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EDITORIAL COMMENT

Aortic Stenosis Is Still Very Tricky, Especially When it Is Moderate*

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In this issue of the *Journal*, van Gils et al. (1), addressed a difficult issue: managing patients with both moderate aortic stenosis (AS) and left ventricular (LV) dysfunction, a population that has received little scientific attention (2,3). From our time-tested script of its time course, AS remains silent for many years until the narrowing becomes severe and symptoms develop, at which time we should intervene with aortic valve replacement (AVR) (4). According to this model, moderate AS should be a stable "intermediate" group, not yet needing valve replacement. However, myocardial dysfunction reflects hemodynamic distress; so, how does this reconcile with patients whose AS is only "moderate?" As evidence of this distress, the authors found adverse outcomes of all-cause death, AVR, or heart failure hospitalization in 61% of their 305 patients at 4 years; thus, their population was truly neither intermediate nor stable.

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There are several questions that need to be answered when managing each such patient.

IS IT TRULY MODERATE AS?

This question raises the obvious, important issue of how reliable is AS quantitation. The valve guidelines (5) give well-defined ranges that denote moderate AS, and echocardiography methodology for assessment is well standardized. However, many patients have discordant indexes (6); for example, a mean aortic valve gradient that suggests 1 degree of AS and a valve area that diagnoses more stenosis or less. Unfortunately, discrepancies between various criteria are common in valvular heart disease (7), even when the transthoracic echocardiogram is recorded and measured perfectly by experts. It is also unfortunate that many valve disease patients are difficult to image due to body habitus, lung disease, or inability to ideally position them. The most problematic component of assessing valve area is the left ventricular outflow tract (LVOT) diameter. Errors here are compounded because the diameter is squared in the equation. Measuring it becomes more equivocal with upper septal hypertrophy, or when the upper septal endocardium and the basal anterior leaflet are not parallel or not easily visible. Use of a single diameter to calculate cross-sectional area has served us very well since it was validated over 30 years ago (8–11), but it assumes a circular shape of the LVOT that is, instead, often elliptical in shape (12–15). Notably, both circular echocardiography and elliptical methods for calculating aortic valve area correlate well with clinical outcome (16).

The criterion that patients with moderate AS have a valve area between 1.0 and 1.5 cm^2 was designed for the average-sized human. However, the valve orifice of any given size does not have the same effect for a smaller-than-average person compared with a very large person. A valve area that indicates moderate AS for a patient with a body surface area (BSA) of 1.7 m^2, for example, is a severe obstruction for a large person who weighs 300 lbs and has a BSA of 2.6 m^2. The aortic valve area index (AVAI), which corrects for the patient's BSA (17), addresses this issue. In this new paper in the *Journal*, the authors re-evaluated AVAI in their population and found that 33% of their group of "moderate AS" patients actually had an AVAI <0.6 cm^2/m^2, the criterion for severe AS. They

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concluded that some of their patients "might have had severe AS ...." (1). The authors opined that AVAI might overestimate AS severity in obese patients, and a higher percentage (one-half) of their patients with an AVAI <0.6 cm^2/m^2 had a body mass index >30 kg/m^2. Nevertheless, we must accept their population as having moderate, not severe, AS based on the criteria chosen. All of their patients were assessed by 1 of 4 hospitals that are among the best heart centers in the world.

IS THIS AS SYMPTOMATIC?

It is notable that 76% of the patients studied by van Gils et al. (1) were symptomatic, 32% were in New York Heart Association functional class III or IV, and many had required hospitalization for heart failure. Yet, the stenosis in all of them was only moderate.

Aortic stenosis and the symptoms it may cause do not always progress in parallel. Many patients with severe AS are completely asymptomatic (18–20). Also, patients with moderate AS may have symptoms from a separate cause. Lung disease, for example, does not show up in the echocardiographic qualifying data of a multicenter study. Additionally, moderate AS may be well tolerated by a ventricle with normal systolic function but be poorly tolerated by a failing ventricle (2).

IS THE LV DYSFUNCTION CAUSED BY THE AS?

Myocardial dysfunction may result from unrecognized coronary artery disease (CAD), which is common in patients with AS. Unfortunately, cause and effect is difficult to prove in this business. The only potential proof is to fix the AS and see if the LV dysfunction resolves, or at least stops its progression (21). It would be interesting to do follow-up imaging of all AVR survivors in the study by van Gils et al. (1) to see what happens to their LV dysfunction after surgery.

The presence of symptoms moves us toward AVR. Among patients with moderate AS and LV dysfunction, those with heart-related symptoms are different than those who are asymptomatic (22). van Gils et al. (1) found greater symptoms were associated with adverse outcome, as were male sex and higher initial aortic jet velocity. For these complex management decisions, there are many additional questions: Is the AS advancing rapidly? Is there severe calcification, concomitant CAD, aortic regurgitation, or ascending aortic dilation? How old is the patient chronologically and physiologically? Does the patient have additional comorbidities such as subaortic obstruction, vascular disease, renal disease, lung disease, or dementia?

Transthoracic echocardiography is the obvious objective test to define moderate AS and select patients for any investigation of AS, but many other assessments about the effect of AS are important for management decisions. Clinical history and physical examination help stage all clinical assessments (23,24). Dobutamine echocardiography provides a second chance to calculate AVA, both at rest and at a higher flow rate, to clarify low-flow AS (25,26) or to separate "pseudo stenosis" from true AS (27). Exercise echocardiography clarifies symptoms and exercise capacity in AS patients (28). Calculation of LV strain may help decision making (29,30). Computed tomography can be used to diagnose coronary artery disease using gating and contrast (31), define coronary calcium (32), assess aortic valve calcium (33,34), visualize leaflet motion, measure the LVOT with its elliptical shape, and identify thoracic aortic enlargement. Transesophageal echocardiography visualizes aortic valve leaflets to accurately measure valve area and LVOT area with its elliptical shape. Cardiac catheterization defines CAD, which is common in the AS population (35,36), and commonly presents with similar symptoms as AS. If the patient needs bypass surgery, AVR for moderate AS "while we are there" has a survival benefit over coronary artery bypass graft surgery alone (37).

LOADING CONDITIONS

LV function, assessed by any imaging method, is affected by the LV's afterload, which might change with various clinical influences. With greater valvular-arterial impedance (38), LV size might increase, especially in systole, reducing ejection fraction. If the patient has uncontrolled hypertension in addition to AS (39), the total resistance to LV outflow is even higher. Studies that have taken into account the total LV afterload (calculated using valvulo-arterial impedance) have illustrated the potential for uncontrolled hypertension to worsen the clinical presentation compared with that from the AS alone (40). In such patients, it is ideal—although not always possible—to control blood pressure and then reassess the aortic valve, to be more certain what is specifically due to the AS.

In the current era of transcatheter aortic valve replacement (TAVR), we must be even more diligent to fully assess patients with AS. Additional questions abound, including arterial access, LVOT size, annular calcification, risk of paravalvular regurgitation, location of the coronary ostia, and others (41,42). Although early data are encouraging, it is unclear what criteria will allow low-risk patients to qualify