PERSPECTIVE

Heart Failure in Aortic Stenosis — Improving Diagnosis and Treatment

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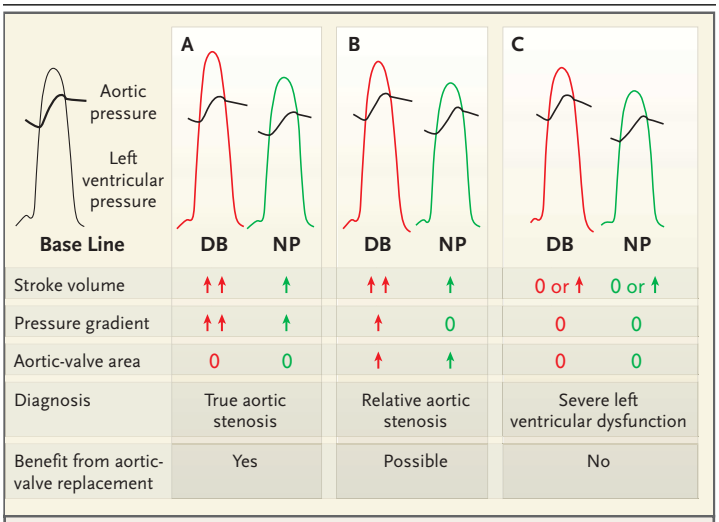
The development of heart failure in patients with aortic stenosis is associated with a high mortality rate — unless aortic-valve replacement is performed. There is an especially high risk of death among patients with aortic stenosis and a decreased ejection fraction. Before surgery is performed in such patients, initial management must include an evaluation of the severity of the stenotic lesion and the functional state of the left ventricle; in addition, the heart failure must be treated and the patient's condition stabilized. It is possible to pursue both of these goals simultaneously with echocardiographic techniques or cardiac catheterization techniques, together with selected pharmacologic interventions.

Proper evaluation and treatment require an understanding of the pathophysiology of heart failure in patients with aortic stenosis. Hypertrophic remodeling provides a compensatory mechanism by which the left ventricle can generate increased systolic pressures while maintaining normal systolic wall stress (afterload) and a normal ejection fraction. If, however, the hypertrophic remodeling is inadequate, systolic wall stress will be increased. There is an inverse relation between wall stress and the ejection fraction: the presence of afterload excess results in a decline in the ejection fraction. Aortic-valve replacement can increase the ejection fraction by correcting the afterload excess created by a truly stenotic valve.

A second mechanism that can produce a depressed ejection fraction in patients with aortic stenosis is a decline in the intrinsic contractility of the myocardium. Aortic-valve replacement may have little or no effect on the ejection fraction if decreased contractility coexists with "relative" aortic stenosis (or "pseudo" aortic stenosis) or if there is a primary cardiomyopathy (see Figure).

In true severe aortic stenosis, the aortic-valve area is constant (or nearly constant) and is proportional to the stroke volume divided by the square root of the pressure gradient. Therefore, if the stroke volume declines, as it does in some patients with aortic stenosis in whom heart failure has developed, there is a proportional decline in the pressure gradient. Under these low-flow conditions, the calculated effective aortic-valve area may indicate the presence of severe aortic stenosis, despite a low transvalvular pressure gradient. A mean pressure gradient that is less than 30 mm Hg in a patient with what appears to be severe aortic stenosis (an aortic-valve area of <1 cm^2) indicates what is referred to as "low-gradient aortic stenosis."

An example of a low pressure gradient in a pa-



Hemodynamic Response to Dobutamine (DB) and Nitroprusside (NP) in Patients with Aortic Stenosis and a Low Transvalvular Pressure Gradient.

The base-line panel shows an example representing a typical patient with low-gradient aortic stenosis. The hemodynamic response to treatment with dobutamine and nitroprusside helps to clarify whether such a patient has true aortic stenosis (Panel A), relative aortic stenosis (Panel B), or severe left ventricular dysfunction (Panel C). A zero denotes no change, a single arrow an increase in the value for the particular variable, and two arrows a large increase in the value.

tient with true severe aortic stenosis is shown in Panel A of the Figure. The low pressure gradient is a consequence of a low stroke volume, which results in large part from increased systolic wall stress (afterload excess). The intravenous administration of dobutamine or nitroprusside produces an increase in the stroke volume and an increase in the systolic pressure gradient across the aortic valve, but there is no change in the calculated aortic-valve area. The absence of a change in the valve area under different hemodynamic conditions indicates the presence of true severe aortic stenosis. Patients with true stenosis have a salutary response to aortic-valve replacement.

However, not all patients with a low pressure gradient and a calculated aortic-valve area of less than 1 cm^2 in fact have true severe aortic stenosis. Some of these patients have aortic-valve disease without severe stenosis (relative aortic stenosis). In these patients, the decreased ejection fraction and low pressure gradient are caused primarily by decreased contractility. It is difficult to differentiate patients with true aortic stenosis from those with relative aortic stenosis, because low-flow states limit the accuracy of the valve-area calculation. It is under these circumstances that selected pharmacologic interventions can be helpful.

An example of a low pressure gradient in a patient with relative aortic stenosis is shown in Panel B of the Figure. Such patients have a variable aortic-valve area that is dependent on the stroke volume. The administration of dobutamine or nitroprusside produces an increase in flow across the aortic valve that is well out of proportion to the increase in the transvalvular pressure gradient; during infusion of nitroprusside, the gradient may even decrease. As a result, the calculated aortic-valve area increases by at least one third, or 0.3 cm^2, and may exceed 1 cm^2. Such a patient has relative aortic stenosis, and the value of aortic-valve replacement in this condition remains in doubt. It is not known whether medical treatment significantly alters the outcome, nor is it clear that the response to dobutamine or nitroprusside is predictive of the subsequent response to medical therapy. Given the rapid advances in surgery and valve design, some patients with relative aortic stenosis may benefit from aortic-valve replacement. In general, however, although optimal treatment remains uncertain, treatment of relative aortic stenosis should be focused on medical therapy.

A third group of patients has little or no response to dobutamine or nitroprusside (Panel C). These patients have severe and generally irreversible left ventricular dysfunction and a poor prognosis. Although these patients have aortic-valve disease, the valve disease itself does not contribute substantially to the left ventricular dysfunction. Medical therapy is directed at the cardiomyopathic failing ventricle.

Once heart failure develops in patients with true aortic stenosis, aortic-valve replacement should be performed as soon as the patient is medically stable. Medical treatment includes the judicious use of diuretics and may, in selected cases, require the use of a positive inotropic agent or a vasodilator. Vasodilators such as nitroprusside have generally been thought to be contraindicated in patients with aortic stenosis because of the danger of hypotension. In this issue of the *Journal*, Khot et al. (pages 1756–1763) report their experience with the therapeutic use of nitroprusside in patients with true aortic stenosis and a decreased ejection fraction. They reasoned that aortic valvular obstruction and increased total vascular resistance act in concert to load the left ventricle and that such a doubly loaded ventricle might benefit from a reduction in systemic resistance. They found a substantial increase in cardiac output (with both high-gradient and low-gradient aortic stenosis), and they concluded that nitroprusside was a safe and effective therapeutic bridge to aortic-valve replacement. However, the patients they studied were highly selected, were invasively monitored, and were being treated in an intensive care unit. There are substantial risks associated with this approach that should limit its wide application. Whether treatment with positive inotropic agents would produce a similar effect with fewer risks remains to be determined.

Patients with aortic stenosis, a depressed ejection fraction, and a low transvalvular pressure gradient continue to pose a management challenge. Judicious use of pharmacologic interventions in an invasive setting has the potential to improve diagnosis and treatment.

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