Exercise-Induced Regurgitation in Mitral Valve Prolapse: Is It a New Disease?*

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Since the initial description of mitral valve prolapse as billowing mitral leaflets leading to regurgitation (1-4), physicians have had to contend with the problem of its noninvasive diagnosis (5-9). Lack of specificity of diagnostic criteria led to a “disease by definition” frequently diagnosed in otherwise normal subjects (10-22). Recent efforts have attempted to restore prolapse to the category of a disease more consistent with its surgical and pathologic manifestations (23-25) and to identify those patients at greatest risk for its valve-related complications, namely, the need for mitral valve surgery and the development of endocarditis (26-35).

Exercise-induced regurgitation in mitral valve prolapse. The study by Stoddard et al. (36) in the current issue of the Journal begins with the anticipation that exercise-induced regurgitation might be able to predict the development of complications in patients with mitral valve prolapse and no regurgitation at rest. Conceptually, exercise could potentially reveal valves more susceptible to augmented stresses on the prolapsing leaflets and attached papillary muscles (37-39). Nevertheless, although postural and pharmacologic changes in left ventricular volume have been shown to alter the timing of prolapse (40-42), there is virtually no information concerning exercise-induced changes in its associated mitral regurgitation. Bashore et al. (43) found no exercise-induced regurgitation by left/right ventricular stroke-count ratio in 16 patients. The only other studies have used mental stress (44) to increase both click amplitude and the degree of prolapse by two-dimensional echocardiography without evaluating mitral regurgitation (45,46). The concept underlying the current study is therefore highly original.

A new disease? The results initially appear to introduce a new condition or variant affecting 32% of patients without mitral regurgitation at rest, affecting relatively young subjects (mean age 38 years), over two-thirds women, and having an aggressive natural history with complications in >50% of patients, including the need for mitral valve surgery in 10% for regurgitation progressing over a relatively short interval (mean follow-up 3.2 years). Although never previously explored in this manner, such a new natural history stands in contrast to the overall picture of a disease typically progressing over decades, with valve-related complications most frequent in men ≥50 to 60 years of age (27,47-53). Although unstated, these results could lead us to infer that routine exercise testing to identify such high-risk patients is reasonable and indicated.

The same disease? However, several points that emerge from closer analysis of the data suggest that this study may actually be describing the more typical natural history of mitral valve prolapse in a small subset of the subjects studied and that their condition only appears to be more severe because it stands in contrast to a benign natural history in the remainder: 1) If we remove the nonspecific complication of syncope, which was heterogeneous in mechanism and frequently present at the time of patient selection, we are left primarily with three patients who needed mitral valve surgery for New York Heart Association functional class II to III symptoms. These patients fit the classical mold: In contrast to the other patients with exercise-induced regurgitation, they tended to be older (51 ± 16 vs. 36 ± 12 years) and to have larger left atria (56 ± 11 vs. 43 ± 19 cm³), higher mitral valve prolapse scores (7.7 ± 2.3 vs. 5.1 ± 1.9) and a longer duration of follow-up (50 ± 7 vs. 36 ± 13 months; data from the original manuscript). 2) The diagnosis of mitral valve prolapse was based on criteria such as leaflet displacement in the apical four-chamber view, which can lead to the diagnosis in 13% to 21% of subjects who are otherwise apparently normal (10,18-21). This raises the logical possibility, noted by Stoddard et al., that many of the subjects without inducible regurgitation really had structurally normal hearts: In other words, the differences described in their study may be mainly between normality and the disease mitral valve prolapse, not between subgroups of patients with the disease. 3) Forty-two (45%) of the 94 subjects studied were volunteers who responded to an advertisement for patients with mitral valve prolapse, raising at least the theoretic possibility that patients presented for study because of indications leading to concern that they had a more severe form of the illness (10). 4) Mitral valve surgery was ultimately required only in the four patients with severe exercise-induced regurgitation. At this time, therefore, there is no evidence of adverse prognosis associated with mild or moderate induced regurgitation, which constituted 87% of the observed lesions.

Observations. The combination of increased heart rate and the limited frame rate of Doppler color flow mapping tends to decrease apparent jet size (54); this would not detract from the positive findings of regurgitation during exercise. However, uncertainties in assessing both prolapse and the mechanism of regurgitation in these patients make it harder to evaluate the results. As Stoddard et al. note in the Discussion, exercise-induced changes in the degree of mitral valve pro-
Although increased leaflet billowing from a small cavity was lapse, the fundamental lesion, unfortunately could not be easily assessed in these patients. The mechanism of exercise-induced regurgitation therefore remains to be determined. Although increased leaflet billowing from a small cavity was lapse, the fundamental lesion, unfortunately could not be giving increased force to close the apically tented leaflets more providing increased stresses on the prolapsing leaflets (37,38). This behavior would be different from that of the orifice in putting increased stresses on the prolapsing leaflets (37,38).

Redundant leaflets to cover.

the degree of billowing by providing a greater area for the redundant leaflets to cover.

Pressure and prolapse. The fundamental concept remains intriguing that the regurgitant orifice in mitral valve prolapse should be susceptible to increased left ventricular pressure, putting increased stresses on the prolapsing leaflets (37,38). This behavior would be different from that of the orifice in dilated cardiomyopathy and ischemic heart disease, which decreases as left ventricular pressure increases (56–58), providing increased force to close the apically tented leaflets more effectively. This concept of exercise-induced changes in the regurgitant orifice, if confirmed, would have potential implications for therapy (59,60) as well as for exercise recommendations (61) in patients with mitral valve prolapse. However, on the basis of these considerations, and as Stoddard et al. note, “it would be premature to advocate modifications in level of exercise” or in insurance premiums. At this time, it is prudent to reserve judgment until the presence and natural history of exercise-induced regurgitation in mitral valve prolapse have been confirmed and evaluated further.

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References


