A new option for the Diagnosis and Management of Valvular Heart Disease

Oregon Comprehensive Valve Center
I have no disclosures
Oregon Comprehensive Valve Center

• Weekly multidisciplinary case conferences to discuss optimal treatment of complex patients.
• Involvement of primary care physicians through case conferences, phone consultations, or telemedicine.
• Use of evidence-based guidelines for the evaluation, treatment and follow-up of patients with valve disease.
• Automated reminders to patients for clinical follow-up and testing with their primary care physician and the valve center.
• Access to investigational procedures and techniques for patients who are not candidates for conventional therapy.
Burden of Valve Diseases in the US

Year 2000 → 2030

Disease  | AS  | 2.5 millions → 4.6 millions  | MR  | 2.7 millions → 4.8 millions
Aortic stenosis
The new presentation
Degenerative AS
Aortic Stenosis
What do we know about AS?

What is the current Clinical Outcome of AS?
Survival in Asymptomatic AS

Event-free survival

Time from enrollment (months)

Vmax <3.0 m/s

3.0-4.0 m/s

>4.0 m/s

Otto CM et al: Circ 95(9):2262, 1997
Aortic Stenosis

- **Echocardiogram** is recommended if clinical exam detects:
  - New murmur
  - Diminished or absent S2
  - Murmur in patients with symptoms (chest pain, dyspnea, syncope or pre-syncope)

- **Exercise testing** is discouraged for aortic stenosis patients due to safety concerns, however can be performed in selected patients. Dobutamine ECHO

- **Serial testing in asymptomatic patients:**
  - Mild AS: Echo every three to five years
  - Moderate AS: Echo every one to two years
  - Severe AS: Annual echocardiogram
Treatment options:

- **Medication.** Treat symptoms of heart failure (diuretics are the mainstay). Counter to initial research, statins probably do not prevent disease progression.

- **Aortic valve replacement (AVR).** For the vast majority of adults, AVR is the only effective treatment for severe aortic stenosis.

- **Balloon valvuloplasty.** This method is largely palliative for patients of advanced age and/or with severe co-morbidities.

- **AVR: Percutaneous valve insertion.** To a large extent, the patient base for this new procedure is similar to that for balloon valvuloplasty (those of advanced age and/or with severe co-morbidities). More to come.
AS in the Elderly

Usual Management

- Asymptomatic elderly with severe VHD: “You are doing too well to consider a risky surgery”

- Symptomatic elderly with VHD: “You are too old to be operated”
Current limitations for balloon valvuloplasty in the elderly with calcific aortic stenosis

- Modest gains in AVA using traditional retrograde arterial techniques
  \[0.5-0.6 \rightarrow 0.8-1.0 \text{ cm}^2\]
- 60% hemodynamic restenosis rates at 6 months (>80% at 1 year)
- Palliative with no apparent effect on survival
Role of BAV in TAVI Era

- Stand Alone BAV
  - Patients with very limited longevity from other comorbidities (<1 year)
  - Patients with poor access or unsuitable cardiac anatomy for TAVI
  - Diagnostic challenge in the presence of other potential causes for symptom complex (e.g., lung disease)
- BAV as bridge to TAVI in unstable patients
- BAV to predilate for TAVI and size AV annulus
Study Devices

Edwards-SAPIEN THV

23mm and 26mm valve sizes

Retroflex 1

22F and 24F sheath sizes
Purpose

To assess the safety and effectiveness of TAVI compared with standard therapy, in patients with severe aortic stenosis and cardiac symptoms, who cannot undergo surgery ("inoperable"), using rigorous evidence-based clinical trial methodologies.
Transcatheter Aortic Valve Implantation in Inoperable Patients with Severe Aortic Stenosis

PARTNER TRIAL
Inclusion Criteria

- Severe calcific aortic stenosis defined as echo derived valve area of < 0.8 cm\(^2\) (EOA index <0.5cm\(^2\)), and mean gradient > 40 mmHg or jet velocity > 4.0 m/s
- NYHA functional class II or greater
- Risk of death or serious irreversible morbidity as assessed by cardiologist and two surgeons must exceed 50%
PARTNER Study Design

Symptomatic Severe Aortic Stenosis

ASSESSMENT: High Risk AVR Candidate
3105 Total Patients Screened

Total = 1058 patients

2 Parallel Trials: Individually Powered

n= 700
High Risk

ASSESSMENT: Transfemoral Access

High Risk TF
1:1 Randomization
TAVI Trans femoral VS Surgical AVR

High Risk TA
1:1 Randomization
TAVI Trans femoral VS Surgical AVR

Primary Endpoint: All Cause Mortality (1 yr) (Non-inferiority)

n=358
Inoperable

ASSESSMENT: Transfemoral Access

1:1 Randomization

Primary Endpoint: All Cause Mortality over length of trial (Superiority)

TAVI Trans femoral VS Standard Therapy (usually BAV)

Not In Study
All Cause Mortality

The graph compares the all-cause mortality rates between TAVI and Standard Rx over a period of 24 months. The mortality rates are as follows:

- **Standard Rx**
  - 1 yr = 50.7%
  - 2 yr = 60.0%
  - 3 yr = 66.7%
  - 4 yr = 70.7%

- **TAVI**
  - 1 yr = 30.7%
  - 2 yr = 32.0%
  - 3 yr = 33.3%
  - 4 yr = 33.3%

The difference at 1 year (Δ) is 20.0%, with an NNT of 5.0 pts.

Numbers at Risk:

<table>
<thead>
<tr>
<th></th>
<th>1 yr</th>
<th>2 yr</th>
<th>3 yr</th>
<th>4 yr</th>
<th>5 yr</th>
<th>6 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAVI</td>
<td>179</td>
<td>138</td>
<td>122</td>
<td>67</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Standard Rx</td>
<td>179</td>
<td>121</td>
<td>83</td>
<td>41</td>
<td>12</td>
<td></td>
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</table>
All Cause Mortality (ITT)

Crossover Patients Censored

All Cause Mortality (%)

HR [95% CI] = 0.56 [0.43, 0.73]

p (log rank) < 0.0001

Δ at 2 yr = 24.7%

NNT = 4.0 pts

Numbers at Risk

<table>
<thead>
<tr>
<th></th>
<th>TAVR</th>
<th>Standard Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>19 Months</td>
<td>179</td>
<td>179</td>
</tr>
<tr>
<td>12</td>
<td>138</td>
<td>121</td>
</tr>
<tr>
<td>6</td>
<td>124</td>
<td>85</td>
</tr>
<tr>
<td>0</td>
<td>110</td>
<td>62</td>
</tr>
<tr>
<td>0%</td>
<td>83</td>
<td>42</td>
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</table>

TAVR

Standard Rx
Mean Gradients Over Time

P < 0.0001

Mean Gradient (mm Hg)

<table>
<thead>
<tr>
<th>Time</th>
<th>Standard Rx</th>
<th>TAVI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>44.6</td>
<td>43.2</td>
</tr>
<tr>
<td>30 Day</td>
<td>33.0</td>
<td>10.8</td>
</tr>
<tr>
<td>6 Months</td>
<td>39.5</td>
<td>11.3</td>
</tr>
<tr>
<td>1 Year</td>
<td>44.4</td>
<td>12.1</td>
</tr>
</tbody>
</table>

Error bars = ± 1 Std Dev

N=163
N=143
N=100
N=89
Conclusions (2)

At 2 years, in patients with symptomatic severe AS who are not suitable candidates for surgery...

- There were more neurologic events in TAVR patients vs Standard Rx (16.2% vs 5.5%; p = 0.003) with 5 new events (3 strokes and 2 TIAs) between 1-2 years in TAVR patients.

- After 30 days, differences in stroke frequency were largely due to increased hemorrhagic strokes in TAVR patients.

- A subgroup analysis according to surgical risk score suggests that the most pronounced benefit of TAVR is in patients without extreme clinical co-morbidities.
Conclusions (1)

**At 2 years**, in patients with symptomatic severe AS who are not suitable candidates for surgery...

- TAVR remained superior to standard therapy with incremental benefit from 1 to 2 years, markedly reducing the rates of...
  - All cause mortality
  - Cardiovascular mortality
  - Repeat hospitalization
- TAVR improved NYHA functional status and decreased Class III/IV symptoms compared to standard therapy (17% vs 64%; p < 0.001).
F/U 2 YEARS

- To evaluate the clinical outcomes of TAVR compared to standard therapy at 2 years in “inoperable” aortic stenosis patients.

- To assess valve hemodynamics and durability using echocardiography.

- To perform subgroup analyses to better define the impact of co-morbidities on outcomes.
There has been explosive growth in transcatheter aortic valve implantation (TAVI) since the first procedure in 2002.

Although patient selection, operator skills, and technology have improved, all previous TAVI studies have been observational registries, without standardization of endpoint definitions.

There is a paucity of evidence-based clinical data to substantiate incremental benefits of TAVI compared with current standard therapies.
ANIMATION
Transfemoral Deployment of Edwards SAPIEN Transcatheter Heart Valve in Calcified Aortic Valve
TRANSAPICAL AORTIC VALVE IMPLANTATION:
2 Year Outcomes from The SOURCE Registry
Mean follow-up: 14.96 ± 9.28 months

<table>
<thead>
<tr>
<th>Survival</th>
<th>Transapical (N=1387)</th>
<th>All (N=2307)</th>
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</thead>
<tbody>
<tr>
<td>30 Days</td>
<td>89.1%</td>
<td>90.5%</td>
</tr>
<tr>
<td>1 Year</td>
<td>74.1%</td>
<td>76.5%</td>
</tr>
<tr>
<td>2 Years</td>
<td>65.3%</td>
<td>68.2%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>N @ Risk</th>
<th>Transapical (N=1387)</th>
<th>All (N=2307)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 Days</td>
<td>1229</td>
<td>2079</td>
</tr>
<tr>
<td>1 Year</td>
<td>903</td>
<td>1550</td>
</tr>
<tr>
<td>2 Years</td>
<td>326</td>
<td>610</td>
</tr>
</tbody>
</table>
BACKGROUND

• Technical safety and feasibility of TA-AVR has been proven.

• Accepted alternative option for patients unsuitable or seen as high-risk for AVR.

• Only limited data on long-term outcome available.

• Using data from The SOURCE Registry we analyse 2 year outcomes after TA-AVR in a large patient series.
CONCLUSION

• T-AVR using TA access is resulting in excellent 2 year survival of more than 65%.

• Initial mortality during the first 2 months is slightly higher compared to the overall SOURCE T-AVR cohort, which may be explained with the higher risk profile of TA patients.

• Over the mid-term follow-up, survival curves are parallel.

• Majority of deaths up to 2 year are mainly non-cardiac and related to comorbidities.
Index Admission Costs

TF-TAVR

- Procedure: $34,863
- Non-Procedure: $4,742
- Total MD Fees: $31,192

AVR

- Procedure: $54,228
- Non-Procedure: $5,773
- Total MD Fees: $54,228

Transfemoral

Index Admission Costs

$74,452

$71,955

∆ = ($2,496)

P = 0.53
Costs

- **TAVR and AVR procedures**: Measured resource utilization (procedure duration, supplies) multiplied by unit costs
  - SAPIEN valve estimated commercial price = $30,000
  - Cath lab overhead used for all TF-TAVR cases; cardiac OR overhead used for AVR and TA-TAVR cases

- *All other costs for index admission*: bills collected from consenting patients enrolled at participating US sites
Conclusions

• TAVI improved cardiac symptoms (NYHA class, $P < 0.0001$) and six minute walking distance ($P = 0.002$), after 1-year follow-up

• TAVI resulted in more frequent complications at 30 days, including…
  - major vascular complications, 16.2% vs. 1.1%, $P < 0.0001$
  - major bleeding episodes, 16.8% vs. 3.9%, $P < 0.0001$
  - major strokes, 5.0% vs. 1.1%, $P = 0.06$
Conclusions

• TAVI was superior to standard therapy, markedly reducing the rate of...
  ➢ all-cause mortality by 46%, \( P < 0.0001 \), NNT = 5.0 pts
  ➢ cardiovascular mortality by 61%, \( P < 0.0001 \), NNT = 4.1 pts
  ➢ all-cause mortality and repeat hospitalization
    ▪ hierarchical (FS method), \( P < 0.0001 \)
    ▪ non-hierarchical (KM analysis) by 54%, \( P < 0.0001 \), NNT = 3.4 pts
Conclusions

In patients with severe AS and symptoms, who are not suitable candidates for surgery…

- Standard therapy (including BAV in 83.8% of pts) did not alter the dismal natural history of AS; all-cause and cardiovascular mortality at 1 year was 50.7% and 44.6% respectively
- Transfemoral balloon-expandable TAVI, despite limited operator experience and an early version of the system, was associated with acceptable 30-day survival.
Clinical Implications

- Two year data continues to support the role of TAVR as the standard-of-care for symptomatic patients with aortic stenosis who are not surgical candidates.

  - The ultimate value of TAVR in “inoperable” patients will depend on careful selection of patients who are not surgical candidates, and yet do not have extreme co-morbidities that overwhelm the benefits of TAVR and render the intervention futile.
Clinical Implications

- Balloon-expandable TAVI should be the new standard of care for patients with aortic stenosis who are not suitable candidates for surgery!
- Next generation devices (e.g. SAPIEN XT) may help to reduce the frequency of procedure-related complications in the future.
- The ultimate value of TAVI will depend on careful assessment of bioprosthetic valve durability, which will mandate obligatory long-term clinical and echocardiography FU of all TAVI patients.