Overview of Aortic Stenosis and Transcatheter Aortic valve Replacement/Implantation (TAVR/TAVI)

Gaurav R. Parikh, MD, MRCP(UK)
Interventional Cardiology
Aortic Stenosis

• Restricted opening of the aortic valve
  – Thickening and calcification of leaflets
  – Fusion of commissures (rheumatic)
  – Intrinsically narrowed orifice (congenital)

• When orifice is decreased by more than 50% it becomes flow-limiting
  – Pressure gradient develops across valve
  – LV hypertrophy maintains wall stress
  – Eventual LV failure and coronary insufficiency result in symptomatology
Aortic Stenosis
Pathophysiology of AS

**VALVE HISTOLOGY SHOWING PROGRESSION OF THE DISEASE**

- **Initiating factors:**
  - Bicuspid valve
  - Genetic factors
  - Shear stress

- **Early lesion**
  - T cell
  - LDL
  - Monocyte

- **Disease progression:**
  - Age and sex
  - Increased serum lipids
  - Increased blood pressure
  - Diabetes and metabolic syndrome
  - Smoking

- **Phenotypic transformation**
  - Wnt3, Lrp5, and β-catenin

- **Calcification**
  - Increased alkaline phosphatase
  - Increased BMP-2
  - Increased osteocalcin

**AORTIC-VALVE ANATOMY**

- **B** Normal
- **Aortic sclerosis**
- **Mild-to-moderate aortic stenosis**
- **Severe aortic stenosis**

**DOPPLER AORTIC JET VELOCITY**

- **Normal**
- **Aortic sclerosis** (<2.5 m/sec)
- **Mild-to-moderate aortic stenosis** (2.5–4.0 m/sec)
- **Severe aortic stenosis** (>4 m/sec)
Increasing Prevalence of Valvular Heart Disease with Age

**Population-based Studies**

- **All valve disease**
- **Mitral valve disease**
- **Aortic valve disease**

**Olmsted County, MN**

Prevalence of mild or severe VHD (%)

Prevalence Moderate/Severe AS 2.4 % in Those Age >75

*Nkomo VT at al. Lancet 2006;368:1005-1011*
Clinical Presentation

• Classic symptoms:
  – Murmur
  – Dyspnea
  – Chest pain
  – Syncope
  – Heart Failure
Natural History of Aortic Stenosis

- **Survival (percent)**
- **Age (years)**
- **Increasing obstruction, myocardial overload**
- **Latent Period**
- **Symptoms**
- **Average Age Death**
Mortality with Medical Rx Perspectives

5 Year Survival: Metastatic Cancer

- Breast: 23%
- Lung: 5%
- Colorectal: 12%
- Prostate: 30%
- Ovarian: 28%
- Severe Inoperable AS: 3% *

* Constant Hazard Model

Courtesy Murat Tuzcu
Therapeutic Options

• Mechanical problem = Mechanical solution

• No medical therapy effective in delaying progression or altering outcome of AS

• Surgical AVR:
  – Mechanical vs Bioprosthetic

• Transcatheter therapy:
  – BAV and TAVR
At Least 30% of Patients with Severe Symptomatic AS are “Untreated”!

Severe Symptomatic Aortic Stenosis
Percent of Cardiology Patients Treated

<table>
<thead>
<tr>
<th>Year</th>
<th>AVR (%)</th>
<th>No AVR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999</td>
<td>59</td>
<td>41</td>
</tr>
<tr>
<td>2004</td>
<td>68</td>
<td>32</td>
</tr>
<tr>
<td>2005</td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td>2006</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>2009</td>
<td>52</td>
<td>48</td>
</tr>
<tr>
<td>2005</td>
<td>69</td>
<td>31</td>
</tr>
<tr>
<td>2009</td>
<td>55</td>
<td>45</td>
</tr>
</tbody>
</table>

Unmet Clinical Need

2. Iung B et al. A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on Valvular Heart Disease. European Heart Journal 2003:24:1231-1243 (*includes both Aortic Stenosis and Mitral Regurgitation patients)
NO ONE Likes Surgery (of any kind)!
Alain Cribier: 
First human transcatheter valve replacement (2002)
TAVR – Current Landscape

Edwards SAPIEN 3
Balloon Expandable

Medtronic CoreValve Evolut
Self Expanding

- Intermediate-, high- and extreme-risk
- Valve-in-valve
The TAVR Revolution

First Generation Devices

Edwards Lifesciences
Approved Nov 2011

Medtronic CoreValve
Approved Jan 2014
TAVR and SAVR* Procedures In the TVT Registry and STS ACSD*

* SAVR= isolated surgical aortic valve replacement; ACSD=Adult Cardiac Surgery Database

Source: STS/ACC TVT Registry Database as of Oct 18, 2016; STS ACSD 2015 Annual Report
TAVR now accounts for 41% of all AV replacements

U.S. Medicare AV Cases in 2016

FY2015 MedPAR, all cases on file regardless of IPPS status
TAVR Sites in US = 477 and counting

Alaska: 1
Hawaii: 1
FIND A TAVR CENTER

Use this tool to find a multi-disciplinary Heart Team that can determine whether transcatheter aortic valve replacement (TAVR) is an option for you or someone you care for. Search to find TAVR Centers and view details about each listing.

*Enter city and/or state, zip code, or hospital name and select from the list.

91767

Show the closest 10 TAVR Centers

Search ▶

Showing 10 closest TAVR Centers

- CITRUS VALLEY INTERCOMMUNITY HOSPITAL
  210 W. San Bernardino Road
  Covina, CA 91723
  Distance: 8mi

- ST. JOSEPH HOSPITAL
  1100 W. Steward Drive
  Orange, CA 92866
  Distance: 21mi

- HUNTINGTON HOSPITAL
  100 West California Boulevard
  Pasadena, CA 91105
  Distance: 23mi

- KECK MEDICAL CENTER OF USC
  1500 San Pablo
  Los Angeles, CA 90033
  Distance: 26mi

- DIGNITY HEALTH ST. BERNARDINE MEDICAL CENTER
  2101 North Waterman Ave.
  San Bernardino, CA 92404
  Distance: 26mi

- LOMA LINDA UNIVERSITY HEALTH
  11234 Anderson St.
  Loma Linda, CA 92354
Class 1 recommendation: Patients with severe VHD should be evaluated by a multidisciplinary Heart Valve Team when intervention is considered.
Risk Assessment: Beyond The Risk Scores

• STS risk score provides a reasonable preliminary estimate of risk for the majority of patients

• The STS score fails to account for many important factors affecting surgical risk
  – Porcelain aorta
  – Chest wall radiation or deformity (hostile chest)
  – Previous sternotomy with adhesion of IMAs to chest wall
  – Severely compromised respiratory function
  – Severe liver disease
  – Severe pulmonary hypertension
  – Dementia and/or severe cerebrovascular disease
  – Frailty: “eyeball” test vs objective assessment

• Clinical judgment of experienced operators plays a key role in assessment of surgical risk status
Classic TAVR Patient #1

- 68 y.o. male
- Recurrent CHF admissions

<table>
<thead>
<tr>
<th>Clinical History</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic Heart Failure</td>
<td>Severe low gradient low flow AS</td>
</tr>
<tr>
<td>CABG x 4 - 2005</td>
<td>HTN</td>
</tr>
<tr>
<td>Stent to RCA graft x2 (1/4/17)</td>
<td>ICD</td>
</tr>
<tr>
<td>Ischemic cardiomyopathy</td>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td>EF 20 – 25%</td>
<td></td>
</tr>
</tbody>
</table>

**Risk determination:**
- Intermediate risk based on STS score of 6%
- Severe Pulmonary hypertension – 77/32 (48)mmHg
- Severe biventricular dysfunction
- Redo sternotomy
Classic TAVR Patient #2

90 year old female

Severe AS with reduced EF of 35% now with CHF symptoms

History:  
- Severe AS
- Hyperlipidemia
- PPM 6/14
- Left hip fx with fixation
- CHF
- Extremely HOH

Patient factors:

* Independent for ADLs
* Lives with daughter and son-in-law
* Enjoys going out to dinner, casino, knitting, and frequent trips to the river.
* Has been dx with AS for several years, but was asymptomatic until recently, and would now like treatment.
* 1/31/17 Admitted from ER with SOB, trop 0.52, 0.59.

TAVR Candidate Risk Determination:

* High Risk Candidate based on STS score of 13
* Frailty
Workup for TAVR

- Transthoracic echocardiogram
- Cardiac catheterization
- MDCT gated CT scan of heart, abd pelvis
- Risk assessment (STS score, technical issues)
- Frailty assessment
- Heart Team meeting
Workup - Echocardiogram
Workup- Cardiac catheterization
Retrospective Gated MDCT—Annulus Sizing

**Example**

- Min. Ø: 23.7 mm
- Max. Ø: 26.6 mm
- Avg. Ø: 25.9 mm
- Area derived Ø: 25.9 mm
- Perimeter derived Ø: 25.3 mm
- Area: 528.7 mm²
- Perimeter: 82.7 mm

**Example**

- Min. Ø: 23.7 mm
- Max. Ø: 27.8 mm
- Avg. Ø: 26.3 mm
- Area derived Ø: 25.4 mm
- Perimeter derived Ø: 25.5 mm
- Area: 503.9 mm²
- Perimeter: 80.4 mm
Retrospective Gated MDCT – Annulus Sizing

**SOV**
- Ø 35.4 mm
- Ø 34.8 mm
- Compress: 50.0 mm
- Distance: 12.1 mm

**STJ**
- Min. Ø: 29.6 mm
- Max. Ø: 31.2 mm
- Compress: 50.0 mm
- Distance: 25.3 mm

**STJ Height 25.3 mm/LCA 20.6 mm**

**RCA Height 19.2 mm**

[InteleViewer Series#]

[InteleViewer Image #]
Retrospective Gated MDCT
Access Vessels on CT Angiogram
Workup for TAVR

- Transthoracic echocardiogram
- Cardiac catheterization
- MDCT gated CT scan of heart, abd pelvis
- Risk assessment (STS score, technical issues)
- Frailty assessment
- Heart Team meeting
TAVR Procedure & Hospital Course

- Done in Cardiac Catheterization Lab / Hybrid OR
- General Anesthesia/moderate sedation
- Both Interventional Cardiologist and Cardiac surgery in the room
- Both groins accessed
  - 14 - 16 French for catheter for valve (arterial)
  - Temporary pacer (venous) & Pigtail (arterial)
- Percutaneous arterial access and closure
- Patient extubated in cathlab on table
- Patient to CICU for < 12-24 hrs
- LOS: 2 or 3 days
S/p Successful Trans-femoral TAVR
Sapien 3 Valve

#1
• Tolerated procedure well
• Extubated next day
• Was able to get diuresed and now tolerate HF meds
• Discharged Home after 7 days
• Has not had any more CHF admission
• Able to walk > 30 min upon DC

#2
• Tolerated procedure well
• Extubated on table
• Ambulating next day
• Discharged home within 48 hours
• Continues to do well
PARTNER Study Design

Symptomatic Severe Aortic Stenosis

ASSESSMENT: High-Risk AVR Candidate
3,105 Total Patients Screened

Total = 1,057 patients
2 Parallel Trials: Individually Powered

High Risk
N = 699

Yes
ASSESSMENT: Transfemoral Access

Transfemoral (TF)
1:1 Randomization
N = 244
TF TAVR vs SAVR

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

No
Transapical (TA)
1:1 Randomization
N = 248
N = 104
N = 103

Inoperable
N = 358

Yes
ASSESSMENT: Transfemoral Access

Not In Study

1:1 Randomization
N = 179
TF TAVR vs SAVR

N = 179

Standard Therapy

Primary Endpoint: All-Cause Mortality Over Length of Trial (Superiority)
Co-Primary Endpoint: Composite of All-Cause Mortality and Repeat Hospitalization (Superiority)
PARTNER trial established that TAVR improves survival in extreme risk patients with AS and is an alternative to surgery in high risk patients

Key points to remember

- Enrollment started in 2007 - <100 TAVRs performed in US and only 6 sites had experience prior to trial
- First generation device used (24F sheath, no nosecone on delivery catheter and original SAPIEN device used)
Patients treated with standard therapy were rehospitalized twice as often as TAVR patients.

Of the 358 patients, 87.3% of patients with standard therapy were rehospitalized for cardiac issues.

39.7% absolute reduction of rehospitalization at 5 years.
Pivotal Trial Design

CoreValve US Pivotal Trial

- Extreme Risk
  - Iliofemoral Access > 18 Fr Sheath
    - CoreValve Iliofemoral
    - CoreValve Non-Iliofemoral

- High Risk
  - Randomization* 1:1
    - CoreValve (any route)
    - SAVR

* Randomization stratified by intended access site
All-Cause Mortality

Transcatheter
Surgical

Δ = 6.5
Δ = 4.8
18.9%
14.1%
22.2%
28.6%

Log-rank P=0.04

No. at Risk
Transcatheter: 391 378 354 334 219
Surgical: 359 343 304 282 191
The PARTNER II Trial: Intermediate-risk cohort

Intermediate-risk symptomatic severe aortic stenosis

Intermediate-risk assessment by Heart Valve Team

PARTNER II S3i  
( n = 1078 )

- Assessment for optimal valve delivery access
  - Transfemoral (TF)
    - TF TAVR SAPIEN 3 valve
  - Transapical (TA)/Transaortic (TAo)
    - TA / TAo TAVR SAPIEN 3 valve

PARTNER IIA  
( n = 2032 )

- Assessment transfemoral access
  - Yes
    - Transfemoral (TF)
      - 1:1 Randomization
        - TA TAVR SAPIEN XT valve vs Surgical AVR
  - No
    - Transapical (TA)/Transaortic (TAo)
      - 1:1 Randomization

The most robust, rigorous study in more than 3,000 intermediate-risk patients
Is TAVR Superior to Surgery?

The evidence builds...

PARTNER 2A – Primary Endpoint
All-Cause Mortality or Disabling Stroke (ITT)

![Graph showing TAVR and Surgery outcomes over time with statistical data]

Smith, ACC 2016
### Other unadjusted clinical events
At 30 days and 1 year (AT)

<table>
<thead>
<tr>
<th>Events (%)</th>
<th>30 Days</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PARTNER II S3i trial SAPIEN 3 valve (n = 1,077)</td>
<td>PARTNER IIA trial surgery (n = 944)</td>
</tr>
<tr>
<td>Re-hospitalization</td>
<td>4.6</td>
<td>6.8</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0.3</td>
<td>1.9</td>
</tr>
<tr>
<td>Major vascular complication</td>
<td>6.1</td>
<td>5.4</td>
</tr>
<tr>
<td>Life-threatening / disabling bleeding</td>
<td>4.6</td>
<td>46.7</td>
</tr>
<tr>
<td>New atrial fibrillation</td>
<td>5.0</td>
<td>28.3</td>
</tr>
<tr>
<td>New permanent pacemaker</td>
<td>10.2</td>
<td>7.3</td>
</tr>
<tr>
<td>Re-intervention</td>
<td>0.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>0.2</td>
<td>0.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mean total hospitalization LOS (days)</th>
<th>PARTNER II S3i trial SAPIEN 3 valve (n = 1,077)</th>
<th>PARTNER IIA trial surgery (n = 944)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ICU stay (days)</td>
<td>2.7</td>
<td>5.6</td>
</tr>
</tbody>
</table>
Evolution of the Edwards Balloon-Expandable Transcatheter Valves

- SAPIEN (2006)
- SAPIEN XT (2009)
- SAPIEN 3 (2013)

* Sheath compatibility for a 23 mm valve
Mortality rates continue to decline

- **PARTNER IB trial** (transfemoral): 6.3%
- **PARTNER IA trial** (overall): 5.2%
- **PARTNER IIB trial** (transfemoral): 4.5%
- **PARTNER IIA trial** (overall): 3.6%
- **PARTNER II HR trial** (overall): 3.4%
- **PARTNER II S3i trial** (overall): 2.2%
- **PARTNER II S3i trial** (overall): 1.1%

### Valve Types
- **SAPIEN valve**: 175
- **SAPIEN XT valve**: 271
- **SAPIEN 3 valve**: 1,011
Stroke rates continue to decline

Neurologist evaluations (pre and post)

- PARTNER I B (TF) 7.3%
- PARTNER II B (TF) 4.4%
- PARTNER II B (TF) 4.3%
- PARTNER II HR (TF) 1.4%

SAPIEN valve
- 179
- 271

SAPIEN XT valve
- 282

SAPIEN 3 valve
- 491
TAVR in 2018

New performance benchmarks for high-risk AS patients (@ 30 days)

- All-cause mortality < 3%
- Major (disabling) strokes < 3%
- Major vascular complications < 5%
- Major bleeding complications < 5%
- Mod-severe para-valvular regurgitation < 5%
- New pacemaker requirement < 10%
Discharge Instructions Highlights

• Cardiology follow-up 4 – 5 days, 30 days, 1 year

• Aspirin 81 mg daily and Plavix 75 mg daily x 3-6 months

• Standard Post Cath precautions

• **Antibiotics prophylaxis prior to dental work**
The Future of TAVR?

- Multiple valve choices
  - How many do we need?
  - Different learning curves
  - How do we choose?
- Expanding indications
  - Bicuspid valves
  - Valve in valve
  - Lower risk patients
  - Moderate AS
  - Asymptomatic patients