MANAGEMENT OF AORTIC STENOSIS IN THE PRIMARY CARE SETTING

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Special Thanks to Dr. Walter Tan, Wake Med Structural Heart Program, for his assistance with this presentation.
Aortic stenosis (AS) is progressive obstruction of the left ventricular outflow tract.

Images courtesy Walter Tan, MD; Edwards Life Sciences & Renu Virmani, MD at the CV Path Institute
AS is most common in patients > 65 years of age.

Most Common

• Aortic valve calcification as people age

Less Common

• Rheumatic heart disease
• Other infections
• Congenital: e.g. bicuspid aortic valve
Prevalence of Aortic Stenosis in the Elderly

- Overall rate of 12.4%
- Rate of severe AS 3.4%
- Among those with severe AS, 75.6% were symptomatic
- 40.5% were not treated surgically

AV Anatomy:
Tricuspid (normal) & Bicuspid Valves
Which patients are at risk of developing AS?

<table>
<thead>
<tr>
<th>Older Age</th>
<th>Elevated Lipoprotein A Levels</th>
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<tbody>
<tr>
<td>Male</td>
<td>Elevated LDL</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Metabolic Syndrome</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Tobacco</td>
</tr>
</tbody>
</table>

Other AS Risk Factors

- Mediastinal radiation
- End-stage renal disease
- Elevated serum phosphorus levels
- Disorders of calcium metabolism
- Familial hypercholesterolemia

Hodgkin’s Lymphoma pre-treatment
Disease Progression in Calcific Aortic Stenosis, Showing Changes in Aortic-Valve Histologic Features, Leaflet Opening in Systole, and Doppler Velocities.
Surgically excised calcific aortic valve.
Disease Mechanisms and Time Course of Calcific Aortic Stenosis.

- Risk genotype
- Risk valve morphology
- Older age, male sex
- Dyslipidemia
- Diabetes or metabolic syndrome
- Hypertension
- Smoking
- Renal insufficiency
- Increased serum phosphate

Shear stress
- Inflammation
- Lipid infiltration
- Myofibroblast differentiation

Oxidative stress
- Increased angiotensin II
- Procalcific stimuli
- OPG–RANKL
- Wnt–LRP

Hydroxyapatite nodules
- Cartilage and bone formation

Average Yearly Changes in AS

<table>
<thead>
<tr>
<th>Metric</th>
<th>Change</th>
<th>Per Year</th>
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<tbody>
<tr>
<td>Aortic Valve Area (AVA)</td>
<td>Decreases</td>
<td>0.1 cm²</td>
</tr>
<tr>
<td>Transvalvular Velocity</td>
<td>Increases</td>
<td>0.1 – 0.3 meters/second</td>
</tr>
<tr>
<td>Mean Gradient</td>
<td>Increases</td>
<td>3 – 10 mm Hg</td>
</tr>
</tbody>
</table>

Helpful information to know, but it is hard to predict when aortic valve replacement (AVR) will be needed.

Hemodynamic progression of AS varies from person to person.

AS progresses faster as the stenosis becomes more severe.

Anatomical Changes Associated with Aortic Stenosis.
## Stages of Progression of AS

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
<th>Description</th>
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<tbody>
<tr>
<td>A</td>
<td>At Risk for AS</td>
<td>Patients with risk factors for developing AS</td>
</tr>
<tr>
<td>B</td>
<td>Progressive AS</td>
<td>Asymptomatic patients with mild to moderately severe AS</td>
</tr>
<tr>
<td>C</td>
<td>Asymptomatic Severe</td>
<td>C1: Asymptomatic Patients Left Ventricle is able to compensate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C2: Asymptomatic Patients Left Ventricle is <strong>unable</strong> to compensate for VHD</td>
</tr>
<tr>
<td>D</td>
<td>Symptomatic Severe</td>
<td>Symptomatic Patients</td>
</tr>
</tbody>
</table>

Physical Findings in AS are not sensitive for evaluating its severity.

- Grade 3/6, late-peaking systolic murmur heard best the base of the heart & that radiates to the carotid arteries
  - May be soft or radiate towards the apex
- Single S2 heart sound (due to stiff valve leaflets)
- Paradoxically split second heart sound (left bundle branch block or left ventricle dysfunction)
- Delayed and diminished carotid upstroke
  - May be normal in elderly patients


Progressive AS Signs & Symptoms

- 4th heart sound due to stiff LV
- Angina: 5 year mortality is 50%
  - First occurs on exercise due to increased MVO₂
  - May see LV strain pattern on EKG
    - ST depression & T wave inversion due to subendocardial ischemia
- Chest pressure, increasing dyspnea on exertion
- Pre-syncope or syncope (usually exertional)
- ? Fixed cardiac output (fixed stroke volume)
- CHF—2 year mortality rate is 50%
- Systolic & diastolic dysfunction
Comorbid Issues in AS

• Coronary artery disease (CAD) is common in patients with AS.
• 5% will have calcium in the myocardium that leads to AV block.
• 10-15% will have atrial fibrillation
• Approximately 75% of patients with AS will also have some degree of aortic insufficiency (AI).

MEDICAL MANAGEMENT OF MILD TO MODERATE AS
Indications for Transthoracic Echocardiogram (TTE)

- Initial evaluation of suspected aortic stenosis
  - AS severity
  - Presence of left ventricular (LV) hypertrophy
  - Left ventricular ejection fraction (EF)

<table>
<thead>
<tr>
<th>AS Severity</th>
<th>Time-Frame for Repeating TTE</th>
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<tbody>
<tr>
<td>Mild</td>
<td>3-5 years</td>
</tr>
<tr>
<td>Moderate</td>
<td>1-2 years</td>
</tr>
<tr>
<td>Severe</td>
<td>Annually</td>
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</table>

Repeat echo in patients with worsening symptoms regardless of time frame.

# AS Severity Scale

<table>
<thead>
<tr>
<th>Degree of AS</th>
<th>Mean Gradient (mmHg)</th>
<th>AV Area (cm²)</th>
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</thead>
<tbody>
<tr>
<td>Mild</td>
<td>&lt; 25</td>
<td>&gt; 1.5</td>
</tr>
<tr>
<td>Moderate</td>
<td>25 - 40</td>
<td>1.0 – 1.5</td>
</tr>
<tr>
<td>Severe</td>
<td>&gt; 40</td>
<td>&lt; 1.0</td>
</tr>
<tr>
<td>Critical</td>
<td>&gt; 70</td>
<td>&lt; 0.6</td>
</tr>
<tr>
<td>Stage</td>
<td>AVA</td>
<td>Velocity</td>
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<tr>
<td>-------</td>
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</tr>
<tr>
<td>A</td>
<td></td>
<td>$V_{\text{max}} &lt; 2 \text{ m/s}$</td>
</tr>
<tr>
<td>B</td>
<td></td>
<td>$V_{\text{max}} 2.0-2.9 \text{ m/s (mild)}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$V_{\text{max}} 3.0-3.9 \text{ m/s (mod)}$</td>
</tr>
<tr>
<td>C1</td>
<td>$\leq 1.0 \text{ cm}^2$</td>
<td>$V_{\text{max}} \geq 4 \text{ m/s}$</td>
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<td></td>
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</tr>
<tr>
<td>C2</td>
<td>$\leq 1.0 \text{ cm}^2$</td>
<td>$V_{\text{max}} \geq 4 \text{ m/s}$</td>
</tr>
<tr>
<td>D1</td>
<td>$\leq 1.0 \text{ cm}^2$</td>
<td>$V_{\text{max}} &gt; 4 \text{ m/s}$</td>
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<tr>
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</tr>
<tr>
<td>D2</td>
<td>$\leq 1.0 \text{ cm}^2$</td>
<td>$V_{\text{max}} &lt; 4 \text{ m/s}$</td>
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<tr>
<td>D3</td>
<td>$\leq 1.0 \text{ cm}^2$</td>
<td>$V_{\text{max}} &lt; 4 \text{ m/s}$</td>
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Statins and Other Lipid-Lowering Agents Do Not Affect Progression of AS

Simvastatin and Ezetimibe in Aortic Stenosis (SEAS) Trial

• Small, prospective trial
• Lipid lowering agents v. placebo
• Failed to demonstrate that aggressively lowering lipids had any effect on the progression of AS in adults.

Aortic Stenosis Progression Observation: Measuring Effects of Rosuvastatin (ASTRONOMER) Trial

- Patients with mild to moderate AS
- Randomly assigned to lipid lowering agents v. placebo
- No change in mortality, rates of AS progression, or time to valve replacement.

Cautiously Use Diuretics

• Beneficial if a patient has fluid volume overload.

• Don’t routinely use diuretics in patients with AS.

• Over diuresis can cause:
  • Hypovolemia
  • Decreased left ventricular stroke volume
  • Decreased cardiac output
  • Orthostatic hypotension
Use of ACEI/ARBs in AS

• May improve outcomes
• Start with low-dose
• Gradually titrate up dose to prevent hypotension

Beta-Blockers in AS

- Should generally be avoided in AS, unless there are specific indications for an individual patient where the benefit out weighs the risk.
  - e.g.: Heart rate or rhythm control, comorbid disease where BB are indicated.

- Risks of BB in AS:
  - Decreased myocardial contractility
  - May lead to LV failure in patients: fixed stroke volume relies on increased heart rate to increase cardiac output during activity or times of stress

\[
\text{Cardiac Output} = \text{Stroke Volume} \times \text{Heart Rate}
\]

SURGICAL MANAGEMENT OF SEVERE AORTIC STENOSIS

When and how to refer a patient for evaluation for aortic valve replacement.
Indications for Aortic-Valve Replacement (AVR).

Otto CM, Prendergast B.
The patients with symptomatic aortic stenosis that are at the highest risk of mortality, have low cardiac outputs, low EFs, & low-transvalvular gradients.

Pericardial (Tissue) Replacement Valves

• Made from either bovine or porcine pericardial tissue
• Indicated in older patients, those with bleeding issues
• Younger patients with active lifestyles may prefer this type.

Pros: Does not require anticoagulation

Cons: Requires reoperation if/when valve deteriorates
Mechanical Replacement Valves

- Indicated in younger patients
- May not be the best for women of child bearing age
- Often used for patients who are on life-long anticoagulation for another reason

- Pros:
  - Valve longevity
  - Freedom from re-operation

- Cons:
  - Life-long anticoagulation with warfarin
  - Goal INR for AVR is 2.0-3.0
Surgical AVR (SAVR)
Surgical AVR Procedure
ALTERNATIVES TO TRADITIONAL SURGICAL AVR FOR HIGH-RISK PATIENTS
How is High Risk Defined?

- Society of Thoracic Surgeons (STS) Predicted Risk of Mortality (STS-PROM)
  - Mortality risk > 10%
- Calcified ascending aorta; “porcelain aorta”
- Multi-valve disease
- Severe lung disease
- Severe liver disease
- Frailty (multiple frailty scales exist)
- “Hostile” chest
Aortic Arch Atheroma: High Risk

Image courtesy of Walter Tan, MD.
“The opinion of an experienced heart team is the best indicator of risk.”

Balloon Aortic Valvuloplasty

- Modest benefit
- Risks: Stroke, aortic insufficiency, and vascular complications
- Short-lived results:
  - Fracturing the valve leads to tissue damage.
  - Tissue repair mechanisms such as granulation tissue development and valve fibrosis lead to restenosis.
  - Restenosis occurs 50% of patients by 6 months, and the majority of patients at 1 year.
- Indications: bridge to surgical or transcatheter AVR in symptomatic or hemodynamically unstable patients.


Transcatheter Aortic Valve Replacement (TAVR)

- Allows for replacement of stenotic aortic valves without stopping the heart and putting the patient on the cardiopulmonary bypass pump in patients who are too high risk for surgical AVR..

- Successfully performed in 2002.

- Routes of valve deployment:
  - Transfemoral (most common)
  - Transapical
  - Transaortic
  - Transaxillary
  - Transsubclavian
Edwards LifeScience SAPIEN Valves

CoreValve ReValving System (Medtronic)

- Now indicated for TAVR in patient with failed surgical implanted bioprosthetic aortic valves.

Permission to use photo request sent to Medtronic.

PARTNER TRIAL

• Large-scale trial: 26 centers
• Predicted risk of operative mortality is ≥15% and/or a minimum STS score of 10
• Findings: TAVR was superior to medical management of AS
• Absolute Mortality Reduction:
  • 1 year: 20%
  • 2 years: 36%
• TAVR was non-inferior to surgical AVT (SAVR) at 1 & 2 years
  • Benefit: Decreased morbidity

Referring Patients for TAVR

1. **Patient with severe AS**
2. **Decision discussed with patient, family, & referring provider**
3. **Multidisciplinary Heart Team Reviews Findings**
4. **Diagnostic Testing**
5. **Referred to TAVR Clinic**
6. **Functional Testing**
TAVR Candidate?

CABG '91 (stents 2010, 2011): Grafts are patent on cardiac catheterization

PAD: L Internal Carotid Artery Stent; Renal Artery Stent

Permanent pacemaker
Paroxysmal atrial fibrillation (PAF) (CHADS = 4)

Type 2 DM on insulin

COPD – 72 pack years
Stage 3 chronic kidney disease (CKD)
Echo

AVA = 0.43 cm²

Mean gradient = 41 mmHg

Courtesy of Walter Tan, MD
<table>
<thead>
<tr>
<th>Procedure Name</th>
<th>Isolated AVRepl</th>
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<tbody>
<tr>
<td>Risk of Mortality</td>
<td>12.5%</td>
</tr>
<tr>
<td>Morbidity or Mortality</td>
<td>39.1%</td>
</tr>
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</table>

- **Coronary Artery Bypass**
  - Options: Yes, No, Missing

- **Ventricular Assist Device**
  - Options: Yes, No, Missing

- **Valve Surgery**
  - Options: Yes, No, Missing

- **Aortic**
  - Options: No, Replacement, Repair/Reconstruction, Root Reconstruction with Valve Conduit, Replacement + aortic graft conduit (not a valve conduit), Root Reconstruction with Valve Sparing, Resuspension Aortic Valve with replacement of ascending Aorta, Resuspension Aortic Valve without replacement of ascending Aorta, Resection Sub-Aortic Stenosis, Missing

- **Mitral**
  - Options: No, Replacement, Repair/Reconstruction, Root Reconstruction with Valve Conduit, Replacement + aortic graft conduit (not a valve conduit), Root Reconstruction with Valve Sparing, Resuspension Aortic Valve with replacement of ascending Aorta, Resuspension Aortic Valve without replacement of ascending Aorta, Resection Sub-Aortic Stenosis, Missing
CTA 3D RECON (.625 MM CUTS):

Image courtesy of Walter Tan, MD
Coronal (widest)

Sagittal (smaller diameter)

AP fluoroscopy

TTE parasternal long axis

Courtesy of Walter Tan, MD.
Left Main Height – distance from annulus

Coronal oblique images

Courtesy of Walter Tan, MD
TAVR Procedure Video
Courtesy of Walter Tan, MD
Two-Year Mortality, Stratified According to the Society of Thoracic Surgeons (STS) Risk Score.

- **STS <5%**
  - Hazard ratio, 0.37 (95% CI, 0.13–1.01)
  - P=0.04
- **STS 5–14.9%**
  - Hazard ratio, 0.58 (95% CI, 0.41–0.81)
  - P=0.002
- **STS ≥15%**
  - Hazard ratio, 0.77 (95% CI, 0.46–1.28)
  - P=0.31

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<th>Months</th>
<th>TAVR</th>
<th>Standard therapy</th>
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Two-Year Mortality, Stratified According to the Society of Thoracic Surgeons (STS) Risk Score.

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No. at Risk

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CoreValve ReValving System (Medtronic)

- Now indicated for TAVR in patient with failed surgical implanted bioprosthetic aortic valves.

Permission to use photo request sent to Medtronic.

Potential TAVR Complications

- Embolic stroke: 1-4%
- Paravalvular regurgitation: Common & usually mild.
- Significant paravalvular leak may occur
  - May require an additional procedures or conversion to SAVR.
- AV nodal blocks (risk varies by type of valve used)
  - Risk of requiring permanent pacemaker varies between 5-30%
- Left main coronary artery obstruction: < 1%
- Arterial injury
- Bleeding
- Infection

TAVR Durability & Longevity

- Paravalvular regurgitation is common & usually mild.
- Estimated that the valves can last 10 years.
- Not much data after 3-5 years post-insertion available.
- Valves can fail
- No evidence at this time that the valves will be durable enough to implant in younger patients.
Conclusions

- AS is progressive and severely affects patients’ quality of life and functional abilities
- Mitigating risk factors and treating comorbidities such as hypertension and dyslipidemia early may help prevent AS.
- More research is needed before specific medical therapies can be recommended to prevent the progression of AS
- Medical management is indicated for patients with mild to moderate stenosis
- Patients with severe AS can benefit from referral to a valve clinic.
- Both SAVR and TAVR improve mortality, decrease symptoms of AS, & improve quality of life.
Questions?
References


References