New Therapies for Treatment of Valvular Heart Disease – Is Open Heart Surgery Still Necessary?
Part 1: Identifying Candidates & When Intervention is Required

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Disclosures

• Nothing to disclose.
• Chuckles approved this talk
What we will do this morning

• Primarily this will focus on Aortic Valve Stenosis
• Prevalence and types of Aortic Valve Disease
• Natural History of Aortic Stenosis
• Diagnosis and Evaluation
• The New Guidelines for the Treatment of Patients with Valvular Heart Disease from the American College of Cardiology
You don’t have to look far....

• Aortic Valve Stenosis is the commonest valve lesion in the World.

• In Park Ridge, estimates are:
  – ~ 400 bicuspid Aortic Valves
  – ~ 450 Degenerative Calcific Aortic Valves of varying degree
  – An unknown number of rheumatic aortic valves predominantly in the immigrant populations.
Etiology of Valve Disease

- **Congenital Malformations**: Most are rare except for Bicuspid Aortic Valves which constitutes 1% of the US population. Inherited *genetic* disease. Associated with aortic aneurysms. Seventy percent become stenotic or narrowed in the person’s lifetime. Half of all aortic valve replacements in the US are for bicuspid valve disease.

- **Rheumatic Fever**: These valves are scarred due to the *infectious* process. This involved the mitral, aortic, tricuspid and pulmonic valves in that order.

- **Degenerative Disease**: This is an *age related* process. All valves can either become stenotic or insufficient over one’s lifetime particularly the aortic valve. Degenerative (age related aortic stenosis) is seen in ~2% of the over 65 yr population; 5-7% of over 75 yr population.
Mechanisms of Disease

NORMAL

BICUSPID

RHEUMATIC

DEGENERATIVE

Braunwald’s Heart Disease, 9th edition.
ASE Guidelines: Figure 1 Aortic stenosis aetiology: morphology of calcific AS, bicuspid valve, and rheumatic AS (Adapted from C. Otto, Principles of Echocardiography, 2007).
Bicuspid Aortic Valve

The Good, the Bad and the Ugly

John Ritter

Terminator

Ugly
The Bicuspid Aortic Valve

- The commonest genetic cardiac disease.
- Congenital fusion or poor development of the raphae.
- Most are autosomal dominant, ~ 1% of the population.
- Valves may be stenotic, insufficient or both to varying degree.
- Associated Aortopathy should not be forgotten:
  - 80X increase in proximal aortic aneurysm
  - 8X increase in proximal aortic dissection
  - Unknown number of coarctations
  - Unknown number of cervical-cerebral dissections
  - Association with other genetic syndromes (eg. Turner’s)
Degenerative (formerly Senile) Calcific Aortic Valve Stenosis
Degenerative Aortic Valve Stenosis

• This is a disease of the aortic valve cusps. The commissures are intact but the fold line in the cusp after a billion heart beats begins to fibrose and calcify.
• Like holding a rock in your palm while trying to make a fist.
• If we live long enough, we will all get this.
Primary Symptoms are the same for all forms of Aortic Valve Stenosis

Dyspnea, Shortness of Breath, Heart Failure

Syncope or Fainting, particularly with exertion

Chest Pain, Angina Pectoris from coronary ischemia
Aortic Valve Stenosis

• This is the commonest valve lesion.
• There is no medical treatment for this.
• It is a lethal disease in which 50% of patients will be dead within 2 years of the onset of symptoms.
• Surgical Aortic Valve Replacement (SAVR) can be performed at low risk even in the elderly.
• For those who are too ill or too frail to tolerate surgery, transcatheter valve replacement (TAVR) is feasible and available.
Historical Aortic Stenosis
PROGNOSIS & NATURAL HISTORY

• As you can see from the prior graph, once symptoms of shortness of breath, fainting or chest pain occur, there is a steep mortality curve.
• About 50% will be dead at 2 years and nearly all will be dead at 5 years.
• Despite this chart being 47 years old, the current transcatheter trials (PARTNER) shows much the same for severe aortic stenosis now.
• Progressive debility rather than preserved functional capacity is the rule.
Why Detection and Treatment are Important

• There are large numbers of patients with treatable aortic valve disease in the US.
• Surgical and catheter based treatments are available and are feasible to do and are cost effective. There is no medical therapy for this disease.
• The estimation from the American College of Cardiology is that ~ 40% of all patients with treatable aortic valve stenosis get no therapy at all. Poor recognition, poor detection, lack of understanding by the lay and medical communities are likely to be the reason for this.
Echocardiography for AS

- With the visual 2D and 3D echocardiographic reconstruction of the heart and with the application of Doppler/Color, we can measure the degree of leakage and the degree of narrowing of all heart valves.

- The Doppler Principle tells us that as the orifice narrows, the blood velocity must increase to eject the same volume. Thus the continuity equation (conservation of mass) applies with $A_1 \times V_1 = A_2 \times V_2$.
Doppler and Planimetry

Severe increase in velocity to 5.4m/sec (Normal 1-2m/sec)

2D Planimetry of Degenerative Aortic stenosis with AVA 0.6cm² (Normal 2-4cm²)
2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Short Summary with Emphasis on Aortic Valve Stenosis

## Stages of Valvular AS.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
<th>Valve Anatomy</th>
<th>Valve Hemodynamics</th>
<th>Hemodynamic Consequences</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At risk of AS</td>
<td>• Bicuspid aortic valve (or other congenital valve anomaly) &lt;br&gt;• Aortic valve sclerosis</td>
<td>• Aortic $V_{max} &lt; 2$ m/s</td>
<td>• None</td>
<td>• None</td>
</tr>
<tr>
<td>B</td>
<td>Progressive AS</td>
<td>• Mild-to-moderate leaflet calcification of a bicuspid or trileaflet valve with some reduction in systolic motion or&lt;br&gt;• Rheumatic valve changes with commissural fusion</td>
<td>• Mild AS: &lt;br&gt;Aortic $V_{max} 20–2.9$ m/s or mean $\Delta P &lt; 20$ mm Hg &lt;br&gt;Moderate AS: &lt;br&gt;Aortic $V_{max} 30–3.9$ m/s or mean $\Delta P 20–39$ mm Hg</td>
<td>• Early LV diastolic dysfunction may be present&lt;br&gt;• Normal LV EF</td>
<td>• None</td>
</tr>
<tr>
<td>C</td>
<td>Asymptomatic severe AS</td>
<td>• Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening</td>
<td>• Aortic $V_{max} &gt; 4$ m/s or mean $\Delta P &gt; 40$ mm Hg&lt;br&gt;AVA typically is $&lt; 1.0$ cm$^2$ (or $AVA &lt; 0.6$ cm$^2$/m$^2$)</td>
<td>• LV diastolic dysfunction&lt;br&gt;• Mild LV hypertrophy&lt;br&gt;• Normal LV EF</td>
<td>• None: Exercise testing is reasonable to confirm symptom status</td>
</tr>
<tr>
<td>C1</td>
<td>Asymptomatic severe AS</td>
<td>• Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening</td>
<td>• Aortic $V_{max} &gt; 4$ m/s or mean $\Delta P &gt; 40$ mm Hg&lt;br&gt;AVA typically $&lt; 1.0$ cm$^2$ (or $AVA &lt; 0.6$ cm$^2$/m$^2$)</td>
<td>• LV diastolic dysfunction&lt;br&gt;• Mild LV hypertrophy&lt;br&gt;• Normal LV EF</td>
<td>• None</td>
</tr>
<tr>
<td>C2</td>
<td>Asymptomatic severe AS with LV dysfunction</td>
<td>• Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening</td>
<td>• Aortic $V_{max} &gt; 4$ m/s or mean $\Delta P &gt; 40$ mm Hg&lt;br&gt;AVA typically $&lt; 1.0$ cm$^2$ (or $AVA &lt; 0.6$ cm$^2$/m$^2$)</td>
<td>• LV diastolic dysfunction&lt;br&gt;• Mild LV hypertrophy&lt;br&gt;• Normal LV EF</td>
<td>• None</td>
</tr>
<tr>
<td>D</td>
<td>Symptomatic severe AS</td>
<td>• Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening</td>
<td>• Aortic $V_{max} &gt; 4$ m/s or mean $\Delta P &gt; 40$ mm Hg&lt;br&gt;AVA typically $&lt; 1.0$ cm$^2$ (or $AVA &lt; 0.6$ cm$^2$/m$^2$) but may be larger with mixed AS/AR&lt;br&gt;Dobutamine stress echocardiography shows &lt;br&gt;$AVA &gt; 1.0$ cm$^2$ with $V_{max} &gt; 4$ m/s at any flow rate</td>
<td>• LV diastolic dysfunction&lt;br&gt;• LV hypertrophy&lt;br&gt;• Pulmonary hypertension may be present</td>
<td>• Exertional dyspnea or decreased exercise tolerance&lt;br&gt;• Exertional angina&lt;br&gt;• Exertional syncope or presyncope</td>
</tr>
<tr>
<td>D1</td>
<td>Symptomatic severe high-gradient AS</td>
<td>• Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening</td>
<td>• Aortic $V_{max} &gt; 4$ m/s or mean $\Delta P &gt; 40$ mm Hg&lt;br&gt;AVA typically $&lt; 1.0$ cm$^2$ (or $AVA &lt; 0.6$ cm$^2$/m$^2$)</td>
<td>• LV diastolic dysfunction&lt;br&gt;• LV hypertrophy&lt;br&gt;• LVEF $&lt; 50%$</td>
<td>• HF&lt;br&gt;• Angina&lt;br&gt;• Syncope or presyncope</td>
</tr>
<tr>
<td>D2</td>
<td>Symptomatic severe low-flow/low-gradient AS with reduced LVEF</td>
<td>• Severe leaflet calcification with severely reduced leaflet opening</td>
<td>• Aortic $V_{max} &gt; 4$ m/s or mean $\Delta P &gt; 40$ mm Hg&lt;br&gt;Indexed $AVA &lt; 0.6$ cm$^2$/m$^2$ and&lt;br&gt;$V_{max}$ indexed by body surface area&lt;br&gt;Stroke volume index $&lt; 35$ mL/m$^2$&lt;br&gt;Measured when patient is normotensive (systolic BP $&lt; 140$ mm Hg)</td>
<td>• Increased LV relative wall thickness&lt;br&gt;Small LV chamber with low stroke volume&lt;br&gt;Restrictive diastolic filling&lt;br&gt;LVEF $&lt; 50%$</td>
<td>• HF&lt;br&gt;• Angina&lt;br&gt;• Syncope or presyncope</td>
</tr>
<tr>
<td>D3</td>
<td>Symptomatic severe low-gradient AS with normal LVEF or paradoxical low-flow severe AS</td>
<td>• Severe leaflet calcification with severely reduced leaflet opening</td>
<td>• Aortic $V_{max} &gt; 4$ m/s or mean $\Delta P &gt; 40$ mm Hg&lt;br&gt;Indexed $AVA &lt; 0.6$ cm$^2$/m$^2$ and&lt;br&gt;$V_{max}$ indexed by body surface area&lt;br&gt;Stroke volume index $&lt; 35$ mL/m$^2$&lt;br&gt;Measured when patient is normotensive (systolic BP $&lt; 140$ mm Hg)</td>
<td>• Increased LV relative wall thickness&lt;br&gt;Small LV chamber with low stroke volume&lt;br&gt;Restrictive diastolic filling&lt;br&gt;LVEF $&lt; 50%$</td>
<td>• HF&lt;br&gt;• Angina&lt;br&gt;• Syncope or presyncope</td>
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</table>

AR indicates aortic regurgitation; AS, aortic stenosis; AVA, aortic valve area; LVEF, left ventricular ejection fraction; $\Delta P$, pressure gradient; and $V_{max}$, maximum aortic velocity.
For Aortic Valve Stenosis...

**Stages of Aortic Stenosis**

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<th>Stage</th>
<th>Definition</th>
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<tr>
<td>A</td>
<td>Risk of valve disease (BAV, RF, CVD risk)</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  
| D1: High gradient AS  
| D2: Low gradient, LV dysfunction  
| D3: Low gradient, normal LV function |
Low Flow, Low Gradient Aortic Stenosis

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

- Normal EF if clinical, hemodynamic and anatomic data support severe AS
  - class Ila

- Reduced EF, with contractile reserve
  - class Ila

- Normal EF only after careful confirmation of severe AS
  - class Ila

2014 Valve Summit
General treatment algorithm for patients with severe symptomatic aortic stenosis

Patient with severe, symptomatic aortic stenosis:
- Maximal velocity > 4 m/s
- Aortic valve area < 1.0 cm²
- Mean gradient > 40 mm Hg

Candidate for open heart surgery

Surgical aortic valve replacement

Not a candidate for open heart surgery

Candidate for percutaneous aortic valve replacement

Percutaneous aortic valve replacement

Not a candidate for percutaneous aortic valve replacement

Candidate for bridging therapies (aortic valvuloplasty, intra-aortic balloon counterpulsation, or sodium nitroprusside)

Bridging therapy
Reconsider candidacy for surgical or percutaneous aortic valve replacement

FIGURE 1
Aortic Stenosis

• Severe AS Symptomatic: Easy. Class I indication for intervention – SAVR
• Contraindication or High Risk: Clear. Class IIA – TAVR
• Severe AS Asymptomatic: If over 5 m/sec Class IIA indication for intervention. If not, stress testing for clarity of symptoms.
Aortic Stenosis: Less Clear indications.

- **Reduced EF/Low flow/Low Gradient**: Dobutamine Echocardiographic Stress Testing

- This is when the EF is low and Mean gradient is $<40$ mmHg and peak velocity is $<4$ m/sec. Incremental dobutamine infusion which increases contractility which gives a gradient or velocity of severe range at any dose of dobutamine infusion indicates need for intervention.
Aortic Stenosis: Less Clear Indications

• **Normal EF, Low Flow, Low Gradient**
• A very unclear area. Small people, hypertension, vascular resistance may play a role.
• You have to decide whether the AS of Normal EF/Low Flow/Low Gradient is actually the cause of symptoms (dyspnea, angina, syncope).
• Would refer to a center of excellence as we have limited data on this and it may take multiple opinions with advanced imaging.
Questions?

• This is not an easy topic and there are no silly questions.
So, a 94 yo male comes in....

- Healthy and workes as a comedian
- Normal kidney/liver function
- No exercise
- Smokes cigars
What is his surgical risk for AVR?

- 1%
- 5%
- 10%
- 20%

By the Society of Thoracic Surgery Database: Less than 4%. Nonetheless, most patients seem to want noninvasive or limited surgery or TAVR.
THANK YOU FOR YOUR TIME. I HOPE YOU FOUND THIS USEFUL

Sadly, Chuckles did not.