Severe Aortic Stenosis and TAVR: An Update for 2016

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Disclosures

Medtronic - speaker
Edwards - TAVR education
**Symptomatic Severe Aortic Stenosis**

*Breast, Lung, Colon, Prostate, Ovarian*

<table>
<thead>
<tr>
<th>Tissue</th>
<th>5-year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>23%</td>
</tr>
<tr>
<td>Lung</td>
<td>4%</td>
</tr>
<tr>
<td>Colon</td>
<td>12%</td>
</tr>
<tr>
<td>Prostate</td>
<td>30%</td>
</tr>
<tr>
<td>Ovarian</td>
<td>28%</td>
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</tbody>
</table>

Severe Inoperable AS*

3%

**5-year Survival: Metastatic Cancer**

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<td>Ovarian</td>
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Onset of severe symptoms

**Percent Survival**

Severe AS in the old days ...

Angina
Syncope
Heart failure

Peak vel >4 m/s
Grad >40 mmHg
Area <1.0 cm²

50% referral
CT
Surgeon
40%
AVR

Classic symptoms are late manifestations.
Initial sx: DOE or ↓exercise tolerance.
80 year old farmer with HF, syncope and angina.

Mean gradient - 43 mmHg
AV Area - 0.4 cm²

VTI 105 cm
Vel 4.5 m/s

VTI 14 cm
Vel 0.7 m/s
Symptoms may be subtle like reduced exercise tolerance or dyspnea on exertion. Pts may reduce activity to below symptoms threshold. Risk of sudden death is high once any symptoms develop – even mild ones.

Management of Aortic Stenosis

Asymptomatic pts with AS have outcomes similar to age-matched adults. But progression with symptoms is common.

AVR is based largely on the presence or absence of symptoms attributed to severe AS and not on absolute valve area or gradient. (EF 30% HF I or III)

Symptoms may be subtle like reduced exercise tolerance or dyspnea on exertion. Pts may reduce activity to below symptoms threshold. Risk of sudden death is high once any symptoms develop – even mild ones.

Exercise testing in asymptomatic severe AS is safe and underutilized. May help to unmask symptoms!

Bonow. ACC/AHA Valvular Heart Disease Guidelines. JACC 2008:52:e1-142
Walks 2 miles/day - no symptoms!

75 yr old wants a 2nd opinion

Peak velocity – 5.5 m/s
Mean gradient - 75 mmHg
AV Area - 0.5 cm²

197 pts, No sx, valve <0.75 cm² plus vel >4.5 m/s or >50mmHg
(Excluded pts with CAD, EF <50%, significant AI or MR, age >85)

Peak velocity – 5.5 m/s was an indep marker for mortality

Is it Aortic Stenosis or Age?

75 male – followed in clinic for severe AS. He may be “slowing some” although attributes it to his age. Denies CP, dyspnea, or syncope. Continues to work out twice a week for at >1 hour on each occasion – jogging, rapid walking, cycles with a high tension and lifts weights. No symptoms.

Treadmill - 7 METS. Stops due to leg weakness, fatigue.

BP at rest - 167/62. BP with exercise - 130/60.
AS: Complex “systemic” disease

1. Hypertension which adds to total afterload.
2. CAD which can impact ventricular function.
In 2016, it looks like this …

- Age > 80+
- Tired / fatigue
- Heart failure (?)
- COPD / Renal

High gradient AS

Low flow, low gradient

Paradoxical low-flow

- Treadmill stress (IIa)
- Dobutamine echo (IIa)
  if EF <50%, AVA <1.0, and <4m/s or <40 mmHg

Trial TAVR

SAVR ± ?

TAVR

Truly symptomatic severe AS or futility

Clinic

TAVR Clinic

In 2016, it looks like this …
Transcatheter Aortic Valve Replacement
Demographic Trends

1.6 M
~548 K
~88 K
~18 K

16.6
20.0
25.6
31.1
34.7
39.4
53.2
69.4
75.2
78.9

AGE > 65 years
Population in Millions

Nearly 3% of subjects >75 years have critical aortic stenosis.

US Census Bureau 2010
TVT 2015: Freed 2010; Bach. Unoperated pts with severe AS. J Heart Valve Dis May 2011
Estimated Global TAVR Growth

In the next 10 years, TAVR growth will increase 4 fold.

Lancet 2015;385:2439-41. TVT 2015 – Source: Credit Suisse TAVI Comment 1/8/15
CE-Approved TAVR Systems

First TAVR – 2002
Alain Cribier, France
Low-Flow/Low-Gradient AS (↓EF)

AV Area - 0.9 cm²

LVOT
17 cm
0.8 m/s

Ao V
62 cm
3.0 m/s
23 mmHg

April 2012
Mean gradient is proportional to the square of the flow.
Low-Flow/Low-Gradient AS (↓EF)

**LVOT**
- Sept 2011: 28 cm, 1.0 m/s
- April 2012: 17 cm, 0.8 m/s

**Ao V**
- Sept 2011: 98 cm, 3.8 m/s, 38 mmHg
- April 2012: 62 cm, 3.0 m/s, 23 mmHg

**AV Area**
- 0.9 cm²

*Note: AV Area - 0.9 cm² is highlighted.*
Paradoxical low-flow severe AS

Chronic exposure to high afterload may eventually lead to intrinsic impairment of myocardial function.

Myocardial function and stroke volume are reduced despite a normal LVEF.

Severe low-gradient AS
### Predicting the Future

<table>
<thead>
<tr>
<th></th>
<th>Low</th>
<th>Intermediate</th>
<th>High Risk</th>
<th>Inoperable</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STS PROM</strong></td>
<td>&lt;4% <strong>and</strong></td>
<td>4 to 8% <strong>or</strong></td>
<td>&gt;8% <strong>or</strong></td>
<td>major morbidity or death &gt;50% at 1 year</td>
</tr>
<tr>
<td><strong>Frailty Index</strong></td>
<td>None <strong>and</strong></td>
<td>1 index - mild <strong>or</strong></td>
<td>≥2 indices <strong>mod-severe</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Major organs compromised</strong></td>
<td>None <strong>and</strong></td>
<td>1 organ system <strong>or</strong></td>
<td>≤ 2 organ systems <strong>or</strong></td>
<td>3 organ systems <strong>or</strong></td>
</tr>
<tr>
<td></td>
<td>Low EF, diastolic or RV dysfx, pulm HTN, CKD stage 3-5, FEV1 &lt;50%, dementia, CVA, albumin &lt;3.0, active malignancy, liver dz / cirrhosis.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Anatomy</strong></td>
<td>None</td>
<td>Possible</td>
<td>Possible</td>
<td>Severe</td>
</tr>
<tr>
<td></td>
<td>Trach, porcelain aorta, chest deformity, grafts against chest wall, radiation</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PARTNER IB - Inoperable

N - 358. Edwards 23mm or 26mm bioprosthetic valve
Age 83, male 45%, HF III-IV 92%, AVA 0.6 cm², EF 52%

All cause mortality

Death from Any Cause (%) 0 20 40 60 80
0 12 24 36 48 60 mo

Med 80% 94%
TAVR 30% 54% 72% 40%

Lancet 2015;385:2485-91  NEJM 2010;363:1597-1607
PARTNER IB - HF Status

Baseline

Patients (%)

TAVI  Standard  TAVI  Standard

Baseline  1 Year

P=0.68  P<0.001

IV  IV  III  III  II  II

NEJM 2010;363:1597-1607  NEJM 2012;366:1696-1704
PARTNER IA - High Risk

N - 699. Randomized to TAVR (TF or TA) or SAVR
Age 84, male 58%, HF III-IV 94%, EF 53%, Prior CABG 41%

All cause mortality

25% TAVR
34% SAVR

FDA approved - Sept 2012

NEJM 2011; 364:2187-98  Lancet 2015;385:2477-84
CoreValve - High surgical risk

Self-expanding system.

N - 747. Randomized to TAVR (TF or TA) or SAVR
Age 83, male 53%, HF III-IV 86%, Prior CABG 30%, DM 40%

All cause mortality

Death from Any Cause (%)

p <0.04

Surgery - 19%

TAVR - 14%

5-Year Prosthesis Performance

3rd generation 18-F CoreValve device

June 2007 to August 2009
Prospective study of 353 consecutive patients in 8 Italian centers
(26 mm and 29 mm CoreValves)
## 30 day Outcomes

<table>
<thead>
<tr>
<th>Trial</th>
<th>N</th>
<th>STS</th>
<th>Death</th>
<th>CVA</th>
<th>&gt;2+ AR</th>
<th>Vasc Injury</th>
<th>Pacer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partner IB</td>
<td>179</td>
<td>11.2</td>
<td>5.0</td>
<td>6.7</td>
<td>11.8</td>
<td>16.2</td>
<td>3.4</td>
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<tr>
<td>Partner 1A</td>
<td>348</td>
<td>11.8</td>
<td>3.4</td>
<td>4.7</td>
<td>12.2</td>
<td>11.0</td>
<td>3.8</td>
</tr>
<tr>
<td>Partner IIB</td>
<td>284</td>
<td>10.3</td>
<td>3.5</td>
<td>4.3</td>
<td>24.0</td>
<td>9.6</td>
<td>6.4</td>
</tr>
<tr>
<td>SAPIEN 3</td>
<td>150</td>
<td>7.4</td>
<td>5.3</td>
<td>2.7</td>
<td>3.5</td>
<td>5.3</td>
<td>13.3</td>
</tr>
<tr>
<td>SAPIEN 3 TF</td>
<td>96</td>
<td>7.5</td>
<td>2.1</td>
<td>1.0</td>
<td>3.5</td>
<td>4.2</td>
<td>12.5</td>
</tr>
</tbody>
</table>

| Core - Extreme | 489| 10.3| 8.4  | 4.0 | 15.3   | 5.9         | 21.6  |
| Core - Pivotal | 390| 7.3 | 3.3  | 4.9 | 10.0   | 5.3         | 19.8  |
| Evolut R       | 60 | 7.0 | 0    | 0   | 3.4    | 8.3         | 11.7  |

Euro PCR 2015. JACC 2014;64;2244-5
Impact of Aortic Regurgitation

Predictors: calcification, valve malposition within annulus, undersized valve, CoreValve vs Sapien (21% vs 13%)*

Outcomes: AI > 2+ is an independent predictor of short- and long-term mortality. The mechanism is still unclear.

2-year Total Mortality

N-699

Mild - Severe

None - Trace

HR 2.11

p 0.0001

months

Total Mortality

N-2939

AR >2

AR - 1

AR - 0

p = 0.001

Days

Partner IA. JACC 2013;61:1125-36

*France 2 Registry. CIRC 2014; 129:1415-1427
PARTNER 1A (high risk): ~ 20% pts had mod or severe MR

Moderate or severe MR was associated with a higher 2 year mortality with SAVR but not with TAVR.

TAVR/SAVR: HF symptoms improved regardless of MR

Barbanti. Circ 2013;128:2776-84
TOPAS study: 220 pts, age 73, HF III-IV 50%
60% underwent AVR (80% surg - 20% TAVR)

30-day Mortality

0/1 TR
2 TR
3/4 TR
Any AVR

Mortality

0/1
2
3/4
Med Rx
TAVR - low flow, low gradient

Retrospective analysis of 385 pts with inoperative or high risk symptomatic severe aortic stenosis.

Low EF-LG AS pts had more CAD, MI, MR. More likely to die of CV causes. Paradoxical LFLG pts - same benefit as HG. Typically 80 yr, ♀, HTN, CAD.

O’Sullivan. Europ Heart J 2013;34:3437-50
Balloon Aortic Valvuloplasty
CoreValve Deployment
LV Function During TAVR

Baseline

Rapid RV Pacing
Rapid Pacing for TAVR

- RV pacing at 180 bpm
- Root injection 70 mmHg
- Deploy valve 40 mmHg
- 10 seconds
- 150 mmHg
PARTNER IA at 5 Years
Balloon-expandable valves versus SAVR

For pts with no or trace paravalvular regurgitation, 5 year mortality reduction for TF-TAVR compared to SAVR was ~16% (45% vs. 61%), emphasizing the need to eliminate paravalvular regurgitation post-procedure.

Better outcomes with TAVR: women, those with smaller annular size and low-flow, low gradient AS.
Typical TAVR Patient

84 year old with class IV HF, EF 20%, valve area - 0.5 cm$^2$ mean gradient - 50 mmHg

Few months later, presents for TAVR: EF 15%, gradient 27 mmHg
Typical TAVR Patient

84 year old with class IV HF, EF 20%, valve area - 0.5 cm² mean gradient - 50 mmHg

Few months later, presents for TAVR: EF 15%, gradient 27 mmHg

Cardiac output doubled and diastolic dysfunction improved.
Severe AS
>4 m/s or 40 mmHg

Symptoms
No Symptoms

EF <50%
V >5 m/s
Abnl ETT

AVR Class I
AVR Class IIa

Symptomatic but
3-4 m/s or 20-40 mmHg

EF <50%
then DSE:
AVA <1cm²
or V >4m/s

If EF >50%
AVA <1cm²,
and AS likely
cause of sx*

AVR Class IIa

* SBP <140
Calcified AV!

ACC/AHA Valvular Heart Disease Guidelines. JACC 2014;63:e57-185
Symptomatic Severe AS

170,000 patients

1. STS Adult Cardiac Database - 2010 Harvest, Isolated AVR.
9. Medtronic data
2014 ACC/AHA: Which Valve?

Symptomatic AS

Heart Team: TAVR / High risk

Prohibitive risk

Partner II (S3) Sur-Tavi (CoreValve)

Risk is low to intermediate

High risk surgery

Bridge to SAVR or TAVR for severe symptoms

BAV (IIb)

TAVR Class I

Palliative Care

Portico (St Jude) for high risk or inoperable.

Predicted post-TAVR survival > 1 yr

YES

NO

ACC/AHA Valvular Heart Disease Guidelines. JACC 2014;63:e57-185
Trans-femoral TAVR should be considered as the first-line therapy for high risk patients with severe aortic stenosis.

TAVR and Clinical Practice

In Germany

<table>
<thead>
<tr>
<th>Year</th>
<th>Surg</th>
<th>TAVR</th>
</tr>
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<tbody>
<tr>
<td>2007</td>
<td>8622</td>
<td>144</td>
</tr>
<tr>
<td>2013</td>
<td>7048</td>
<td>9147</td>
</tr>
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Age >85

Age <75

No of Procedures

Year:
- 2007: 8622 TAVR, 144 Surgical AVR
- 2013: 7048 TAVR, 9147 Surgical AVR

NEJM 2016;373:2438-47
Aortic Stenosis in 2016