Another Chapter in the Complex
Vagaries of Aortic Stenosis
Barone-Rochette et al., in this issue of Circulation: Cardiovascular Imaging, have provided us with an elegant study comparing pertinent echocardiographic measurements in patients with aortic stenosis (AS) with cardiac MRI measurements of similar parameters in the same patients. Reassuringly, they found that aortic flow measured by the 2 techniques was in good agreement, that anatomic aortic valve area (AVA) was slightly larger than physiological area as has been predicted in the past, and they shed new light on the patient with low flow, low gradient normal ejection fraction (EF) AS.

There are 3 ways that a patient with a normal EF can have reduced aortic flow: (1) end-diastolic volume is reduced; (2) there is mitral regurgitation; and (3) small nonstatistically significant differences in the components of aortic flow add up to major differences in stroke volume. Thus, a patient with an end-diastolic volume of 120 cc, an EF of 0.63, and no mitral regurgitation has a stroke volume of 75.6 cc, whereas a patient with an end-diastolic volume of 118 cc, an EF of 0.60, and a regurgitant fraction of 0.09 has a forward aortic stroke volume of 64.4 cc, a 15% reduction. Accordingly, patients in the current study with low flow and high gradient seemed to have more mitral regurgitation than other groups because stroke volume determined volumetrically was substantially more than aortic flow.

Patients with low flow and low gradient had a clinically significant but statistically insignificant 10% reduction in end-diastolic volume compared with the high flow groups and they also had the lowest EF of all groups in the study but still normal at 0.60. Of interest is their finding that in this group the mass:volume ratio was not excessively high in contrast to other reports. Thus, reduced stroke volume in the current study was not because of excessive hypertrophy reducing cavity size. Rather, reduced stroke volume was dependent on the factors noted above. Also, the current study did not find evidence of excessive fibrosis in contrast to a previous report. So then what is the left ventricular (LV) pathology of AS patients with low flow, low gradient normal EF aortic stenosis? Answer: it probably is not a single pathology but many.

Capricious Response of the Left Ventricle to Aortic Outflow Obstruction
Aortic stenosis obstructs left ventricular outflow requiring the left ventricle to generate excess pressure to drive blood into the aorta. This pressure overload results in concentric left ventricular hypertrophy (LVH), the major compensatory mechanism for the pressure overload. Unfortunately, LVH is a double-edged sword, providing increased muscle mass to accomplish the increased work of the LV, on one hand, while at the same time resulting in LV pathology responsible in large part for the symptoms (and outcome) of AS.

The onset of symptoms marks a major change in the natural history of AS, presaging sudden death unless the outflow obstruction is corrected by aortic valve replacement. The typical symptoms of AS are angina, syncope, and dyspnea on exertion, symptoms also caused by a variety other cardiac conditions and also noncardiac conditions. Key questions facing the clinician are if symptoms are present can they be attributed to AS (obviously indicating the need for valve replacement) or if the patient is asymptomatic, is outflow obstruction becoming so severe as to indicate that symptom onset is imminent? The answers to these questions would be simple if a given AVA or other measure reliably predicted symptoms in most patients; but this is simply not the case. Each patient responds to the pressure overload in a nearly unique way wherein a similar pressure overload my cause a remarkably different hypertrophic response confounded by different individual responses to similar amounts of LVH.

Some patients, especially older women seem to have excessive LVH, whereas other patients seem to have inadequate LVH to balance the extra load. Some AS ventricles remodel in such a way as to have reduced volume because of excessive wall thickness, whereas others (emphasized in the current study) have reduced volume because of reduced LV radius. Thus, although obstruction to outflow must surely be the cause of LVH, its magnitude and geometric patterns seem almost infinitely modified by the multitude of biological pathways that lead from load to muscle. As such in some patients with low flow, low gradient there may be increased wall thickness and scarring, whereas in others there may be remodeling in such a way that LV radius is reduced. Because response to load is so variable, we might be able to define arbitrarily what we call severe AS but we cannot define critical AS, that valve area that causes enough obstruction...
to produce symptoms or cause asymptomatic sudden death because criticality is probably different in each patient.

In any case it is the heart’s job to deliver cardiac output and irrespective of the pathological mechanism, Herrmann et al.\textsuperscript{16} have found that reduced stroke volume in AS infers a poorer than normal prognosis, irrespective of mechanism. However, understanding the patient with low flow AS is key to understanding the spectrum of the disease.

What Tools Does the Clinician Have to Judge the Severity of Obstruction and How Good Are They?

Defining critical AS in the patient with an 80 mm Hg gradient and syncope is simple and additional measurements are unlikely to be helpful and could even be confusing. But what about the patient with a 30-mm Hg gradient, a valve area of 1.0 cm\(^2\), and vague complaints of dyspnea? How does the clinician decide if aortic valve replacement is indicated?

Valve Area

Valve area has been a key determinant of the magnitude of orifice obstruction because it takes into account the acceleration through the narrowed orifice as a factor of flow. AVA=F/V, where F is flow and V is velocity. In the echo laboratory, V is measured directly, whereas in the cath laboratory using invasively obtained pressure gradient data, V is calculated as \(V=\sqrt{2gh}\), where g is the acceleration because of gravity and h is the mean pressure gradient. AVA takes into account the fact that flow through the orifice varies widely even among normal subjects of the same body size and flow varies even more so in pathological conditions. In his famous text, Carl Wiggers stated in 1945 “The aortic opening must be reduced to less than a quarter of its natural size in experimental animals before systolic discharge, the blood pressure, or the pulse is affected” and this has often been the source of defining AS severity.\textsuperscript{17} Because the normal AVA is \(=3.0\) cm\(^2\), one quarter of that is 0.75 cm\(^2\), a value used by many as critical. The American College of Cardiology/American Heart Association guidelines use an AVA of 1.0 cm\(^2\) to define severe specifically avoiding the word critical.\textsuperscript{18} Although many patients with an AVA of 1.0 cm\(^2\) demonstrate the physiological orifice smaller than the physical anatomic orifice. Thus, planimetered valve areas probably overestimate the actual physiological valve area calculated by either the continuity or the Gorlin equations as noted in the current study.\textsuperscript{1}

The continuity equation \(A_1\times V_1= A_2\times V_2\) correctly assumes that flow on either side of the valve must be equal so that \(A_2= A_1\times V_1/V_2\). This concept that assumes continuity of flow would be an accurate measure of AVA if each parameter could be measured accurately.

However, measurement of the outflow tract area \(A_1\) is fraught, a potential Achilles heel of that method.

Valve Area Index

The concept of needing to correct valve area for the patient’s size and the cardiac output that relates to his/her body mass has to be inherently correct but the method of anthropomorphic correction is controversial and in doubt.\textsuperscript{20} The body is 3-dimensional as is the volume passing through the valve yet we correct for area, not mass or volume. It may be that some correction such as with body surface area is better than no correction at all but it is not clear that aortic valve area index is superior to AVA in predicting outcome in a wide range of body types and weights.

Because of the inaccuracies and uncertainties noted above I am concerned (and sometimes amused) when my own laboratory and many publications report AVA to the second decimal place, implying that we are accurate in assessing AVA to 0.01 cm\(^2\).

Valve Resistance

Aortic valve resistance (gradient/flow) uses the same measurements for its calculation as the Gorlin formula but avoids the need for determining the discharge coefficients. Although this method has received some attention,\textsuperscript{21,22} it is not held in widespread usage.

Peak Jet Velocity

Jet velocity is also used to define severe AS. It has the obvious advantage of being a single observed parameter requiring no further calculations or assumptions. The technique’s drawbacks include measuring error if the interrogating ultrasound beam is not nearly parallel with the blood flow jet and also because jet velocity depends on the magnitude of flow through the valve.\textsuperscript{23} The latter is most problematic in low flow states where jet velocity could seriously underestimate disease severity.

Transvalvular Gradient

When measured properly, transvalvular pressure gradient is a direct measure of part of the pressure overload on the LV. Like jet velocity, it requires no assumptions in its determination but like jet velocity, pressure gradient is also flow dependent.

Tie Breakers

Thus, none of the measures of AS severity are adequate to be a single arbiter of therapy in difficult cases. In the case of the patient with the 30-mm Hg gradient and AVA of 1.0 cm\(^2\)
posed above, additional correlates of altered physiology must be integrated into the management decision. Physical examination often discounted today by inexperienced observers is key because it sets up Bayes Theorem on pretest probability, affecting the accuracy of the other tests that follow. An elevated B-type natriuretic peptide or elevated LV filling pressure helps to establish a cardiac cause for the patient’s dyspnea.\(^{25}\) The presence of LVH confirms that the patient’s LV has responded to a pressure overload and reduced exercise tolerance and a failure of blood pressure to rise with exercise adds additional evidence of the obstructive severity of the patient’s aortic stenosis.\(^{25}\) All of these parameters may be needed to come to a final management decision.

**Conclusions**

The left ventricle when confronted with the pressure overload of aortic stenosis responds by remodeling in a myriad of ways based on the load itself which is then modified by the genetically determined pathways that transduce load into muscle. Sometimes the pattern of LVH is adaptive, many times it is maladaptive. Management of the symptomatic patient with a tight valve and large transvalvular gradient represents one end of this spectrum which is also one of the easiest decisions in cardiology, perform aortic valve replacement, or consign the patient to a poor outcome. However, the vagaries of the hypertrophic process make the patient with low flow, low gradient AS a management decision requiring all the judgment the clinician can muster to enable relative confidence that AS is the cause of the patient’s symptoms. In these cases there is no simple measurement that can determine management or outcome but rather the clinician must use every tool at his disposal to decide whether the patient will benefit from aortic valve replacement.

**Disclosures**

None.

**References**


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