Evolving Transcatheter Therapies for Tricuspid Valve Disease

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Disclosures

• Speaker:
  • Abbott Vascular, Baylis Medical, Philips Healthcare, Edwards Lifescience

• Institutional Consulting Agreements (no direct compensation):
  • Abbott Vascular, Boston Scientific, Edwards Lifescience, Medronic
  • Core Lab Chief Scientific Officer for multiple Tricuspid Valve Device Trials

• Stock Options with Navigate
New Horizon for Tricuspid Regurgitation

TRANSCATHETER TECHNOLOGIES

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>New Technologies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annuloplasty (Direct and Indirect) Device</td>
<td>TriAlign, Cardioband, 4Tech, Millepede, Pasta, Cardiac Implants, MIA PolyCor Anchors</td>
</tr>
<tr>
<td>Leaflet Device</td>
<td>Forma, MitraClip, PASCAL, Mistral</td>
</tr>
<tr>
<td>Heterotopic Valve (in IVC/SVC)</td>
<td>Trinity /Sapien, TriCentro, SAPIEN in IVC, TricValve</td>
</tr>
<tr>
<td>Orthotopic Valve Replacement</td>
<td>Navigate, Trisol, LUX, Tri-Cares, Intrepid, EVOQUE, V-dyne</td>
</tr>
</tbody>
</table>
Transcatheter Annular Repair

Intra-procedural Imaging for Tricuspid Valve Interventions

2D and 3D TEE Imaging

TV 3D en face view

Trialign™

Cardioband™

4Tech TriCinch™ Coil System

Baseline

Final

POST
Tricuspid valve repair with the Cardioband system: two-year outcomes of the multicentre, prospective TRI-REPAIR study

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Table 3. Adverse events, number of patients.

<table>
<thead>
<tr>
<th>Event</th>
<th>One year n (%)</th>
<th>Two years n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>5 (16.7)</td>
<td>8 (26.7)*</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (3.3)</td>
<td>2 (6.7)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Breeding complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(extensive, life-threatening, or fatal)*</td>
<td>6 (20.0)</td>
<td>7 (23.3)</td>
</tr>
<tr>
<td>Coronary complications</td>
<td>3 (10.0)</td>
<td>3 (10.0)</td>
</tr>
<tr>
<td>Device-related secondary intervention</td>
<td>1 (3.3)</td>
<td>2 (6.7)</td>
</tr>
<tr>
<td>Device-related cardiac surgery</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Renal failure*</td>
<td>1 (3.3)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Conduction system disturbance</td>
<td>1 (3.3)</td>
<td>2 (6.7)</td>
</tr>
<tr>
<td>Ventricular arrhythmia</td>
<td>3 (10.0)</td>
<td>3 (10.0)</td>
</tr>
</tbody>
</table>

*CEC adjudicated. *Defined according to MVARC guidelines. *Occurrence in the first week post procedure and required haemodialysis. *None of the deaths between 30 days and two years were cardiovascular-related. *Patient experienced bleeding after secondary intervention.
April 30, 2018—Edwards Lifesciences announced that it has received European CE Mark approval for its Cardioband tricuspid valve reconstruction system for the treatment of tricuspid regurgitation.

Nickenig G et al. EuroIntervention. 2021 Feb 5;16(15):e1264-e1271
Challenges with Annuloplasty Devices

- Imaging of the annulus and catheter navigation can be difficult
  - New imaging tools: 3D ICE
- Annulus is not distinct fibrous structure that offers support leading to anchor pullout
- Challenging to achieve annular and TR reduction
  - Less effective when leaflet tethering is the primary pathology
DaVinci™ TR System

FIGURE 1: Multimodality Imaging at Baseline and Follow-up


Transcatheter Leaflet Coaptation Devices

Leaflet Coaptation Devices

Can treat primary and secondary Tricuspid Regurgitation!
NYHA class showed significant improvement, with the percentage of patients categorised as class I–II increasing from 25% (21 of 83 patients) at baseline to 80% (67 of 84) after 30 days (p<0.0001) and 86% (63 of 73) after 6 months (p<0.0001).

Assessment with the Kansas City Cardiomyopathy Questionnaire (KCCQ) showed a mean improvement in self-assessed heart failure symptoms of 14·2 points (SD 16·7) from baseline to 30 days (p<0.0001) and of 18·4 points (21·5) from baseline to 6 months (p<0.0001).

April 9, 2020 -- Abbot announced that its TriClip™ Transcatheter Tricuspid Valve Repair System has received CE Mark.
Summary

- Twenty-nine patients (85%) received implants.
- 52% with moderate or less TR and 85% achieved a TR severity reduction of at least 1 grade (p < 0.001).
- MAE rate was 5.9%, and none of the patients experienced cardiovascular mortality, stroke, myocardial infarction, renal complication, or reintervention.
- 89% improved to NYHA functional class I/II (p < 0.001),
- 6MWD improved by a mean of 71 m (p < 0.001)
- KCCQ score improved by a mean of 15 points (p < 0.001).

May 18, 2020 — Edwards Lifesciences announced that it received CE Mark approval for its Pascal transcatheter valve repair system for treating tricuspid valve regurgitation.
Survival and heart failure hospitalization rates

CEC-adjudicated survival and freedom from HFH

Kaplan-Meier analysis estimate ± std error.

HFH, heart failure hospitalization; CEC, clinical events committee

Days alive and not hospitalized for heart failure at one year: 363.1

Annualized HFH*

P=0.005

56.4% reduction

*Pre-enrollment HFH data collected via site-reported medical history. Post-procedure HFH data was CEC adjudicated. Error bars represent 95% confidence interval. P value derived from two sample z test for incidence rate ratio on natural log scale.
Challenges of Leaflet Devices

- Leaflet and Chordal variability
- Limited gap size that can be addressed
- Difficulty maneuvering through dense chordae or with pacemaker impingment
- Difficulty imaging to assess:
  - Leaflets and subvalvular apparatus intra-procedurally
  - TR severity post device (intra-procedural and at follow-up)

Pascal


Novel Devices: Tricuspid Valve Spacers

**CroiValve**

- Proximal Handle in subcutaneous pocket
- Intended Human Use
- Potential to adjust occluder dimensions
- Adapts to positive remodelling of heart
- Easily repositionable/removable

**Coramaze**

- Distal Occluder & Anchor
  - Exo-skeleton made of Nitinol mesh
  - Internal membrane of polyester fabric
  - Easily manipulated into ellipsoid, spherical or disc shapes

**TV Occluder**

- Potential to adjust occluder dimensions
- Adapts to positive remodelling of heart
- Easily repositionable/removable

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@hahn_rt
Heterotopic Valve Implantation

TricValve

NVT TriCento

Trillium
Challenges for Heterotopic TTVR: Patient Eligibility

Clinical
- NYHA ≥ III
- EF ≥ 40%
- 6MWT ≥ 60m
- Life expectancy ≥ 12 month

Absence of:
- Untreated left-sided Valvular heart disease,
- Severe renal failure
- Liver cirrhosis Child C

Anatomic

Hemodynamic
- V-Wave in IVC and SVC ≥ 25mmHg
- TAPSE ≥ 14mm
- sPAP ≤ 65mmHg

NOTE: patients with proven systolic flow reversal in the caval veins and preserved RV function potentially benefit from this treatment.
Transcatheter Tricuspid Valve Replacement Devices

Can treat primary, secondary and CIED-related Tricuspid Regurgitation!
Caval veins for TF Approach to Tricuspid Valve

Quantification of anatomical dimensions and orientation
### 30 day results

<table>
<thead>
<tr>
<th>Safety profile</th>
<th>N=25</th>
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<tbody>
<tr>
<td>Mortality</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Reintervention</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>HF hospitalization</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Renal failure requiring dialysis</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>Device embolization</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Conduction system disturbance requiring PPM</td>
<td>8%</td>
<td></td>
</tr>
</tbody>
</table>

### Procedural results

<table>
<thead>
<tr>
<th>Technical success</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 unsuccessful procedure due to non-coaxial approach</td>
</tr>
<tr>
<td>1 low placement requiring valve-in-valve (SAPIEN 3, Edwards Lifesciences)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Delivery system insertion to removal, minutes; mean (min, max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>68 (37, 101)</td>
</tr>
</tbody>
</table>

![Graph showing TR severity and NYHA functional class](image)
### Inclusion Criteria

- Age ≥ 18 years
- Signs and/or symptoms or prior heart failure hospitalization from TR despite optimal medical therapy (OMT) per the local Heart Team
- Functional or degenerative TR ≥ moderate
- Patient appropriate for transcatheter tricuspid valve replacement

### Exclusion Criteria

- Tricuspid valve anatomy precludes proper device deployment and function
- Previous tricuspid intervention interfering with the device
- Severe right ventricular dysfunction
- LVEF < 25%
Challenges with Orthotopic TTVR

- Annulus size large
- RV function with ↑ afterload
- Conduction disturbance
- Leaflet thrombosis
- Durability

Risk for New PPM

Pre-existing PPM
Current transcatheter treatment options in Europe

- Leaflet Approximation
- Annular Repair
- Heterotopic Valve Replacement
- Orthotopic Valve Replacement

1. Who are the appropriate patients for TTVI?
2. What anatomy is suitable for TTVI?
3. Can we improve outcomes with TTVI?