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Evaluation of the relationship between Mitral Valve Prolapse (MVP) and Body Mass Index (BMI): a review article

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ABSTRACT

Background: Mitral valve prolapse (MVP) is a valvular heart disease in which the two valve flaps of the mitral valve do not close equally, and part of the mitral valve slips backward loosely into the left atrium during systole. In general, MVP is associated with low body mass index (BMI), as confirmed by several studies. However, the reason for the higher prevalence of MVP in patients with low BMI remains unknown.
Objectives: There is no reliable evidence on the role of genetics or pathophysiological factors in this correlation, and the hypothesis that the size of BMI may lead to MVP or vice versa has not yet been established.
Materials and Methods: In this study, all the articles were evaluated in terms of the inclusion criteria. In total, we found 546 articles via PubMed and Google scholar, out of which 30 articles were mainly focusing on MVP, MVR as the major complication of MVP, and BMI, which were included in this systematic review.
Results: Among these reviewed studies, patients with MVP had a lower BMI score compared to the subjects without MVP. The low and high BMI score were 28±5 kg/m and 31±6 kg/m, respectively.
Conclusions: In the present study, we concluded that low BMI is directly associated with the occurrence of MVP.

Keywords: Mitral Valve Prolapse, Body Mass Index.
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INTRODUCTION

Mitral valve prolapses (MVP), also known as "systolic click murmur syndrome" or "floppy mitral valve syndrome", is the systolic billowing of one or both mitral valve leaflets into the left atrium. In MVP, the two valve flaps of the mitral valve do not close evenly, and part of the mitral valve slips loosely backward into the left atrium. Therefore, the left ventricle squeezes during each heartbeat letting a small amount of blood leak backward through the valve in some cases.[1,2]

In most cases, the cause of MVP remains unknown. The disease could be triggered by genetic factors or conditions where cartilage is not in normal condition. MVP is a common cardiac valve abnormality which affects women more than men, and its prevalence ranges between 2-3% in the population.[2]

Mitral valve regurgitation (MVR), arrhythmias, and endocarditis are among the most frequent complications caused by MVP, and MVR is the most common problem in this regard. The association between MVP and MVR is normally the main cause of mitral valve surgery.[3-5]

MVP is inherited as an autosomal and X-linked dominant inheritance. No specific genes are considered as the underlying cause of MVP; however, three different loci on chromosomes 11, 13 and 16 have been found to be associated with the occurrence of MVP. MVP is prevalent in patients with connective tissue diseases, such as Marfan's syndrome, Ehlers-Danlos syndrome and Osteogenesis imperfecta.[6]

As mentioned above, MVP might lead to several complications, which, in some cases, require surgical intervention. According to a study by Grau et al., the rate of in-hospital mortalities caused by heart valve surgery ranges between 4-8%. The same study also indicated small body mass index (BMI) to be a significant risk factor for in-hospital mortalities among patients undergoing heart valve surgery.[7]

Furthermore, another study indicated the rate of in-hospital mortality rate of double-valve surgery (DVS) to be about 6.9%, which was significantly higher in patients with smaller BMI.[8] Therefore, the evaluation of BMI in patients with MVP and MVR is of paramount importance in order to assess and predict the rate of in-hospital mortalities.

The study of the common features between MVP, MVR and other complications associated with MVP could lead us to a better understanding of the main causes and risk factors of this disorder. Several studies have attempted to determine the association between MVP, its complications and BMI. However, information on the exact causes of this association is scarce.

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MATERIALS AND METHODS

Literature Search Strategy

In the current study, we reviewed the literature in order to find articles related to mitral valve prolapsed, BMI and symptoms affecting MVP and MVR. We searched in databases such as PubMed and Google Scholar using the following keywords: mitral valve prolapses, body mass index, low weight, high weight, mitral valve regurgitation and complication.

Exclusion Criteria

The following studies were excluded from this review: 1) qualitative studies; 2) case reports, 3) editorials and letters 4) expert opinions, and 5) review articles. In addition, all the collected studies were original articles published in English, and studies written in other languages were excluded from the present review.

Search Strategy

In this study, all the articles were evaluated in terms of the inclusion criteria. In total, we found 546 articles via PubMed and Google scholar, out of which 30 articles were mainly focusing on MVP, MVR as the major complication of MVP, and BMI, which were included in this systematic review.

The collected data from these articles were summarized in different subsections, while all the repetitive and irrelevant findings were excluded. The selected articles were evaluated as to determine the association between MVP, MVR, and BMI. Finally, all the articles in their full text were closely reviewed, and the obtained results were gathered based on aims of this article. The screening procedures are shown in the PRISMA flow diagram.

RESULTS AND DISCUSSION

The Evaluation of BMI in patients with MVP

MVP is a frequent clinical condition, which commonly occurs in the general population and there are selective advantages associated with it. Moreover, MVP is associated with mitral MVR and infective endocarditis, which are considered as dangerous disorders.[9] In a study by Theal et al., the prevalence of MVP has been reported to be between 5-15% among the general population.[10]

Atypical chest pain, palpitations, low blood pressure and autonomic nervous system dysfunction are other frequent complications caused by MVP. Furthermore, low body weight is one of the common physical manifestations of MVP.[11,12]

As we know, the mitral valve is located between the left atrium (LA) and left ventricle. According to one study, the patient's age and body weight were independently predictive of the left atrium diameter (P<0.0001).[13]

On the other hand, a study by Aufderheide et al. investigated whether dehydration could induce MVP in normal male individuals, and the results were indicative of a significant decrease in weight were in all the subjects. These findings emphasize the significant association of gender and weight with dehydration-induced MVP.[6]

Another study by Movahed and Hepner was performed using two databases; the primary database included MVP patients, and the secondary consisted of young athletes. In the first database, MVP was observed in 0.6% and 0.2% of the patients with low and high BMI, respectively (P<0.0001) while in the second database, it was observed in 2% and 0.6% of the patients with low and high BMI, respectively (P=0.03).

In total, a significant association was observed between MVP and low BMI, in addition to mitral and tricuspid regurgitation. The mean age of the MVP patients in the aforementioned studies was 49.6±18.2 versus 51.3±18.6 years in subjects without MVP in the first database, while it was 18.9±9.6 versus 17.5±8.2 years in subjects without MVP in the second database.

Consequently, age was not found to be associated with MVP, while according to the further results, MVP was observed to be associated with male gender (P=0.01) and tricuspid regurgitation only in the large database (primary) (P=0.0001). Additionally, there was no association between bicuspid aortic valve disease, low or high BMI or MVP, and aortic regurgitation.[5]

In a study by Devereux et al., the prevalence of MVP was estimated to be 1.6% and 1.8% in male and female patients, respectively. Moreover, the MVP patients had a lower BMI and blood pressure, as well as lower levels of fasting glucose, triglycerides, serum creatinine, and log of the urine albumin/creatinine ratio (ACR) compared to the patients without MVP. Furthermore, MVP was observed to be associated with a higher prevalence of mild and severe mitral regurgitation. In total, the aforementioned study was indicative of low ventricular wall thickness, high mid-wall function, and low urine ACR to be associated with MVP, regardless of the patients' age, gender and BMI.[9] On the other hand, the relationship between MVP and BMI was confirmed in a study by Koren et al., which was indicative of a significant association between MVP and markers of preclinical cardiovascular disease such as higher left ventricular relative wall thickness,[14] which is compatible with the findings of Devereux et al.

In a study by Theal et al., the prevalence of MVP was calculated to be 2.7%, which was higher than the results of Devereux et al., and similar to

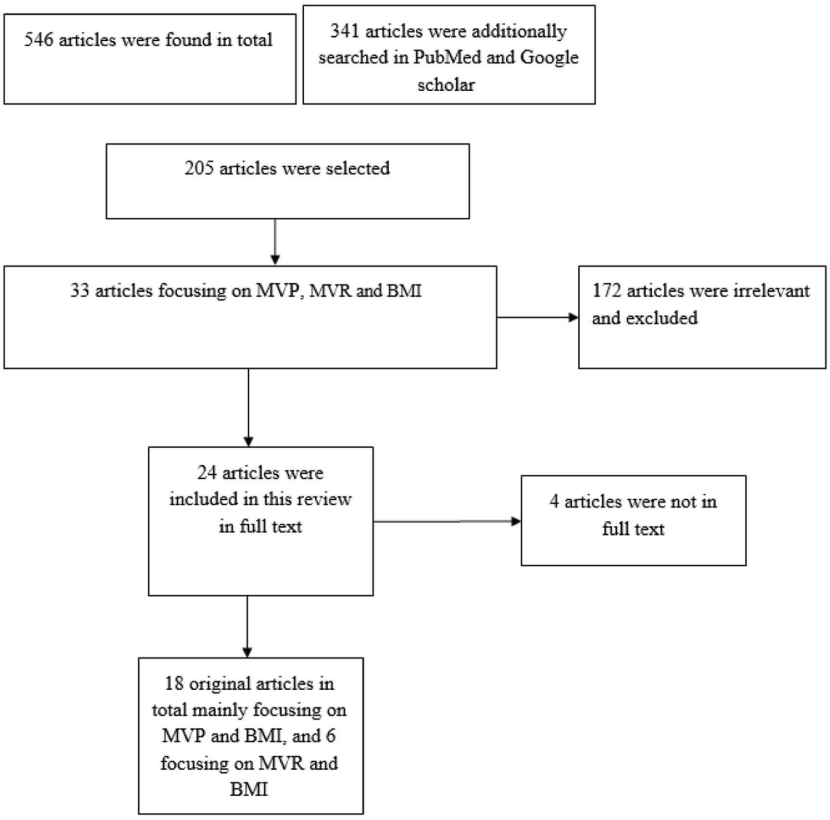

Figure 1 PRISMA Flow Diagram: The Screening Process of Articles in The Current Study

the findings of Devereux et al., the BMI in MVP patients was observed to be lower than the subjects without MVP. However, the mean of the BMI scores in the study of Theal et al. was lower than that of the study of Devereux et al.

According to the findings of Theal et al., a few serious cardiovascular complications were observed to be associated with the occurrence of MVP. Furthermore, MVP was found to be more prevalent among the patients with mitral regurgitation in the general population, and it was also associated with diabetes. In addition, MVP was observed to be associated with blood pressure, which was compatible with the obtained results of Devereux et al.[10] In a study by Oke et al., the mean of the BMI in the patients with clinical features of MVP was similar to the findings of Theal et al.[15]

Similar to the results of Devereux et al. and Theal et al., the echocardiographic findings of Flack et al. indicated that MVP patients had a lower BMI compared to healthy subjects. Moreover, these patients were taller, leaner, and had severe mitral regurgitation than the subjects compared to the normal echocardiograms. However, since the majority of self-reported MVP status were inconsistent with the definite echocardiographic MVP diagnoses, that study considered a constellation of anthropometric, physiological, and psycho-behavioral characteristics to be associated with echocardiographic MVP in young adults.[3]

Another study was conducted in order to determine the extra-valvular findings associated with MVP in patients with Marfan's syndrome, and according to the obtained results, patients with Marfan's syndrome and MVP had a lower BMI compared to those without MVP. In addition, they were younger and presented with systolic blood pressure,[16] which was also confirmed by Devereux et al.[9]

Given the hypothesis that MVP patients tend to have distinctive anthropometric characteristics, Hickey et al evaluated 100 MVP patients identified by echocardiography. Consistent with other studies in this regard, their results indicated that MVP patients had a lower BMI compared to the subjects in the control group. In addition, both male and female patients were observed to have a lower body weight compared to the subjects in the control group. Further results of that study revealed no significant difference between the BMI of male and female patients,[17] which was also confirmed by the findings of Devereux et al., while it was incompatible with the results of Van Der Ham et al.

According to Van Der Ham et al., weight and BMI were significantly lower in female patients compared to the male ones, which might be due to geographical differences. The studies by Hickey et al. and Devereux et al. were conducted in Australia and United State, respectively, while the study of Van Der Ham et al. was performed in South Africa. South Africa is an underdeveloped country with insufficient health care access for women.

In the study of Van Der Ham et al, children presented with MVP were evaluated and compared with the clinical profile of adults, and the observed symptoms of MVP children younger than 13 years of age were not similar with those of the MVP adults, and most of the MVP children were observed to be asymptomatic.[18]

Another study by Friedman et al. claimed that mild dehydration could lead to echocardiographic symptoms of MVP in healthy women more than men, while the BMI of the female subjects was also observed to be significantly lower than the male ones.[19]

A number of studies conducted on the relationship between MVP and BMI are depicted in Table 1.

Among these reviewed studies, patients with MVP had a lower BMI score compared to the subjects without MVP. The low and high BMI score were 28±5 kg/m and 31±6 kg/m, respectively. This was also observed in by Devereux et al., which might be a result of geographical differences, as well as the larger mean weight in American individuals compared to other countries.

Table 1 The relationship between MVP and BMI

Author/Publication/ Year/ (Reference)	Country	Other findings and clinical determinants of MVP	The relationship between BMI and MVP
Movahed and Hepner 2007 (5)	Arizona state (USA)	Significant difference between prolapsed, male gender (P=0.01) and tricuspid regurgitation only in the large database (first) (P=0.0001), and mitral regurgitations in both databases (P=0.007, P=0.001 in the first and second databases, respectively) No association between bicuspid aortic valves, and low or high BMI and MVP with aortic regurgitation No association between age and MVP	In the first database, MVP was observed in 0.6% and 0.2% of patients with low and high BMI, respectively (P< 0.0001) In the second database, MVP was observed in 2% and 0.6% of patients with low and high BMI, respectively (P=0.03). Significant association between MVP and low BMI, in addition to mitral and tricuspid regurgitation
Matos-Souza et al. 2010 (20)	Brazil	Mean age: 37.9 ± 0.3 years Subjects with MVP had a higher AoR diameter (30.4 ± 0.1 vs. 29.5±0.1 cm, P < 0.0001) compared to control group, regardless of confounding variables (P<0.0001)	Mean BMI: 23.7 ±0.1 kg/m
Bitar et al. 2006 (21)	Kuwait	MVP was observed in 37.5% of PSP patients and 7.5% of subjects in control group (P=0.008)	Similar to MVP, BMI was lower in patients with progressive supranuclear palsy (PSP) (P=0.001)
Van Der Ham et al. 2003 (18)	South Africa	Most of the MVP children were asymptomatic Pulse rate was lower in male patients than female ones (P=0.002)	Weight (P=0.005) and BMI (P=0.003) were lower in female MVP patients than male ones
Friedman et al. 1998 (19)	Tucson city (USA)	MVP was more prevalent in female individuals than male ones	BMI was significantly lower in female patients (20.8±0.7 kg/m (2) than male ones (23.7±0.3 kg/m (2) (P< 0.05).
Devereux et al. 2001 (9)	USA	Prevalence of MVP estimated 1.8% in female subjects and 1.6% in male ones MVP patients had lower blood pressure (124.71 ± 19.10 mmHg vs. 130.75 ± 21.10 mmHg, P <0.05) Lower levels of fasting glucose, triglycerides, serum creatinine, and log of urine ACR (P <0.001)	MVP patients had a lower BMI (28±5 kg/m (2) vs. 31±6 kg/m (2), P=0.001) compared to subjects without MVP
Flack et al. 1999 (3)	USA	Subjects with echocardiographic MVP were taller (P<0.01), leaner (P<0.01), and more often with Doppler mitral regurgitation (34.8% vs. 11. 8%, P<0.01) compared to subjects with normal echocardiogram	Subjects with echocardiographic MVP had a lower BMI (22.0 kg/m (2) vs. 26.2 kg/m (2), P <0.01) compared to subjects with normal echocardiogram
Theal et al. 2004 (10)	Canada	MVP was common among patients with mitral regurgitation in general population, associated with lower blood pressure and higher prevalence of diabetes	Low BMI in MVP patients (24.5±5.5 kg/m (2) vs. 26.0±4.3 kg/m (2), P=0.10) compared to subjects without MVP
Pini et al. 1989 (16)	USA	Marfan's syndrome and MVP patients were younger (29 ±12 vs. 38 ± 15 years, P<0.02), had systolic blood pressure (120 ± 20 vs. 133 ± 20 mm Hg, P≤0.05) compared to subjects without MVP	Marfan's syndrome and MVP patients had a lower BMI (19.8 ± 2.7 vs. 23.9 ± 2.9 kg/m^2, P<0.00005) compared to subjects without MVP
Hickey et al. 1985 (17)	Australia	Female MVP patients had a lower body weight compared to control group (P> 0.001), and the same trend was observed in male patients (P=0.14)	Both male and female MVP patients had lower BMI compared to control group (P<0.01 and P<0.001, respectively).
Oke et al. 2000 (15)	Nigeria	Vague chest discomfort and chest pain were observed in 42% and 28% of patients. The most common auscultatory sign and clinical association were apical clicks (8%) and hypertension (12%), respectively.	Mean BMI of patients with clinical features of MVP was 20.8 ± 5.56 kg/m^2

Table 1 (continued)

Author/Publication/ Year/ (Reference)	Country	Other findings and clinical determinants of MVP	The relationship between BMI and MVP
Szombathy et al. 2000 (22)	Taiwan	---	BMI of patients with MVP (24.2 ± 4 vs. 24.5 ± 4, P=0.50).
Koren et al. 1991 (14)	USA	Association between low blood pressure, MVP and indices of preclinical cardiovascular diseases such as higher left ventricular relative wall thickness	Patients with MVP were leaner Risk factors of MVP were influenced by body weight
Savage et al. 1983 (23)	USA	Lower blood pressure and higher prevalence of diabetes were more common in MVP patients	Lower body weight was more common in patients with MVP compared to the control group

In general, MVP is associated with lower BMI, as confirmed by several studies. However, the main cause of the higher prevalence of MVP in patients with lower BMI remains unknown. This might be due to the smaller body size and simultaneously smaller heart of the patients, which predispose the mitral valve to prolapse. There is no reliable evidence of the role of genetic or pathophysiological factors in this association.[3-5]

The Evaluation of BMI in Patients with MVR

In most cases, patients with MVP do not experience any complications; however, this diseases is commonly associated with serious complications, and mitral valve regurgitation (MVR) is the most common problem caused by MVP.[5] MVR is recognized as a cardiac disorder in which the mitral value does not close properly and leads to valve blood leaks back into the left atrium. MVR is the most prevalent form of valvular heart diseases.[24]

Male gender and blood pressure are considered as the two main risk factors of MVR. According to a study by Come et al., mitral and aortic regurgitation are common complications in the patients with MVP.[25] The association between MVP and MVR has been confirmed by several studies.[5,9,10] This association is also the main cause of surgical interventions on the mitral valve.[3-5]

The study of the relationship between MVR and high BMI plays a pivotal role in the recognition of MVP and its contributing factors. On the other hand, evidence suggests the appetite suppressants could also affect the prevalence of MVR resulting in obesity.[26] Several studies have indicated that the high body weight and blood pressure might involve an increasing risk of MVP as well.[27]

The study of common features between MVP, MVR and other complications of MVP could lead to a better understanding of the main causes and risk factors of this disease.

In a study by Jones et al., mitral regurgitation (MR) was observed to be correlated with low BMI. Other results of that study also indicated older age, high systolic blood pressure, high serum creatinine, and high urine ACR to be correlated with the occurrence of MR. Moreover, the severity of MR was observed to be independently associated with low BMI, mitral stenosis, MVP, renal dysfunction, and older age.[26] Unlike MVP,[10] MR is not associated with complications such as dyslipidemia or diabetes.[26]

A number of studies focusing on different variables associated with MVP have revealed a significant relationship between MVP and low BMI. Other variables such as blood pressure, levels of serum creatinine and log of urine ACR were also observed to be lower in patients with MVP compared to those without MVP.[9]

However, low BMI could not always be a proper indicator for MR. In a study by Singh et al., patients with severe MR associated with MVP were compared with individuals with uncomplicated MVP. According to their findings, overweight, higher systolic and diastolic blood pressure and hypertension were observed to be more prevalent in patients with severe MR compared to other subjects. It is also noteworthy that the majority of patients with severe MR were older and male.

Further results of that study indicated that blood pressure and body weight in male patients with MVP were higher compared to female patients. Furthermore, there was a significant correlation between the severity of MR and older age, higher BMI and hypertension. During follow-up, 59% of the patients who underwent mitral valve surgery were more overweight compared to those not requiring any surgical interventions. Moreover, overweight patients with MVP were at a higher risk of severe MR and valve surgery compared to those with normal body weight.[27]

Another study by Singh et al. aimed to evaluate the prevalence of MR, and tricuspid and aortic regurgitation in the general population. According to their findings, the prevalence and severity of MR were equally observed in both genders. The clinical

Table 2 The Relationship between MVR and BMI

Author/ Publication/ Year/ Reference	Country	Other findings and clinical determinants of MR	The relationship between BMI and MR
Singh et al. 1999 (28)	USA	Age (OR: 1.3/9.9 years, 95% CI, 1.2-1.5), Hypertension (OR: 1.6, 95% CI, 1.2-2.0)	BMI (OR: 0.8/4.3 kg/m^2, 95% confidence interval (CI) , 0.7-0.9)
Singh et al. 2000 (27)	USA	Hypertension (P=0.0001) age (P<0.00005), higher systolic (P=0.0003) and diastolic blood pressure (P=0.007) and male gender (P<0.001) were observed more in patients with severe MR Gender-specific cumulative risk for requiring valvular surgery in patients with severe MR	Overweight (P=0.002) was more prevalent in patients with severe MR than other subjects During follow-up, 59% of patients who underwent mitral valve surgery were more overweight than those not requiring surgery
Jones et al. 2001 (26)	New York (USA)	MR was correlated with old age (P<0.001), high systolic blood pressure (P=0.003), high serum creatinine (P<0.001) and high urine ACR (P<0.001). Severity of MR was independently associated with MVP and old age	MR was associated with low BMI (P<0.001) Severity of MR was independently associated with low BMI
Reid et al. 2006 (29)	California (USA)	Combined AR and MR was observed in 0.5% of subjects Mean of left ventricular mass was 155 ± 48 g in patients with MR Increased left atrial size and larger left ventricular internal dimensions	No associations between BMI and the prevalence or severity of MR

determinants of MR were age, hypertension, and BMI of the patients. The odds ratio (OR) of BMI was 0.8/4.3 kg/m^2, and the majority of healthy men and women were observed to have detectable valvular regurgitation.[28]

In a study by Reid et al., Isolated MR by color Doppler was detected in 10.4% of the subjects, which was indicative of no associations between BMI and the prevalence or severity of MR.[29] The relationship between MVR and BMI, as evaluated by some studies, is depicted in Table 2.

CONCLUSION

The hypothesis that BMI might lead to MVP or vice versa has not yet been confirmed. In addition, we cannot consider mutations associated with obesity and the consequences as proper predictors for MVP. It is mainly because the genetic mutations responsible for MVP have not been clearly identified; however, it could be concluded that low BMI is directly associated with the occurrence of MVP.

Limitations of The Study

In the current study, we collected data only from databases such as PubMed and Google scholar. Furthermore, there was lack of access to more recent studies conducted on this subject.

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