Aortic Stenosis: Background

Severe Symptomatic Aortic Stenosis: 50% 2-year Mortality

* Ross and Braunwald 1968, Circulation
* Bouma B J et al. Heart. 1999;82:143-146
* Iung B et al. European Heart Journal 2003;24:1231-1243
* Pellikka, Sarano et al. Circulation 2005
Initial TAVR Trials

**PARTNER I TRIAL**

- **n = 699**
  - **High-Risk**
  - **Inoperable**

**Symptomatic Severe Aortic Stenosis**
1057 Total Patients Enrolled

**ST** ≥ **10; Predicted Mortality > 15%**

**Predicted death, serious morbidity > 50%**

TAVR v SAVR

TAVR v Standard Tx

**CoreValve US Pivotal Trial**

- **n = 487**
  - **High-Risk**
  - **Extreme Risk**

**Symptomatic Severe Aortic Stenosis**
1381 Total Patients Enrolled

**Predicted Mortality > 15%**

**Predicted death, serious morbidity > 50%**

TAVR v SAVR

TAVR v Performance Goal

**TAVR Candidacy in August 2014**

- **n = 699**
- **TAVR v SAVR**
- **TAVR v Standard Tx**
- **TAVR v Performance Goal**
Current TAVR Candidacy

<table>
<thead>
<tr>
<th>STS 0-3</th>
<th>STS 4-8</th>
<th>STS &gt; 8</th>
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<td>EuroScore 0-2</td>
<td>EuroScore 3-5</td>
<td>EuroScore &gt; 6</td>
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- LOW
- INTERMED
- HIGH
- INOPERABLE

- SAPIEN
- CORE
- SAVR

OBSERVANT
- Prospective registry
- TAVR or SAVR
- 93 sites in Italy, 2010-2012
- EuroScore < 4
- Mean age 80
- 85% preserved EF
- Propensity Matched n = 355

All-cause mortality lower with SAVR at 3 years
**OBSERVANT**
- Prospective registry
- TAVR or SAVR
- 93 sites in Italy, 2010-2012
- EuroScore < 4
- Mean age 80
- 85% preserved EF
- Propensity Matched n = 355

* MACE* lower with Surgical AVR at 3 years

* mortality, stroke, AMI, coronary revascularization

**NOTION**
- TAVR or SAVR (1:1, n=280)
- 81% were low-risk (STS < 4)
- 2009-2013
- 3 centers, Denmark, Sweden
- Mean age 79

All-cause mortality no different at 12 months
NOTION
- TAVR or SAVR (1:1, n=280)
- 81% were low-risk (STS < 4)
- 2009-2013
- 3 centers, Denmark, Sweden
- Mean age 79

Stroke incidence no different at 12 months

The Low Risk Question...

OBSERVANT (CoreValve)
- Observational Registry
- Low Risk TAVR in 44% overall
  - Indication creep?
  - Patient discretion?
  - Uncaptured features?
- Favors SAVR

NOTION (SAPIEN)
- Randomized Trial
- Relatively small (n = 280)
- Randomized 18% screened
- More transfemoral (96%)
- TAVR and SAVR equivalent

Transfemoral access, newer generation valves, randomized trials
TAVR Candidacy in 2016

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<td>EuroScore &gt; 6</td>
<td></td>
</tr>
<tr>
<td>&lt; 70 yo, no comorbidities</td>
<td>80 years old, 1-2 comorbidities</td>
<td>80 years old Prior sternotomy</td>
<td></td>
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</tbody>
</table>

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**What 1st endpoint is appropriate?**

**SAVR**

- CORE
- SAPIEN

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**TAVR Success and Complications: Stroke**

- Initially 5-7% incidence at 30d
- 95% Ischemic, Higher mortality
- Now 2-3%, comparable to SAVR
- Positioning, Deployment

**EARLY ( < 1 Day; 54%)**
- Experience
- Diabetes
- Balloon-dilation
- New atrial fibrillation

**LATE (30 Days; 46%)**
- Chronic Atrial fibrillation
- Peripheral arterial disease
- Cerebrovascular disease
- Anticoagulation

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Reardon et al., NEJM 2017, 37(6); Vahl et al., JACC 2016, 67(12); Nombela-Franco et al. Circ 2012 26(25)
TAVR Success and Complications: Vascular

- 15% Major, 12% Minor
- Female (HR 2.3)
- Sheath/Femoral Art > 1.05
- Diabetes
- Calcified vessels
- Recent PCI
- 1-Yr Mortality (HR 2.3)
- Rate likely decreasing*

Evolving Populations and Risks

- Procedural Issues
  - Vascular Complications
  - Stroke
  - Bleeding
  - Procedural Mortality
  - Hemodynamic Support

- Valve Considerations
  - Pacemaker
  - Valve Durability

- Procedural Issues
- Low Surgical Risk
- Moderate Aortic Stenosis
- Aortic Insufficiency
- Bicuspid Aortic Stenosis

Holmes et al. 2015, NEJM 66(25); Genereux 2012, JACC 60(12)
Challenges to Success in Low-Risk Patients

Procedural Considerations Have Greater Relevance

- Continue to reduce paravalvular leak
- Continue to reduce vascular complications
- Continue to reduce incidence of heart block
- Continue to reduce incidence of stroke

Device Considerations Will be More Longstanding

- More clinical experience to observe valve durability
- Valve-in-valve potential
- Access to coronary arteries

TAVR Success and Complications: VHD

Valvular Hemodynamic Deterioration

>10% mm Hg increase in gradient

Trigo et al. 2016, JACC 67:644-655

N = 1,521; Multicenter registry

4.5% (n = 68) VHD at mean of 20-mo

Independent predictors:
- No anticoagulation
- Valve in valve
- Smaller valves
- BMI

Vemulapalli et al., ACC.16

N = 22,271; TVT registry

2.1% at 30-d, 2.5% at 12-mo

Not associated with adverse outcomes

> 20 mm Hg gradient or > mod AI

Dvir et al., EuroPCR 2016

N = 387 from 2 sites, 2002-2011

2/387 (0.55) survived 10 years

9% at 5 yrs

20% at 6 yrs

60% at 8 yrs

2/3 from AI, 1/3 from stenosis

Independent of age

Independent predictors:
- Renal failure

Bioprosthetic surgical valve

durability is up to 20 years
Reduced Leaflet Motion/Thrombosis

PORTICO IDE Study, High-Extreme Risk Patients

PORTICO vs Commercial TAVR Valve, CT at 30d

A patient had a stroke, and CT finding of reduced leaflet motion. Another asymptomatic patient had similar CT finding.

Study temporarily suspended, now resumed

Makkar et al. (2015) NEJM

Reduced Leaflet Motion Observed

- Grading Leaflet motion
  - Normal
  - Mild reduction ( < 50%)
  - Moderate reduction (50-70%)
  - Severe reduction (> 70%)
  - Immobile

<table>
<thead>
<tr>
<th>PORTICO TRIAL (30-d CT)</th>
<th>Registries (median 87-d CT)</th>
</tr>
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<tbody>
<tr>
<td>PORTICO 13/37 (40%)</td>
<td>5/15 (33%)</td>
</tr>
<tr>
<td>SAPIEN 6/14 (43%)</td>
<td>7/58 (12%)</td>
</tr>
<tr>
<td>CoreValve 0/4 (0%)</td>
<td>2/24 (8.3%)</td>
</tr>
<tr>
<td>Lotus Valve --</td>
<td>1/8 (12.5%)</td>
</tr>
<tr>
<td>Surgical Valves --</td>
<td>2/27 (7.4%)</td>
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Net 34%                 Net 13%

No difference in mean gradient at this time

Makkar et al. (2015) NEJM
## U.S. Low Risk Trials

<table>
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<tr>
<th>LOW Risk</th>
<th>TRIAL</th>
<th>DESIGN</th>
<th>ENDPOINTS</th>
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<tbody>
<tr>
<td>SAPIEN</td>
<td>PARTNER III</td>
<td>STS &lt; 4%</td>
<td>MORTALITY</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N = 1300</td>
<td>STROKE</td>
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<tr>
<td></td>
<td></td>
<td>50 Sites</td>
<td>REHOSPITALIZATION</td>
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<tr>
<td>CORE</td>
<td>MDT Low-Risk</td>
<td>STS &lt; 3%</td>
<td>MORTALITY</td>
</tr>
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<td>N = 1200</td>
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<td>Both in enrollment</td>
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<td>Leaflet motion substudies</td>
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### Conclusions

- Rapid adoption of TAVR among lower risk populations
- Outcomes, procedural considerations are different
- Valve durability issue is fundamental to success in younger patients
- Additional device and procedural iterations will likely expand potential TAVR population
TALENT IS GOD GIVEN. BE HUMBLE. FAME IS MAN-GIVEN. BE GRATEFUL. CONCEIT IS SELF-GIVEN. BE CAREFUL.

Thank You