Published by Elsevier Inc.

ISSN 0735-1097/04/$30.00
doi:10.1016/j.jacc.2004.08.012

EDITORIAL COMMENT

Low Flow–Low Gradient Aortic Stenosis

The Pathologist Weighs In*

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Approximately 2% of the population older than 65 years of age has aortic stenosis (AS) (1). Assuming this prevalence, the number of individuals with AS older than 65 years of age in the U.S. in the year 2000 was approximately 700,000 (2). In contemporary clinical practice, the initial diagnosis of AS is often made when a patient with a systolic ejection murmur undergoes echocardiography. Given the ubiquity of echocardiography and the increasing mean age of the population, cardiologists will become increasingly occupied with issues related to the management of the patient with AS in the ensuing decades.

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Doppler echocardiography is the method used in most AS cases to quantitate hemodynamic severity. Invasive hemodynamic measurements are also used to quantitate AS severity, but in many centers, catheterization is reserved for those patients in whom coronary artery disease is suspected, particularly when aortic valve replacement surgery (AVR) is being considered. In this issue of the *Journal*, Roberts and Ko (3) introduce a third, albeit retrospective, method of quantitating AS severity—weighing the excised aortic valve.

PRINCIPAL FINDINGS

These investigators report aortic valve weights in a series of 324 patients who underwent AVR with or without concomitant coronary artery bypass graft surgery. The individuals included in the study were culled from among 580 patients undergoing AVR for AS from 1998 to 2003. The 324 patients who comprised the final study population were selected only if: 1) hemodynamic data were available, and 2) the valve was available to be weighed by Dr. Roberts. This work extends previous observations by the same authors, wherein the weights of aortic valves were tabulated but no hemodynamic data were reported (4).

The principal findings of the paper are that: 1) aortic valve weights were inversely correlated with the number of cusps: trileaflet valves weighed the least, and the heaviest valves were usually bicuspid; 2) there was a positive correlation between the peak pressure gradient obtained at catheterization and valve weight; and 3) the correlation between valve area—estimated by the Gorlin equation—and valve weight was not as close as that between valve gradient and valve weight.

LOW FLOW–LOW GRADIENT AS

In the opinion of the authors, the major importance of their observations is that their data are not consistent with the conventional wisdom concerning "low flow–low gradient" AS (5–7). This term is usually used to describe the condition in which AS coexists with severe left ventricular (LV) systolic dysfunction, usually related to coronary artery disease. A consensus definition of low flow–low gradient AS, however, is lacking. Many require a mean gradient <30 mm Hg and a valve area below 1 cm^2 (6). Roberts and Ko (3) do not give mean gradient data, so it is difficult to compare their data with prior studies.

An inspection of Figures 2 and 3 in the Roberts and Ko study (3) shows that low gradients are commonly seen in patients undergoing AVR for AS: about one-fifth of the patients had a *peak* transvalvular gradient below 30 mm Hg, even when the patients undergoing concomitant coronary artery bypass graft surgery were excluded. It is likely that many more individuals in their study would have a mean gradient below this number. In such patients, especially those with very low ejection fraction, it may be difficult for the clinician to interpret a small (e.g., <1 cm^2) Gorlin formula-derived valve area. Is the calculated effective orifice area small because of true stenosis or because of deficient opening-force generation by the ventricle, or are the data unreliable because of the flow dependence of aortic valve area formulae?

A number of hemodynamic studies have shown that some individuals experience an increase in valve area when flow is augmented with either exercise or dobutamine (5–9). Some of these individuals probably do not have true severe AS (5–8), underscoring the flow dependence of current methods of assessing effective valve orifice area. Roberts and Ko (3) interpret their finding of a higher correlation coefficient between pressure gradient and valve weight than that between valve area and valve weight as evidence of the unreliability of the Gorlin formula. They suggest that true AS is not present unless a significant transvalvular gradient is present.

VALVE WEIGHT: THE COURT OF HIGHEST APPEAL?

Certainly these provocative observations provide a novel insight into the pathophysiology of AS. However, there are some reasons to be cautious in accepting these findings. We would offer no argument to the proposition that the valve gradient and valve weights are direct measurements, and are

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

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likely to be more accurate than a derived valve area. This does not necessarily invalidate the valve area calculation. A number of studies have confirmed a poor outcome in individuals with AS and a low transvalvular gradient: the operative mortality associated with low flow–low gradient AS has been in the range of 33% in several studies (5,7,10,11). Some of these studies have also reported operative confirmation of a severely stenotic aortic valve. Secondly, it is difficult at this time to know whether the valve weight represents "the court of highest appeal" in the assessment of AS severity. We are inclined to trust the principal author on this issue, and, given the rarity of rheumatic disease as a significant cause for AS in the U.S., it seems reasonable to assume that a heavier valve means more calcification and worse stenosis. At this time, however, little literature exists on the weights of excised aortic valves, and no other study has correlated in vivo hemodynamic data with aortic valve weights. It is likely that the current study (3) will stimulate further validation work in this area.

There are also limitations related to the fact that this study is retrospective. As the authors acknowledge, there was a lack of a rigorous hemodynamic standard used for measurements of gradients and valve areas, although it could be argued that errors so encountered would not necessarily be clustered in one anatomic/weight subtype. It is also possible, given the recent attention being paid the importance of prosthesis-patient mismatch (12), that indexation of the valve area for body surface area might have improved the correlation between valve area and valve weight.

Finally, the clinician's rationale regarding the decision to perform AVR cannot be assessed in a retrospective study. Figures 2 and 3 of their study (3) seem to show a slightly higher frequency of coronary artery bypass graft surgery among the patients with a low transvalvular gradient. This suggests the possibility that some of these individuals might have had symptomatic coronary artery disease (and related LV dysfunction) as the more compelling reason for surgery.

IMPORTANCE OF THESE FINDINGS

These limitations notwithstanding, this study represents an important contribution to our understanding of AS. The results emphasize that the AS many of us learned about in medical school is very different from the one we are encountering in contemporary practice. Increasingly this "newer" AS is degenerative (calcification of a trileaflet valve) in contrast to inherently pathological (bicuspid, unicuspid, and other). This is underscored by the fact that 54% of the patients in this study had a trileaflet aortic valve, an even greater percentage than was observed in the 1980s (13). In the current study, more than one-half the patients underwent coronary artery bypass graft surgery at the same time, with many, as we have seen, having a low transvalvular gradient documented at catheterization. Therefore, it is difficult to argue with the possibility, raised by the authors, that this current version of AS might be more affected by the hemodynamic vagaries of the valve area equation or formula.

Secondly, if the importance of valve weights is confirmed by other investigators, it is conceivable that dissemination of Roberts and Ko's (3) results might alter practice patterns, as clinicians might be compelled to check on the valve weights in patients in whom surgery was recommended. It is even possible that the frequency of heavy valves excised at surgery might be used as a parameter to judge the quality of a cardiology/cardiothoracic surgery program.

One might argue that from the patient's perspective, the most important criterion of the appropriateness of an AVR is whether he or she feels better or lives longer following the procedure. The cardiologist can measure end points such as improvement in ejection fraction and LV mass regression, both of which occur after AVR (14). Some patients with low flow–low gradient AS also experience a dramatic increase in ejection fraction after AVR, even in the presence of significant coronary disease (15,16). If future work is stimulated by the findings of Roberts and Ko (3), as we suspect will happen, perhaps the relationship between valve weight and regression of hypertrophy and improvement in ejection fraction will be clarified. Quantitation of symptom improvement, as it relates to valve characteristics, will help us to improve on patient selection for AVR.

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