MHIF Research Highlights: JANUARY 2020

**SHARING EXPERTISE:**
Dr. Miedema was featured in *Men’s Health Magazine*... in an article, “The Great Millennial Blood Pressure Problem,” addressing why high blood pressure is rising for millennials.

**FEATURED MHIF STUDIES**
Open for Enrollment and Referrals!

**HITSOVA** for heparin induced thrombocytopenia
   CONTACTS: Carina Benson, 612-863-4393 and Jane Fox, 612-863-6289

**VESALIUS** for high cardiovascular risk without prior myocardial infarction or stroke
   CONTACT: Ezi Ebere, 612-863-4393

**REDUCE LAP-HF RCT II** for heart failure
   CONTACT: Jane Fox, 612-863-6289

**MARK YOUR CALENDARS**
Heart Valve Awareness Event for Patients!
Thursday, February 20
Minnesota Valley Country Club

**MHIF on KSTP Channel 5 News!**
Dr. Scott Sharkey and patient, Kristen Bowlds were interviewed by the local KSTP, Channel 5 news for a story about women’s heart research and Kristen’s experience with SCAD.

Shout out of gratitude for Dr. Wang’s support of research...

Dr. Wang is appreciated by research staff for always being so open to research and speaking with his patients about the studies! After he gives the introduction, patients are often interested in participating and we are grateful!

**REGISTER:**
Mplsheart.org/valveday
UPDATE ON TRICUSPID REGURGITATION – Evaluation and Treatment

ANENE UKAIGWE, MB;BS
Structural Heart Disease Fellow
Minneapolis Heart Institute/ Abbot Northwestern Hospital
Minneapolis, MN

DISCLOSURES

• None
• Off label use and Investigational devices
OBJECTIVES

• Understand burden of Tricuspid Regurgitation and clinical implications
  • Clinical problem, implications, prognosis
• Outline how to evaluate a patient with Tricuspid Regurgitation
  • Annulus, severity, coaptation, RV chambers, PA pressures, planning
• Outline transcatheter treatment options and outcomes.

Classification and Etiology

CENTRAL ILLUSTRATION: Schematic Drawing of the Different Morphologic Types of Tricuspid Regurgitation

<table>
<thead>
<tr>
<th>MORPHOLOGIC TYPES OF TRICUSPID REGURGITATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
</tr>
<tr>
<td>Primary Tricuspid Regurgitation</td>
</tr>
</tbody>
</table>

TR is common and Multifactorial

**Primary TR**
- Cardiac Implantable Device
- Endocarditis
- Congenital
- Rheumatic Tricuspid
- Myxomatous

**Secondary TR**
- Left systolic dysfunction
- Mitral or aortic valve disease
- PH due to Pul disease
- Idiopathic
- HFpEF
- Primary Pulmonary Hypertension

35,000 patient echo based study in Madrid
~5% Torrential or massive TR.
22% TR

417 patients with ≥moderate TR
Olmstead County

Zamarano JL et al (in press) courtesy PCR online.com

---

TR is common and impacts Survival

5223 Patients in VA 4-y follow up.
90% had TR

13,026 Patients with HFpEF
88% had FTR
FTR is associated with more dyspnea, impaired renal function and low CO (P < 0.003 for all)

417 Patients 10 yrs mod TR or greater.
8% had isolated TR
Associated with –old age, female gender, atrial fibrillation

TR impacts on survival even after transcatheter valve interventions on left heart valves

TR in 80% of TAVR pts, severe in 5%

Impact on survival persists after adjustments

Pooled analysis of all studies reporting outcomes for TR patients, n = 32, 601
Moderate to Severe on 3 scale grading
- 1.95 fold increase in All cause mortality
- 2.56 increase in cardiac mortality
- 1.73 fold increase in HF hospitalization

- All cause mortality
- 1.25 fold increase with Mild
- 1.61 fold increase with moderate
- 3.44 fold increase with severe

Possible reasons for under-treatment of TR

• Under-estimation of TR severity pre-operatively or under general anesthesia
• Over-estimation of surgical risk of concomitant TV surgery
• Misconception that TR resolves after treatment of mitral valve disease.
**RV volume overload**

- **Eccentric RV remodeling**
- **Reduced CO, Chronic neurohumoral activation**
- **Peripheral congestion, Liver dysfunction, ascites, Renal dysfunction, AF**

**SYMPTOMS**

**TV annular dilation**
- **Loss of coaptation, Leaflet tethering**
- **VICIOUS CYCLE “TR begets TR”**

- **RA Volume overload**
- **RV volume overload**

---

**A Natural History Construct for TR**

- **RA dilation → Tricuspid annulus dilation occurs → Begets more TR**
- **Circularization of Tricuspid Annulus → LA+RA dilation → AFIB**

- **Moderate**
  - RV dilatation, preserved RV function, minimal symptoms
  - Impairment already
  - Years of indolence

- **Severe**
  - RV dilatation and RV failure, a late phenomenon
  - Massive Torrential
  - Very steep both ways

- **Massive RA- and RV-Dilatation**
  - RV Dysfunction, Chronic Congestion.

**Courtesy of Paul Sorajja, MD**
Right-Sided Chamber Remodeling
RA, RV, and Tricuspid Annulus

Tricuspid Annulus and RA volume Change First

Nemoto N et al. JTCVS 2015

Clinical Presentation

- Usually have prolonged asymptomatic interval.
- May be very subtle
- Hepatic congestion, hepatic fibrosis.
- Worsening renal dysfunction
- Low cardiac output
- Atrial tachycardias, Atrial fibrillation.

TR seen on Echo
GOALS OF IMAGING

• Diagnosis
• Severity
• Etiology
• Concomitant lesions
• RA and RV assessment
• Pulmonary hypertension
• Plan intervention – Morphology of TV apparatus, Geometry of Landing zone, Anatomic relationships, vascular access assessment, angle of deployment.

TR and RV assessment on TTE can be challenging

### ASE Guidelines → Multiple parameters

#### Tricuspid Regurgitation

<table>
<thead>
<tr>
<th>A. Color Flow Doppler (2D and 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Advantages</strong></td>
</tr>
<tr>
<td>Color Doppler assessment</td>
</tr>
</tbody>
</table>

#### B. Pulsed Wave Doppler

<table>
<thead>
<tr>
<th><strong>Advantages</strong></th>
<th><strong>Disadvantages</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Portable, simple to use</td>
<td>May not distinguish between TR and MR</td>
</tr>
</tbody>
</table>

#### C. Continuous Wave Doppler

<table>
<thead>
<tr>
<th><strong>Advantages</strong></th>
<th><strong>Disadvantages</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-invasive, high precision</td>
<td>May not distinguish between TR and MR</td>
</tr>
</tbody>
</table>

#### Example...

**Mild**

**Moderate**

**Massive/Torrential**

---

Slide Courtesy Joao Cavalcante MD

In Reality.....Additional Views with Color Doppler -

Unable to define flow convergence zone for PISA calculation

Slide Courtesy Joao Cavalcante MD

Doppler of TR jet

Slide Courtesy Joao Cavalcante MD
### Grading the Severity of Chronic TR by Echocardiography

<table>
<thead>
<tr>
<th>TR Severity</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Structural</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TV morphology</td>
<td>Normal or mildly abnormal leaflets</td>
<td>Moderately abnormal leaflets</td>
<td>Severe valve lesions (e.g., flail leaflet, severe retraction, large perforation)</td>
</tr>
<tr>
<td>RV and RA size</td>
<td>Usually normal</td>
<td>Normal or mild dilatation</td>
<td>Usually dilated</td>
</tr>
<tr>
<td>Inferior vena cava diameter</td>
<td>Normal &lt;2cm</td>
<td>Normal or mildly dilated 2.1-2.5cm</td>
<td>Dilated &gt;2.5cm</td>
</tr>
<tr>
<td><strong>Qualitative Doppler</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Color flow jet area</td>
<td>Small, narrow, central</td>
<td>Moderate central</td>
<td>Large central jet or eccentric wall-impinging jet of variable size</td>
</tr>
<tr>
<td>Flow convergence zone</td>
<td>Not visible, transient or small</td>
<td>Intermediate in size and duration</td>
<td>Large throughout systole</td>
</tr>
<tr>
<td>CWD jet</td>
<td>Faint/paritial/parabolic</td>
<td>Dense, parabolic or triangular</td>
<td>Dense, often triangular</td>
</tr>
</tbody>
</table>

- **Semi-quantitative**: Bolded signs are considered specific for their AR grade.
  - Color flow jet area (cm²)
    - Not defined
    - Not defined
    - >10
  - VCO (cm²)
    - <0.3
    - 0.3-0.69
    - ≥0.6
  - PISA radius (cm)
    - ≤0.6
    - 0.6-0.9
    - >0.9
  - Hepatic vein flow
    - Systolic dominance
    - Systolic blunting
    - **Systolic flow reversal**
  - Tricuspid inflow
    - A-wave dominant
    - Variable
    - E-wave >1.0m/sec

- **Quantitative**
  - ENPA (cm²)
    - ≤0.20
    - 0.20-0.39
    - ≥0.40
  - RV (ml/beat)
    - <20
    - 20-40
    - ≥45

1 RV and RA size can be within the "normal" range in patients with acute severe TR.
2 With Nyquist limit >50-70 cm/sec.
3 With baseline Nyquist limit shift of 28 cm/sec.
4 Signs are nonspecific and are influenced by many other factors (RV diastolic function, atrial fibrillation, RA pressure).
5 There are little data to support further separation of these values.

---

**Slide Courtesy Joao Cavalcante MD**


---

**Same patient, same day, different probes... (3D TTE)**

![3D Vena Contracta Area](image)

Slide Courtesy Joao Cavalcante MD
### Proposed Grading Scheme

**Table 1: 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></td>
<td></td>
<td>75-94 mm²</td>
<td>95-114 mm²</td>
<td>≥115 mm²</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.


---

### Proposed grading scheme

- Need to integrate degree of RV dysfunction, remodeling and Leaflet changes

Santoro C et al. Eur Heart J Cardiovasc Imaging. 2019 Sep 1;20(9):1035-1042
Echocardiographic/clinical evaluation of TR disease by main pathogenic/prognostic mechanisms

<table>
<thead>
<tr>
<th>TR quantitative parameters</th>
<th>Vena contracta width (biplane average)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PSV EROA and RegVol</td>
</tr>
<tr>
<td></td>
<td>Quantitative Doppler EROA and RegVol</td>
</tr>
<tr>
<td></td>
<td>3D vena contracta area and RegVol</td>
</tr>
</tbody>
</table>

| Annular dilation           | ≥40 mm or ≥21 mm/m² from apical 4ch view |
|                           | Note: Annular dilation may be a surrogate for severe TR in absence of adequate quantitative measures. |

| Leaflet coaptation         | Tenting length and area (2D echo, 4Ch view) |
|                           | Tenting volume (3D echo)                     |
|                           | Note: Coaptation parameters may be a surrogate for severe TR in absence of adequate quantitative measures. |

| Right ventricle remodeling, dilation, dysfunction | Multiparametric assessment of global right ventricle function: TAPSE, STDI, 2D-longitudinal strain, FAC%, 3D-RVEF% |

| RV-PA coupling             | Measure of RV contractile function indexed to afterload |

| Clinical features          | High CVP, renal dysfunction, liver dysfunction, ascites, edema |

Severe leaflet tethering - advanced
May not benefit for TV repair and need replacement.
Combination transcatheter therapies

Coaptation gap – for edge to edge repair
Functional CTA for Quantification of right-sided function and Remodeling

**RV 2ch View**

**RV 4ch View**

**RV 3ch View**

**RV “centric” SAX Reconstruction allow for quantification of RA, RV volumes and EF**

- Right Atrium
- Right Ventricle
**Anatomical ROA – Average Systolic Frames**

Systolic Frame 10%  
Systolic Frame 20%  
Systolic Frame 30%

Average Anatomical ROA = 0.629 cm²

Slide Courtesy Joao Cavalcante MD  

---

**Tricuspid Annulus, tethering height and Anatomic ROA**

4ch Diameter  
4ch Area and Height  
2ch Diameter Area & Major/Minor Diameter  
2ch Area and Height  
Anatomical ROA

Slide Courtesy Joao Cavalcante MD
Endoluminal 3D Views
- Leaflet Motion
- Visualization of the valve gap
  - Evaluation of TR severity
  - Individualization of therapy
- Best angles for leaflet grasping and coplanar alignment for commissures

Slide Courtesy Joao Cavalcante MD

Patient with prior large inferior MI with RV infarct.
Tethering of the posterior leaflet

Endoluminal 3D Views
- Leaflet Motion
- Visualization of the valve gap
- Evaluation of TR severity
- Individualization of therapy
- Best angles for leaflet grasping and coplanar alignment for commissures
CTA for Procedural Planning


CTA for Fluoroscopy Angle Planning
**CTA for Procedural Planning**

A distance between RCA and TV annulus of ≤2 mm is considered less favorable.

Curved spline for RCA segmentation and tricuspid annulus, important for tricuspid annular devices (Tricinch, Millipede, Cardioband, etc).


---

**Importing CT for tricuspid leaflet segmentation and angles for fluoro overlay**
CMR produces Echo like images!
CMR Scanning of patients with Pacemaker and Defibrillator is feasible and safe

TR Quantification is Feasible Despite PM/ICD

TR Volume = 102 - 42 = 60 ml/beat
TR Fraction = 60 / 102 = 59%
IVC systolic flow reversal on CMR

CMR Technology Continues to Evolve for patients with Afib and unable to perform breath-hold

Breath-Held Segmented  Free Breathing Real-Time

Free Breathing Real-Time with Averaging of Multiple Beats and Gadgetron Image Reconstruction

Same patient, same scanner, different pulse sequence...  Superior and diagnostic image quality

Both RVEF and RVEDVi are prognostically important prior to TV surgical intervention

| Table 4 |

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cardiac Death</th>
<th>Major Postoperative Cardiac Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV EF, per 5% higher</td>
<td>Hazard Ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td>RV EDVi, per 10ml/m² higher</td>
<td>Hazard Ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age and sex adjusted</td>
<td>1.158</td>
<td>1.001, 1.367</td>
</tr>
<tr>
<td>Age and NYHA class adjusted</td>
<td>1.158</td>
<td>1.000, 1.367</td>
</tr>
<tr>
<td>Age, sex, NYHA class, and etiology level adjusted</td>
<td>1.158</td>
<td>1.000, 1.367</td>
</tr>
<tr>
<td>Age, sex, NYHA class, and etiology level, and GFR adjusted</td>
<td>1.158</td>
<td>1.000, 1.367</td>
</tr>
</tbody>
</table>

Park JB et al. Radiology. 2016 Sep;280(3):723-34

Cardiac death-free survival rate (%)
Why Quantify and assess etiology

Topilsky et al, Eur Heart J. 2018 Jul 27

Why assess RV size and Pulmonary Pressures

Benfari et al, Circulation, 2019;140;196–206
Why assess RV size and function

A.

B.

Park JB et al. Radiology. 2016 Sep;280(3):723-34

Multi-modality Imaging for Assessment of Tricuspid Regurgitation Severity

TREATMENT

• “……Treating Tricuspid regurgitation and right heart failure is an art rather than evidence based medicine”.
  Prof Zamarano PCRLV 2019
  Madrid, Spain

Paraphrased –
“TR is a part of a spectrum of complex cardiac, pulmonary, arrhythmia and right heart failure syndromes. Treating TR is as much a team sport as it is an art and a science”.
Goals of Medical Therapy

- Preload management.
- Optimize Left sided heart disease
- Manage right heart failure
- Afterload reduction
- Prevent / Treat end organ damage

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Recommendation</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013 ACC/AHA HF</td>
<td>Right heart failure is an indicator of poor outcomes in acute decompensated HF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2014 ACC/AHA Valve</td>
<td>• Diuretics can be useful for patients with severe TR and signs of right-sided HF (stage D).&lt;br&gt;• Medical therapies to reduce elevated PAP and/or PVR might be considered in patients with severe functional TR (stages C,D)</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>2017 ESC Valve</td>
<td>• Diuretics are useful in the management of RHF but are of limited long term efficacy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2016 ESC HF</td>
<td>• Severe TR causes/deteriorates RHF, thus diuretics are used to reduce peripheral oedema.&lt;br&gt;• As hepatic congestion is often present in these patients MRA may improve decongestion&lt;br&gt;• Management of HF which underlies secondary TR should be optimized&lt;br&gt;• Indications for surgical correction of secondary TR complicating HF are not clearly established</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**ACC/AHA Valve 2014**

No Class I indications for surgery in isolated TR
Heterogenous group
No trials

**ESC Valve 2017**

**Recommendations on primary tricuspid regurgitation**

- Surgery is indicated in patients with severe primary tricuspid regurgitation undergoing left-sided valve surgery.
  - Class I
  - Recommendation

- Surgery is indicated in asymptomatic patients with severe isolated primary tricuspid regurgitation without severe RV dysfunction.
  - Class I
  - Recommendation

- Surgery should be considered in patients with moderate primary tricuspid regurgitation undergoing left-sided valve surgery.
  - Class IIIa
  - Recommendation

- Surgery should be considered in asymptomatic or mildly symptomatic patients with severe isolated primary tricuspid regurgitation and progressive RV dilatation or deterioration of RV function.
  - Class IIIa
  - Recommendation

**Recommendations on secondary tricuspid regurgitation**

- Surgery is indicated in patients with severe secondary tricuspid regurgitation undergoing left-sided valve surgery.
  - Class I
  - Recommendation

- Surgery should be considered in patients with mild or moderate secondary tricuspid regurgitation with a dilated annulus (>40 mm or >25 mm² by 2D echocardiography) undergoing left-sided valve surgery.
  - Class IIIa
  - Recommendation

- Surgery may be considered in patients undergoing left-sided valve surgery with mild or moderate secondary tricuspid regurgitation even in the absence of annular dilatation when previous repair/valvuloplasty had been documented.
  - Class IIIb
  - Recommendation

“Although asymptomatic severe isolated TR respond well to diuretic therapy, delaying surgery is likely to result in irreversible RV damage, organ failure and poor results of late surgical intervention.”
Accepted surgical risk was defined as:
1. Age ≤ 75 years
2. SPAP < 50 mmHg
3. Prohibitive general conditions
   - GFR < 40 mL/min/1.73 m²
   - AST < 35 U/L, ALT < 60 U/L, Bil < 1 mg/dL
4. No RV dilatation (RVEDD < 40 mm)
5. No RV dysfunction (TAPSE ≥ 20 mm, TDI ≤ 10 cm/s)
6. No LV dysfunction (LVEF > 45%)

---

### SURGICAL TRICUSPID VAVE THERAPIES

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Image 1</th>
<th>Image 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suture annuloplasty</td>
<td><img src="image1.png" alt="Suture annuloplasty" /></td>
<td><img src="image2.png" alt="Suture annuloplasty" /></td>
</tr>
<tr>
<td>Ring annuloplasty</td>
<td><img src="image1.png" alt="Ring annuloplasty" /></td>
<td><img src="image2.png" alt="Ring annuloplasty" /></td>
</tr>
<tr>
<td>Coaptation enhancement</td>
<td><img src="image1.png" alt="Coaptation enhancement" /></td>
<td><img src="image2.png" alt="Coaptation enhancement" /></td>
</tr>
<tr>
<td>Replacement</td>
<td><img src="image1.png" alt="Replacement" /></td>
<td><img src="image2.png" alt="Replacement" /></td>
</tr>
<tr>
<td>Leaflet augmentation</td>
<td><img src="image1.png" alt="Leaflet augmentation" /></td>
<td><img src="image2.png" alt="Leaflet augmentation" /></td>
</tr>
<tr>
<td>Neochordae repair</td>
<td><img src="image1.png" alt="Neochordae repair" /></td>
<td><img src="image2.png" alt="Neochordae repair" /></td>
</tr>
</tbody>
</table>

---


COMPARING TV surgery strategies

A. Long-term Survival (%)
- No Ring: 36 ± 8%
- Ring: 49 ± 5%
- p=0.007
- 15 yrs
- 0 5 10 15
- Years Postoperatively

B. Event-Free Survival (%)
- No Ring: 17 ± 6%
- Ring: 34 ± 5%
- p<0.01
- 15 yrs
- 0 5 10 15
- Years Postoperatively

PREDICTORS OF RECURRENT TR AFTER ANNULOPLASTY
- ↑ TR severity
- ↑ TV annulus
- ↑ Leaflet tethering >1cm, 1.6cm²
- Severe Pulmonary hypertension
- ↓ LV function
- Pacemaker leads
- Mitral valve replacement

=> Consider Replacement or alternate repair techniques

Min SY et al Eur Heart J. 2010 Dec;31(23):2871-80.
WHY TRANSCATHETER OPTIONS

Jan 1 2003 – Dec 31 2014
12,562 underwent TV surgery
TV surgery increased 48% from 2003 to 2014
Isolated TV Surgery 15%.
Concomitant with left heart surgery 85%.

Isolated TV replacement 10.9% in hospital mortality
5.5% New Dialysis, PPM 34%
Isolated TV repair mortality 8.1%,
PPM 11%, New dialysis 4.4%

**CENTRAL ILLUSTRATION:** Temporal Trends in Surgical Volume and Mortality for Isolated Tricuspid Valve Surgery


Isolated TV surgery 5005, Mortality 8.8%

Alqahtani F et al J Am Heart Assoc. 2017 Dec 22;6(12). pii: e007597
WHY SUCH OUTCOMES?

397 TV repairs and 52 TV replacement at a Single center 1997-2020
Factors that had no impact on mortality
  Procedure Type
  Etiology of TR

---

**Independent Predictors of Mortality**

- Male gender
- Age
- NYHA IV
- Liver Cirrhosis
- GFR
- Albumin
- Pre-operative hemoglobin

---

WHY SUCH BAD OUTCOMES??

TRIVALVE REGISTRY

Propensity score matched Age, EuroScore, PASP – 268 matched pairs

Baseline characteristics similar - RV dysfunction, PASP MR, AF, Pacemaker


TRIVALVE Procedural success impact on outcomes

Procedural Failure 14%
Higher with severe RV dysfunction

Patients being treated with transcatheter options currently have advanced TV disease and multiple co-morbidities

<table>
<thead>
<tr>
<th>Baseline clinical profile of the overall study population</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
</tr>
<tr>
<td><strong>Female gender (n, %)</strong></td>
</tr>
<tr>
<td><strong>EuroScore II (mean ± SD)</strong></td>
</tr>
<tr>
<td><strong>TR Etiology (n, %)</strong></td>
</tr>
<tr>
<td>Functional</td>
</tr>
<tr>
<td>Degenerative</td>
</tr>
<tr>
<td>Mixed</td>
</tr>
<tr>
<td>Pacemaker induced</td>
</tr>
<tr>
<td>Previous left side valve intervention (surgical/transcatheter)</td>
</tr>
<tr>
<td>Trans-valvular tricuspid lead (n, %)</td>
</tr>
<tr>
<td>Atrial fibrillation (n, %)</td>
</tr>
<tr>
<td>eGFR (ml/min)</td>
</tr>
<tr>
<td>NT pro-BNP (median; IQR – pg/ml)</td>
</tr>
<tr>
<td><strong>Ascites (n, %)</strong></td>
</tr>
<tr>
<td><strong>Peripheral oedema (n, %)</strong></td>
</tr>
<tr>
<td><strong>NYHA functional class III-IV (n, %)</strong></td>
</tr>
<tr>
<td><strong>Previous admission for RV failure (n, %)</strong></td>
</tr>
</tbody>
</table>
ANATOMY

- Anterior, oriented Vertically.
- Larger than mitral valve
- Fibrous annulus, size varies with loading conditions
- Variable papillary muscles
- Thin leaflets
- Variable leaflets
- Adjacent structures – RCA, CS, AVN

CS – btw IVC orifice and Septal leaflet
ANATOMIC CONSIDERATIONS

Access
- RV complex shape and thin walled – Transapical/transventricular is not desirable
- Angulation between IVC and TV can be challenging for TF esp if prominent Eustachian valve
- TJ approach – ergonomically challenging in cath lab
- Large profile delivery systems needed due to large size of TV annulus

Imaging
- TEE is limited due to anterior location of the valve
- Esophagus is not axial or close to TV so mid esophageal views are not axial and difficult to orient
- Thin leaflets obscured by shadowing from left heart structures
- 3D – shows all 3 leaflets but poor acoustic windows

ANATOMIC CONSIDERATIONS

- Device design
  - Anchoring – No calcification, oversizing for dynamic TV annulus.
  - Leaflet repair – Thin, fragile leaflets, varying anatomy
- Surrounding structures
  - Annuloplasty – RCA
  - TTVR – AV node
  - All - RV trabeculations limit movements below the TV plane
COAPTATION ENHANCEMENT

- Leaflet repair – MitraClip, PASCAL
- Spacer - FORMA

MITRACLIP/TRICLIP (Abbott Vascular)

- Trans-catheter edge-to-edge repair
  - Goal is to recreate normal coaptation
- MitraClip
  - Modified steering
- TriClip
  - Designed for the right atrium and access all areas of the leaflets
- Impossible without echocardiographic guidance. Tricuspid imaging is difficult
- TEE – can’t see all leaflets at same time
  - Multi-level imaging needed
- Alternatives
  - Intravascular imaging in RA right above the leaflets – better anatomic and temporal resolution
  - 3D ICE
Predictors of Procedural failure - NT

- Coaptation gap
  - Coaptation gap >10mm had a 30% predicted success.
- Tethering distance/Area
- Non-central and non-anteroseptal jets
- EROA >0.65cm²
- VC 11mm
- Large flail gap >10mm (from MitraClip)

Transcatheter Edge to Edge repair in the TRIVALVE registry

249 patients, centers in Europe and North America. June 2015 and June 2018
24% ascites, 84% peripheral edema, and 74% HF hospitalizations
Predisposing factors for TR HFrEF 26%, left-sided valve disease in 68%, COPD 25%, AF 74%, and ICD of pacemaker lead in 30% of patients.
Secondary TR in 90%
MitraClip

Transcatheter edge-to-edge repair for reduction of tricuspid regurgitation: 6-month outcomes of the TRILUMINATE single-arm study

Georg Nicksmig*, Marcel Weber*, Philipp Lurz, Ralph Stephan von Bardeleben, Marta Sitges, Paul Sonnja, Jörg Hausleiter, Paolo Denti, Jean-Noël Tesche, Michael Naber, Abdellaziz Dahou, Rebecca Tritshn

• Prospective Single arm, multi center trial enrolling 85 subjects across Europe and USA
• To evaluate performance of a purpose built clip delivery system to the tricuspid valve in patients with ≥ Moderate TR
• Primary Endpoint - Echo TR reduction ≥ 1 grade at 30d Composite MAE at 6 months
Procedural data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>TVRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implant Success Rate</td>
<td>100%</td>
</tr>
<tr>
<td>Acute Device Success</td>
<td>100%</td>
</tr>
<tr>
<td>Acute Procedural Success</td>
<td>91.6%</td>
</tr>
<tr>
<td>Device Time, min</td>
<td>75.2±49.4</td>
</tr>
<tr>
<td>Total Procedure Time, min</td>
<td>152.7±57.8</td>
</tr>
<tr>
<td>Fluoroscopy Duration, min</td>
<td>23.3±17.8</td>
</tr>
</tbody>
</table>

Primary Safety End Point

<table>
<thead>
<tr>
<th>Event</th>
<th>(n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Adverse Event (MAE) through 6 months</td>
<td>3</td>
</tr>
<tr>
<td>Cardiovascular Mortality</td>
<td>2</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>0</td>
</tr>
<tr>
<td>Stroke</td>
<td>0</td>
</tr>
<tr>
<td>New Onset Renal Failure</td>
<td>1</td>
</tr>
<tr>
<td>Non-elective CV surgery, TVRS</td>
<td>0</td>
</tr>
<tr>
<td>Device-related AE</td>
<td>0</td>
</tr>
</tbody>
</table>

Device Effectiveness

Additional Safety Endpoints

Symptom Improvement

Right cardiac chamber remodeling

- p=0.0001
- p=0.001
- p=0.038
- p=0.032
- p=0.008
- p=0.051
- p=0.045
- p=0.005
- p=0.050
MHIF Featured Study: TRILUMINATE PIVOTAL

**CONDITION:** Severe Tricuspid Regurgitation (TR)

**NATIONAL PI:** Paul Sorajja, MD
**CONTACT:** Kate Jappe, RN
Kate.jappe@alhna.com; 912-883-7347

**SPONSOR:** Abbott Vascular, Inc.

**DESCRIPTION:** Prospective, randomized, multicenter trial of Tricuspid Valve Incessant Mitral Valve (Tricuspid) device in symptomatic patients with severe tricuspid regurgitation (TR) who have been determined to be at intermediate or greater estimated risk for mortality with tricuspid valve surgery.

**ACTION:**
Are the patients you see experiencing symptoms of severe TR?
If so, please contact Dr. Sorajja or Kate Jappe, RN (Study Coordinator).

**PARTIAL CRITERIA LIST / QUALIFICATIONS:**
- **Inclusion**
  - **Primary:** Moderate to severe TR despite optimal medical therapy (drug and/or device)
  - Adverse event history per applicable standards and stable for 30 days
  - Intermediate or greater surgical risk on mortality with tricuspid valve surgery

- **Exclusion**
  - **Primary:** Carotid artery stenosis > 0%
  - Major uncontrolled hypertension (systolic blood pressure > 180 mmHg)
  - Left ventricular ejection fraction (LVEF) < 20%
  - History of atrial fibrillation
  - Peripheral vascular disease
  - Known history of coagulation disorder
  - History of thromboembolism
  - History of endocarditis
  - History of pacemaker or ICD

**PASCAL — (Edwards Lifesciences, Irvine CA)**

**PAddlesSpacerClaspAlfieri**

- **22F Delivery System**
- **Central Spacer to fill the ROA**
- **Spacer + Broad contoured paddles reduce stress on leaflets.**
- **Independent leaflet capture**
COMPASSIONATE USE - PASCAL

<table>
<thead>
<tr>
<th>Procedural Data</th>
<th>TR Reduction</th>
<th>Functional Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Procedural Success</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>86% (24)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mean # of Devices Implanted</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.4 ± 0.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Independent Leaflet Grasping</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>90%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Procedure Time (Skin to Skin), mins</strong></td>
<td>134 ± 68</td>
<td></td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Conversion to Surgery</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FORMA (Edwards Lifesciences, Irvine CA)

- Coaptation enhancement with Forma, a foam filled expandable device anchored in septal portion of RV
- Fills central TV annulus and provides new coaptation area.

Before spacer | After spacer

- **Systole**
- **Diastole**
ANNULOPLASTY

- 4Tech Tricinch – Bicuspidization by cinching
- Trialign - Bicuspidization
- Cardioband –Incomplete ring
- Millipede – Complete Semi-rigid ring
TRIALIGN – Mitralign Tewksbury MA

Early feasibility of a Percutaneous Tricuspid Valve Annuloplasty System for Symptomatic Chronic Functional Tricuspid regurgitation (SCOUT I) Study

(excluded pacemaker leads, ACHD, Transplanted hearts)

3 Pledget dehiscence
No death
Reduced severity of TR
Improved QoL

SCOUT II registered.

TriCinch (4TECH Cardio, Galway, Ireland)

• Single 25F Delivery System
• Epicardial placement of coil for secure anchoring
• Single anchor
• Recapturable self expanding stent attached to a Dacron band deployed in the subhepatic region of the IVC to maintain tension.
• Multiple stent sizes cover a range of IVC diameters
• PREVENT (Percutaneous Treatment of Tricuspid Valve Regurgitation With the TriCinch System) trial
• 24 Patients
• Successful implant in 18 patients (81%)
• Significant (≥1 grade) acute TR reduction in 94% of cases.
• Hemopericardium in 2 patients (8%)
• 5 patients (23%) experienced late annular anchor detachment.
• Preliminary data showed severe 4+ TR reduction
• from ~80% to ~40%,
• Sustained improvement in NYHA and QoL at 6-month follow-up
Minimally Invasive Annuloplasty (MIA Microinterventional Devices, Newton PA)

Sutureless Transcatheter annuloplasty system
thermoplasty elastomer (Myolast), low mass polymeric self-tensioning anchors (Polycor)

Via RUJV to the posterior annulus
Fixation elements connected by cable which
is cinched and then fixed by locking of a
cable
STTAR feasibility Arm
10 patients
No device adverse events
no dehiscence
TR reduced and maintained at 1 yr
CARDIOBAND (Edwards Lifesciences, Irvine CA)

25F steerable sheath
Sutureless adjustable dacron band

Polyester sleeve with radiopaque markers
Up to 17 stainless steel anchors, 6mm long.
Repositionable and retrievable until deployed
Implant size controlled via a Spool

May be limited as a stand alone therapy if -
Severe annular dilation
Severe leaflet tethering (Tethering height >0.51cm)
Primary TR

CT planning - RCA is<2mm to annulus is a contra-indication
Mark first anchor

Understanding the proximity between anatomical landmarks and device to guide procedure and prevent complications

TRI-REPAIR Cardioband

- Single arm study to evaluate safety and efficacy of Cardioband Tricuspid system for (TR 30 patients)
- Excluded patients with device leads impinging the TV
- In early experience the
  - Complications – related to RCA (side branch occlusion, worsening distal RCA lesion, tamponade from anchor in RCA)
  - Significant reduction in EROA through annular reduction at 30d and sustained in 1 year
  - Clinically and statistically significant improvements in functional status, QoL, 6MWT at 30d and through 1 year
  - One year survival 83%
- CE Mark Approval
Trans-atrial intra-pericardial tricuspid annuloplasty system (Cook Medical, Bloomington IN)

- Memory shaped delivery system
- Access through femoral vein into pericardium vis right atrial appendage (RAA)
- Adjustable circumferential implant along atrioventricular groove externally compressing the TV annulus
- RAA access closed with a nitinol occlude

- A newer version of the device—including a balloon anchor pericardial sheath, the annuloplasty system, and a bioresorbable closure device—for human use is currently being developed by the National Institutes of Health and Cook Medical (EFS is planned)

MILLIPEDE IRIS (Boston Scientific, Marlborough, MA)

- Semirigid complete ring
- Customized repositioned and retrievable
- Leave options open for future interventions
- Catheter for Tricuspid is in development
- No anticoagulation needed
- Allows concomitant procedures
- Serves as a dock for TTVR
Orthotopic Valve Implantation

- Native Valve
- Valve-in Valve or Valve-in-ring

NAVIGATE (Navigate Cardiac Structures, Lake Forest CA)

- Self expanding nitinol tapered stent,
- 3 pericardial valve
- Atrial Winglet and Ventricular graspers
- 21mm Height, truncated cone
- Delivery system
  - 42F sheath in RIJV
  - 35F at distal capsule,
  - 24F shaft
- 2 degrees of motion at the tip
- 80 degrees articulation
- Only one tried in humans yet
Transjugular and Transatrial

Initial valve deployment with RCA injection

Retracting the capsule: Exposing Ventricular Tines

Coaxial View 1

Coaxial View 2

Short-axis View
Final Result

- Trivial central and trivial paravalvular regurgitation
- Peak/mean transtricuspid gradient = 1.5 and 0.3 mmHg

Efficacy and Functional Improvement

Tricuspid Regurgitation Severity

Pre: 56% (44%), 61% (39%)
Post: 50% (46%), 46% (37%)

NYHA Class

Pre: 53
Postop: 7.5

0 50 100
Pre Postop
Complications

30 D mortality – 13%
• Trans-atrial
  • D9 VSD, re-operation
  • D28 AKI multiorgan failure
  • D2 Premature deployment, canted valve, ECMO, bioprosthetic valve
• Transjugular
  • D9 AKI, multiorgan failure

• Malpositioning needing surgical conversion
  • gross oversizing ~ 10mm
  • Undersizing and premature deployment
  • Small RA and deep RV deployment in Carcinoid patient
  • Canting while trying to capture septal leaflet
• RV perforation due to guidewire
• HIT
• Pacemaker D2,5,150
• AKI on CKD

NAVIGATE COMPASSIONATE USE

• Feasible via TA or TJ, coaxial deployment is key
• Low RVOT risk
• Rapid pacing not necessary
• Confirm leaflet insertion
• Confirm sizing with TEE – oversizing VSD or PPM
• Implanted in PPM patients without dislodgment or change in thresholds
CARDIOVALVE

- 3 bovine pericardium leaflets sutured via a Dacron fabric to a dual self-expanding nitinol frame design.
- 24 grasping points that fixate the device to the native tricuspid annulus.
- The Dacron fabric is also used to cover the nitinol frame for promoting atraumatic interface with the heart tissue and enhanced sealing.

TRISOL

- Single dome shaped leaflet.
- Large diameter and low profile
- Axial anchoring
- Bovine pericardium
- Leaflet
LUX valve (Jenscare Biotechnology Ningbo China)

- Self expanding bovine pericardial tissue valve mounted on a nitinol stent frame and inserted trans-atrially
- Adaptive skirt to minimize paravalvular regurgitation
- Special anchoring mechanism for secure anchoring within right ventricle

Rationale of caval valve implantation

- Reduce TR volume by increasing RA pressure
- Decongest hepatic and renal veins by reducing peak IVC pressure
- Prospective, open-label, single center, RCT
- Symptomatic TR (NYHA ≥2) despite established optimal medical therapy, age ≥50 years, and IVC diameter <31 mm
- Excluded: LVEF < 30%, severe MR, dialysis
Within 7-48 hours post CAVI – 2 valve dislocations and stent migrations
All surgical bail out
All died - bleeding, RHF, Sepsis 1, 8, 49 and 60 days after the index procedure
Recruitment was stopped prematurely after patient 28 (40 pts. planned)

TRICAVAL TRIAL

• Prospective, open-label, single center, RCT
• Symptomatic TR (NYHA ≥2) despite established optimal medical therapy, age ≥50 years, and IVC diameter <31 mm
• Excluded: LVEF < 30%, severe MR, dialysis
• Primary outcome: Peak VO2 after 3 months
• Secondary : safety, 6MWT, NYHA class, NT-proBNP levels, right heart function, HF hospitalization, QoL
**TRICENTO** (NVT GmBH, Hechingen)

- Self expanding covered nitinol stent with a bicuspid porcine pericardium valve
- Bicaval anchored
- Custom made with CT measurements
- 24F TF
- Fully repositionable and re-sheathable up to final release

<table>
<thead>
<tr>
<th>SYMPTOMS</th>
<th>STAGE 1</th>
<th>STAGE 2</th>
<th>STAGE 3</th>
<th>STAGE 4</th>
<th>STAGE 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>None</td>
<td>Vague</td>
<td>Current or previous episodes of RHF</td>
<td>Overt RHF+/- end organ damage from chronic RV/VO</td>
<td></td>
</tr>
<tr>
<td>TR GRADE</td>
<td>&lt;moderate</td>
<td>≥ moderate</td>
<td>Severe</td>
<td>Severe</td>
<td>Torrential</td>
</tr>
<tr>
<td>ANNUAL REMODELING</td>
<td>Normal &lt;40mm</td>
<td>Normal or mild</td>
<td>Present</td>
<td>Moderate to severe</td>
<td>Severe</td>
</tr>
<tr>
<td>LEAFLET COAPTATION</td>
<td>Normal 5-6mm</td>
<td>mildly abnormal &lt;3mm</td>
<td>Abnormal</td>
<td>Coaptation gap</td>
<td>Large coaptation gap</td>
</tr>
<tr>
<td>TETHERING</td>
<td>None</td>
<td>None or mildly abnormal</td>
<td>Abnormal &lt;8mm</td>
<td>Significantly abnormal, varying degrees of tethering &gt;8mm, 1.8cm²</td>
<td>Significantly abnormal</td>
</tr>
<tr>
<td>RV FUNCTION AND REMODELING</td>
<td>None</td>
<td>Mildly abnormal</td>
<td>Mild RV dysfunction +/- remodeling</td>
<td>&gt; Moderate dysfunction and remodeling</td>
<td>Severe RV dysfunction and remodeling</td>
</tr>
<tr>
<td>MEDICAL TREATMENT</td>
<td>None</td>
<td>Normal function Mild remodeling Diuretic</td>
<td>Diuretics</td>
<td>Moderate to high dose diuretics and/or IV diuretic requirements</td>
<td>Multiple RHF hospitalizations, Frequent need for IV diuretics and/or high dose combination diuretics</td>
</tr>
<tr>
<td>SURGICAL TREATMENT</td>
<td>No</td>
<td>At time of Left heart (LH) surgery</td>
<td>At time of LH surgery Isolated if symptoms, RV remodeling, comorbidities</td>
<td>Isolated TVR in absence of severe PHTN and comorbidities High risk of peri-operative RV dysfunction</td>
<td>Prohibitive intra-operative and peri-operative risk</td>
</tr>
<tr>
<td>TRANSCATHETER TREATMENT</td>
<td>No</td>
<td>Potential future target</td>
<td>Potential candidates for surgery enrolled in IDE RCTs</td>
<td>Currently in EFS IF High surgical risk May require combination anuloplasty + leaflet repair TVTR</td>
<td>Prohibitive risk Potentially futile Palliative procedures in highly selected patients</td>
</tr>
</tbody>
</table>

Dreyfus G et al J Am Coll Cardiol. 2015 Jun 2;65(21):2331-6
<table>
<thead>
<tr>
<th>STAGE 1</th>
<th>STAGE 2</th>
<th>STAGE 3</th>
<th>STAGE 4</th>
<th>STAGE 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>SYMPTOMS</td>
<td>None</td>
<td>Vague</td>
<td>Current or previous episodes of RHF</td>
<td>Overt RHF+/- end organ damage from chronic RVOD</td>
</tr>
<tr>
<td>TR GRADE</td>
<td>&lt;moderate</td>
<td>2 moderate</td>
<td>Severe</td>
<td>Severe</td>
</tr>
<tr>
<td>TV ANNULUS</td>
<td>Normal &lt;40mm</td>
<td>Normal or mild</td>
<td>Present</td>
<td>Moderate to severe</td>
</tr>
<tr>
<td>LEAFLET COAPTATION</td>
<td>Normal</td>
<td>mildly abnormal</td>
<td>Abnormal</td>
<td>Coaptation gap</td>
</tr>
<tr>
<td>TETHERING</td>
<td>None</td>
<td>5-6mm</td>
<td>Abnormal &lt;8mm</td>
<td>Significantly abnormal, varying degrees of tethering &gt;8mm</td>
</tr>
<tr>
<td>RV FUNCTION AND REMODELING</td>
<td>None</td>
<td>Mildly abnormal</td>
<td>Mild RV dysfunction +/- remodeling</td>
<td>&gt; Moderate dysfunction and remodeling</td>
</tr>
<tr>
<td>MEDICAL TREATMENT</td>
<td>None</td>
<td>Surveillance</td>
<td>Normal function</td>
<td>Diuretics</td>
</tr>
<tr>
<td>SURGICAL TREATMENT</td>
<td>No</td>
<td>At time of Left heart surgery</td>
<td>Isolated if symptoms, RV remodeling, comorbidities</td>
<td>Prohibitive intra-operative and peri-operative risk</td>
</tr>
<tr>
<td>TRANSOCATHETER TREATMENT</td>
<td>EARLY</td>
<td>RV initial dilation</td>
<td>Leaflet – mild coaptation defects</td>
<td>Leaflet approximation</td>
</tr>
<tr>
<td>PROGRESSIVE</td>
<td>RV progressive dilation</td>
<td>TA progressive dilation</td>
<td>Leaflet – lack of coaptation</td>
<td>Leaflet approximation</td>
</tr>
<tr>
<td>LATE</td>
<td>RV and TA severe dilation</td>
<td>Leaflet tethering</td>
<td>Annuloplasty</td>
<td>+/- Annuloplasty</td>
</tr>
</tbody>
</table>

**SUMMARY**

- Tricuspid regurgitation is BAD, Early diagnosis is key for successful therapies.
- Careful echocardiography and use of cross sectional imaging is crucial for diagnosis.
- Transcatheter tricuspid interventions is rapidly developing and shows promise in early feasibility studies
- Standardization of outcomes (Valve Academic Research consortium) and Registry.
- Determination of best timing for intervention “Early TTVI”
- Combination therapies – sequential or simultaneous.
- More Trials
ACKNOWLEDGEMENTS

• Dr. Paul Sorajja
• Dr. Santiago Garcia
• Dr. Michael Mooney
• Dr. Mario Goessl
• Dr. Joao Cavalcante
• Dr. Richard Bae
• Cardiac Surgery
• Cardiac Imaging
• Marcus Burns DNP and Lynelle Schneider PA-C
• Aisha Ahmed BS and Kate Jappe RN
• MHIF Research Team, Cath Lab staff, Clinic Nurses and Staff
• Referring Cardiologists
• Patients

THANKS FOR LISTENING

QUESTIONS??
TR PH-related and AF-Related (12%)

**Annulus Diameter**

- **A**: Controls vs. PHTN-FTR (p=0.03 vs. TTR)
- **B**: Leaflet to Annulus Ratio

**Leaflet to Annulus Ratio**

- **C**: Controls vs. Id-FTR (p=0.01 vs. TTR)

Toplisky et al, Circ Cardiovasc Im 2011
Restricted Mobility  
41%  

Adherence & Scarring  
37%  

Chordal Entrapment  
< 10%  

Perforation  
12%