiter, 12.5% had diffuse goiter and 25% had hyperthyroidism. During the follow-up of 36 months no major adverse events occurred in patients with MVP during the follow-up.

**CONCLUSIONS:** This finding suggests that MVP is a benign disorder and the prevalence of MVP is lower than previously studies. There might be a relationship between MVP and goiter, and depression.

*Key Words:*

Epidemiology, Mitral valve prolapse, Prevalence.

## Introduction

Mitral valve prolapse (MVP) is the most common cardiac valvular abnormality in industrial-

ized countries and the leading cause of mitral valve surgery for isolated mitral regurgitation<sup>1,2</sup>. MVP is generally understood to be the systolic displacement of an abnormally thickened, redundant mitral leaflet into the left atrium during systole<sup>3</sup>. Its prevalence has been estimated to be between 2% to 4%<sup>4,5</sup>. However, the studies by Flack et al, and Hepner et al found the prevalence of MVP less than 1%<sup>6,7</sup> which is significantly lower than the prevalence reported in the Framingham Heart Study.

The purpose of this study was to determine the prevalence, demographic, clinical and echocardiographic characteristics of MVP in a large population-based epidemiologic study.

## Materials and Methods

### *Study Design*

This is an observational, cross-sectional study.

### *Study Population*

The rationale, methodology and basic results of the MELEN study were published before<sup>8-12</sup>. The MELEN Study is a prospectively designed survey on the prevalence of cardio metabolic risk factors in Turkish adults. A total of 2,298 subjects with a mean age of 50 (age range 18-92) were interviewed. The study protocol was approved by the Ethics Committee of Duzce University and every subject signed a consent form.

### *Study Protocol*

Demographic and clinical data were obtained by a validated questionnaire, physical examination of the cardiovascular system, sampling of

blood, recording of a resting electrocardiogram, echocardiography and thyroid ultrasonography. The participants who refused echocardiography measurement and had poor image quality and blood sampling were excluded (n = 70).

### **Echocardiography**

An echocardiography machine utilizing 2-5 MHz probe specific for field studies (M Turbo, SonoSite Inc., Bothell, WA, USA) was used. Echocardiographic measurements were performed according to the recommendations of the American Society of Echocardiography<sup>13</sup>. All Doppler echocardiographic and tissue Doppler imaging (TDI) recordings were obtained during normal respiration. The LV ejection fraction was calculated using the biplane Simpson's method. The displacement of each leaflet was measured in the parasternal long-axis view above a line connecting the mid portions of the annular hinge points<sup>14</sup>. The thickness of the mitral valve was measured by M mode recording. Each leaflet was measured, and maximal thickness was used for categorization<sup>15</sup>. A measurement of  $\geq 5$  mm identified a thickened leaflet<sup>15</sup>. The degree of mitral regurgitation was assessed by the method recommended by current guideline<sup>16</sup>.

### **Thyroid Ultrasonography**

Thyroid ultrasonography was performed and interpreted by the same experienced physician, using the same equipment with a 5-12-MHz linear-array transducer (M Turbo, SonoSite Inc., Bothell, WA, USA). Size of the thyroid lobes and characteristics of thyroid parenchyma and nodules were determined. Goiter prevalence was defined according to Gutekunst's criteria. Gutekunst reference values for adults ( $> 18$  cm<sup>3</sup> in women and  $> 25$  cm<sup>3</sup> in men) were used<sup>17</sup>.

### **Definitions**

Hyper and hypothyroidism: A thyroid stimulating hormone (TSH) level of  $< 0.35$   $\mu$ IU/mL was accepted as hyperthyroidism and  $> 4.5$   $\mu$ IU/mL as hypothyroidism. The questionnaire included an extensive list of questions that operationalize DSM-IV criteria<sup>18</sup> for major depression. A minimum of 5 out of 9 possible depression symptoms were required to have occurred during the period of disturbance, and 1 of these must have been depressed mood or anhedonia. Social and/or occupational dysfunction must have also occurred.

### **Follow-up**

The follow-up was done 36 months after the baseline admission via telephone call. The participants were asked whether they had myocardial infarction or stroke during the follow-up period. Mortality data was gathered from first degree relatives. Questions related with in-hospital death with a medical diagnosis, sudden death possibly due to cardiovascular origin and other causes such as accidents. Major adverse event was defined as cardiovascular mortality or myocardial infarction or stroke.

### **Statistical Analysis**

The SPSS statistical software (SPSS for windows 13, Inc., Chicago, IL, USA) was used for all statistical calculations. Continuous variables are given as mean  $\pm$  SD; categorical variables were defined as percentages.

## **Results**

The final cohort included 2,228 participants (1,424 women 804 men, with a mean age of  $49 \pm 15$ ). The echocardiographic prevalence of MVP was 0.36%. The prevalence of MVP was 0.35 % in female (n = 5) and 0.37% in male (n = 3) patients. The mean age of patients with MVP was  $39 \pm 10.7$  (22-53) years. Four patients (50%) had prolapse of the anterior leaflet, 1 (12.5%) had prolapse of the posterior leaflet and 2 (25%) had prolapse of both anterior and posterior leaflet. Only one patient had mild mitral regurgitation on color Doppler echocardiography. One patient had arrhythmia (sinus tachycardia). Baseline demographic and clinical characteristics of patients were as follows; 1 (12.5%) had hypertension, 3 (37.5%) had depression, 1 (12.5%) had migraine, 1 (12.5%) had diabetes mellitus, 1 (12.5%) had diastolic dysfunction, 2 (25%) had multi-nodular goiter, 1 (12.5%) had diffuse goiter and 2 (25%) had hyperthyroidism (Table I).

### **Follow-up**

During the follow-up of 36 months (4485 patient years) in MELEN study, 42 major adverse events occurred. Among them, 16 were death (1 stroke, 2 cancer, 13 cardiac related), 12 were stroke and 14 were myocardial infarction. No major adverse events occurred in 8 patients with MVP during the follow-up.

**Table I.** Demographic and clinical characteristics of patients.

Characteristics	N 1	N 2	N 3	N 4	N 5	N 6	N 7	N 8
Age, years	26	22	39	53	38	47	39	48
Gender (male)	+	-	-	+	-	-	+	-
Prolapse of AML	+	+	+	+	+	+	+	-
Prolapse of PML	-	-	-	-	+	-	+	+
Mild mitral regurgitation	-	-	-	-	-	-	+	-
Hypertension	-	-	-	-	-	+	-	-
Diabetes mellitus	-	-	-	-	-	-	-	+
Multinodular goiter	-	-	-	-	-	+	-	+
Diffuse goiter	-	-	-	+	-	-	-	-
Hyperthyroidism	-	-	-	+	+	-	-	-
Depression	-	-	+	+	-	+	-	-
Deafness	-	-	-	-	-	-	-	+
Migraine	-	-	+	-	-	-	-	-
Sinus tachycardia	-	-	-	-	+	-	-	-

AML: anterior mitral leaflet; N: number of MVP patients; PML: posterior mitral leaflet.

## Discussion

In this study, the echocardiographic prevalence of MVP was 0.36%. During the follow-up no major adverse events occurred in 8 patients with MVP during the follow-up.

Mitral valve prolapse (MVP) is the most common cardiac valvular abnormality in industrialized countries<sup>1,2</sup>. MVP is generally understood to be the systolic displacement of an abnormally thickened, redundant mitral leaflet into the left atrium during systole<sup>3</sup>. Its prevalence has been estimated to be between 2% to 4%<sup>4,5</sup>. However, some studies found the prevalence of MVP less than 1%<sup>6,7</sup> which is significantly lower than the prevalence reported in the Framingham Heart Study. In our study, the echocardiographic prevalence of MVP was 0.36%. The prevalence of MVP was 0.35% in female (n = 5) and 0.37% in male (n = 3) patients. During the past decade, studies with new echocardiographic criteria have shed new light on the prevalence and complications of MVP in the general population<sup>4,19</sup>.

MVP is associated with serious complications including severe MR with or without chordae tendineae rupture, congestive heart failure, infective endocarditis, possible ischemic neurological events, and possible increase in the risk of sudden death<sup>20</sup>. Additionally, arrhythmias have been reported to occur frequently in symptomatic patients with MVP.<sup>21</sup> We previously showed that presence of moderate to severe mitral regurgitation was the only independent predictor of atrial and ventricular arrhythmias in patients with

MVP<sup>22,23</sup>. In this study, only one patient had mild mitral regurgitation on color Doppler echocardiography and one patient had arrhythmia (sinus tachycardia).

An association between MVP and several comorbidities including thyroid disease and anxiety disorders has been suggested in several studies. Increased prevalence of MVP has been reported in patients with Graves disease and chronic lymphocytic thyroiditis, but not in toxic multinodular goiter<sup>24-26</sup>. However, a study done by our group showed no significant relationship between MVP and hyperthyroidism<sup>27</sup>. Vazquez et al<sup>28</sup> showed that prevalence of MVP was 10 fold higher among patients with idiopathic sudden sensorineural hearing loss and they supported the hypothesis that MVP could be one of the etiological factors of idiopathic sudden sensorineural hearing loss. Clinical characteristics of our studies patients were as follows; 12.5% had hypertension, 37.5% had depression, 12.5% had migraine, 12.5% had diabetes mellitus, 12.5% had diastolic dysfunction, 25% had multi-nodular goiter, 12.5% had diffuse goiter and 25% had hyperthyroidism (Table I).

Avierinos et al<sup>28</sup> investigated the rates of mortality and morbidity associated with MVP and contrasted these findings with the earlier report from the Framingham study that described MVP as a "benign" condition in the general population<sup>29,30</sup>. During the follow-up of 36 months (4485 patient years) in MELEN study, no major adverse events occurred in 8 patients with MVP during the follow-up.

These results might apply only to that specific region or ethnical group; they suggest a possible overestimation of the real prevalence of mitral prolapse. Because of the small size of the prolapse group we did not provide any further statistics.

## Conclusions

This finding suggests that MVP is a benign disorder and the prevalence of MVP is lower than previously studies. There might be a relationship between MVP and goiter, and depression.

## Conflict of Interest

The Authors declare that there are no conflicts of interest.

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