Cardiol Young 2007; 17: 172–174

ISSN 1047-9511
doi: 10.1017/S1047951107000108

Original Article

Mitral valvar prolapse is significantly associated with low body mass index in addition to mitral and tricuspid regurgitation

Mohammad-Reza Movahed,[1] Absalom D. Hepner[2]

[1]*University of Arizona Sarver Heart Center, Tucson, Arizona;* [2]*Department of Medicine, Division of Cardiology, University of California, Irvine Medical Center, Orange, California, United States of America*

Abstract *Introduction:* An association between mitral valvar prolapse and low body mass index has been proposed. The goal of this study was to evaluate this suggested association using two independent and large databases. For comparison, we evaluated the association, if any, between bicuspid aortic valve and low body mass index. *Methods:* We retrospectively analyzed, using uni- and multivariate analysis, 1742 echocardiograms that were performed as a part of a cardiac screening of teenage athletes and 24,265 echocardiograms performed between 1984 and 1998 for various clinical indications. *Results:* The first database included a total of 12,926 (53%) female and 11,339 (47%) male patients. The second database included a total of 1172 male (67%) and 570 female (33%) high school athletes. Mitral valvar prolapse was independently associated with low body mass index in addition to mitral regurgitation in both data bases. An index less than 30 occurred in 78 of 13,874 (0.6%) as opposed to 7 of 3236 (0.2%) in the echo data base, p equal to 0.03, odds ratio: 2.4 confidence intervals: 1.1–5.2, and an index less than 20 occurred in 7 of 354 (2%) as opposed to 6 of 944 (0.6%) in the athletic data base, p equal to 0.03, odds ratio: 3.2 confidence intervals: 1.05–9.5. The finding of a bicuspid aortic valve did not have any association with low body mass index. *Conclusion:* In our two independent databases, mitral valvar prolapse was independently associated with low body mass index in addition to mitral and tricuspid regurgitaton. The cause of this association remains unknown.

Keywords: Congenital cardiac disease; valvar regurgitation; echocardiography; athletes; body habit

MITRAL VALVAR PROLAPSE IS A COMMON abnormality, and an association has been reported with low body mass index.[1–5] Previous studies, however, have been limited due to bias in terms of geographic location and selection of populations. The goal of our study was to evaluate the purported association by analyzing the data contained in two independent large databases performed for various clinical reasons or as a screening test. Furthermore, as a control, we evaluated any association between bicuspid aortic valve and body mass index.

Correspondence to: Mohammad-Reza Movahed, MD, PhD, FACC, FACP, FCCP, Associate Professor of Medicine, Director of Coronary Care Unit, University of Arizona Sarver Heart Center, 1501 North Campbell Ave., Tucson, AZ, 85724, United States of America. Tel: +5206266223, +9494000091; E-mail: rmovahed@email.arizona.edu, rmova@aol.com

Accepted for publication 31 May 2006

One database was from our non-invasive laboratory, and was created using echocardiographic studies that were performed at our institution between 1984 and 1998 for various clinical reasons. The second database was collected from echocardiographic examinations of healthy young athletes by a non-profit organization, A Heart for Sports, for routine screening of young athletes using echocardiography for the detection of asymptomatic hypertrophic cardiomyopathy. These two databases contained over 25,000 echocardiograms, representing as far as we are aware the largest study to date for the evaluation of any association between mitral valvar prolapse and body mass index. In addition, the databases were gathered and interpreted completely independently, reducing the possibility of bias. Our study was approved by the institutional review board.

Methods

We retrospectively analyzed two large databases. The first included 24,265 echocardiogram reports from our institution between 1984 and 1998. Echocardiograms were performed for various clinical indications, and had been interpreted by different cardiologists at our institution. The diagnosis of mitral valvar prolapse was based on visual estimation, and the criterions accepted by the reading cardiologist at the time of interpretation. The reading cardiologists were board certified or eligible for cardiovascular disease, and had been trained at least to the second level for interpretation of echocardiograms. Trace regurgitations were not included in the diagnosis of valvar regurgitation. This database, therefore, reflects an unbiased, real-world representation of an echocardiagraphic diagnosis of mitral valvar prolapse by various cardiologists. The second database was a retrospective study of 1742 echocardiograms performed during the screening of a large number of healthy teenage athletes in Southern California. The screenings were organized by "A Heart for Sports". The athletes were recruited through advertisements and by contacting local schools. The echocardiograms were performed by experienced echocardiographers and interpreted by volunteer cardiologists onsite. The echocardiographers and interpreting cardiologist were instructed to report any cardiac abnormalities, including mitral valvar prolapse and bicuspid aortic valve. This database was generated after the year 2000, by which time more strict criterions had been proposed to substantiate the diagnosis of mitral valvar prolapse.[2] The screenings were free of charge, and were sponsored by various donations from the community. The index of body mass was calculated using recorded heights and weights. We evaluated any association between this index and either mitral valvar prolapse or bicuspid aortic valve, in addition to mitral and tricuspid regurgitation. Due to smaller body size of young athletes, we chose the lower cut of point 20 for the index for statistical analysis in order to have comparable control.

Results

The first database included a total of 12,926 (53%) female and 11,339 (47%) male patients. The second database included a total of 1172 male (67%) and 570 female (33%) high school athletes. Both uni- and multivariate analysis showed that mitral valvar prolapse was independently associated with a lower body mass index in both databases. In the larger echo database, using a cutoff of less than 30, mitral valve prolapse was found in 78 of 13,874 (0.6%) of patients with lower body mass index, versus 7 of 3236 (0.2%) of those with a higher index (p less than 0.0001, odds ratio 2.4 confidence intervals: 1.1–5.2). In the database of young athletes, when using a cutoff of less than 20, prolapse was found in 7 of 354 (2%) of patients with lower body mass and 6 of 944 (0.6%) of those with higher body mass index (p equal to 0.03, odds ratio: 3.2 confidence intervals: 1.05–9.5) (see Tables 1 and 2). Bicuspid aortic valve did not have any association with either low or high body mass index. The mean age of patients with prolapsing mitral valves in the larger of the two echocardiographic databases was 49.6 plus or minus 18.2, as opposed to 51.3 plus or minus 18.6 years in those without mitral valvar prolapse. Age was not associated with prolapse, the mean age of athletes with prolapse being 18.9 plus or minus 9.6, as opposed to 17.5 plus or minus 8.2 years in those without prolapse. Furthermore, prolapse was independently associated with significant mitral regurgitations in both databases, with almost identical odds ratios (8.8, with confidence intervals of 1.8–42.6, p equal to 0.007, for the athletes, and 8.3, with confidence intervals of 5.2–13.2, p less than 0.001 for the larger database) (Tables 1 and 2). Prolapse was associated with male gender only in the large database (the odds ratio being 1.8, with confidence intervals: 1.1–2.7, p equal to 0.01) (Tables 1 and 2). Moreover, tricuspid regurgitation was independently associated with mitral valva prolapse in the larger database (the odds ratio being 2.7, with confidence intervals: 1.7–4.3, p less than 0.0001) (Tables 1 and 2). Using multivariate analysis, there was no association between mitral valvar prolapse with aortic regurgitation. Bicuspid aortic valve, as a control, was not associated with lower body mass index nor mitral regurgitation in either database.

Discussion

Using two large independent databases, we found that the presence of mitral valvar prolapse is associated with lower body mass index in addition to mitral and tricuspid regurgitations, confirming previous studies of selected populations.[1–3] One of the strengths of our study is the large size of our samples. We have analysed more patients, over 24,000, than the sum of all of the other studies. Additionally, our findings represent a "real-world" sample, as all examinations were included regardless of the age of the subject, gender, ethnicity or reason for referral, and included random screenings of young healthy athletes. The strikingly similar findings from both of these independent databases are remarkable, and support the validity of our results. The reason for the higher prevalence of mitral valvar prolapse in patients with lower body mass index, however, is not known. It is possible that smaller body size, and a concomitantly

https://doi.org/10.1017/S1047951107000108 Published online by Cambridge University Press

Table 1. Multivariate odds ratios and confidence intervals for the association between mitral valvar prolapse and tricuspid regurgitation, aortic regurgitation, gender and body mass in the larger echocardiographic database.

	Odds ratio	95% Confidence intervals	p
Mitral regurgitation	8.3	5.2–13.2	<0.0001
Tricuspid regurgitation	2.7	1.7–4.3	<0.0001
Body mass index <30	2.4	11–5.2	<0.0001
Male gender	1.8	1.1–2.7	0.01
Aortic regurgitation	1.4	0.97–2.1	0.1

Table 2. Multivariate odds ratios and confidence intervals for the association between mitral valvar prolapse and tricuspid regurgitation, aortic regurgitation, gender and body mass in the athletic screening data base.

	Odds ratio	95% Confidence intervals	p
Mitral regurgitation	8.8	1.8–42.6	0.007
Body mass index < 20	3.2	1.05–9.5	0.03
Tricuspid regurgitation	3.3	0.4–26.2	0.2
Male gender	1.2	0.7–1.03	0.2
Aortic regurgitation	0.9	0.99–1.00	0.8

smaller heart, predispose the mitral valve to prolapse into the left atrium during systole. Rosenberg et al.[6] suggested the association between hypomastia and mitral valvar prolapse as an evidence for possible mesenchymal dysplasia, and a partial explanation for the increased occurrence of prolapse in patients with smaller body size. There are no studies available, however, evaluating detailed genetic or pathophysiological reasons for this association. The association between prolapse and mitral regurgitation has been well established as a one major cause of surgery on the mitral valve in this population.[1–3,7–11] One of the striking findings of our study is the independent association between mitral valvar prolapse and tricuspid regurgitation. Namiki et al.[12] found such an increase incidence of tricuspid regurgitation only in female patients with prolapsing mitral valves. It is possible that the increased prevalence of tricuspid regurgitation in patients with mitral valve prolapse is related to secondary increases in the pulmonary arterial pressure. It is also possible that the apparatus of the tricuspid valve is similarly affected by the same abnormalities of connective tissue that are responsible for the occurrence of mitral valvar prolapse. Unlike ourselves, Come et al.[13] found a higher incidence of mitral regurgitation and aortic regurgitation in patients with mitral valve prolapse.

There are limitations to our study. Our data was extracted from databases, and not from a prospective randomize trial. The echocardiograms were interpreted by different cardiologists. The inter-observer variability, or adherence to established guidelines, therefore, could not be confirmed.

In conclusion, we have shown that lower body mass index is directly associated with the occurrence of mitral valvar prolapse using two independent databases, thus confirming previous findings in a broader populations. The cause of this association is not known at this time, warranting future investigations.

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