Valvular Heart Disease 2016: Challenges and Future Prospects

Robert O. Bonow, MD, MS
Northwestern University Feinberg School of Medicine
Bluhm Cardiovascular Institute
Northwestern Memorial Hospital
Editor-in-Chief, JAMA Cardiology

No Relationships to Disclose
2008 Focused Update Incorporated Into the ACC/AHA 2006 Guidelines for the Management of Patients With Valvular Heart Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease)

Endorsed by the Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons

2006 Writing Committee Members

Robert O. Bonow, MD, MACC, FAHA, Chair
Blase A. Carabello, MD, FACC, FAHA
Kama Chatterjee, MB, FACC
Antonio C. de Leon, Jr, MD, FACC, FAHA
David P. Faxon, MD, FACC, FAHA
Michael D. Freed, MD, FACC, FAHA
William H. Gaasch, MD, FACC, FAHA
Bruce W. Lytle, MD, FACC

Rick A. Nishimura, MD, FACC, FAHA
Patrick T. O’Gara, MD, FACC, FAHA
Robert A. O’Rourke, MD, MACC, FAHA
Catherine M. Otto, MD, FACC, FAHA
Pravin M. Shah, MD, MACC, FAHA
Jack S. Shanewise, MD*
The evidence base is limited by an inadequate number of randomized clinical trials.
Hence, virtually all of the recommendations are based on expert consensus (Level C)
2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease
A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the American Association for Thoracic Surgery, American Society of Echocardiography, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthetists, and Society of Thoracic Surgeons

Writing Committee Members

Rick A. Nishimura, MD, MACC, FAHA, Co-Chair
Catherine M. Otto, MD, FACC, FAHA, Co-Chair
Robert O. Bonow, MD, MACC, FAHA
Blase A. Carabello, MD, FACC
John P. Lewin III, MD, FACC
Robert A. Guyton, MD, FACC
Patrick T. O’Gara, MD, FACC
Carlos E. Ruiz, MD, PhD, FACC
Nikolaos J. Skakas, MD, FASE

Paul Sorajja, MD, FACC, FAHA*
Thordahl M. Sandi, III, MD††
James D. Thomas, MD, FASE, FACC, FAHA‡

*Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry and other entities may apply. See Appendix 1 for revised information. †ACC/AHA representatives. ‡ACC/AHA Task Force on Performance Measures liaison. §ESC/ESC/AHA Task Force on Practice Guidelines liaison. ‖Society of Cardiovascular Anesthetists representative. #Society for Cardiovascular Angiography and Interventions representative. *American Association for Thoracic Surgery representative. †|Society of Thoracic Surgeons representative. ||Society of Echocardiography representative.
<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Risk of valve disease</td>
</tr>
<tr>
<td>B</td>
<td>Mild - moderate asymptomatic disease</td>
</tr>
</tbody>
</table>
| C     | Severe valve disease but asymptomatic  
C1: Normal LV function  
C2: Depressed LV function |
| D     | Severe, symptomatic valve disease |

RHD, BAV, MVP, HF, CVD risk
Mitral regurgitation

Degenerative MR: primary valve disease

Functional MR: primary myocardial disease
Mitral regurgitation

Degenerative MR: primary valve disease

Functional MR: primary myocardial disease
Mitral regurgitation

Indications for mitral valve surgery for degenerative MR?
Mitral regurgitation

Indications for mitral valve surgery for degenerative MR?

• Symptomatic patients

class I
Indications for mitral valve surgery for degenerative MR?

- Symptomatic patients
- Asymptomatic patients
- LV systolic dysfunction
Mitral regurgitation

Indications for mitral valve surgery for degenerative MR?

- Symptomatic patients
- Asymptomatic patients
- LV systolic dysfunction

LVEF <60%

class I
Mitral regurgitation

Indications for mitral valve surgery for degenerative MR?

- Symptomatic patients
- Asymptomatic patients
  - LV systolic dysfunction

LVEF <60%
LVSD >40mm
Mitral regurgitation

Indications for mitral valve surgery for degenerative MR?

- Symptomatic patients (class I)
- Asymptomatic patients
  - LV systolic dysfunction (class I)
  - Pulmonary hypertension (class IIa)
Mitral regurgitation

Indications for mitral valve surgery for degenerative MR?

- Symptomatic patients  
  - LV systolic dysfunction  
  - Pulmonary hypertension

- Asymptomatic patients

PASP >50 mmHg at rest

class I

class I

class IIa
Mitral regurgitation

Indications for mitral valve surgery for degenerative MR?

- Symptomatic patients
- Asymptomatic patients
  - LV systolic dysfunction
  - Pulmonary hypertension
  - Atrial fibrillation

class I
class I
class IIa

class IIa
Mitral regurgitation

Indications for mitral valve surgery for degenerative MR?

- Symptomatic patients  
- Asymptomatic patients
  - LV systolic dysfunction
  - Pulmonary hypertension
  - Atrial fibrillation
  - Normal LV function, repair feasible?

- class I
- class I
- class IIa
- class IIa
Mitral regurgitation

Indications for mitral valve surgery for degenerative MR?

- Symptomatic patients
- Asymptomatic patients
  - LV systolic dysfunction
  - Pulmonary hypertension
  - Atrial fibrillation
  - Normal LV function, repair feasible?

MV repair to improve survival?
Mitral regurgitation

Indications for mitral valve surgery for degenerative MR?

- Symptomatic patients
- Asymptomatic patients
  - LV systolic dysfunction
  - Pulmonary hypertension
  - Atrial fibrillation
  - Normal LV function, repair feasible?

MV repair to improve survival?
What is the natural history?
Mitral regurgitation

Indications for mitral valve surgery for degenerative MR?

- Symptomatic patients
- Asymptomatic patients
  - LV systolic dysfunction
  - Pulmonary hypertension
  - Atrial fibrillation
  - Normal LV function, repair

Asymptomatic severe degenerative MR:

- 66% come to surgery in 5 years because of symptoms, LV dysfunction, pulmonary hypertension or AF
- Long-term postoperative survival is worse if surgery is performed after patients become symptomatic
Late outcomes of mitral valve repair for floppy valves: Implications for asymptomatic patients

Tirone E. David, MD
Joan Ivanov, PhD
Susan Armstrong, MSc
Harry Rakowski, MD

J Thorac Cardiovasc Surg 2003;125:1143-1152
Mitral Regurgitation
Survival After Mitral Valve Surgery

Survival (percent)

Time (years)

n=488

64%
p<0.001

David et al, J Thorac Cardiovasc Surg 2003;125:1143-1152
Mitral Regurgitation
Survival After Mitral Valve Surgery

FC I-II
81%

FC III-IV
58%

Survival (percent)

Time (years)

n=488

p<0.001

David et al, J Thorac Cardiovasc Surg 2003;126:1143-1152
Late Outcomes of Mitral Valve Repair for Mitral Regurgitation Due to Degenerative Disease

Tirone E. David, MD; Susan Armstrong, MSc; Brian W. McCrindle MD; Cedric Manlhiot, BSc

Background—The pathological spectrum of mitral regurgitation (MR) is broad, and there are various underlying pathologies. This study examined 840 patients who underwent mitral valve surgery for isolated degenerative MR.

Methods and Results—All patients were prospectively followed for a mean of 10.4 years. Clinical, hemodynamic, catheter, age, left ventricular ejection fraction were included in multivariable analysis. MF repair patients had repeat MV surgery for severe MR developed in 35% of patients. A degree of myxomatous changes was associated with increased freedom from moderate or severe MR.

Conclusions—MV repair for MR was well tolerated. Improved outcomes may be tied to lower recurrence rates, which may be due to lower recurrence rates resulting from reduced MR.

David et al, Circulation 2013;127:1485-1492
Indications for MV repair for asymptomatic primary MR:

- Chronic severe MR
- Preserved LV function
- Experienced surgical center
- Likelihood of durable repair without residual MR > 95%

Class IIa
Mitral regurgitation

Indications for MV repair for asymptomatic primary MR:

- Chronic severe MR
- Preserved LV function
- Experienced surgical center
- Likelihood of durable repair without residual MR > 95%

class Ila

- Preserved LV function
- Likelihood of durable repair and low risk for surgery, and
- LA dilatation >60 ml/m2
  -- or --
  Exercise PAP >60 mmHg

class IIB
Mitral regurgitation

Indications for MV repair for asymptomatic primary MR:

- Chronic severe MR
- Preserved LV function
- Experienced surgical center
- Likelihood of durable repair without residual MR > 95%.

- Repair better than mitral valve replacement
- Patients should be referred to centers experienced in repair

class I

class Ila
Centers of Excellence in Mitral Valve Repair

Criteria:
- MV surgery volume requirement (center and surgeon)
- Expert periprocedural imaging capabilities
- Access to transcatheter technology
- Transparency regarding outcomes including: repair rates, mortality rates, stroke rates, repair durability
Mitral regurgitation

Primary MR: primary valve disease

Secondary MR: primary myocardial disease
Mitral regurgitation

Primary MR: primary valve disease

Secondary MR: primary myocardial disease

- Diagnostic dilemmas
- Therapeutic dilemmas
Imprecision in grading severity of secondary MR

What is “severe” secondary MR?
Ischemic Mitral Regurgitation
Long-Term Outcome and Prognostic Implications With Quantitative Doppler Assessment

Francesco Grigioni, MD; Maurice Enriquez-Sarano, MD; Kenton J. Zehr, MD; Kent R. Bailey, PhD; A. Jamil Tajik, MD


Survival After MI

- MI without MR
- ERO 1-19
- ERO ≥20

Survival (percent)

Time (years)

Grigioni et al. *Circulation* 2001;103:1759-1764
Independent prognostic value of functional mitral regurgitation in patients with heart failure. A quantitative analysis of 1256 patients with ischaemic and non-ischaemic dilated cardiomyopathy

Andrea Rossi,1 Frank L Dini,2 Mariantonietta Cicoira,1 Silvia Stefano Ghio,5 Maurice Enriquez-Sarano

Heart 2011;97:1675–1680

Rossi et al. Heart 2011;97:1675-1680
Independent prognostic value of functional mitral regurgitation in patients with heart failure. A quantitative analysis of 1256 patients with ischaemic and non-ischaemic dilated cardiomyopathy

Andrea Rossi,† Frank L Dini,‡ Mariantonietta Cicoira,† Silvia Stefano Ghio,§ Maurice Enriquez-Sarano

Heart 2011;97:1675–1680

Rossi et al. Heart 2011;97:1675-1680
Valvular Heart Disease

Influence of Mitral Regurgitation Repair on Survival in the Surgical Treatment for Ischemic Heart Failure Trial

Marek A. Deja, Paul A. Grayburn, Benjamin Sun, Vivek Rao, Lilin She, Michal Krejea, Anil R. Jain, Yeow Leng Chua, Richard Daly, Michele Senni, Krzysztof Mokrzycki, Lorenzo Menicanti, Jae K. Oh, Robert Michler, Krzysztof Wróbel, Andre Lamy, Eric J. Velazquez, Kerry L. Lee and Robert H. Jones

*Circulation. 2012;125:2639-2648*

**Ischemic Cardiomyopathy**

![Graph showing mortality rates over time for different levels of mitral regurgitation (MR): No MR (30%), Mild MR (47%), and Mod-Severe MR (55%). The graph indicates a statistically significant difference (p<0.001) in mortality rates across the three categories.]
Valvular Heart Disease

Influence of Mitral Regurgitation Repair on Survival in the Surgical Treatment for Ischemic Heart Failure Trial

Marek A. Deja, Paul A. Grayburn, Benjamin Sun, Vivek Rao, Lilin She, Michal Krejea, Anil R. Jain, Yeow Leng Chua, Richard Daly, Michele Senni, Krzysztof Mokrzycki, Lorenzo Menicanti, Jae K. Oh, Robert Michler, Krzysztof Wróbel, Andre Lamy, Eric J. Velazquez, Kerry L. Lee and Robert H. Jones

_Circulation_. 2012;125:2639-2648

---

Ischemic Cardiomyopathy

- **EF 25%**: ESVI 90 mL/m²
- **EF 27%**: ESVI 80 mL/m²
- **EF 30%**: ESVI 73 mL/m²

**Mild MR**
- EF 27%
- ESVI 80 mL/m²

**Mod-Severe MR**
- EF 25%
- ESVI 90 mL/m²

**No MR**
- EF 30%
- ESVI 73 mL/m²

Mortality (percent)

- p<0.001

Time (years)

0 1 2 3 4 5 6

Deja et al. _Circulation_ 2012;125:2639-2648
# Prevalence of MR in Patients with LV Dysfunction

<table>
<thead>
<tr>
<th>Study</th>
<th>Journal</th>
<th>N</th>
<th>Prevalence</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yiu et al</td>
<td><em>Circulation</em> 2000</td>
<td>128</td>
<td>63%</td>
<td></td>
</tr>
<tr>
<td>Grigioni et al</td>
<td><em>Circulation</em> 2001</td>
<td>303</td>
<td>64%</td>
<td></td>
</tr>
<tr>
<td>Koelling et al</td>
<td><em>Am Heart J</em> 2002</td>
<td>1436</td>
<td>49%</td>
<td>*</td>
</tr>
<tr>
<td>Trichon et al</td>
<td><em>Am J Cardiol</em> 2003</td>
<td>2057</td>
<td>56%</td>
<td></td>
</tr>
<tr>
<td>Robbins et al</td>
<td><em>Am J Cardiol</em> 2003</td>
<td>221</td>
<td>59%</td>
<td></td>
</tr>
<tr>
<td>Cleland et al</td>
<td><em>N Engl J Med</em> 2004</td>
<td>605</td>
<td>50%</td>
<td>*</td>
</tr>
<tr>
<td>Grayburn et al</td>
<td><em>J Am Coll Cardiol</em> 2005</td>
<td>336</td>
<td>77%</td>
<td></td>
</tr>
<tr>
<td>Bursi et al</td>
<td><em>Circulation</em> 2005</td>
<td>303</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Acker et al</td>
<td><em>J Thorac CV Surg</em> 2006</td>
<td>300</td>
<td>66%</td>
<td></td>
</tr>
<tr>
<td>Di Mauro et al</td>
<td><em>Ann Thorac Surg</em> 2006</td>
<td>239</td>
<td>75%</td>
<td></td>
</tr>
<tr>
<td>Rossi et al</td>
<td><em>Heart</em> 2011</td>
<td>1300</td>
<td>74%</td>
<td></td>
</tr>
<tr>
<td>Deja et al</td>
<td><em>Circulation</em> 2012</td>
<td>599</td>
<td>63%</td>
<td></td>
</tr>
<tr>
<td>Onishi et al</td>
<td><em>Circ Heart Fail</em> 2013</td>
<td>277</td>
<td>48%</td>
<td>*</td>
</tr>
</tbody>
</table>

* *Patients with moderate to severe MR*
Secondary mitral regurgitation:
...a marker of a sicker LV
- or -
...a contributor to a sicker LV?
Secondary mitral regurgitation:
...a marker of a sicker LV
- or -
...a therapeutic target?

Therapies that produce beneficial reverse remodeling also reduce severity of functional MR
Secondary mitral regurgitation

Guideline-directed medical therapy for heart failure, including CRT

class I
Secondary mitral regurgitation

Guideline-directed medical therapy for heart failure, including CRT

Indications for mitral valve surgery:

- Patients with severe MR undergoing CABG or AVR

Class I

Class IIa
Secondary mitral regurgitation

Guideline-directed medical therapy for heart failure, including CRT

Indications for mitral valve surgery:

• Patients with severe MR undergoing CABG or AVR

• Severe MR, persistent symptoms despite optimal medical therapy, including CRT
Indications for mitral valve surgery:

- Patients with severe MR, persistent symptoms despite optimal medical therapy, including CRT (class IIb)
- Patients with severe MR undergoing CABG or AVR (class IIa)
- Severe MR, persistent symptoms despite optimal medical therapy, including CRT (class IIb)
- Patients with moderate MR undergoing CABG or AVR (class IIb)
Baseline

Optimized Medical Therapy and Biventricular Pacing
Correction of Mitral Regurgitation in Nonresponders to Cardiac Resynchronization Therapy by MitraClip Improves Symptoms and Promotes Reverse Remodeling

Angelo Auricchio, MD, PtID,* Wolfgang Schillinger, MD;† Sven Meyer, MD;‡ Francesco Maisano, MD;§ Rainer Hoffmann, MD;¶ Gian Paolo Ussia, MD,¶ Giovanni B. Pedrazzini, MD,* Jan van der Heyden, MD,# Simona Fratini, MD, PtID,*** Catherine Klersy, MD, MSc,†† Jan Komtebedde, DVM,* Olaf Franzen, MD,‡ on behalf of the PERMIT-CARE Investigators

*Lugano, Switzerland; Göttingen, Hamburg, and Aachen, Germany; Milan, Catania, L’Aquila, and Pavia, Italy; and Nieuwegein, the Netherlands
Secondary mitral regurgitation

Indications for transcatheter MV repair for severe secondary MR:

- Severe secondary MR
- Severely symptomatic
- Prohibited or high surgical risk
- Reasonable life expectancy

class IIb
# Prevalence of MR in Patients with LV Dysfunction

<table>
<thead>
<tr>
<th>Authors</th>
<th>Journal</th>
<th>Year</th>
<th>N</th>
<th>Prevalence MR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yiu et al</td>
<td><em>Circulation</em> 2000</td>
<td>2000</td>
<td>128</td>
<td>63%</td>
</tr>
<tr>
<td>Grigioni et al</td>
<td><em>Circulation</em> 2001</td>
<td>2001</td>
<td>303</td>
<td>64%</td>
</tr>
<tr>
<td>Koelling et al</td>
<td><em>Am Heart J</em> 2002</td>
<td>2002</td>
<td>1436</td>
<td>49% *</td>
</tr>
<tr>
<td>Trichon et al</td>
<td><em>Am J Cardiol</em> 2003</td>
<td>2003</td>
<td>2057</td>
<td>56%</td>
</tr>
<tr>
<td>Robbins et al</td>
<td><em>Am J Cardiol</em> 2003</td>
<td>2003</td>
<td>221</td>
<td>59%</td>
</tr>
<tr>
<td>Cleland et al</td>
<td><em>N Engl J Med</em> 2004</td>
<td>2004</td>
<td>605</td>
<td>50% *</td>
</tr>
<tr>
<td>Grayburn et al</td>
<td><em>J Am Coll Cardiol</em> 2005</td>
<td>2005</td>
<td>336</td>
<td>77%</td>
</tr>
<tr>
<td>Bursi et al</td>
<td><em>Circulation</em> 2005</td>
<td>2005</td>
<td>303</td>
<td>50%</td>
</tr>
<tr>
<td>Acker et al</td>
<td><em>J Thorac CV Surg</em> 2006</td>
<td>2006</td>
<td>300</td>
<td>66%</td>
</tr>
<tr>
<td>Di Mauro et al</td>
<td><em>Ann Thorac Surg</em> 2006</td>
<td>2006</td>
<td>239</td>
<td>75%</td>
</tr>
<tr>
<td>Rossi et al</td>
<td><em>Heart</em> 2011</td>
<td>2011</td>
<td>1300</td>
<td>74%</td>
</tr>
<tr>
<td>Deja et al</td>
<td><em>Circulation</em> 2012</td>
<td>2012</td>
<td>599</td>
<td>63%</td>
</tr>
<tr>
<td>Onishi et al</td>
<td><em>Circ Heart Fail</em> 2013</td>
<td>2013</td>
<td>277</td>
<td>48% *</td>
</tr>
</tbody>
</table>

*Patients with moderate to severe MR*
Burden of valvular heart diseases: a population-based study

Vuyisile T Nkomo, Julius M Gardin

Moderate-Severe Mitral Valve Disease

<table>
<thead>
<tr>
<th>Age</th>
<th>ARIC, CHS, CARDIA (n=11,911)</th>
<th>Olmstead County (n=16,501)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;45</td>
<td>28,412 subjects</td>
<td></td>
</tr>
<tr>
<td>45-54</td>
<td></td>
<td></td>
</tr>
<tr>
<td>55-64</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥75</td>
<td>9.6%</td>
<td>7.3%</td>
</tr>
</tbody>
</table>

Burden of valvular heart diseases: a population-based study

Vuyisile T Nkomo, Julius M Gardener

Moderate-Severe Aortic Valve Disease

ARIC, CHS, CARDIA (n=11,911)
Olmstead County (n=16,501)
28,412 subjects

<table>
<thead>
<tr>
<th>Age</th>
<th>ARIC, CHS, CARDIA</th>
<th>Olmstead County</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>45-54</td>
<td></td>
<td></td>
</tr>
<tr>
<td>55-64</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td>4.4</td>
<td>6.0</td>
</tr>
<tr>
<td>≥75</td>
<td>6.0</td>
<td>4.4</td>
</tr>
</tbody>
</table>

Nkomo et al, Lancet 2006;368:1005-1011
Aortic Stenosis

Rheumatic AS

Congenital AS

Calcific AS

from Bonow and Braunwald, Valvular Heart Disease
Braunwald's Heart Disease, 7th ed, 2004
Aortic Stenosis

Rheumatic AS

Congenital AS

Calcific AS

Age >60

All patients 47%

Men 51%

from Bonow and Braunwald, Valvular Heart Disease
Braunwald's Heart Disease, 7th ed, 2004

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

Rheumatic AS

Congenital AS

Calcific AS

Age >80

All patients: 28%

Men: 32%

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

from Bonow and Braunwald, Valvular Heart Disease
*Braunwald's Heart Disease*, 7th ed, 2004
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.
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...
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 aortic stenosis because of the incidence of sudden death as disease and the grave prognoses to accompany the onset of.

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

Supplement V to Circulation, Vol. XXXVI.
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 aortic stenosis because of the recorded incidence of sudden death as well as the grave prognosis and to accompany the onset of symptoms in 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

*From the Cardiology Branch, National Heart Institute, Bethesda, Maryland.
Supplement V to Circulation, Vol. XXXVI.
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 H. Pao, MD

Bach et al, Circ Cardiovasc Qual Outcomes 2009;2:533-539
Aortic Stenosis

Indications for AVR

- Symptomatic patients with severe AS

...if it is likely that the symptoms are cardiac in origin
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
- 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
• Hypotension

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:
- Vmax: >4.0 m/s
- Mean Δ: >40 mmHg
-AVA: <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?
Aortic Stenosis

84 year old man with severe AS

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

* What is the risk of death while waiting for symptoms to trigger valve replacement?
Indications for valve replacement:

- Very severe AS: $V_{max} \geq 5 \text{ m/s}$  

**Asymptomatic Aortic Stenosis**

class IIa
Asymptomatic Aortic Stenosis

Indications for valve replacement:

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

class IIa

class IIb
Asymptomatic Aortic Stenosis

Indications for valve replacement:

- **Very severe AS:** $V_{max} \geq 5$ m/s  
  **class IIa**

- **Rapid progression and low surgical risk**  
  **class IIb**

- **Very severe AS:** $V_{max} > 5.5$ m/s  
  **class IIa**
Asymptomatic Aortic Stenosis

Indications for valve replacement:

- **Very severe AS: Vmax ≥5 m/s**
  - class IIa

- **Rapid progression and low surgical risk**
  - class IIb

- **Very severe AS: Vmax >5.5 m/s**
  - class IIa

- **Severe valve calcification and rate of progression ≥0.3 m/s / year**
  - class IIa
### Asymptomatic Aortic Stenosis

**Indications for valve replacement:**

<table>
<thead>
<tr>
<th>Level</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IIa</strong></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>Very severe AS: $V_{\text{max}} \geq 5$ m/s</td>
</tr>
<tr>
<td>2.</td>
<td>Rapid progression and low surgical risk</td>
</tr>
<tr>
<td><strong>IIb</strong></td>
<td>Very severe AS: $V_{\text{max}} &gt; 5.5$ m/s</td>
</tr>
<tr>
<td>1.</td>
<td>Severe valve calcification and rate of progression $\geq 0.3$ m/s/year</td>
</tr>
<tr>
<td>2.</td>
<td>Markedly elevated BNP</td>
</tr>
<tr>
<td>3.</td>
<td>Increase in gradient with exercise $&gt;20$ mmHg</td>
</tr>
<tr>
<td>4.</td>
<td>Excessive LVH</td>
</tr>
</tbody>
</table>
Asymptomatic Aortic Stenosis

Indications for valve replacement:

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

- Severity of AS
- Severity of calcification
- Left ventricular function
- Exercise response
Asymptomatic Aortic Stenosis

Indications for valve replacement:

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

- Severity of AS
- Severity of calcification
- Left ventricular function
- Exercise response
- BNP?
B-Type Natriuretic Peptide Clinical Activation in Aortic Stenosis
Impact on Long-Term Survival

Marie-Annick Clavel, DVM, PtD, Joseph Malouf, MD, Hector I. Michelen, MD, Rakesh M. Suri, MD, DPhIII, Ali Daniel Deramo, Anand S. Jayanth, and Maurice Enriquez-Sarano, MD
Rochester, Minnesota

J Am Coll Cardiol 2014;63:2016-2025

Asymptomatic AS with Normal EF

<table>
<thead>
<tr>
<th>BNP ratio</th>
<th>Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.0</td>
<td>83%</td>
</tr>
<tr>
<td>1.0-1.9</td>
<td>66%</td>
</tr>
<tr>
<td>2.0-2.9</td>
<td>53%</td>
</tr>
<tr>
<td>≥3.0</td>
<td>33%</td>
</tr>
</tbody>
</table>

n=562
p<0.001

Clavel et al, J Am Coll Cardiol 2014;63:2016-2025
Aortic stenosis

Management challenges:

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

Systole

Low Gradient Aortic Stenosis

LV Dysfunction

Normal LV Function

Dobutamine: Echocardiography or Catheterization

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
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
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
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
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
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
Diastole

Systole

Low Flow
Low Gradient
Normal LV Function

- Treat hypertension
- Catheterization
- Valve calcification
- Advanced imaging
- Clinical skills
Low Flow, Low Gradient Aortic Stenosis

Indications for valve replacement:

**Reduced EF:**
- Dobutamine study showing:
  - $V_{max} > 4$ m/s or
  - Mean $\Delta > 40$ mmHg or
  - $AVA \leq 1$ sq cm

**Reduced EF:**
- With contractile reserve

**class Ila**
Low Flow, Low Gradient Aortic Stenosis

Indications for valve replacement:

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

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

**Reduced EF:**
- With contractile reserve
Low Flow, Low Gradient Aortic Stenosis

Indications for valve replacement:

**Reduced EF:**
- Dobutamine study showing:
  - $V_{\text{max}} > 4$ m/s or
  - Mean $\Delta > 40$ mmHg or
  - $\text{AVA} \leq 1$ sq cm

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

**Reduced EF:**
- With contractile reserve

**Normal EF:**
- Only after thorough confirmation of severe AS
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
  - class I

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

  TAVR as alternative?

  - class I

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

  TAVR alternative for patients at high surgical risk
  - 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

N=33,441

7.6%

4.2%
Aortic Valve Replacement
Hospital Mortality

Medicare 1999-2011

30 Day AVR Mortality (percent)

Year

Age ≤65
Age 65-74
Age 75-84
Age ≥85

12.3%
5.9%
5.8%
3.3%

Barreto-Filho et al, JAMA 2013;210:2078-2085
Valvular heart disease 1
Management strategies and future challenges for aortic valve disease

Robert O Bonow, Martin B Leon, Darshan Doshi, Neil Moat

Lancet 2016; 387: 1312-23
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 or 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
Aortic 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 the surgeon with a major problem to be solved, and its solution requires a high degree of technical skill. It may be studied only incidentally during the operation for mitral disease, when the early diagnosis of aortic stenosis may determine the choice of the operation of mitral relief. 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 absence.

Wood P, Am J Cardiol 1958;1:553-571

The 1958 Morris H. Nathanson Lecture, University of Southern California, Los Angeles.

...it's not simple any more
Valvular heart disease:
Have the guidelines filled the gap?