Dobutamine Stress Echocardiography in Patients With Low-Gradient Aortic Stenosis

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In adults with moderate or severe aortic stenosis (AS), valve replacement surgery is recommended when symptoms (ie, angina, syncope, or congestive heart failure) appear. In such patients, valve replacement surgery alleviates symptoms and improves survival, even in those with a depressed left ventricular ejection fraction (LVEF). Although a minority of patients with symptomatic AS have a reduced LVEF, these individuals present challenges in evaluation and management.

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In the patient with AS and a depressed LVEF, the latter may be caused by inadequate compensatory LV hypertrophy (so-called afterload mismatch) in which myocyte function is normal but LVEF is low because of inadequate LV mass. In such an individual, symptomatic status and LVEF improve with valve replacement surgery because the operation eliminates the preexisting excessive LV afterload, thereby restoring the balance between LV myocardial mass and afterload. Alternatively, a depressed LVEF may be caused by a superimposed and separate myocardial disease process such as cardiomyopathy, ischemia, or fibrosis in which myocyte function is abnormal. In these individuals, operative risk is increased, symptomatic status often does not improve, and LVEF remains depressed after valve replacement surgery.

**Low-Gradient AS**

Several previously published studies in subjects with AS and depressed LVEF have attempted to identify variables that may help to differentiate patients with afterload mismatch from those whose depressed LVEF is due to a separate disease process. Carabello and colleagues found that individuals with severe AS, depressed LVEF, and a transvalvular pressure gradient >30 mm Hg were likely to survive valve replacement surgery and to manifest symptomatic improvement postoperatively. In contrast, those with severe AS, depressed LVEF, and a low (<30 mm Hg) transvalvular pressure gradient did not benefit from valve replacement surgery; of 4 such subjects, 3 died perioperatively, and the 1 survivor did not manifest symptomatic improvement. From the outcome of these 4 patients—all of whom underwent valve replacement surgery in the 1970s, when intraoperative cardioprotection was relatively primitive—it seemed imprudent to perform valve replacement surgery in individuals with severe AS and a low transvalvular pressure gradient.

In 1993, Brogan et al reported on 18 patients with severe AS and a low (<30 mm Hg) transvalvular pressure gradient who underwent valve replacement surgery between 1988 and 1992 (at a time when intraoperative cardioprotection had improved compared with the 1970s). Although 6 (33%) died perioperatively, 10 of the 12 survivors noted substantial symptomatic improvement. Subsequently, several reports of even larger numbers of such patients, most of whom underwent valve replacement surgery in the 1990s (when intraoperative cardioprotection had improved further), noted even lower perioperative mortalities (8% to 21%) and symptomatic improvement in most survivors.

In short, although patients with AS and a low transvalvular pressure gradient who undergo valve replacement surgery in the modern era appear to have an increased operative mortality compared with those with a larger gradient, the risk is by no means prohibitive, and successful surgery usually results in symptomatic improvement. Unfortunately, none of the aforementioned studies successfully identified clinical or hemodynamic variables predictive of an adverse operative outcome in this patient population. Accordingly, dobutamine stress echocardiography (DSE) has been proposed as a means of assessing LV contractility and aortic valve area in patients with AS and a low transvalvular pressure gradient to identify those who are likely (or not likely) to benefit from valve replacement surgery.

**DSE in Low-Gradient AS**

The accurate assessment of aortic valve area in patients with a reduced stroke volume is difficult because the calculated valve area is proportional to stroke volume and the constant of the Gorlin equation varies with transvalvular flow. As a result, some patients with AS and a low transvalvular pressure gradient have a reduced valve area because of inadequate stroke volume in the presence of thickened valve leaflets rather than a fixed, anatomic stenosis. Cannon et al described 8 such patients who were identified as having severe AS using the Gorlin equation but only mild AS during inspection of the valve at the time of surgery. These individuals were thought to have “pseudo-AS”; ie, their aortic valve had thickened leaflets, which opened in direct relation to systolic blood flow. If the stroke volume was small, the leaflets opened poorly, resulting in a demonstrable transvalvular pressure gradient and a small calculated valve area. As
the stroke volume increased, the leaflets opened more effectively, resulting in a larger valve area. Subsequently, deFilippi et al. demonstrated that DSE could be used to distinguish individuals with fixed AS from those with pseudo-AS. In patients with fixed AS, dobutamine induced an increase in peak velocity, mean transvalvular pressure gradient, and valve resistance and no change in valve area. In contrast, in those with pseudo-AS, dobutamine caused a considerable increase in valve area (≥0.3 cm²) without a substantial change in peak velocity, mean transvalvular pressure gradient, or valve resistance. Therefore, DSE clearly can help to differentiate patients with fixed low-gradient AS (who will benefit from valve replacement surgery) from those with pseudo-AS (in whom valve replacement surgery is not indicated).

In patients with fixed low-gradient AS, can (and should) DSE be used to determine whether the depressed LVEF is due to LV afterload mismatch or primary LV contractile dysfunction resulting from a separate disease process? In these subjects, would the presence or absence of LV contractile reserve alter management? According to the proponents of DSE, subjects with low-gradient AS who manifest an increase in peak velocity (>0.6 m/s), stroke volume (>20%), or mean transvalvular pressure gradient (>10 mm Hg) with DSE have LV contractile reserve and would benefit from valve replacement surgery. In contrast, the absence of these changes with DSE identifies patients without LV contractile reserve whose operative risk might be prohibitively high and whose symptomatic status would be unlikely to improve after surgery.

In subjects with severe AS and a low transvalvular pressure gradient, does the presence or absence of LV contractile reserve help to predict operative mortality? The answer appears to be “yes.” Several recent studies showed that patients with severe AS, a low transvalvular pressure gradient, and LV contractile reserve by DSE had a perioperative mortality of only 5% to 8%, whereas those without LV contractile reserve had a distinctly higher perioperative mortality (as high as 32%). In the study of Quere et al., published in this issue of Circulation, the operative mortalities for those with and without LV contractile reserve were 6% and 33%, respectively.

In subjects with severe AS and a low transvalvular pressure gradient, does the presence or absence of LV contractile reserve help to predict postoperative symptomatic status, long-term prognosis, and LVEF if the patient survives valve replacement surgery? The answer appears to be “no.” From a previously reported French multicenter trial, Quere et al. identified 66 patients with symptomatic AS, a mean transvalvular pressure gradient ≤40 mm Hg, and an LVEF ≤40% who survived valve replacement surgery and underwent an evaluation of functional status and LVEF postoperatively. Before valve replacement surgery, 89% were New York Heart Association functional class III or IV. LV contractile reserve was present in 46 of patients (70%) and absent in 20 (30%). Compared with those with LV contractile reserve, those without reserve had a similar (1) symptomatic status postoperatively (New York Heart Association functional class I or II in 93% versus 85%, respectively), (2) survival at 2 years (92% versus 90%, respectively), (3) increase in LVEF (19% versus 17%, respectively), and (4) postoperative LVEF (47% versus 48%, respectively) after valve replacement surgery. In short, most patients with severe AS and a low transvalvular pressure gradient manifested a substantial improvement in symptomatic status and LVEF after valve replacement surgery, and these improvements occurred with similar frequency in subjects with and without LV contractile reserve.

**Recommendations for the Evaluation and Management of the Patient With Low-Gradient AS**

In symptomatic patients with severe AS and a low transvalvular pressure gradient, DSE should be used to distinguish fixed from pseudo-AS. The patient with pseudo-AS should not have valve replacement surgery. In the patient with fixed AS and a low transvalvular pressure gradient, DSE can be used to estimate operative mortality, after which the patient should be considered for valve replacement surgery regardless of the DSE results. Although the absence of LV contractile reserve portends an increased operative mortality, the majority of these patients survive valve replacement surgery, and most of the survivors manifest an improvement in symptoms and LVEF. One thing is clear: If such individuals do not undergo valve replacement surgery, their prognosis is abysmal. Therefore, we agree with Quere and colleagues that the absence of LV contractile reserve should not preclude consideration of valve replacement surgery in symptomatic subjects with severe AS and a low transvalvular pressure gradient. Even for these individuals, valve replacement surgery is the treatment of choice.

**Disclosures**

None.

**References**


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