THE IMPORTANCE OF CLINICAL TRIALS: WHY THEY MATTER

Advancing Innovation Through Clinical Trial Education
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• The PDF version of the slides, as well as the recording of this presentation, will be available on the Mended Hearts ® website following the event.
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Moderator
The Importance of Clinical Trials: Why they Matter

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Professor of Medicine
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Clinical Chief, Division of Cardiology
Medical Director, Bluhm Cardiovascular Institute
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Aortic Stenosis

Age and type of abnormality at autopsy

Stenotic UAV*

Stenotic BAV

Stenotic Tricuspid

* Unicuspid aortic valve (UAV) (uni) usually manifest stenosis

Mean Age

- Uni: 33
- Bi: 39
- Tricuspid (Stenotic): 78

59% M, 73% M, 84% M
Aortic Stenosis
Survival without Intervention

Ross J. Circ 1968; 37, Suppl V
Isolated SAVR volumes doubled from 2005 to 2013 with 30,679 cases in 2013

TAVR > isolated SAVR volumes in 2015
Northwestern: 75% of patients with AS are treated with TAVR

Since 2008, NMH has performed over 2000 TAVRs
SAPIEN TAVR Evolution

Valve Technology

SAPIEN

SAPIEN XT

SAPIEN 3

Sheath Compatibility

22-24F

16-20F

14-16F

Available

23 mm  26 mm

PARTNER 1
2011

23 mm  26 mm  29 mm

PARTNER 2
2014

20 mm  23 mm  26 mm  29 mm

PARTNER 3

FDA Approval of Valve:
Sapien 3 Deployment
Final Aortogram
Extreme Risk Compared to Medical Therapy
All-Cause Mortality 5 Years

Leon et al NEJM 2014

* In an age and gender matched population without comorbidities, the mortality at 5 years is 40.5%.
Edwards SAPIEN Valves All-Cause Mortality at 30 Days

AT Populations- KM Event Rates (%)
Death or Disabling Stroke Compared to Surgery

HR [95% CI] = 0.34 [0.12, 0.97]
P = 0.03
Functional Outcomes

**NYHA Class II/III/IV**

- Percentage of Patients (%):
  - TAVR: 20, 18
  - Surgery: 33, 17

  - 30 Days: P < 0.01
  - 1 Year: P = 0.76

**Six-Minute Walk Distance**

- Percentage Change from Baseline (%):
  - TAVR: 32, 7
  - Surgery: 32, 17

  - 30 Days: P < 0.01
  - 1 Year: P = 0.94

**KCCQ Overall Summary Score**

- Percentage Change from Baseline (%):
  - TAVR: 38, 13
  - Surgery: 40, 39

  - 30 Days: P < 0.01
  - 1 Year: P = 0.19
The PARTNER3 Trial
Clinical Implications

• Based upon these findings, TAVR, through 1-year, should be considered the preferred therapy in low surgical risk aortic stenosis patients!

• PARTNER randomized trials over the past 12 years, clearly indicate that the relative value of TAVR compared with surgery is independent of surgical risk profiles.

• The choice of TAVR vs. surgery in aortic stenosis patients should be a shared-decision making process, respecting patient preferences, understanding knowledge gaps (esp. in younger patients), and considering clinical and anatomic factors.
No Surgery for me!
Mitral VIV
MitraClip Procedural Steps
**All-cause Mortality**

- **MitraClip + GDMT**
- **GDMT alone**

**HR [95% CI] = 0.62 [0.46-0.82]**

**P<0.001**

**NNT (24 mo) = 5.9 [95% CI 3.9, 11.7]**

<table>
<thead>
<tr>
<th>Time After Randomization (Months)</th>
<th>No. at Risk: MitraClip + GDMT</th>
<th>No. at Risk: GDMT alone</th>
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<tr>
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</table>
Transcatheter Valve Replacement – Partial List

Intrepid Medtronic

Evoque Edwards

Navigate

Tendyne Abbott

Sapien M3 Edwards

AND Many Others…
Tricuspid Valve Disease – The “Forgotten Valve”

Cardiac surgery for severe isolated TR was rarely performed (16±5%, 5 years after diagnosis). 

The Impact of Tricuspid Regurgitation

Impacts 1.6 million patients in the U.S.

Early Feasibility Study of Cardioband Tricuspid System for Functional Tricuspid Regurgitation

30-Day Outcomes

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ABSTRACT

OBJECTIVES The study reports for the first time the 30-day outcomes of the first U.S. study with the Cardioband tricuspid valve reconstruction system for the treatment of functional tricuspid regurgitation (TR).

BACKGROUND Increasing severity of TR is associated with progressively higher morbidity and mortality; however, treatment options for isolated significant disease are limited.

METHODS In this single-arm, multicenter, prospective Food and Drug Administration-approved early feasibility study (EFS), 30 patients with severe or greater symptomatic functional TR were enrolled who were deemed candidates for transcatheter tricuspid repair with the Cardioband tricuspid system by the local heart team and multidisciplinary screening committee.

RESULTS The mean patient age was 77 years, 80% were women, 97% had atrial fibrillation, 70% were in New York Heart Association functional class III to IV with mean left ventricular ejection fraction of 58%, and 27% had severe, 20% massive, and 53% torrential TR. Device success was 93% and all patients were alive at 30 days. Between baseline and 30 days, septalateral tricuspid annular diameter was reduced by 13% (p < 0.001), 85% of patients had ≥1 grade TR reduction and 44% had ≤moderate TR, 75% were in New York Heart Association functional class I to II (p < 0.001), and overall Kansas City Cardiomyopathy Questionnaire score improved by 16 points (p < 0.001).

CONCLUSIONS In patients with severe symptomatic functional TR, this is the first study in the United States with the Cardioband tricuspid system for direct transcatheter annular reduction. This early feasibility study demonstrates high procedural feasibility with no 30-day mortality. There is significant reduction of functional TR with clinically significant improvements in functional status and quality of life. (Edwards Cardioband Tricuspid Valve Reconstruction System Early Feasibility Study, NCT03882467) (J Am Coll Cardiol Intv 2021;14:41-50) © 2021 by the American College of Cardiology Foundation.
# Cardioband Annular Reduction

<table>
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<th>Illustration</th>
<th>CT/Fluoroscopy</th>
<th>4D-ICE/TEE</th>
<th>Pre-procedural/Baseline</th>
<th>Partial implant deployment</th>
<th>Full implant deployment</th>
<th>Implant contraction</th>
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<td>B</td>
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</tr>
</tbody>
</table>

- **Cardioband** implant
- **ICE catheter**
- **Size adjustment tool**
- **RCA**
- **Implant Catheter**
- **Aortic Valve**
- **Right Atrium**
- **Right Ventricle**
- **TV Leaflet**
- **High Flow**
- **Cardioband implant**
- **Cardioband implant**

Davidson, C, Abramson, S, Smith R et al. JACC 2021
Early Feasibility Study of the Cardioband Tricuspid Functional Tricuspid Regurgitation: 30-day Outcomes

Davidson, Lim, Smith, Gray et al. JACC Int 2021; 14: 41-50
Feasibility Study of the Transcatheter Valve Repair System for Severe Tricuspid Regurgitation

Susheel Kodali, MD, * Rebecca T. Hahn, MD, * D. Mackram F. Eleid, MD, Robert Kipperman, MD, Robert Smith, MD, D. Scott Lim, MD, William A. Gray, MD, Akhil Narang, MD, Sotin V. Petrus, MD, Konstantinos Kouloulias, MD, Paul Grayburn, MD, Dale Fowler, MD, Katie Hawthorne, MD, Abdelaziz Dahoun, MD, Shekar H. Deo, MBBS, PhD, Prashanthi Vandurangi, PhD, Florian Busch, MD, Michael J. Mack, MD, Martin B. Leon, MD, Ted Feldman, MD, Charles J. Davidson, MD, on behalf of the CLASP TR DFS Investigators

ABSTRACT

BACKGROUND  Tricuspid regurgitation (TR) is a prevalent disease with limited treatment options.

OBJECTIVES  This is the first 30-day report of the U.S. single-arm, multicenter, prospective CLASP TR early feasibility study of the PASCAL transcatheter valve repair system in the treatment of TR.

METHODS  Patients with symptomatic TR despite optimal medical therapy, reviewed by the local heart team and central screening committee, were eligible for the study. Data were collected at baseline, discharge, and the 30-day follow-up and were reviewed by an independent clinical events committee and echocardiographic core laboratory. Feasibility endpoints included safety (composite major adverse event [MAE] rate), echocardiographic, clinical, and functional endpoints.

RESULTS  Of the 34 patients enrolled in the study, the mean age was 76 years, 53% were women, the mean Society of Thoracic Surgeons score was 7.3%, 88% had atrial fibrillation, 57% had severe or greater TR, and 79% had New York Heart Association (NYHA) functional class III/IV symptoms. Twenty-nine patients (85%) received implants at 30 days, 85% of them achieved a TR severity reduction of at least grade 1, with 52% with moderate or less TR (p < 0.001). The MAE rate was 5.9%, and none of the patients experienced cardiovascular mortality, stroke, myocardial infarction, renal complication, or reintervention. Eighty-nine percent of the patients improved to NYHA functional class II (p < 0.001), the mean 6-min walk distance improved by 7 m (p < 0.001), and the mean Kansas City Cardiomyopathy Questionnaire score improved by 15 points (p < 0.001).

CONCLUSIONS  In this early experience, the repair system performed as intended, with substantial TR reduction, favorable safety results with a low MAE rate, no mortality or reintervention, and significant improvements in functional status, exercise capacity, and quality of life. (Edwards CLASP TR EFS [CLASP TR EFS], NCT03423131)

(J Am Coll Cardiol 2021;77(18):54-56) © 2021 by the American College of Cardiology Foundation.
Pascal Tricuspid Clip: First in US Compassionate Use Case
EVOQUE Tricuspid Valve

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

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

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

**Multiple sizes** offer treatment for a broad range of tricuspid pathologies and anatomies
Does TTVI improve survival?

Taramasso et al JACC 2019
thank you!

What is Involved in a Clinical Trial? Learn from the Experts

Register at www.mendedhearts.org

June 10, 2021
3:00 PM ET