1-year outcomes of Transcatheter Mitral Valve Replacement in Native Mitral Valve Disease With Severe Mitral Annular Calcification

Update from the first global registry
Speaker's name: Mayra Guerrero

- I have the following potential conflicts of interest to report:
  - Proctor: Edwards Lifesciences
  - Institutional grant/research support: Edwards Lifesciences
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
TMVR in MAC Global Registry

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Institutions

- Bichat Hospital. Univ of Paris, Paris, France
- Henry Ford Hospital Detroit, USA
- Mayo Clinic, Rochester, USA
- Evanston Hospital, Evanston, USA
- Columbia University Medical Center, New York, USA
- Cedars Sinai Medical Center, Los Angeles, USA
- University of Washington Medical Center, Seattle, USA
- Leipzig Heart Center, Leipzig, Germany
- Banner University Medical Center, Phoenix, USA
- Aurora St. Lukes Medical Center, Milwaukee, USA
- Mount Carmel East Hospital, Columbus, USA
- University of California San Francisco, San Francisco, USA
- Rangueil University Hospital, Toulouse, France
- Laval University, Quebec, Canada
- Royal Victoria Hospital, Montreal, Canada
- Cardiocentro Ticino Foundation, Lugano, Switzerland
- Saint Francis Medical Center, Peoria, USA

Collaborators

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- R Makkar, T Chakravarty
- M Reisman, M Mathur, B MacKensen, G Aldea
- D Holzhey
- A Pershad, T Byrne K Fang, M Morris, M Tassett
- D O’Hair
- N Jones, M Gibson, P Wells, K Phillips-Burkhardt
- V Mahadevan
- N Dumontiel
- Josep Rodes-Cabau
- Nicolo Piazza
- E Ferrari
- D Ciaburri
TMVR in MAC Global Registry

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Institutions
- Centre Cardiologique du Nord, St. Denis, France
- Albany Medical Center Hospital, Albany, USA
- Abbott Northwestern Hospital, Minneapolis, USA
- University of Iowa Hospitals and Clinics, Iowa City, USA
- Piedmont Heart Institute, Atlanta, USA
- Intermountain Heart Institute, Salt Lake City, USA
- Brigham and Women’s Hospital, Boston, USA
- Central Manchester University Hospital, Manchester, UK
- Heart Center Bonn, University Hospital, Bonn, Germany
- Rabin Medical Center, Petah Tikva, Israel
- St. Paul’s Hospital, Vancouver, Canada
- Cardiologia de Occidente, Cali, Colombia
- King’s College Hospital, London, UK
- Institute of Cardiology, Warsaw, Poland
- St. Thomas’ Hospital, London, UK
- St. Michael’s Hospital, Toronto, Canada
- Univ of Rouen's Charles Nicolle Hosp, Rouen, France

Collaborators
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- P Shah, T Kaneko
- V Mahadevan
- JM Sinning, G Nickenig
- R Kornowski
- D Dvir, J Webb
- P Martinez-Clark, A Dager
- O Wendler, P MacCarthy
- A Witkowski, K Kuśmierski, M Dąbrowski
- V Bapat, ZY Lim,
- S Alnasser, A Chema, D Deva, M Peterson
- A Cribier, E Durand, H Eltchaninoff, Litzler
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Institutions

- Ntnl Institute of Cardiovascular Diseases, Bratislava, Slovakia
- University Hospitals Case Medical Center, Cleveland, USA
- UCLA Medical Center, Los Angeles, USA
- Complexo Hospitalar de Niteroi, Niteroi, Brasil
- Escola Paulista de Medicina, Sao Paolo, Brazil
- The Iowa Heart Center, Des Moines, USA
- Hôpital de La Tour, Geneva, Switzerland
- The Nebraska Medical Center, Omaha, USA
- Heart Hospital of Austin, Austin, USA
- Buffalo General Medical Center, Buffalo, USA
- Cooper University Hospital, Camden, USA
- Einstein Medical Center, Philadelphia, USA
- Nebraska Heart Hospital, Lincoln, USA
- Praire Heart Institute, Springfield, USA
- INOVA Fairfax Hospital, Falls Church, USA
- Medstar Washington Hospital Center, Washington, USA
- Massachusetts General Hospital, Boston, USA

Collaborators

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- R Shemin, W Suh, G Vorobiof, O Aksoy, M Kwon
- J Sobrinho, Nagela SV Nunes, C Eiras Falcão,
- J Honorio Palma, D Gaia
- D McAllister, B Jensen
- A Fassa
- G Pavlides, M Moulton, N Sricharoen
- F Kerendi, F Zidar, S Dewan, J Karhna
- V Iyer
- G Kaddissi, MR Sardar
- C Witzke
- J Wudel
- G Mishkel, N Goswami
- B Raybuck
- R Waksman, L Satler, A Pichard
- I Palacios, I Inglessis.
1-Year Follow-up TMVR in MAC Registry
Data lock May 1st, 2017

116 patients with severe MAC underwent TMVR
With aortic THVs

29/116 deaths < 30 days

106 patients had procedure 1-year prior to Data Lock
May 1st, 2017
(eligible for 1-year follow-up)

10 had procedure after May 2016
Mean follow-up 5 months (range 2-10)

77 patients alive after 30 days
and eligible for 1-year follow-up

29/77 deaths after 30 days

48 patients alive 1-year after TMVR
### Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>n (%), or mean (±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>73 (±12)</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>79/116 (68.1%)</td>
</tr>
<tr>
<td><strong>NYHA</strong></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>10%</td>
</tr>
<tr>
<td>III</td>
<td>45%</td>
</tr>
<tr>
<td>IV</td>
<td>45%</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td>46%</td>
</tr>
<tr>
<td><strong>COPD</strong></td>
<td>42.3%</td>
</tr>
<tr>
<td><strong>Atrial Fibrillation</strong></td>
<td>42.8%</td>
</tr>
<tr>
<td><strong>Renal Failure</strong></td>
<td>53.2%</td>
</tr>
<tr>
<td><strong>Prior CABG</strong></td>
<td>32.1%</td>
</tr>
<tr>
<td><strong>Prior AVR</strong></td>
<td>52.6%</td>
</tr>
<tr>
<td><strong>STS score</strong></td>
<td><strong>15.3 (±11.6)</strong></td>
</tr>
</tbody>
</table>
### Baseline Echo Characteristics

<table>
<thead>
<tr>
<th></th>
<th>n (%) or mean (±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ejection fraction (%)</strong></td>
<td>60 (±10.3)</td>
</tr>
<tr>
<td><strong>Mean MVG (mmHg)</strong></td>
<td>11.5 (±4.2)</td>
</tr>
<tr>
<td><strong>MVA (cm²)</strong></td>
<td>1.3 (±0.7)</td>
</tr>
<tr>
<td><strong>Systolic PAP (mmHg)</strong></td>
<td>58 (±19.2)</td>
</tr>
<tr>
<td><strong>Peak LVOT gradient (mmHg)</strong></td>
<td>5.8 (±15)</td>
</tr>
<tr>
<td><strong>Degree or MR</strong></td>
<td></td>
</tr>
<tr>
<td>0-1 (+)</td>
<td>24/103 (23.3%)</td>
</tr>
<tr>
<td>2 (+)</td>
<td>40/103 (38.9%)</td>
</tr>
<tr>
<td>3 (+)</td>
<td>23/103 (22.3%)</td>
</tr>
<tr>
<td>4 (+)</td>
<td>16/103 (15.5%)</td>
</tr>
</tbody>
</table>

7/116 (6%) had only MR without stenosis
Lotus and Direct flow valves were excluded from this analysis.
Delivery Approach

Transatrial

Transapical

Transeptal
# Procedural Outcomes

**n=116**

<table>
<thead>
<tr>
<th>Event</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technical success by MVARC criteria</td>
<td>89 (76.7%)</td>
</tr>
<tr>
<td>LVOT obstruction with hemodynamic compromise</td>
<td>13 (11.2%)</td>
</tr>
<tr>
<td>Valve embolization</td>
<td>5 (4.3%)</td>
</tr>
<tr>
<td>Need for second valve (migration=6, MR=11)</td>
<td>17 (14.7%)</td>
</tr>
<tr>
<td>LV perforation</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>Conversion to open surgery (embolization=2, LV perforation=1, LVOTO=1)</td>
<td>4 (3.4%)</td>
</tr>
</tbody>
</table>
## Clinical Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>30 Days n=116</th>
<th>1 Year n=106</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-Cause Mortality</td>
<td>29 (25%)</td>
<td>58 (54.7%)</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>15 (13%)</td>
<td>26 (24.5%)</td>
</tr>
<tr>
<td>Non-Cardiac death</td>
<td>14 (12%)</td>
<td>32 (30.2%)</td>
</tr>
</tbody>
</table>
# Clinical Outcomes

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<th>1 Year n=106</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular Deaths</td>
<td>15 (13%)</td>
<td>26 (24.5%)</td>
</tr>
<tr>
<td>LVOT Obstruction</td>
<td>6 (5.2%)</td>
<td>7 (6.6%)</td>
</tr>
<tr>
<td>LV Perforation</td>
<td>2 (1.7%)</td>
<td>2 (1.8%)</td>
</tr>
<tr>
<td>Late embolization</td>
<td>2 (1.7%)</td>
<td>2 (1.8%)</td>
</tr>
<tr>
<td>MI</td>
<td>1 (0.85%)</td>
<td>2 (1.8%)</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>1 (0.85%)</td>
<td>4 (3.8%)</td>
</tr>
<tr>
<td>Valve Thrombosis</td>
<td>0 (0%)</td>
<td>2 (1.8%)</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>0 (0%)</td>
<td>3 (2.8%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (0.85%)</td>
<td>2 (1.8%)</td>
</tr>
<tr>
<td>Complete AV Block</td>
<td>1 (0.85%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Sudden Death</td>
<td>1 (0.85%)</td>
<td>2 (1.8%)</td>
</tr>
</tbody>
</table>
## Clinical Outcomes

<table>
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<th>Outcomes</th>
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<th>1 Year n=106</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Cardiac Deaths</td>
<td>14 (12%)</td>
<td>32 (30.2%)</td>
</tr>
<tr>
<td>Multi-organ failure</td>
<td>6 (5.2%)</td>
<td>6 (5.7%)</td>
</tr>
<tr>
<td>Non-cardiac Infection</td>
<td>3 (2.6%)</td>
<td>8 (7.6%)</td>
</tr>
<tr>
<td>Ischemic bowel or perforation</td>
<td>2 (1.7%)</td>
<td>3 (2.8%)</td>
</tr>
<tr>
<td>Bleeding</td>
<td>1 (0.85%)</td>
<td>3 (2.8%)</td>
</tr>
<tr>
<td>Failure to Thrive</td>
<td>0 (0%)</td>
<td>5 (4.7%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (0.85%)</td>
<td>2 (1.8%)</td>
</tr>
</tbody>
</table>
## Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th>30 Days n=116</th>
<th>1 Year n=106</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>5 (4.3%)</td>
<td>7 (6.6%)</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>1 (0.8%)</td>
<td>2 (1.8%)</td>
</tr>
<tr>
<td>Mitral Valve Reintervention</td>
<td>9 (7.7%)</td>
<td>13 (12.3%)</td>
</tr>
<tr>
<td>Valve Embolization</td>
<td>5 (4.3%)</td>
<td>5 (4.7%)</td>
</tr>
<tr>
<td>Valve migration after procedure</td>
<td>2 (1.7%)</td>
<td>3 (2.8%)</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>0 (0%)</td>
<td>3 (2.8%)</td>
</tr>
<tr>
<td>Hemolytic anemia</td>
<td>4/109 (3.7%)</td>
<td>4 (3.8%)</td>
</tr>
<tr>
<td>Valve Thrombosis</td>
<td>0 (0%)</td>
<td>2 (1.8%)</td>
</tr>
</tbody>
</table>
## Mitral Valve Reintervention

<table>
<thead>
<tr>
<th></th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Within 30-Days (n=9/116, 7.7)</strong></td>
<td></td>
</tr>
<tr>
<td>PVL Closure</td>
<td>4</td>
</tr>
<tr>
<td>Transseptal VinV (1 central MR, 1 PVL)</td>
<td>2</td>
</tr>
<tr>
<td>Transatrial TMVR (1 embolization, 1 LVOTO)</td>
<td>2</td>
</tr>
<tr>
<td>Surgical MVR (for MR)</td>
<td>1</td>
</tr>
<tr>
<td><strong>After 30 days (n=4/77, 5.2%)</strong></td>
<td></td>
</tr>
<tr>
<td>PVL Closure</td>
<td>1</td>
</tr>
<tr>
<td>Transseptal Valve-in-Valve (for PVL)</td>
<td>1</td>
</tr>
<tr>
<td>Transatrial TMVR (for LVOTO)</td>
<td>1</td>
</tr>
<tr>
<td>Surgical MVR (late migration)</td>
<td>1</td>
</tr>
</tbody>
</table>
Outcomes of LVOT Obstruction

LVOT Obstruction
With hemodynamics compromise
n=13 (11.2%)

Medical Treatment
n=5
- Died Cath Lab=1
- Pneumonia=1
- 1 day post=1
- 2 days post=1
- 2m post=1
- Dead n=5

Kissing BAV and BMV
n=1
- Dead n=1

Surgery
n=1
- Dead n=1

Alcohol Septal Ablation
n=6
- Died In-Hosp n=2
- Discharged n=4
- GI bleed at 45 days
- Unknown at 3 months
- Alive at 1 y n=2

Discharged
n=4
# Multivariate Cox Regression Analysis

## Independent Predictors of 1 Year Mortality

<table>
<thead>
<tr>
<th></th>
<th>HR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technical success (yes vs no)</td>
<td>0.22</td>
<td>0.09-0.51</td>
<td>0.0005</td>
</tr>
<tr>
<td>LVOT obstruction</td>
<td>2.63</td>
<td>1.14-6.06</td>
<td>0.0227</td>
</tr>
</tbody>
</table>

HR: Hazard ratio; 95% CI: 95% confidence intervals of hazard ratio
Predicting LVOT Obstruction

Alcohol Septal Ablation as bail out for LVOTO

6 patients treated with alcohol ablation as bail out for LVOTO post TMVR
Reduction in LVOT gradient in all 6 patients
4 were discharged from the hospital after successful rescue

The role of preemptive Alcohol Septal Ablation prior to TMVR to decrease the risk of LVOT obstruction will be presented today by Dr. Dee Dee Wang at 3pm Room Ternes 2

Kaplan-Meier Freedom from All-Cause Mortality

Survival Probability vs. time_days

At Risk: 116 86 70 61 58 56 53 51 49 48

Censored
Kaplan-Meier Freedom from All-Cause Mortality

After 30 Days

Survival Probability

At Risk

0 30 60 90 120 150 180 210 240 270 300 330 360

time_days

0.0 0.2 0.4 0.6 0.8 1.0

At Risk

79 79 68 63 58 57 56 53 52 51 50 49 48

+ Censored

NorthShore University HealthSystem

Evanston Hospital
## Echocardiographic Data at 1-Year

<table>
<thead>
<tr>
<th></th>
<th>30 Days n=58</th>
<th>1 Year n=34</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection Fraction (%)</td>
<td>60.9 (±8.5)</td>
<td>58.6 (±11.2)</td>
</tr>
<tr>
<td>Mean MVG (mmHg)</td>
<td>6.2 (±2.5)</td>
<td>5.8 (±2.2)</td>
</tr>
<tr>
<td>MVA (cm²)</td>
<td>2.48 (±0.9)</td>
<td>1.9 (±0.5)</td>
</tr>
<tr>
<td>MR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None to Trace</td>
<td>49/58 (84.5%)</td>
<td>24/32 (75%)</td>
</tr>
<tr>
<td>Mild 2(+)</td>
<td>5/58 (8.6%)*</td>
<td>7/32 (21.9%)**</td>
</tr>
<tr>
<td>≥3 (++)</td>
<td>4/58 (6.9%)</td>
<td>1/32 (3.1%)</td>
</tr>
<tr>
<td>Peak LVOT gradient (mmHg)</td>
<td>10.9 (±12.8)</td>
<td>7.3 (±10.2)</td>
</tr>
</tbody>
</table>

*All Paravalvular
** All Central except for 1 which location was not documented
Mean Mitral Valve Gradient at 1-Year

Baseline
n=100

30 Days
n=58

1 Year
n=34

Error bars= ± 1 SD
NYHA Class at 1-Year

Baseline (n=111) 30 day (n=58) 1 year (n=39)

- Class I
- Class II
- Class III
- Class IV
Conclusions

- TMVR with balloon expandable aortic THVs is feasible in severe MAC
- It is associated with procedural complications and high 30-day mortality
- LVOT obstruction is an independent predictor of mortality
- Efforts should be made to predict and prevent LVOTO
- Cardiac CT analysis is crucial to predict LVOTO
Conclusions

- Patients who survive the 30-day procedural period have sustained improvement of symptoms at 1 year.

- Reintervention rate after 30 days is low.

- Valve performance is maintained at 1 year.

- Most deaths after 30 days were non-cardiac... *we must avoid cohort C patients to improve long term outcomes.*

- Prospective clinical trials are needed and ongoing.
Thank You

mayraguerrero@me.com