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EDITORIAL COMMENT

Valve Regurgitation With LV Dysfunction

How Did We Get There?*

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Valve regurgitations can cause left ventricular (LV) dysfunction. Historically, we came to this conclusion by observing poor results of valvular surgery, whereby patients who presented with post-operative heart failure often had normally functioning prostheses or repairs but a poorly contracting left ventricle. The advent of echocardiography allowed more generalized measurement of LV characteristics and the confirmation that LV dysfunction affects patients with mitral regurgitation (MR) or aortic regurgitation (AR). The consequences of LV dysfunction are serious, causing excess rates of heart failure and death after "successful" surgery. The question of whether surgery itself caused the LV dysfunction was promptly resolved by observing that patients with post-operative LV dysfunction had presented, in the vast majority, with worse LV characteristics before the operation. Subsequently, it was shown that signs of LV dysfunction also had severe outcome implications under medical management, while patients were waiting for the "optimal" timing of surgery. The quest to understand how we got to the point of overt LV dysfunction has been frustrating because of the complex hemodynamics of valve regurgitations, the complexity of assessing true LV contractility, and the limited knowledge of the biochemical and genetic factors that govern a "good" versus a "bad" left ventricle. In this issue of *iJACC*, Kusunose et al. (1) attempt to uncover the link between overload and progression of LV dysfunction in patients with organic MR and AR.

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The study (1) was based on cohorts of patients with AR or MR, with no signs of LV dysfunction at baseline, matched according to age and regurgitant volume and who had at least 1 follow-up evaluation by echocardiography 1 year later (and at subsequent years for some patients). The authors analyzed rates of decline of LV function, measured by using various indices, volumes, ejection fractions, end-systolic stress and pressure/volume ratios, and preload recruitable stroke work, by direct comparison and by complex mixed models to account for those lost to follow-up over time. The results showed that a decline in LV function was observed only in patients with severe regurgitation, defined by a regurgitant volume $\geq$30 ml/m^2, and that rates of decline were similar in MR and AR. Based on their data, the authors suggest that yearly echocardiographic monitoring may be excessive in patients with moderate regurgitation but is reasonable in patients with severe regurgitation.

The contributions of this study (1) to our knowledge of valve regurgitations are important. First, the demonstration that larger volume overload, measured by using the regurgitant volume, is a key determinant of LV function deterioration was not previously proven, although it was perceived as such because patients with moderate regurgitation rarely develop LV dysfunction. This finding adds proof to the existing literature based on quantified valvular regurgitations, that severity of AR (2) and of MR (3) is a major determinant of clinical outcome under medical management and thereby reinforces the mandate to use these quantitative measures in clinical practice. Second, measures of AR and MR severity indexed to body surface area have been used but are not yet recommended. This point is important because analysis of valve regurgitations in women has shown that women have smaller bodies and left ventricles and that absolute measurements nonindexed to their body size are part of underestimating their valve disease severity and of their worse outcome compared with men. Although this key clinical process has to be refined (i.e., determining if body surface area or another measure for indexation should be used), it must be present in the mind of clinicians. Third, the

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equal LV progression of AR and MR is more disputable. It has long been known that LV response to regurgitation is different in MR cases versus AR cases, which have a higher afterload and generally more severe LV enlargement (4). This difference was also demonstrated by the study's contrasting baseline data of AR and MR.

This third point leads to a discussion of the limitations of the study (1). Indeed, age-matching of AR and MR patients who present in clinical practice at different ages (2,3) may bias the similarity to real-life LV dysfunction progression. Furthermore, follow-up was no more than 1 or 2 years in a large proportion of the patients with severe regurgitation, reducing the power to detect a difference. Also, selection of patients on the basis of performance of exercise testing, although no exercise data were analyzed, probably biases the study in contrast to the general pool of AR and MR. Finally, valve regurgitations generally progress with increasing regurgitant volume (5), which was not accounted for in the study. Hence, the conclusion that MR and AR display similar progression of LV dysfunction is tenuous and warrants longer and more comprehensive data in future studies.

What are the take-home messages of this study (1) as integrated with the literature? First, it is reasonable to determine the frequency of follow-up of patients with AR and MR on the basis of quantitative measures of regurgitation. We use a general rule in patients with moderate regurgitation, based on average progression that would bring the patient close to severe regurgitation. New data on regurgitation progression are needed to refine the timing of follow-up. Second, body size should be taken into account in the assessment of regurgitation severity and consequences. New research is necessary to specify how best to achieve body size indexation. Third, quantitative assessment of valve regurgitations is a must, and the present study shows again that it is feasible. Once the numbers are obtained, interpretation in the specific context of the patient and his or her valve disease is essential. Fourth, the occurrence of LV dysfunction is rare and is far from being the single marker of poor outcome. A wide array of such markers of poor outcome under medical management should be gathered in patients with valve regurgitations. In turn, this comprehensive approach will allow the major outcome benefits of early surgery to be acknowledged (6).

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