Treatment Paradigms for Complex Heart Valve Disease

Saurabh Gupta, MD, FACC
Director, Cardiac Catheterization Laboratories
Co-Director, Complex Heart Valve Clinic
Oregon Health Sciences University

Presenter Disclosure Information

- I WILL discuss off label use or investigational use in my presentation.
- I HAVE financial relationships to disclose:
  - Employee of: OHSU
  - Consultant for: Biotronik (national PI for pivotal bare metal stent trial)
  - Significant Stockholder (more than $25K): None
  - Research support from: Site PI for several national trials (no conflicts)
  - Honoraria (last 5 years): No drug/ device manufacturer
  - Travel support from Edwards for TAVR training

OBJECTIVES

- Learn about surgical and catheter based options for correction of mitral valve disease.
- Recognize and identify patients with significant aortic valve disease and discuss results of surgical and transcatheter aortic valve replacement and triage those patients to medical management, SAVR or TAVR.

THE PAST

Early Inflation

Full expansion
THE PRESENT

THE FUTURE
.....OR ARE WE ALREADY THERE?

Current MR Surgical Options
Complications, Mortality, Procedures

Mitral Valve Repair is the preferred treatment of choice

<table>
<thead>
<tr>
<th>Mitral Valve Procedure</th>
<th>Any Complication*</th>
<th>Mortality*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Replacement</td>
<td>52.6%</td>
<td>5.5%</td>
</tr>
<tr>
<td>Repair</td>
<td>39.9%</td>
<td>1.5%</td>
</tr>
</tbody>
</table>

MV Procedure Distribution*:
- 54% Repair
- 46% Replacement

*Sor database, 2007 in-hospital data, isolated 2198 MVR 2536 repair

Surgical View of the Mitral Valve

Anterior
Left lateral
Posterior
Medial
antero-lateral
antero-medial
A1, A2, A3

Adapted from: Dist. Valvular
Annal invasive, Society 1999
MITRAL VALVE REPAIR

Mitrval valve repair usually preferable to mitral valve replacement.

- **Leaflet resection:**
  - Remodeling the valve by removing some portion of leaflet tissue and reattaching them with sutures.

- **Anuloplasty:**
  - Implanting a ring (collar-like structure) around the mitral valve's base, in order to remodel the annulus (opening) and support the repair.

- **Edge to Edge:**
  - Fastening the leaflets together where the valve leaks.

- **Chordal Transposition:**
  - Repositioning and re-attaching fibers (chordae tendineae) that connect to muscles in the LV and that control movement of the mitral valve leaflets.

Percutaneous approaches to Mitral Valve Repair based on surgical principles

<table>
<thead>
<tr>
<th>Technique</th>
<th>Device</th>
<th>Surgical Principle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leaflet Repair</td>
<td>MitraClip (Edwards Lifesciences)</td>
<td>Annuloplasty</td>
</tr>
<tr>
<td>Percutaneous Mitral Annuloplasty</td>
<td>Artificial Chords</td>
<td>Surgical edge to edge repair</td>
</tr>
<tr>
<td>+Coronary Sinus Annuloplasty</td>
<td>Monarch (Medtronic)</td>
<td>Surgical Artificial chords</td>
</tr>
<tr>
<td></td>
<td>+Carillon (Cardiac Dimensions)</td>
<td>Surgical annuloplasty</td>
</tr>
<tr>
<td></td>
<td>+PTMA device (Viscogen)</td>
<td></td>
</tr>
<tr>
<td>Direct Annuloplasty</td>
<td>+MitraClip (Cardiac Dimensions)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>+Radiol Frequency ablation of annulus (CardioCor)</td>
<td></td>
</tr>
<tr>
<td>Chamber and annular remodeling</td>
<td>+Coapsys (Myocor)</td>
<td>Left ventricular anteroposterior reshaping using the surgical Coapsys.</td>
</tr>
<tr>
<td>+Left Ventricle Remodeling</td>
<td>+PS3 System (Ample Medical)</td>
<td>Reshaping annulus by creating a tension bridge between coronary sinus and interatrial septum</td>
</tr>
<tr>
<td>+Trans-Atrial Shape Change</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Leaflet Repair

Surgical Edge to Edge Repair "Alfieri Stitch"

Surgical Isolated Central Alfieri mitral repair intentionally without annuloplasty*  
"Clinical proof of principle for an endovascular approach"  

Edge to Edge MitraClip Concepts

- Facilitates leaflet coaptation
  - Mechanical solution for mechanical problem
  - Reduces regurgitant volume & LV volume overload

- Creates tissue bridge
  - Limits dilatation of annulus
    - Septal-lateral (A-P) dimension
    - Supports durability of repair

- Restrains LV wall
  - Limits LV dilatation

* No leaflet or chordal surgery

Percutaneous Edge to Edge Repair using MitraClip

- First Percutaneous Mitral Valve repair system to receive CE Mark approval
- Based on surgical edge to edge repair
- Effective for both degenerative and functional Mitral regurgitation (MR)

Conditions treated with the MitraClip device

- Mal-coaptation of the A2-P2 leaflet scallops:
  - Degenerative mitral valve disease
    - Posterior leaflet prolapse/flail
    - Anterior leaflet prolapse/flail
    - Bi-leaflet Prolapse
  - Functional mitral regurgitation
    - Non ischemic dilated cardiomyopathy
    - Ischemic cardiomyopathy with restriction of A2 or P2.

EVEREST (Endovascular Valve Edge-to-Edge REpair STudy)

EVEREST Initial Cohort
Efficacy Results through Discharge
N = 107

Clip Procedure Attempted
N = 107 (100%)

Clip Implanted
n=98 (90%)

No Clip Implanted
n=9 (10%)

Acute Procedural Success
MR = 2+
N=81 (86%)

MR = 3+
N=15 (16%)

Acute Procedural Success (APS): placement of ≥1 Clips resulting in discharge MR severity of 2+ or less (determined by Core Lab)

EVEREST Initial Cohort
Patients with 30 Day MACE (N=107)

Freedom from Major Adverse Events 91%

- Death - Unrelated to Clip 1
- Stroke (>72 hours) 1
- Myocardial Infarction 0
- Re-operation for failed surgery 1
- Non-elective Cardiac Surgery (transseptal comp) 2
- Renal failure 0
- Deep wound infection and Sepsis 0
- Ventilation > 48 hrs 0
- GI complication requiring surgery 0
- Bleeding requiring transfusion ≥ 2 units 5

10/107 (9%)

Clinical Experience with the MitraClip Device

- High acute success rate: percutaneous mitral valve repair using the MitraClip is safe and effective in selected patients with MR
- Partial Clip detachment decreasing from 10% to under 2% with the learning curve
- Surgical Options are preserved
- Durable Mid term results
- There is clinical need for percutaneous repair
  - High risk surgical patients
  - Younger patients who prefer a less invasive approach
### Table 2: Comparative summary of published MitraClip clinical trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Feasibility patients</th>
<th>Pre-randomized patients</th>
<th>Non-randomized patients (High Risk Study)</th>
<th>Randomized patients (2:1 Clip to Surgery)</th>
<th>Non-randomized patients</th>
<th>Non-randomized patients</th>
<th>Commercial patients</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVEREST I (Feasibility)</td>
<td>55</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EVEREST II (Pivotal)</td>
<td>60</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EVEREST II (Pivotal)</td>
<td>78</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>REALISM (Continued Access)</td>
<td>716</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compassionate/Emergency Use</td>
<td>43</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACCESS Europe Phase I</td>
<td>506</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACCESS Europe Phase II</td>
<td>162</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Commercial Use</td>
<td>3,984</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>5,668</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+65 surgery</td>
</tr>
</tbody>
</table>

**Worldwide Experience**

**Commercial MitraClip Implant Experience**
- Treating Centers: 164
- Patients: 4,732
- Implant Rate: 96%
- Acute MR reduction of implants
- Etiology:
  - Functional MR: 67%
  - Degenerative MR: 25%
  - Mixed: 8%

**MitraClip Therapy Current Global Adoption**

**Rationale of Coronary Sinoplasty**

**Edwards MONARC System**

- Foreshortening Implant
- Distal Anchor
- Proximal Anchor
Conclusions

- Percutaneous mitral repair is a reality
- Most devices are in the early clinical phase
- Improvements of technology will improve clinical success rates
- Combination of annuloplasty with leaflet repair techniques likely will increase the early and long term success rates in certain patient groups

Percutaneous Transcatheter Closure of Prosthetic Mitral Paravalvular Leaks

ARE WE THERE YET?

Conclusions

- Trans-catheter mitral PVL closures is challenging but technically feasible.
- Advanced image guidance with 3D echo significant enhancement.
- Long-term clinical success, however, is dictated by the limitations associated with the use of existing devices for PVL closure and the need to design a PVL-specific closure device.

Severe AS should be treated

Survival Percent

Onset severe symptoms

Latest Period (increasing Obstruction, Myocardial overload)

Angina, syncope, failure

Avg. survival Years

0 40 80 60 40 20 0


Euro Heart Survey
Symptomatic AS (elderly)
Euro Heart Survey on VHD

31.8% of patients were not operated, despite NYHA class III/IV Sx

- **CARDIAC REASONS**
  - decrease Sx after treatment 45%
  - "end-stage" cardiac disease 30%

- **EXTRA-CARDIAC REASONS**
  - age 27%
  - co-morbidities 27%
  - patient refusal 16%


There is a need for alternatives to surgery in high risk aortic stenosis patients...

**Percutaneous Aortic Valves**

- Cribier-Edwards/Sapien™ Valve
  - Balloon expandable
- CoreValve
  - Self expandable

**Edwards SAPIEN™ THV**

Bovine pericardial valve
Mounted on stainless steel balloon expandable stent

Two sizes: 23 and 26 mm

Transfemoral

Transapical

**PARTNER Study Design**

- Symptomatic Severe Aortic Stenosis
  - AS score ≥3 high risk
  - NYHA class IV or severe heart failure

N = 699

High Risk

Inoperable N = 358
CONCLUSIONS FROM THE PARTNER TRIAL

- TAVR is superior to best medical therapy in patients deemed inoperable.
- TAVR is non-inferior to surgical AVR in high risk patients.
- Death at 30 days was lower than expected in both arms of the trial:
  - TAVR mortality (3.4%) lowest reported in any series
  - AVR mortality (6.5%) was lower than the expected operative mortality (11.8%)
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 TIs) between 1-2 years in TAVR patients.
- After 30 days, differences in stroke frequency were largely due to increased hemorrhagic strokes in TAVR patients.

TAVR Admission Costs

![Bar chart showing TAVR Admission Costs](chart)

- ICU: 4.0 (2.0) days
- Non-ICU: 6.1 (3.0) days
- Total: 10.1 (7.0) days
- Post-Procedure: 8.8 (8.0) days (N=175)

TAVR Procedure Costs

![Bar chart showing TAVR Procedure Costs](chart)

- Physician Fees: $3,432
- Other Devices: $7,460
- OR Costs: $46,293
- Study Device: $32,057

Results: 12-Month Follow-up Costs

![Bar chart showing Results: 12-Month Follow-up Costs](chart)

- Total F/U Costs (12 months):
  - TAVR: $29,352
  - Control: $32,724

Published Cost Effectiveness Estimates

![Bar chart showing Published Cost Effectiveness Estimates](chart)

- Dollars per life year at QALY (Discounted)
Valve Clinic

- Multidisciplinary Approach
- Patient seen simultaneously by CTS and IC
- Allied specialties: pulmonary, renal, hematology, palliative care
- Close collaboration with interventional radiology/vascular surgery
- Valve conference for final determination of patient treatment strategy
- Close involvement of patient’s current care team/referring MD
**TAVR Service**

![TAVR Service Diagram]

**HEART VALVE Cardiologists SERVICE**
- Outpatient Clinic
- Bi-Weekly Clinical Service Meeting
- TAVR
- Inpatient Rounds
- Angiography
- PCI
- BAV

**Surgical AVR**

**Initials: AB**
**Age: 87**
**Sex: Male**

- **CLINICAL HISTORY**
  - COPD
  - CHF
  - PAD - s/p Right CEA (95)
  - Dementia
  - Transient Atrial Fib/Flutter
  - CAD
  - Presented with Class 4 heart failure and significant decrease in EF from Dec 2011.
  - Underwent BAV with prolonged CHF → PPM

- **NYHA Class: 3**
- **Labs:**
  - Cr: 1.22
  - Hgb: 12
  - Platelets: 164

**SURGICAL RISK ASSESSMENT**
- STS Score: 14%
- EUROScore II: 30%

- Deemed inoperable for the following reasons:
  - Not a surgical candidate due to his age, low EF, frailty (unable to walk, low grip strength, low albumin) confusion/dementia

**STS Busters**
- Porcelain Aorta
- Hostile Chest
- Pulmonary Disease
  - Pulmonary HTN
  - Pulmonary Fibrosis
- LIMA/RIMA across midline or adherent to sternum
- Cirrhosis
- Frailty

**CORONARY ANGIOGRAPHY (Date: April 2012)**

- LCA: 50% Stenosis of LAD
- RCA: Non dominant with severe disease

**Echocardiography (4/27/12)**

- [Echocardiogram Image]
Valve Size Selection

- The SAPIEN valve is intended to be implanted in a native annulus size range comparable to the following TEE measurements:

<table>
<thead>
<tr>
<th>Valve Size to Annulus Diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annulus Diameter</td>
</tr>
<tr>
<td>Size of SAPIEN Valve</td>
</tr>
<tr>
<td>Minimum Valve Diameter</td>
</tr>
<tr>
<td>Minimum Veal Diameter</td>
</tr>
<tr>
<td>Minimum Veal Diameter</td>
</tr>
</tbody>
</table>

CT Abdomen and Pelvis

CT: Right Ileo-femoral system

CT: Left Ileo-femoral system
Transfemoral Room Setup

Rapid Ventricular Pacing:
Test Run

- Set output to high setting to ensure proper capture
- Note that there can be a delay between pacing onset and effective reduction of cardiac output

Surgeons as Partners

Beware - Cardiologists appear closer than they actually are.

Center for Advanced valve therapies

NO MA’AM. “CASH FOR CLUNKERS” IS NOT A HEALTH CARE PROGRAM