Transcatheter Mitral Valve Replacement
How Close Are We?

Gregory Pavlides, MD, PhD, FACC, FESC
Professor of Medicine
Miscia Chair of Interventional Cardiology
Director, Cardiac Catheterization Laboratories, Interventional Cardiology and Structural Heart Disease Program
University of Nebraska Medical Center
Omaha, NE, USA
The Mitral Valve Apparatus is a Complex Structure
Mitral Valve Challenges to Percutaneous Treatments

- The mitral valve is large
- It is difficult to access
- It is asymmetrical
- It lacks an anatomically well-defined annulus to which to anchor the replacement valve
- Its geometry changes throughout the cardiac cycle
- It is close to LVOT and placing a replacement valve in it entails the risk of obstruction
Mitral Valve Pathology Amenable to Interventional Therapy

- Mitral Valve Regurgitation
  
  **Primary (degenerative)**
  - Myxomatous degeneration
  - Chordal detachment
  - Fibroelastic deficiency
  - Endocarditis
  - Rheumatic
  
  **Secondary (functional)**
  - Apical tethering to a dilated ventricle
  - Reduced closing forces with left ventricular dysfunction
  - Annular dilation

- Mitral valve stenosis
  - Rheumatic
  - Degenerative calcification (MAC)

- Bioprosthetic Valve or Valve Ring Failure
Native Mitral Valve Regurgitation
Sequence of Therapeutic Steps

Degenerative Mitral Regurgitation
• Cardiac surgery remains the standard of care, at a hospital experienced with mitral valve repair
• When surgical risk is prohibitive, percutaneous edge-to-edge leaflet repair using the MitralClip is the best option in suitable anatomy
• If not amenable to MitralClip, transcatheter mitral valve replacement (TMVR) could be considered in a setting of a clinical trial

Functional Mitral Regurgitation
• Restoration of NSR in cases of atrial fibrillation
• Guideline directed medical therapy for left ventricular dysfunction
• Cardiac resynchronization therapy, when indicated
• MitralClip in high surgical risk patients (enroll in a study)
• Enroll in a TMVR study
<table>
<thead>
<tr>
<th>Type of repair</th>
<th>Device</th>
<th>Technique</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edge-to-edge repair</td>
<td>MitraClip</td>
<td>V-shaped clip applied via femoral vein</td>
<td>FDA approval for patients with degenerative mitral regurgitation COAPT trial for patients with functional mitral regurgitation</td>
</tr>
<tr>
<td>Indirect annuloplasty</td>
<td>Carillon</td>
<td>Nitinol wire placed in the coronary sinus via the internal jugular vein</td>
<td>US trial being planned CE Mark approval</td>
</tr>
<tr>
<td>Direct annuloplasty</td>
<td>Mitralign</td>
<td>Anchors placed in the posterior annulus via femoral artery</td>
<td>Feasibility trial published</td>
</tr>
<tr>
<td></td>
<td>Valtech Cardioband</td>
<td>Anchors placed in the posterior annulus via the femoral vein</td>
<td>Feasibility trial published</td>
</tr>
<tr>
<td>Chordal repair</td>
<td>NeoChord</td>
<td>Transapical approach</td>
<td>CE Mark approval</td>
</tr>
<tr>
<td>Valve spacer</td>
<td>Mitra-Spacer</td>
<td>Balloon placed in the mitral valve to reduce regurgitant orifice and improve coaptation, transfemoral and transapical delivery</td>
<td>First-in-man completed Technology licensed for possible tricuspid valve use</td>
</tr>
<tr>
<td>Chamber remodelling</td>
<td>Basal annuloplasty of the cardia externally (BACE)</td>
<td>Silicone band placed externally at the atrioventricular groove and inflated</td>
<td>First-in-man completed</td>
</tr>
</tbody>
</table>
TMVR Devices Implanted in Humans

- Fortis (Edwards Lifesciences, Irvine, CA)
- Tendyne (Tendyne Holding Inc., Roseville, MN)
- NaviGate (NaviGate Cardiac Structures Inc., Lake Forest, CA)
- Intrepid (Medtronic, Minneapolis, MN)
- CardiAQ (Edwards Lifesciences, Irvine, CA)
- Tiara (Neovasc Inc., Richmond, BC)
Transcatheter mitral valve replacement
Characteristics of Proposed Devices

All devices in development are comprised of three components:
1. Occluding component (leaflets)
2. Supporting frame (usually nitinol frame)
3. Anchoring mechanism

4. Delivery
Self-expandable nitinol frame
Bovine pericardium
Trans-apical approach

13 patients
12/13 functional MR
EF 34%
Procedural success 10/13
5 patients died in 6 months
Trial on hold
The Tendyne Valve

Self-expanding valve
Porcine epicardial leaflets
Tethered to apex
Trans-apical placement
Up to 80 valves implanted worldwide.
Transcatheter Mitral Valve Replacement for Patients With Symptomatic Mitral Regurgitation: A Global Feasibility Trial

David W.M. Muller, MBBS, MD,1 Robert Saied Farivar, MD,1 Paul Jansz, MBBS, PhD,1 Richard Bae, MD,1

**TABLE 3 30-Day Clinical Outcomes**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0.0 (0/30)</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>0.0 (0/30)</td>
</tr>
<tr>
<td>Noncardiovascular death</td>
<td>3.3 (1/30)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.0 (0/30)</td>
</tr>
<tr>
<td>Disabling stroke</td>
<td>0.0 (0/30)</td>
</tr>
<tr>
<td>Nondisabling stroke</td>
<td>0.0 (0/30)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0.0 (0/30)</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td></td>
</tr>
<tr>
<td>New-onset atrial fibrillation</td>
<td>3.3 (1/30)</td>
</tr>
<tr>
<td>New LBBB</td>
<td>10.0 (3/30)</td>
</tr>
<tr>
<td>Ventricular arrhythmia</td>
<td>0.0 (0/30)</td>
</tr>
<tr>
<td>Prosthesis dysfunction</td>
<td></td>
</tr>
<tr>
<td>Thrombosis</td>
<td>3.3 (1/30)</td>
</tr>
<tr>
<td>Embolism or migration</td>
<td>0.0 (0/30)</td>
</tr>
<tr>
<td>Hemolysis</td>
<td>3.3 (1/30)</td>
</tr>
<tr>
<td>Mitral valve surgery</td>
<td>0.0 (0/30)</td>
</tr>
<tr>
<td>Rehospitalization for heart failure</td>
<td>13.8 (4/29)</td>
</tr>
</tbody>
</table>

*(J Am Coll Cardiol 2017;69:381-91)*
Self-expending nitinol
Bovine pericardial leaflets
Limited experience
Outer stent to anchor in the annulus
Inner stent to house the valve
Bovine pericardial leaflets
Self-expending
Trans-apical approach
Fair experience
A trial under way (Europe)
Bovine pericardial leaflets
Native leaflet anchoring system
Trans-apical and Trans-septal delivery.
12 patient compassionate use with high mortality
Still in phase 1 trials
Self-expending
Bovine pericardial leaflets
Trans-apical placement

11 patients in a special Canadian Registry
STS score 15.6, EF 29%
9 patients with functional MR
2 patients converted to open heart and died
One additional patient died day 4
Total mortality 3/12
Phase 1
Mitral Annular Calcification-Degenerative Mitral Stenosis

Transcatheter Mitral Valve Replacement in Native Mitral Valve Disease With Severe Mitral Annular Calcification

Results From the First Multicenter Global Registry

Mayra Guerrero, MD,a Danny Dvir, MD,b Dominique Himbert, MD,c Marina Urena, MD,d Mackram Eleid, MD,e Dee Dee Wang, MD,f Adam Greenbaum, MD,g Vaikom S. Mahadevan, MBBS, MD,h David Holzhey, MD, PhD,i Daniel O’Hare, MD, h Nicolas Dumonteil, MD, j Josep Rodés-Cabau, MD, k Nico Piazza, MD,l Jose H. Palma, MD, MSc,l Augustin DeLago, MD, t Enrico Ferrari, MD, t Adam Witkowski, MD, PhD, g Olaf Wendler, MD, PhD,p Ran Kornowski, MD, q Pedro Martinez-Clark, MD, r Daniel Ciaburri, MD, s Richard Shemin, MD, t Sami Alnasser, MD, u David McAllister, DO, v Martin Bena, MD, w Faraz Kerendi, MD, x Gregory Pavilides, MD, y Jose J. Sobrinho, MD, z Guilherme F. Attizzani, MD, rr Isaac George, MD, ss George Nickenig, MD, tt Amir-Ali Fassa, MD, uu Alain Cribier, MD, vv Vinnie Bapat, MD, w Ted Feldman, MD, x Charanjit Rihal, MD, y Alec Vahanian, MD, z John Webb, MD, a William O’Neill, MD a
30 day mortality 29.7%

TMVR in patients with MAC is feasible
Associated with significant adverse effects
Bioprosthetic Valve or Valve-in Ring Failure
(Valve In Valve International Data)

- 349 with valve-in-valve and 89 with valve-in-ring patients
- STS score 12.9
- Trans-apical approach with Sapien XT valve in the majority
- Stroke: ViV 2.9, ViR 1.1%
- Residual MR: ViV 14.8, ViR 2.6%
- LVOT obstruction: ViV 8, ViR 2.6%
- 30 day mortality: ViV 11.4, ViR 7.7%
Bioprosthetic Valve or Valve-in Ring Failure
Trans-catheter Mitral Valve Replacement
Conclusions (May 2017)

• TMVR in regurgitant mitral valves, failing mitral valve bioprosthesis and rings, and calcified mitral annuli is feasible and it has been conducted in a limited number of patients with NO surgical option
• The Valve-in-Valve procedure using a TAVR prosthesis has been the most successful and clinically applicable
• The Valve-in-Ring procedure using a TAVR prosthesis has also been proven successful, however LVOT obstruction remains a significant risk
• TMVR for regurgitant native valves is still in clinical infancy. Only a small number of patients have been enrolled in studies with relatively high mortality rate in this early phase. As we speak, TMVR for native regurgitant valves should be considered only in the setting of a clinical trial and only for patients who have no surgical option.
We Are in Our Way, But Not There Yet