

EDITORIAL COMMENT

Management Decisions in Aortic Regurgitation

Has the Time for Exercise Assessment Finally Arrived?*

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Aortic regurgitation (AR) is a problem of moderate but increasing frequency. Current data suggest that AR of some degree affects approximately 5% to 10% of the population and increases in frequency and severity with age (1). When severe, AR gradually leads to irreversible left ventricular (LV) dysfunction, heart failure, and death; indeed, sudden death occurs in asymptomatic patients when intrinsic myocardial dysfunction is severe, even if LV ejection fraction (EF)

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is normal (2). Aortic valve replacement (AVR) can reliably minimize or obviate symptoms. However, management of the asymptomatic patient is a problem. In the absence of hypertension (3), no evidence supports “prophylactic” drug therapy for outcome improvement (4). Inferences from observational series have led to consensus guidelines defining indications for AVR (5), but no randomized trials ever have been performed to rigorously evaluate the life-prolonging efficacy of surgery, with resulting uncertainty and controversy. Therefore, current

opinions are based on interpretation of imperfect data. It seems intuitively reasonable that, because myocardial damage from exogenous mechanical overloads is the mediate cause of debility and death in AR, AVR is appropriate before symptoms develop but when irreversible dysfunction is imminent. But how shall we identify this instant? Clearly, identifying specific pathogenic myocardial cellular/molecular processes would be best, but, despite tantalizing information (6,7), we are far from data sufficient for this purpose. Thus, for the best current answer, we must interrogate indices of myocardial structure and function.

As indicated by Tamas et al. (8) in this issue of *JACC*, the clearest predictors often are apparent too late. Subnormal LVEF at rest and moderately abnormal LV systolic, and possibly diastolic, dimensions are relatively reliable predictors of imminent death and debility (5), but we have no evidence that surgery performed when these first become apparent will normalize survival. Rate of progression to these predictors probably is informative (9), but appropriate rate-based risk segregators and their accuracy are not clearly apparent. With the development of radionuclide cineangiography more than 3 decades ago (10), it became practical to employ exercise to unmask potentially important intrinsic myocardial dysfunction that is not apparent at rest. When first applied to AR, this approach frequently revealed otherwise unanticipated abnormalities (11). However, though clearly predictive of outcome (2,9), optimizing the prognostic value of exercise testing in the unoperated patient required combining it with echocardiography to normalize EF for afterload, defining intrinsic contractility (9). Unfortunately, the technical requirements of radionuclide cineangiography have limited its use; other modalities, including echocardiography, are difficult to apply until after exercise is completed, altering hemodynamic loads and resulting functional data. Thus, the poten-

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tial of exercise imaging has not been realized in routine clinical practice. The work of Tamas et al. (8) reminds us of the opportunity that is being lost, demonstrating that myocardial functional reserve generally improves but may not be normalized by AVR even when indexes measured at rest are normal before operation and that the residual deficit can be predicted only from pre-AVR exercise-induced LV performance changes (Δ EF). However, the goal of surgery is not normalization of LV function but prevention of clinical debility and death. Tamas et al. (8) provide no insight into the predictive value of Δ EF for this purpose, because no clinical follow-up is provided for their small series. In addition, their decision to continue medication during testing may have affected their results: the drugs employed have multiple pharmacological effects on the myocardium, some potentially deleterious (4) and possibly altering exercise response. Tamas et al. (8) raise additional questions: If systolic function prognostically is most important, but development of symptoms indicates that AVR has been excessively delayed, why were both resting and Δ EF normal in some symptomatic patients? Are symptoms related to some other, unmeasured, pathophysiological process, or are symptoms, per se, less prognostically important than previously inferred? Also, because the Tamas et al. (8) patients with the most markedly subnormal Δ EF were those with

hypertension, a known risk marker in AR (4), and because hypertension persisted after surgery, the functional reserve deficit in this group may have been more related to afterload than to intrinsic myocardial dysfunction both before and after AVR. Responses to some of these issues are provided by recent preliminary data from our ongoing study of the natural history of AR and its predictors (12): among multiple commonly employed clinical, echocardiographic, and radionuclide cineangiography descriptors, long-term survival after AVR is, indeed, best predicted by Δ EF when it is adjusted for afterload, independent of symptoms—and mortality excess, compared with the age- and sex-matched U.S. census cohort, begins with disturbingly modest contractility deficits. The latter finding highlights the need for continuing evaluation of the adequacy of current consensus indications for surgery.

With recent technical advances, methods other than radionuclide cineangiography may now enable collection of the relevant data. However, as Tamas et al. (8) remind us, the well-established method remains viable and, far more importantly, it is high time to accept the utility of exercise-induced LV functional changes in management decision making for patients with AR.

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