S
evere symptomatic aortic stenosis (AS) is a lethal
disease, the only effective therapy for which is me-
chanical relief of the obstruction to outflow, ie, aortic
valve replacement (AVR). Generally held tenets about AS
include the following. (1) Patients with preserved systolic
function have an excellent outcome after AVR.1 (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.2,3 (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.4,5 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.6 (5) Even some low-EF, low-
gradient patients without inotropic reserve benefit from
AVR.7 However, 2 studies of AS published in this issue of
Circulation raise many interesting questions about our man-
agement of patients with AS.8,9 These studies help to confirm
some of our concepts of managing this disease while raising
questions about others.

The study by Hachicha et al8 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 dysfunc-
tion 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 sarco-
mere shortening is ≈10%. The normal EF of 60% is obtained
because sarcomeres thicken as they shorten, displacing blood
from the LV cavity.10,11 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 dysfunc-
tion 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 al8 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
perhaps 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 colleagues9 is
exciting and at the same time provocative. This study ad-
dressed 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.12 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 values <550 pg/mL survived. Remarkably, 17

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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 obfuscated important trends. Another explanation could be that patients with high BNP 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 BNP 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 not accurate enough to make a useful clinical distinction.

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

Key Word: Editorials ■ aorta ■ stenosis ■ valves ■ ventricular ejection fraction
Aortic Stenosis: Two Steps Forward, One Step Back
Blase A. Carabello

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