Transcatheter Therapies for Tricuspid Regurgitation

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Smidt Heart Institute, Cedars-Sinai Medical Center, Los Angeles CA
Tricuspid Regurgitation is highly prevalent

- Is more common with age
- Similar in prevalence to aortic stenosis

Yan Topilsky, et al. Burden of Tricuspid Regurgitation in Patients Diagnosed in the Community Setting
J Am Coll Cardiol Img. 2019 Mar, 12 (3) 433-442
## TR Prevalence amongst different populations

<table>
<thead>
<tr>
<th>Population</th>
<th>TR severity</th>
<th>TR prevalence (%)</th>
<th>FU</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>MitraClip</td>
<td>Moderate to severe</td>
<td>11</td>
<td>1 y</td>
<td>Ohno (2014)</td>
</tr>
<tr>
<td>TAVI</td>
<td>Moderate to severe</td>
<td>21</td>
<td>30 d</td>
<td>Barbanti (2015)</td>
</tr>
<tr>
<td>TAVI</td>
<td>Moderate to severe</td>
<td>16</td>
<td>1 y</td>
<td>Lindman (2015)</td>
</tr>
<tr>
<td>SAVR</td>
<td>Mild to severe</td>
<td>21</td>
<td>4,4 y</td>
<td>Jeong (2014)</td>
</tr>
<tr>
<td>Valvuloplasty for rheumatic MS</td>
<td>Moderate to severe</td>
<td>19</td>
<td>12 y</td>
<td>Lee, S.-P (2013)</td>
</tr>
<tr>
<td>MV surgery for degenerative MV disease</td>
<td>Severe</td>
<td>6</td>
<td>&gt; 5 y</td>
<td>Rajbanshi (2014)</td>
</tr>
<tr>
<td>MV repair in dilated cardiomyopathy</td>
<td>Moderate to severe</td>
<td>20</td>
<td>7,3 y</td>
<td>De Bonis (2015)</td>
</tr>
</tbody>
</table>
TR is associated with adverse outcomes

Yan Topilsky, et al. Burden of Tricuspid Regurgitation in Patients Diagnosed in the Community Setting
J Am Coll Cardiol Img. 2019 Mar, 12 (3) 433-442
TR Risk of mortality increases with severity

TR Risk of mortality increases with severity

In patients with PASP <40mmHg

In patients with LVEF > 50%

P = .003

P < .0001

Patients are largely undertreated with surgery

- **1,600,000**
  Number of moderate to severe TR cases

- **250,000**
  Number of new TR cases annually

- **<8,000**
  Number of TR surgeries

- **<0.5%**
  Number of TR cases treated surgically

- **90%**
  Are repair

Agarwal et al. Interventional Cardiology Perspective on fTR
Circ Cardiovascular Intervention 2009; 565-573
Operative Mortality for TR remains high

J Am Coll Cardiol, 70 (2017), pp. 2953-2960
Highly Prevalent

Limited Therapies

Operative mortality ~ 9%

Poor Prognosis

>50% three-year mortality with > moderate TR

~ 1.6 million Americans with > moderate TR
There is a significant unmet clinical need to find novel therapies for patients with tricuspid regurgitation.
Tricuspid Valve – No longer the forgotten valve
ETIOLOGIES OF TRICUSPID REGURGITATION

**PRIMARY 15%**
- Organic
  - Rheumatic
  - Myxomatous
  - Ebstein anomaly
  - Endomyocardial fibrosis
  - Endocarditis
  - Carcinoid disease
  - Traumatic (blunt chest injury, laceration)
- Prolapse
- Iatrogenic (pacemaker/ defibrillator)

**SECONDARY 85%**
- Left Valve Disease
  - Aortic
  - Mitral
- Pulmonary Hypertension
  - WHO group 2
- Left heart disease
  - Systolic (HFrEF)
  - Diastolic (HFpEF)
- Idiopathic
  - AF

*The TriClip Implant is not indicated for patients with severe mitral regurgitation.*

TR has Poor Long Term Survival\textsuperscript{1}

36\% of Patients with Severe TR die within 1 year of diagnosis\textsuperscript{2}
10 Year Survival = 14\%\textsuperscript{1}

- The poorest survival was seen with functional TR associated with left valvular disease, or associated with LV systolic dysfunction\textsuperscript{1}
- Followed by functional TR associated with PHTN and organic TR\textsuperscript{1}
- Was ominous even in isolated TR, with no other systemic or cardiac comorbidity\textsuperscript{1}

*The TriClip Implant is not indicated for patients with severe mitral regurgitation.


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Current options to treat tricuspid regurgitation

Off-label use of commercially available devices

Emerging dedicated devices in research protocols

TriClip™ NT

~6mm*

~9 mm**
Off-label MitraClip in Tricuspid Valve

- 22-year-old female transferred from OSH on pressors
- History of HOCM treated with OHT in 2003
  - Complicated by rejection in 2013
- Severe TR of the transplanted heart due to flail of the tricuspid valve secondary to RV biopsy
- Transferred for consideration of transcatheter therapies
MitraClip x 2 to the tricuspid valve

Patient successfully weaned from dobutamine and discharged home in 4 days

Final result: Mild-moderate TR
Off-label MitraClip in Tricuspid Valve

- Insights from the TriValve Registry
- 249 patients treated with off-label or compassionate MitraClip

Off-label MitraClip in Tricuspid Valve

Transcatheter tricuspid edge-to-edge repair can achieve TR reduction at 1 year, resulting in significant clinical improvement.

Predictors of procedural failure and 1-year mortality identified here may help select patients who will benefit most from this therapy.
Dedicated Device: TriClip

- Clip
- Steerable Guide Catheter
- Steerable Sleeve
- Clip Delivery System

TriClip™ NT

~6mm *

~9 mm **
## TRILUMINATE | Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Patients (n=85)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (years)</td>
<td>77.8 ± 7.9</td>
</tr>
<tr>
<td>Male / Female (%)</td>
<td>34% / 66%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>86%</td>
</tr>
<tr>
<td>Prior MI</td>
<td>17.6%</td>
</tr>
<tr>
<td>A-fib</td>
<td>92%</td>
</tr>
<tr>
<td>Prior Aortic Intervention</td>
<td>11%</td>
</tr>
<tr>
<td>Prior Mitral Intervention</td>
<td></td>
</tr>
<tr>
<td>Replacement – Surgery</td>
<td>25%</td>
</tr>
<tr>
<td>Replacement – Percutaneous</td>
<td>7.1%</td>
</tr>
<tr>
<td>Repair – Surgery</td>
<td>28.6%</td>
</tr>
<tr>
<td>Repair – Percutaneous</td>
<td>32.1%</td>
</tr>
<tr>
<td>Other</td>
<td>14.3%</td>
</tr>
<tr>
<td>CRT/ICD/PPM</td>
<td>14%</td>
</tr>
<tr>
<td>Renal Disease</td>
<td>46%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>22%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Patients (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV End Diastolic Dimension (cm)</td>
<td>5.27 ± 0.67 (81)</td>
</tr>
<tr>
<td>NYHA FC III/IV</td>
<td>75%</td>
</tr>
<tr>
<td>EuroSCORE II</td>
<td>8.6 ± 10.9%</td>
</tr>
<tr>
<td>LVEF</td>
<td>59.39 ± 8.09% (73)</td>
</tr>
<tr>
<td>TAPSE</td>
<td>1.44 ± 0.31 (79)</td>
</tr>
<tr>
<td>PA Pressure, systolic (mmHg)</td>
<td>38.9 ± 16.0</td>
</tr>
<tr>
<td>6MWT (m)</td>
<td>277.47 ± 137.20 (76)</td>
</tr>
<tr>
<td>BNP</td>
<td>534.13 ± 353.84</td>
</tr>
<tr>
<td>NT-proBNP</td>
<td>3626.78 ± 13579.21</td>
</tr>
<tr>
<td>Tricuspid Regurgitation Grade</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>6% (5)</td>
</tr>
<tr>
<td>Severe</td>
<td>29% (24)</td>
</tr>
<tr>
<td>Massive</td>
<td>29% (24)</td>
</tr>
<tr>
<td>Torrential</td>
<td>37% (31)</td>
</tr>
</tbody>
</table>
TRILUMINATE Study
Essential Results:

Mean Age = 77.8 + 7.9 year
65.9% Female
100% Implant success rate
90.5% Acute Procedural Success rate
87% TR reduction of at least 1 grade at 1 Year
Mean Improvement in KCCQ-OS score of 20 points from baseline to 1 Year

On average number of clips used
2.2

Average procedure time
152 min

At 1 Year, a significantly greater proportion (83%) of subjects were categorized as NYHA class I or II compared to 31% of subjects at baseline.

1. Lurz, Philip MD, PhD as presented at PCR eCourse 2020
TRILUMINATE Pivotal Study - Trial Overview

Subject has Symptomatic Severe TR and is at intermediate or greater risk of mortality and morbidity with TV Surgery

TR Severity Confirmed by the Echo Core Laboratory

Subject Meets all Inclusion/Exclusion Criteria and the Eligibility Committee Confirms that the Tricuspid Valve Anatomy is Suitable for TR Reduction by TriClip™

Eligibility Committee Determines that TR can be Reduced to Moderate or Less

Randomization (1:1) (N=450)

TriClip Device (Device)

Medical Therapy (Control)

Single Arm (N=100)

TriClip Device (Device)

Exclude Subject

Exclude Subject

NO

NO

NO

YES

YES

YES

Principle Investigators:
Dr. David Adams (Mt.Sinai)
Dr. Paul Sorajja (Abbott Northwestern)
Real-world Outcomes for Tricuspid Edge-to-Edge Repair: Initial 30-Day Results from the TriClip™ bRIGHT Study

Philipp Lurz, Robert Schueler, Bjoern Goebel, Helge Moellmann, Georg Nickenig, Raffi Bekeredjian, Rodrigo Estevez, Iskandar Atmowihardjo, Alexander Schmeisser, Erwan Donal

TriClip™ bRIGHT Study is sponsored by Abbott
90% of subjects had TR reduced by at least 1 grade at 30 days with the majority (66%) reduced to moderate or less.
Significant Clinical Improvements

Majority of subjects experienced significant improvements in NYHA functional class and KCCQ-OS score.

NYHA FUNCTIONAL CLASS

- **Baseline (N=167)**
  - NYHA I: 19%
  - NYHA II: 71%
  - NYHA III: 2%
  - NYHA IV: 2%

- **30 Days (N=167)**
  - NYHA I: 10%
  - NYHA II: 66%
  - NYHA III: 76%
  - NYHA IV: 10%

KCCQ – OS

- **Baseline (N=161)**
  - KCCQ-OS: 76%

- **30 Days (N=161)**
  - KCCQ-OS: 95%

\[ \Delta = 19 \pm 25, p < 0.0001 \]
PASCAL Platform for Tricuspid Regurgitation

Central Spacer
Bridge the coaptation gap

Elongation
Navigate in dense chordae

Nitinol Design
Passive closure, acute implant flexing

Independent Clasps
Staged leaflet capture and adjustment

PASCAL Ace
A narrow profile and central spacer designed to complement PASCAL and provide additional options for patients

CAUTION: Investigational device. Limited by Federal (or United States) law to investigational use.
Prospective, multicenter, single-arm study

Purpose:
Evaluate the safety and performance of the Edwards PASCAL Transcatheter Valve Repair System in tricuspid regurgitation

Principal Investigator:
Susheel K. Kodali, MD

The Edwards PASCAL Transcatheter Valve Repair System in Tricuspid Regurgitation (CLASP TR) Early Feasibility Study

CLASP TR EFS

Patients with Symptomatic Severe Tricuspid Regurgitation

Heart Team Assessment

• Severe functional or degenerative TR
• Symptomatic despite optimal medical therapy
• Patient appropriate for the device

PASCAL Repair System

Follow-up: 30 days, 6 months, 1 year and annually through 5 years

Primary Endpoints:
• Freedom from device or procedure-related adverse events at 30 days

NCT03745313
PASCAL Transcatheter Valve Repair System in Tricuspid Regurgitation

<table>
<thead>
<tr>
<th></th>
<th>N = 63</th>
<th>% (n/N) or Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful implant rate¹,² (ITT)</td>
<td></td>
<td>91% (57/63)</td>
</tr>
<tr>
<td>Successful implant rate¹ (AT)</td>
<td></td>
<td>100% (57/57)</td>
</tr>
<tr>
<td>Procedural success³</td>
<td></td>
<td>98% (44/45)</td>
</tr>
<tr>
<td>Clinical success⁴</td>
<td></td>
<td>87% (40/46)</td>
</tr>
<tr>
<td>Mean number of devices implanted per patient</td>
<td></td>
<td>1.5 ± 0.57 (57)</td>
</tr>
<tr>
<td>Device time (implant insertion to release), mins</td>
<td></td>
<td>159 ± 129 (56)</td>
</tr>
</tbody>
</table>

¹Implant deployed as intended and delivery system retrieved as intended at the time of the patient’s exit from the cardiac catheterisation laboratory.
²Implants were successfully retrieved in six patients whose leaflets were unable to be captured due to complex anatomy with no adverse sequelae.
³Implant success with at least one grade reduction in TR at the end of the procedure without surgical or percutaneous intervention prior to hospital discharge.
⁴Procedural success without MAEs at 30 days. MAEs, major adverse events; ITT, intention to treat; AT, as treated.
Significant Improvements in Echocardiographic Outcomes at 6 Months by Core Lab¹

89% achieved ≥1 grade reduction and 70% achieved ≥2 grade reductions at 6 months

¹Cardiovascular Research Foundation. Two patients initially considered to have severe TR at baseline by transoesophageal echocardiography (TEE) were reclassified as moderate TR by transthoracic echocardiography (TTE).

Graphs show unpaired data. *Wilcoxon signed-rank test for moderate TR or less. a n=51; baseline=4%; 30 days=67%. b n=27; baseline=7%; 6 months=78%. Paired t-test for mean±SD PISA EROA. c n=34; baseline=0.75±0.28 cm²; 30 days=0.4±0.26 cm². d n=20; baseline=0.75±0.32 cm²; 6 months=0.32±0.19 cm². Paired t-test for mean±SD vena contracta width. e n=49; baseline=1.4±0.45 cm; 30 days = 0.69±0.33 cm. f n=27; baseline=1.4±0.49 cm; 6 months=0.64±0.32 cm. PISA EROA, proximal isovelocity surface area effective regurgitant orifice area; TR, tricuspid regurgitation.
Improved Clinical, Functional, and Quality of Life Outcomes Sustained at 6 Months

NYHA Class

Graphs show unpaired data. *Wilcoxon signed-rank test for NYHA. \(^{a}\)n=51; baseline=30%; 30 days=88%; \(^{b}\)n=38; baseline=32%; 6 months=84%. *Paired t-test for mean±SD for 6MWD. \(^{c}\)n=47; baseline=202±104 m; 30 days=265±112. \(^{d}\)n=30; baseline=210±109 m; 6 month=248±109. *Paired t-test for mean±SD for KCCQ. \(^{e}\)n=51; baseline=54±21; 30 days=71±23. \(^{f}\)n=39; baseline=54±22; 6 months=73±26. NYHA Class, New York Heart Association; 6MWD, 6-minute walk distance; KCCQ, Kansas City Cardiomyopathy Questionnaire.
Prospective, multicenter, randomized, controlled pivotal trial

Purpose:
Evaluate the safety and effectiveness of the PASCAL Transcatheter Tricuspid Valve Repair System and optimal medical therapy (OMT) compared to OMT alone in patients with Tricuspid Regurgitation.

Patients with symptomatic severe TR despite medical therapy

Multidisciplinary Heart Team Assessment

- ≥ severe TR as assessed by echo core lab
- NYHA Class II-IVa
- ≥ intermediate mortality risk with tricuspid valve surgery

PASCAL Repair System + OMT

OMT alone

Primary Endpoint at 24 months
- Composite endpoint including all-cause mortality, RVAD implantation or heart transplant, tricuspid valve intervention, heart failure hospitalizations, and Quality of Life improvement (measured by KCCQ score)

NCT04097145
Transcatheter Tricuspid Valve Replacement

Devices with FIM experience

Navigate  Lux  Intrepid  Evoque
EVOQUE Tricuspid Valve Replacement System
Transfemoral replacement may address current tricuspid challenges
What did we study?

EVOQUE Tricuspid Valve Replacement System

**Unique valve design** engages leaflets, chords, and annulus to achieve secure placement

**Atraumatic anchors** compatible with pre-existing leads and respect the native anatomy

**Conforming frame** designed to achieve optimal retention force

**Multiple sizes** offer treatment for a broad range of tricuspid pathologies and anatomies (44, 48, 52 mm)

**28F transfemoral delivery system** compatible with all valve sizes
Transcatheter Tricuspid Valve Replacement

- 74-year-old female with worsening peripheral oedema and shortness of breath.
- History of atrial fibrillation, permanent pacemaker insertion, and previous TIA.
- Two hospital admissions with right sided heart failure
  - Echo demonstrated severe TR
  - Referred for consideration of transcatheter therapy
CT Screening to assess RV & TV anatomy

90% Diastole

30% Systole
Safari wire advanced on septal side of both RA and RV leads

A combination of LAO and RAO fluoro projections were used to confirm wire positioning in relation to pacing leads
Interaction of the tapered tip with the RV was preventing the capsule from getting coaxial to the TV in A-P.

Procedure: Establish depth, position & trajectory
Procedure: Establish depth, position & trajectory

We were able to regain coaxiality and continue to expose the anchors, in a controlled way with the EVOQUE delivery system.
Complete capture of all leaflets/ scallops.
Confirmed RV pacing lead position in posteroseptal commissure, as planned.
Procedure: Valve Release

Stable release with no change in final valve position.
**Procedure: Final Result**

**TR reduction:** Severe to None

**Mean PG 1mmHg**
Patients with severe tricuspid regurgitation

Randomise 2:1

EVOQUE + OMT
N = 200

OMT
N = 100

Registry
N = 150
<table>
<thead>
<tr>
<th>STUDY OUTCOMES:</th>
</tr>
</thead>
</table>

**Thirty Days:**
- Major adverse events

**Six Months:**
- TR reduction
- QoL Indices
- Functional Indices

**Twelve Months: pre-specified hierarchical composite outcomes**
1. All-cause mortality
2. RVAD implantation or heart transplant
3. Tricuspid valve surgery or percutaneous tricuspid intervention
4. HF hospitalizations
5. QOL improvement
6. NYHA functional class improvement
7. 6MWD improvement
91-year-old female with severe functional tricuspid regurgitation

NYHA III Heart Failure Symptoms,
Hx SAVR,
Dual chamber pacemaker,
Hx of DVT s/p IVC filter,
Hypertension
91 year old female with severe functional tricuspid regurgitation - treated with 44mm EVOQUE TTVR

Day 30 Follow-up
EVOQUE Example 4: MICRA positioning
EVOQUE Example 4: Result

84-year-old female with severe functional TR
- Treated with 44mm EVOQUE TTVR
- CHB treated with MICRA Implantation

Day 30 Follow-up
Transfemoral tricuspid valve replacement in patients with TR: the TRISCEND study 6-month outcomes
How was the study executed?

Participating Sites

- CA Cedars Sinai Medical Center
- IL Northwestern Medical Center
- OR Oregon Health & Science University
- NY Columbia University Medical Center/NYPH
- MI Henry Ford Hospital
- GA Piedmont Heart Institute
- TX Baylor Heart Hospital Plano
- GA Emory University Hospital
- CA Stanford University
- PA Hospital of the University of Pennsylvania
- MA Massachusetts General Hospital
- VA University of Virginia Health System
- NY Montefiore Medical Center
- MA Brigham and Women’s Hospital
### Study Enrollment

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>N=132</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>79.2 ± 7.39</td>
</tr>
<tr>
<td>Female</td>
<td>97 (74%)</td>
</tr>
<tr>
<td>EuroSCORE II (%)</td>
<td>5.3 ± 4.3</td>
</tr>
<tr>
<td>STS score (MV repair)</td>
<td>7.4 ± 5.39</td>
</tr>
<tr>
<td>NYHA functional class III or IV</td>
<td>76%</td>
</tr>
<tr>
<td>TR grade ≥severe</td>
<td>113 (88%)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>119 (90%)</td>
</tr>
<tr>
<td>Pulmonary hypertension (sPAP ≥30 mmHg)</td>
<td>104 (79%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>25 (19%)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>73 (55%)</td>
</tr>
<tr>
<td>History of ascites</td>
<td>26 (20%)</td>
</tr>
<tr>
<td>Prior stroke</td>
<td>16 (12%)</td>
</tr>
<tr>
<td>CABG surgery</td>
<td>26 (20%)</td>
</tr>
<tr>
<td>Prior valve surgery/intervention</td>
<td>50 (38%)</td>
</tr>
<tr>
<td>Pacemaker or ICD</td>
<td>46 (35%)</td>
</tr>
<tr>
<td>TR etiology</td>
<td></td>
</tr>
<tr>
<td>Functional</td>
<td>93 (70.5%)</td>
</tr>
<tr>
<td>Degenerative</td>
<td>9 (6.8%)</td>
</tr>
<tr>
<td>Mixed/other</td>
<td>30 (22.7%)</td>
</tr>
</tbody>
</table>

Enrolled patients N=132

Follow up not due n=29
Pending visit n=27
Missed visit n=10
All-cause mortality n=5
Exited for other reasons n=5
What are the essential results?

### Procedural Characteristics and Hospital Disposition

#### Procedural Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n/N (%) or Mean ± SD (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percutaneous</td>
<td></td>
</tr>
<tr>
<td>• Right femoral vein access</td>
<td>132/132 (100%)</td>
</tr>
<tr>
<td>• Left femoral vein access</td>
<td>125/132 (94.7%)</td>
</tr>
<tr>
<td>• Left femoral vein access</td>
<td>7/132 (5.3%)</td>
</tr>
<tr>
<td>Device success (per device)*</td>
<td>128/133 (96.2%)</td>
</tr>
<tr>
<td>Device time (implant insertion to release), mins</td>
<td>72.8 ± 28.15 (130)</td>
</tr>
</tbody>
</table>

*Device deployed and delivery system retrieved at exit from the cardiac catheterization laboratory. One patient had two device attempts.

#### Hospital Disposition

<table>
<thead>
<tr>
<th>Disposition</th>
<th>n/N (%) or Median (Min,Max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of Stay (days)</td>
<td>3 (0,35)</td>
</tr>
<tr>
<td>Discharge Location</td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>114/129 (88.4%)</td>
</tr>
<tr>
<td>Home with Services</td>
<td>6/129 (4.7%)</td>
</tr>
<tr>
<td>Skilled Nursing Facility</td>
<td>6/129 (4.7%)</td>
</tr>
<tr>
<td>Other</td>
<td>3/129 (2.4%)</td>
</tr>
</tbody>
</table>
What are the essential results?

Major Adverse Events (MAEs) at 30 Days

<table>
<thead>
<tr>
<th>CEC Adjudicated Events</th>
<th>N=124&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular mortality</td>
<td>3 (2.4%)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Renal complications requiring unplanned dialysis or renal replacement therapy</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Severe bleeding&lt;sup&gt;b&lt;/sup&gt;</td>
<td>22 (17.7%)</td>
</tr>
<tr>
<td>Major access site and vascular complications</td>
<td>2 (1.6%)</td>
</tr>
<tr>
<td>Non-elective tricuspid valve re-intervention, percutaneous or surgical</td>
<td>2 (1.6%)</td>
</tr>
<tr>
<td>Major cardiac structural complications</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Device-related pulmonary embolism</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Composite MAE Rate</strong></td>
<td><strong>23 (18.5%)</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other Events</th>
<th>N=132&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td></td>
</tr>
<tr>
<td>All cause mortality</td>
<td>4 (3.3%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Site-Reported Events</th>
<th>N=76&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td></td>
</tr>
<tr>
<td>New permanent pacemaker</td>
<td>8 (10.5%)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Denominator for % calculation includes all patients who reached 30-day follow-up as well as any patients who experienced an MAE prior to follow-up. <sup>b</sup>Severe bleeding is defined as major, extensive, life-threatening or fatal bleeding per Mitral Valve Academic Research Consortium (MVARC). <sup>c</sup>Of 132 enrolled patients, 4 patients died of all causes. <sup>d</sup>76 patients did not have a pre-existing pacemaker and reached 30-day follow-up.

81.5% of patients had no MAEs at 30 days
What are the essential results?

**Significant Reduction in TR Severity by Core Lab\(^1\) at 6 Months**

### TR Severity at Discharge

- **p < 0.001\(^a\)**
- Patients (%)
  - Baseline: \(n=116\)
  - Discharge: \(n=116\)

<table>
<thead>
<tr>
<th>Severity</th>
<th>Baseline</th>
<th>Discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Torr/Partial</td>
<td>22%</td>
<td>3%</td>
</tr>
<tr>
<td>Severe</td>
<td>21%</td>
<td>37%</td>
</tr>
<tr>
<td>Moderate</td>
<td>45%</td>
<td>60%</td>
</tr>
<tr>
<td>Mild/None/Trace</td>
<td>13%</td>
<td>97%</td>
</tr>
</tbody>
</table>

**No residual TR post implant with EVOQUE valve**

≥1 grade reduction in 100% at discharge and 6 months

≥2 grade reduction in 95% at discharge and 98% at 6 months

### TR Severity at 6 Months

- **p < 0.001\(^a\)**
- Patients (%)
  - Baseline: \(n=43\)
  - 6 Months: \(n=43\)

<table>
<thead>
<tr>
<th>Severity</th>
<th>Baseline</th>
<th>6 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Torr/Partial</td>
<td>14%</td>
<td>100%</td>
</tr>
<tr>
<td>Severe</td>
<td>26%</td>
<td>51%</td>
</tr>
<tr>
<td>Moderate</td>
<td>49%</td>
<td>51%</td>
</tr>
<tr>
<td>Mild/None/Trace</td>
<td>9%</td>
<td>0%</td>
</tr>
</tbody>
</table>

\(^1\)Core lab: Baylor, Scott and White Research Institute; \(^a\)Wilcoxon signed-rank test

TR, tricuspid regurgitation
What are the essential results?

Composite Major Adverse Events (%) to 6 Months

Kaplan-Meier Analysis

CEC adjudicated MAEs between 30 days and 6 months included: 2 non-elective tricuspid valve re-interventions (PODs 49 and 110), 2 severe bleeds (traumatic hematoma at POD 32 and GI bleed at POD 127), 1 cardiovascular death (cardiac arrest POD 70)
What are the essential results?

High Survival Rate and Freedom from Heart Failure Hospitalization to 6 Months

Kaplan-Meier analysis

<table>
<thead>
<tr>
<th>Survival</th>
<th>Freedom from Heart Failure Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>At Risk 120</td>
<td>At Risk 114</td>
</tr>
<tr>
<td>97 ± 2%</td>
<td>95 ± 2%</td>
</tr>
<tr>
<td>66</td>
<td>61</td>
</tr>
<tr>
<td>96 ± 2%</td>
<td>94 ± 2%</td>
</tr>
</tbody>
</table>

Kaplan-Meier analysis

Survival Percentage

Freedom from HHF
Significantly Improved Functional and Quality of Life Outcomes at 6 Months

NYHA Class

- **p < 0.001**
- **89%**

6MWD

- **p < 0.001**
- **Δ=56 m**

KCCQ Score

- **p < 0.001**
- **Δ=27 points**

Data are presented as Mean ± SD, 95% CI by normal approximation. *Wilcoxon signed-rank test; *Paired t-test.

NYHA Class, New York Heart Association functional classification; 6MWD, 6-minute walk distance; KCCQ, Kansas City Cardiomyopathy Questionnaire.
The essentials to remember

<table>
<thead>
<tr>
<th>What?</th>
<th>The transfemoral EVOQUE Tricuspid Valve Replacement System may be an important therapy for an undertreated TR patient population</th>
</tr>
</thead>
<tbody>
<tr>
<td>How?</td>
<td>We report the 6-month outcomes from the prospective, single-arm, multicentre TRISCEND study in patients with ≥moderate TR</td>
</tr>
<tr>
<td>What are the results?</td>
<td>Significant TR reduction by core laboratory assessment, with 100% of patients having mild or less TR at 6 months in patients with predominantly ≥severe TR at baseline</td>
</tr>
<tr>
<td></td>
<td>96% survival rate and 94% freedom from heart failure hospitalization</td>
</tr>
<tr>
<td></td>
<td>Significant improvements in NYHA class, KCCQ score, and 6MWD</td>
</tr>
<tr>
<td>Why is this important?</td>
<td>Transfemoral tricuspid valve replacement with the EVOQUE system demonstrated favorable 30-day outcomes sustained at 6 months</td>
</tr>
<tr>
<td></td>
<td>Randomized pivotal trial (TRISCEND II, NCT04482062) is underway</td>
</tr>
</tbody>
</table>
Transcatheter Therapies for Tricuspid Regurgitation

• There is renewed interest and focus on the tricuspid valve in the era of transcatheter valve technologies
• There are a number of concepts that have been shown to be feasible with early acceptable safety and efficacy results
• Increasing experience with off-label use of existing technologies:
  • Increasing experience with edge-to-edge repair using the MitraClip/Triclip system with good early results, but questions on long-term durability
  • Tricuspid valve-in-valve and valve-in-ring using TAVR devices is straightforward procedure with excellent risk benefit profile
• On-going protocols with dedicated devices to treat TR with valve replacement look promising in EFS. Pivotal trials are ongoing.

Key question: TR is associated with adverse outcomes but does treating functional TR result in improved clinical outcomes
60-year-old female with severe mitral regurgitation
- Deemed not a surgical candidate
- Considered for TMVR

NYHA Class III,
Congestive Heart Failure
Atrial Fibrillation
Obesity (previously 400lbs)
Severe PAH
Excellent symptomatic response 1 year later returns with peripheral oedema - No MR but severe functional TR

NYHA Class III, Severe MR s/p MVR with SM3 device Congestive Heart Failure A-fib on Eliquis Severe PAH
M3 & EVOQUE Example

61-year-old female with severe functional TR
- Treated with 48mm EVOQUE TTVR

Day 30 Follow-up