Transcatheter Tricuspid Valve Therapies: What Are We Doing Now and What Will be Doing in Five Years?

Christopher U. Meduri, MD MPH
Co-Director Marcus Heart Valve Center
Piedmont Heart Institute
Atlanta, GA

Disclosures

Affiliation
- Proctor/Speaker/Ad Board
- Proctor/Speaker/Grant
- Proctor/Grant

Company
- Boston Scientific
- Medtronic
- Edwards

National Co-PI
Steering Committee

Scout I (Trialign)
Apollo
The Forgotten Valve?

The forgotten valve: lessons to be learned in tricuspid regurgitation

Julia Michosherer and Gerald Maurer

European Heart Journal (2010) 31 3291-3293

TRI...
How are ~ 8MM Tricuspid Patients Forgotten?

EU-22
Prev. 4,700,000
Incid. 331,000

USA
Prev. 2,500,000
Incid. 217,000

13,000
10,000

Patients w/ Moderate or Severe TR
Annual TR Surgeries

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TR Treatment Options

• Pharmaceuticals are suboptimal
  • Renal congestion
  • Hepatic congestion
  • Resulting edema difficult to manage

• Surgery is suboptimal
  • Operative mortality as high as 26 %
  • Concomitant with left sided surgery
  • Few isolated TR surgeries are performed

* Marcus Heart Valve Center
* Piedmont HEART
What Are We Doing Now?
Temporal Trends in Isolated Tricuspid Surgery

- Less than 800 Isolated Surgeries/year
- Mortality rate of 8.8%
- Tricuspid Replacement mortality 2.2x Repair
- Avg LOS 11 days
- Avg cost $161,000

Untreated Tricuspid Regurgitation: Impact on Survival

5507 patients, echocardiography at Veterans Centers

After adjustment for age, LVEF, IVC size, RV size and RV function, S-PAP

P < 0.001
Why Treatment is Important

SCOUT I 30 Day‡, MLWHF in Perspective
SCOUT in Tricuspid and MitraClip in Mitral

Annuloplasty
ERO: Space Filling
Leaflet

Repair Treatment Modalities: Annulus, Leaflet, ERO
**Trialign for FTR**

- Based on a surgical predicate (Kay Procedure)
- Small Footprint: Pledgets & Lock
- Ability to titrate Therapy: Location, # of pledgets

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**SCOUT I**

**30-Day Safety and implant success**

<table>
<thead>
<tr>
<th>Category</th>
<th>n/N</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Implant Success</td>
<td>15/15</td>
<td>100%</td>
</tr>
<tr>
<td>Unplanned intervention</td>
<td>1/15</td>
<td>7%</td>
</tr>
<tr>
<td>Intraprocedural stenting of RCA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 Day Follow Up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Freedom from death</td>
<td>15/15</td>
<td>100%</td>
</tr>
<tr>
<td>Technical Success</td>
<td>12/15</td>
<td>80%</td>
</tr>
<tr>
<td>3 single pledget dehiscence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major Adverse Events</td>
<td>0/15</td>
<td>0%</td>
</tr>
</tbody>
</table>

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Investigational Device: Not Available for Commercial Use.
SCOUT I Patient Flow

Patients Enrolled Intent to treat n=15

Technical Success Per Protocol n=12

30 Day
Death n=1*

6 Months
Elective Re intervention n=1

-12 Months

Technical Success Per Protocol n=11

Technical Success Per Protocol n=10

Pledget Dehiscence n=3

Death n=1*

Elective Re intervention n=1

3/2/2018

PISA EROA Reduction

<table>
<thead>
<tr>
<th>Time</th>
<th>Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 Days</td>
<td>-33.2%</td>
</tr>
<tr>
<td>6 Month</td>
<td>-18.9%</td>
</tr>
<tr>
<td>12 Month*</td>
<td>-21.6%</td>
</tr>
</tbody>
</table>

*Change from baseline to 12 months computed on paired data, *1 patient excluded from 12 month due to reintervention for per protocol.
LVOT Stroke Volume Gain

- Change from baseline to 12 months computed on paired data.
- *n=1* patient excluded from 12 month due to reintervention for per protocol.

Clinical Outcomes through 12 months

- \( \Delta \) 61% change in NYHA classification.
- \( \Delta \) 21% change in 6 MWT (m).

<table>
<thead>
<tr>
<th>MLWHF</th>
<th>NYHA Classification</th>
<th>6 MWT (m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>p = 0.003</td>
<td>p = 0.023</td>
<td>p = 0.115</td>
</tr>
</tbody>
</table>

‡All patients with 30 day technical success (n=12); Excludes 1 death at 6M & 1 re-intervention at 12M.
Edwards Cardioband System:

- Percutaneous partial ring
- Originally designed for Mitral
- 15 consecutively placed screws
- Ring is reduced to size once implanted
- 30 patients treated to date
- Organized data reported

Edwards Cardioband (n=30)

- 20% Major Adverse Event rate
  - 2 Deaths
  - 1 Stroke
  - 2 life threatening bleeds
  - 1 extensive bleed

- Efficacy
  - At 30 days
    - 50% reduction in PISA EROA
    - 31% reductions in vena contracta
    - 7% improvement in stroke volume by core lab at 30 days

- 82% of patients in NYHA Class I or II
  - Only 15% in Class I (asymptomatic)
  - Quality of Life increase of 17% (KCCQ)
Edwards TRI-REPAIR Study
50% reduction in PISA EROA, 31% reductions in vena contracta. And 7% improvement in stroke volume by core lab at 30 days

- Large proportion of patients treated with "torrential TR"
- Improvements resulted in most patients achieving lower severity or moderate TR at 30 days

Edwards TRI-REPAIR Study
Functional improvement at 30 days
4Tech, The TriCinch System:

- 4Tech places a single anchor into the side wall of the heart at the Tricuspid Valve Annulus, then deploys a stent in the IVC to apply tension and pull the Valve together.

| Corkscrew implant in Antero-Posterior Commissure | Coupling Mechanism | Tension Applied | Stent Deployment in Inferior Vena Cava |

TriCinch™ Gen 2
Alternative anchoring mechanism

- Nitinol wire transforming in an hemi-spiral shaped anchoring system
- Deployed in the pericardial space
- Independence from RCA location and tissue quality
Edwards, Forma System:

- Positioned within regurgitant orifice
- Provides surface for native leaflets to coapt
- Advanced from left subclavian vein
- Anchored at RV apex and subclavian vein

Forma Early Feasibility Study

Study Flow

Intent to Treat
n=30

- Procedure aborted (n=1)
  - Venogram revealed occluded subclavian vein

Enrolled
n=29

- RV perforation (n=2)
  - 1 patient death day 0
  - 1 patient converted to surgery

Implanted
n=27

- Device migration (n=1)
  - Device explanted day 2, death day 36

- Device explant (n=1)
  - Device explanted day 21 due to infection

30 Day Echo Follow Up
n=25*

*2 anchor dislodgements. Spacer remained in the transvalvular position, patients stable at 30 day follow-up

Kodali S, TCT 2017
## FORMA Early Feasibility Study
### Baseline Echocardiography (1)

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD N = 29</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF (%)</td>
<td>56.9 ± 12.8</td>
</tr>
<tr>
<td>TAPSE (cm)</td>
<td>1.4 ± 0.4</td>
</tr>
<tr>
<td>TV Annular Diameter (cm)</td>
<td>4.5 ± 0.7</td>
</tr>
<tr>
<td>TR Vena Contracta mean (cm)</td>
<td>1.6 ± 0.5</td>
</tr>
<tr>
<td><strong>PISA EROA (cm²)</strong></td>
<td><strong>1.2 ± 0.6</strong></td>
</tr>
<tr>
<td>Tricuspid Regurgitant EROA 2D or 3D (cm²)</td>
<td>2.2 ± 1.5</td>
</tr>
<tr>
<td><strong>Tricuspid Regurgitant volume (mL)</strong></td>
<td><strong>129.0 ± 65.8</strong></td>
</tr>
<tr>
<td>TV mean gradient (mmHg)</td>
<td>1.9 ± 1.1</td>
</tr>
</tbody>
</table>

## FORMA Early Feasibility Study
### Clinical Outcomes at 30 Days

<table>
<thead>
<tr>
<th></th>
<th>Patients N = 29</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death (All-Cause)</td>
<td>2</td>
<td>6.9</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Vascular Injury</td>
<td>1</td>
<td>3.4</td>
</tr>
<tr>
<td><strong>Bleeding</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life Threatening or Disabling</td>
<td>2</td>
<td>6.9</td>
</tr>
<tr>
<td>Major</td>
<td>4</td>
<td>13.8</td>
</tr>
<tr>
<td>Device Related Cardiac Surgery</td>
<td>3</td>
<td>10.3</td>
</tr>
<tr>
<td>AKI ≥ Stage 2*</td>
<td>3</td>
<td>10.3</td>
</tr>
</tbody>
</table>

* VARC-2 Guidelines

20/29 patients (69%) had none of the above events
FORMA Early Feasibility Study
Echocardiography Outcomes at 30 Days
( echo core lab, paired analysis)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>30 Days</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF (%)</td>
<td>55.9 ± 13.8</td>
<td>58.6 ± 12.9</td>
<td>0.074</td>
</tr>
<tr>
<td>RV TAPSE (cm)</td>
<td>1.4 ± 0.4</td>
<td>1.5 ± 0.4</td>
<td>0.592</td>
</tr>
<tr>
<td>LVOT Stroke Volume (mL)</td>
<td>58.0 ± 14.7</td>
<td>60.8 ± 16.1</td>
<td>0.331</td>
</tr>
<tr>
<td>TV Annular Diameter (cm)</td>
<td>4.4 ± 0.7</td>
<td>4.5 ± 0.9</td>
<td>0.577</td>
</tr>
<tr>
<td>RV Diameter Base (cm)</td>
<td>5.9 ± 0.9</td>
<td>5.5 ± 1.0</td>
<td>0.020</td>
</tr>
<tr>
<td>PISA EROA (cm²)</td>
<td>1.1 ± 0.6</td>
<td>0.6 ± 0.4</td>
<td>0.001</td>
</tr>
<tr>
<td>2D or 3D Quantitative EROA (cm²)</td>
<td>2.1 ± 1.8</td>
<td>1.1 ± 0.9</td>
<td>0.012</td>
</tr>
<tr>
<td>Mean Vena Contracta Width (cm)</td>
<td>1.6 ± 0.5</td>
<td>1.1 ± 0.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

FORMA Early Feasibility Study
NYHA Class at 30 Days

P = 0.0002

<table>
<thead>
<tr>
<th>% Population</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>100%</td>
<td>84%</td>
<td>28%</td>
<td>28%</td>
</tr>
<tr>
<td>30 Days</td>
<td>100%</td>
<td>84%</td>
<td>28%</td>
<td>28%</td>
</tr>
</tbody>
</table>

n=25
Abbott Mitraclip for TR

- Same clip as mitral
- Attempting to clip Septal-Anterior leaflets or Post-Septal
  - Multiple clips can be required
  - ~300 off label cases performed world-wide
Transcatheter Treatment of Severe Tricuspid Regurgitation With Edge-to-Edge MitraClip Technique

<table>
<thead>
<tr>
<th>All patients (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedures duration, min</td>
</tr>
<tr>
<td>Concomitant mitral clip, n (%)</td>
</tr>
<tr>
<td>In-hospital mortality, n (%)</td>
</tr>
<tr>
<td>Myocardial infarction, n (%)</td>
</tr>
<tr>
<td>Cardiac Tamponade, n (%)</td>
</tr>
<tr>
<td>Bleeding requiring transfusion, n (%)</td>
</tr>
<tr>
<td>Device migration, n (%)</td>
</tr>
<tr>
<td>Stroke/TIA, n (%)</td>
</tr>
<tr>
<td>Leaks subtotal/total, n (%)</td>
</tr>
<tr>
<td>Number of clips implanted, n (%)</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>Implantation site, n (%)</td>
</tr>
<tr>
<td>Anterior/posteromedial commissure</td>
</tr>
<tr>
<td>Posteroanterior commissure</td>
</tr>
<tr>
<td>Anterolateral commissure</td>
</tr>
</tbody>
</table>

Procedural outcomes and safety

Abbott Tricuspid Clip
Transcatheter Treatment of Severe Tricuspid With Edge-to-Edge Mitraclip Technique

Changes in echocardiographic TR-defining parameters

EROA: 0.9 to 0.4 (P<0.001)

VC 1.1 to 0.6 (P<0.001)

RV 57.2 to 30.8 (P<0.001)
Transcatheter Treatment of Severe Tricuspid Regurgitation With Edge-to-Edge Mitraclip Technique

Results: Symptomatic and functional changes

NYHA class

6 minutes walking distance

Baseline NYHA class

Follow-up NYHA class

0
20
40

0
145
155
245
345

NYHA class

p=0.001

p=0.007

6 minutes walking test baseline

6 minutes walking test 30 days

NaviGate

Tricuspid Valved Stent and Delivery Systems

Components Specifications

• Temperature Shape Memory NiTiNol Tapered Stent
• Height profile 21 mm, Truncated Cone configuration with a Diffuser Effect
• Annular Winglets for secure anchoring of TV annulus and tricuspid valve leaflet
• Sizes: 36mm, 40mm, 44mm, 48mm, 50mm, and 52mm.
• Chemically Preserved Xenogeneic Pericardium

Delivery System

• Presently 35F profile at the distal capsule
• 18F catheter shaft
• Two degrees of motion at tip
• 90° Articulation
• Controlled Valve Release
• All modes of delivery use the same valve configuration

Navia J. EuroPCR 2017
Comparison of Technologies

<table>
<thead>
<tr>
<th>Type of Study</th>
<th>Trialign</th>
<th>Forma</th>
<th>Cardioband</th>
<th>Mitraclip</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>15</td>
<td>30</td>
<td>30</td>
<td>64</td>
</tr>
</tbody>
</table>

**Safety**

- **30 Day Mortality**: 0% 7% 7% 4.6%
- **Major Bleeding**: 0% 21% 10% 4.6%
- **Cardiac Surgery**: 0% 10% 0%

**Efficacy**

- **PISA EROA**: 38% 45% 50% 55%
- **Stroke Volume**: 19% NR 7% NR

**Clinical Outcomes**

- **MLWH/KCCQ**: 56% (MLWH) 73% (KCCQ) 17% (KCCQ)
- **6MWT (m)**: 22% 21% 11.87% 6.4%
- **NYHA Class I/II**: 100% 82% 72% 37%

- Modest Reductions in TR
- Variable Safety Profiles (but very early!)
- Impressive Improvements in QOL
- Long Procedures

What Do We Need In 5 Years

- Further TR Reduction
- Proven Long-term Efficacy
- Tailoring Treatment for Each Process
- Safer Replacement
- Earlier Treatment

- What do we need to attain this???
“When I want to understand what is happening today or try to decide what will happen tomorrow, I look back”

-- Omar Khayyam
In 5 Years: Technologies and Operators Must Evolve

- **Safety:**
  - ¾ studies with 30d mortality of 5%
  - ¾ MACE 10-20%
- **Success:**
  - ~20% pullout with Trialign
  - 4Tech reengineered for pullouts
- **TR reduction**
  - <50% on average
  - Reoccurs

In 5 Years: Physicians Must Evolve

- We will learn to identify and treat earlier
- We will learn to tailor devices to anatomy
  - Annulus
  - Leaflets
  - Degree of TR
  - ? Likely etiology of FTR
- We will continue to focus on repair but if safe options for replacement develop, may be treatment of choice for “late” patients
Thank You

Christopher.Meduri@piedmont.org
404-673-0902