Valve Workup and Indications for Intervention: What the 2014 Guidelines Tell Us

Vasant Jayasankar, MD, MS, FACS
Overview

• Aortic Stenosis
  o Undertreatment
  o Workup overview
# Levels of Evidence

<table>
<thead>
<tr>
<th>Class I</th>
<th>Benefit &gt;&gt; Risk</th>
<th>Procedure/Treatment SHOULD be performed/administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class IIA</td>
<td>Benefit &gt;&gt; Risk</td>
<td>Additional studies with focused objectives needed</td>
</tr>
<tr>
<td>Class IIB</td>
<td>Benefit ≥ Risk</td>
<td>Additional studies with broad objectives needed; additional registry data would be helpful</td>
</tr>
<tr>
<td>Class III</td>
<td>No Benefit or Class III</td>
<td>Harm</td>
</tr>
<tr>
<td>Procedure/Test</td>
<td>Treatment</td>
<td></td>
</tr>
<tr>
<td>COR III: Not Helpful</td>
<td>COR III: Excess Cost w/o Benefit or Harmful</td>
<td></td>
</tr>
<tr>
<td>COR III: Harmful</td>
<td>No Proven Benefit</td>
<td></td>
</tr>
</tbody>
</table>

## Level A
- Multiple populations evaluated*
- Data derived from multiple randomized clinical trials or meta-analyses
- Recommendation that procedure or treatment is useful/effective
- Sufficient evidence from multiple randomized trials or meta-analyses

## Level B
- Limited populations evaluated*
- Data derived from a single randomized trial or nonrandomized studies
- Recommendation that procedure or treatment is useful/effective
- Evidence from single randomized trial or nonrandomized studies

## Level C
- Very limited populations evaluated*
- Only consensus opinion of experts, case studies, or standard of care
- Recommendation that procedure or treatment is useful/effective
- Only expert opinion, case studies, or standard of care
## Stages of Valve Disease

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At risk</td>
<td>Patients with risk factors for development of VHD</td>
</tr>
<tr>
<td>B</td>
<td>Progressive</td>
<td>Patients with progressive VHD (mild-to-moderate severity and asymptomatic)</td>
</tr>
<tr>
<td>C</td>
<td>Asymptomatic severe</td>
<td>Asymptomatic patients who have the criteria for severe VHD:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C1: Asymptomatic patients with severe VHD in whom the left or right</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ventricle remains compensated</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C2: Asymptomatic patients with severe VHD, with decompensation of the</td>
</tr>
<tr>
<td></td>
<td></td>
<td>left or right ventricle</td>
</tr>
<tr>
<td>D</td>
<td>Symptomatic severe</td>
<td>Patients who have developed symptoms as a result of VHD</td>
</tr>
</tbody>
</table>

VHD indicates valvular heart disease.
Aortic Stenosis

• Severe AS is a lethal disease
  o Especially once symptomatic

• AS is undertreated in the U.S.

• Many patients would benefit from AS treatment with increased longevity and QOL

• Many “asymptomatic” severe AS patients in fact have symptoms
  o Provocative testing can demonstrate this
Aortic Stenosis

Normal

Aortic Stenosis
Bicuspid Valve

- Arnold Schwarzenegger
- Develop Stenosis by age 60
U.S. PREVALENCE OF AORTIC STENOSIS

U.S. Pop. >65
Prevalence Rate
Prevalence
Surgical (%)
Addressable Patients Today

37M
~4%
~1.5M
20%
300,000

~27% of pool is treated each year

Annual Valve Replacements

~80,000

U.S. Census 2008
HRI 2009
Calculation
L.E.K. Consulting, STS Database
Calculation

Estimated from available data
Aortic stenosis is life-threatening, progresses rapidly, and severely limits quality of life

- Survival after onset of symptoms is 50% at two years and 20% at five years\(^1\)

- “...valve surgery is appropriate with even mild symptoms.”\(^2\)

Sources
UNDERTREATMENT IN PRIMARY CARE

The Journal
of
HEART VALVE
DISEASE

Decision-Making and Outcomes in Severe Symptomatic Aortic Stenosis
Erik Charlson¹, Anna T. R. Legedza², Mary Beth Hamel²
¹Mayo Clinic College of Medicine, ²Division of General Medicine and Primary Care, Harvard Medical School, Boston, USA

“Primary care managed patients: 75% of severe symptomatic AS untreated”

The benefits of early valve replacement in asymptomatic patients with severe aortic stenosis


*J Thorac Cardiovasc Surg* 2008;135:308-315
DOI: 10.1016/j.jtcvs.2007.08.058

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://jtcvs.ctsnetjournals.org/cgi/content/full/135/2/308
622 patients
- Aged 72 ± 11 years
- Isolated asymptomatic severe aortic stenosis

Peak systolic velocity of > 4 m/s by transthoracic echocardiography

Monitored for the onset of symptoms and need for AVR

SURVIVAL BENEFIT IN SURGICALLY TREATED PATIENT COHORT

Patient survival

AVR SURVIVAL COMPARABLE TO AGE-MATCHED POPULATION

Survival after AVR for severe aortic stenosis

% Survival

0 10 20 30 40 50 60 70 80 90 100

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

Years

CARDIAC SURGERY IN THE ELDERLY

- 459 pts age >80
- Includes CABG, valve, and combined procedures
CARDIAC SURGERY IN THE ELDERLY

![Survival Curve]

Cumulative Survival vs. Postoperative Year

- BWH Elderly patients
- US pop >75yo expected

N=459 373 343 310 280 248 198 133 89 41 16
Updated Guidelines

2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Rick A. Nishimura, Catherine M. Otto, Robert O. Bonow, Blase A. Carabello, John P. Erwin III, Robert A. Guyton, Patrick T. O'Gara, Carlos E. Ruiz, Nikolaos J. Skubas, Paul Sorajja, Thoralf M. Sundt III and James D. Thomas

*Circulation.* published online March 3, 2014;

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Indications for AVR – Severe AS

• Severe symptomatic AS (Class I)
  o AVA < 1 cm²
  o Mean gradient > 40
  o Vmax > 4 m/s

• Severe asymptomatic AS with any one of the following:
  o **Class I**
  o EF < 50%
  o Performing other cardiac surgery
  o **Class IIa**
  o Very severe AS (Mean gradient > 60, Vmax > 5 m/s)
  o Abnormal Stress Test
Indications for AVR – Moderate AS

- Mean gradient 20-39 mm Hg, Vmax 3-3.9 m/s
- All class IIa

- Symptomatic, EF < 50%, positive stress test

- Symptomatic, EF > 50%, AVA < 1 cm$^2$, symptoms likely related to AS

- Asymptomatic, having other cardiac surgery
Low Flow State

• Can be challenging to elicit high gradients and velocities with failing ventricle

• Severe AS can exist with low numbers

• Dobutamine stress test can assist

• Look for increase in gradient and/or velocity to demonstrate severe AS
Asymptomatic Severe AS

- Hard to determine if truly Asx
- Exercise stress test very helpful
- Increased gradients/velocity with echo after exercise
- Development of symptoms
- Fall in BP or <20 mm Hg rise in SBP
- ≥ 2mm ST depression
Exercise Testing

Asymptomatic Severe AS

Event-free Survival

Normal ETT

Abnormal ETT

Months
ASYMPTOMATIC PATIENTS HAVE SIGNIFICANT MORTALITY BENEFIT

### Summary of Recommendations for AS: Timing of Intervention

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVR is recommended with severe high-gradient AS who have symptoms by history or on exercise testing (stage D1)</td>
<td>I</td>
<td>B</td>
<td>(10, 57-59)</td>
</tr>
<tr>
<td>AVR is recommended for asymptomatic patients with severe AS (stage C2) and LVEF &lt;50%</td>
<td>I</td>
<td>B</td>
<td>(61, 62)</td>
</tr>
<tr>
<td>AVR is indicated for patients with severe AS (stage C or D) when undergoing other cardiac surgery</td>
<td>I</td>
<td>B</td>
<td>(63, 64)</td>
</tr>
<tr>
<td>AVR is reasonable for asymptomatic patients with very severe AS (stage C1, aortic velocity ≥5.0 m/s) and low surgical risk</td>
<td>IIa</td>
<td>B</td>
<td>(65, 66)</td>
</tr>
<tr>
<td>AVR is reasonable in asymptomatic patients (stage C1) with severe AS and decreased exercise tolerance or an exercise fall in BP</td>
<td>IIa</td>
<td>B</td>
<td>(27, 38)</td>
</tr>
<tr>
<td>AVR is reasonable in symptomatic patients with low-flow/low-gradient severe AS with reduced LVEF (stage D2) with a low-dose dobutamine stress study that shows an aortic velocity ≥4.0 m/s (or mean pressure gradient ≥40 mm Hg) with a valve area ≤1.0 cm² at any dobutamine dose</td>
<td>IIa</td>
<td>B</td>
<td>(67-69)</td>
</tr>
<tr>
<td>AVR is reasonable in symptomatic patients who have low-flow/low-gradient severe AS (stage D3) who are normotensive and have an LVEF ≥50% if clinical, hemodynamic, and anatomic data support valve obstruction as the most likely cause of symptoms</td>
<td>IIa</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>AVR is reasonable for patients with moderate AS (stage B) (aortic velocity 3.0–3.9 m/s) who are undergoing other cardiac surgery</td>
<td>IIa</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>AVR may be considered for asymptomatic patients with severe AS (stage C1) and rapid disease progression and low surgical risk</td>
<td>IIb</td>
<td>C</td>
<td>N/A</td>
</tr>
</tbody>
</table>

AS indicates aortic stenosis; AVR, aortic valve replacement by either surgical or transcatheter approach; BP, blood pressure; COR, Class of Recommendation; LOE, Level of Evidence; LVEF, left ventricular ejection fraction; and N/A, not applicable.
Management of Patients With Severe AS

- Naturally history of severe AS is malignant—medical Rx ineffective.

- Exercise/dobutamine testing can be important component of AS evaluation in asymptomatic patient

- Even asymptomatic patients can benefit from AVR

- Elderly patients have significant benefit and can do quite well—perception of very high risk unfounded

- Substantial quality of life improvement—not just about survival
Mitral Regurgitation

- Normal Closure
- Prolapse Closure
Types of MR

• Primary (Degenerative)
  o Due to problem with valve leaflets andor supporting structures (chordae, papillary muscles)
  o Not primarily due to ventricular dysfunction

• Secondary (Functional)
  o Due to ventricular dysfunction
  o MR is a secondary result of abnormal ventricle dilatation
Mitral Valve Repair
<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>MV surgery is recommended for symptomatic patients with chronic severe primary MR (stage D) and LVEF &gt;30%</td>
<td>I</td>
<td>B</td>
<td>(156, 179)</td>
</tr>
<tr>
<td>MV surgery is recommended for asymptomatic patients with chronic severe primary MR and LV dysfunction (LVEF 30%-60% and/or LVESD ≥40 mm, stage C2)</td>
<td>I</td>
<td>B</td>
<td>(150-153, 180-182)</td>
</tr>
<tr>
<td>MV repair is recommended in preference to MVR when surgical treatment is indicated for patients with chronic severe primary MR limited to the posterior leaflet</td>
<td>I</td>
<td>B</td>
<td>(155, 183-198)</td>
</tr>
<tr>
<td>MV repair is recommended in preference to MVR when surgical treatment is indicated for patients with chronic severe primary MR involving the anterior leaflet or both leaflets when a successful and durable repair can be accomplished</td>
<td>I</td>
<td>B</td>
<td>(195-197, 199-203)</td>
</tr>
<tr>
<td>Concomitant MV repair or replacement is indicated in patients with chronic severe primary MR undergoing cardiac surgery for other indications</td>
<td>I</td>
<td>B</td>
<td>(204)</td>
</tr>
<tr>
<td>MV repair is reasonable in asymptomatic patients with chronic severe primary MR (stage C1) with preserved LV function (LVEF &gt;60% and LVESD &lt;40 mm) in whom the likelihood of a successful and durable repair without residual MR is &gt;95% with an expected mortality rate of &lt;1% when performed at a Heart Valve Center of Excellence</td>
<td>IIa</td>
<td>B</td>
<td>(149, 203, 205-209)</td>
</tr>
<tr>
<td>MV repair is reasonable for asymptomatic patients with chronic severe nonrheumatic primary MR (stage C1) and preserved LV function in whom there is a high likelihood of a successful and durable repair with 1) new onset of AF or 2) resting pulmonary hypertension (PA systolic arterial pressure &gt;50 mm Hg)</td>
<td>IIa</td>
<td>B</td>
<td>(154, 205, 210-215)</td>
</tr>
<tr>
<td>Concomitant MV repair may be considered in patients with chronic moderate primary MR (stage B) undergoing cardiac surgery for other indications</td>
<td>IIa</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>MV surgery may be considered in symptomatic patients with chronic severe primary MR and LVEF ≤30% (stage D)</td>
<td>IIb</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>MV repair may be considered in patients with rheumatic mitral valve disease when surgical treatment is indicated if a durable and successful repair is likely or if the reliability of long-term anticoagulation management is questionable</td>
<td>IIb</td>
<td>B</td>
<td>(194, 202, 203)</td>
</tr>
<tr>
<td>Transcatheter MV repair may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe primary MR (stage D) who have a reasonable life expectancy but a prohibitive surgical risk because of severe comorbidities</td>
<td>IIb</td>
<td>B</td>
<td>(216)</td>
</tr>
<tr>
<td>MVR should not be performed for treatment of isolated severe primary MR limited to less than one half of the posterior leaflet unless MV repair has been attempted and was unsuccessful</td>
<td>III: Harm</td>
<td>B</td>
<td>(195-198)</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; COR, Class of Recommendation; LOE, Level of Evidence; LV, left ventricular; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; MR, mitral regurgitation; MV, mitral valve; MVR, mitral valve replacement; N/A, not applicable; NYHA, New York Heart Association; and PA, pulmonary artery.
Aortic Insufficiency
AR indicates aortic regurgitation; AVR, aortic valve replacement (valve repair may be appropriate in selected patients); ERO, effective regurgitant orifice; LV, left ventricular; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction.
### AI Recommendations

**Table 10. Summary of Recommendations for AR Intervention**

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVR is indicated for symptomatic patients with severe AR regardless of LV systolic function (stage D)</td>
<td>I</td>
<td>B</td>
<td>(33, 92, 93)</td>
</tr>
<tr>
<td>AVR is indicated for asymptomatic patients with chronic severe AR and LV systolic dysfunction (LVEF &lt;50%) (stage C2)</td>
<td>I</td>
<td>B</td>
<td>(92, 94-96)</td>
</tr>
<tr>
<td>AVR is indicated for patients with severe AR (stage C or D) while undergoing cardiac surgery for other indications</td>
<td>I</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>AVR is reasonable for asymptomatic patients with severe AR with normal LV systolic function (LVEF ≥50%) but with severe LV dilation (LVESD &gt;50 mm, stage C2)</td>
<td>IIa</td>
<td>B</td>
<td>(97-99)</td>
</tr>
<tr>
<td>AVR is reasonable in patients with moderate AR (stage B) who are undergoing other cardiac surgery</td>
<td>IIa</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>AVR may be considered for asymptomatic patients with severe AR and normal LV systolic function (LVEF ≥50%, stage C1) but with progressive severe LV dilation (LVEDD &gt;65 mm) if surgical risk is low*</td>
<td>IIb</td>
<td>C</td>
<td>N/A</td>
</tr>
</tbody>
</table>

*Particularly in the setting of progressive LV enlargement.
Mitral Stenosis

- Severe MS: MVA \leq 1.5 \text{ cm}^2
<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMBC is recommended for symptomatic patients with severe MS (MVA ≤1.5 cm², stage D) and favorable valve morphology in the absence of contraindications</td>
<td>I</td>
<td>A</td>
<td>(109-113, 115)</td>
</tr>
<tr>
<td>Mitral valve surgery is indicated in severely symptomatic patients (NYHA class III/IV) with severe MS (MVA ≤1.5 cm², stage D) who are not high risk for surgery and who are not candidates for or failed previous PMBC</td>
<td>I</td>
<td>B</td>
<td>(137-142)</td>
</tr>
<tr>
<td>Concomitant mitral valve surgery is indicated for patients with severe MS (MVA ≤1.5 cm², stage C or D) undergoing other cardiac surgery</td>
<td>I</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>PMBC is reasonable for asymptomatic patients with very severe MS (MVA ≤1.0 cm², stage C) and favorable valve morphology in the absence of contraindications</td>
<td>IIa</td>
<td>C</td>
<td>(121, 143-145)</td>
</tr>
<tr>
<td>Mitral valve surgery is reasonable for severely symptomatic patients (NYHA class III/IV) with severe MS (MVA ≤1.5 cm², stage D), provided there are other operative indications</td>
<td>IIa</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>PMBC may be considered for asymptomatic patients with severe MS (MVA ≤1.5 cm², stage C) and favorable valve morphology who have new onset of AF in the absence of contraindications</td>
<td>IIb</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>PMBC may be considered for symptomatic patients with MVA &gt;1.5 cm² if there is evidence of hemodynamically significant MS during exercise</td>
<td>IIb</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>PMBC may be considered for severely symptomatic patients (NYHA class III/IV) with severe MS (MVA ≤1.5 cm², stage D) who have suboptimal valve anatomy and are not candidates for surgery or at high risk for surgery</td>
<td>IIb</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>Concomitant mitral valve surgery may be considered for patients with moderate MS (MVA 1.6–2.0 cm²) undergoing other cardiac surgery</td>
<td>IIb</td>
<td>C</td>
<td>N/A</td>
</tr>
</tbody>
</table>
### Table 4. Frequency of Echocardiograms in Asymptomatic Patients with VHD and Normal Left Ventricular Function

<table>
<thead>
<tr>
<th>Stage</th>
<th>Aortic Stenosis*</th>
<th>Aortic Regurgitation</th>
<th>Mitral Stenosis</th>
<th>Mitral Regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progressive (stage B)</td>
<td>Every 3–5 y (mild severity $V_{\text{max}}$ 2.0–2.9 m/s) every 1–2 y (moderate severity $V_{\text{max}}$ 3.0–3.9 m/s)</td>
<td>Every 3–5 y (mild severity) Every 1–2 y (moderate severity)</td>
<td>Every 3–5 y (MVA &gt;1.5 cm$^2$) Every 1–2 y (moderate severity)</td>
<td>Every 3–5 y (mild severity) Every 1–2 y (moderate severity)</td>
</tr>
<tr>
<td>Severe (stage C)</td>
<td>Every 6-12 mo ($V_{\text{max}}$ ≥4 m/s)</td>
<td>Every 6–12 mo Dilating LV: more frequently</td>
<td>Every 1–2 y (MVA 1.0–1.5 cm$^2$) Once every year (MVA &lt;1.0 cm$^2$)</td>
<td>Every 6–12 mo Dilating LV: more frequently</td>
</tr>
</tbody>
</table>

Patients with mixed valve disease may require serial evaluations at intervals earlier than recommended for single valve lesions.

*With normal stroke volume.

LV indicates left ventricle; MVA, mitral valve area; VHD, valvular heart disease; and $V_{\text{max}}$, maximum velocity.
Thank You!