Tricuspid Valve Disease: Pathophysiology and Evolving Therapies

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Conflicts of Interest

• Consultant to Boston Scientific, Abbott Vascular, Medtronic, Edwards Lifesciences, WL Gore

• Co-Principal Investigator for PINNACLE FLX, trial, CHAMPION AF (Boston scientific)

• Co-Principal Investigator for EXPAND Registry and REPAIR-MR trial (Abbott Vascular)

• Steering committee member: Triluminate Trial
Pathophysiology of Tricuspid valve disease
Anatomy of the Tricuspid Valve

Anatomic Changes In Tricuspid Regurgitation

(A) Tricuspid valve (TV) anatomy and adjacent structures. (B) Three-dimensional shape of the tricuspid annulus at systole. Reprinted with permission from Fawzy et al. (20). (C) Progressive tricuspid annulus dilation occurs in its anteroposterior plane. Red arrows show the increasing intercommissural distance with progressive annular dilation. Reprinted with permission from Dreyfus et al. (5). A = anterior annulus; AA = ascending aorta; Ant. = anterior; AP = anteroposterior commissure; AS = anteroseptal commissure; CS = coronary sinus; LCx = left circumflex artery; MV = mitral valve; MPA = main pulmonary artery; P = posterior annulus; Post. = posterior; PS = posteroseptal commissure; RCA = right coronary artery; S = septal annulus; Sept. = septal.

TRICUSPID REGURITATION

**Etiology**

- **Primary (25%)**
  - Ebstein’s anomaly
  - Carcinoid tumors
  - Infective endocarditis
  - Drug related “Fen-phen” diet pills
  - Radiation therapy
  - Rheumatic
  - Iatrogenic
  - **Pacemaker, ICD, Biopsy**

- **Secondary (75%)**
  - Left heart disease
  - Right heart dysfxn
  - Pulmonary hypertension
    - Chronic jung disease
    - Thromboembolism
  - Annular dilation
    - Usually from A-fib

Courtesy: Adam Greenbaum
80 yr old lady fatigue, abdominal pain, leg edema 7 months after pacer
80 yr old lady fatigue, abdominal pain, leg edema 7 months after pacer

Transgastric view

ICD lead pinning the septal leafet
2 months post lead removal

- Some improvement of symptoms
- Still has severe TR
- Septal leaflet was mobile
- Patient was enrolled in the Triluminate Trial
New proposed grading of TR

Table I  Proposed expansion of the ‘Severe’ grade

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Massive</th>
<th>Torrential</th>
</tr>
</thead>
<tbody>
<tr>
<td>VC (biplane)</td>
<td>&lt;3 mm</td>
<td>3-6.9 mm</td>
<td>7–13 mm</td>
<td>14–20 mm</td>
<td>≥21 mm</td>
</tr>
<tr>
<td>EROA (PISA)</td>
<td>&lt;20 mm²</td>
<td>20–39 mm²</td>
<td>40–59 mm²</td>
<td>60–79 mm²</td>
<td>≥80 mm²</td>
</tr>
<tr>
<td>3D VCA or quantitative EROA</td>
<td>75–94 mm²</td>
<td>95–114 mm²</td>
<td>≥115 mm²</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VC, vena contracta; EROA, effective regurgitant orifice area; 3D VCA, three-dimensional vena contracta area.

3D VCA and quantitative Doppler EROA cut-offs may be larger than PISA EROA.

• Need to integrate the severity of RV function and remodeling

Courtesy: Hahn R
Significant tricuspid regurgitation affects prognosis

- 1-year survival rates
  - No TR: 91.7%
  - Mild TR: 90.3%
  - Mod TR: 78.9%
  - Severe TR: 63.9%

- Independent of:
  - LVEF
  - PA pressure
  - Age
  - RV size
  - IVC dilation

Figure 1. Kaplan-Meier survival curves for all patients with tricuspid regurgitation (TR). Survival is significantly worse in patients with moderate and severe TR.

- n=5223 VA patients
- Follow up available for 4 years
Evolving Therapies
Introduction

- Tricuspid regurgitation affects prognosis

- Tricuspid valve once a forgotten valve is become the point of attention surgeons and cardiologists

- Isolated tricuspid valve surgery is not common and carries a high mortality

- In the era of transcatheter therapies for left heart valves there is a need for transcatheter treatment options for Tricuspid valve disease
# New Transcatheter Tricuspid Therapies

## Mechanism

### Annuloplasty (Direct and Indirect) Device

- Cardioband
- 4Tech
- Millepede
- Pasta
- Cardiac Implants
- MIA PolyCor Anchors

### Leaflet Device

- MitraClip
- PASCAL
- Mistral

### Heterotopic Valve (in IVC/SVC)

- Trinity /Sapien
- TriCentro
- SAPIEN in IVC

### Orthotopic Valve Replacement

- Navigate
- Trisol
- LUX
- Tri-Care
- Intrepid
- Evoque
- Cardiovalve

_Sources: Hahn R_
Leaflet Grasping devices

MitraClip NTR and XTR (Abbott Vascular)

PASCAL system (Edwards Lifesciences)
FTR is predominantly a consequence of RV enlargement and antero-posterior dilatation: rationale of leaflet apposition

A = Anterior leaflet; P = Posterior leaflet; S = Septal leaflet
TriClip™ Transcatheter Tricuspid Valve Repair System (Abbott)

Two Clip sizes

NTR

XTR

Clip Strategy

TriClip™ Transcatheter Tricuspid Valve Repair System (Abbott) Guide and Clip Delivery System
80 yr old lady with pacer induced TR treated successfully with 3 Triclips following pacer removal
Clinical experience with TriClip

• Most common transcatheter treatment of TR
• Off label commercial usage of MitraClip in Tricuspid position > 5000 cases
• Triluminate Study (US and Europe): completed enrollment
• CE Mark approval in 2020
• Pivotal Triluminate Study: (US) Ongoing
  • Randomized study: Triclip vs medical therapy
86.6% showed at least 1 grade improvement at 30 days. The 97.5% lower confidence limit was 77.3%, which is greater than the performance goal of 35%, thus the primary effectiveness endpoint is met.
Triluminate Trial
Results - Clinical Outcomes

**NYHA Functional Class**

- **Baseline**: NYHA I/II: 55.6%
  - Class I: n=21
  - Class II: n=57
- **30-day**: NYHA I/II: 80.5%
  - Class I: n=18
  - Class II: n=47

\[ \Delta = 14.20 \pm 16.74 \]
\[ p < 0.0001 \text{ (paired, n=82)} \]

**KCCQ Score**

- **Baseline**: n=16
- **30-day**: n=47

\[ \Delta = 14.20 \pm 16.74 \]
\[ p < 0.0001 \text{ (paired, n=83)} \]

*5 pt improvement is considered clinically meaningful. MVARC recommends 10 point improvement for MR.*

61% of patients experienced >10 point improvement.

*5 pt improvement is considered clinically meaningful.*
Trial Overview

Subject has Symptomatic Severe TR and is at intermediate or greater risk of mortality 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 Clippable

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

Randomization (1:1) (N=450)

TriClip Device (Device)  Medical Therapy (Control)

Up to 3 Roll-Ins Permitted per Site

Exclude Subject

Exclude Subject

Single Arm (N=100)

TriClip Device (Device)
Edwards PASCAL Transcatheter Valve Repair System

**Implant**

Central spacer intended to fill the regurgitant orifice area

Spacer and broad, contoured paddle design reduce stress on leaflets

Clasps allow for independent leaflet capture and the ability to fine-tune leaflet position
Compassionate use of PASCAL for TR (28 pts)  
Significant Reduction in TR Severity at 30 Days  

- Significant reduction in TR severity in 85% of patients with TR ≤2+ at 30 days  

N=28  

Wilcoxon Signed-Rank Test
Clinical experience with PASCAL device for TR

- CE Mark approved based on the compassionate data

- Pivotal CLASP TR trial (US) Ongoing
  - Randomized study: Triclip vs medical therapy
Cardioband Tricuspid System Procedure

1. Femoral Access & System Insertion
2. Implant Deployment
3. Implant Size Adjustment

CAUTION: Investigational device. Limited by Federal (or United States) law to investigational use.
Clinical experience with Cardioband for TR

- CE Mark approved based on early feasibility trial
- Early experience in US
- Procedure is safe, moderate reduction of TR, and moderate reduction of annular diameter
- The procedure time is long
- Pivotal study is on hold in US
- Could be used in conjunction with edge to edge repair
Transcatheter Valve replacement

• It is difficult to repair torrential tricuspid regurgitation
• It may be safer to perform transcatheter tricuspid valve replacement than mitral valve replacement
• Will abolish TR and not just reduce TR
• Will require long term anticoagulation
• There are concerns whether failing RV can tolerate sudden abolishment of TR
Components Specifications

• Temperature Shape Memory NiTinol Tapered Stent
• Height profile all Sizes <22 mm,
• Annular Winglets for secure anchoring of TV annulus and tricuspid valve leaflet
• Sizes = 36mm, 40mm, 44mm, 48mm and 52mm.
• Chemically Preserved Xenogeneic Pericardium

• 42 F sheath required
• Two degrees of motion at tip
• 90° Articulation (Steering control)

Not approved for use in USA
Navigate valve: Successful deployment

- Trivial central and trivial paravalvular regurgitation
- Peak/mean transtricuspid gradient = 1.5 and 0.3 mmHg
CAUTION: Investigational device. Limited by Federal (or United States) law to investigational use.

- Unique anchoring mechanism utilizes annulus, leaflets, and chords, respecting the native mitral anatomy

- Intra-annular sealing skirt and frame to minimize PV leak

- Low atrial and ventricular profile to reduce procedural complications

- Integrates Edwards bovine pericardial leaflet design and tissue treatment

- Both valve sizes (44 and 48 mm) compatible with one size delivery system
EVOQUE valve for TR: Clinical update

• Early feasibility Trial: 25 patients (completed enrollment)
  • Encouraging data

• TRISEND II Pivotal Study
  • Multicenter randomized study 300 pts (2:1 randomization) Device vs Medical treatment
  • Single arm registry: (100 pts)
Conclusions

- Tricuspid valve is not a forgotten valve anymore
- Significant tricuspid valve disease affects prognosis
- In the era of transcatheter therapies, there are several transcatheter treatment options
- Leaflet repair using the TriClip or off label use of the MitraClip is the most well studied procedure
- Encouraging data on use of Transcatheter Valve replacement has lead to starting of PIVOTAL Trial
- The treatment of TR is a tool box: there is role of repair and replacement
QUESTIONS?