Health Status after Transcatheter Mitral-Valve Repair in Patients with Heart Failure and Secondary Mitral Regurgitation: Results from the COAPT Trial

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On behalf of the COAPT Investigators

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Disclosures

• The COAPT trial was sponsored by Abbott and designed collaboratively by the principal investigators and the sponsor.

• The health status analysis was conducted independently at Saint Luke’s Mid America Heart Institute (Kansas City, Missouri).

• I have no disclosures other than support from a Career Development Grant Award (K23 HL116799) from the NIH/NHLBI.
The 2 major goals in treating heart failure are to prolong survival and to improve health status (i.e., patients’ symptoms, functional limitations, and quality of life).

Recently, the COAPT trial demonstrated that treatment of patients with symptomatic heart failure and secondary (functional) MR with transcatheter mitral valve repair (TMVr) using MitraClip resulted in improved survival and fewer heart failure hospitalizations.

To fully define the benefits of TMVr, it is important to understand its impact on health status as well.
Objectives

1. To compare the early and late health status outcomes of TMVr versus standard care

2. To examine whether the health status benefit of TMVr differs according to patient factors

3. To explore the impact of differences in mortality on the health status benefits of TMVr
Study Design

- Multicenter, open-label RCT in patients with heart failure and 3+ or 4+ secondary MR who remained symptomatic despite maximally-tolerated GDMT
- Enrollment between December 2012 and June 2017 at 78 sites in the US and Canada
- Follow-up through 2 years, with a minimum of 1 year of follow-up in all patients
- Crossover not permitted before 2 years
Patient-reported health status assessed at baseline and 1, 6, 12, and 24 months

- Kansas City Cardiomyopathy Questionnaire
  - Scores 0-100; higher=better; MCID=5 points
- SF-36 Physical and Mental Summary Scores
  - Higher=better; population mean 50 SD 10; MCID=2.5 points

**Primary outcome:** KCCQ-overall summary score (KCCQ-OS) over 24 months
Statistical Analysis

• Health status over 24 months compared between groups using piecewise linear regression
  - Differs from the NEJM analysis in which patients who died of HF had their KCCQ score imputed to the worst observed value
• Subgroups explored with interaction terms
  - Age, sex, COPD, cause of cardiomyopathy (ischemic vs. nonischemic), LV end diastolic volume index, effective regurgitant orifice (ERO), walk speed, ADL dependency
• Categorical analyses performed in order to integrate survival and health status
• Sensitivity analysis jointly modeled health status and survival using a Bayesian approach

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>TMVr (n=302)</th>
<th>Standard Care (n=309)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>71.7 ± 11.8</td>
<td>72.7 ± 10.6</td>
</tr>
<tr>
<td>Male</td>
<td>66.6%</td>
<td>61.8%</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>31.3 ± 9.1</td>
<td>31.2 ± 9.6</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>35.1%</td>
<td>39.5%</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>1.8 ± 1.2</td>
<td>1.8 ± 1.4</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>55.6%</td>
<td>50.8%</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>23.5%</td>
<td>23.0%</td>
</tr>
<tr>
<td>Ischemic cardiomyopathy</td>
<td>60.9%</td>
<td>60.6%</td>
</tr>
</tbody>
</table>
## Baseline Health Status

<table>
<thead>
<tr>
<th></th>
<th>TMVr (n=302)</th>
<th>Standard Care (n=309)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>KCCQ</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall Summary</td>
<td>53.2 ± 22.8</td>
<td>51.6 ± 23.3</td>
</tr>
<tr>
<td>Physical Limitations</td>
<td>58.3 ± 24.5</td>
<td>55.7 ± 26.0</td>
</tr>
<tr>
<td>Symptoms</td>
<td>60.3 ± 24.9</td>
<td>58.9 ± 24.7</td>
</tr>
<tr>
<td>Quality of Life</td>
<td>45.2 ± 25.6</td>
<td>44.7 ± 25.8</td>
</tr>
<tr>
<td>Social Limitation</td>
<td>49.5 ± 29.2</td>
<td>46.8 ± 30.4</td>
</tr>
<tr>
<td><strong>SF-36</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical Summary</td>
<td>33.0 ± 9.0</td>
<td>32.6 ± 10.0</td>
</tr>
<tr>
<td>Mental Summary</td>
<td>46.7 ± 12.7</td>
<td>45.4 ± 13.0</td>
</tr>
</tbody>
</table>
Primary Outcome: KCCQ-OS

Months

KCCQ-OS score

Standard Care
Primary Outcome: KCCQ-OS

Δ 15.9, p<0.001
Δ 15.3, p<0.001
Δ 14.5, p<0.001
Δ 12.8, p<0.001

MCID=5 points

TMVr

KCCQ-OS score

Standard Care

Months
KCCQ Domains

- **Physical Limitations**
  - TMVr vs Std Care
  - *p*<0.001 at all timepoints

- **Quality of Life**
  - TMVr vs Std Care
  - *p*<0.001 at all timepoints

- **Total Symptoms**
  - TMVr vs Std Care
  - *p*<0.01 at all timepoints

- **Social Limitations**
  - TMVr vs Std Care
  - *p*<0.001 at all timepoints
SF-36 Physical Summary

- Δ 5.3 p<0.001
- Δ 4.9 p<0.001
- Δ 4.5 p<0.001
- Δ 3.6 p=0.001

MCID=2.5 points

Standard Care

TMVr
SF-36 Mental Summary

- TMVr
- Standard Care

MCID=2.5 points

Δ 5.2 p<0.001
Δ 4.9 p<0.001
Δ 4.4 p<0.001
Δ 3.6 p=0.011
## Subgroup Analyses

<table>
<thead>
<tr>
<th>Category</th>
<th>n</th>
<th>Mean Difference (95% CI)</th>
<th>Interaction P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>&lt;74 years</td>
<td>297</td>
<td>14.7 (9.6, 19.8)</td>
<td>0.24</td>
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<tr>
<td>≥74 years</td>
<td>317</td>
<td>14.1 (9.0, 19.2)</td>
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</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td>0.67</td>
</tr>
<tr>
<td>Male</td>
<td>393</td>
<td>15.3 (10.8, 19.8)</td>
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</tr>
<tr>
<td>Female</td>
<td>221</td>
<td>12.8 (6.8, 18.8)</td>
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</tr>
<tr>
<td><strong>COPD</strong></td>
<td></td>
<td></td>
<td>0.33</td>
</tr>
<tr>
<td>Yes</td>
<td>143</td>
<td>14.0 (6.3, 21.8)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>471</td>
<td>14.4 (10.3, 18.5)</td>
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<tr>
<td><strong>Cardiomyopathy</strong></td>
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<td>0.02</td>
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<tr>
<td>Ischemic</td>
<td>373</td>
<td>18.3 (13.6, 22.9)</td>
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<tr>
<td>Nonischemic</td>
<td>241</td>
<td>8.4 (2.7, 14.1)</td>
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<tr>
<td><strong>LVEDV Index</strong></td>
<td></td>
<td></td>
<td>0.27</td>
</tr>
<tr>
<td>&lt;94 mL/m²</td>
<td>269</td>
<td>14.3 (8.9, 19.7)</td>
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</tr>
<tr>
<td>≥94 mL/m²</td>
<td>298</td>
<td>15.3 (10.1, 20.4)</td>
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<tr>
<td><strong>ERO</strong></td>
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<td>0.64</td>
</tr>
<tr>
<td>&lt;0.4 cm²</td>
<td>325</td>
<td>14.7 (9.8, 19.6)</td>
<td></td>
</tr>
<tr>
<td>≥0.4 cm²</td>
<td>266</td>
<td>15.3 (9.8, 20.9)</td>
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</tr>
<tr>
<td><strong>Walk Speed</strong></td>
<td></td>
<td></td>
<td>0.90</td>
</tr>
<tr>
<td>&lt;0.8 m/s</td>
<td>268</td>
<td>14.9 (9.3, 20.5)</td>
<td></td>
</tr>
<tr>
<td>≥0.8 m/s</td>
<td>343</td>
<td>13.5 (8.9, 18.1)</td>
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<tr>
<td><strong>ADL Dependency</strong></td>
<td></td>
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<td>0.80</td>
</tr>
<tr>
<td>Yes</td>
<td>107</td>
<td>17.6 (8.6, 26.6)</td>
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</tr>
<tr>
<td>No</td>
<td>505</td>
<td>13.4 (9.6, 17.3)</td>
<td></td>
</tr>
</tbody>
</table>

-30 Favors Standard Care  Favor Standard Care  Favor TMVr  30

**Mean KCCQ-OS Difference**
Health status can only be assessed in survivors, but those with worse health status are more likely to die.

Challenges in Health Status Assessment

Impact of Differential Mortality

Health status can only be assessed in survivors, but those with worse health status are more likely to die.

[Graph showing mortality rates over time for Standard Care and TMVr treatments.]
Challenges in Health Status Assessment

*Impact of Differential Mortality*

- Strategies to address this challenge:
  - Categorical analyses that integrate survival and health status
  - Jointly modeling health status and mortality, which allows us to understand the expected health status benefit of TMVr assuming the patient survives
Categorical Outcomes at 24 Months

NNT 5.1

- Alive with a moderate improvement: 36%
P<0.001

- Alive with a large improvement: 17%

Alive and well:
- KCCQ-OS ≥ 60 points and ΔKCCQ-OS ≥ -10 points
Joint Model Results: KCCQ-OS

Primary Analysis

MCID=5 points

KCCQ-OS Score

TMVr

Standard Care

Months

0 6 12 18 24
Joint Model Results: KCCQ-OS

Bayesian Analysis

KCCQ-OS Score

Δ 18.5 (14.3, 22.7)  Δ 18.6 (14.6, 22.6)  Δ 18.7 (14.1, 23.3)  Δ 18.9 (11.4, 26.0)

Months

TMVr

Standard Care

MCID=5 points
Limitations

• Non-blinded study/possibility of placebo effect

• Durability of the health status results beyond 24 months is unknown

• The health status results may not be generalizable beyond the strict inclusion/exclusion criteria of the COAPT trial and outside of experienced centers and operators
Summary

- In patients with heart failure and 3+ or 4+ secondary MR, TMVr with MitraClip provided substantial benefits in terms of symptoms, functional status, and quality of life.
- The difference in health status between groups was moderately large, fully evident by 1 month, and generally sustained through 24 months.
- The health status benefit of TMVr was also consistent across most key subgroups.
Conclusion

Considering the previously reported benefits of TMVr on survival and heart failure hospitalization, these health status results further support the use of MitraClip for patients with heart failure and 3+ or 4+ secondary MR who remain symptomatic despite maximally-tolerated GDMT.
Acknowledgments

- **HETA/Outcomes group at MAHI**: David Cohen, Khaja Chinnakondepalli, Kaijun Wang, Elizabeth Magnuson, Suzanne Baron, John Spertus

- **COAPT PIs and investigators**: William Abraham, JoAnn Lindenfeld, Michael Mack, Gregg Stone, Saibal Kar, D. Scott Lim, Jacob Mishell, and others

- **Abbott team**: Julie Prillinger, Scott Goates

- **COAPT patients**
Health Status After Transcatheter Mitral-Valve Repair in Heart Failure and Secondary Mitral Regurgitation

COAPT Trial

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Elizabeth A. Magnuson, ScD, a Suzanne J. Baron, MD, MSc, a Saibal Kar, MD, b D. Scott Lim, MD, c
Jacob M. Mishell, MD, d William T. Abraham, MD, e JoAnn A. Lindenfeld, MD, f Michael J. Mack, MD, g
Gregg W. Stone, MD, h David J. Cohen, MD, MSc, a on behalf of the COAPT Investigators

ABSTRACT

BACKGROUND In the COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation) trial, transcatheter mitral valve repair (TMVR) led to reduced heart failure (HF) hospitalizations and improved survival in patients with symptomatic HF and 3+ to 4+ secondary mitral regurgitation (MR) on maximally-tolerated medical therapy. Given the advanced age and comorbidities of these patients, improvement in health status is also an important treatment goal.
Back-up slides
Health Status in COAPT in Perspective

- **12-month mortality**
  - 18.9%
  - 23.0%
  - 30.7%

- **KCCQ-OS**
  - **1 month**
    - Δ 16.9
    - Δ 24.8
    - Δ 24.8
  - **12 months**
    - Δ 17.0
    - Δ 29.1
    - Δ 31.8

- **Months**: 0, 6, 12

- **Graph**
  - TMVr (COAPT)
  - TMVr (TVT)
  - TAVR (PARTNER IB)
SF-36 Physical Summary

Bayesian Analysis Results

MCID=2.5 points

Δ 5.5 (3.9, 7.1)  Δ 5.2 (3.8, 6.7)  Δ 4.9 (3.3, 6.5)  Δ 4.2 (1.8, 6.5)

SF-36 Physical Summary

Standard Care

TMVr

Months

0  6  12  18  24
SF-36 Mental Summary

MCID=2.5 points

Bayesian Analysis Results

<table>
<thead>
<tr>
<th>Months</th>
<th>TMVr</th>
<th>Standard Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Δ5.7 (3.8, 7.8)</td>
<td>Δ5.2 (2.2, 8.3)</td>
</tr>
<tr>
<td>6</td>
<td>Δ5.6 (3.8, 7.5)</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Δ5.5 (3.5, 7.5)</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td></td>
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</tr>
</tbody>
</table>

Δ = 2.5 points


KCCQ scores for patients who died of heart failure were imputed as the worst observed KCCQ score

## TVT Health Status Results

### Factors associated with 30-day KCCQ-OS after TMVr

<table>
<thead>
<tr>
<th></th>
<th>Estimate (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline KCCQ-OS (per 10-points)</td>
<td>3.9 (3.6 to 4.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (per 5-years)</td>
<td>-0.5 (-1.0 to -0.0)</td>
<td>0.030</td>
</tr>
<tr>
<td>Hemoglobin (per 1 g/dL)</td>
<td>0.6 (0.1 to 1.1)</td>
<td>0.018</td>
</tr>
<tr>
<td>Atrial fibrillation or flutter</td>
<td>-2.2 (-3.7 to -0.6)</td>
<td>0.007</td>
</tr>
<tr>
<td>Severe chronic lung disease</td>
<td>-3.9 (-6.2 to -1.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Home oxygen use</td>
<td>-2.7 (-4.9 to -0.4)</td>
<td>0.021</td>
</tr>
<tr>
<td>Permanent pacemaker</td>
<td>-2.1 (-3.7 to -0.4)</td>
<td>0.013</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>2.0 (0.3 to 3.7)</td>
<td>0.022</td>
</tr>
</tbody>
</table>

Factors in the model that were not significantly associated with QOL (p>0.05): sex, race, BSA, prior MI, PCI, PAD, LV EF, prior stroke, current smoker, diabetes, GFR, current dialysis, moderate/severe aortic insufficiency, moderate/severe tricuspid insufficiency, acuity of case.
<table>
<thead>
<tr>
<th>KCCQ Domain</th>
<th>Mean Between Group Difference (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical Limitations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month</td>
<td>13.7 (9.9, 17.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>6 months</td>
<td>13.3 (9.8, 16.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>12 months</td>
<td>12.9 (9.1, 16.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24 months</td>
<td>12.1 (6.3, 18.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Total Symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month</td>
<td>14.2 (10.6, 17.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>6 months</td>
<td>12.7 (9.4, 15.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>12 months</td>
<td>10.9 (7.4, 14.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24 months</td>
<td>7.3 (2.1, 12.5)</td>
<td>0.006</td>
</tr>
<tr>
<td><strong>Quality of Life</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month</td>
<td>18.0 (14.0, 22.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>6 months</td>
<td>17.5 (13.8, 21.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>12 months</td>
<td>16.9 (12.9, 20.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24 months</td>
<td>15.7 (9.6, 21.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Social Limitation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month</td>
<td>17.5 (12.8, 22.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>6 months</td>
<td>16.7 (12.4, 21.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>12 months</td>
<td>15.8 (11.1, 20.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24 months</td>
<td>13.9 (6.8, 20.9)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Eligible Patients
N=614

Randomized 1:1

TMVr
N=302

N=302/302 (100%)

Baseline

N=219/239 (92%)

12-month

(primary endpoint minimum)

N=128/142 (90%)

Died 56
Withdraw 7
No KCCQ 20

Died 78
Withdraw 16
Did not reach timepoint 66
No KCCQ 14

Standard Care
N=312

No KCCQ 3

N=309/312 (99%)

12-month

Died 69
Withdraw 21
Did not reach timepoint 1
No KCCQ 32

N=189/221 (86%)

24-month

(eligible patients)

N=90/103 (87%)

Died 115
Withdraw 32
Did not reach timepoint 62
No KCCQ 13
# Key Inclusion/Exclusion Criteria

## Key Inclusion Criteria

1. LVEF 20%-50% and LVESD ≤70 mm
2. NYHA II-IVa despite maximally-tolerated GDMT and CRT (if indicated)
3. Not appropriate for mitral valve surgery by local heart team assessment

## Key Exclusion Criteria

1. ACC/AHA stage D HF, hemodynamic instability, or cardiogenic shock
2. Untreated CAD requiring revascularization
3. COPD requiring continuous home oxygen or chronic oral steroid use
4. Severe pulmonary hypertension or right ventricular dysfunction
5. Life expectancy <12 months due to non-cardiac conditions