Calcific Aortic Valve Disease: New Concepts

Catherine M. Otto, MD

Our understanding of calcific aortic stenosis has changed dramatically during the past 3 decades, with the concept of a "mechanical" disease of aging now replaced by the concept of an active disease process at the tissue level that may be amenable to medical therapy. The ability of echocardiography to provide early diagnosis and an accurate measurement of disease severity has increased our knowledge of the natural history of this disease process and allows us to follow individual patients over time, long before valve replacement is needed. We now recognize that even mild symptoms are an indication for valve replacement when severe obstruction is present. This review discusses the optimal approach to measurement of disease severity, the presymptomatic disease course, and the underlying causes of calcific valve disease, followed by a summary of clinical trials of medical therapy and the current indications and choices for valve replacement.

Semin Thoracic Surg 22:276-284 © 2010 Elsevier Inc. All rights reserved.

Keywords: aortic stenosis, valve replacement, natural history, bicuspid aortic valve

Aortic valve stenosis (aortic stenosis [AS]) is the most common indication for valve replacement in the United States, and the prevalence of this disease is likely to increase with the aging of our population. In adults with symptomatic severe valvular obstruction, the only effective treatment is replacement of the calcified valve with a prosthetic valve. However, severe stenosis is the end-stage of a disease spectrum ranging from minor focal leaflet thickening with normal valve function, termed aortic sclerosis, to severe calcification and increased stiffness of the leaflets resulting in significant obstruction to left ventricular (LV) outflow.[1]

In the past, most adults with AS were not diagnosed until late in the disease course—typically at symptom onset with severe valve obstruction—so the time interval between diagnosis and valve replacement was quite short. Now, nearly all patients are diagnosed much earlier in the disease course, most often because a systolic murmur is noted in an asymptomatic patient or because echocardiography is requested for other reasons. The ability to detect early disease and follow each patient prospectively as valve obstruction gradually worsens has improved patient outcomes by ensuring intervention right at symptom onset, before clinical deterioration occurs. However, early diagnosis has also introduced the clinical dilemma of defining the optimal timing of intervention relative to disease severity in asymptomatic patients.

Division of Cardiology, University of Washington, Seattle, Washington.

Address reprint requests to Catherine M. Otto, MD, J. Ward Kennedy-Hamilton Endowed Chair in Cardiology, Professor of Medicine, Director, Cardiology Fellowship Programs, Division of Cardiology, Box 356422, University of Washington, Seattle, WA 98195. E-mail: cmotto@u.washington.edu

MEASUREMENT OF DISEASE SEVERITY

Measurement of the severity of AS is clinically important for 3 reasons. First, the severity of obstruction provides critical data for decision making about timing of valve replacement. Second, quantitative measures allow us to follow and predict disease progression in individual patients. Third, and most importantly, measurement of stenosis severity helps ensure that valve obstruction is the cause of the patient's symptoms, signifying that valve replacement will relieve symptoms and improve long-term outcome.[2]

Cause of Aortic Stenosis

Echocardiography allows noninvasive detection of aortic valve disease, determination of the cause of valve dysfunction and accurate quantitation of disease severity. Calcific AS is seen both in patients with congenital bicuspid aortic valve disease and in those with an anatomically normal trileaflet aortic valve. Early in the disease course, the number of valve leaflets can be reliability determined by echocardiography. Care is needed to identify the number of leaflets and commissures in the open systolic position because a bicuspid valve with a raphe may be mistaken

doi:10.1053/j.semtcvs.2011.01.009

for a trileaflet valve on a diastolic image. Careful analysis of valve morphology in surgical series shows that more than 50% of aortic valve replacements (AVRs) are for AS attributable to a bicuspid aortic valve. In patients younger than 70 years of age, approximately 60% of stenotic aortic valves are bicuspid but even in those older than 70 years of age, about 40% of patients with severe AS have a congenital bicuspid valve. Rheumatic valve disease also can present with calcified valve leaflets but is distinguished from primary calcific valve disease by the presence of commisural fusion and concurrent mitral valve involvement.

Hemodynamic Severity of Valve Obstruction

The recommended measurements for quantitation of aortic valve hemodynamics are the AS maximum velocity (V_{max} in m/s), the transaortic mean systolic pressure gradient (mean ΔP in mm Hg), and the continuity equation aortic valve area (aortic valve area (AVA) in cm^2).[3]

Aortic maximum velocity is a direct measurement based on continuous-wave Doppler recording of the transaortic flow signal. Aortic V_{max} is the strongest predictor of clinical outcome and should be the primary parameter used in clinical decision making.[4-8] Accurate aortic velocity measurements depend on a parallel intercept angle between the Doppler beam and flow signal which requires careful patient positioning, an experienced sonographer, adequate instrumentation and use of multiple acoustic windows. Note that aortic velocity is best measured on transthoracic, not transesophageal, imaging. The most common error in Doppler evaluation of AS is underestimation of severity attributable to a nonparallel intercept angle between the Doppler beam and aortic jet; a repeat study or alternate approaches should be considered when the Doppler data are discrepant with clinical or physical examination findings. Less frequently, the Doppler velocity may be erroneously overestimated if gain settings are too high or if other intracardiac flow velocities are mistaken for the aortic flow signal.

Mean transaortic gradient is calculated from the aortic velocity signal using the Bernoulli equation which states that the pressure difference across a stenosis is 4 times the velocity squared:

$$\Delta P = 4V^2$$

There is a consistent relationship between Doppler V_{max} and mean ΔP in adults with native AS, so this calculation does not provide additional diagnostic information and is not additive to velocity data on multivariate analysis of predictors of clinical outcome. However, many clinicians are more comfortable with the concept of mean ΔP because of the historical role of cardiac catheterization in evaluation of valvular heart disease.

Aortic valve area is a measure of the degree of leaflet opening in systole and reflects the functional cross sectional area of flow in midsystole. Functional valve area may be slightly less than anatomic orifice size because of fluid dynamic effects, but the functional valve area is the appropriate parameter for clinical decision making. The continuity equation states that volume flow rates are equal just proximal to and in the narrowed aortic valve orifice. Because volume flow rate at any site can be calculated from the cross-sectional area (CSA) of flow times the velocity time integral (VTI) of flow at that site, AVA can be calculated from 2D and Doppler left ventricular outflow tract (LVOT) and AS (AS) measures as:

$$AVA \times VTI_{AS} = CSA_{LVOT} \times VTI_{LVOT} \text{ or}$$

$$AVA = \left(CSA_{LVOT} \times VTI_{LVOT}\right)/VTI_{AS}$$

Continuity equation valve area measurements have been well validated, but data acquisition requires careful attention to technical details in the clinical setting. In particular, LVOT tract diameter measurements are made immediately adjacent and parallel to the aortic valve leaflet insertions in midsystole with imaging to clearly show the endocardial edge of the septum and the leading edge of the anterior mitral leaflet. Small errors in outflow tract diameter measurements lead to large errors in valve area calculations because LVOT radius is squared to obtain a circular cross sectional area. In adults, outflow tract diameter rarely changes over time so that use of the same value facilitates comparison of sequential studies. Careful measurement of LVOT or aortic annulus diameter is especially important in patients being considered for transcatheter aortic valve implantation (TAVI).

Definition of Severe AS

Potential approaches to defining severe AS include valve hemodynamics, the degree of leaflet calcification, the response of the LV to pressure overload, and the presence or absence of clinical symptoms.[9,10] Current guidelines base definitions of AS severity on valve hemodynamics, which provides a useful framework for patient follow-up and clinical decision making (Table 1).[3,11,12] These hemodynamic measures have been validated on the basis of clinical outcomes, with a greater rate of symptom onset and adverse cardiovascular events in adults with severe AS compared with those with mild or moderate stenosis. However, there is marked individual variability in the degree of ob-