Aortic Stenosis
Two Steps Forward, One Step Back
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Severe symptomatic aortic stenosis (AS) is a lethal disease, the only effective therapy for which is mechanical relief of the obstruction to outflow, i.e., aortic valve replacement (AVR). Generally held tenets about AS include the following. (1) Patients with preserved systolic function have an excellent outcome after AVR. (2) Patients with reduced ejection fraction (EF) and high afterload also have an excellent response to AVR because AVR reduces afterload and allows ejection performance to return toward normal. (3) Patients with low flow, reduced EF, and pseudo-AS would not benefit from AVR. Pseudo-AS has been defined as a condition in which calculated aortic valve area falsely overestimates the severity of AS when aortic valve area is calculated at low flow. Because in such cases the AS is in fact not severe, it has been reasoned that AVR would not be of benefit. (4) Patients with truly severe AS, low EF, and low gradient benefit from AVR when such patients demonstrate inotropic reserve. (5) Even some low-EF, low-gradient patients without inotropic reserve benefit from AVR. However, 2 studies of AS published in this issue of Circulation raise many interesting questions about our management of patients with AS. These studies help to confirm some of our concepts of managing this disease while raising questions about others.

The study by Hachicha et al seems to confirm at least 1 of the aforementioned concepts: that AS patients with only mild left ventricular (LV) systolic dysfunction have an excellent outcome after AVR. Their group of patients with impaired mid-wall shortening and reduced forward stroke volume, but normal EF, who underwent AVR had a survival rate that was virtually identical to that of the group with better systolic function. Unfortunately, many in the group with LV dysfunction did not undergo AVR. In fact, only 47% of the group with mild LV dysfunction underwent AVR compared with 65% in the group with normal LV function. The question is why this disparity existed. Perhaps the LV dysfunction group failed to manifest symptoms. This seems unlikely because the group had lower cardiac output and greater relative wall thickness, which should have caused higher LV filling pressure and the symptoms of dyspnea. More likely, the treachery of using crude measures of LV function such as EF for evaluating the patient with valvular heart disease together with the reduced gradient caused by reduced valvular flow may have caused the treating physicians to believe the AS in these patients was not severe and that their patients had preserved contractility. It must be noted that normal sarcomere shortening is ~10%. The normal EF of 60% is obtained because sarcomeres thicken as they shorten, displacing blood from the LV cavity. The more sarcomeres that exist in parallel, the more it is possible that thickening can occur. Thus, in the presence of concentric LV hypertrophy, impaired sarcomere shortening can still yield normal EF but not normal mid-wall shortening, as was the case here. Thus, LV dysfunction was masked by a normal EF that possibly caused a false sense of security.

Another interesting aspect of the LV dysfunction group in the study of Hachicha et al was their small heart volumes. Calculated end-systolic volume index was virtually identical in the 2 groups (19 mL/m² normal function group, 20 mL/m² LV dysfunction group), which is curious in light of their increased afterload. Reduced stroke volume and reduced flow were primarily due to decreased end-diastolic volume even though body surface area was identical in the 2 groups. Perhaps the LV dysfunction group had more fibrosis, or genetic variation led to differences in remodeling in response to AS. In either case, the study by Hachicha et al should heighten our awareness that this group of patients exists and that their outcome treated medically is poor, while at the same time we should be reassured that such patients do well after AVR.

The excellent article by Bergler-Klein and colleagues is exciting and at the same time provocative. This study addressed the most problematic group of AS patients, those with low-gradient and low EF. They reported on 69 such patients who underwent inotropic challenge. Patients with aortic valve area of <1.0 cm² at a normal projected flow rate were considered to have true AS, and those with larger aortic valve area were considered to have pseudo-AS. The authors then related outcome to B-type natriuretic peptide (BNP). Their study included 29 patients with true AS and 40 patients with pseudo-AS. A BNP of >550 pg/mL portended a poor outcome for both groups, with only 47% of such patients surviving for 1 year compared with 97% survival in patients with lower BNP values. It was amazing that neither the status of true AS versus pseudo-AS nor medical versus surgical therapy affected outcome. Four of 4 true AS patients (100%) treated medically and 8 of 8 true AS patients (100%) treated with AVR with BNP <550 pg/mL survived. Remarkably, 17
of 19 pseudo-AS patients (89%) treated medically and 4 of 5 (80%) treated surgically survived when BNP was <550 pg/mL. In contradistinction, only 3 of 5 true AS patients (60%) survived with medical therapy versus 6 of 12 (50%) who survived with AVR when BNP was >550 pg/mL. Seven of 12 pseudo-AS patients (58%) survived with medical therapy versus 2 of 4 (50%) who survived with AVR with BNP >550 pg/mL.

The authors were very careful to caution against overinterpretation of data from such small groups, and, admittedly, my analysis fails to heed that caution. Nonetheless, there does not even seem to be a trend toward the concept that true AS patients treated with AVR should have a better outcome.

What explains these findings? Why didn’t the true AS patients fare better with AVR? Obviously, the small group sizes and relatively short follow-up could have obscured important trends. Another explanation could be that patients with high BNPs have such a poor prognosis and such advanced disease that therapy makes little difference. However, it must be noted that of the 33 patients with high BNP, almost half survived, and this proportion is too large to ignore. We obviously must find out more about this group to discern which of these patients would benefit from which therapies. What about the results for pseudo-AS? As a whole, 22 of 31 (71%) treated medically and 6 of 9 (67%) treated with AVR survived. Perhaps surgery may benefit some patients by relieving even modest obstruction, or perhaps our rather arbitrary definition of what constitutes true versus pseudo-AS is not accurate enough to make a useful clinical distinction.

From the articles on AS presented in this week’s issue of Circulation, it seems likely that patients with severe AS, mild LV dysfunction, and reduced flow may be overlooked, an unfortunate occurrence because such patients seem to have excellent outcome with AVR. It also seems that AS patients with a low gradient and reduced EF who have high BNPs have a greatly reduced prognosis. The current data place in doubt which of these low-EF, low-gradient patients will benefit from AVR and also whether our current concept of what constitutes true AS versus pseudo-AS is helpful in clinical decision making. We must reconcile previous data that indicate that patients with far-advanced AS who have low gradient and low EF and inotropic reserve (but in whom BNP was unknown) have an excellent outcome with AVR. With these new data that suggest that high BNP portends a poor prognosis regardless of other factors thought to be important. Only a large randomized trial or registry can help to solve these issues. Until then, it seems appropriate to use BNP as a factor but certainly not the only factor in deciding how to manage this very difficult group of patients. Indeed, several patients with low EF, low gradient, and high BNP will still have a good outcome. Now we must define which of these patients will benefit from which therapy.

Disclosures

None.

References


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