Motivation for Percutaneous Treatment of Valvular Heart Disease

- Mechanical treatment of valvular heart disease has traditionally been the domain of the cardiac surgeon
  - First cardiac surgical procedure = mitral commissurotomy
  - Nearly 1/3 of current cardiac surgical procedures involve some treatment of valve disease
- However, many patients may not be optimally served by this treatment paradigm
  - Morbid procedures and imperfect prostheses → strategy of waiting for the "golden moment"
  - Watchful waiting may lead to irreversible LV dysfunction in some individuals and tolerating mild/moderate sx in others
  - Many patients are poor candidates for surgery due to comorbidity/advanced age

Changing Treatment for Mitral Stenosis

- Historically, mitral commissurotomy (closed or open) was the standard of care from 1950s through 1980s
- Balloon mitral valvuloplasty (BMV, PTMC) introduced by Inoue and Locke in 1984
- As techniques and results have improved, BMV is now first-line treatment for mitral stenosis
  - Single balloon, double balloon, Inoue balloon, Cribier valvulotome
**Balloon Mitral Valvuloplasty**

**BMV vs. Open Surgical Commissurotomy**

- BMV performed with double-balloon technique
- No difference in acute results or complications
- 3 year results similar but tend to favor BMV

Reyes et al.

- BMV vs. Open Surgical Commissurotomy

**Relationship Between Valve Deformity and Acute Results of BMV**

- Valve characteristics scored independently on 0-4 scale
  - Leaflet mobility
  - Valvular thickening
  - Subvalvular thickening
  - Valvular calcification
- Higher score closely correlated with acute success (esp. <8)

Reyes et al. NEJM. 1994; 331:961-997

Abascal VM, Circulation. 1990;82:448-456
Aortic Stenosis

• Most common form of acquired valvular heart disease in adults
• Incidence likely to increase substantially over next 2 decades due to aging population
• Etiology varies with age

- Degenerative/Calcific (70-80)
- Bicuspid (50-60)
- Rheumatic (variable)

Natural History of Aortic Stenosis

Treatment of Aortic Stenosis

• Standard treatment is surgical aortic valve replacement
• Generally well-tolerated, even in octogenarians (operative mortality ~5% with isolated AVR)
• However, many patients are poor surgical candidates because of multiple adverse prognostic factors
  - Advanced age (esp. > 80 yo)
  - Advanced NYHA class CHF
  - Severely reduced LV fn (EF < 30%)
  - Concomitant CABG
• Led to the development of balloon aortic valvuloplasty in the mid-1980s
Balloon Aortic Valvuloplasty

Results of Balloon Aortic Valvuloplasty

BIDMC Experience
- Acute results good
  - Typical 50% reduction in gradient
  - Mean AVA 0.6 → 0.9 cm²
  - Low periprocedural mortality and stroke
- Long-term results poor
  - 82% developed recurrent sx during follow-up
  - No difference in overall survival c/w medical rx

Kuntz RE et al. NEJM 1990

Current Indications for BAV

1) Severe, symptomatic AS in non-operative candidate
   - Extensive comorbidity (cancer, pulm dz)
   - Severe LV dysfunction
   - Inoperable coronary disease

2) Low gradient / low output aortic stenosis
   - Diagnostic BAV (response to BAV may distinguish reversible from irreversible LV dysfunction)

3) Asymptomatic, severe AS in a patient who requires major non-cardiac surgery

4) Bridge to percutaneous valve replacement

Edwards SAPIEN Transcatheter Aortic Valve
MAHI THV #4: L.D.

- 87 y.o. woman with severe AS → hospitalized x 2 in last 2 months for Class IV CHF and refractory angina

PMHx
- Severe 3-vessel CAD → BMS to LAD and LCX placed for refractory angina in 6/08
- Steroid-dependent COPD x 15 yrs

Exam
- Ht: 4’10” Wt: 92 lbs
- BP: 110/64
- Cardiac: S1 S2 + III/VI late-peaking SEM

STS Risk Score
- Perioperative Mortality: 14.6%
- Major morbidity: 38.2%

Aortic Regurgitation

<table>
<thead>
<tr>
<th>Grade</th>
<th>Pre</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>0</td>
<td>6</td>
<td>2</td>
</tr>
</tbody>
</table>

- Less AI in recent series due to development of larger valve prostheses (26 vs. 23 mm)

Hemodynamics

Pre-THV

Post-THV

Assessment for Femoral Access
MAHI Transapical THV #1: DHC

85 y.o. woman with severe AS → NYHA Class III

PMHx
- Single-vessel CAD, s/p BMS to LAD 1 month prior
- Moderate renal insufficiency (Creat 1.5-1.7)
- Mild interstitial lung dz.

Exam:
- Ht: 5'0" Wt: 192 lbs BP: 110/64
- Cardiac: S1 S2 + III/VI late-peaking SEM

STS Risk Score
- Perioperative Mortality 10.3%
- Major morbidity 29.5%

Baseline TTE
- EF 70%
- AVA = 0.7cm²
- Peak grad= 71 mmHg
- Mean grad= 42 mmHg
- LVOT = 1.9 cm
- PA = 36 mmHg

Baseline TEE
- Ao Annulus = 2.0 cm
Other Aortic Valve Approaches

**CoreValve**
- Self-expanding stent, 18F
- Extends above coronaries
- Approved in Europe

**Other stent-valve designs**
- Bonhoeffer (Bovine jugular valve)
- Direct Flow (inflatable cuff)

**Corazone**
- In vivo valve decalcification
- Several surgical cases done
- Percutaneous use planned

**CoreValve Revalving™ System**
- Nitinol, self-expanding stent design
- Multi-level stent design incorporates 3 levels of radial force
  - Low radial force (for orientation)
  - Constrained: Avoid coronary ostia
  - High radial force (valve dilation, anchoring)

**18F Delivery Catheter System**
- Loading/Release Handle
- 18F Capsule
- 15F Shaft
- Over-the-wire 0.035 compatible

**Lesson Learned**
- Slow and Stepwise Deployment Allows Repositionability
  - No need to “rush” since...
PARTNER Trial: Edwards Lifesciences

Patients with severe, symptomatic AS
High-risk for AVR (n=1040)

High risk surgical candidate
(Predicted mortality >10%)

Non-surgical candidate

Perc AVR
Surgical AVR
Perc AVR
Continued medical Rx

N=690 (minimum)
1° endpoint = 1-year mortality
Non-inferiority comparison
2° endpoint: death, MI, stroke

N=350
1° endpoint = 1-year survival
Superiority comparison

Mitral Regurgitation: Structural

- Abnormalities of valve leaflets
  - Floppy mitral valve/MVP
  - Rheumatic heart disease → deformity of cusps

- Abnormalities of chordae and papillary muscles
  - Chordal rupture
  - Endocarditis, MVP
  - Ischemic papillary muscle dysfunction or rupture
Mitral Regurgitation: Functional

- Left ventricular dilatation with normal leaflets
- Generally due to ischemic or idiopathic cardiomyopathy

Mitral Repair

Mitral Annuloplasty Rings

- Reduce annular circumference
- Push posterior leaflet forward for better coaptation

Issues with Coronary Sinus Approach

- Ability to substantially reduce annulus due to anatomic constraints
  - CS over LA
  - Mitral annular calcification?
- Potential pinching of circumflex coronary artery
- Risk of CS thrombosis/occlusion
- Risk of CS erosion/perforation over long term

If it works, however, this approach would be simple and practical for many interventional cardiologists
**Mitral Repair**

**Edge-to-Edge Repair: “Alfieri Stitch”**

- Introduced in 1990 by Ottavio Alfieri (Milan)
- Suture in center → create double orifice
- Approximates leaflets in early systole and substantially reduces MR
- Preserves ventricular shape and dynamics
- May be combined with annuloplasty

**Percutaneous Mitral Repair System**

**EVEREST Feasibility Study**

- Clip procedure attempted (n=104)
- Clip Implant = 93 (89%)
- No Clip = 11 (11%)
- Acute Success MR ≤ 2+ by core lab = 79 (85%)
- No Acute Success = 7 (15%)

**Inclusion Criteria**
- Patients with 3-4+ MR and either:
  - Symptoms
  - or EF <60% with LVEDD = 45 mm
  - MR originates from A2-P2 mal-coaptation
  - Candidate for mitral valve surgery

**LV Volumes (46 Matched Pairs)**

- End Diastolic Volume
  - Baseline: 172, 12 months: 146 (P<0.001)
  - Baseline: 72, 12 months: 63 (P=0.002)
EVEREST II Pivotal Trial

• Prospective, randomized clinical trial
  – Patients with 3-4+ MR with good LV function
  – Randomized to E-valve clip vs. mitral valve surgery (2:1)
  – PI: Ted Feldman (Evanston Hosp)

• Primary efficacy endpoint
  – Freedom from death, re-intervention for valve dysfunction, >2+ mitral regurgitation by echo at 12 months
  – Non-inferiority comparison

• Primary safety endpoint
  – 1 month major adverse events
  – Superiority comparison

Issues with Edge-to-Edge Repair

• Large device size (24Fr) and complexity
  – Unfamiliar anatomic/functional considerations for most interventionalists
  – Need for non-angiographic real-time imaging

• Anatomic considerations may limit application

• Durability of repair
  – Alfieri f/u studies suggest some increased MR over time

• Will it work without concomitant annuloplasty?
  – ? Eventual role for device synergy

Percutaneous Heart Valve Rx

• Although devices for percutaneous valve repair/replacement are still early stage, they are promising even now

• Initial candidates for such therapy will likely be patients who are either too healthy (moderate MR) or too sick (advanced CHF, comorbidity) for current surgical techniques

• Direct competition with open valve surgery in surgical candidates will take proven long-term results comparable to those of surgery

Percutaneous Heart Valve Rx

• Progress will best be made by close collaboration among:
  – Cardiac Surgeons – they really know valve disease
  – Interventional Cardiologists – they know catheters but need to learn about the valves and special access issues
  – Echocardiographers – they provide the best real-time imaging
  – Engineers – they know what can be made, and how to make it