TEER vs. TMVR for Severe MR: The State of the Art in 2024

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Interventional Cardiology, IRCCS Pol. S. Donato, Milan
Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Grant/Research Support</td>
<td>Medtronic, Philips, Abbott, Boston Scientific, Cardionovum, Meril, Concept Medical</td>
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<tr>
<td>• Consulting Fees/Honoraria</td>
<td>Medtronic, Philips, Abbott, Boston Scientific, Cardionovum, Meril, Concept Medical</td>
</tr>
<tr>
<td>• Proctoring Activity</td>
<td>Abbott, Boston Scientific, Cardionovum, Meril, Concept Medical</td>
</tr>
</tbody>
</table>
Expanding portfolio of transcatheter mitral repair and replacement

- **Chordal Replacement**
  - NeoChord
- **Leaflet Repair**
  - MitraClip
  - PASCAL
- **Annuloplasty**
  - Cardioband
  - Carillon
- **Replacement**
  - Tendyne, Intrepid, Tiara, Cardiovalve, HighLife, etc.
- **Combo procedures**
  - NeoChord Harpoon
  - MitraClip XTR/W & NTR/W
  - PASCAL

- **Tendyne**
- **Intrepid**
- **Harpoon**
2021 ESC/EACTS Guidelines for the management of valvular heart disease

Developed by the Task Force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)
16+ Years Dedicated to the Treatment of Valvular Regurgitation
Proven clinical results show significant MR reduction

MitraClip™ TEER 1-11*#
MR Severity at Discharge or 30 Days*

*Discharge rate was used if 30-day data not available. Mack et. al. did not report MR≤1+, rate assumed from Mitra.FR, > Sorajja TVT 2017. # all study years based on end of enrollment (trials), analysis period (TVT, STS registries), or publication year. Note: Data not from head-to-head studies. Data are provided for informational purposes only.

References 1-11: Please see slide 31
**Durable MR reduction up to five years in a broad range of anatomies**

<table>
<thead>
<tr>
<th>ALL MR ≤ 2+</th>
<th>PMR ≤ 2+</th>
<th>SMR ≤ 2+</th>
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</thead>
<tbody>
<tr>
<td><strong>30-day</strong></td>
<td><strong>30-day</strong></td>
<td><strong>30-day</strong></td>
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<tr>
<td><strong>1-yr</strong></td>
<td><strong>1-yr</strong></td>
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<td><strong>2-yr</strong></td>
<td><strong>2-yr</strong></td>
<td><strong>2-yr</strong></td>
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<tr>
<td><strong>3-yr</strong></td>
<td><strong>3-yr</strong></td>
<td><strong>3-yr</strong></td>
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<tr>
<td><strong>5-yr</strong></td>
<td><strong>5-yr</strong></td>
<td><strong>5-yr</strong></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>EII RCT (N=184)</th>
<th>REALISM HR (N=628)</th>
<th>EXPAND (N=1041)</th>
<th>EXPAND G4 (N=1164)</th>
<th>EII PRDMR (N=127)</th>
<th>COAPT (N=614)</th>
</tr>
</thead>
<tbody>
<tr>
<td>84%</td>
<td>90%</td>
<td>98%</td>
<td>98%</td>
<td>98%</td>
<td>93%</td>
</tr>
<tr>
<td>81%</td>
<td>84%</td>
<td>84%</td>
<td>82%</td>
<td>95%</td>
<td>95%</td>
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<tr>
<td>85%</td>
<td>85%</td>
<td>87%</td>
<td>86%</td>
<td>99%</td>
<td>99%</td>
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<tr>
<td>84%</td>
<td>88%</td>
<td></td>
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</tbody>
</table>


Note: Only residual MR ≤ 2+ reported; data on residual MR ≤ 1+ is limited. Data not from head-to-head studies. Data provided for informational purposes only.
Complication Rate across the Trials

The low mortality rate in EXPAND compared to prior registries is an indicator of current clinical outcomes at experienced, high volume MitraClip centers.

- **EVEREST II Prohibitive Risk DMR (1)**: 6.3%
- **ACCESS-EU (2)**: 3.4%
- **TRAMI (3)**: 2.5%
- **TVT Registry (4)**: 5.2%
- **EXPAND**: 1.5%
- **GIOTTO**: 3.8%

MR Reduction by Core Lab

MR ≤1+ at 6 months: 83.7% for PASCAL and 71.2% for MitraClip

Graph shows paired analysis and p values relative to baseline were calculated using the Wilcoxon signed rank test. ¹Echocardiographic core lab: Atlantic Health System Morristown Medical Center, Morristown, NJ, USA. MR severity assessed by transthoracic echocardiography (TTE).
### TMVR in Functional MR

Different pts → different results

<table>
<thead>
<tr>
<th></th>
<th>GIOTTO (n= 890)</th>
<th>Mitra.FR (n= 152) Percutaneous repair group</th>
<th>COAPT (n=302) Percutaneous repair group</th>
<th>Mitraclip Expand (n= 1041)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>73 ± 8</td>
<td>70,1 ± 10,1</td>
<td>71,1 ± 11,8</td>
<td>77.3 ± 9.7*</td>
</tr>
<tr>
<td>Male</td>
<td>637 (71.6%)</td>
<td>120 (78,9%)</td>
<td>201 (66,6%)</td>
<td>571 (54.9%) *</td>
</tr>
<tr>
<td>NYHA I</td>
<td>5 (0.6%)</td>
<td>-</td>
<td>1 (0,3%)</td>
<td>2.8%*</td>
</tr>
<tr>
<td>NYHA II</td>
<td>138 (15.5)</td>
<td>56 (36,8%)</td>
<td>129 (42,7%)</td>
<td>18.7%*</td>
</tr>
<tr>
<td>NYHA III</td>
<td>650 (73.0%)</td>
<td>82 (53,9%)</td>
<td>154 (51,0%)</td>
<td>67.2%*</td>
</tr>
<tr>
<td>NYHA IV</td>
<td>97 (10.9%)</td>
<td>14 (9,2%)</td>
<td>18 (6,0%)</td>
<td>11.3%*</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>33 ± 10</td>
<td>33,3 ± 6.5</td>
<td>31.3 ± 9.1</td>
<td>38.6 ± 13.3</td>
</tr>
<tr>
<td>LVEDVi (mL/m²mean, SD)</td>
<td>98 ± 35</td>
<td><strong>135 ± 35</strong></td>
<td>101 ± 34*</td>
<td>97.8 ± 43</td>
</tr>
<tr>
<td>EROA (mm²)</td>
<td>35 ± 14</td>
<td>31 ± 10</td>
<td>41 ± 15</td>
<td>47 ± 24*</td>
</tr>
<tr>
<td>MR 2+</td>
<td>12 (2.3%)</td>
<td>-</td>
<td>-</td>
<td>7.9%</td>
</tr>
<tr>
<td>MR 3+</td>
<td>213 (23.9%)</td>
<td>-</td>
<td>148 (49,0%)</td>
<td>29.2%</td>
</tr>
<tr>
<td>MR 4+</td>
<td>665 (74.7%)</td>
<td>-</td>
<td>154 (51,0%)</td>
<td>62.8%</td>
</tr>
<tr>
<td>ICD</td>
<td>423 (47.5%)</td>
<td>90 (59,2%)</td>
<td>91 (30,1%)</td>
<td>18.7%*</td>
</tr>
</tbody>
</table>
Mortality according to post-procedural MR

A. Overall Population

- MR1+ vs. MR2+ vs. MR3+ vs. MR4+
- Log-rank p value ≤ 0.001
- MR1+ vs. MR2+ p ≤ 0.001

B. FMR

- MR1+ vs. MR2+ vs. MR3+ vs. MR4+
- Log-rank p value ≤ 0.001
- MR1+ vs. MR2+ p ≤ 0.001

C. DMR

- MR1+ vs. MR2+ vs. MR3+ vs. MR4+
- Log-rank p value ≤ 0.001
- MR1+ vs. MR2+ p ≤ 0.001

Number at risk:

- MR1+: 911, 822, 520, 481, 333
- MR2+: 465, 373, 267, 199, 128
- MR3+/4+: 50, 39, 23, 14, 10
- MR1+ vs. MR2+ vs. MR3+ vs. MR4+:
  - 568, 518, 393, 313, 224
  - 275, 221, 165, 128, 87
  - 31, 19, 15, 10, 7

p ≤ 0.001
Post Procedural MR and Survival

STS/ACC TVT registry for Mitraclip

S.Lym TCT 2017
Many patients treated with TEER may not achieve MR grade $\leq$ mild at 30-days.

The data is not intended to be a comparison of these devices as there is no head-to-head clinical study, but rather is intended to summarize the clinical results of TEER therapies. Multiple factors contribute to clinical study outcomes and need to be considered in making any assessments across different devices.

<table>
<thead>
<tr>
<th>Device</th>
<th>Study</th>
<th>Study Date</th>
<th>Primary MR Etiology</th>
<th>Secondary MR Etiology</th>
<th>Study Cohort Size</th>
<th>MR $\leq$ Mild at 30-days</th>
</tr>
</thead>
<tbody>
<tr>
<td>MitraClip$^1$</td>
<td>Global EXPAND G4</td>
<td>2020-2022</td>
<td>41.6%</td>
<td>58.4%</td>
<td>1164</td>
<td>91%</td>
</tr>
<tr>
<td>MitraClip$^2$</td>
<td>Global EXPAND</td>
<td>2018-2019</td>
<td>50.5%</td>
<td>49.5%</td>
<td>1041</td>
<td>89%</td>
</tr>
<tr>
<td>MitraClip$^3$</td>
<td>STS/ACC TVT Registry</td>
<td>2014-2022</td>
<td>100%</td>
<td>0%</td>
<td>19,088</td>
<td>66%</td>
</tr>
<tr>
<td>MitraClip$^4$</td>
<td>COAPT PAS</td>
<td>2019-2020</td>
<td>0%</td>
<td>100%</td>
<td>5000</td>
<td>62.5%</td>
</tr>
<tr>
<td>PASCAL$^5$</td>
<td>CLASP IID</td>
<td>2018-2021</td>
<td>100%</td>
<td>0%</td>
<td>199</td>
<td>81%</td>
</tr>
<tr>
<td>PASCAL$^6$</td>
<td>CLASP IID Registry</td>
<td>2019-2021</td>
<td>100%</td>
<td>0%</td>
<td>98</td>
<td>58%</td>
</tr>
<tr>
<td>PASCAL$^7$</td>
<td>CLASP</td>
<td>2017-2020</td>
<td>31.5%</td>
<td>68.5%</td>
<td>124</td>
<td>77%</td>
</tr>
</tbody>
</table>
The Dream of TMVR...

Design and Procedure Goals
- Ease of implantation
- Agnostic to etiology of MR
- Reliable elimination of MR
- Less recurrence of MR
Transcatheter Mitral Valve Replacement

CardioValve
Valtech (Edwards)

CardiAQ
Edwards

EVOQUE
Edwards

Sapien M3
Edwards

Fortis
Edwards

EPYGON
Affluent Medical

AccuFit
SINOMED

MValve
Mvalve Tech

Tiara
Neovasc

HighLife
HighLife Medical

Mi-thos
Shanghai NewMed

Caisson
Livanoval

Corona
Valcare

Permavalve
Micro Interventional

SATURN
InnovHeart

Intrepid
Medtronic

AltaValve
4C Medical

CEPHEA
Abbott

Tendyne
Abbott

NaviGate
NCSI
Current TMVR Clinical Pivotal Trial Landscape

TMVR clinical trials are earlier in development compared with TEER, with only one RCT currently enrolling.

<table>
<thead>
<tr>
<th></th>
<th>Tendyne SUMMIT Trial</th>
<th>Intrepid APOLLO Trial</th>
<th>SAPIEN M3 ENCIRCLE Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sponsor</strong></td>
<td>Abbott</td>
<td>Medtronic</td>
<td>Edwards Lifesciences</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>≥Mod-severe MR Grade III-IV</td>
<td>≥Mod-Severe MR</td>
<td>≥3+ MR</td>
</tr>
<tr>
<td><strong>Design</strong></td>
<td>Randomized and non-randomized arms</td>
<td>Non-randomized</td>
<td>Non-randomized</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>1:1 against TEER w/MAC cohort</td>
<td>Single-Arm w/MAC Cohort</td>
<td>Single-Arm</td>
</tr>
<tr>
<td><strong>Primary Endpoint</strong></td>
<td>Survival free of HFH at 1 year</td>
<td>All-cause mortality or HFH post-30 days or KCCQ improvement &lt;10 composite</td>
<td>Non-hierarchical composite of death and HFH at 1 year</td>
</tr>
<tr>
<td><strong>Patients (Est)</strong></td>
<td>958</td>
<td>1350</td>
<td>500</td>
</tr>
</tbody>
</table>

Table data from clinicaltrials.gov
# Current TMVR Clinical Early Feasibility Trials

The TMVR early feasibility trial landscape continues to evolve and grow with the introduction of new devices.

<table>
<thead>
<tr>
<th>Sponsor</th>
<th>HighLife Feasibility Study</th>
<th>AltaValve Feasibility Study</th>
<th>Cephea Feasibility Study</th>
<th>CardioValve AHEAD Trial</th>
<th>EVOQUE MiSCEND Study</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
<td>Severe MR</td>
<td>Mod to severe or severe MR</td>
<td>MR ≥ Grade III</td>
<td>Severe MR, Grade 3-4+</td>
<td>Clinically significant, symptomatic MR</td>
</tr>
<tr>
<td><strong>Design</strong></td>
<td>Non-randomized</td>
<td>Non-randomized</td>
<td>Non-randomized</td>
<td>Non-randomized</td>
<td>Non-randomized</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Single-Arm</td>
<td>Single-arm</td>
<td>Single-arm</td>
<td>Single-arm</td>
<td>Single-arm</td>
</tr>
<tr>
<td><strong>Primary Endpoint</strong></td>
<td>Freedom from MAE at 30 day; continued intended performance of the bioprosthetic valve at 30 days; and technical success</td>
<td>Major adverse cardiac event at 30 days</td>
<td>Freedom from all-cause mortality at 30 days and proportion of subjects with MR &lt;2+ at 30 days</td>
<td>Freedom from all-cause mortality and MAE at 30 days, 6 months, 1 year, and 2 years</td>
<td>Composite MAE at 30 days</td>
</tr>
<tr>
<td><strong>Patients (Est)</strong></td>
<td>5 (actual)*</td>
<td>15</td>
<td>30</td>
<td>30</td>
<td>123</td>
</tr>
</tbody>
</table>

Table data from clinicaltrials.gov
Deployment and release of a Tendyne
Next Generation Intrepid Transfemoral System

**Consistent Intrepid* Valve Design**
- Optimized for 29Fr Profile & LVOT
- Increased Patient Eligibility with Larger Valve Size

**Updated TF System**
- 29Fr Profile
- Designed for Improved Steering
- Streamlined Accessories
2-Year Clinical and Echocardiography Follow-Up of Transcatheter Mitral Valve Replacement With the Transapical Intrepid System

Vinayak Bapat, MBBS, MS, MCh, Eric Weiss, MD, Tanvir Bajwa, MD, Vitool H. Thourani, MD, Pradeep Yadav, MD, Jeremy J. Thaden, MD, D. Scott Lim, MD, Michael Brendan, MD, Sean Pinney, MD, David H. Adams, MD, Steven J. Yalagud, MD, Thomas Modine, MD, Paul Simon R. Redwood, MD, Antony Walter, MD, Konstantinos Spangias, MD, Angie Zhang, MD, Michael Maki, MD, Martin B. Leon, MD

2-Year Outcomes After Transcatheter Mitral Valve Replacement With the Transapical Intrepid System

A Mitral Regurgitation (Paired)

- Baseline (N = 123)
- 1 Month (N = 123)
- 2 Years (N = 123)

Proportion of Patients

- None/Trace/Mild
- Moderate
- Moderate-Severe
- Severe

- 63.4%
- 35.8%
- 0.8%
- 100.0%
- 100.0%

Data includes discharge if 1 month unavailable; 2 years ± 6 months

B All-Cause Mortality

- Months Postprocedure
- All-Cause Mortality
- 13.1% 27.3% 36.2%

- Pilot
- APOLLO
- Pilot + APOLLO

- No. at Risk:
- Pilot 95 63 55
- APOLLO 157 116 99
- Pilot + APOLLO 252 179 154

• Marked and sustained reduction in mitral regurgitation over 2 years
• Significant early morbidity and mortality among this high-risk cohort

Bapat V, et al. J Am Coll Cardiol Intv. 2024; [ ] [ ] [ ].
TEER Treatment Suitability for Mitral Regurgitation

• TEER is a safe and effective treatment for MR and supported by the largest patient experience for any transcatheter intervention.

• However, there are potential challenges that suggest alternative therapeutic approaches are needed to address mitral valve complexities:

  **Anatomical Suitability**
  - Numerous anatomies potentially unsuitable for TEER.

  **Treatment Efficacy**
  - Patients Left with Residual MR

  **Treatment Durability**
  - Risk of MR Recurrence
TEER Treatment Challenge | Anatomical Suitability

Only 26% of EXPAND G4 Study Population Classified as TEER Suitable\(^1\).

---

**TEER SUITABLE**
- Baseline MR Severity 3+/4+ and ALL of the following:
  - No Secondary Jet
  - No Severe Mitral Annular Calcification
  - No Severe Leaflet Calcification
  - No Significant Cleft/Scallop
  - MVA ≥ 3.5 cm\(^2\)
  - No prior annuloplasty
  - No Barlow’s disease
  - No bi-leaflet prolapse/fail
  - No severe degenerative leaflets with large gaps
  - No minimal leaflet tissue

**EXPAND G4**
- N=1164

**RISK OF STENOSIS**
- Baseline MR Severity 3+/4+ and at least ONE of the following:
  - Severe Annular Calcification
  - Severe Leaflet Calcification
  - Prior Mitral Annuloplasty
  - MVA < 3.5 cm\(^2\)

**RISK OF INADEQUATE MR REDUCTION**
- Baseline MR Severity 3+/4+ and at least ONE of the following:
  - Barlow’s disease
  - Bi-leaflet flail/prolapse
  - Significant secondary jet
  - Severe leaflet degeneration with large gaps
  - Minimal leaflet tissue
  - Significant cleft or scallop

---

**BASELINE MODERATE MR OR LESS**
- Baseline MR Severity < 3+
  - assessed by Echo Core Lab per ASE guidelines

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\(^1\)Rogers, et al. JACC Intv. 2023 Jun 26;16(12):1474-1485
CHOICE-MI Registry: TEER vs TMVR

- Transcatheter mitral valve replacement (TMVR) is emerging as a viable option to manage MR, but there is a current evidence gap on whether it is comparable to the more established TEER therapy.
- A large PS-matched comparative analysis of secondary MR patients undergoing TMVR or TEER reported similar mortality between groups but better MR reduction with TMVR\(^1\).
- TMVR results are encouraging, especially with the majority using a transapical approach\(^2\).

---

## Head to Head

<table>
<thead>
<tr>
<th>Device</th>
<th>Safety</th>
<th>Efficacy</th>
<th>Ease of use</th>
<th>Lifetime</th>
<th>Eligibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>MitraClip</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Pascal</td>
<td></td>
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<tr>
<td>Intrepid</td>
<td>Safety profile being established through early clinical experience: valve thrombosis?</td>
<td>Consistent, Predictable &amp; Durable Elimination of MR</td>
<td>Variable for each device</td>
<td></td>
<td></td>
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<tr>
<td>Sapien M3</td>
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<tr>
<td>Tendyne</td>
<td></td>
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<tr>
<td>Highlife</td>
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</table>

- **TEER** consistently demonstrates low all-cause mortality at 30-days (up to 1.8% in EXPAND G4)
- ~10-30% of patients do not receive optimal outcomes
- Leaflet grasping results in challenging imaging & procedure in complex anatomies & significant learning curve
- Prevents re-intervention on the Mitral Valve due to “bridge” across the valve (or requires complex procedure to remove the clip)
- Several anatomical restrictions, 15% screen out

- Should Enable Future Re-Intervention; anticoagulation?
- Estimated 80% screen out rate: small LVOT!!

**Safety profile**

- Safety profile being established through early clinical experience: valve thrombosis?

**Efficacy**

- Consistent, Predictable & Durable Elimination of MR

**Ease of use**

- Variable for each device

**Lifetime**

- Should Enable Future Re-Intervention; anticoagulation?

**Eligibility**

- Estimated 80% screen out rate: small LVOT!!
Conclusions

• A Toolbox of transcatheter mitral valve repair devices will likely be available in the future

• TEER is and will be the mainstream of TMVrepair in particular for suitable anatomies and COAPT-like patients, at least until a reasonable TMV replacement platform will come....