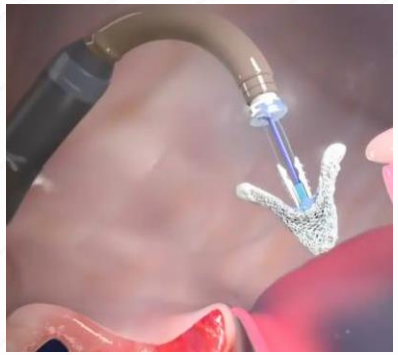
Transcatheter Therapies for Tricuspid Regurgitation: Has the Future Arrived?



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Disclosure

- Co-investigator in CLASP and TRISCEND trials

Functional Tricuspid Regurgitation is a Progressive Disease

- Time to TR progression
  - Trivial/mild to mod/severe 5.3 ± 3 yrs

- Independent Risk factors for TR progression:
  - PASP change (p<0.0001)
  - Permanent AF OR=14.3 (p <0.0001)
  - CAD OR (p =0.015)

- Progression-to-severe TR independently predicted subsequent mortality.

1-year survival with severe TR 64%

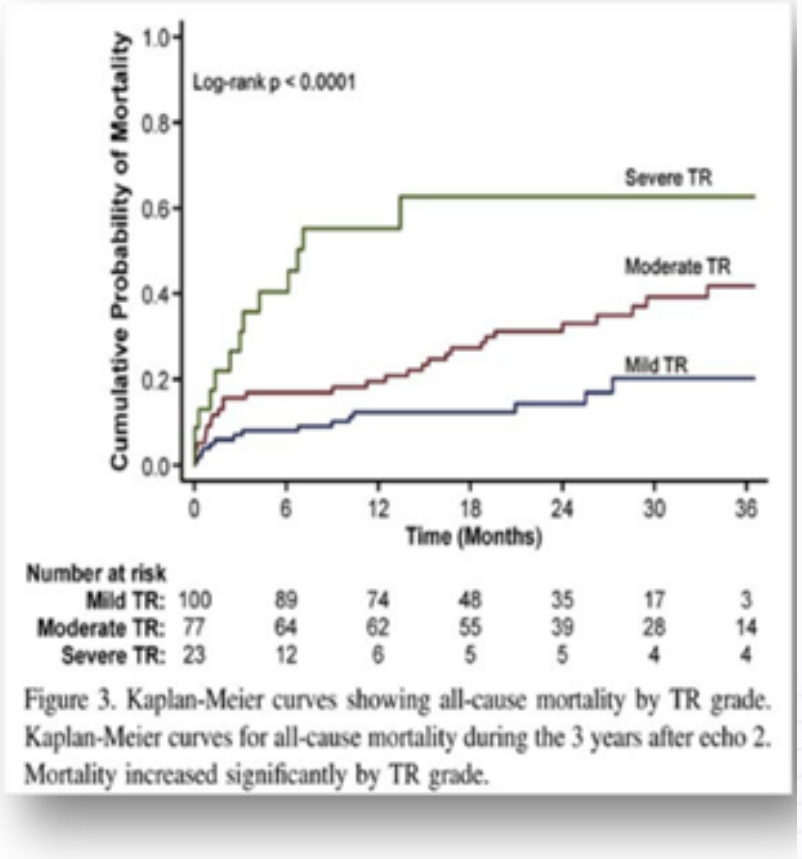


Figure 3. Kaplan-Meier curves showing all-cause mortality by TR grade. Kaplan-Meier curves for all-cause mortality during the 3 years after echo 2. Mortality increased significantly by TR grade.

Shiran A et al *Am J Cardiol* 113:995-1000; 2014

Tricuspid Valve Operations (2002-2014)
STS Database

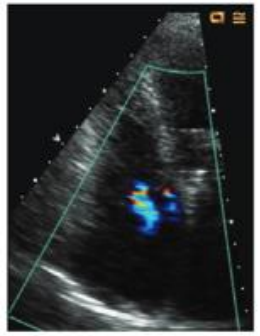
- Isolated Tricuspid Valve Operations n=2,050

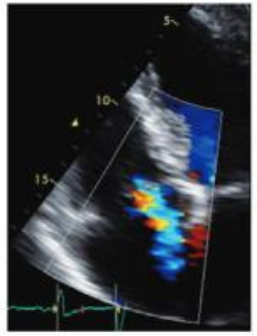
  - Operative Mortality (9%)
  - 170 Cases Per Year in US
  - Major Morbidity (42%)

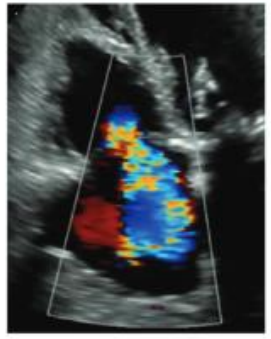
Courtesy of Charles Davidson, MD

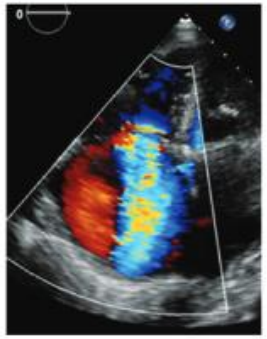
Imaging Assessment of Tricuspid Regurgitation Severity

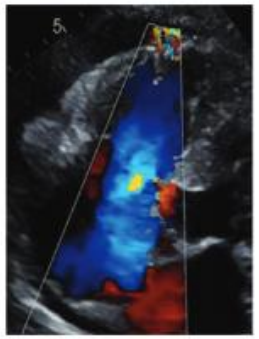
Parameters	MILD	MODERATE	SEVERE	MASSIVE	TORRENTIAL
Vena Contracta width (biplane average)	<3 mm	3-6.9 mm	7 mm - 13 mm	14-20 mm	≥21 mm
EROA by PISA	<20 mm^2	20-39 mm^2	40-59 mm^2	60-79 mm^2	≥80 mm^2
3D Vena Contracta Area or Quantitative Doppler EROA	-	-	75-94 mm^2	95-114 mm^2	≥115 mm^2





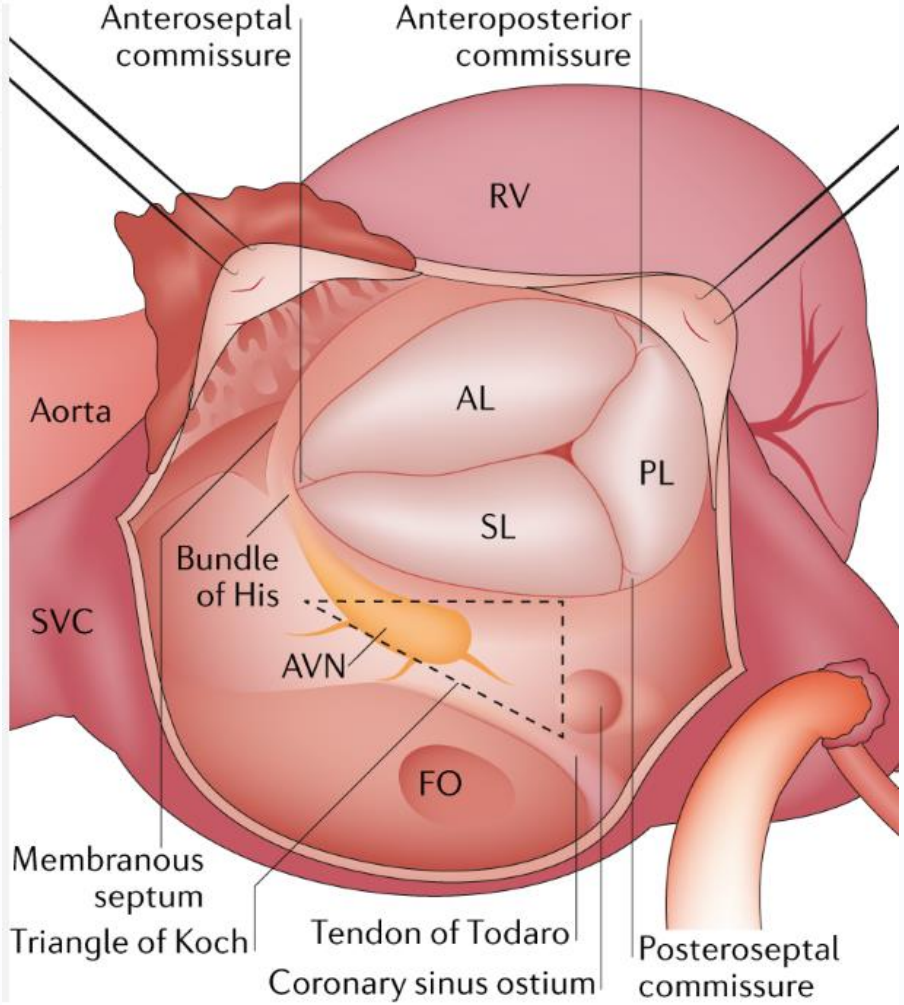






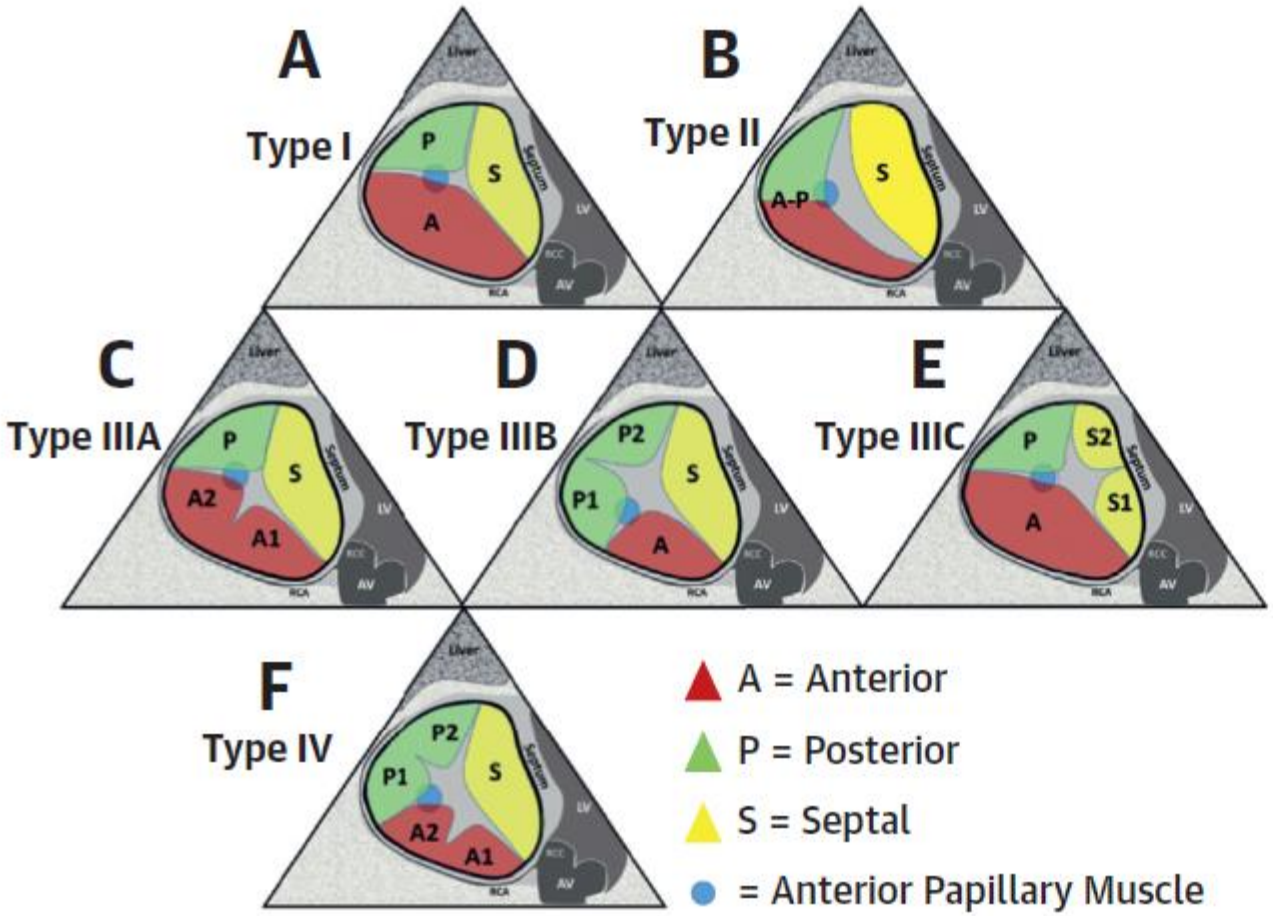
Hahn JACC Imaging 2019;12:469-90

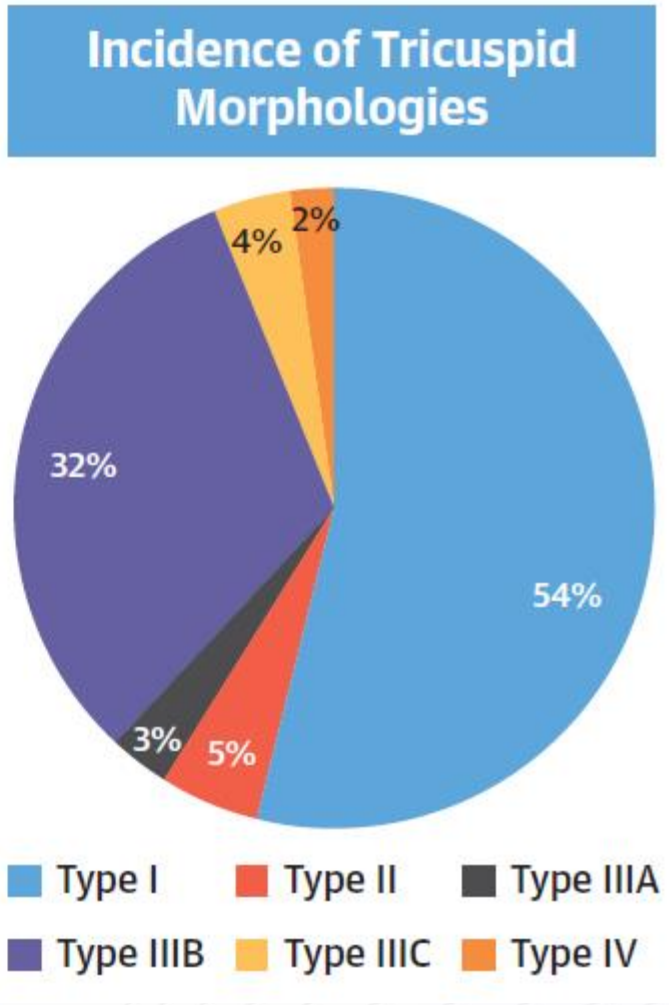
Tricuspid Valve Anatomy



Asmarats et al *Nat Rv Card* 2019;16:538-54

Tricuspid Valve Variability





Hahn et al *JACC Imaging* 2021;14:1299-305

Transcatheter Tricuspid Valve Therapies Landscape

Transcatheter Edge to Edge Repair

- Devices: TriClip, PASCAL
- Favorable Indications

1. Small leaflet coaptation gap (<7 mm)
2. "True" tricuspid (3 leaflets) morphology
3. Confined prolapse or flail of any leaflet
4. Jet location: Anteroseptal

TriClip

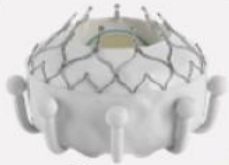
PASCAL

Tricuspid Valve Replacement

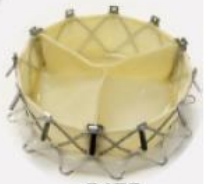
- Devices: Evoque, LuxValve, GATE
- Favorable Indications

1. Greater leaflet coaptation gap (>8.5 mm)
2. Valve tethering (more than moderate)
3. Previous Tricuspid Valve Replacement (ViV)
4. Thickened leaflets (heavily calcified)

LuxValve



Evoque



GATE

Annuloplasty

- Devices: Cardioband
- Favorable Indications

1. Dilated tricuspid annulus as the key pathophysiological mechanism
2. Valve tethering preferably mild
3. Jet location: Central

Cardioband

Heterotopic Caval Valve Implantation

- Devices: Tricento, TricValve
- Favorable Indications

1. Venous congestion – significant backflow in caval veins
2. Not suitable for orthotopic valve implantation
3. Appropriate cava anatomy-size

Tricento

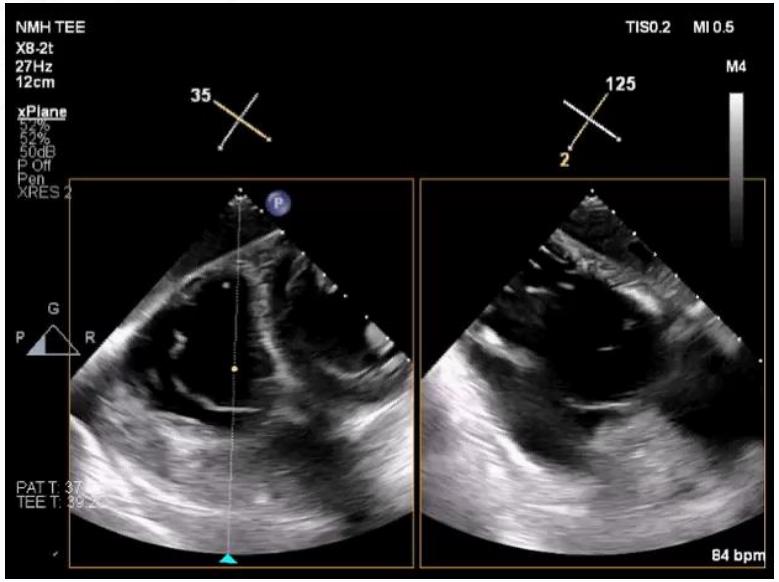
TricValve

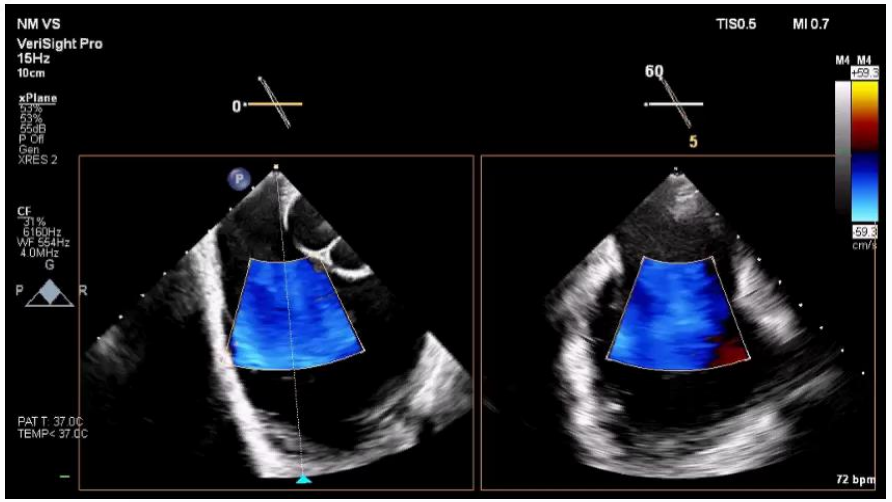
K Dimitriadis et al *Life* 13:1417; 2023

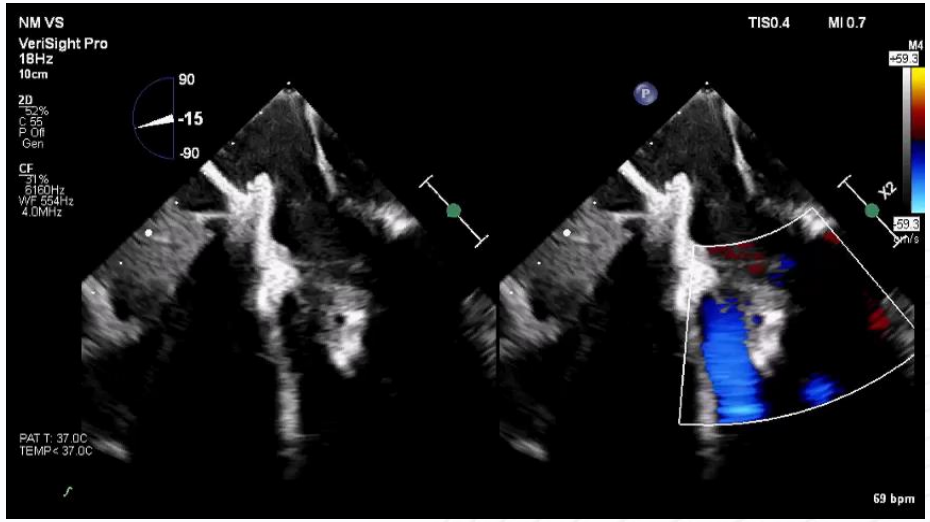
Case 1

- 61 y/o man s/p OHT
- Posterior-septal flail
- Torrential TR (ROA-PA 123, RV 56)
- Good leaflet length, narrow gap
- Annulus mildly dilated

Choice: TEER



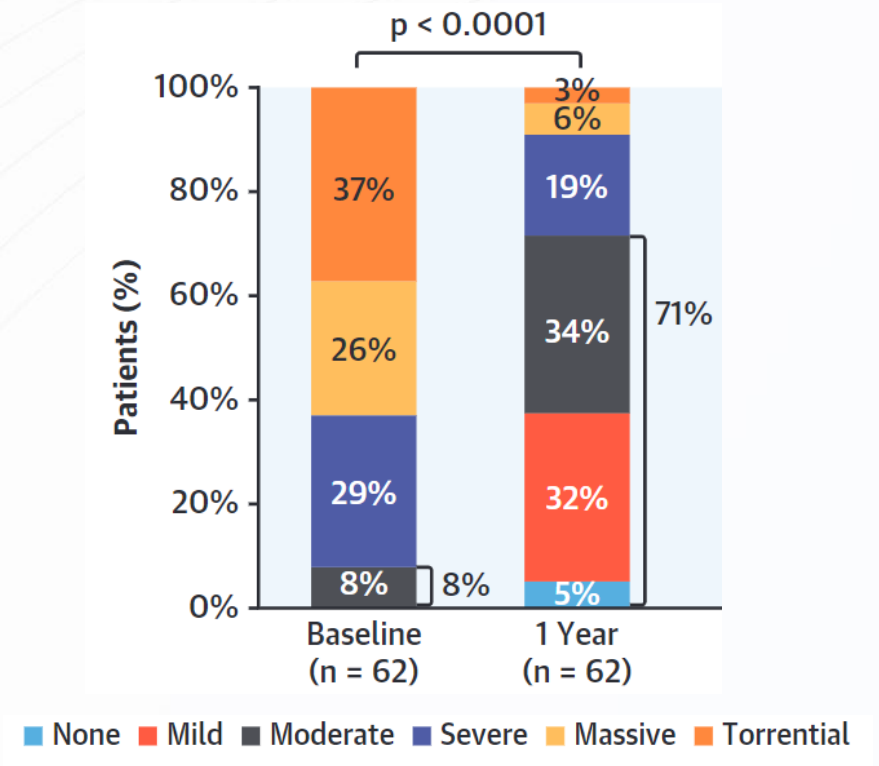


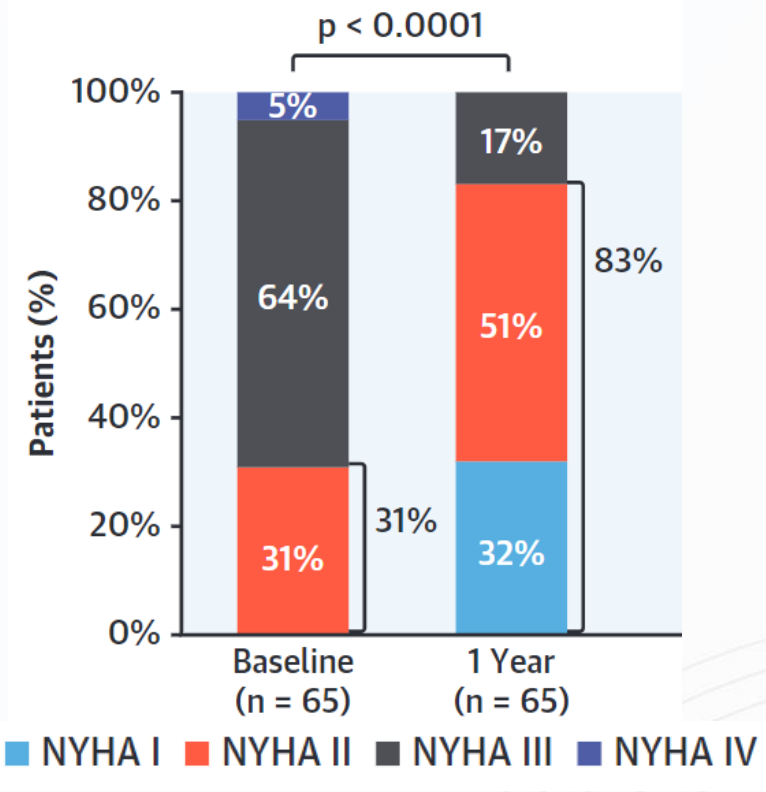


TEER for Tricuspid Regurgitation

TRILUMINATE (“*MitraClip*” for TR)

Transcatheter Edge-to-Edge Repair for Treatment of Tricuspid Regurgitation



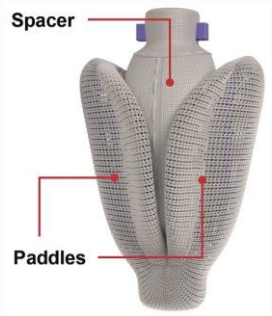


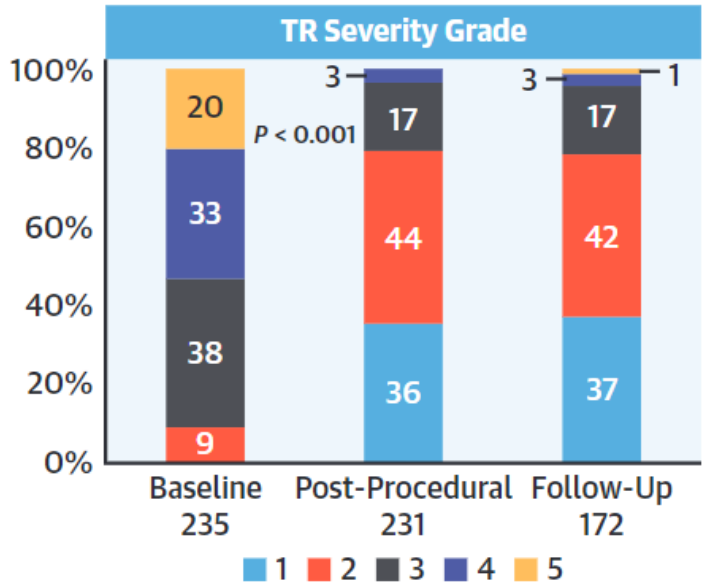
P Lurz et al JACC 77:229-39; 2021

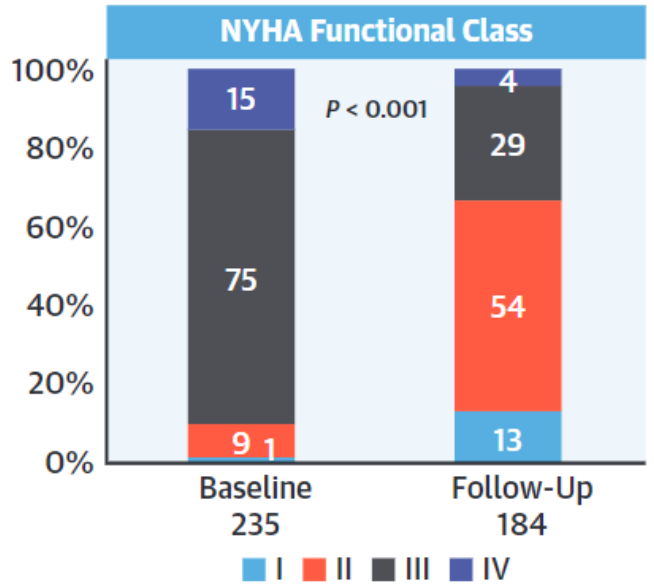
TEER for Tricuspid Regurgitation

PASTE (and CLASP TR - *PASCAL* for TR)

Multicenter Experience With the Transcatheter Leaflet Repair System for Symptomatic Tricuspid Regurgitation







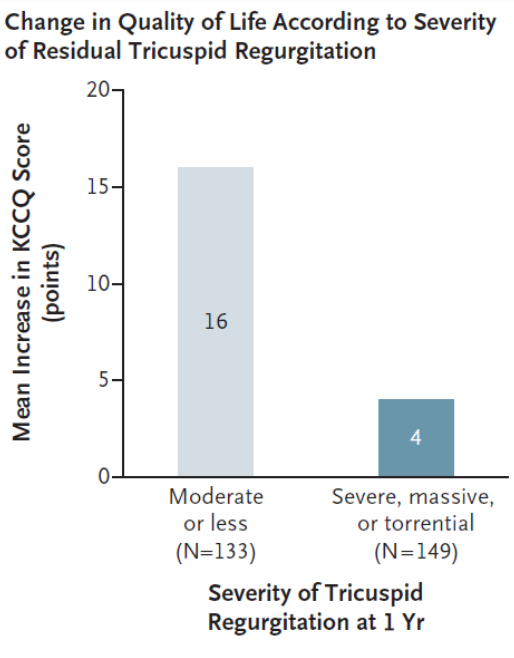
MG Wild et al JACCInt 15:1352-63; 2022

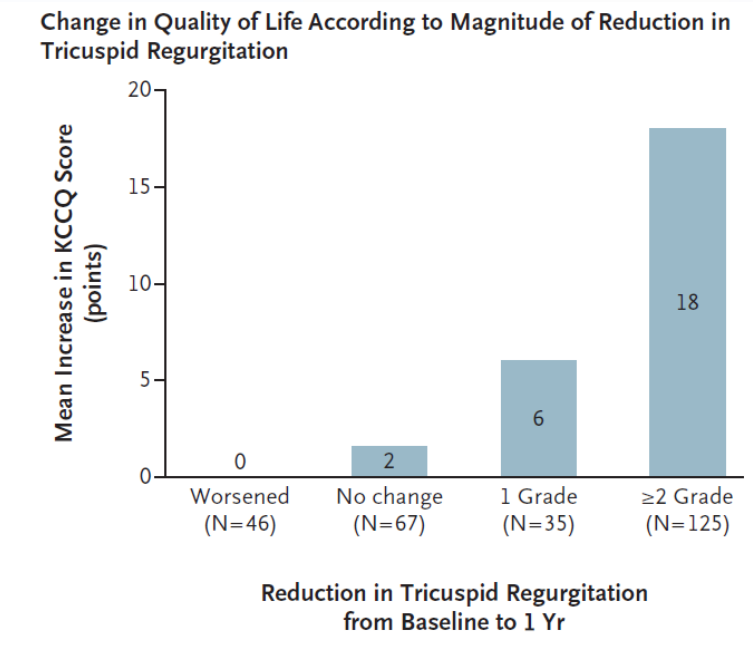
The NEW ENGLAND JOURNAL of MEDICINE

Transcatheter Repair for Patients with Tricuspid Regurgitation

TRILUMINATE

- 350 patients: TEER vs. Med Tx alone
- Composite primary end point at 1 year:
  Death/TV surg/HF hosp/+15 KCCQ
- At 30 days, 87% TEER gp ≤ moderate TR (vs. 4.8%)
- Win ratio 1.48 (1.06-2.13, p=0.02) for TEER
- Driven entirely by QoL (KCCQ +12.3% vs. +0.6%)





Sorajja et al 388:1833-42; 2023

The NEW ENGLAND JOURNAL of MEDICINE

Transcatheter Repair for Patients with Tricuspid Regurgitation

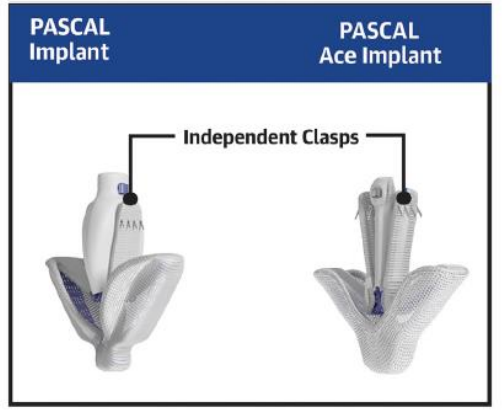
- Is this a Win?
- Too selective? (1573 consented, 795 screen failures)
  - ESRD and severe pulmonary HTN excluded
- Is a sham arm necessary for a QoL trial?
- Hawthorne effect?
- Is one-year enough follow-up?

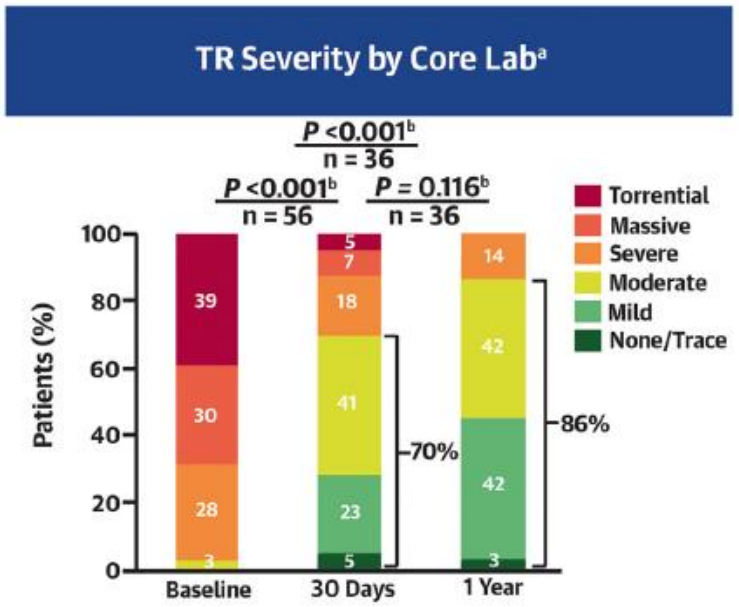
Sorajja et al 388:1833-42; 2023

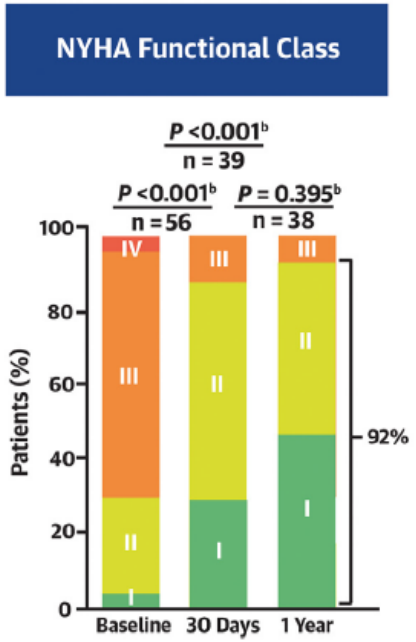
JACC: Cardiovascular Interventions

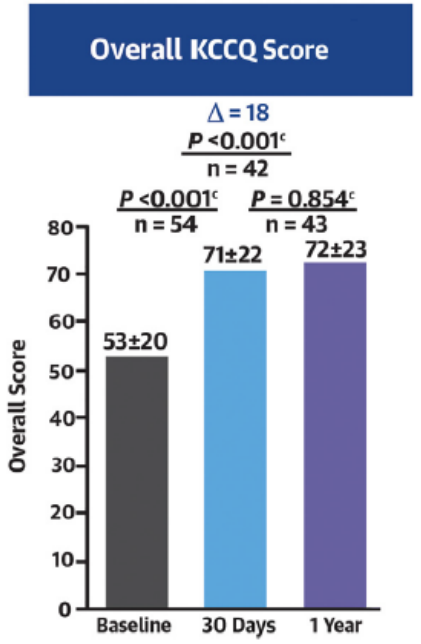
1-Year Outcomes of Transcatheter Tricuspid Valve Repair

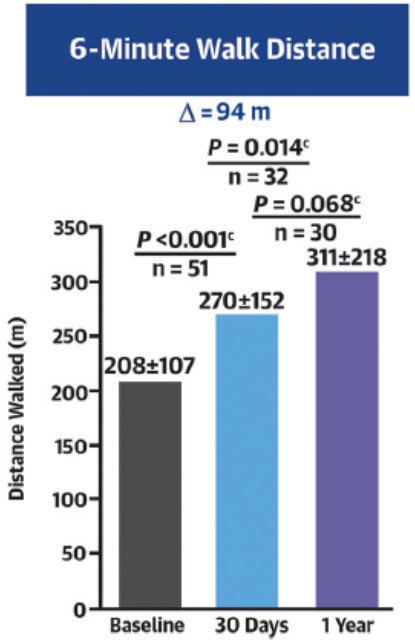
- 65 patients
- 97% with severe to torrential TR
- 86% achieved moderate or less TR







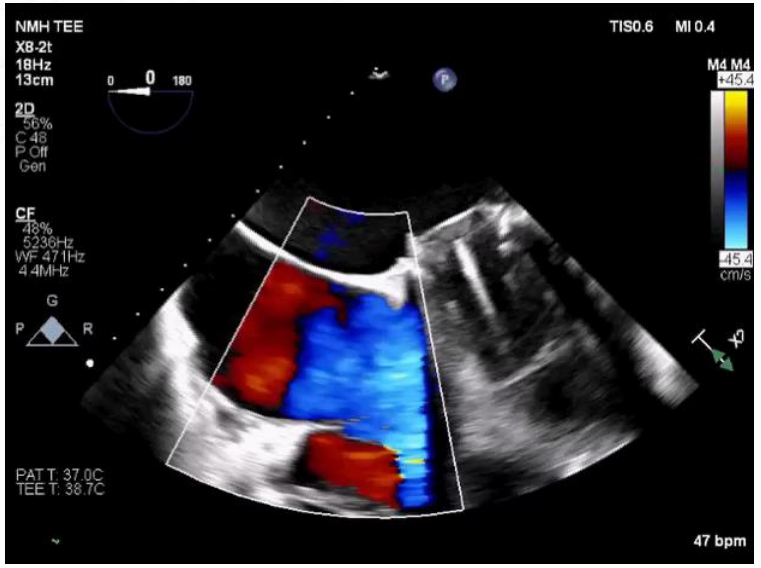




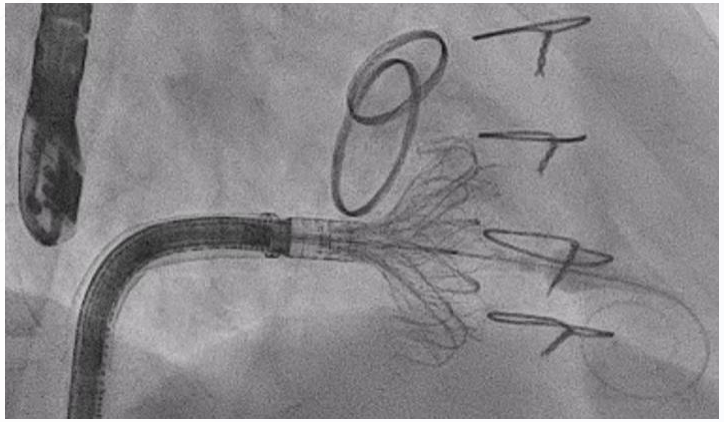
Kodali et al 2023;81:1766-76

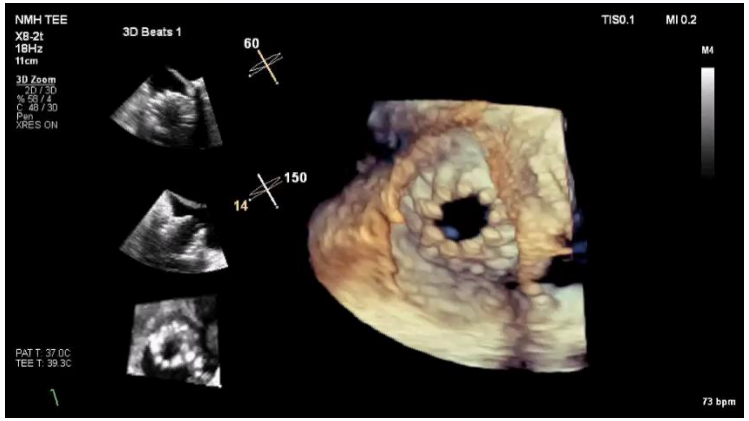
Case 2

- 75 y/o man, persistent A-fib
- Severe Annular Dilation
- Massive TR (ROA-PA 70, RV 45)
- Short restricted septal leaflet



Choice: TTVR

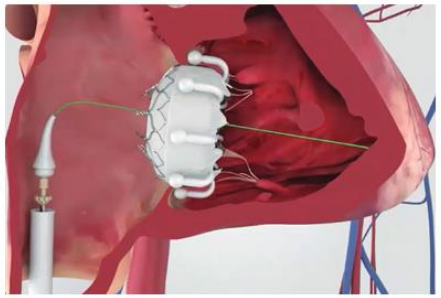


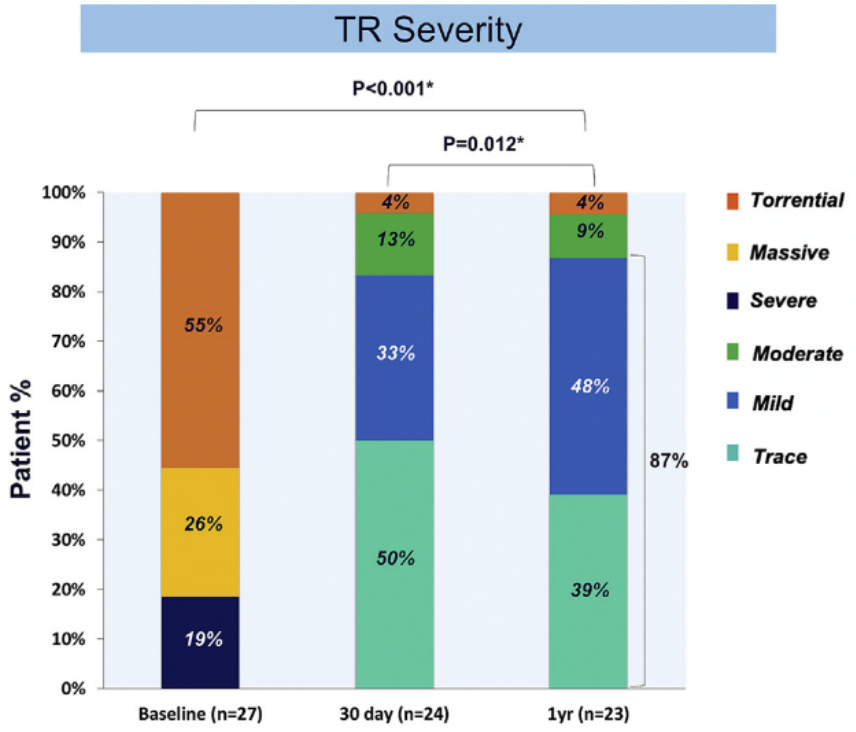


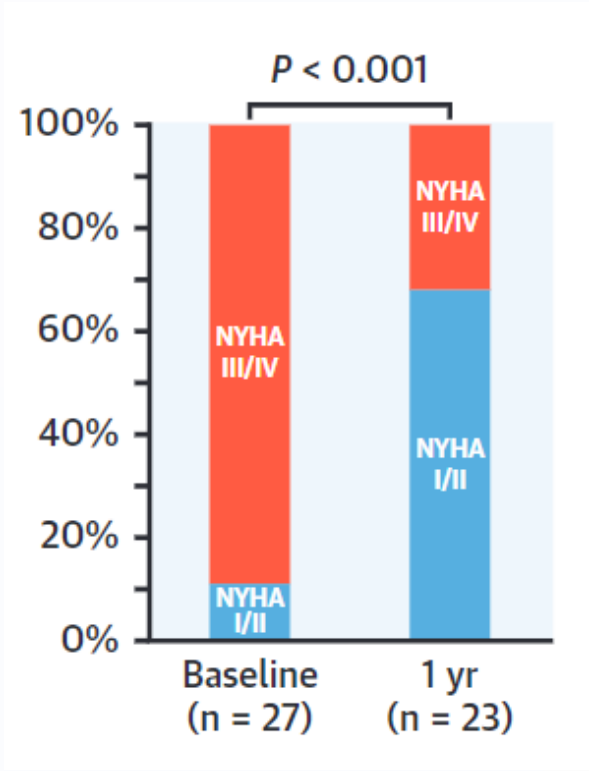
JACC: Cardiovascular Interventions

Transcatheter Tricuspid Valve Replacement With the EVOQUE System

1-Year Outcomes of a Multicenter, First-in-Human Experience







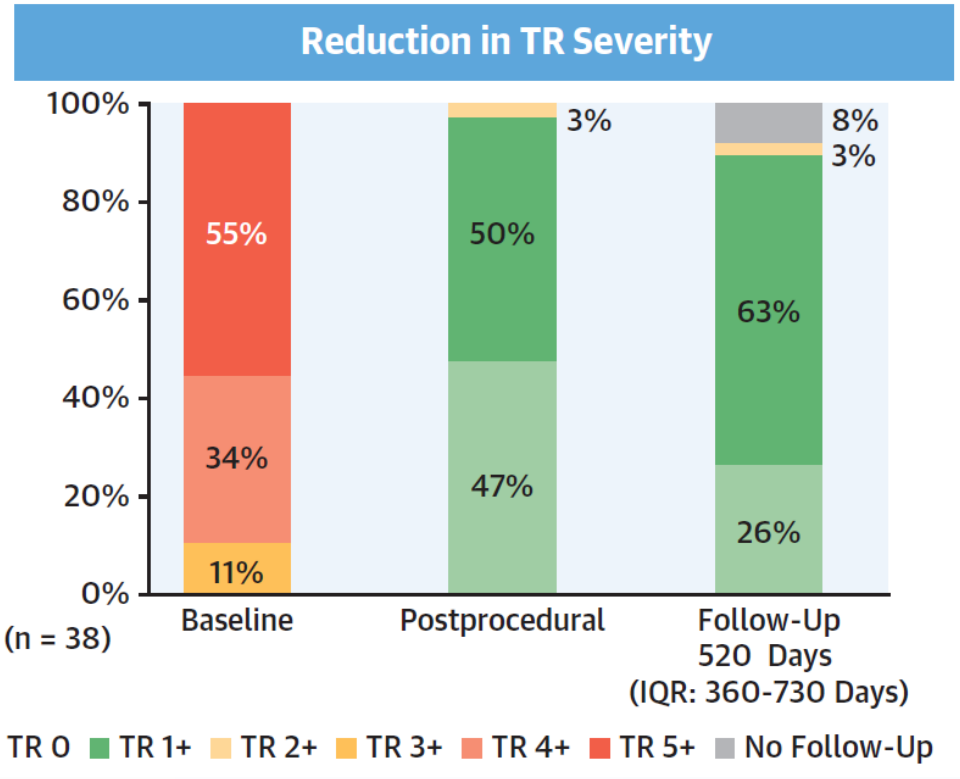
All-cause mortality: 7%
HF hospitalization: 7%
New pacemaker: 7% within 30 days, 4% beyond 30 days

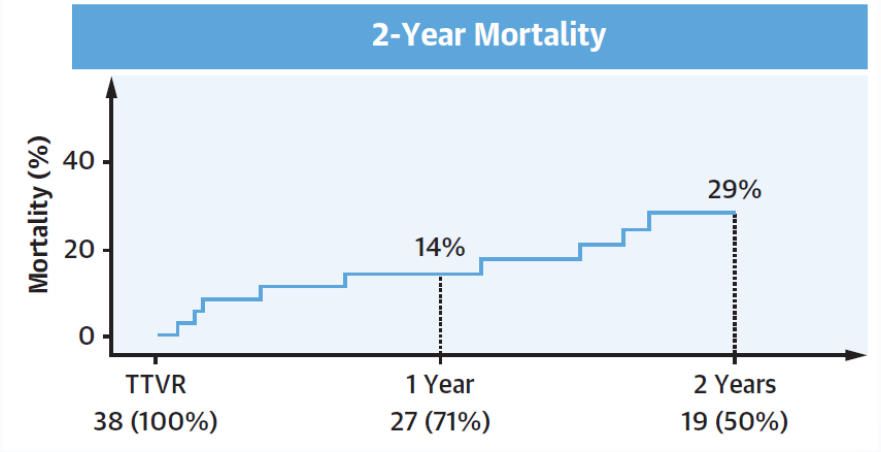
JG Webb et al 15:481-91; 2022

2-Year Outcomes Following Transcatheter Tricuspid Valve Replacement Using the EVOQUE System

JACC
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Letter to the Editor





- 1 surgery for valve migration
- 3 permanent pacers in first week
- All d/c'd on oral anti-coagulation
- 9/25 (36%) had HALT on f/u CTA

L Stolz et al 81:2374-76; 2023

TRISCEND Global Registry

- 176 high-risk patients
- ≥mod TR (40% ≥ massive) & refractory HF
- Implant success 96.2%
- 90.1% 1 year survival
- ~ 12% hospitalization at 1 year
- 97.6% ≤ mild TR
- KCCQ score 46.0 → 71.7
- 6-min walk +56 meters

THE TRISCEND II PIVOTAL TRIAL

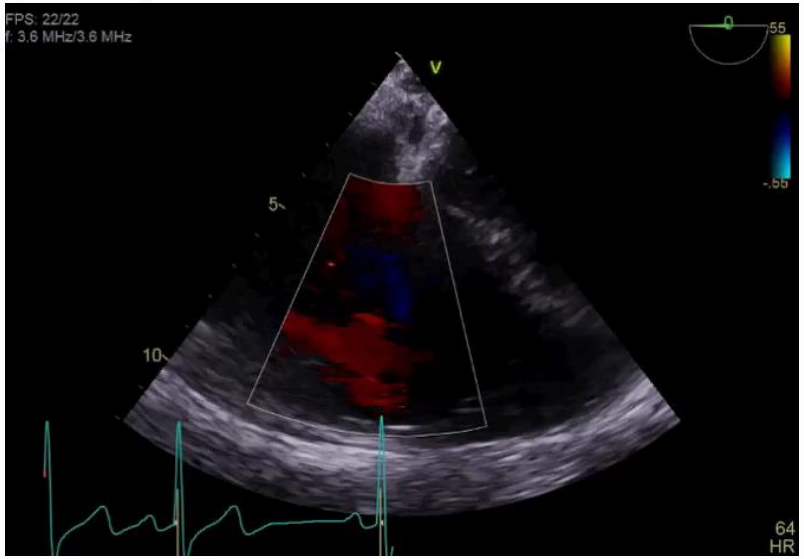
250 pts

TTVR with EVOQUE + OMT randomized (2:1) vs. OMT alone followed through 5 years.

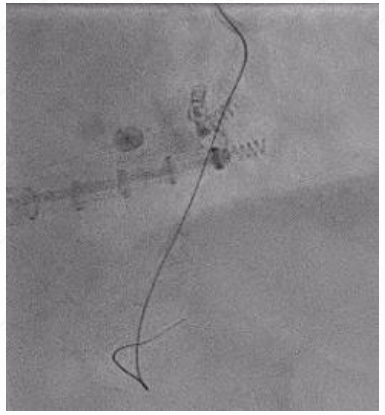
S Windecker London Valves Nov 2022

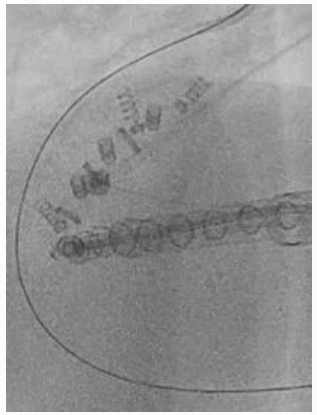
Case 3

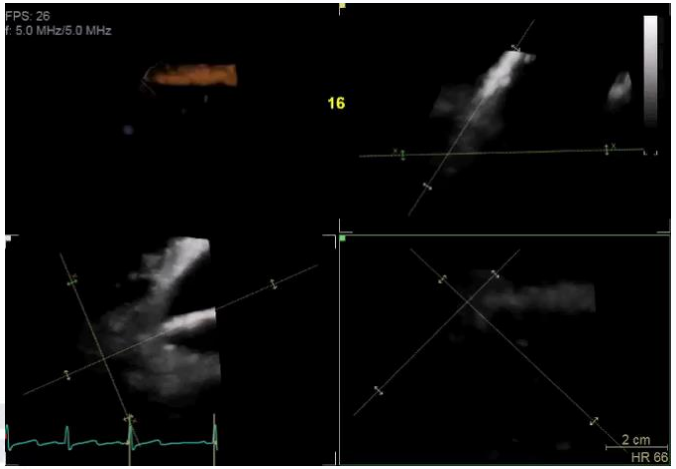
- 71 y/o woman, CAD and A-fib
- Massive Annular Dilation
- Sev-Massive TR (ROA-PA 55, RV 51)
- Large coaptation gap

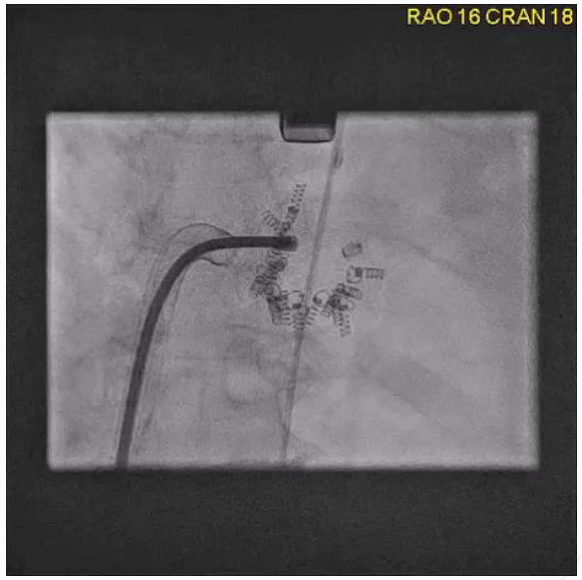


Choice: Annuloplasty



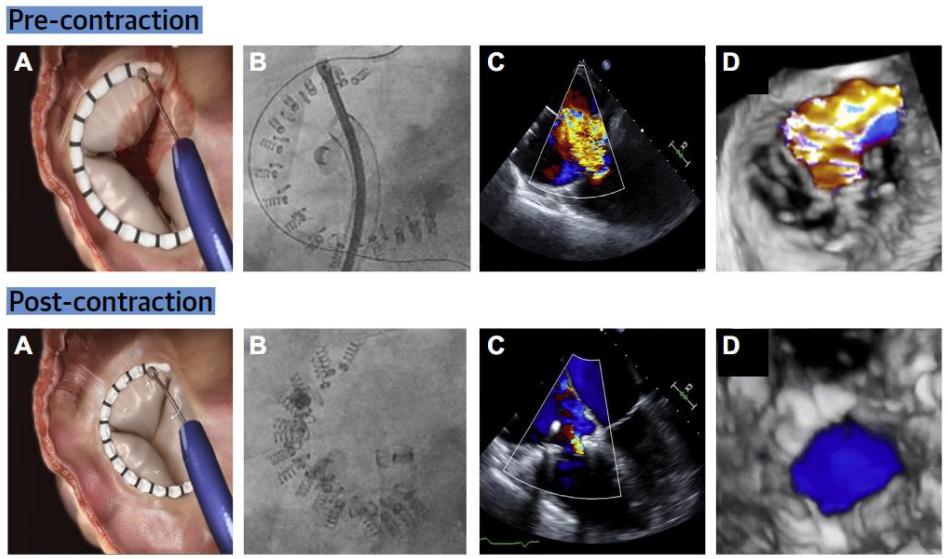


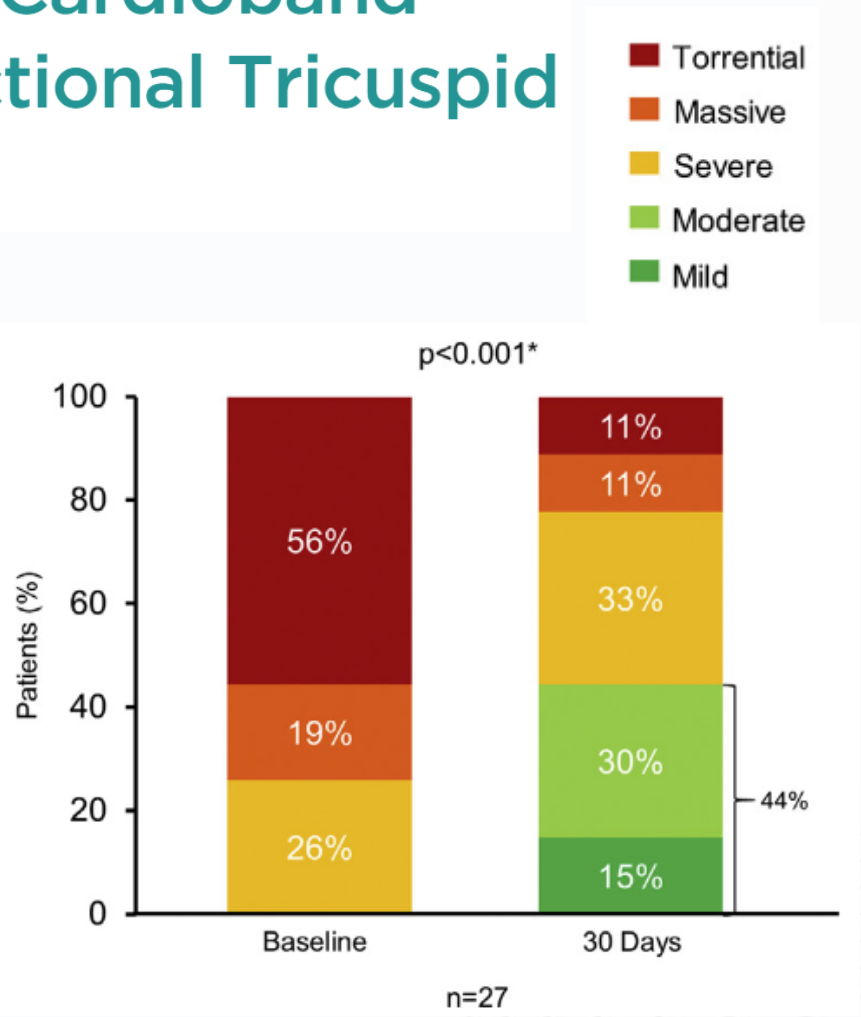




JACC: Cardiovascular Interventions

Early Feasibility Study of Cardioband Tricuspid System for Functional Tricuspid Regurgitation



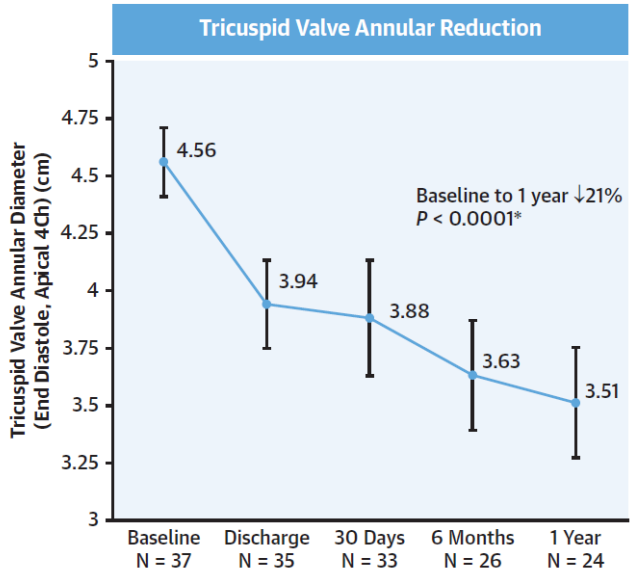


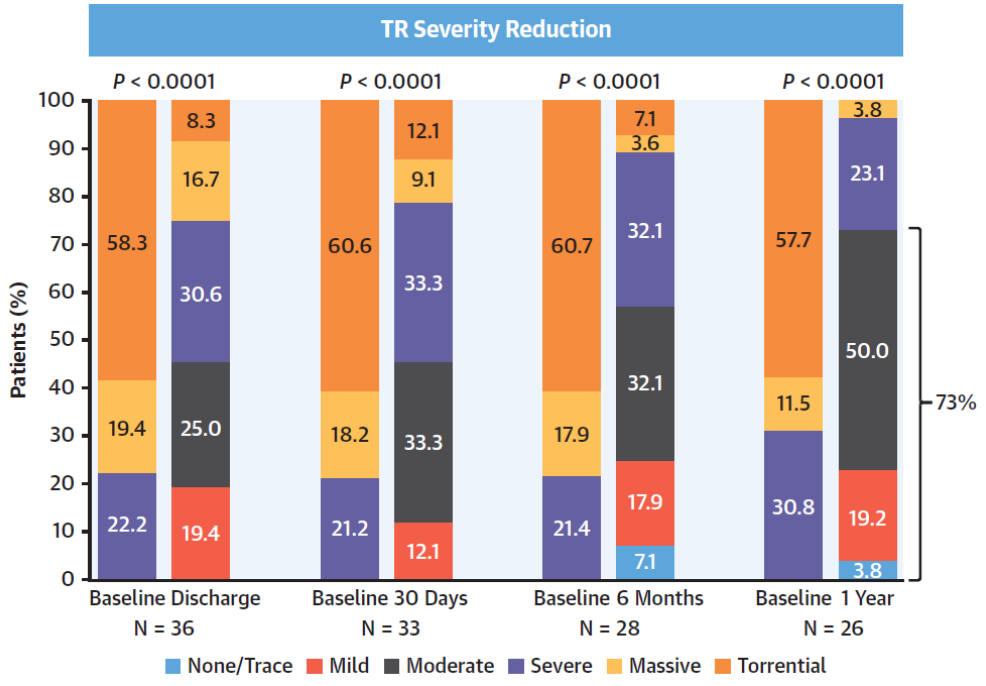
CJ Davidson et al 14:41-50; 2021

JACC: Cardiovascular Interventions

1-Year Outcomes of Cardioband Tricuspid Valve Reconstruction System Early Feasibility Study

Reduction in Tricuspid Valve Annular Diameter and TR Severity at 1 Year With Cardioband System



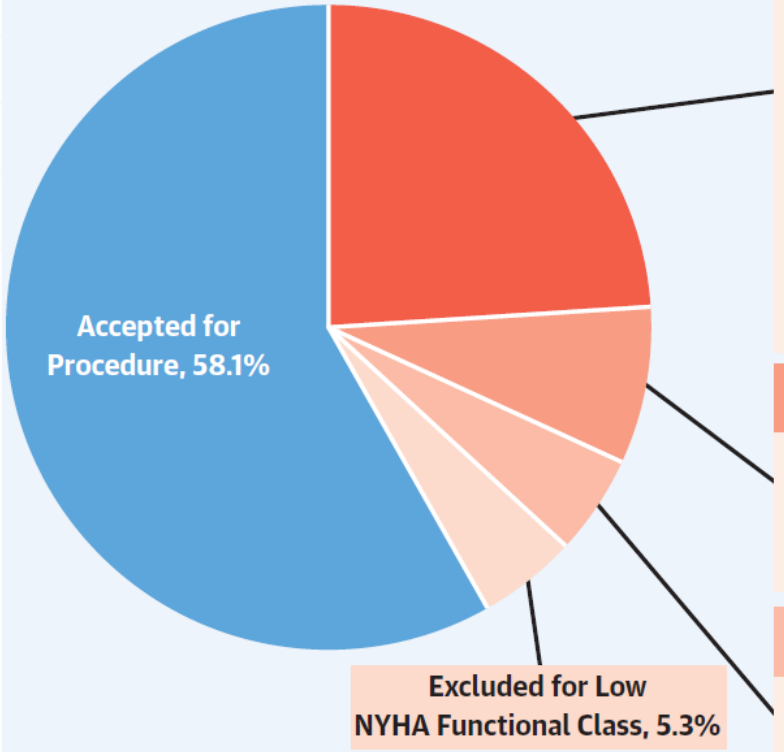


W Gray et al 19:1921-32; 2022

Screen Failure Rates for Trials is High

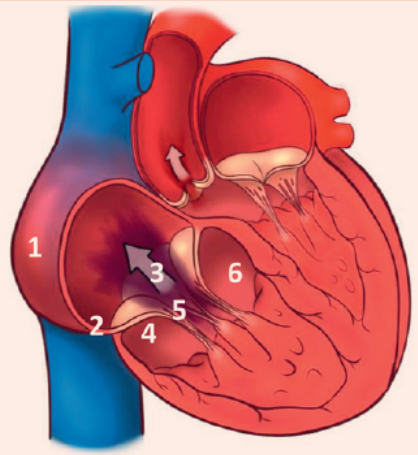
Characterization of Screen Failures Among Patients Evaluated for TTVr

547 Patients evaluated for TTVr (2016-2021) at 3 centers in the U.S. and Germany



Excluded for Anatomy or Morphology, 23.8%*

1. Right Atrial Dilation, mm^2
   OR: 1.04 (95% CI: 1.02-1.07)
2. Tricuspid Valve Annular Dilation, mm
   OR: 1.08 (95% CI: 1.03-1.13)
3. Tricuspid Valve Coaptation Deficit, cm^2
   OR: 1.14 (95% CI: 1.07-1.20)
4. Leaflet Tethering, cm^2
   OR: 2.15 (95% CI: 1.50-3.06)
5. Tricuspid Valve Coaptation Depth, cm^2
   OR: 1.28 (95% CI: 1.14-1.45)
6. Right Ventricular Dilation, mm
   OR: 1.06 (95% CI: 1.03-1.10)



Excluded for Clinical Futility, 7.5%

- Poor clinical status/frailty, 36.6%
- Pulmonary hypertension, 34.1%
- Other comorbid diseases, 24.4%
- Recurrent HF with need for VAD/HTX, 4.9%

Excluded for Limitations, 5.3%

- Poor imaging quality, 55.2%
- Pacemaker lead with leaflet leaflet impingement or attachment, 44.8%

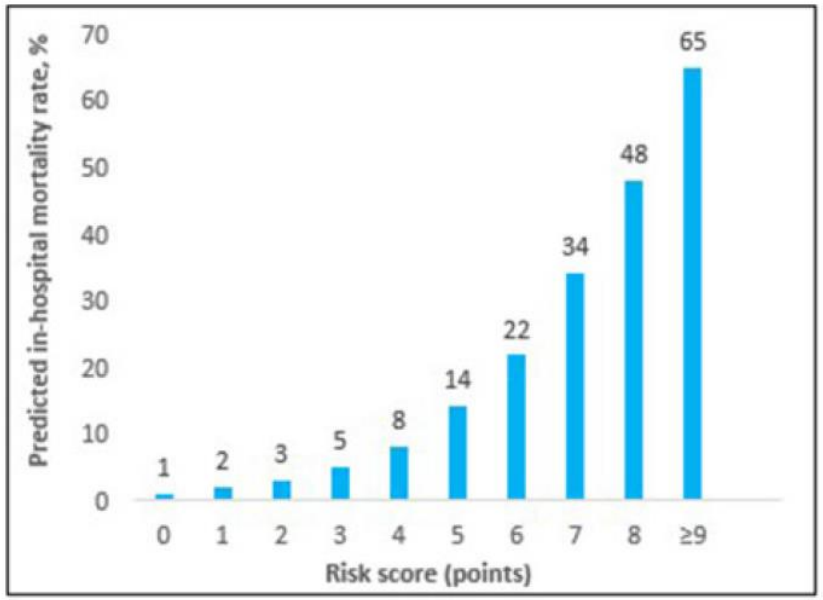
M Gercek et al *JACC Intv* 16:1579-89; 2023

European Heart Journal

TRI-SCORE: a new risk score for in-hospital mortality prediction after isolated tricuspid valve surgery

- 12 French centers
- 466 patients
- 2007-2017
- 10% in-hospital mortality
- Reliable TR reduction

Risk factors (final model from multivariate analysis)	Scoring
Age ≥ 70 years	1
NYHA functional class III-IV	1
Right-sided heart failure signs	2
Daily dose of furosemide ≥ 125mg	2
Glomerular filtration rate < 30 ml/min	2
Elevated total bilirubin	2
Left ventricular ejection fraction < 60%	1
Moderate/severe right ventricular dysfunction	1
Total	12



J Dreyfus et al *EHJ* 43:654-62; 2022

Unanswered ?’s About Transcatheter TR Therapies

- What is the appropriate outcome target for TV trials?
  - QoL, mortality, rehospitalization
- Are the promising results with TV device therapy durable?
  - Duration of anti-coagulation after TTVR?
  - Does TEER preclude future options?
- Should we be treating TR earlier?
- Should we be more aggressive treating A-fib and pulmonary HTN and avoid placing pacemaker leads across the TV?

TEER

CLASP II TR

TRICI-HF

TRI-FR

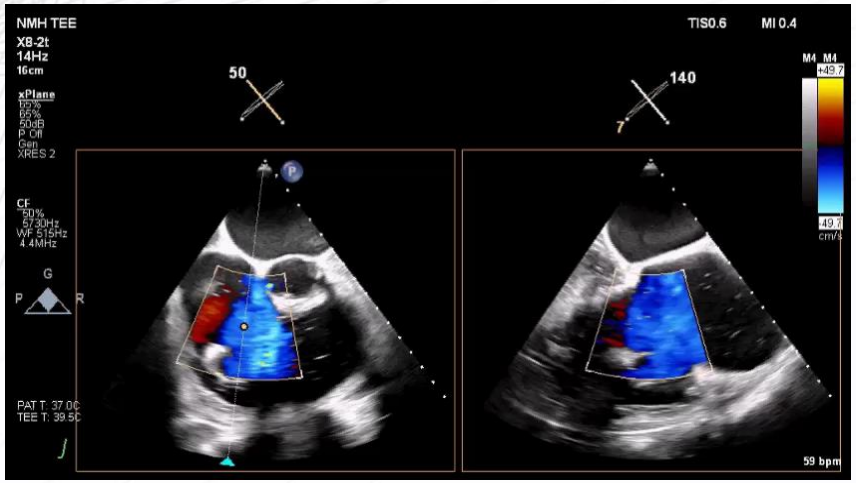
TRILUMINATE 5 year follow-up*

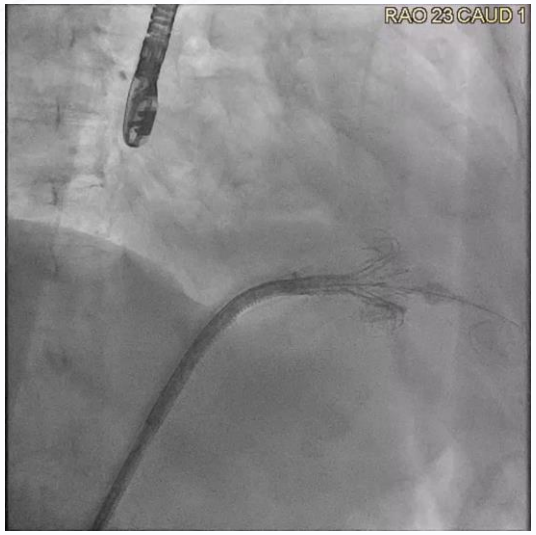
TTVR

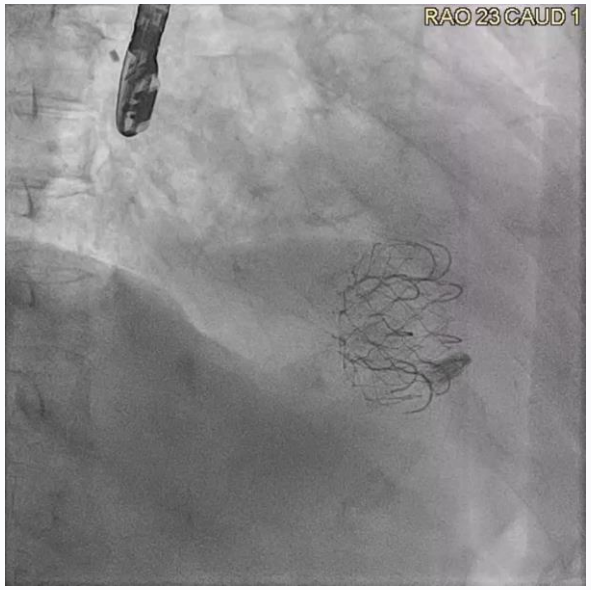
TRISCEND II

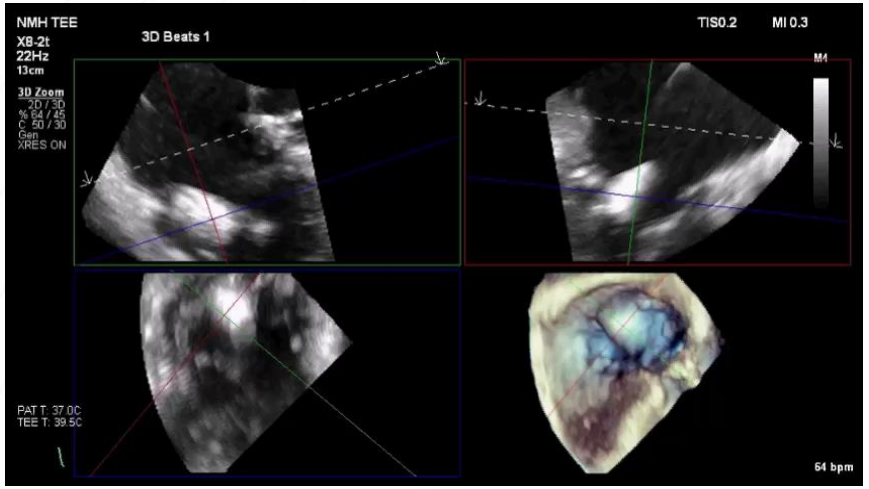
*Cross-over permitted at 1 year

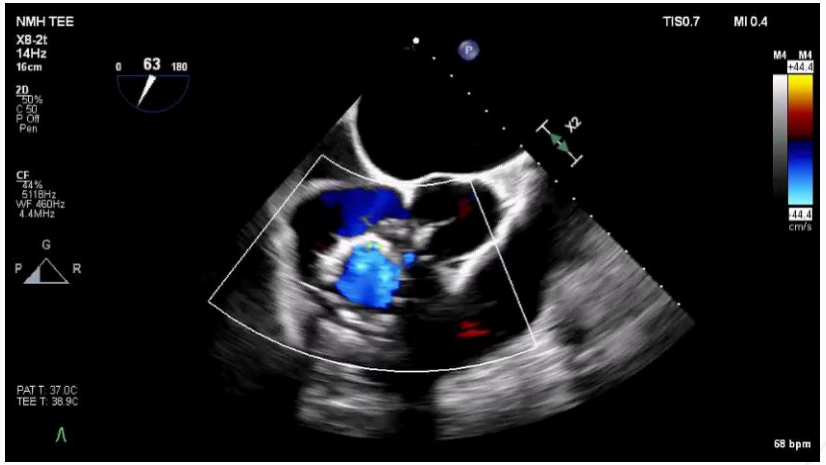
TTVR and after failed TEER











Conclusion

- Tricuspid regurgitation portends a poor prognosis
- Surgical therapy for tricuspid regurgitation has historically been associated with poor outcomes, but may be making a comeback
- An array of percutaneous tricuspid valve therapies has emerged and is showing promise to change the therapeutic landscape of tricuspid regurgitation and right ventricular failure
- There remain many unanswered questions about TR therapies that may be answered in ongoing clinical trials and with longer follow-up