Aortic Stenosis: When to Refer for Valve Replacement?

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Editor-in-Chief
JAMA Cardiology

No Relationships to Disclose
Aortic Stenosis

Age >60

All patients 47%  
Men 51%

Roberts and Ko, *Circulation*  
2005;111:920-925

from Otto and Bonow, Valvular Heart Disease  
*Braunwald’s Heart Disease*, 10th ed, 2014
Aortic Stenosis

Age >80

All patients 28%
Men 32%

Roberts and Ko, *Circulation* 2005;111:920-925

from Otto and Bonow, Valvular Heart Disease
*Braunwald’s Heart Disease*, 10th ed, 2014
## Stages of Aortic Stenosis

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|       | C1: Normal LV function  
|       | C2: Depressed LV function |
| D     | Severe, symptomatic valve disease |

BAV, RHD, CAD risk
## Stages of Aortic Stenosis

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| D     | Severe, symptomatic valve disease  
|       | D1: High gradient AS  
|       | D2: Low gradient, LV dysfunction  
|       | D3: Low gradient, normal LV function |

BAV, RHD, CAD risk
Aortic-Valve Stenosis — From Patients at Risk to Severe Valve Obstruction

Catherine M. Otto, M.D., and Bernard Prendergast, D.M.

Aortic Stenosis

By John Ross, Jr., M.D. and Eugene Braunwald, M.D.

The advent of corrective operations for various forms of heart disease has placed increasing emphasis upon the need for accurate information concerning the natural history of patients with potentially correctible lesions. An understanding of the natural course assumes particular importance in the case of aortic stenosis because of the significant incidence of sudden death associated with this disease and the grave prognosis that appears to accompany the onset of certain symptoms, patients with isolated valvular aortic stenosis of rheumatic etiology and patients without a history of rheumatic fever who have isolated calcific aortic stenosis; many of the latter patients are now considered to have developed calcification and stenosis of a congenitally bicuspid valve. The review will focus primarily on the prognostic significance of three major symptoms—angina pectoris, syncope, and symptoms related to left ventricular failure.

...the grave prognosis that appears to accompany the onset of certain symptoms
Aortic Stenosis

By John Ross, Jr., M.D. and Eugene Braunwald, M.D.

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From the Cardiology Branch, National Heart Institute, Bethesda, Maryland.

Supplement V to Circulation, Vol. XXXVI.
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Evaluation of Patients With Severe Symptomatic Aortic Stenosis Who Do Not Undergo Aortic Valve Replacement
The Potential Role of Subjectively Overestimated Operative Risk

David S. Bach, MD; Derrick Siao, MD; Steven E. Girard, MD, PhD; Claire Duvernoy, MD; Benjamin...
Indications for AVR

- Symptomatic patients with severe AS

...if it is likely that the symptoms are cardiac in origin
Aortic Stenosis

Management challenges:

• The asymptomatic patient with severe AS
• Low-flow, low gradient severe AS
• Indications for TAVR
**Aortic Stenosis**

*Management challenges:*

- The asymptomatic patient with severe AS
- Low-flow, low gradient severe AS

Are asymptomatic patients with severe AS *really* asymptomatic?
Aortic stenosis

Indications for valve replacement

Exercise test results:

• Symptoms
  - class I
• Hypotension
  - class IIa

How are *symptoms* determined?
  • Everyone has symptoms on stress test
  • Are the symptoms cardiac in origin?
  • What level of exercise?

How is *hypotension* defined?
  • Less than 20 mmHg increase (?)
Aortic stenosis

Indications for valve replacement

*Exercise test results:*
- Symptoms (class I)
- Hypotension (class IIa)

Should *asymptomatic* patients with severe AS undergo AVR? …when they are *really* asymptomatic?
Vmax: 4.6 m/s
Mean Δ: 52 mmHg
AVA: 0.7 sq cm

Severe AS:
>4.0 m/s
>40 mmHg
<1.0 sq cm
Aortic Stenosis

84 year old man with severe AS

- Watchful waiting? *
- More data (more testing)?
- Aortic valve replacement?

* Wait until he develops symptoms in 5-6 years and then recommend TAVR?
Natural History of Severe Asymptomatic AS

Average hospital mortality: 8.8%
- Low volume centers: 13.0%
- High volume centers: 6.0%

Medicare data

Natural History of Severe Asymptomatic AS


Event-Free Survival (%)

Otto

Rosenhek

Time (years)

Vmax > 4.0 m/s
Average hospital mortality: 8.8%
- Low volume centers: 13.0%
- High volume centers: 6.0%

Medicare data

Natural History of Severe Asymptomatic AS

Vmax > 4.0 m/s

Event-Free Survival (%)

Time (years)

Pellikka et al. *Circulation* 2005;111:3290-2395
Natural History of Severe Asymptomatic AS

Pellikka et al. Circulation 2005;111:3290-2395
Stewart et al. Eur Heart J 2010;31:2216-2222
Average hospital mortality: 8.8%

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Event-Free Survival (%)

Vmax > 4.0 m/s

Average hospital mortality: 8.8%

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Medicare data

![Graph showing event-free survival vs time]

Event-Free Survival (%)

- No or mild calcification
- Moderate or severe calcification

Time (years)

n=128
p<0.001

Average hospital mortality: 8.8%

- Low volume centers: 13.0%
- High volume centers: 6.0%

Medicare data

Event-Free Survival (%)

Natural History of Severe Asymptomatic AS

Rosenhek et al. Circulation 2010;121:151-156

Vmax 4.0 – 5.0 m/s

Vmax 5.0 – 5.5 m/s

Vmax >5.5 m/s

n=198
p<0.001

Time (years)
<table>
<thead>
<tr>
<th>Month</th>
<th>Vmax</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aug 2006</td>
<td>3.7</td>
</tr>
<tr>
<td>Jan 2009</td>
<td>4.0</td>
</tr>
<tr>
<td>Dec 2009</td>
<td>4.1</td>
</tr>
<tr>
<td>Nov 2010</td>
<td>4.4</td>
</tr>
<tr>
<td>Sept 2011</td>
<td>5.2</td>
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Management challenges:

- The asymptomatic patient with severe AS
- Low-flow, low gradient severe AS

What is the risk of death while waiting for symptoms to trigger AVR?
Natural History of Severe Asymptomatic AS

Average hospital mortality: 8.8%  
- Low volume centers: 13.0%  
- High volume centers: 6.0%

Medicare data

Survival (%)

Time (years)

Kang et al. *Circulation* 2010;121:1502-1509
Average hospital mortality: 8.8%

- Low volume centers: 13.0%
- High volume centers: 6.0%

Medicare data

Survival (%)

- Kang et al. *Circulation* 2010;121:1502-1509
- Nistri et al. *Am J Cardiol* 2012;109:718-723
Average hospital mortality: 8.8%
- Low volume centers: 13.0%
- High volume centers: 6.0%

Medicare data

Survival (%)

100
80
60
40
20
0
0 1 2 3 4 5
Time (years)

Natural History of Severe Asymptomatic AS

Kang et al. Circulation 2010;121:1502-1509
Nistri et al. Am J Cardiol 2012;109;718-723
Taniguchi et al. J Am Coll Cardiol 2105;66:2827-2838
Natural History of Severe Asymptomatic AS

Taniguchi et al. J Am Coll Cardiol 2105;66:2827-2838
Natural History of Severe Asymptomatic AS


31% of patients who developed symptoms did not have AVR → 17 deaths

Taniguchi
Aortic stenosis

Indications for valve replacement in asymptomatic patients:

• Very severe AS: Vmax ≥5 m/s

class IIa
Aortic stenosis

Indications for valve replacement in asymptomatic patients:

- Very severe AS: Vmax ≥5 m/s
- Rapid progression and low surgical risk

class IIa

class IIb
Aortic stenosis

The ACC/AHA guidelines have lowered the threshold for surgery in asymptomatic patients with AS

- Severity of AS
- Severity of calcification
- Left ventricular function
- Exercise response
Aortic stenosis

The ACC/AHA guidelines have lowered the threshold for surgery in asymptomatic patients with AS

• Severity of AS
• Severity of calcification
• Left ventricular function
• Exercise response
• BNP?
Aortic stenosis

The ACC/AHA guidelines have lowered the threshold for surgery in asymptomatic patients with AS

- Severity of AS
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- Left ventricular function
- Exercise response
- BNP?
Aortic stenosis

The ACC/AHA guidelines have lowered the threshold for surgery in asymptomatic patients with AS.

...but there needs to be renewed emphasis on the class I indications for surgery in symptomatic patients with severe AS.
Aortic stenosis

Management challenges:

- The asymptomatic patient with severe AS
- Low-flow, low gradient severe AS
- Indications for TAVR
Diastole

Normal Flow
High Gradient
Normal LV Function

Low Flow
Low Gradient
LV Dysfunction

Systole

Low Flow, Low Gradient AS
Indications for valve replacement

Reduced EF:
Dobutamine study showing:
- Vmax >4 m/s or
- Mean Δ >40 mmHg or
- AVA ≤1 sq cm

class IIa
Diastole

- Normal Flow
  - High Gradient
  - Normal LV Function

- Low Flow
  - Low Gradient
  - LV Dysfunction

Systole

- Low Flow
  - Low Gradient
  - Normal LV Function

- Dobutamine echocardiography

- Treat hypertension
- Catheterization
- Valve calcification
- Advanced imaging
- Clinical skillset

from Pibarot and Dumesnil, J Am Coll Cardiol 2012:60:1845-1853
Inconsistent grading of aortic valve stenosis by current guidelines: haemodynamic studies in patients with apparently normal left ventricular function

Jan Minners, Martin Allgeier, Christa Gohlke-Baerwolf, Rolf-Peter Kienzle, Franz-Josef Neumann, Nikolaus Jander

Heart 2010;96:1463–1468
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*Heart* 2010;96:1463–1468
Outcome and Impact of Aortic Valve Replacement in Patients With Preserved LVEF and Low-Gradient Aortic Stenosis

Victor Dayan, MD, PhD,* Gustavo Vignolo, MD,* Julien Magne, PhD,† Marie-Annick Clavel, DVM, PhD,‡ Dania Mohty, MD,† Philippe Pibarot, DVM, PhD†

J Am Coll Cardiol 2015;66:2594-603

Mortality According to Treatment

- Low gradient AS
- High gradient AS

Odds Ratio

AVR Protective

Conservative Management Protective
Valvular Heart Disease

Impact of Aortic Valve Replacement on Symptomatic Patients With Left Ventricular Outflow Gradient and Preserved Left Ventricular Ejection Fraction

Alper Ozkan, MD; Rory Hachamovitch, MD; E. Murat Tuzcu, MD; The Circulation Study Investigators


![Graph showing survival rates](image)
Impact of Aortic Valve Replacement on Symptomatic Patients With Low-Gradient and Preserved Left Ventricular Ejection Fraction

Alper Ozkan, MD; Rory Hach, MD; E. Murat Tuzcu, MD; Tazeh Kardan, MD; Andrew Escaned, MD; M. Ridwan M. Azar, MD; Benjamin B. Young, MD; and the PARTNER Investigators

Circulation 2013;128:622-631

Survival in Low Flow AS with Normal LVEF

from Ozkan et al, Circulation 2013;128:622-631

Low-Gradient, Low-Flow Severe Aortic Stenosis With Preserved Left Ventricular Ejection Fraction

Characteristics, Outcome, and Implications for Surgery

Christophe Tribouilloy, MD, PhD,*† Dan Rusinaru, MD, PhD,*‡ Sylvestre Maréchaux, MD, PhD,§ Anne-Laure Castel, MD,* Nicolas Debray, MD,* Julien Maizel, MD, PhD,† Romuald Montaverri, PharmD, PhD,‡ Said Kamel, PharmD, PhD,† Michel Slama, MD, PhD,† Franck Lévy, MD*†

J Am Coll Cardiol 2015;65:55-66
Valvular Heart Disease

Impact of Aortic Valve Replacement in Symptomatic Patients With Low-Gradient and Preserved Ejection Fraction

Alper Ozkan, MD; Rory Hachamovitch, MD; E. Murat Tuzcu, MD; Thomas L. forearm, MD

Survival in Low Flow AS with Normal LVEF

- AVR: n=123
- Medical: n=137

p<0.05

Survival (percent)

Time (years)

from Ozkan et al, Circulation 2013;128:622-631

Low-Gradient, Low-Flow Aortic Stenosis With Preserved Ventricular Ejection Fraction

Characteristics, Outcome, Follow-up

Christophe Tribouilloy, MD, PhD,* † Dan Rust, BSc; Anne-Laure Castel, MD,* Nicolas Debray, MD; Said Kamel, PharmD, PhD, † Michel Slama, MD; * J Am Coll Cardiol

Survival in Low Flow AS with Normal LVEF

- AVR
- Medical

HR 0.75 (0.14, 4.05)
p=0.74

Survival (percent)

Time (years)

from Tribouilloy et al, J Am Coll Cardiol 2015;65:55-66
Impact of Aortic Valve Replacement vs. Medical Management in Symptomatic Patients With Normal Left Ventricular Ejection Fraction and Low Left Ventricular Systolic Aortic Blood Flow

Alper Ozkan, MD; Rory Hachamovitch, MD; E. Murat Tuzcu, MD; ... 

Survival in Low Flow AS with Normal LVEF

from Ozkan et al, Circulation 2013;128:622-631

Survival in High Gradient AS

from Tribouilloy et al, J Am Coll Cardiol 2015;65:55-66
Low Flow, Low Gradient AS

Indications for valve replacement:

**Normal EF:**
Only if clinical, anatomic, and hemodynamic data support severe AS

class Ila
Aortic stenosis

Management challenges:

• The asymptomatic patient with severe AS
• Low-flow, low gradient severe AS
• Indications for TAVR
Indications for TAVR vs surgical AVR:

- Evaluation by a Heart Team

*class I*
Indications for TAVR vs surgical AVR:

- Evaluation by a Heart Team
- Surgical AVR for patients at low or intermediate risk
Indications for TAVR vs surgical AVR:

- Evaluation by a Heart Team
- Surgical AVR for patients at low or intermediate risk
- TAVR for patients with prohibitive surgical risk and life expectancy >12 months
**Intervention for Severe AS**

Indications for TAVR vs surgical AVR:

- **Evaluation by a Heart Team**

- **Surgical AVR for patients at low or intermediate risk**
  - class I

TAVR as alternative?

- **TAVR for patients with prohibitive surgical risk and life expectancy >12 months**
  - class I

TAVR alternative for patients at high surgical risk

TAVR as alternative?

- class I?
  - ?

- class IIa?
Aortic Valve Replacement

Hospital Mortality

Medicare 1999-2011

30 Day AVR Mortality (percent)

Year

1999 2001 2003 2005 2007 2009 2011

N=24,900

7.6%

N=33,441

4.2%

Barreto-Filho et al, JAMA 2013;210:2078-2085
Aortic Valve Replacement

Hospital Mortality

Medicare 1999-2011

Year

30 Day AVR Mortality (percent)

Age 65-74

Age 75-84

Age ≥85

1999 2001 2003 2005 2007 2009 2011

5.9%

12.3%

5.8%

3.3%

Barreto-Filho et al, JAMA 2013;210:2078-2085
TAVR Now

- TAVR has been truly transformative
- Surgical AVR remains the standard with proven durability and safety for most patients
- TAVR provides treatment options for patients who previously had no options other than a predictably very poor short term outcome
- TAVR is an alternative to SAVR in patients at high and intermediate surgical risk
- The threshold for TAVR is declining in clinical trials, registries and clinical practice
- All patients want this
- Determining when to withhold TAVR is difficult
TAVR in the Future

Guidelines will need to adapt to the rapidly evolving TAVR evidence base

TAVR in intermediate and low risk surgical patients

Availability of TAVR is likely to inform new indications for valve replacement

- Moderate AS in primary cardiomyopathy
- Asymptomatic severe AS?

Judgment of the Heart Team remains essential in patient selection for TAVR

Appropriate use criteria and performance measures are needed to define quality
Aortie stenosis is a simple mechanical fault, which, if severe enough, imposes a heavy burden on the left ventricle and sooner or later overcomes it. An obstructive lesion of this sort presents a problem to any surgeon. This problem may be stated as follows: can we prescribe just the right degree of intervention, and at the right time, and over the right portion of the valve, to prevent catastrophic failure of the heart to meet, and on the other hand, to prevent excessive proliferation of the stenotic aortic valve leaflets which may lead to mitral valve incompetence? The definition of severe stenosis is one with sufficient hypertrophy of the left ventricle to cause inversion of the T wave of the electrocardiogram in left ventricular surface leads or their equivalents. It is in this setting that the surgical emphasis is placed on the management of the mitral valve. It is important to understand that aortic stenosis may be treated medically, surgically, or both.

...it's not simple any more