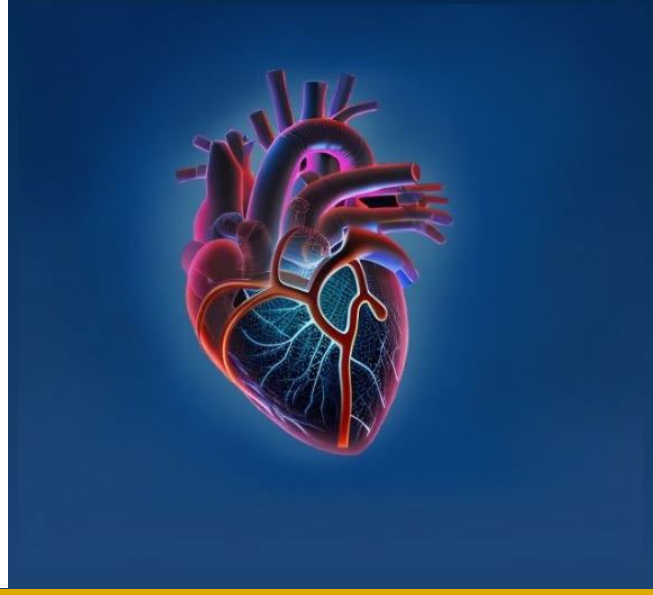
2024 Northern California Structural Heart Summit



Grasping the Clinical Need and Supporting Data for T-TEER

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Disclosures

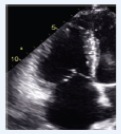
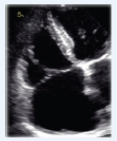
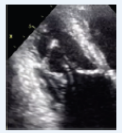
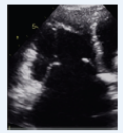
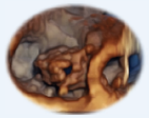
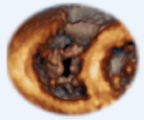
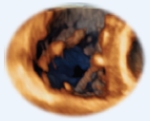
- **Edwards Lifesciences:** Physician proctor, consultant, speaker.

Objectives

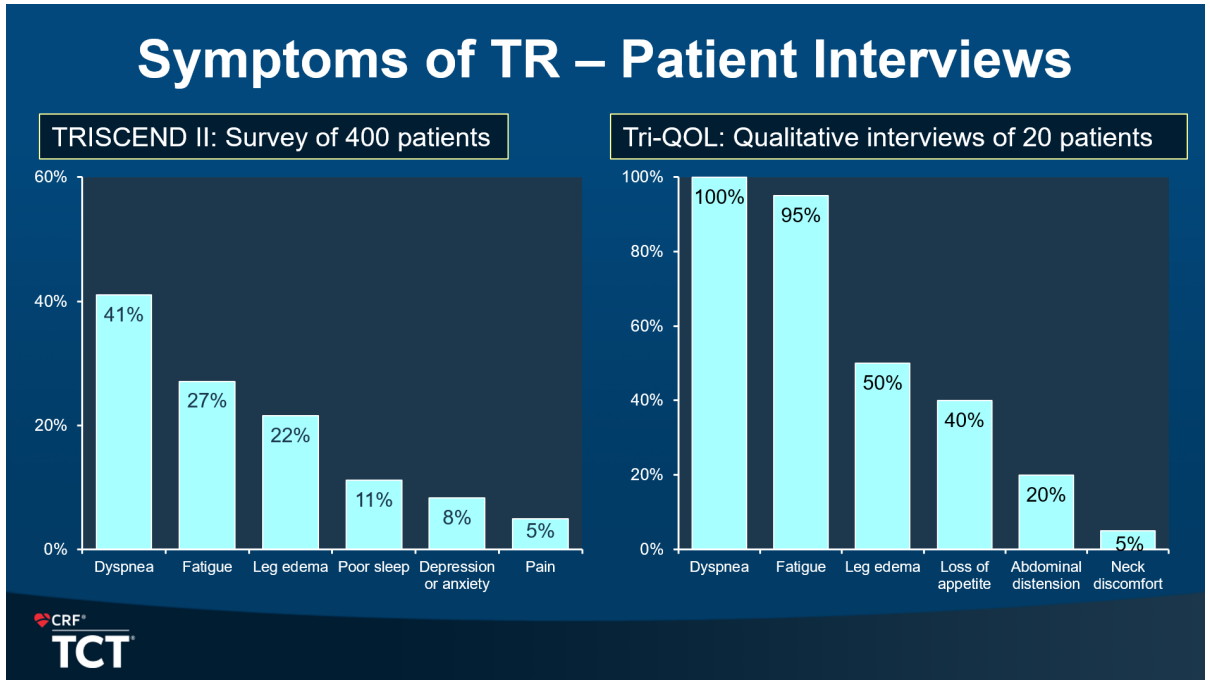
- Understand the clinic significance of tricuspid regurgitation.
- Review the options for treatment of tricuspid regurgitation including tricuspid transcatheter edge-to-edge repair (T-TEER).
- Discuss key clinical trial data supporting T-TEER

Tricuspid Valve Regurgitation

FIGURE 1 Classification of TR Etiology

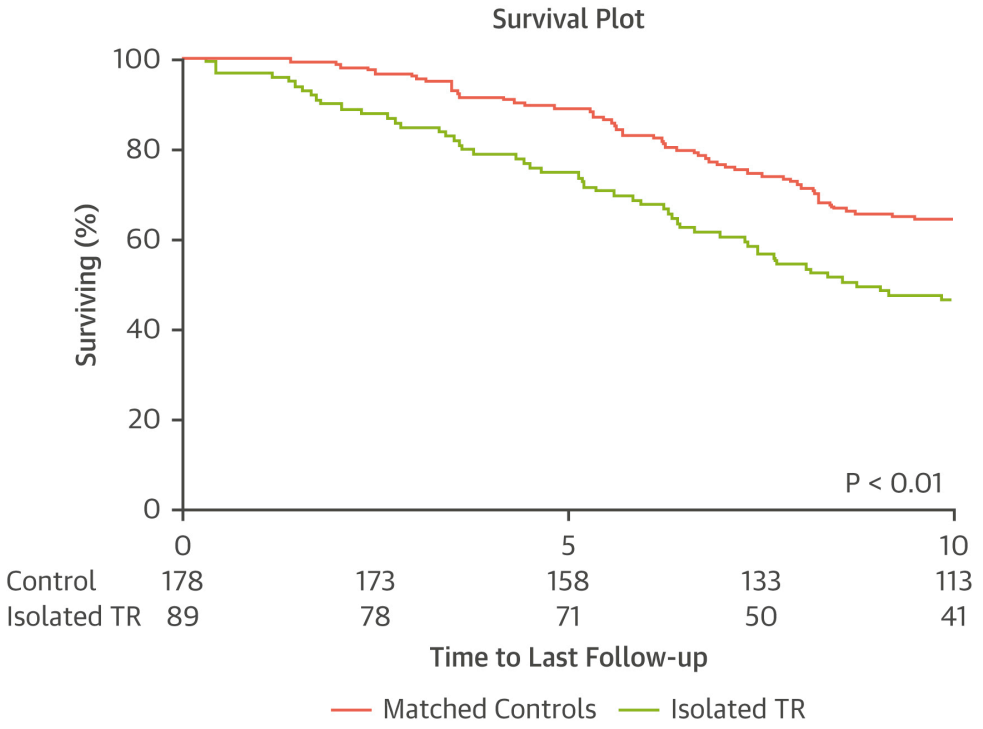
	Secondary		CIED (A)	Primary	
2D TTE					
3D TTE					
Parameter	**Ventricular**	**Atrial**	**CIED Type A**	**Primary TR**	
Carpentier Class	*IIIb*	*I*	*I, IIIa, IIIb*	*Prolapse II*	*RHD IIIa*
TV Tethering	++++	+/−	++	−	−
Leaflet Restriction	Systole	−	Systole/Diastole	−	Diastole
RA/TA Dilatation	++	++++	+/−	++	+++
RV Dilatation	+++	+/−	+/−	+/−	+/−
RV Dysfunction	+++	+/−	+/−	+/−	+/−

Hahn R et al. JACC 2023;82(17):1711-35

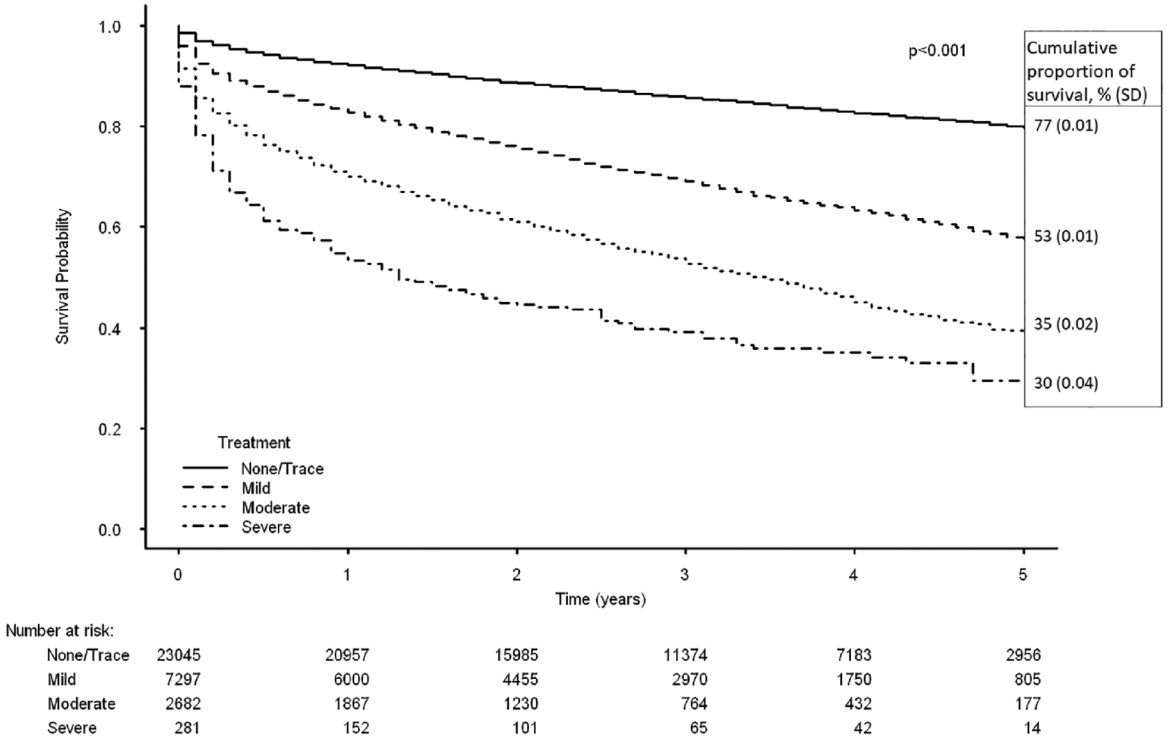


Arnold S. TCT 2024

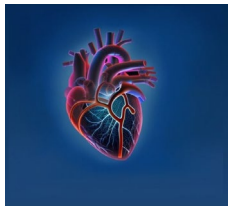
Survival with Tricuspid Regurgitation



Topilsky Y et al. JACC Imaging 2019;12(3):433-42.



Chorin E et al. Eur Heart J Cardiovasc Imaging 2020;21(2):157-65.



2020 ACC/AHA and 2021 ESC/EACTS Valve Guidelines

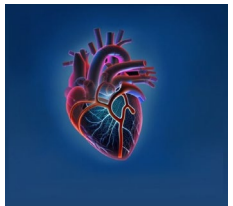
Recommendations for Medical Therapy for TR

COR	LOE	RECOMMENDATIONS
2a	C-EO	1. In patients with signs and symptoms of right-sided HF attributable to severe TR (Stages C and D), diuretics can be useful.
2a	C-EO	2. In patients with signs and symptoms of right-sided HF attributable to severe secondary TR (Stages C and D), therapies to treat the primary cause of HF (eg, pulmonary vasodilators to reduce elevated pulmonary artery pressures, GDMT for HF with reduced LVEF, or rhythm control of AF) can be useful (1,2)

Recommendations for Timing of Intervention
Referenced studies that support the recommendations are summarized in Online Data Supplement 32.

COR	LOE	RECOMMENDATIONS
1	B-NR	1. In patients with severe TR (Stages C and D) undergoing left-sided valve surgery, tricuspid valve surgery is recommended (1-8).
2a	B-NR	2. In patients with progressive TR (Stage B) undergoing left-sided valve surgery, tricuspid valve surgery can be beneficial in the context of either 1) tricuspid annular dilation (tricuspid annulus end diastolic diameter >4.0 cm) or 2) prior signs and symptoms of right-sided HF (3-10).
2a	B-NR	3. In patients with signs and symptoms of right-sided HF and severe primary TR (Stage D), isolated tricuspid valve surgery can be beneficial to reduce symptoms and recurrent hospitalizations (11-14).
2a	B-NR	4. In patients with signs and symptoms of right-sided HF and severe isolated secondary TR attributable to annular dilation (in the absence of pulmonary hypertension or left-sided disease) who are poorly responsive to medical therapy (Stage D), isolated tricuspid valve surgery can be beneficial to reduce symptoms and recurrent hospitalizations (11,12,15-19).
2b	C-LD	5. In asymptomatic patients with severe primary TR (Stage C) and progressive RV dilation or systolic dysfunction, isolated tricuspid valve surgery may be considered (12,20).
2b	B-NR	6. In patients with signs and symptoms of right-sided HF and severe TR (Stage D) who have undergone previous left-sided valve surgery, reoperation with isolated tricuspid valve surgery may be considered in the absence of severe pulmonary hypertension or severe RV systolic dysfunction (1,2,11,18).

Recommendations on primary tricuspid regurgitation		
Surgery is recommended in patients with severe primary tricuspid regurgitation undergoing left-sided valve surgery.	I	C
Surgery is recommended in symptomatic patients with isolated severe primary tricuspid regurgitation without severe RV dysfunction.	I	C
Surgery should be considered in patients with moderate primary tricuspid regurgitation undergoing left-sided valve surgery.	IIa	C
Surgery should be considered in asymptomatic or mildly symptomatic patients with isolated severe primary tricuspid regurgitation and RV dilatation who are appropriate for surgery.	IIa	C
Recommendations on secondary tricuspid regurgitation		
Surgery is recommended in patients with severe secondary tricuspid regurgitation undergoing left-sided valve surgery.[423–427]	I	B
Surgery should be considered in patients with mild or moderate secondary tricuspid regurgitation with a dilated annulus (≥40 mm or >21 mm/m^2 by 2D echocardiography) undergoing left-sided valve surgery.[423,425–427]	IIa	B
Surgery should be considered in patients with severe secondary tricuspid regurgitation (with or without previous left-sided surgery) who are symptomatic or have RV dilatation, in the absence of severe RV or LV dysfunction and severe pulmonary vascular disease/hypertension.[418,433 e]	IIa	B
Transcatheter treatment of symptomatic secondary severe tricuspid regurgitation may be considered in inoperable patients at a Heart Valve Centre with expertise in the treatment of tricuspid valve disease.[f]	IIb	C



Contemporary Isolated TV Surgery Outcomes

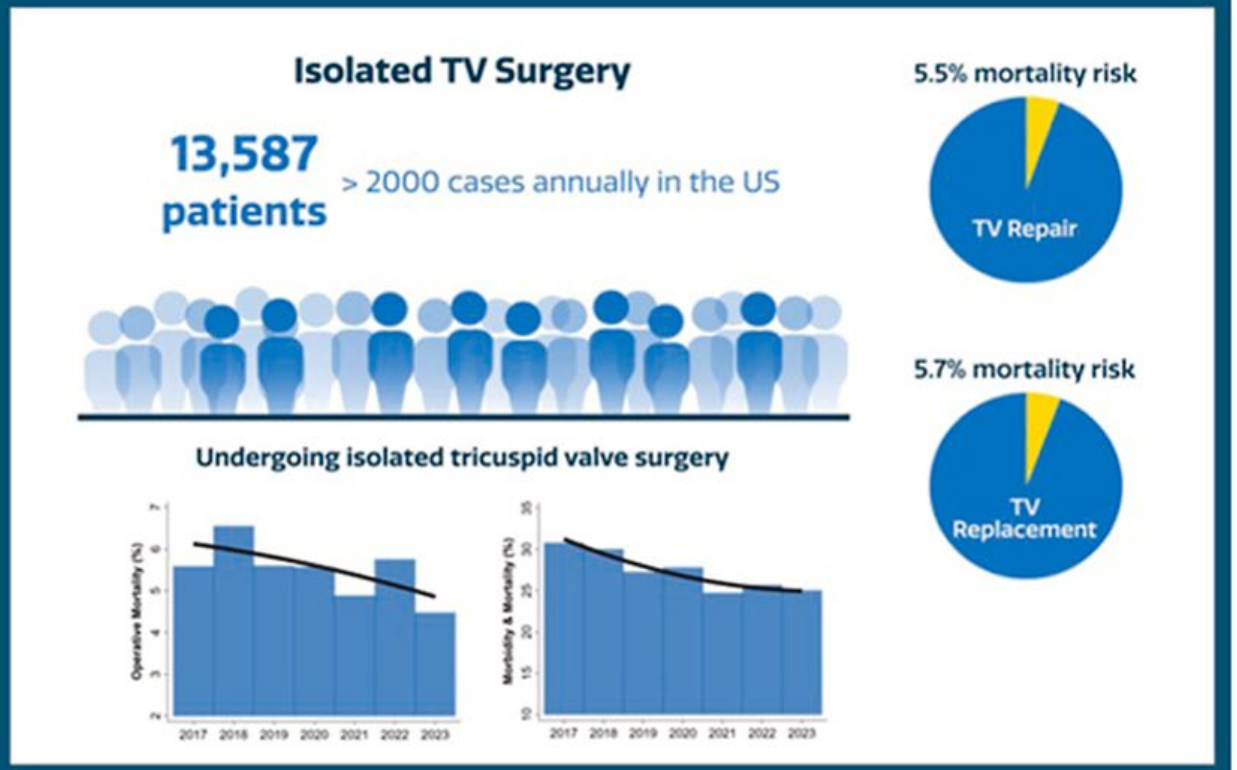
Operative mortality of 6-7% in patients without IE

STUDY POPULATION

13,587 isolated tricuspid valve surgeries at 842 hospitals

Overall operative mortality of TV repair 5.5%, TV replacement 5.7%

Enhanced and robust risk models with new STS Risk Calculator to help inform heart team decision-making

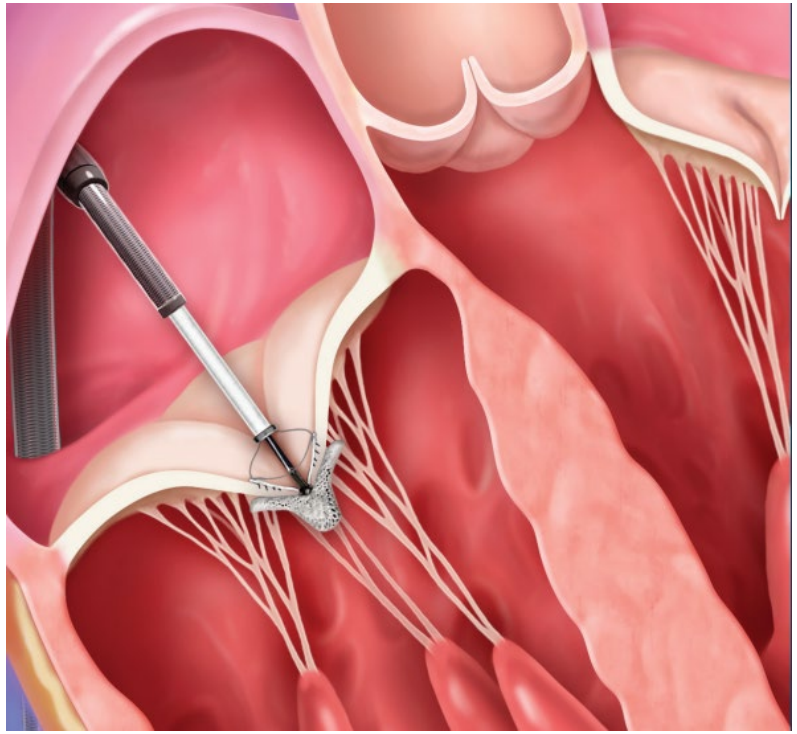


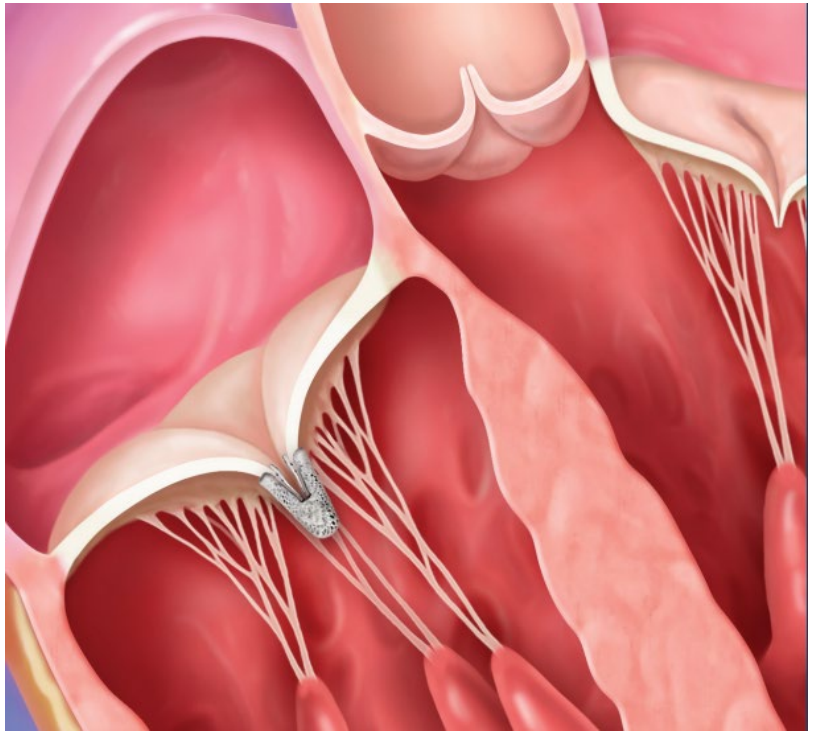
Isolated TV Surgery Outcomes Improving

Thourani V et al. Ann Thorac Surg 2024;118(4):873-81

Transcatheter Edge-to-Edge Repair (TEER)

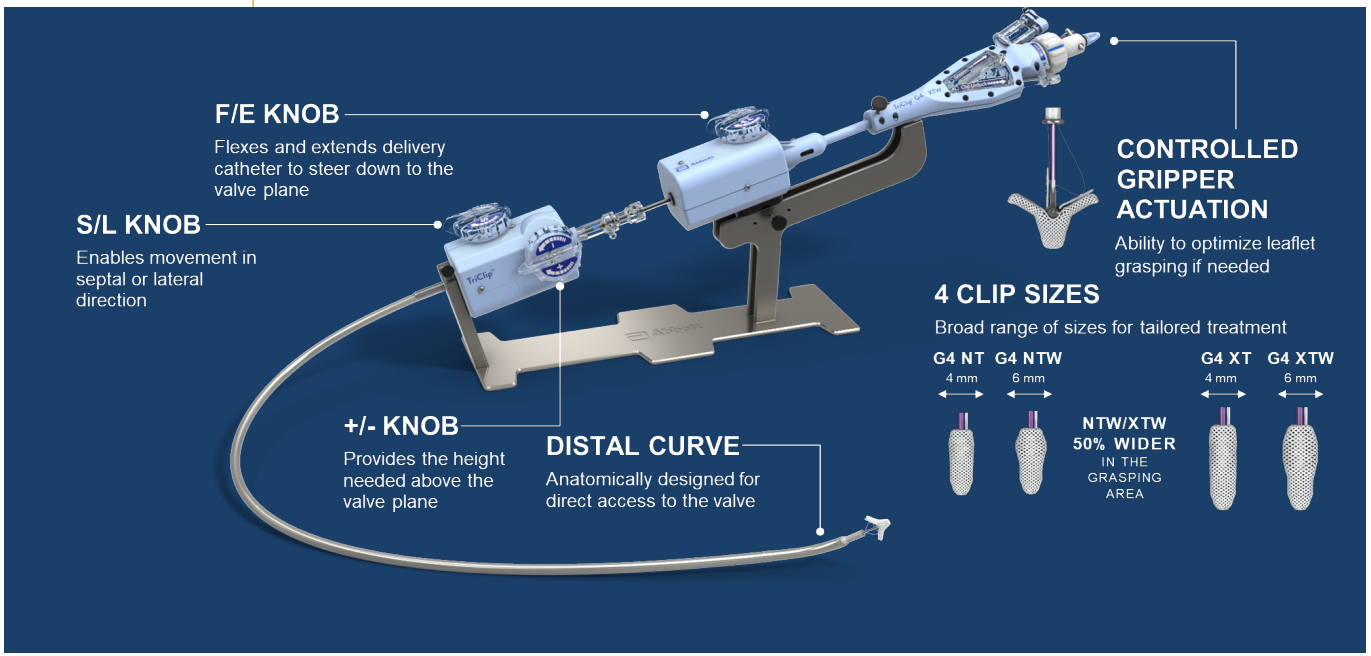
- Mechanism: TEER mimics surgical edge-to-edge repair by clipping the valve leaflets together, reducing regurgitation without open surgery.
- Advantages: Lower morbidity and mortality compared to surgical repair.



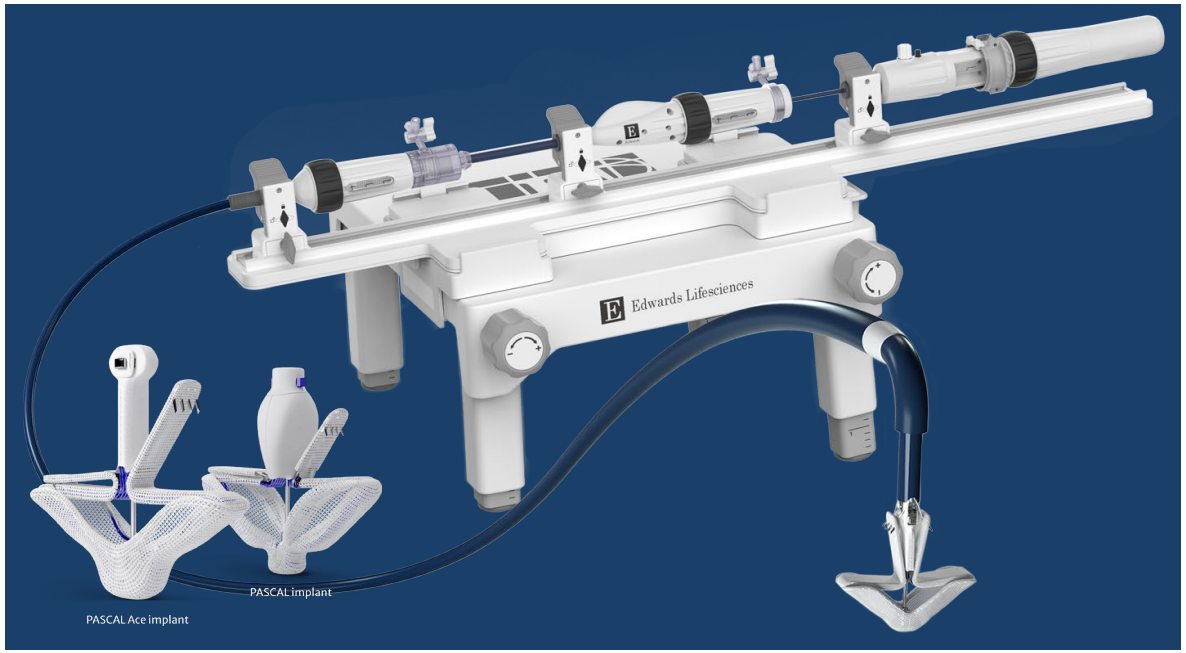


TEER Devices

TriClip (FDA Approved)



PASCAL (Investigational in US)



TRILUMINATE Pivotal Study Design

	Patients with severe TR who remain symptomatic despite medical therapy
	Randomized
Patient Population	Ability to reduce TR to Moderate or less
Randomization	1:1 TriClip: Control (Medical Therapy)
Endpoint	Hierarchical composite of all-cause mortality or tricuspid valve surgery, HFH, and KCCQ improvement ≥ 15 points at 12 months
Primary Analysis	**350**
Total Enrolled (Randomized)	**589 (572)**

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TRILUMINATE™ PIVOTAL TRIAL

Baseline Characteristics

Characteristic	Device N=285	Control N=287
Age (years)	78.1 ± 7.9 (285)	78.1 ± 7.6 (287)
Female sex	58.9% (168)	58.9% (169)
BMI	26.8 ± 5.8 (285)	27.1 ± 5.5 (287)
Atrial fibrillation	82.8% (236)	92.7% (266)
Dyslipidemia	62.8% (179)	54.0% (155)
Hypertension	81.1% (231)	81.5% (234)
Diabetes	17.2% (49)	15.7% (45)
Peripheral vascular disease	7.7% (22)	9.4% (27)
CABG	16.8% (48)	17.8% (51)
Prior percutaneous coronary intervention	15.1% (43)	14.3% (41)
Kidney disease	31.9% (91)	34.8% (100)
Liver disease	7.0% (20)	7.3% (21)
COPD	13.0% (37)	15.7% (45)
CRT, CRT-D, ICD, or permanent pacemaker	16.5% (47)	16.4% (47)
Previous aortic/mitral intervention	37.9% (108)	34.5% (99)
HFH within 1 year before enrollment	24.9% (71)	22.6% (65)
NT-proBNP (pg/mL)	1871.1 ± 1483.9 (121)	2420.7 ± 3416.1 (113)
NYHA Class III/IV	56.1% (160)	54.0% (155)
KCCQ score	55.6 ± 22.9 (285)	54.6 ± 23.8 (286)
6-minute walk distance (m)	240.5 ± 116.4 (272)	249.6 ± 125.5 (279)

Data shown as % (n) or mean±standard deviation (n).

Echocardiographic and Hemodynamic Characteristics

Characteristic	Device N=285	Control N=287
TR Etiology		
Functional	95.7% (270/282)	93.9% (263/280)
Degenerative	2.1% (6/282)	1.8% (5/280)
Mixed	2.1% (6/282)	3.9% (11/280)
CIED lead-related	0% (0/282)	0.4% (1/280)
Baseline TR Severity		
Moderate	2.2% (6/279)	1.5% (4/274)
Severe	25.1% (70/279)	28.5% (78/274)
Massive	24.0% (67/279)	18.6% (51/274)
Torrential	48.7% (136/279)	51.5% (141/274)
Coaptation gap (mm)	5.3 ± 1.8 (219)	5.2 ± 1.8 (229)
RV TAPSE (cm)	1.7 ± 0.4 (279)	1.6 ± 0.4 (271)
RVEDD, mid (cm)	3.7 ± 0.7 (278)	3.7 ± 0.8 (274)
Right atrial volume (mL)	140.9 ± 81.2 (279)	146.7 ± 78.0 (278)
Tricuspid annulus diameter (cm)	4.3 ± 0.8 (280)	4.4 ± 0.8 (274)
Cardiac output (L/min)	4.6 ± 1.4 (285)	4.6 ± 1.4 (285)
Left ventricular ejection fraction (%)	59.4 ± 9.0 (267)	59.7 ± 9.2 (260)

Data shown as % (n/N) or mean±standard deviation (n).

Procedural Characteristics (Device Only)

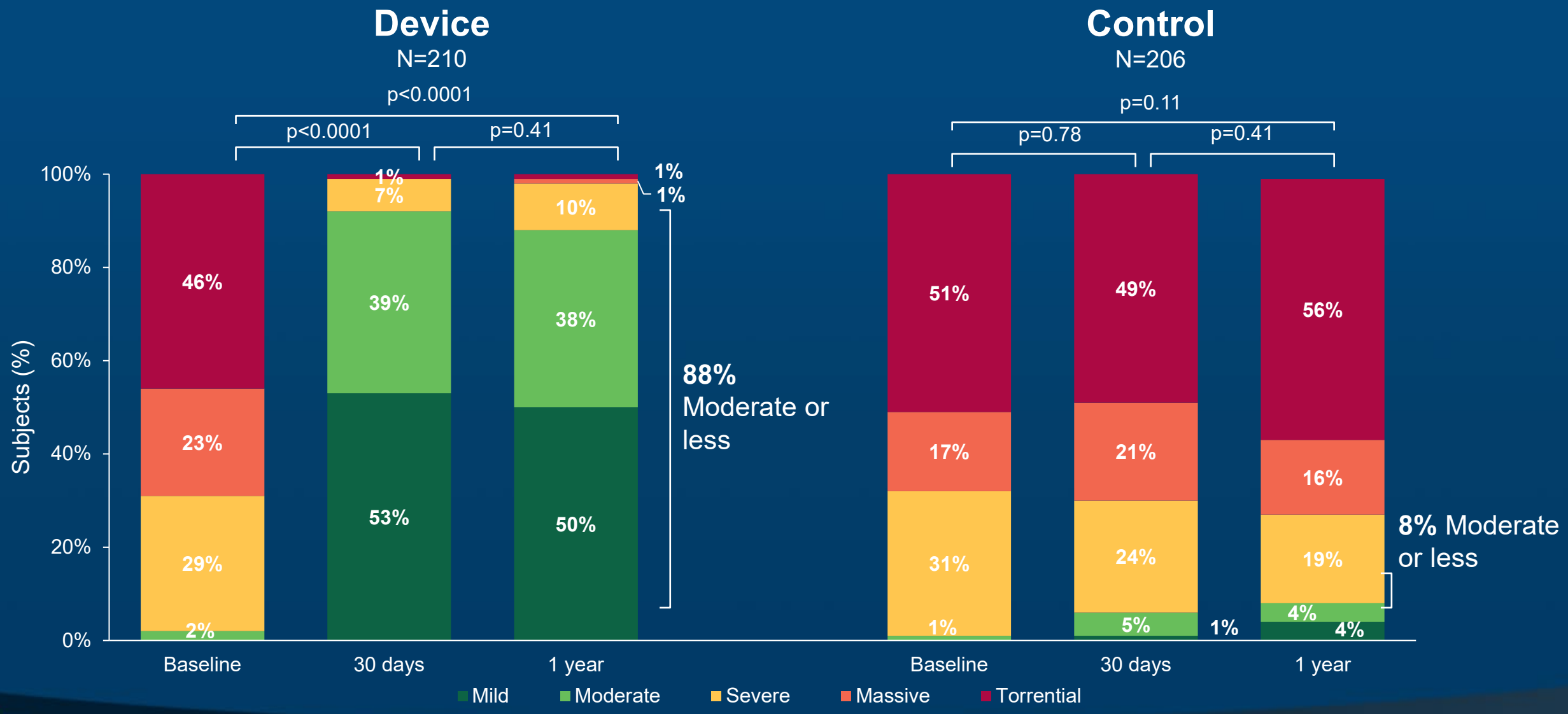
Variable	Device N=281
System	
TriClip	29.9% (84)
TriClip G4	70.1% (197)
Number of devices implanted	
0	1.1% (3)
1	14.9% (42)
2	60.5% (170)
3	20.6% (58)
4	2.8% (8)
Device type	
NT	10.0% (59/588)
XT	32.0% (188/588)
NTW	5.6% (33/588)
XTW	52.4% (308/588)
Device time (minutes)	85.6 ± 63.0 (274)
Procedure time (minutes)	147.2 ± 72.0 (279)
Length of hospital stay (days)	1.5 ± 1.3 (281)
In-hospital death	0% (0)
Home discharge	97.9% (275)

Adverse Events through 30 Days	Device N=281
Major Adverse Events through 30 Days	
Cardiovascular mortality	0.4% (1)
New-onset renal failure	0.7% (2)
Non-elective cardiac surgery	0% (0)
Endocarditis requiring surgery	0% (0)
Other Adverse Events through 30 Days	
Myocardial infarction	0% (0)
Stroke	0.4% (1)
Major bleeding	3.2% (9)
Device embolization	0% (0)
Single leaflet device attachment (SLDA)	5.7% (16)
Device thrombosis	0% (0)

No in-hospital deaths and low rates of adverse events

Data shown for attempted procedure population. Data shown as % (n), % (n/N # of total clips), or mean±standard deviation (n).

Tricuspid Regurgitation Severity



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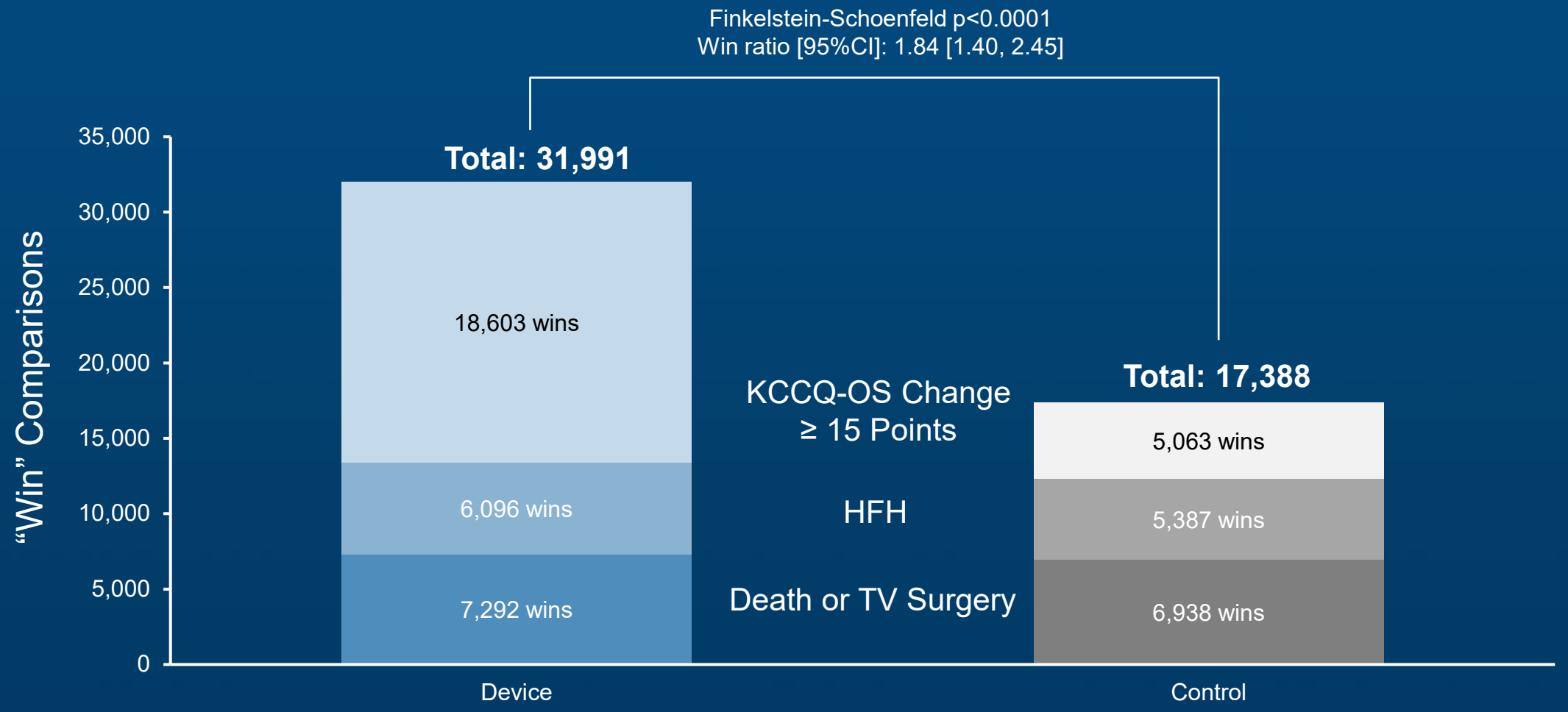
Paired data shown.

TRILUMINATE™ PIVOTAL TRIAL

Primary Endpoint for Full Randomized Cohort (N=572)



Device subjects **84% more likely** to have better outcome

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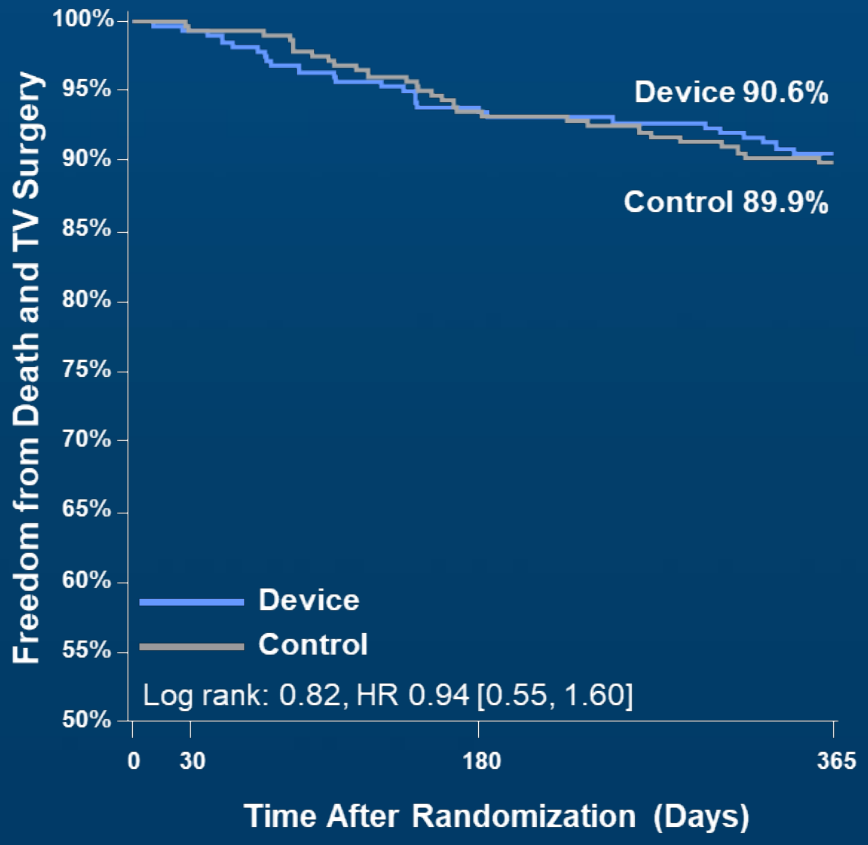
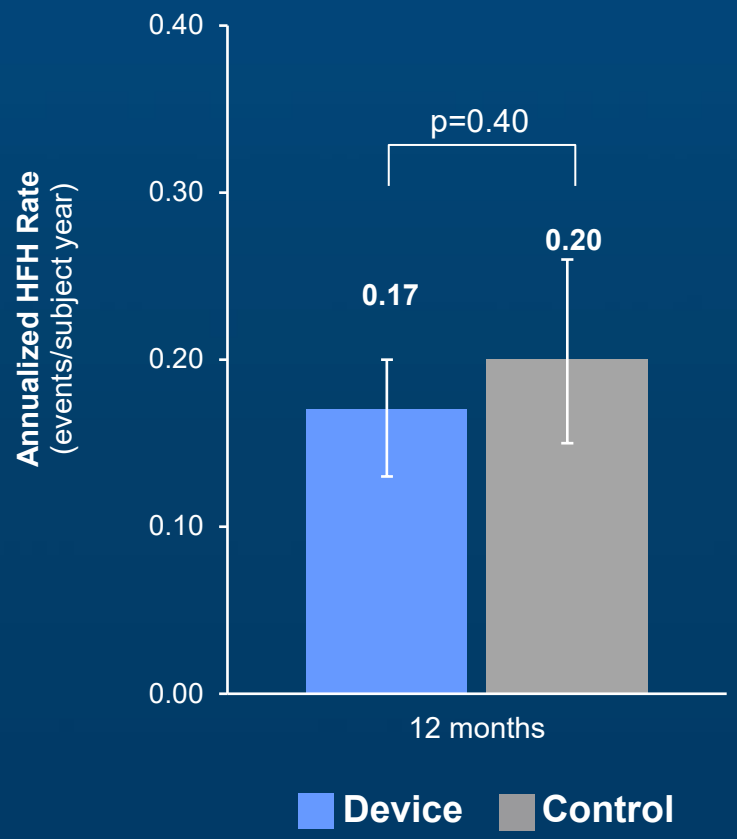
TRILUMINATE™ PIVOTAL TRIAL

Primary Endpoint Components

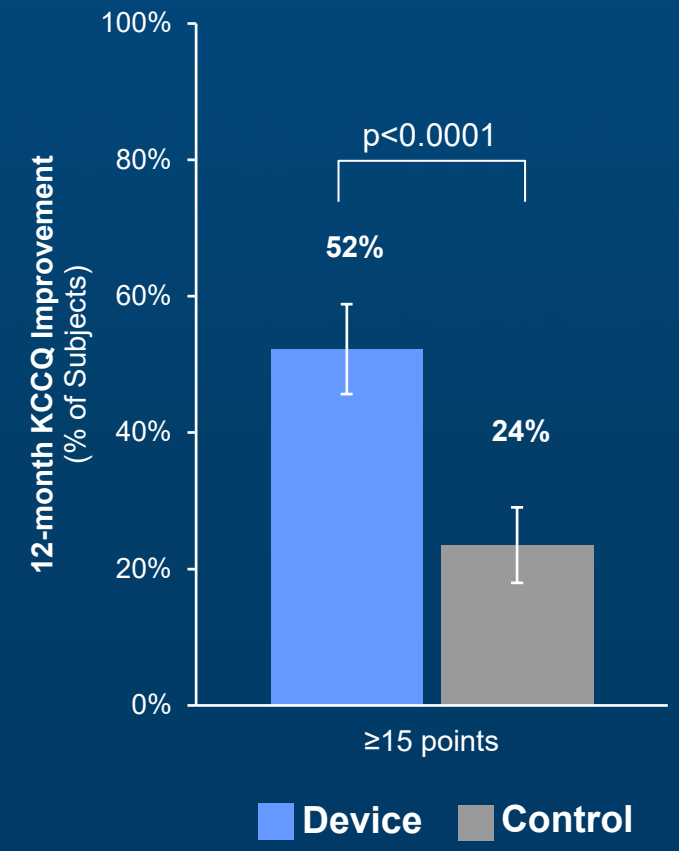
Freedom from Mortality and TV Surgery



Annualized HFH

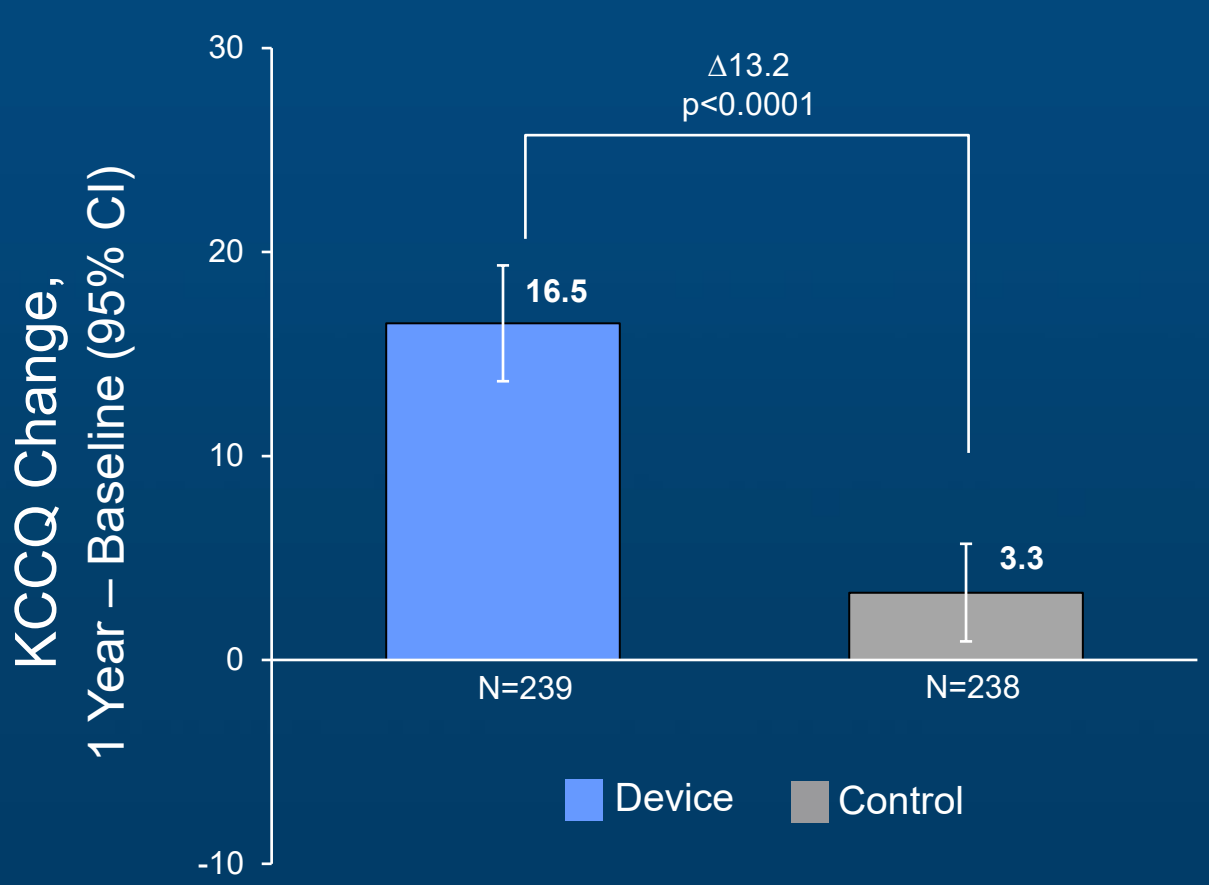


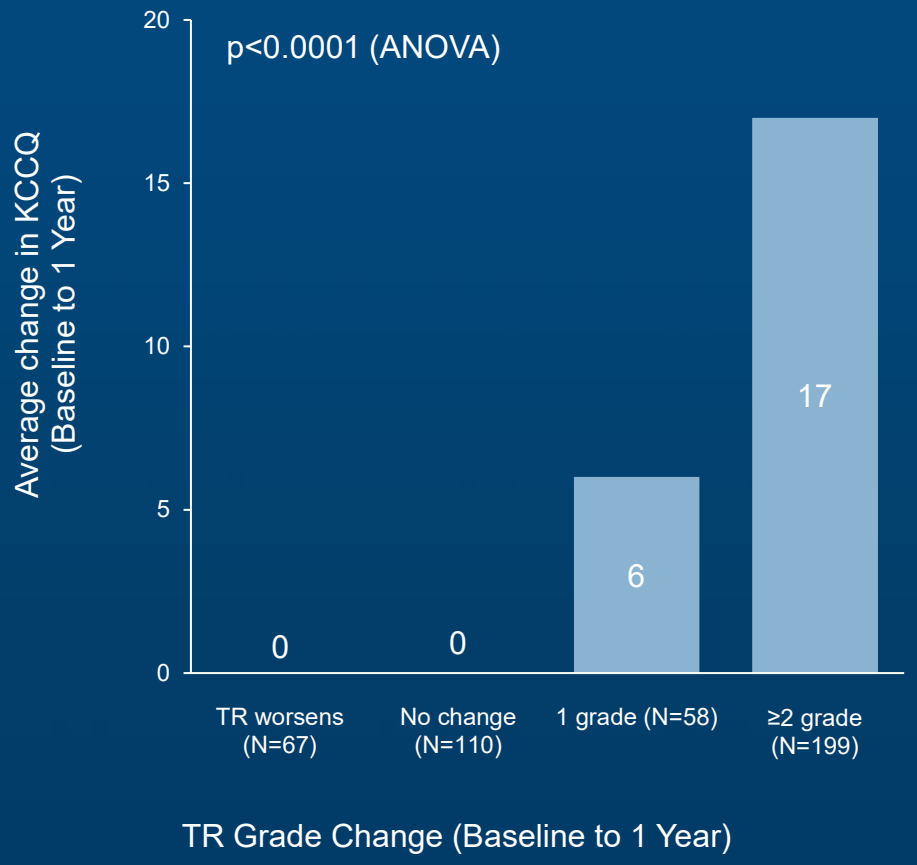
ΔKCCQ-OS



Data shown as mean±95%CI.

Change in KCCQ by TR Reduction





Significantly greater improvement in quality of life in the device group and change in KCCQ was associated with TR reduction

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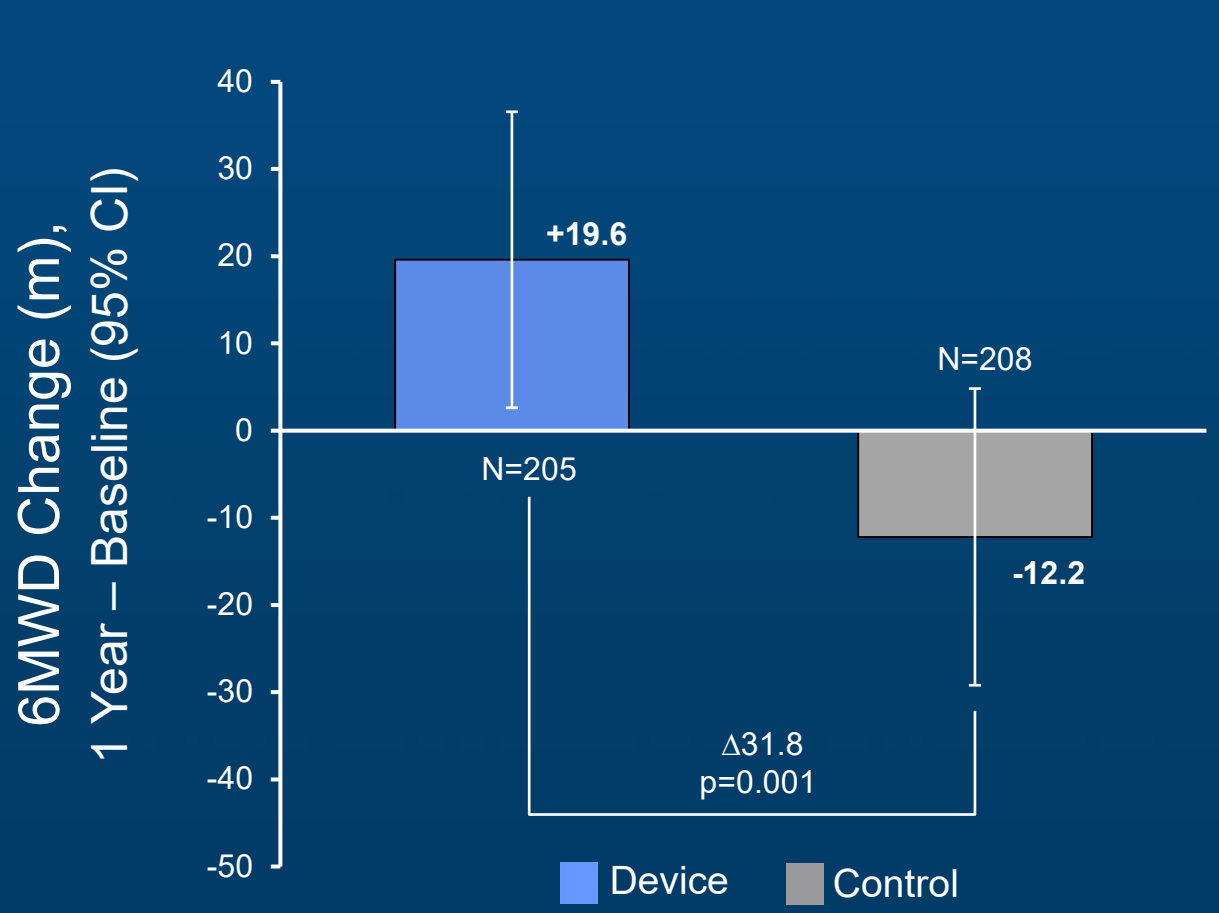
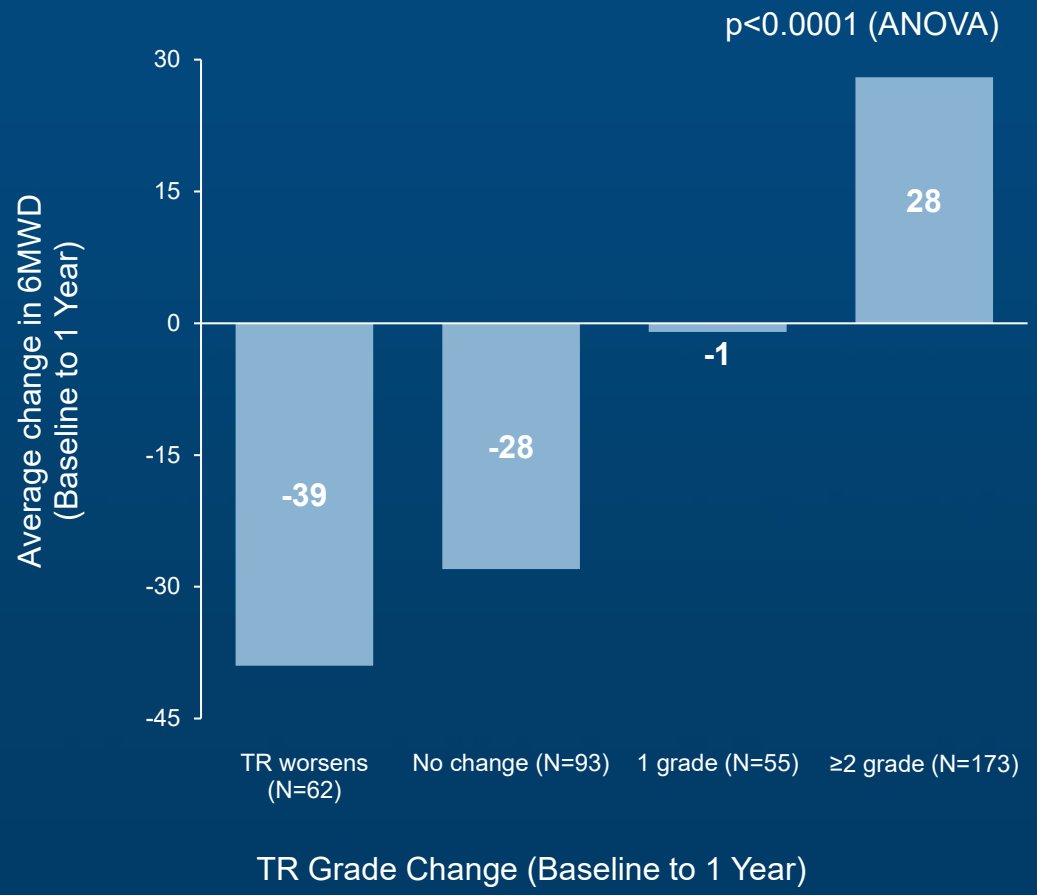
Data shown as mean±95%CI. For change in KCCQ by TR, data shown for device and control subjects.

TRILUMINATE™ PIVOTAL TRIAL

Change in 6MWD by TR Reduction





Significantly greater improvement in 6MWD in device group and change in 6MWD was associated with TR reduction

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Data shown as mean±95%CI. For change in 6MWD by TR, data shown for device and control subjects.

TRILUMINATE™ PIVOTAL TRIAL

Single-arm Cohort of TRILUMINATE Pivotal

Patient Population	Low likelihood of achieving moderate or less, with ability to reduce TR by 1 grade, considering factors such as: • TR severity • Presence and location of pacing lead • Coaptation gap size
Randomization	TriClip Only
Endpoint	Survival through 12 months with KCCQ improvement ≥ 10 points compared to baseline
Primary Analysis	100

Primary Endpoint

Survival through 12 months with a quality-of-life improvement (assessed using KCCQ overall score) of **at least 10 points** compared to baseline.

Single-arm and All Randomized Baseline Characteristics

Variable	Single-arm N=100	All Randomized N=572
Age, mean (years)*	**80.4 ± 6.2**	**78.1 ± 7.8**
Female	53% (53)	59% (337)
NYHA Class III or IV	59% (59)	55% (315)
KCCQ Score, mean	54.5 ± 22.6	55.1 ± 23.3
Renal disease	36% (36)	33% (191)
Liver disease	3% (3)	7% (41)
Atrial fibrillation	96% (96)	88% (502)
COPD	22% (22)	14% (82)
Presence of cardiac leads*	**35% (35)**	**16% (94)**
Prior aortic or mitral intervention*	**44% (44)**	**36% (207)**
Prior tricuspid intervention	4% (4)	0.3% (2)

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*Bolded gold font indicates p<0.05 (compared with all randomized cohort)

Single-arm and All Randomized Baseline Characteristics

Variable, cont.	Single-arm N=100	All Randomized N=572
TR Severity		
Moderate	0% (0)	2% (10)
Severe	9% (9)	27% (148)
Massive	17% (16)	21% (118)
Torrential*	**74% (71)**	**50% (277)**
Functional TR	86% (85)	95% (533)
Coaptation gap, mean (mm)*	**7.4 ± 2.7**	**5.3 ± 1.8**
RVEDD (mid, cm)*	**4.0 ± 0.8**	**3.7 ± 0.7**
RAV (mL)*	**182 ± 84**	**144 ± 80**
TV annulus diameter (cm)	4.6 ± 0.8	4.3 ± 0.8
RV TAPSE (cm)	1.6 ± 0.4	1.7 ± 0.4
LVEF (%)	58.9 ± 9.5	59.6 ± 9.1
CO (L/min)	4.3 ± 1.3	4.6 ± 1.4

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*Bolded gold font indicates $p<0.05$ (compared with all randomized cohort)

Single-arm and All Randomized Procedural Outcomes

Variable	Single-arm N=100	All Randomized TEER Subjects N=281
Technical Success	98.0%	98.9%
Device Time, mean (min)	84 ± 59	86 ± 63
Total Procedure Time, mean (min)	154 ± 65	147 ± 72
Number of clips, mean	2.2 ± 0.8	2.1 ± 0.7
Discharge to Home	96% (96)	98% (275)
Length of Stay, mean (days)	1.8 ± 2.1	1.5 ± 1.3
In-Hospital Mortality	0% (0)	0% (0)

Adams D, TCT 2023

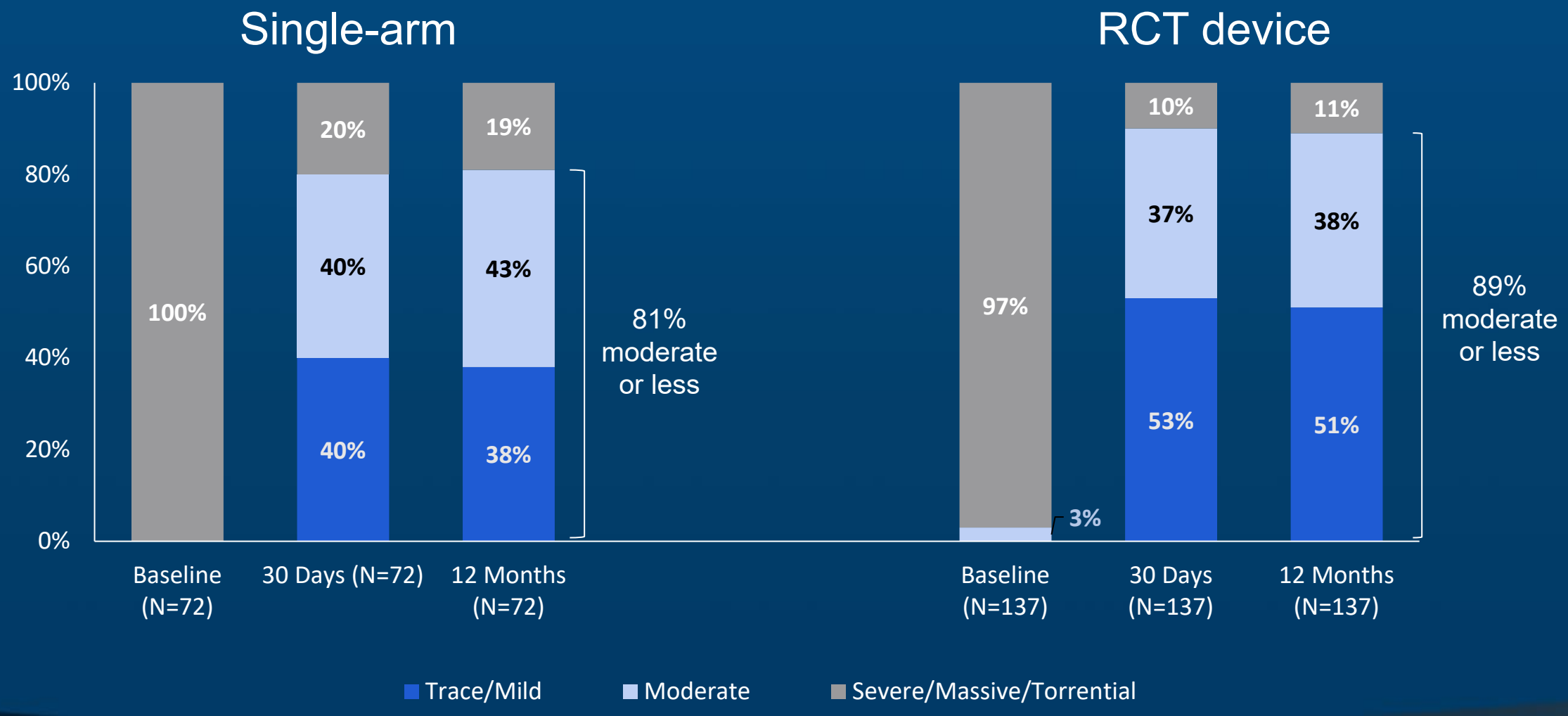
Adverse Events Through 30 Days

Major Adverse Events (MAEs)	Single-arm N=99
Total	0%
Cardiovascular mortality	0%
Endocarditis requiring surgery	0%
New-onset renal failure	0%
Non-elective CV Surgery, TVRS for device-related AE	0%

Other AEs	Single-arm N=99
Any-cause mortality	0%
Tricuspid valve surgery	0%
Tricuspid valve re-intervention	2%
Major bleeding	5%
Tricuspid mean gradient ≥5mmHg	3%
SLDA	7.5%
Stroke	0%
Myocardial Infarction	0%
Embolization	0%
Device thrombosis	0%
New pacemaker	0%

Adams D, TCT 2023

Sustained TR Reduction (Paired)



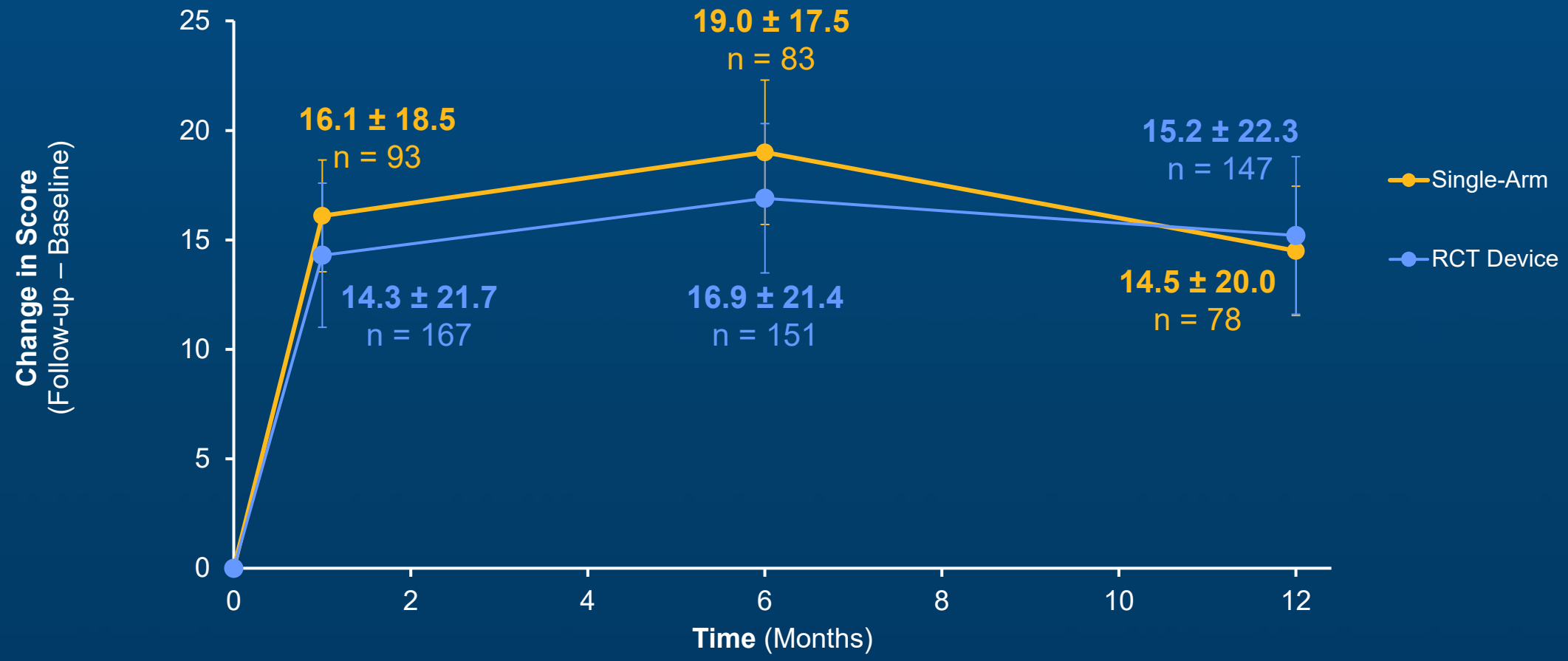
Adams D, TCT 2023

12-month All-cause Mortality and HFH

Variable	Single-arm N=100	RCT Device N=175
All-cause mortality	15.0%	8.6%
Heart failure hospitalization	24.0%	14.9%

Adams D, TCT 2023

KCCQ-OS Improvement



Adams D, TCT 2023

Single-arm Primary Endpoint

Single-arm	Estimate*	Lower 98.75% CI	Performance Goal	P value
Primary endpoint	46.2% (42/91)	34.3%	30%	0.0008

*Nine subjects excluded from analysis: Missing KCCQ score (n=6), COVID related death/hospitalization prior to 12 months (n=2), withdrew prior to 12 months (n=1).

Primary Endpoint

Survival through 12 months with a quality-of-life improvement (assessed using KCCQ overall score) of at least 10 points compared to baseline (performance goal of 30%).

✓ **Primary endpoint met despite more anatomically complex patients.**

Adams D, TCT 2023

Conclusions

- T-TEER with TriClip showed an excellent safety profile with low rates of adverse events
- The primary endpoint was strengthened in the full randomized cohort
  - Primary endpoint continues to be primarily driven by improvements in health status
  - HFH favored the device group in the subsequently enrolled cohort
- All secondary endpoints significantly favored the Device group (KCCQ, 6MWD, and TR reduction)
- Despite the complex anatomies present in the single-arm cohort, outcomes between single-arm and randomized cohorts were comparable, including 30-day safety, sustained TR reduction, and 12-month change in KCCQ-OS.

Clinical Data – TRI.fr Trial

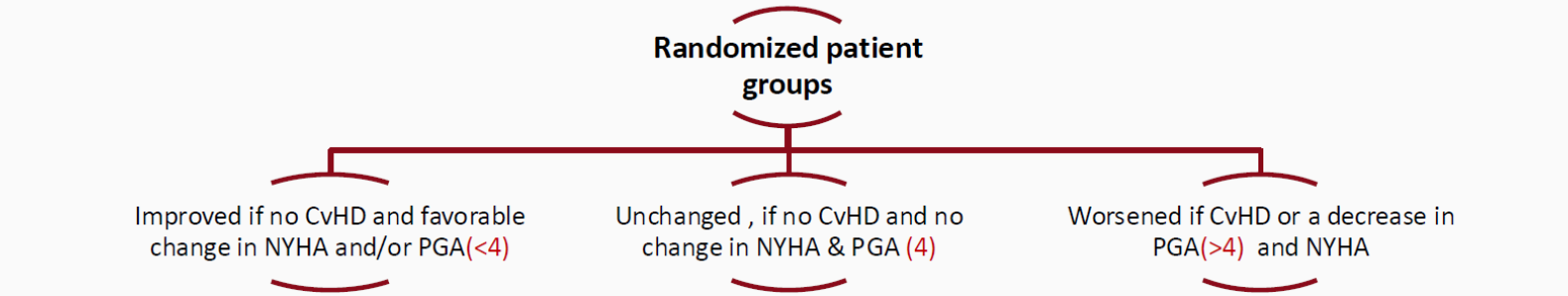
Primary Endpoint: Clinical Composite Score

The **Clinical Composite Score:**
at 12-month post randomization

- Occurrence of major cardio-vascular events (cardiovascular hospitalization and/or death (CvHD)
- Changes in the NYHA class, or
- Patient global assessment (PGA) and

PGA
Patients were asked how they felt:

- ○ 1. Markedly improved
- ○ 2. Moderately improved
- ○ 3. Mildly improved
- ○ 4. No change
- ○ 5. Slightly worse
- ○ 6. Moderately worse
- ○ 7. Markedly worse



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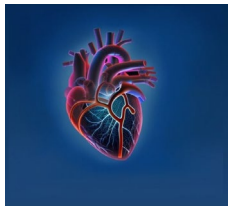
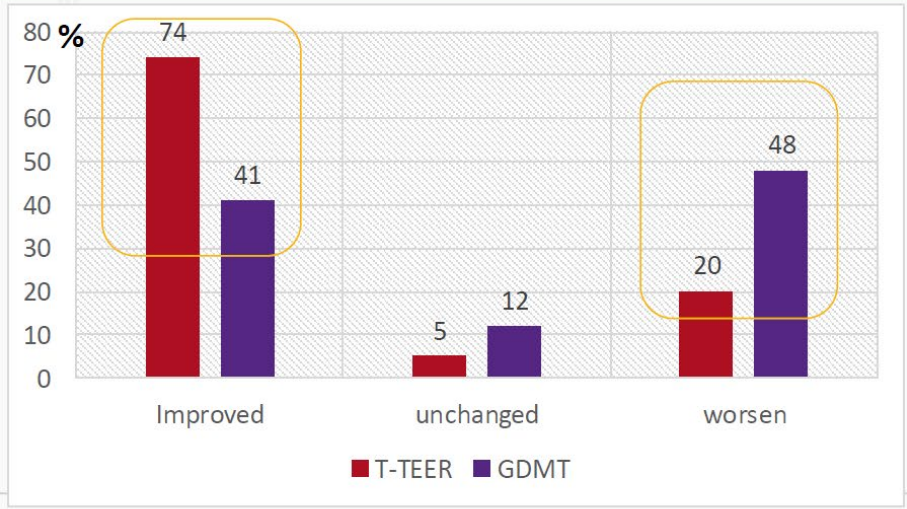


Clinical Data – TRI.fr Trial

Primary Endpoint (ITT) (1)

At 1-year follow-up, 109 patients (74.1%) in the T-TEER group improved, compared to 58 patients (40.6%) in the GDMT group

The T-TEER group has a probability of a better rank of 0.67; 95% confidence interval, 0.61 to 0.72; P <.0001



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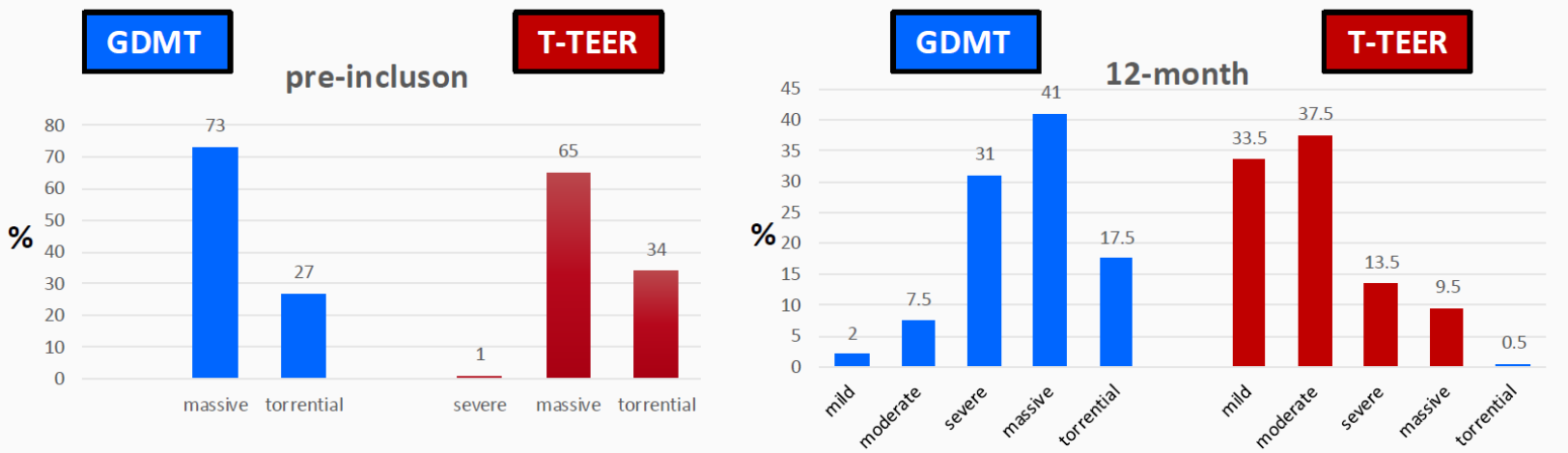
Clinical Data – TRI.fr Trial

Secondary endpoint: TR-Grade



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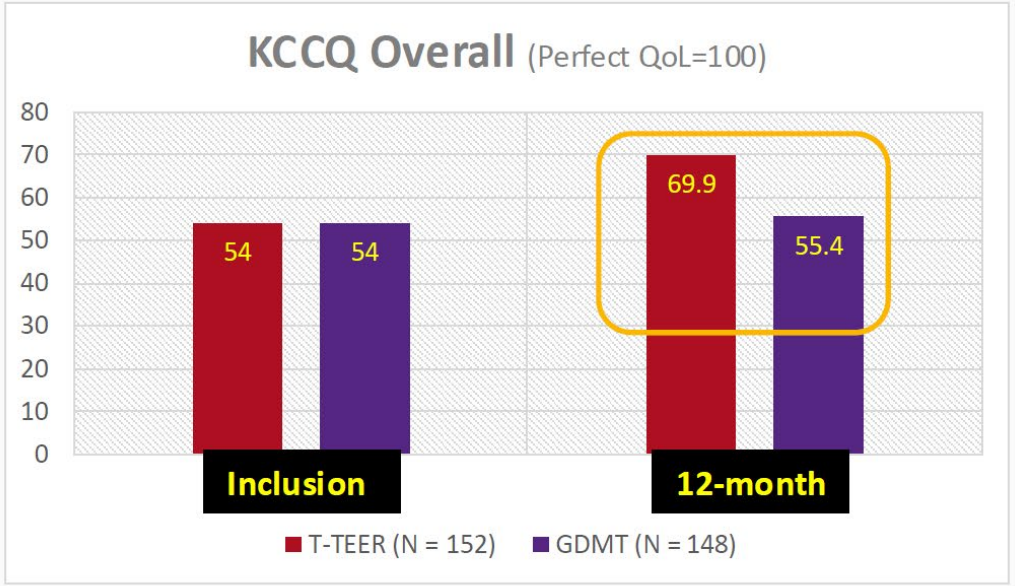
Clinical Data – TRI.fr Trial

Secondary endpoints: KCCQ



Overall KCCQ Summary Score at the 1-year follow-up:

T-TEER (69.9 ± 25.5) vs. control group (55.4 ± 28.8)

Absolute difference = 14.5±27.2, p<0.001

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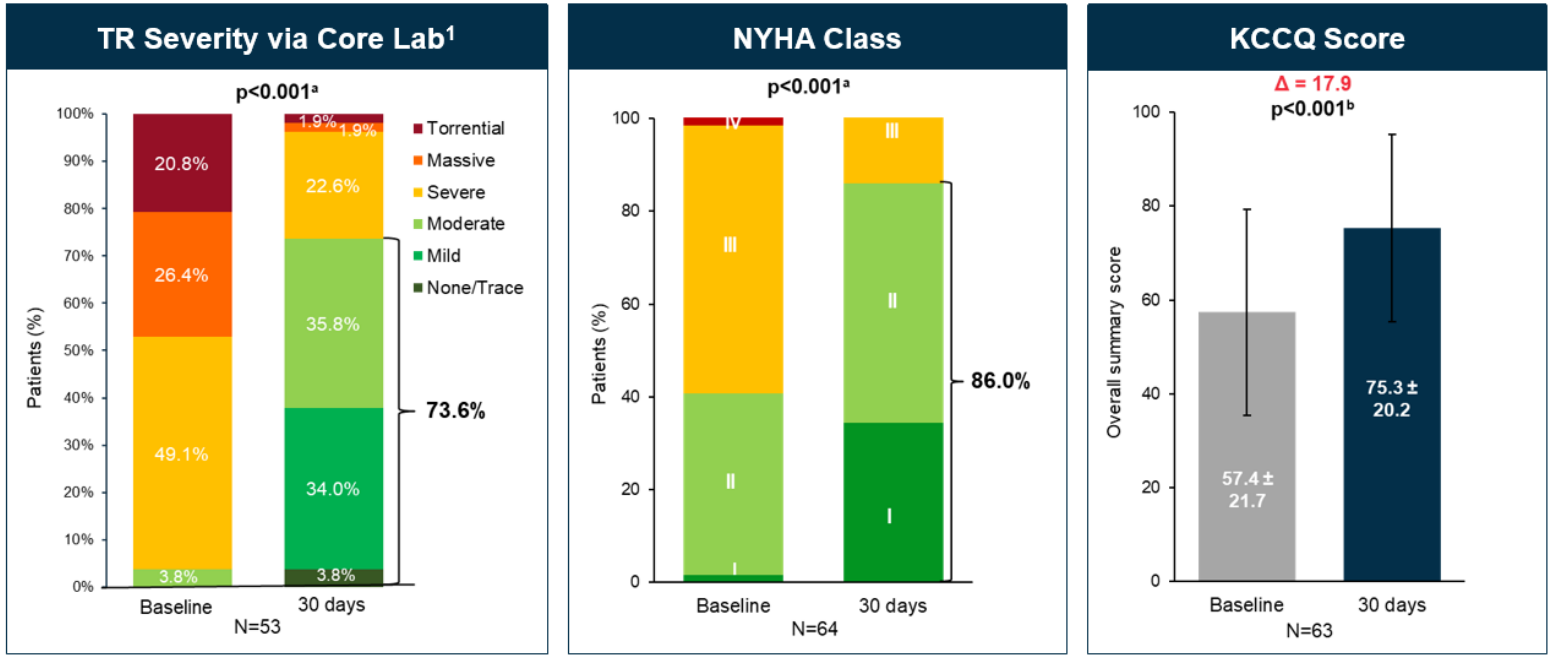
Clinical Data – CLASP II TR Trial (Roll-in Cohort)

Roll-in cohort:

THE CLASP II TR TRIAL

TR Reduction with Clinical and Quality-of-Life Improvements



83.0% improved by ≥ 1 TR grade, 62.3% by ≥ 2 grades, and 73.6% reached ≤ moderate TR at 30 days

[1]Core laboratory: Cardiovascular Research Foundation. [a]Wilcoxon signed-rank test. [b]Paired t-test. *TR*, tricuspid regurgitation; *NYHA*, New York Heart Association; *KCCQ*, Kansas City Cardiomyopathy Questionnaire

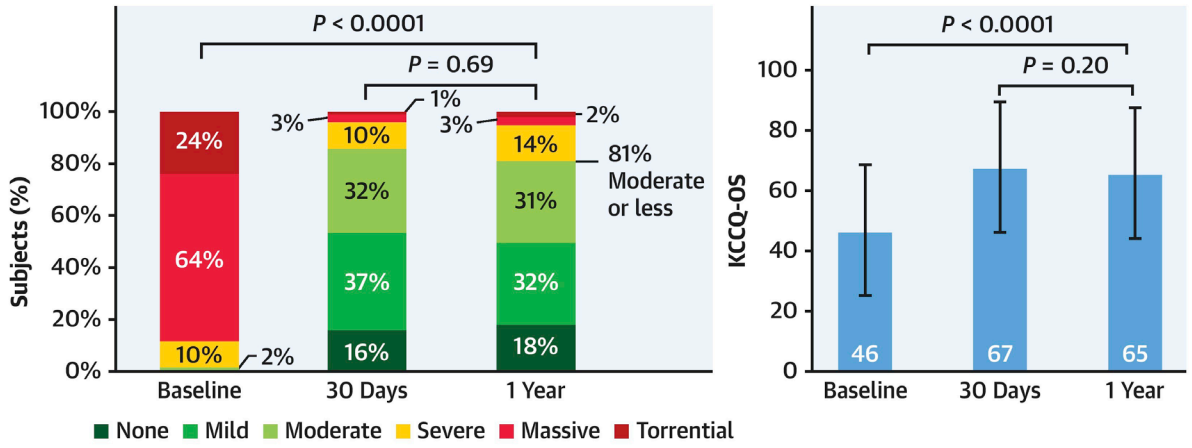
Wang D, TVT 2023

Real-World Data – bRIGHT and PASTE Registries

CENTRAL ILLUSTRATION: 1-Year Tricuspid Regurgitation Reduction and Quality-of-Life Improvement With Tricuspid Transcatheter Edge-to-Edge Repair

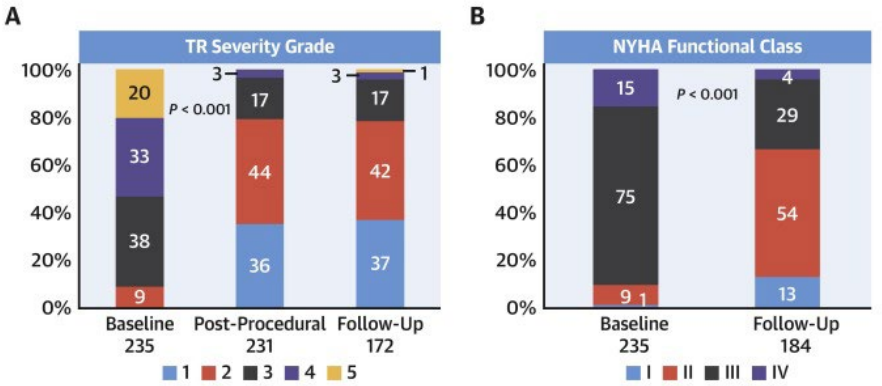
Diverse Real-World Population Treated With Tricuspid Transcatheter Edge-to-Edge Repair

Significant and Sustained 1-Year TR Reduction and Quality-of-Life Improvement



Lurz P, et al. J Am Coll Cardiol. 2024;84(7):607-616.

CENTRAL ILLUSTRATION: Multicenter Experience With Transcatheter Tricuspid Leaflet Repair (N = 235)



C

10 mm

PASCAL, (n = 149)		PASCAL Ace, (n = 82)
93%	Technical success	93%
77%	TR ≤ moderate	78%
1.6 ± 0.6	No. of devices	1.8 ± 0.7
103 ± 46 min	Procedure time	111 ± 60 min

5-6 mm

Wild MG, et al. J Am Coll Cardiol Intv. 2022;15(13):1352-1363.

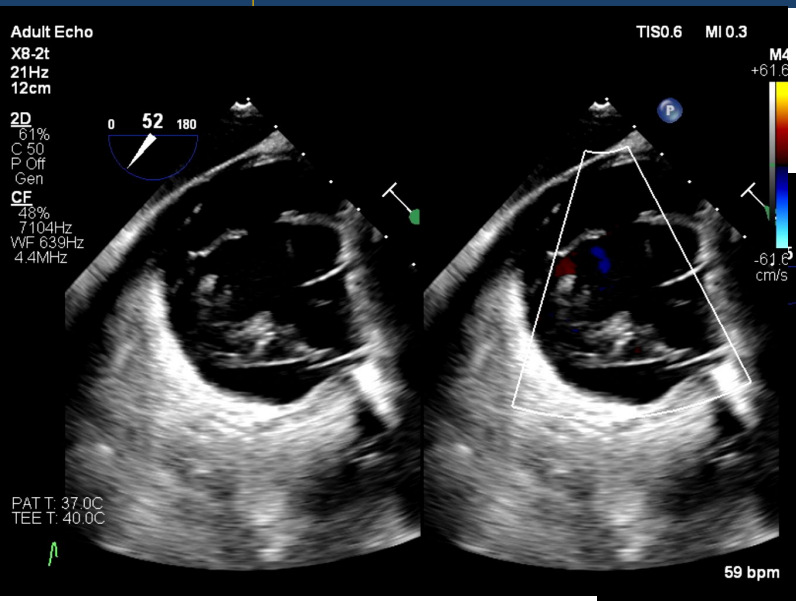
TEER vs Medical Management - Common Theme

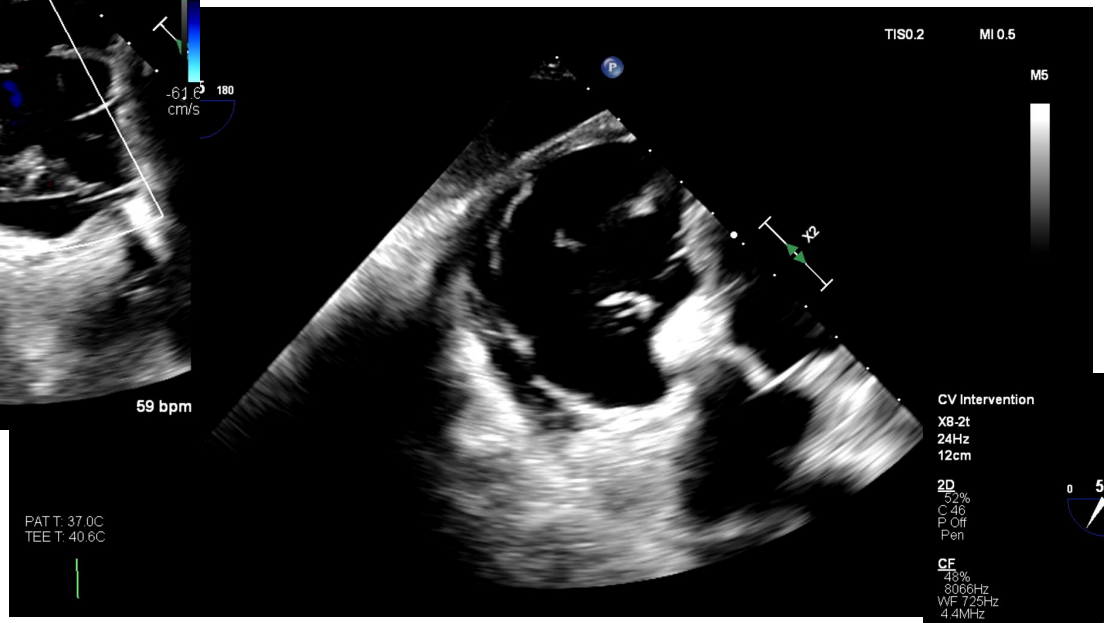
- T-TEER is a safe procedure that reduces TR to moderate or less in 70% to 90% of patients.
- T-TEER reduces symptoms to improves quality of life and may reduce HF hospitalizations.
- T-TEER has not been shown to reduce mortality.

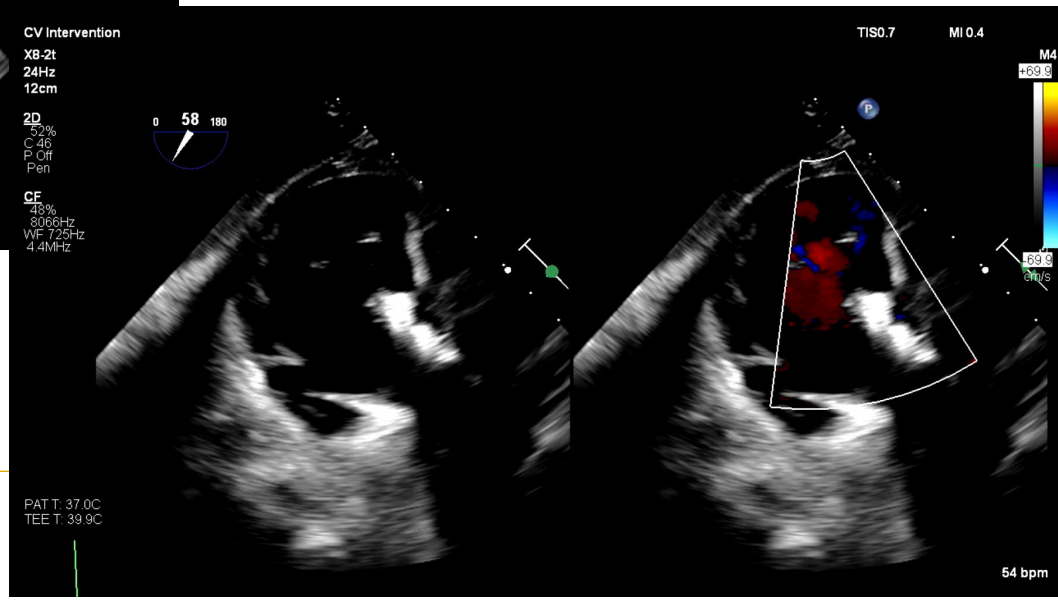
Case – 82yo F with dyspnea and fatigue

- Hx emergent hemiarch replacement for Type A aortic dissection at 79yo
- CKD 3b
- PAF – anticoagulation w/apixaban
- Pulm HTN
- Hx liver biopsy for abnormal LFTs, severe fibrosis by US w/elastography
- RHC – RA 23, PA 40/25/30, PCW 25, TD CO/CI 1.5/0.89, Fick CO/CI 1.39/0.82
- RHC – RA 9, PA 36/16/23, PCW 13, TD CO/CI 2.78/1.68, Fick CO/CI 2.08/1.26

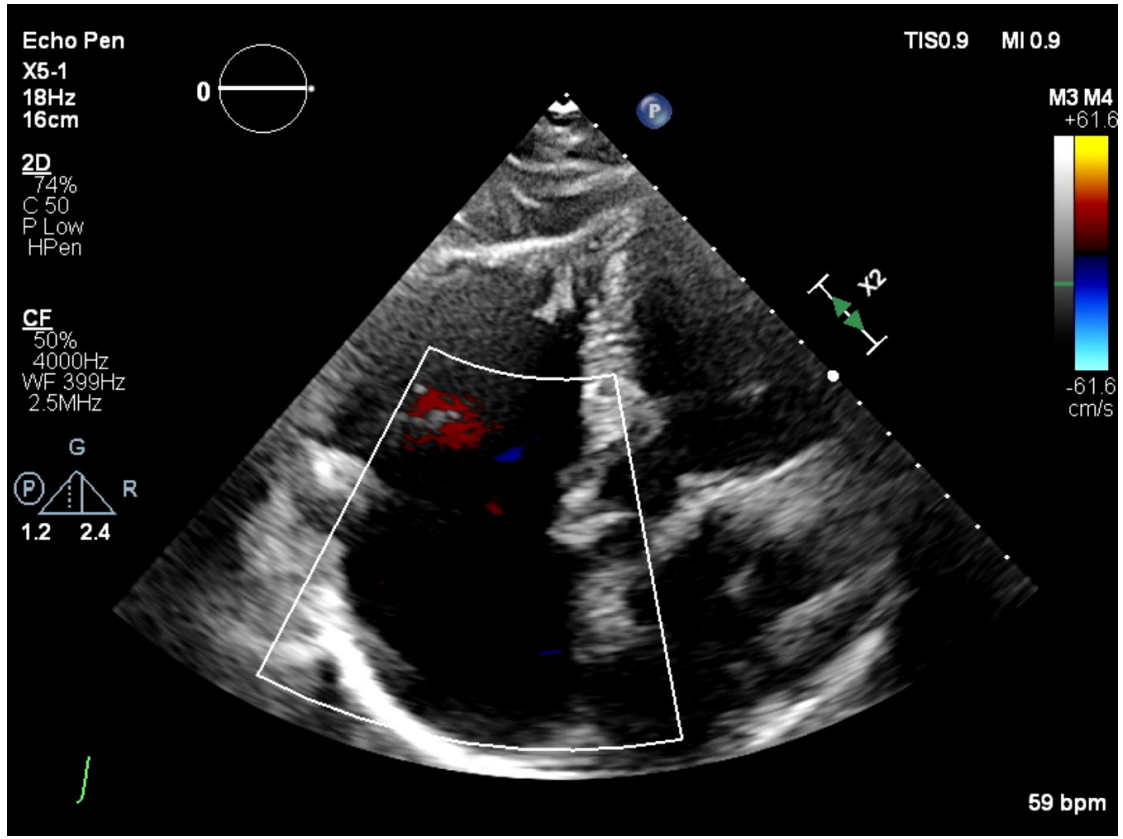
Case – 82yo F with dyspnea and fatigue

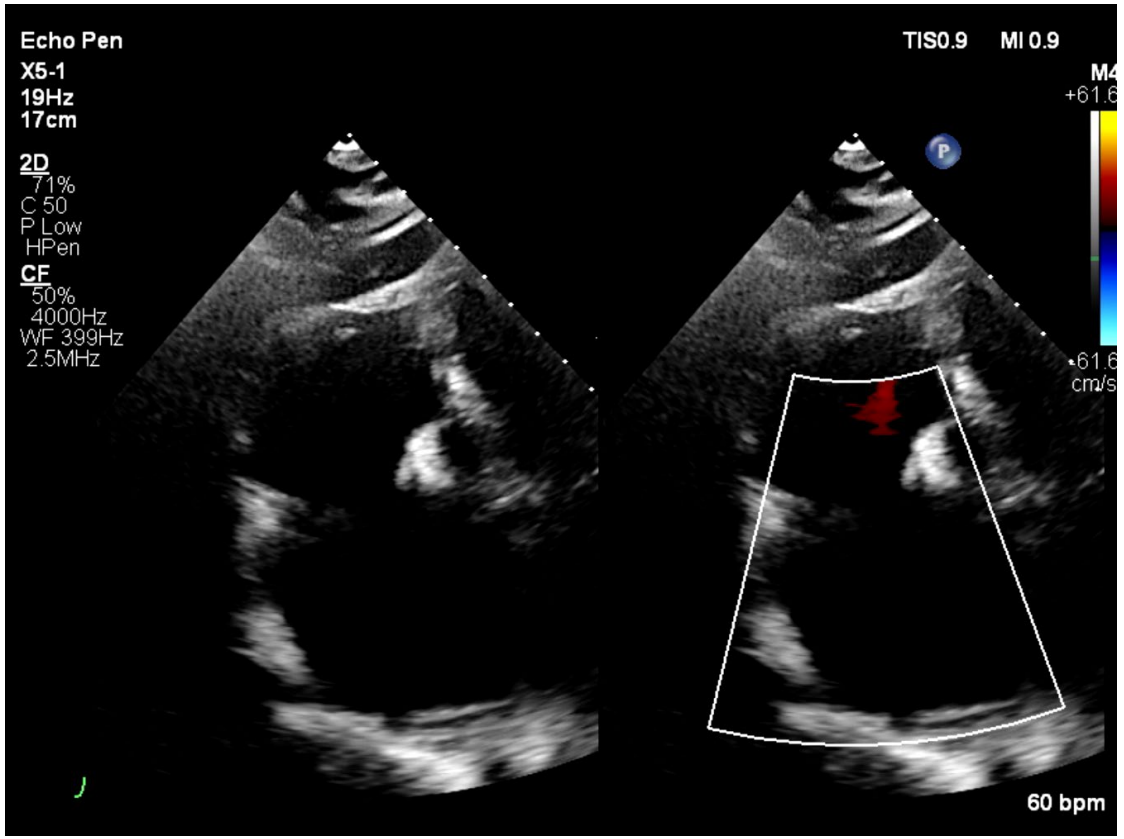






Case – 82yo F with dyspnea and fatigue





Conclusion

- Untreated severe or greater TR is associated with increased mortality.
- Medical management of TR primarily consists of diuretics and treatment of underlying etiologies such as pulmonary hypertension or left heart disease when indicated.
- Contemporary outcomes for isolated tricuspid valve surgery have improved but mortality remains elevated.
- T-TEER is a safe treatment option that can significantly reduce TR, improve quality of life, and may also reduced heart failure hospitalizations for patients who are at increased risk for surgery.

THANK YOU