Transcatheter Aortic Valve Replacement: Evolving Therapy for Severe Aortic Stenosis

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Evolving Therapy for Severe Aortic Stenosis

• Review pathophysiology, natural history, and prevalence of severe aortic stenosis.
• Review recent clinical trials transcatheter aortic valve replacement
• Touch on the future of TAVR
• Review cases

The Human Heart

Aortic Stenosis
Pathogenesis of Aortic Stenosis

**Law of Laplace**

Wall Stress = $\frac{PR}{2\text{thickness}}$

LV thickness increases to offset rise in pressure.

Normalizing wall stress is important for maintaining normal EF and stroke volume.

Prevalence of Aortic Stenosis

- Most common valvular heart disease in the Western World
- Up to 7% of the population over 65y.
- Men >> Women
- 80% of symptomatic cases are in men.

Life Expectancy with Severe Aortic Stenosis
Survival in Severe Symptomatic Aortic Stenosis


Survival in Asymptomatic Severe AS

Pellika PA et al. J Am Coll Cardiol 1990; 15: 1012-17

Treatment Options

- High risk surgery
- Palliative balloon valvuloplasty + medical management
- Medical Tx
Who is high risk or inoperable?

Surgical Risk Score (STS, EuroScore)
Heavily calcified “Porcelain” aorta
Severe chest wall deformity
Severe Oxygen dependant COPD (FEV<50%)
Frailty
Surgical gestalt

STS Risk Score Online Calculator

What defines severe AS?

- Symptoms along with clinical suspicion and objective concerns....
- Maximum transvalvular velocity >4m/s
- Mean gradient >40mmHg
- AVA <1.0cm²
- AVA index (AVA/BSA) <0.6cm²/m²

Risks of Cardiac Surgery by Child-Pugh Score

Mortality

Hepatic decompensation

C-P Score > 7 had 86% sensitivity and 92% specificity for predicting mortality

Low Flow Low Gradient Severe AS

When EF is low (<40%) differentiating true from pseudo-AS can be difficult.

Dobutamine stress (≤20mcg/kg/min)

True Severe AS

Pseudo Severe AS

Paradoxical Low Flow Low Gradient

- Easily missed diagnosis
- Potentially 20% of severe AS patients.
- Defined as “normal EF” with low stroke volume
  - (Stroke Volume Index <35ml/m²)
- May require invasive evaluation.

Transcatheter Aortic Valve Replacement

- Multicenter RCT
- Standard medical therapy vs TAVR via Transfemoral Access
- Primary Endpoint: Rate of death from any cause.
- CoPrimary Endpoint: Rate of composite of death from any cause or time to repeat hospitalization due to valve or procedure related issue.

Transcatheter Aortic Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

What does this mean?

NNT to prevent one death at 1 year:  5
NNT to prevent one death or hospitalization:  3

Perspective:

Statin for primary prevention (mortality): NNT = 83
Aspirin for MI     NNT=40
AICD therapy     NNT=15
Randomized 699 high risk pts with severe symptomatic aortic stenosis to TAVR vs SAVR.

Primary Endpoints: Death rate from any cause at 1 year.

Utilizing Edwards Sapien (1st gen) 23mm and 26mm valves
Time to Event Curves

A. Death from Any Cause, All Patients

B. Death from Any Cause, Transcatheter Placement Cohort

C. Death from Any Cause, Transcatheter Placement Cohort

D. Death from Any Cause or Major Event

Symptom Status

NYHA
- Dead
- IV
- III
- II
- I

Percentage of Patients
- Baseline
- 30 Days
- 6 Months
- 1 Year

Admission Resource Use and Costs

Transfemoral Cohort

<table>
<thead>
<tr>
<th>Resource Category</th>
<th>Trans</th>
<th>TAVR</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalization</td>
<td>594 (47)</td>
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<td>0.99</td>
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<td>Total hospital LOS</td>
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<td>12.9 (12.9)</td>
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</tr>
<tr>
<td>P &lt; 0.0001</td>
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Transapical Cohort

<table>
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<th>Trans</th>
<th>TAVR</th>
<th>p Value</th>
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Health Related Quality of Life In Inoperable

A. Subgroup

B. All Regression

C. Regression of All Regression

D. Regression of All Regression

Interaction

- 0.24
- 0.23
- 0.77
- 0.74
- 0.57
- 0.54
- 0.56
Health Related Quality of Life in High Risk

TAVR-TF vs SAVR

TAVR-TA vs SAVR

Risk of poor outcome or less than expected benefit

- Poor functional capacity (6-min walk test)
- Lower mean gradients
- Severe oxygen dependant COPD
- Chronic kidney disease
- Cognitive impairment

84y/o male candidate for TAVR with EF <47%
Mean gradient 33mmHg
COPD requiring Oxygen
6 min walk distance <14m
MMSE of 25

>55% risk of poor outcome or 37% risk of death at 6mos

TAVR Candidates Under Current Treatment Conditions

Future of TAVR

PARTNER II S3 Study

**Baseline Patient Characteristics**

<table>
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<th>Characteristic (%)</th>
<th>S3HR (n=568)</th>
<th>S3I (n=619)</th>
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<tr>
<td>NYHA Class III or IV</td>
<td>39.1</td>
<td>72.6</td>
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<tr>
<td>Previous CABG</td>
<td>33.1</td>
<td>28.0</td>
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<tr>
<td>Previous CVA</td>
<td>11.0</td>
<td>8.9</td>
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<tr>
<td>Peripheral Vascular Disease</td>
<td>35.2</td>
<td>28.3</td>
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<tr>
<td>Diabetes</td>
<td>34.5</td>
<td>34.1</td>
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<tr>
<td>COPD - O₂ Dependent</td>
<td>11.7</td>
<td>5.0</td>
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<tr>
<td>CKD = Creat. ≥ 2mg/dL</td>
<td>12.6</td>
<td>7.5</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>43.7</td>
<td>36.0</td>
</tr>
<tr>
<td>Permanent Pacemaker</td>
<td>16.3</td>
<td>13.2</td>
</tr>
<tr>
<td>Frailty</td>
<td>30.9</td>
<td>8.6</td>
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**Mortality and Stroke: S3HR**

- All-cause Mortality: S3HR 2.2, S3I 1.4
- Stroke: S3HR 1.8, S3I 0.9

**Mortality and Stroke: S3I**

- All-cause Mortality: S3I 1.1, S3 0.9
- Stroke: S3I 2.6, S3 1.0

- New pacemaker rate ~10% (up from ~6%)
- Major vascular complications ~5% (down from over 16%)
87M with NYHA Class III CHF and severe AS

Pre TAVR mean gradient: 43mmHg
Post TAVR mean gradient: <10mmHg
HPI
81F with prior surgical valve replacement with tissue valve admitted with CHF and unstable angina.

PMH: HTN, PHTN, CAD with AMI in 2005;
STS>15%

Coronary angiography: Moderate non-obstructive CAD

Admission TTE:
LV - moderate LVH, EF 65% RV - normal; RVSP 77mmHg
Aortic Valve: mean gradient 113 mmHg, mod AI
Mitral Valve: Mild MS, Mod MR
TV/PV - unremarkable

Baseline Imaging
Mean Gradient: 16mHg
Peak Gradient: 30mmHg
Expected: 13 +/- 5.3mmHg
30-day f/u NYHA I, CCS 0

Questions?

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Nilto De Oliveira, MD
Shahab Akhter, MD

Website: www.uwhealth.org/heart-valve/heart-valve-clinic/32422

Survival in low gradient, low EF without contractile reserve

Pellika PA et al. Circulation 2005; 111: 3290-95