Advances in the Treatment of Structural Heart Disease: TAVR in 2016

Jonathan A. Sherman, MD FACC
Case #1

- 92 yo followed by Dr. John Ord for many years.

- Known AS but never wanted surgery and never was apparently symptomatic.

- Lived with Daughter for the last several years but has been very independent, performing her own ADLs, cooking, shopping, etc. Loves to garden but has been limited in that activity.

- Admitted initially in the Spring of 2015 with a GI Bleed. Echo at that time showed severe AS, with progression from previous studies.

- Admitted again in 8/2015 with her first episode of CHF. Met the Heart Team but refused intervention. STS PROM 10.8%

- Admitted again in 9/2015, 10/2015 and 11/2015 for CHF.

- Given repeated admissions underwent Balloon Aortic Valvuloplasty (BAV) in 11/2015.

- CHF symptoms improved post BAV, mean gradient improved from ~90mmHg to ~40mmHg.

- Eventually underwent TAVR 12/2015.

- Recently seen in clinic. Back in her previous living situation, helping to cook, clean and had a great Summer in her garden. Just turned 93.
Calcific Aortic Stenosis

- Mainly solid calcium deposits within the valve cusps
- Similar risk factors to Coronary Artery Disease (CAD)
- High coincidence of CAD and AS in same individual
- 6th, 7th, and 8th decades of life
Prevalence of Aortic Stenosis

• Aortic Stenosis (AS) is the most prevalent native valve disease

• Prevalence:
  - 2% of people over 65
  - 3% of people over 75
  - 4% of people over 85

• Over 100,000 people in the U.S. are diagnosed with severe aortic stenosis each year

• Prevalence of AS and co-morbidities that increase the risk of surgical valve replacement, increase with age
AS is Life Threatening and Progresses Rapidly

- Onset of dyspnea and other heart failure symptoms foretell the worst outlook for AS patients
- Classic symptoms of AS:
  - Angina
  - Syncope
  - Heart failure
- Without intervention, this patient population survival rate is approximately 50% at two years
Echo is the Gold Standard for Diagnosis of AS

- According to the 2014 ACC/AHA guidelines, severe aortic stenosis is defined as:
  - Aortic valve area (AVA) less than 1.0 cm²
  - Mean gradient greater than 40 mmHg or jet velocity greater than 4.0 m/s
2014 ACC/AHA GUIDELINES FOR AORTIC VALVE INTERVENTION IN AORTIC STENOSIS

Abnormal Aortic Valve With Reduced Systolic Opening

Severe AS
- $V_{\text{mas}} \geq 4 \text{ m/s}$
- $\Delta P_{\text{mean}} \geq 40 \text{ mm Hg}$

Symptomatic (stage D1)
- LVEF < 50%
  - Other Cardiac Surgery
  - $V_{\text{mas}} \geq 5 \text{ m/s}$
  - $\Delta P_{\text{mean}} \geq 60 \text{ mm Hg}$
  - Low Surgical Risk
  - Abnormal ETT
  - $\Delta V_{\text{mas}} > 0.3 \text{ m/s/y}$
  - Low Surgical Risk
- AVR (I)
- AVR (II)
- AVR (IIb)

Asymptomatic (stage D)
- LVEF < 50%
  - Other Cardiac Surgery
  - DSE with $\text{AVA} \leq 1 \text{ cm}^2$ and $V_{\text{mas}} \geq 4 \text{ m/s}$
  - (stage D2)
- Yes
- AS Likely Cause of Symptoms
  - AVR (IIa)
  - NO
  - AVR (IIa)

V_{\text{mas}} 3 \text{ m/s} – 3.9 \text{ m/s}
- $\Delta P_{\text{mean}} 20-39 \text{ mm Hg}$

Symptomatic (stage B)
- LVEF < 50%
  - Other Cardiac Surgery
- AVR (IIa)

Class I
Class IIa
Class IIb
Unmet Needs in Patients with AS

- Studies show at least 40% of SAS patients are not treated with an AVR
Current Treatment options for Aortic Stenosis: SAVR

Cardiac surgeons have a robust portfolio of bioprosthetic and mechanical valves that enables them to treat a broad spectrum of patients.

Freestyle® Bioprosthesis
Hancock® II Bioprosthesis
Mosaic® Bioprosthesis
Medtronic Open PivotTM Mechanical Valves
Current Treatment options for Aortic Stenosis: TAVR

Self Expanding

- NITINOL FRAME
- SUPRA-ANNULAR VALVE
- PORCINE TISSUE

Balloon Expandable

1. Outer Sealing Skirt
   - Designed to minimize paravalvular (PV) leak

2. Frame Design
   - Enhanced frame geometry for low delivery profile
   - Cobalt-chromium

3. Bovine Pericardial Tissue
TAVR Timeline

- More than 80,000 TAVR implants globally since 1st introduced commercially in 2007
- More than 60 countries
TAVR Access Options

Direct Aortic

Subclavian

Transfemoral
TAVR in High Risk Subgroups

**The PARTNER Trial Protocol**

- **Severe Symptomatic Native Aortic Valve Stenosis**
  - **Assessment: Operability** (N = 3,105)
    - Yes
      - **Cohort A**
        - High-Risk
        - (n = 699)
      - **2 Cohorts**
        - Individually Powered
        - (n = 1,057)
    - No
      - **Cohort B**
        - Inoperable
        - (n = 358)

- **Assessment: Transfemoral Access**
  - **TF**
    - (n = 492)
    - 1:1 Randomization
      - **TF**
        - TAVR
        - (n = 244)
      - **AVR**
        - (Control)
        - (n = 248)
  - **TA**
    - (n = 207)
    - 1:1 Randomization
      - **TA**
        - TAVR
        - (n = 104)
      - **AVR**
        - (Control)
        - (n = 103)
  - **TF**
    - (n = 179)
    - 1:1 Randomization
      - **TF**
        - TAVR
        - (n = 179)
      - **Standard Therapy**
        - (Control)
        - (n = 179)
  - **Not in Study**
TAVR in High Risk Subgroups

In PARTNER 1, transcatheter aortic valve replacement (TAVR) was superior to standard therapy in patients with symptomatic severe aortic stenosis who were not candidates for surgery AND was equivalent to surgery in high-risk patients.
Background

- The 3rd generation SAPIEN 3 transcatheter heart valve has demonstrated improved clinical outcomes in high-risk patients at 1 year (Partner II HR).

- The 30-day outcomes in *intermediate-risk* patients treated with SAPIEN 3 in PARTNER 2 were...
  - All-cause Mortality: 1.1%
  - Disabling Stroke: 1.0%
  - PVL > Moderate: 3.8%

- There is a paucity of longer-term data in intermediate-risk patients with SAPIEN 3 and there have been no rigorous comparisons with surgery in intermediate-risk patients.
TAVR in Intermediate Risk Patients: Partner 2A/SAPIEN 3

Intermediate Risk Symptomatic Severe Aortic Stenosis

Intermediate Risk ASSESSMENT by Heart Valve Team

P2 S3i
n = 1078

ASSESSMENT: Optimal Valve Delivery Access

- Transfemoral (TF)
  - TF TAVR SAPIEN 3

- Transapical / Transaortic (TA/TAo)
  - TA/TAo TAVR SAPIEN 3

P2A
n = 2032

ASSESSMENT: Transfemoral Access

- Yes
  - Transfemoral (TF)
    - 1:1 Randomization
      - TF TAVR SAPIEN XT vs Surgical AVR
      - TA/TAo TAVR SAPIEN 3 vs Surgical AVR

- No
  - Transapical / TransAortic (TA/TAo)
    - 1:1 Randomization
<table>
<thead>
<tr>
<th>Events (%)</th>
<th>30 Days</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TAVR</td>
<td>Surgery</td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause</td>
<td>1.1</td>
<td>4.0</td>
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<tr>
<td>Cardiovascular</td>
<td>0.9</td>
<td>3.1</td>
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<tr>
<td><strong>Neurological Events</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disabling Stroke</td>
<td>1.0</td>
<td>4.4</td>
</tr>
<tr>
<td>All Stroke</td>
<td>2.7</td>
<td>6.1</td>
</tr>
<tr>
<td><strong>All-cause Death and Disabling Stroke</strong></td>
<td>2.0</td>
<td>8.0</td>
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### Other Unadjusted Clinical Outcomes At 30 Days and 1 Year (AT)

<table>
<thead>
<tr>
<th>Events (%)</th>
<th>30 Days</th>
<th>1 Year</th>
<th>30 Days</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TAVR (n = 1077)</td>
<td>Surgery (n = 944)</td>
<td>TAVR (n = 1077)</td>
<td>Surgery (n = 944)</td>
</tr>
<tr>
<td>Re-hospitalization</td>
<td>4.6</td>
<td>6.8</td>
<td>11.4</td>
<td>15.1</td>
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<tr>
<td>MI</td>
<td>0.3</td>
<td>1.9</td>
<td>1.8</td>
<td>3.1</td>
</tr>
<tr>
<td><strong>Major Vascular Complication</strong></td>
<td>6.1</td>
<td>5.4</td>
<td>---</td>
<td>---</td>
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<tr>
<td><strong>AKI (Stage III)</strong></td>
<td>0.5</td>
<td>3.3</td>
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<tr>
<td><strong>Life-Threatening/Disabling Bleeding</strong></td>
<td>4.6</td>
<td>46.7</td>
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<tr>
<td><strong>New Atrial Fibrillation</strong></td>
<td>5.0</td>
<td>28.3</td>
<td>5.9</td>
<td>29.2</td>
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<tr>
<td><strong>New Permanent Pacemaker</strong></td>
<td>10.2</td>
<td>7.3</td>
<td>12.4</td>
<td>9.4</td>
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<tr>
<td><strong>Re-intervention</strong></td>
<td>0.1</td>
<td>0.0</td>
<td>0.6</td>
<td>0.5</td>
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<tr>
<td><strong>Endocarditis</strong></td>
<td>0.2</td>
<td>0.0</td>
<td>0.8</td>
<td>0.7</td>
</tr>
</tbody>
</table>
Unadjusted Time-to-Event Analysis
All-Cause Mortality and All Stroke (AT)

Number at risk:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Number at risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>P2A Surgery</td>
<td>944</td>
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<tr>
<td>S3 TAVR</td>
<td>1077</td>
</tr>
<tr>
<td></td>
<td>805</td>
</tr>
<tr>
<td></td>
<td>786</td>
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<tr>
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<tr>
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<td>743</td>
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<tr>
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</tr>
<tr>
<td></td>
<td>962</td>
</tr>
<tr>
<td></td>
<td>930</td>
</tr>
</tbody>
</table>
Abnormal Aortic Valve With Reduced Systolic Opening

- Severe AS
  - $V_{\text{max}} \geq 4 \text{ m/s}$
  - $\Delta P_{\text{mean}} \geq 40 \text{ mm Hg}$
  - Symptomatic (stage D1)
  - Asymptomatic (stage D)
    - LVEF < 50%
      - Other Cardiac Surgery
        - $V_{\text{max}} \geq 5 \text{ m/s}$
          - $\Delta P_{\text{mean}} \geq 60 \text{ mm Hg}$
            - Low Surgical Risk
            - Abnormal ETT
              - $\Delta V_{\text{max}} > 0.3 \text{ m/s/y}$
                - Low Surgical Risk
      - AVR (I)
      - AVR (II)
    - AVR (IIb)

- $V_{\text{max}} \geq 3 \text{ m/s} - 3.9 \text{ m/s}$
  - $\Delta P_{\text{mean}} \geq 20-39 \text{ mm Hg}$
  - Symptomatic
    - LVEF < 50%
      - Other Cardiac Surgery
        - AVR (II)
      - NO
        - DSE with $\text{AVA} \leq 1 \text{ cm}^2$ and $V_{\text{max}} \geq 4 \text{ m/s}$
          - (stage D2)
        - AS Likely Cause of Symptoms
          - AVR (IIa)
      - YES
        - $\text{AVA} \leq 1 \text{ cm}^2$ and $\text{LVEF} \geq 50$
          - (stage D3)
          - NO

Class I
Class IIa
Class IIb

Severe AS, Symptomatic
~120,000 Incidence

Low Operative Risk¹
32%
SAVR Indicated

Intermediate Operative Risk¹
25%

High Operative Risk¹
31%

Extreme Operative Risk* 2.9
13%
TAVR Indicated

STS Database
## 2014 ACC/AHA Guideline Risk Stratification for Severe AS

<table>
<thead>
<tr>
<th></th>
<th>Low Operative Risk (Must Meet ALL Criteria in This Column)</th>
<th>Intermediate Operative Risk (Any 1 Criterion in This Column)</th>
<th>High Operative Risk (Any 1 Criterion in This Column)</th>
<th>Prohibitive Operative Risk (Any 1 Criterion in This Column)</th>
</tr>
</thead>
<tbody>
<tr>
<td>STS PROM(^1)</td>
<td>&lt; 4% AND</td>
<td>4% to 8% OR</td>
<td>&gt; 8% OR</td>
<td>Prohibited risk with surgery of death or major morbidity (all-cause) &gt; 50% at 1 year OR</td>
</tr>
<tr>
<td>Frailty(^2)</td>
<td>None AND</td>
<td>1 Index (mild) OR</td>
<td>≥ 2 Indices (moderate to severe) OR</td>
<td></td>
</tr>
<tr>
<td>Major organ system compromise not to be improved postoperatively(^3)</td>
<td>None AND</td>
<td>1 Organ system OR</td>
<td>No more than 2 organ systems OR</td>
<td>≥ 3 organ systems OR</td>
</tr>
<tr>
<td>Procedure specific impediment(^4)</td>
<td>None</td>
<td>Possible procedure-specific impediment</td>
<td>Possible procedure-specific impediment</td>
<td>Severe procedure-specific impediment</td>
</tr>
</tbody>
</table>
“The management of patients with complex severe VHD is best achieved by a Heart Valve Team composed primarily of…”

- Cardiologists
- Surgeons
- Structural valve interventionalists
- Cardiovascular imaging specialists
- Cardiovascular surgeons
- Anesthesiologists
- Nurses

Conclusions

• Aortic stenosis is common, progressive disease that often leads to clinical deterioration and decreased survival.

• A large number of patients with severe, symptomatic AS are not treated with aortic valve intervention.

• Options now exist for high risk or inoperable patients with severe, symptomatic AS.

• TAVR is non inferior, and newer technologies (SAPIEN 3/EvoultR), are superior to surgical AVR in well selected patients.

• TAVR is also indicated in high risk patients with AI and in patients with failed bioprosthetic valves with stenosis or insufficiency (VIV).

• The evaluation of patients with aortic valve disease is complicated. Heart teams exist to thoroughly evaluate patients (echo, CT, frailty, multi-modality thinking) in an effort to offer the safest and best therapy to patients. (Class I AHA/ACC guideline)
Case #2

- 80 yo retired orthopedic surgeon referred to our Heart Valve Team/Clinic. By echo severe AS with mPG of 43mmHg.

- Avid fly fisherman and outdoorsman and was developing DOE with activity over the last several months.

- Other comorbidities include DM, AF, Stage III CKD, Bladder Cancer s/p surgery and neobladder, mild COPD. Also has had postoperative SBO x 2.

- STS risk calculated at 5-6% and frail by grip only. The team felt he was a candidate for either TAVR or SAVR.

- Elected TF TAVR and had a 29mm SAPIEN 3 implanted.

- No post procedural complications.
Mitral Valve Regurgitation

* MR is the most common type of heart valve disorder in the United States.
* Approximately 6 million people have significant mitral valve insufficiency, with an annual incidence of 250,000.\(^1\)
* Mitral valve prolapse remains the most common cause in the USA.
* 1/10 over 70 have significant MR
* Approximately 50,000 of these patients undergo surgery each year in the United States.
* Significant morbidity and mortality.
* Surgery, either mitral valve repair or replacement is the definitive therapy primary mitral regurgitation.
Degenerative vs. Functional MR

- Normal mitral valve
- Degenerative MR caused by mitral valve prolapse
- Degenerative MR caused by flail leaflet
- Functional MR
Cardiac valve surgery—the “French correction”

Michel Carpentier, M.D., Paris, France

Mr. President, I would like to begin by expressing my gratitude to the Association for the privilege of presenting the Honored Guest Lecture at the Sixty-third Annual Meeting of The American Association for Thoracic Surgery. What surprises me most in this setting is my presence on this podium, since this honor is usually reserved for more senior and prominent figures in thoracic surgery. I suppose that you wanted to honor a team rather than a man, so that I would like to share this honor with my co-workers who are present in the room: Drs. Deloché, Fabiani, Chauveau, Galant, Lefrançois, Lapèyre, Mrs. Chauveau, Mrs. Massier, Mrs. Venerian, and with my wife, Sophie, who has participated in my laboratory work throughout these years. I also would like to pay special tribute to my respected teacher, Professor Charles Dubost, and to thank my two colleagues, Professors Blondeau and Falise d'Allaines, who are unfortunately not with us today.

Members of the Association, in the past 14 years, I have attended the annual meeting of your Association 14 times, with the privilege of having presented a paper 17 times. All through these years, wearing a pink identification badge, I observed with great admiration and respect the famous people wearing a white, pressed badge and seated in a carefully delineated area of reserved seats. Permitted me to tell you how proud I am to enter this prestigious circle.

Guests, you are about to enter this circle, but only temporarily. I address you specifically, since you represent the future of thoracic surgery and the future of this august Association.

Members and guests, cardiac surgery has achieved remarkable progress in the past 10 years. Safer techniques of anesthesia, perioperative care, improved extracorporeal circulation and myocardial protection, and sophisticated surgical techniques are new tools which have been instrumental in reducing hospital mortality and increasing the efficiency of our operations. New surgical tools impose new surgical goals. It is not enough to save patients' lives, we must also take into consideration the quality of life given to the patient and the socioeconomic impact of our surgical actions. There already have been some trends in the 1980s, such as operating for congenital malformations at an earlier stage and the development of reconstructive operations to replace palliative techniques. Reconstructive valve surgery can very well be considered another example of this nouvelle chirurgie which justifies making it the subject of today's lecture.

Since everything we do in life has some visible or obscure relationship to the environment in which it occurs, within the context of today's lecture.
The edge-to-edge technique

- First case performed in 1991
- Over 1500 published cases accumulated worldwide
- About 15 yrs follow-up
- Technically simple and reproducible
- Versatile
- Criticized by some surgeons
  - Used only as a bailout
THE ACC/AHA GUIDELINE RECOMMENDS INTERVENTION FOR SEVERE DMR PATIENTS

The ACC/AHA guideline recommends surgical intervention (Class I) for chronic severe DMR¹:
• For symptomatic patients
• For asymptomatic patients with LV dysfunction

When surgery is not an option, the guideline states it is reasonable to consider transcatheter mitral valve repair (TMVR) intervention (Class IIb)¹:
• For severe DMR patients with favorable anatomy for repair, reasonable life expectancy, and who remain severely symptomatic despite guideline-directed medical therapy for heart failure
SURGICAL INTERVENTION IS OFTEN NOT AN OPTION

In one survey of severely symptomatic MR patients (NYHA Class III-IV), as many as half were not candidates for mitral valve surgery due to underlying factors, including:

- Impaired LV ejection fraction
- High operative risk
- Multiple comorbidities
- Advanced age

*Based on a survey of severely symptomatic MR patients in NYHA Class III-IV (n = 396); 10% had surgery the following year. The remainder had no surgery/medical management only.
MitraClip: Reproduction Of The Edge-To-Edge Repair Technique Using A Minimally Invasive Approach Through The Femoral Vein Without Cardiopulmonary Bypass
IDENTIFY OPTIMAL MITRACLIP® CANDIDATES

Optimal candidates for MitraClip® therapy should meet the following criteria:

- Significant DMR (MR $\geq 3+$)
- Severely symptomatic (NYHA Class III/IV)
- Not suitable for surgery because of age or severe comorbidities such as liver disease and pulmonary hypertension
Initial Experience With Commercial Transcatheter Mitral Valve Repair in the United States

Paul Sorajja, MD, Michael Mack, MD, Sreekanth Vemulapalli, MD, David R. Holmes, Jr, MD, Amanda Stebbins, MS, Saibal Kar, MD, D. Scott Lim, MD, Vinod Thourani, MD, Patrick McCarthy, MD, Samir Kapadia, MD, Paul Grayburn, MD, Wesley A. Pedersen, MD, Gorav Ailawadi, MD
CENTRAL ILLUSTRATION Transcatheter Mitral Valve Repair in the United States: Change in Mitral Regurgitation With Transcatheter Mitral Valve Repair

Change in Mitral Regurgitation with Transcatheter Mitral Valve Repair

Major Adverse Clinical Events

In-Hospital Mortality: 2.3%
30-day Mortality: 5.8%
Stroke: 1.8%
Major Bleeding: 3.9%
Myocardial Infarction: 0%

CLINICALLY IMPORTANT IMPROVEMENTS IN OTHER MEANINGFUL MEASURES

Significant reduction in left ventricular size\(^1\,\ast\)

73% reduction in heart failure-related symptoms and hospitalizations\(^1\,\dagger\):
- Between the 1-year periods before and after the procedure\(^1\)

**LEFT VENTRICULAR VOLUMES**
- LV End-Diastolic Volumes:
  - Baseline: 125 mL
  - 1 Year: 109 mL
  - Δ = -16 mL

- LV End-Systolic Volumes:
  - Baseline: 49 mL
  - 1 Year: 46 mL
  - Δ = -3 mL

**HEART FAILURE-RELATED SYMPTOMS AND HOSPITALIZATIONS**
- 1 Year Prior to MitraClip\(^\circ\) (N = 127):
  - 0.67 HF Hospitalization Rate per Patient Year
- 1 Year Post Discharge (N = 120):
  - 0.18 HF Hospitalization Rate per Patient Year

Real-world data shows continued success\(^2\,\dagger\)
In the STS/ACC TVT Registry (n = 564) 93% achieved MR ≤ 2+ within 30 days post procedure, with nearly 64% of patients achieving MR ≤ 1+. 
CONTRAINDICATIONS

* Life expectancy <6 months
* H/O rheumatic mitral valve disease or endocarditis
* LA appendage thrombus
* Moderate to severe mitral stenosis
* Mitral Valve area <3.5 cm²
* Active femoral/IVC thrombus
* Inability to take short term DAPT
TMCA Experience As Of Oct 2016

3 Elective Cases, All With Good Results And Reduction Of MR To Mild Grade, No Significant Mitral Stenosis

1 Urgent/Salvage Case: Clips Deployed But MR Reduction Inadequate

2 Elective Cases Scheduled For November
Future Directions In Transcatheter MVr
THANK YOU!!!