Transcatheter Mitral Valve Implantation in patients with MAC
Lessons from Registries and 3D printing

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I have no disclosures
Mitral Annular Calcification

- **Chronic Degenerative** process involving calcification of the fibrous base of the mitral valve.
- **Surgical mitral valve replacement** carries high mortality risk.
- **Technical Difficulties** include the inability to fully decalcify the annulus, to place sutures or sitting the valve properly.

*D.Ramzy et al, J Am Coll Cardiol. 2018 May 1;71(17):1854-1856*
Surgical Mitral Valve Replacement Results

- Higher risk of adverse outcomes.
- Fewer patients with severe MAC being offered surgery.
- The vast majority are simply deemed inoperable and left untreated.
- Significant unmet need for treatment of this patient population.

D.Ramzy et al, J Am Coll Cardiol. 2018 May 1;71(17):1854-1856
Pericutaneous treatment of mitral valve disease

Early Experience With Transcatheter Aortic Valve Implantation in the Aortic Position

Transcatheter aortic valve replacement with a balloon-expandable valve in 20 patients with calcified native aortic valves

Images in Cardiovascular Medicine

First in Human Transapical Implantation of an Aortic Stented Bifurcated Valve in a Patient With Calcified Native Valve

First in Human Percutaneous Implantation of a Soft Expandable Transcatheter Heart Valve in a Severely Stenosed Native Mitral Valve

M. Barovic et al, Current Problems in Cardiology, 2018

V. Bapat, M. Reardon, K. Spurgeon, S. Ptaszek, J Am Coll Cardiol 2018

M. Guerrero et al, Catheterization and Card. Interventions 2014
Dedicated transcatheter mitral valve devices for MAC

- No dedicated devices exist for treatment of MAC.
- Investigational studies for these devices currently exclude MAC.
- Special consideration include challenges in anchoring devices in MAC.
- Specifically designed devices will need to be developed for treatment of MAC.

Described their 1st experience and focused on feasibility and early outcomes.

Evaluated the clinical results and function of mitral prosthesis at 1 year.
116 patients from 51 centers in 11 countries (Sept 2012-March 2017)
Underwent TMVR with compassionate use of balloon-expandable aortic THVs
106 patients eligible for 1-year follow up
These results show no differences compared with their earlier report.
1 Year Analysis of Outcomes of TMVR in patients with severe MAC

Clinical Outcomes

Most patients who survived the 30 day post procedural period remained alive at 1 year.

Efforts should be made to improve patient selection to achieve better outcomes.

Baseline STS score 15%. STS score much higher than in the Partner I trial.

M. Guerrero et al, J Am Coll Cardiol. 2018 May 1;71(17):1841-1853
1 Year Outcomes of Transcatheter Mitral Valve Replacement in patients with severe MAC
Procedural Results – Not insignificant Complications

<table>
<thead>
<tr>
<th>Event</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technical success*</td>
<td>89/116 (76.7)</td>
<td></td>
</tr>
<tr>
<td>LVOT obstruction with hemodynamic compromise</td>
<td>13/116 (11.2)</td>
<td></td>
</tr>
<tr>
<td>Valve embolization</td>
<td>5/116 (4.3)</td>
<td></td>
</tr>
<tr>
<td>Need for a second valve</td>
<td>17/116 (14.7)</td>
<td></td>
</tr>
<tr>
<td>Due to MR</td>
<td>11/17 (64.7)</td>
<td></td>
</tr>
<tr>
<td>Due to migration</td>
<td>6/17 (35.3)</td>
<td></td>
</tr>
<tr>
<td>LV perforation</td>
<td>2/116 (1.7)</td>
<td></td>
</tr>
<tr>
<td>Pulmonary vein perforation</td>
<td>1/116 (0.85)</td>
<td></td>
</tr>
<tr>
<td>Conversion to open heart surgery</td>
<td>4/116 (3.4)</td>
<td></td>
</tr>
<tr>
<td>Embolization</td>
<td>2/4 (50.0)</td>
<td></td>
</tr>
<tr>
<td>LVOT obstruction</td>
<td>1/4 (25.0)</td>
<td></td>
</tr>
<tr>
<td>LV perforation</td>
<td>1/4 (25.0)</td>
<td></td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>58 ± 10.5</td>
<td></td>
</tr>
<tr>
<td>Mean MVG, mm Hg</td>
<td>4.37 ± 2.37</td>
<td></td>
</tr>
<tr>
<td>MVA, cm²</td>
<td>2.44 ± 0.9</td>
<td></td>
</tr>
<tr>
<td>Residual MR at end of procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trace or none</td>
<td>51/82 (62.2)</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>27/82 (32.9)</td>
<td></td>
</tr>
<tr>
<td>≥3 (+)**</td>
<td>4/82 (4.9)</td>
<td></td>
</tr>
</tbody>
</table>

Despite the additional 2 years of experience it seems to be **no reduction** in complication rates.
This finding is critical as LVOTO is a **primary determinant of survival**. Since reporting all causes was not mandatory it is possible that **selecting reporting** occurred to make the data look better.

*M. Guerrero et al, J Am Coll Cardiol. 2018 May 1;71(17):1841-1853*
1 Year Outcomes of Transcatheter Mitral Valve Replacement in patients with severe MAC

**Predictors of 1-Year Mortality**

Current technology has limitations that are directly translated into **procedural mortality**. It is imperative to drive further innovation to valve technology to **improve procedural failure** and to develop better imaging assessments to **accurately predict LVOT obstruction**.

Pre operative determination of LVOTO must improve, as LVOTO at the time of implantation results in **85% mortality rate** which is unacceptably high.

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**Table: Predictors of 1-Year Mortality**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>HR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (1-yr increase)</td>
<td>1.03 (1.01-1.06)</td>
<td>0.028</td>
</tr>
<tr>
<td>Female</td>
<td>0.82 (0.48-1.42)</td>
<td>0.479</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>1.51 (0.88-2.57)</td>
<td>0.131</td>
</tr>
<tr>
<td>Home oxygen</td>
<td>1.05 (0.52-2.09)</td>
<td>0.893</td>
</tr>
<tr>
<td>STS score (1-U increase)</td>
<td>1.02 (0.99-1.05)</td>
<td>0.062</td>
</tr>
<tr>
<td>NYHA functional class III-IV vs. 1-II</td>
<td>3.98 (1.24-12.75)</td>
<td>0.019</td>
</tr>
<tr>
<td>Technical success (yes vs. no)</td>
<td>0.23 (0.12-0.44)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LVOT obstruction</td>
<td>3.56 (1.81-7.01)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Valve embolization</td>
<td>2.93 (1.16-7.42)</td>
<td>0.023</td>
</tr>
<tr>
<td>Conversion to surgery</td>
<td>3.31 (1.18-9.27)</td>
<td>0.022</td>
</tr>
<tr>
<td>Residual MR 3 (+)</td>
<td>1.91 (0.59-6.14)</td>
<td>0.276</td>
</tr>
<tr>
<td>Need for second valve</td>
<td>1.34 (0.68-2.66)</td>
<td>0.393</td>
</tr>
<tr>
<td>Delivery access</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TA vs. transseptial</td>
<td>1.04 (0.60-1.80)</td>
<td>0.891</td>
</tr>
<tr>
<td>TA vs. transatrial</td>
<td>2.67 (1.09-6.48)</td>
<td>0.030</td>
</tr>
<tr>
<td>Transseptal vs. transatrial</td>
<td>2.56 (1.05-6.26)</td>
<td>0.038</td>
</tr>
</tbody>
</table>

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**Figure 3: Outcomes of Patients Who Had LVOT Obstruction With Hemodynamic Compromise After TMVR**

![Figure 3: Outcomes of Patients Who Had LVOT Obstruction With Hemodynamic Compromise After TMVR](image)
Despite normal hearts mortality rate is high.

Either the procedural risk or another factor contributed to mortality.

Procedural failure and LVOTO were major determinants of mortality.

We must have better procedural success if we are to expand TMVR to patients with low EF as mortality in this patients would be higher.

We don’t have data on RV Function which is an important factor on mortality.

M. Guerrero et al, J Am Coll Cardiol. 2018 May 1;71(17):1841-1853
This study was relatively small (harder to elucidate true statistical differences), many centers with 1-2 cases were included which artificially increased the negative outcomes seen in the second half.
Experience/inexperience with transcatheter technologies

• Would **better outcomes** have occurred if these studies were first limited to centers with operators experienced in **transcatheter aortic valve replacement**?
Evaluates safety and feasibility of Transcatheter Mitral Valve Implantation. We anticipate that this trial will help provide insights to further improve technical success, patient selection and the overall clinical outcomes of this patient population.
Self Expandable Aortic Retrievable Devices for Transcatheter Mitral Valve Implantation in patients with MAC

The experience is limited to a few case reports - none of these valves are built for TMVR. Important Disadvantage - the transapical route is the only delivery option at this time.
3D digital and printed models feasible in planning and guiding complex procedure (TMVR) in patients with severe MAC

Abstract

Introduction: Three-dimensional (3D) prototyping is a novel technology which can be used to plan and guide complex procedures such as transcatheter mitral valve replacement (TMVR).
The digital valve was positioned 40% toward the atrium and 60% toward the ventricle. Checked for prosthesis size matching, paravalvular gaps, LVOT obstruction. Results of 3D printing were then compared to post procedural imaging to see how closely the achieved results mirrored the 3D modeled results.

E. Sabbagk et al, Catheter Cardiovasc Interv. 2018 Jan 23
M.Vukicevick, J Am Coll Cardiol Img. February 2017
Assessment of adequacy of valve anchoring, risk of underexpansion and LVOT obstruction

Valve anchoring – measuring the circumferential extend of MAC, reported as a percentage of the mitral annulus, as well as the location of the calcification.

Valve anchoring - measuring the surface area of the virtual valve in direct contact with the digital mitral annular calcification.

Risk of underexpansion - measuring the volume of calcium overlap.

LVOTO - visual assessment of the 3D digital LVOT model in systole with the digital valve inserted.

3D digital models with the Digital Valve Inserted (Sapien prosthesis)

Neo-LVOT area Calculation

% LVOTO = (native LVOT area (systole) - NeoLVOT area) / Native LVOT area

( > 50% high risk of significant LVOT obstruction)

The threshold values of predicted Neo-LVOT area at which clinical LVOTO is seen are not clear and need to be validated with further studies.
Tamponade after TMVR- 3D digital simulation detected significant extraanular calcification extending to the myocardium.

Visual inspection of **any gaps** between the virtual Sapien valve, mitral annulus and mitral leaflets.

3D models were similar to the findings on post procedural imaging.

3D models were made from static images and printed models did not take into account the cardiac tissue properties. Because of that, it did not track dynamic changes that occur after TMVR such as tissue deformation, device tilting, and underexpansion. This could lead to under or overestimation of measurements.
Advancement of 3D printing technologies
Multi material 3D printed model of the mitral valve

The mitral valve apparatus with all functional elements may be fabricated utilizing a range of flexible materials with different stiffness values.

“The idea is that patient selection could be much safer and much more confident if you can actually practice the exact procedure in a model that has the ability to distend and deform the way the heart would.”

Stephan Little

S.Little et al, Structural Heart The Journal of the Heart Team, 2017
M.Vukicevick, Annals of Biomedical Engineering, Vol. 45, No. 2, February 2017
Transcatheter Bioprosthetic Valve Implantation in a Severely Calcified Mitral Valve Annulus: The role for 3D printing

K. Spargias, M. Chrissoheris, K. Papadopoulos, P. Kourkouli, N. Baumboulis, S. Skardoutsos, I. Nikolaou, S. Pattakos

From the Department of Transcatheter Heart Valves and the 2nd Cardiothoracic Surgery Clinic, HYGEIA Hospital, Athens Greece
"There’s also the potential of cost savings by avoiding subsequent fixes by using 3D printing for as little as $100 to $200 to optimize results for the initial intervention. When you think about the total cost for the procedure, even just one TMVR valve is about $30,000 and for now the need of a second valve due to migration or valvular regurgitation would be another $30,000 to $40,000 just based on the valve cost plus the extra procedure cost. If you can decrease the chance of using the second valve, it is cost-effective.”

Stephan Little
Thank you