Treatment Options in Severe Aortic Stenosis

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Case presentation: An 80-year-old woman is referred for cardiovascular evaluation because of a systolic murmur. She denies symptoms of angina, syncope, or heart failure. The physical examination and echocardiogram are consistent with severe aortic stenosis (AS). What further evaluation is indicated?

Aortic stenosis is becoming more frequent as the average age of the population increases; it affects up to 5% of the elderly population.1 The diagnosis of severe AS is most easily defined by Doppler echocardiography with maximum aortic jet velocity >4.0 m/s, mean transvalvular pressure gradient >40 mm Hg, and continuity equation valve area <1.0 cm² or valve area index <0.6 cm² (Figure 1).2 However, when cardiac output is low, a lower transvalvular gradient and jet velocity may be present. Echocardiography is also used in patients with AS to assess left ventricular hypertrophy, size, and function; left atrial size, and the presence of pulmonary hypertension or other associated valvular disease. Nevertheless, the decision to proceed with aortic valve replacement (AVR) is usually based on the presence of symptoms. So, if this patient really is asymptomatic, the echocardiographic criteria for severe AS would not automatically result in a cardiac surgery referral.3–5

The 1%/y risk of sudden death in asymptomatic patients with AS is not higher than that of historical controls without AS.5 However, because patients may deny or fail to recognize symptoms or avoid them by decreasing physical activity, exercise testing can be useful in asymptomatic patients to confirm that the patient really is symptom free. Exercise-induced symptoms, ventricular tachycardia, or hypotension predict a short symptom-free survival and an increased mortality risk.6,7

Asymptomatic patients with severe AS not referred for AVR should be monitored frequently for change in exercise tolerance, exertional chest discomfort, dyspnea, lightheadedness, or syncope. An annual echocardiogram should be performed to evaluate disease progression in patients with severe AS. The higher the maximum aortic jet velocity, the more likely they are to require AVR within 5 years.3,8 An annual increase in aortic jet velocity >0.3 m·second⁻¹·year⁻¹ or a decrease in valve area >0.1 cm²/y indicates rapid hemodynamic progression. Concomitant coronary artery disease or moderate/severe aortic valve calcification are associated with rapid hemodynamic progression.4 Conditions in which early AVR may be warranted in the absence of symptoms, include very severe AS (maximum jet velocity >5.0 m/s, mean gradient >60 mm Hg, or aortic valve area <0.6 cm²), left ventricular ejection fraction (LVEF) < 0.50, abnormal exercise test result, markedly calcified aortic valve, rapid progression of AS by Doppler criteria, or expected delays in the diagnosis or treatment of disease progression.2 Clinical judgment is particularly required in the elderly to balance the risk of waiting for disease progression and operating when the patient is older versus operating earlier when surgical risk may be lower.

Medical treatment options are limited. Systemic arterial hypertension should be treated cautiously and hypotension avoided. Routine endocarditis antibiotic prophylaxis is no longer recommended. Although the active valvular disease process is characterized by lipid accumulation, inflammation, and calcification, statin therapy does not reduce disease progression in patients with severe AS.9

Case Presentation, Continued

Two years later, the patient was hospitalized in the cardiac care unit with
pulmonary edema. Echocardiography demonstrated severe AS, moderate mitral regurgitation, and a moderately reduced LVEF. Aggressive attempts at diuresis did not normalize her volume status, and renal function declined.

**Inoperable Aortic Stenosis**

Some patients are inoperable because of clinical status or comorbidities. Balloon aortic valvuloplasty (BAV) through a retrograde transfemoral approach can be used as a bridge to AVR or transcatheter aortic valve implantation in unstable patients with high surgical risk to allow for improvement in LVEF, severe mitral regurgitation, pulmonary hypertension, and clinical status. It more commonly is used for palliation for patients in whom AVR cannot be performed because of comorbid conditions. Contraindications include moderate or severe aortic regurgitation, severe peripheral artery disease, and futility. Balloon inflation stretches the annulus, separates fused commissures, and creates microfractures in calcified nodules. However, the procedure results in incomplete relief of outflow obstruction (increase in valve area by 0.4 cm², halving of gradient). The small hemodynamic benefit only lasts months because of early recoil, restenosis, and the failure to alter leaflet pathology. Procedural advances include lower-profile balloon catheters, avoidance of double balloon inflations, balloon sizing based on aortic annular diameter determined by echocardiography, rapid ventricular pacing for more precise balloon positioning, and percutaneous suture arterial closure. Complications occur in 15% to 20% of cases and include aortic regurgitation, stroke, and vascular injury requiring intervention. Procedural mortality is 1% to 2%. Long-term survival is not changed by BAV and is ∼50% at 1 year, 35% at 2 years, and 20% at 3 years.

**Case Presentation, Continued**

Balloon aortic valvuloplasty was performed successfully, renal function normalized, and the patient subsequently became euvolemic with further therapy. After a short stay in a rehabilitation facility, she was discharged home and returned 1 month later to the cardiac surgery clinic for evaluation.

**Surgical Candidates, Normal Risk**

Symptomatic AS is a fatal disease if left uncorrected. Annual mortality in patients with severe AS and symptoms is 25%, and average survival is only 2 to 3 years, so the decision to refer patients for AVR is simple once they become symptomatic. Aortic valve replacement reduces symptoms and improves survival in patients who are not at high risk for perioperative morbidity or mortality. Because of the risk of sudden death, AVR should be performed promptly after the onset of symptoms. Age is not a contraindication for surgery, but comorbid disease may make surgical risk unacceptable.

Surgical risk can be estimated by online risk calculators from the Society of Thoracic Surgeons (http://www.sts.org/quality-research-patient-safety/quality/risk-calculator-and-models/risk-calculator) or the European System for Cardiac Operative Risk Evaluation (EuroSCORE; http://www.euroscore.org). The STS score tends to underestimate risk for AVR, whereas the logistic EuroSCORE overestimates risk for isolated valve surgery. Important comorbidities not captured include an extensively calcified (porcelain) aorta, oxygen-dependent respiratory insufficiency, cirrhosis, history of chest wall radiation or deformity, immobility, dementia, and frailty; these will need to be included in the calculation when an AVR risk score is eventually developed. From 1994 to 1999, average in-hospital mortality for AVR in patients >65 years of age was 8.8% (13.0% in lowest-volume hospitals and 6.0% in highest-volume hospitals). Recent data from the STS database showed an overall in-hospital mortality rate of 2.6% and stroke rate of 1.3% for isolated AVR in 2006, reflecting important advances in patient selection and surgical and perioperative treatment. Other complications included myocardial infarction, bleeding, infection, atrial fibrillation, atrioventricular heart block, and acute kidney injury. Risks increase with advanced age, female sex, LVEF <30%, congestive heart failure, and associated coronary artery disease.

Surgical options for AS include AVR with a mechanical or biopro-
thetic (heterograft) valve, AVR with an allograft (homograft) valve, pulmonic valve autotransplantation (Ross operation), aortic valve repair, and left ventricle–to–descending aorta shunt (Figure 2). Mechanical AVR designs include ball-and-cage valves, single tilting-disc prostheses, and bileaflet prostheses.\textsuperscript{21} Bioprosthetic AVR can be stented or stentless and are reasonable in patients who want to avoid the risks and inconvenience of anticoagulation. Bioprosthetic valve durability is improving but may not be as good as a mechanical valve. Prosthetic valve complications include structural deterioration, symptomatic valve prosthesis–patient mismatch, thrombosis, embolism, bleeding complications from anticoagulation, endocarditis, tissue ingrowth, and hemolysis from periprosthetic aortic regurgitation.

Surgical Candidates Not Referred for AVR

One third of patients with symptomatic AS not referred for AVR have acceptable surgical risk on the basis of objective measures.\textsuperscript{22–23} This represents a major gap between guideline-recommended therapy and clinical practice.\textsuperscript{2} Most of these patients do not receive the benefit of a surgical opinion or a risk score calculation. Advanced age and left ventricular dysfunction appear to be overstressed by primary care physicians and general cardiologists compared with comorbidities in subjective clinical decision making. It is increasingly recognized that a multidisciplinary evaluation by a heart team that includes interventional cardiology, cardiac surgery, anesthesiology, and imaging specialists will improve clinical decision making.

Case Presentation, Continued

The cardiac surgeon reviewed her history, performed a physical examination, examined her test results, and explained the risks and benefits of AVR. Subsequent testing revealed a porcelain aorta and a STS risk score of 15%.

Surgical Candidates, High Risk

Patients may be refused for AVR because of high surgical risk (STS score >10% or logistic EuroSCORE >20%) or coexisting noncardiac conditions that predict poor survival potential. Transcatheter valve implantation is intended for symptomatic patients with severe calcific AS requiring AVR who are at high risk for open heart surgery because of comorbid conditions and for patients who are inoperable. The Edwards SAPIEN valve system (Edwards Lifesciences Inc, Irvine, CA) is a trileaflet bovine pericardial valve mounted on a balloon-expandable stainless steel stent (Figure 3A). The second generation Edwards Sapien XT valve is mounted on a cobalt chromium stent frame. The CoreValve system (Medtronic, Minneapolis, MN) is a trileaflet porcine pericardial valve mounted in a self-expanding nitinol stent (Figure 3B). The devices are usually implanted by a transfemoral retrograde approach; the alternative is a transapical approach for the SAPIEN valve and a subclavian approach for the CoreValve. The devices are not approved for use in the United States but have been commercially available in Europe since 2007.
Exclusion criteria include bicuspid or noncalcified aortic valve, peripheral vascular or aorta disease, coronary artery disease requiring revascularization, severe chronic kidney disease, severe left ventricular hypertrophy, LVEF <20%, severe mitral regurgitation, or significant neurological disease. Procedural success rates are >90%. On average, the aortic valve gradient decreases from ∼45 to 10 mm Hg, and the aortic valve area increases from 0.7 cm² to 1.7 cm². In the Placement of Aortic Transcatheter Valves (PARTNER) trial, 1-year mortality in inoperable patients compared with standard therapy (BAV in 84%) was reduced from 50.7% to 30.7%. Procedural complications include death (2% to 5%), stroke (2% to 5%), acute kidney injury (1% to 2%), coronary occlusion (0.6%), major bleeding (15%), vascular access site complications (10% to 15%), need for permanent pacemaker (5% to 15%), significant perivalvular leak (10%), valve embolization (0.3%), and protracted hospitalization. Thirty-day mortality is 6% to 10%, and 1-year mortality is 20% to 30%. Long-term outcomes reflect patient risk rather than procedural risk. Results will improve with better operator experience, improved devices, refined patient selection, and inclusion of lower-risk patients.

Future technical developments will include reduced device profile; better ways of measuring anatomic valve, aortic root, and peripheral artery dimensions; completely repositionable and retrievable devices; better percutaneous closure systems; and improved device durability. Cerebral protection devices delivered through the radial artery are in development. More observational studies will be needed to improve patient selection and assess safety and durability. The potential of percutaneous valve-in-valve replacement may expand the use of bioprosthetic valves in younger patients.

Conclusion
Severe AS is a fatal disease if left uncorrected. Balloon aortic valvuloplasty can be used as a bridge to therapy in unstable patients or for palliation when valve replacement is not possible. Surgical AVR is the treatment of choice. Transcatheter valve implantation is an alternative for selected high-risk surgical or inoperable patients but is available in the United States only through clinical trials.

Case Presentation, Conclusion
The patient was felt to be a candidate for transcatheter aortic valve implantation and was offered participation in a randomized, clinical trial at another medical center developing a structural heart disease program. She elected to travel to a high-volume experienced European center for further treatment.

Disclosures
None.

References
17. Thourani VH, Myung R, Kilgo P, Thompson K, Puskas JD, Lattouf OM, Cooper WA,


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Circulation. 2011;124:355-359
doi: 10.1161/CIRCULATIONAHA.110.974204
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2011 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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