Tricuspid Regurgitation

Yan Topilsky
Tel Aviv Medical Center

Natural History of Tricuspid Regurgitation

- Etiology based natural history trials
- Outcome with surgery
- Outcome with contemporary heart failure therapy
- The TRILUMINATE control arm
- The Pathophysiology and new Classification of Tricuspid Regurgitation

Journal of the American College of Cardiology
© 2004 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 43, No. 3, 2004
ISSN 0735-1097/04/$30.00
doi:10.1016/j.jacc.2003.09.036

Impact of Tricuspid Regurgitation on Long-Term Survival

Jayant Nath, MD,* Elyse Foster, MD, FACC,† Paul A. Heidenreich, MD*
Palo Alto and San Francisco, California

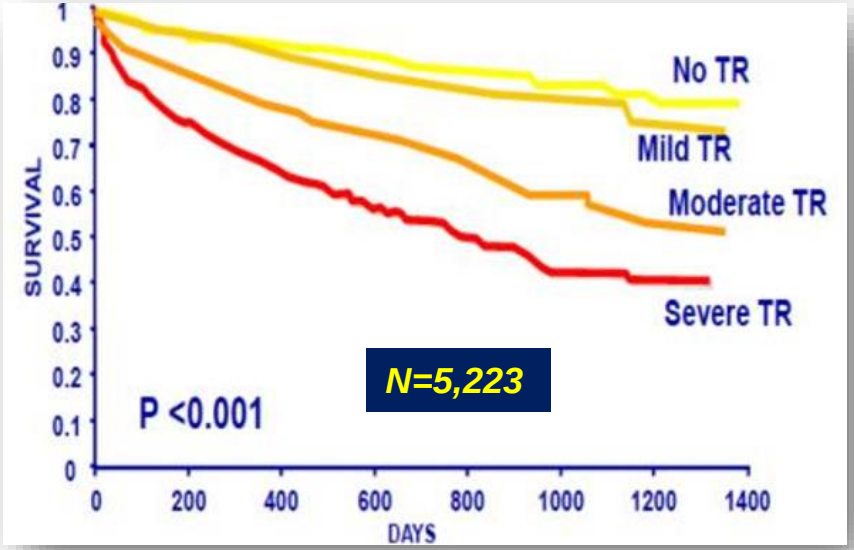


Table 1. Clinical and Echocardiographic Features of Patients With Tricuspid Regurgitation

	No TR (n = 600)	Mild TR (n = 3,804)	Moderate TR (n = 620)	Severe TR (n = 199)	p Value
Age (yrs)	62.2 ± 12.8	66.0 ± 12.6	71.9 ± 11.7	71.9 ± 12.4	< 0.0001
LVEF (%)	57.3 ± 9.1	55.4 ± 11.6	47.1 ± 15.6	40.4 ± 17.2	< 0.0001
RV dilation	8%	11%	35%	66%	< 0.0001
RV dysfunction	3%	8%	30%	61%	< 0.0001
Dilated IVC	6%	11%	44%	76%	< 0.0001

Data are presented as the mean value ± SD or percentage of patients.
IVC = inferior vena cava; LVEF = left ventricular ejection fraction; RV = right ventricular; TR = tricuspid regurgitation.

One year mortality with severe TR was ≈35%

Nath J. et al JACC

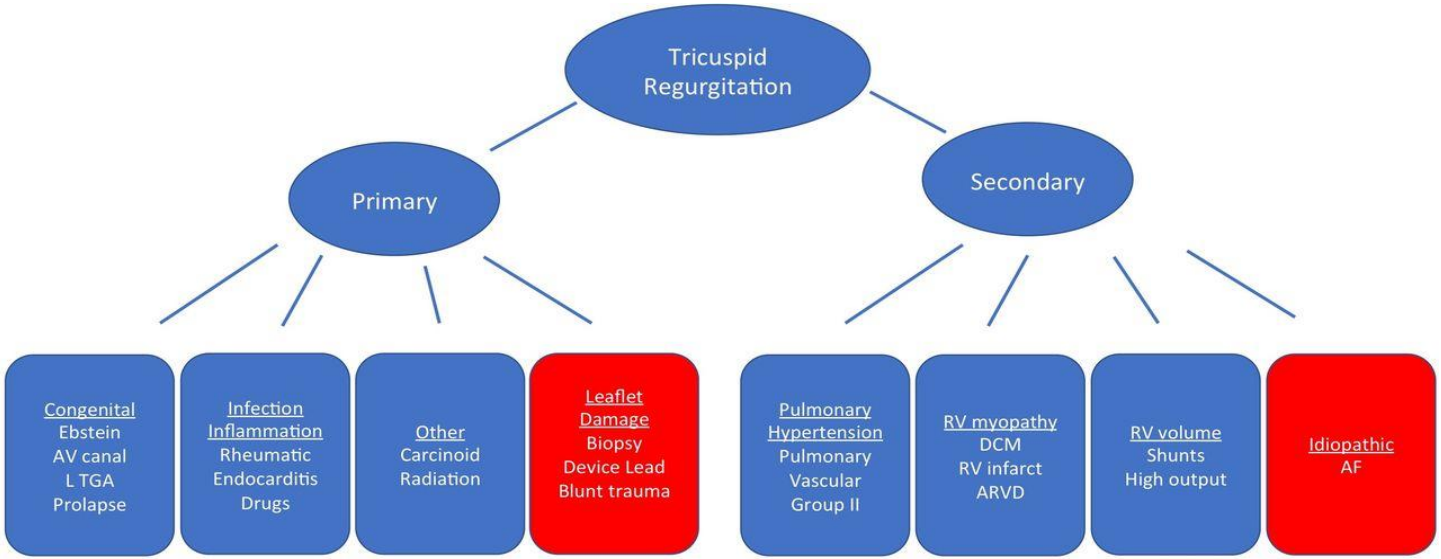
- Systemic co-morbidities were not recorded
- Only hospitalized patients
- Mixed etiologies of TR
- TR was not quantified
- Outdated heart failure therapy

Thus, TR may be just a surrogate of mortality

Etiologic classification of Tricuspid Regurgitation

Isolated tricuspid regurgitation: outcomes and therapeutic interventions

Erin A Fender,[1] Chad J Zack,[1,2] Rick A Nishimura[1]

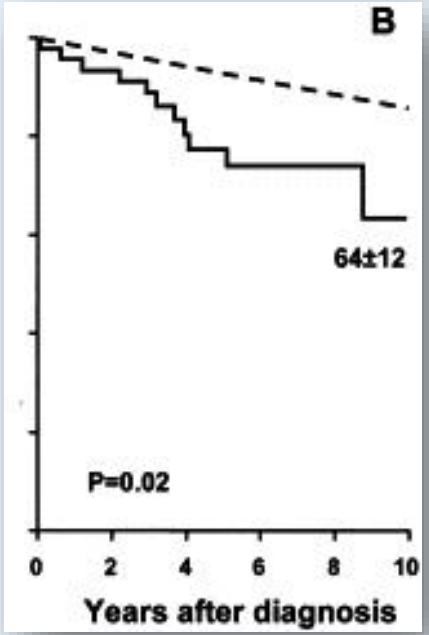


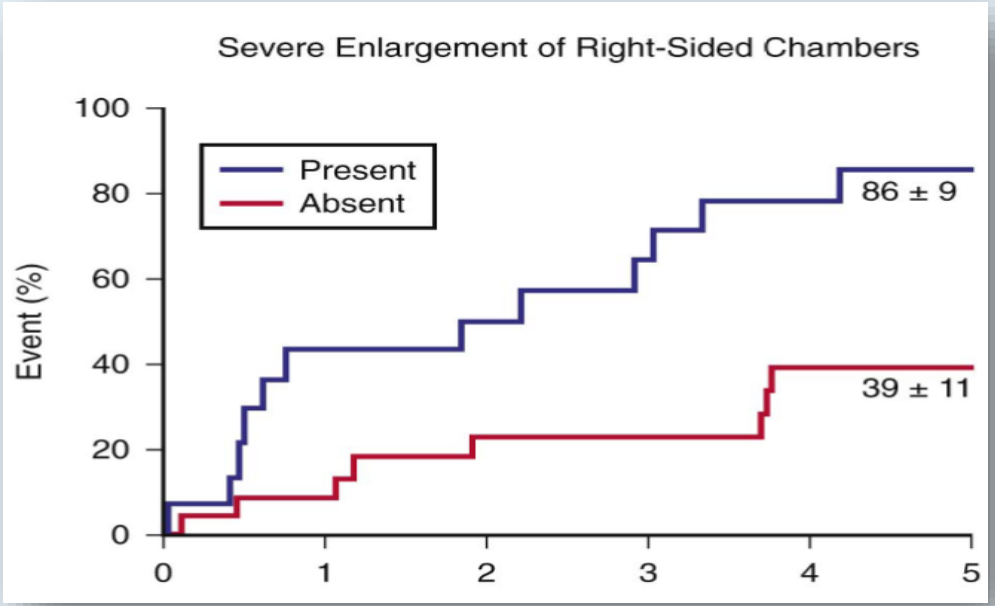
Fender EA, *et al*. *Heart* 2017;**0**:1–9. doi:10.1136/heartjnl-2017-311586

Outcome of untreated TR stratified by etiology
Organic TR

Medical and surgical outcome of tricuspid regurgitation caused by flail leaflets

Messika-Zeitoun D et al. J Thorac Cardiovasc Surg 2004;128:296-302





Significant lead-induced tricuspid regurgitation is associated with poor prognosis at long-term follow-up

Ulas Höke,[1,2] Dominique Auger,[1] Joep Thijssen,[1] Ron Wolterbeek,[3] Enno T van der Velde,[1] Eduard R Holman,[1] Martin J Schalij,[1] Jeroen J Bax,[1] Victoria Delgado,[1] Nina Ajmone Marsan[1]

Höke U, *et al*. *Heart* 2014;**100**:960–968.

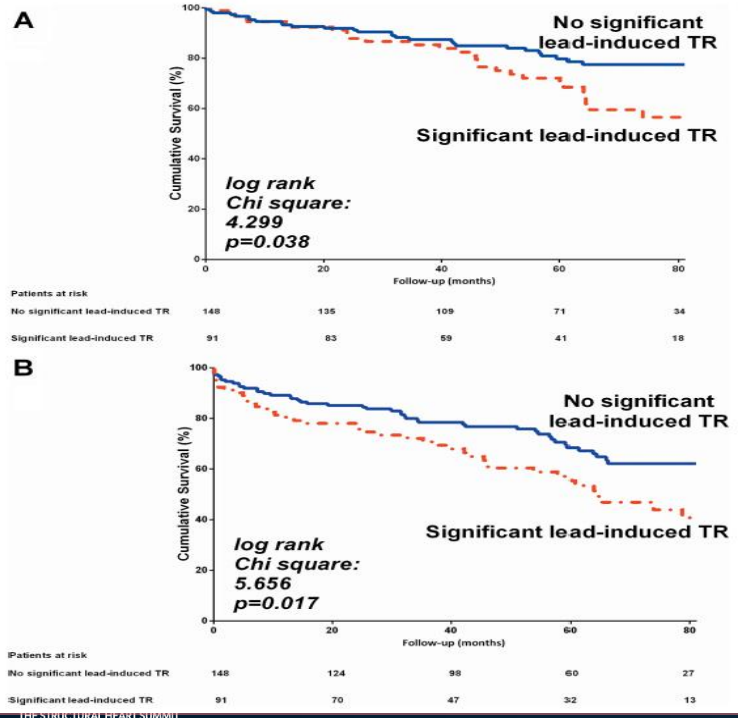


Table 3 Univariate and multivariate Cox regression survival analysis for the primary endpoint (all-cause mortality)

	Univariate analysis			Multivariate analysis		
Variables	**HR**	**95% CI**	**p Value**	**HR**	**95% CI**	**p Value**
Age, per year	1.079	1.048 to 1.112	**<0.001**	1.064	1.032 to 1.098	**<0.001**
Male sex	1.194	0.635 to 2.246	0.582			
Ischaemic aetiology	1.684	0.963 to 2.944	0.068			
Atrial fibrillation	1.373	0.823 to 2.290	0.224			
Diabetes	1.705	0.963 to 3.018	0.067			
ICD system (versus PM)	0.897	0.507 to 1.589	0.710			
Percentage of pacing, per %	1.007	1.002 to 1.013	**0.006**	1.008	1.002 to 1.015	**0.008**
LVEDV, per mL	1.005	1.002 to 1.009	**0.001**			
LVESV, per mL	1.007	1.004 to 1.011	**<0.001**			
LVEF, per %	0.968	0.946 to 0.990	**0.005**	0.973	0.947 to 0.999	**0.041**
Mitral regurgitation grade 0 (reference group)			**0.028**			0.510
Mitral regurgitation grade 1 (vs reference group)	0.449	0.219 to 0.922		1.185	0.522 to 2.691	
Mitral regurgitation grade 2 (vs reference group)	0.840	0.409 to 1.727		1.445	0.626 to 3.336	
Mitral regurgitation grade 3 (vs reference group)	1.815	0.737 to 4.468		2.067	0.695 to 6.146	
Mitral regurgitation grade 4 (vs reference group)	2.695	0.632 to 11.483		2.634	0.662 to 10.488	
RV end-diastolic area, per mm^2	1.069	1.025 to 1.114	**0.002**			
RV fractional area change, per %	0.975	0.953 to 0.996	**0.022**			
TAPSE, per mm	0.914	0.856 to 0.976	**0.007**	0.974	0.910 to 1.042	0.447
Right atrial diameter, per mm	1.412	1.071 to 1.861	**0.014**			
Tricuspid annular diameter, per mm	1.748	1.325 to 2.306	**<0.001**			
sPAP, per mm Hg	1.046	1.029 to 1.063	**<0.001**			
Significant lead-induced TR	1.687	1.023 to 2.780	**0.040**	1.749	1.008 to 3.035	**0.047**

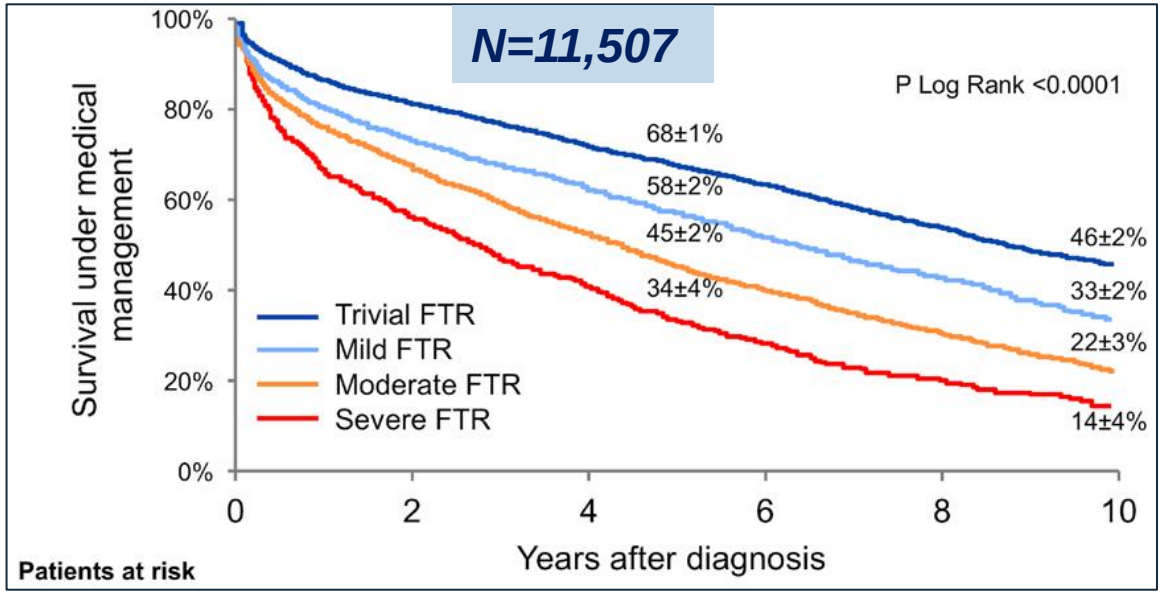
Bold values are statistically significant.
ICD, implantable cardioverter-defibrillator; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular EF; LVESV, left ventricular end-systolic volume; PM, permanent pacemaker; sPAP, systolic pulmonary arterial pressure; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation.

Outcome of untreated TR stratified by etiology
Functional TR

HFrEF

ORIGINAL RESEARCH ARTICLE

Excess Mortality Associated With Functional Tricuspid Regurgitation Complicating Heart Failure With Reduced Ejection Fraction

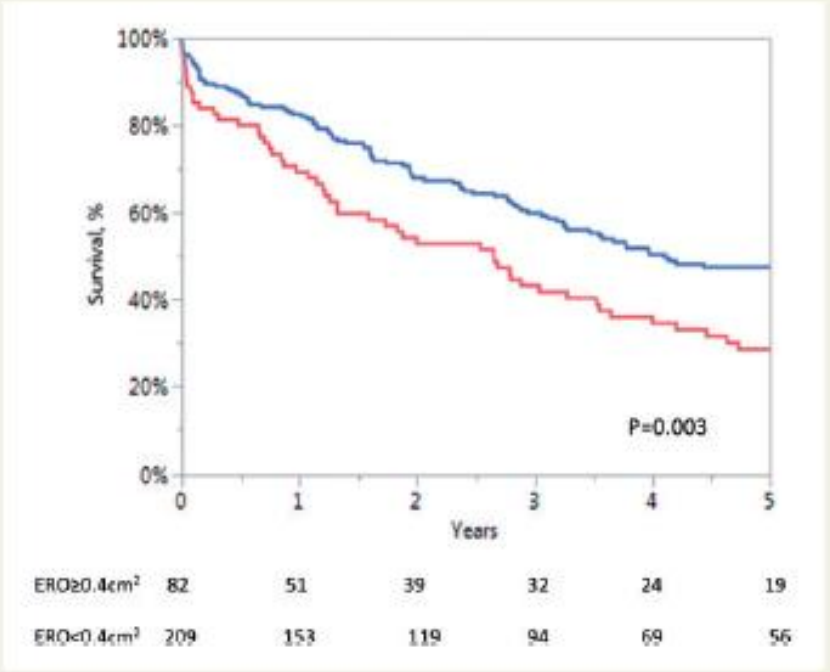


Giovanni Benfari, MD
Clemence Antoine, MD
Wayne L. Miller, MD, PhD
Prabin Thapa, BS
Yan Topilsky, MD
Andrea Rossi, MD
Hector I. Michelena, MD
Sorin Pislaru, MD
Maurice Enriquez-Sarano, MD

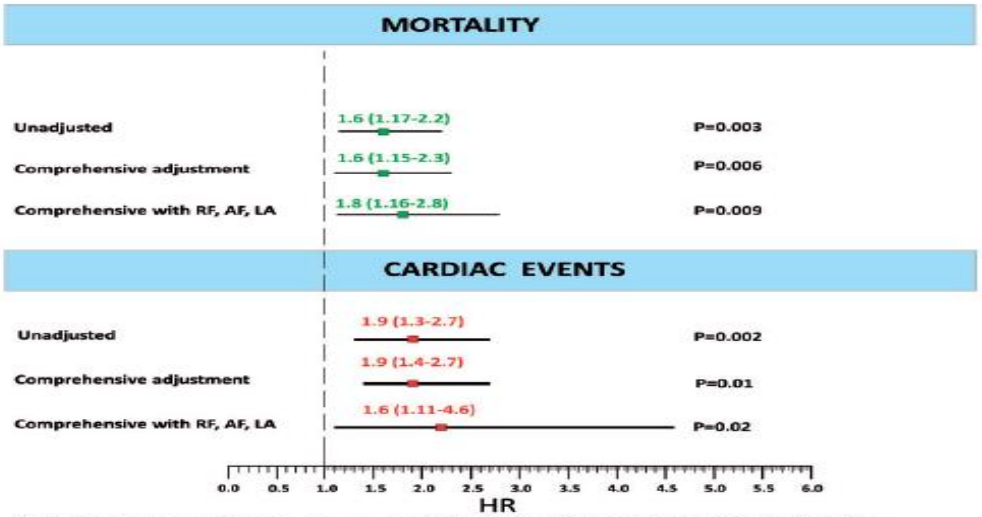
ESC European Society of Cardiology
European Heart Journal (2018) 0, 1–9
doi:10.1093/eurheartj/ehy434

Clinical presentation and outcome of tricuspid regurgitation in patients with systolic dysfunction

Yan Topilsky[1], Jose Medina Inojosa[2], Giovanni Benfari[2], Ori Vaturi[2], Simon Maltais[2], Hector Michelena[2], Sunil Mankad[2], and Maurice Enriquez-Sarano[2]*



Impact of severe regurgitation (effective-regurgitant-orifice ≥ 0.4 cm2), compared to lesser degree of TR, on mortality and cardiovascular events risk after the diagnosis of tricuspid regurgitation in patients with systolic dysfunction.



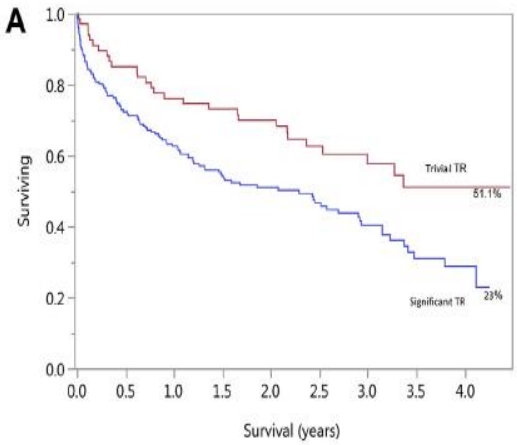
* Adjustment was for age, sex, co-morbidity index, left ventricular ejection fraction, right ventricular dysfunction ≥ moderate and right ventricular systolic pressure.

** Adjustment was for age, sex, co-morbidity index, left ventricular ejection fraction, right ventricular dysfunction ≥ moderate, renal failure(RF), atrial fibrillation(AF), LA size and right ventricular systolic pressure.

Clinical Outcome of Isolated Tricuspid Regurgitation in Patients with Preserved Left Ventricular Ejection Fraction and Pulmonary Hypertension

Nir Bar, MD, Lorin Arie Schwartz, MD, Simon Biner, MD, Galit Aviram, MD, Meirav Ingbir, MD, Ido Nachmany, MD, Gilad Margolis, MD, Ben Sadeh, MD, Rami Barashi, MD, Gad Keren, MD, and Yan Topilsky, MD, *Tel Aviv, Israel*

Journal of the American Society of Echocardiography
■ 2017



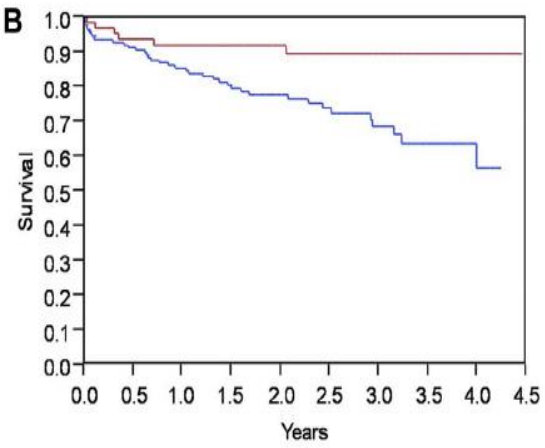


Table 4 Multivariate analysis for associates for survival

	HR	*P* value model
At least moderate to severe TR for mortality		
Univariate analysis	1.8	.004
Adjusted for all clinical parameters*	1.8	<.0001
Adjusted for tricuspid annulus alone	1.7	.005
Adjusted for TAPSE alone	1.7	.0007
Adjusted for echocardiographic parameters†	1.6	<.0001
Adjusted for all echocardiographic† and clinical* parameters	1.5	<.0001
VC for mortality		
Univariate analysis	1.08	.001
Adjusted for tricuspid annulus alone	1.07	.001
Adjusted for TAPSE alone	1.08	<.0001
Adjusted for all clinical parameters*	1.07	.0002
Adjusted for all echocardiographic parameters†	1.06	<.0001
Adjusted for all echocardiographic† and clinical* parameters	1.06	<.0001

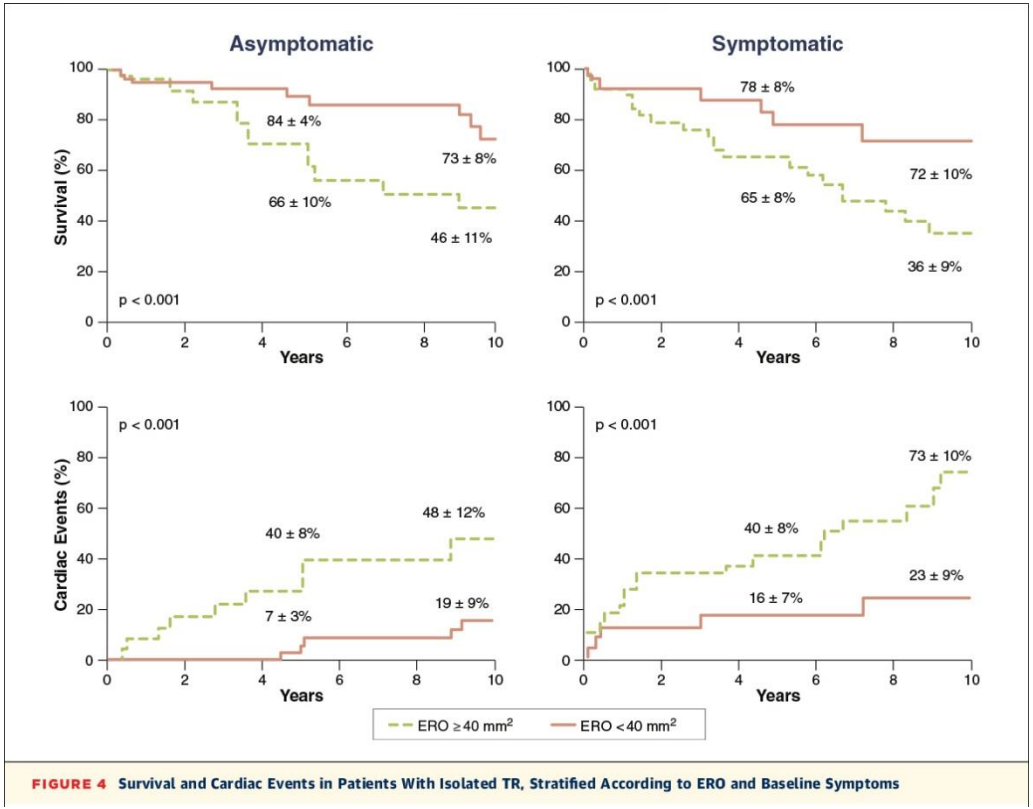


FIGURE 4 Survival and Cardiac Events in Patients With Isolated TR, Stratified According to ERO and Baseline Symptoms

JACC: CARDIOVASCULAR IMAGING
© 2014 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER INC.
VOL. 7, NO. 12, 2014
ISSN 1936-878X/$36.00
http://dx.doi.org/10.1016/j.jcmg.2014.07.018

ORIGINAL RESEARCH

Clinical Outcome of Isolated Tricuspid Regurgitation

Yan Topilsky, MD,* Vuyisile T. Nkomo, MD,† Ori Vatury, MD,† Hector I. Michelena, MD,† Thierry Letourneau, MD,† Rakesh M. Suri, MD, DPhil,‡ Sorin Pislaru, MD,† Soon Park, MD,‡ Douglas W. Mahoney, MSc,§ Simon Biner, MD,* Maurice Enriquez-Sarano, MD†

Topilsky; JACC, 2014

Outcome of TR with surgery

Isolated Tricuspid Surgery

- *290/year in 2004 (67% replacement)*
- *780/year in 2013 (57% replacement)*

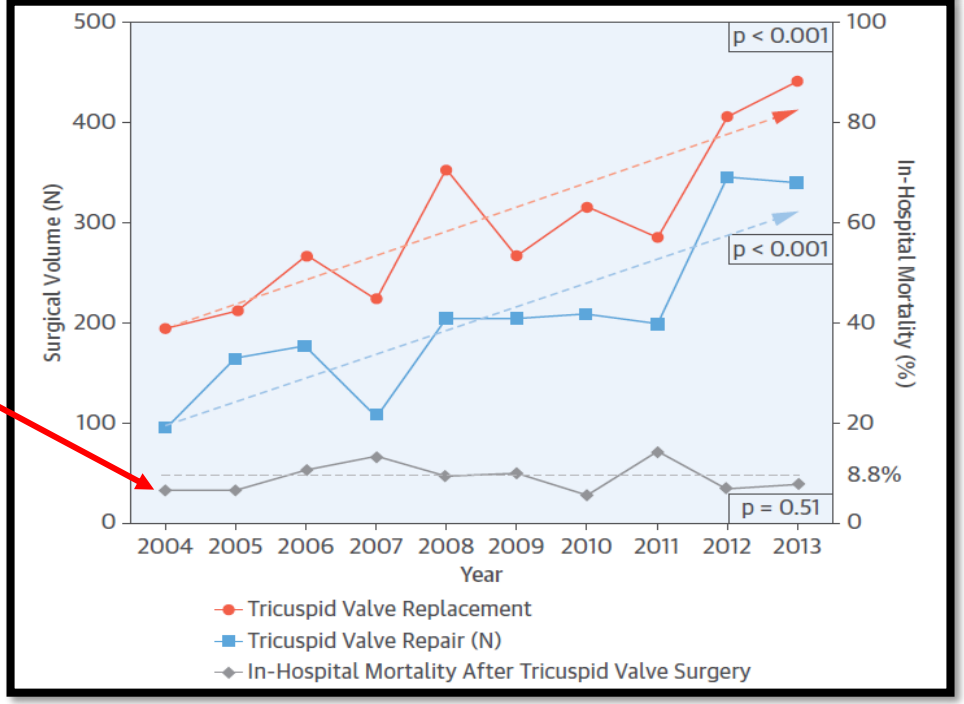
The database represents ≈20% of hospital admissions in the USA (approximately 1000 hospitals

- *Highest mortality (10.9%) for TV replacements*
- *Long hospital stay (median 11 days)*
- *26% pacemakers*

ORIGINAL INVESTIGATIONS

National Trends and Outcomes in Isolated Tricuspid Valve Surgery

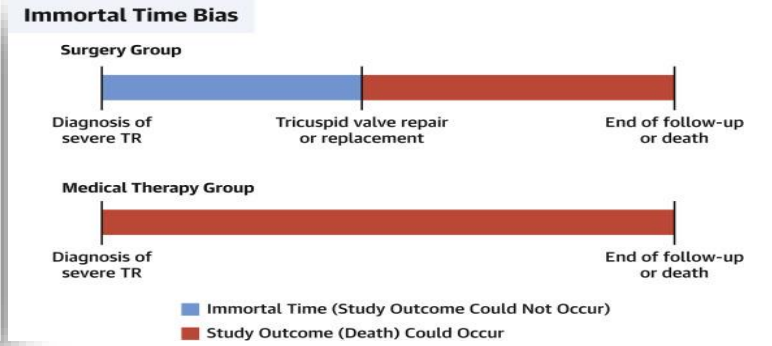
Chad J. Zack, MD,[a] Erin A. Fender, MD,[a] Pranav Chandrashekar, MBBS,[a] Yogesh N.V. Reddy, MBBS,[a] Courtney E. Bennett, DO,[a,b] John M. Stulak, MD,[c] Virginia M. Miller, PhD,[c,d] Rick A. Nishimura, MD[a]



Zack; JACC 2017

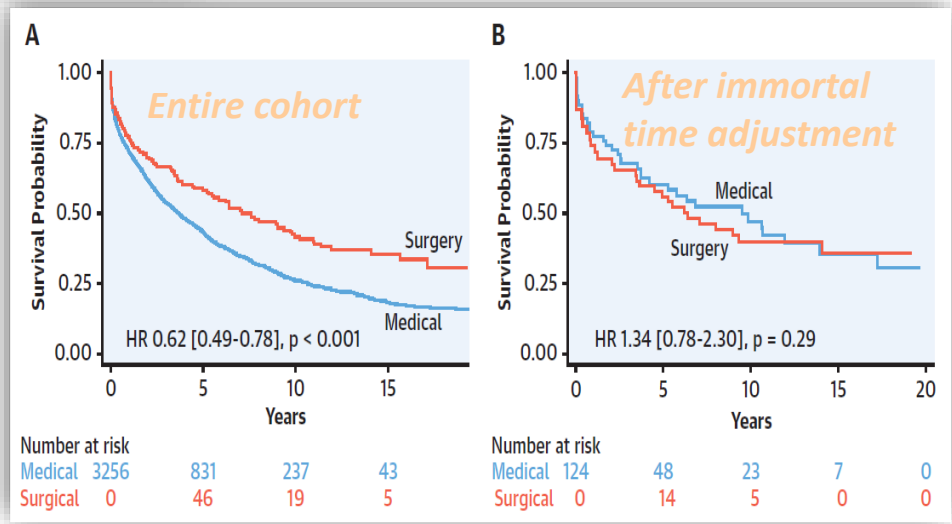
Surgery Does Not Improve Survival in Patients With Isolated Severe Tricuspid Regurgitation

Andrea L. Axtell, MD, MPH,[a,b] Vijeta Bhambhani, MS, MPH,[c] Philicia Moonsamy, MD,[a,d] Emma W. Healy, BS,[c] Michael H. Picard, MD,[c] Thoralf M. Sundt III, MD,[a] Jason H. Wasfy, MD, MPhil.[c]



- *3,276 patients with severe TR*
- *No difference in long-term survival between surgery and medical therapy*

Surgical mortality was adversely affected by delayed operative intervention, especially until severe RV failure, or end-organ damage developed



Axtell ; JACC, August 2019

ESC European Society of Cardiology
European Heart Journal (2022) 43, 654–662
https://doi.org/10.1093/eurheartj/ehab679

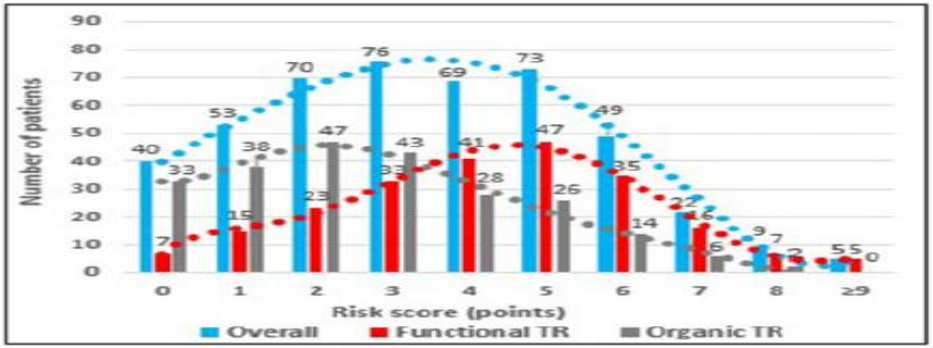
TRI-SCORE: a new risk score for in-hospital mortality prediction after isolated tricuspid valve surgery

Julien Dreyfus [1,*,†], Etienne Audureau[2,3,†], Yohann Bohbot[4,5],

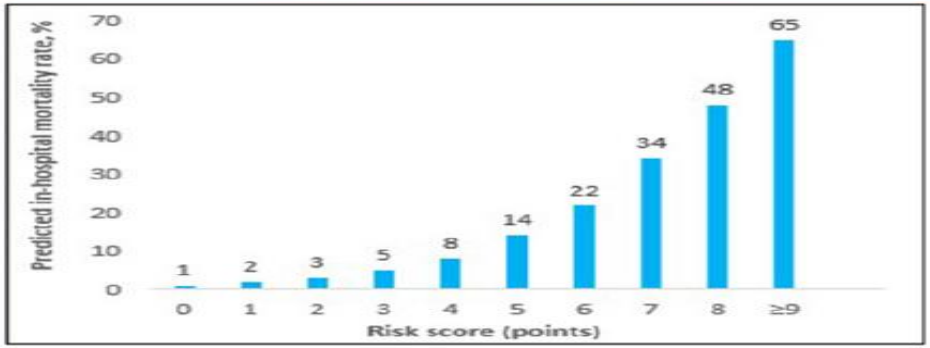
Risk factors and scoring system for in-hospital mortality after isolated tricuspid valve surgery

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

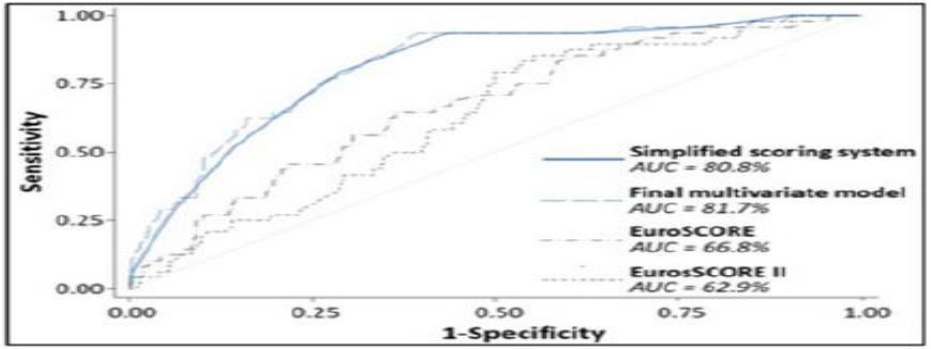
Number of patients presenting with each score value and trends



Predicted in-hospital mortality rate according to the final risk score model



Receiver operating characteristic curves



Outcome of TR with contemporary heart failure therapy

Tricuspid regurgitation and long-term clinical outcomes

Ehud Chorin[1†], Zach Rozenbaum[1†], Yan Topilsky[1], Maayan Konigstein[1], Tomer Ziv-Baran[2], Eyal Richert[1], Gad Keren[1], and Shmuel Banai[1*]

N=33,305

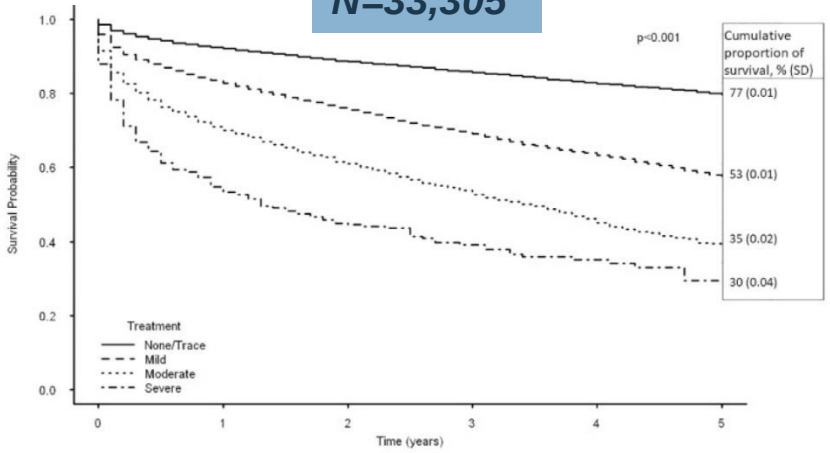


Table 5 Outcomes of sample of hospitalized patients according to TR grade compared to none/minimal adjusted for TAPSE

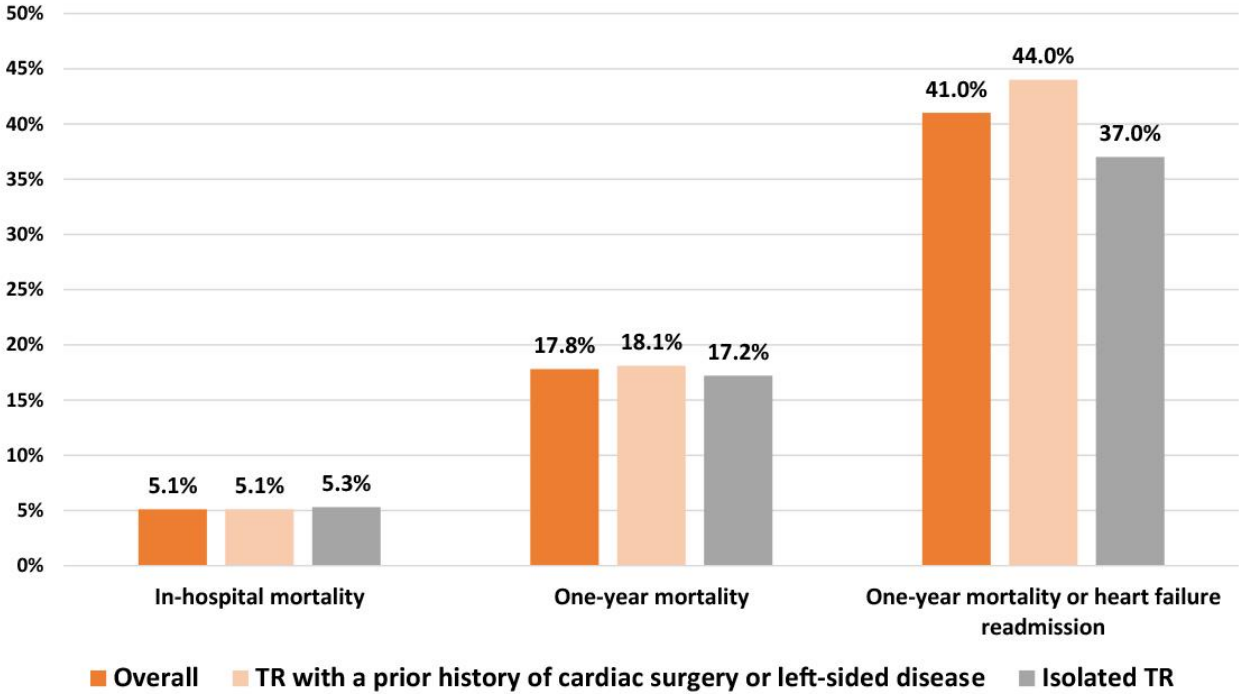
Outcomes	TR	%	Crude HR (95% CI)	*P*-value	Adj HR[a] (95% CI) *n* = 5237	*P*-value
1-year mortality	None/trace	12.4	1		1	
	Mild	20.1	1.7 (1.58–1.84)	<0.001	1.02 (0.85–1.23)	0.823
	Moderate	33.7	3.13 (2.87–3.42)	<0.001	1.22 (0.97–1.54)	0.086
	Severe	51.6	5.44 (4.5–6.58)	<0.001	1.89 (1.29–2.79)	0.001
Overall mortality	None/trace	23.3	1		1	
	Mild	38.7	1.82 (1.72–1.93)	<0.001	1 (0.87–1.15)	0.985
	Moderate	53.1	3.03 (2.83–3.25)	<0.001	1.07 (0.89–1.29)	0.447
	Severe	66.4	4.58 (3.89–5.41)	<0.001	1.41 (1.01–1.98)	0.046
Heart failure re-admission	None/trace	2.9	1	1	1	
	Mild	6.5	2.29 (1.98–2.65)	<0.001	1.48 (1.03–2.12)	0.034
	Moderate	10.6	3.94 (3.33–4.65)	<0.001	1.65 (1.08–2.52)	0.021
	Severe	20.2	7.93 (5.82–10.82)	<0.001	3.52 (1.92–6.47)	<0.001
30-day mortality	None/trace	3.7	1		1	
	Mild	7.0	1.98 (1.73–2.28)	<0.001	1.53 (1.04–2.24)	0.032
	Moderate	13.9	4.23 (3.63–4.93)	<0.001	2.61 (1.68–4.05)	<0.001
	Severe	18.8	6.08 (4.29–8.61)	<0.001	3.96 (1.94–8.07)	<0.001

[a]Age, gender, echocardiographic parameters (diastolic dysfunction, left atrium volume index, E/e, stroke volume, systolic pulmonary artery pressure, ejection fraction, aortic insufficiency, aortic stenosis, mitral stenosis, mitral regurgitation, TAPSE), and comorbidities (lung disease, ischaemic heart disease, pacemaker/implantable cardiac defibrillator, atrial fibrillation/flutter, diabetes mellitus, obesity, hypertension, hyperlipidaemia, renal dysfunction, deep vein thrombosis/pulmonary embolism, malignancy, cerebrovascular accident/transient ischaemic attack).

TR ≥ Moderate is associated with poor survival, regardless of age, echo parameters and comorbidities

Chorin; EHJ CVI 2020

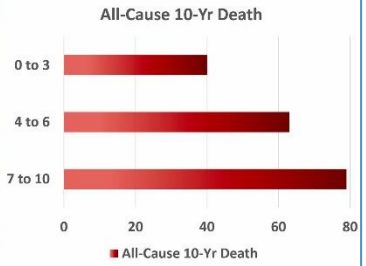
Event rates in patients with tricuspid regurgitation managed conservatively in a nationwide cohort from France



Management and Outcome of Patients Admitted With Tricuspid Regurgitation in France
Messika Zeitun and Maurice Sarano et al.
Canadian Journal of Cardiology, 2021-07-01, Volume 37, Issue 7, Pages 1078-1085

A Risk Model for 10-Year All-Cause Mortality in patients with TR

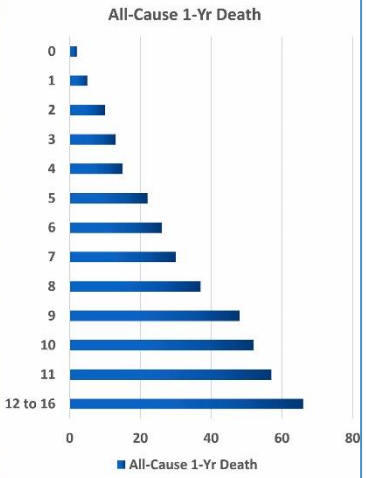
TRIO Score Parameters	Score
Age	
70-79 years	1
≥80 years	2
Male sex	1
Creatinine of ≥2 ml/dl	2
Congestive heart failure	2
Lung disease	1
Aspartate aminotransferase of ≥40 U/L	1
Heart rate 90 bpm or higher	1
Severe TR	1
Total	10



Lara-Breitinger KM. et al. Mayo Clin Proc. 2022 Aug;97(8):1449-1461

B Risk Model for 1-Year All-Cause Mortality in Isolated Secondary TR

Parameter	Score
Age	
65-74 yrs	1
75+ yrs	2
Myocardial infarction	1
Peripheral vascular disease	1
Chronic lung disease	1
Chronic kidney disease (creatinine >1.4 mg/dL)	1
Loop diuretic use	1
Anemia (Hgb <10 g/dL)	1
Thromocytopenia (platelet <15 k/μL)	1
INR >1.5	1
Albumin <3.0 g/dL	2
RV Systolic Fx	
Mildly impaired	1
Moderately impaired	2
Severely impaired	3
Right ventricular systolic pressure >50 mmHg	1
TOTAL	16

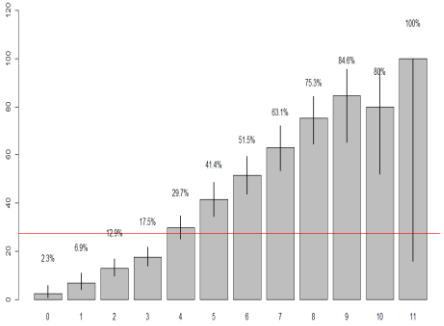


Wang, TKM. et al. J Am Coll Cardiol Img. 2022:15(5):731-744

Hochstadt A, Topilsky Y. et al, Eur Heart J Open. 2022 Oct 14;2(6):oeac067.

Risk Score for 1 year mortality based in patients with ≥Moderate-severe TR

Multivariate predictors
Age≥65 years (1 points)
Age≥75 years (2 points)
Age≥85 years (3 points)
EF≤30% (1 point)
SPAP≥40mmHg (1 points)
GFR≤30 (2 points)
GFR≤20 (4 points)
RV dysfunction (1 point)
Liver disease (2 points)



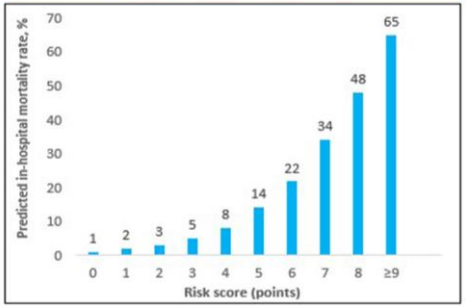
Dreyfus et al. TRISCORE cohort. Eur Heart J, Volume 43, Issue 7, 14 February 2022

All consecutive adult patients who underwent an isolated tricuspid valve surgery for severe tricuspid regurgitation at 12 French centers between 2007 and 2017 (N=466)

Risk factors and scoring system for in-hospital mortality after isolated tricuspid valve surgery

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

Predicted in-hospital mortality rate according to the final risk score model



CRF®
NEW YORK VALVES
THE STRUCTURAL HEART SUMMIT

Trans-catheter Repair for Patients with Tricuspid Regurgitation

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Transcatheter Repair for Patients with Tricuspid Regurgitation

Sorajja P et al. DOI: 10.1056/NEJMoa2300525

CLINICAL PROBLEM

For patients with severe tricuspid regurgitation, transcatheter edge-to-edge repair (TEER) has emerged as a safe and potentially effective treatment option. This percutaneous, transvenous procedure deploys one or more clips to hold the tricuspid-valve leaflets together, thereby reducing regurgitation without the need for cardiac surgery. However, the clinical benefit of tricuspid TEER as compared with medical therapy alone is uncertain.

CLINICAL TRIAL

Design: An international, open-label, randomized, controlled trial evaluated the effectiveness and safety of TEER as compared with medical therapy alone in patients with severe, symptomatic tricuspid regurgitation who were at intermediate or greater surgical risk.

Intervention: 350 patients were assigned to either TEER or medical therapy (control). The primary end point was a hierarchical composite that included death from any cause or tricuspid-valve surgery; hospitalization for heart failure; and an improvement in quality of life as measured with the Kansas City Cardiomyopathy Questionnaire (KCCQ) (≥15-point improvement at 1 year).

RESULTS

Effectiveness: During 1 year of follow-up, the primary outcome favored the TEER group over the control group. The difference between the groups was largely attributable to a significantly greater mean improvement in the quality-of-life score in the TEER group.

Safety: 98% of patients who underwent TEER were free from major adverse events at 30 days, a finding that exceeded the performance goal of the trial (90%).

LIMITATIONS AND REMAINING QUESTIONS

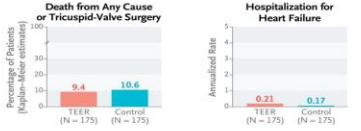
- The open-label nature of the trial could have introduced bias into the interpretation of clinical outcomes.
- The trial was conducted during the Covid-19 pandemic, which could have affected outcomes.
- The results may not apply to patients with hemodynamic or anatomical findings that do not meet the entry criteria used in the trial.

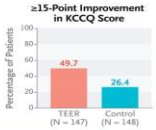
Links: Full Article | NEJM Quick Take | Editorial

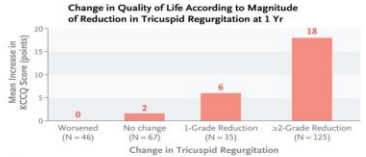
Primary End Point

Win ratio, 1.48 (95% CI, 1.06–2.13); P = 0.02

	TEER Group (N = 175)	Control Group (N = 175)
Hierarchical composite — no. of wins	11,348	7643

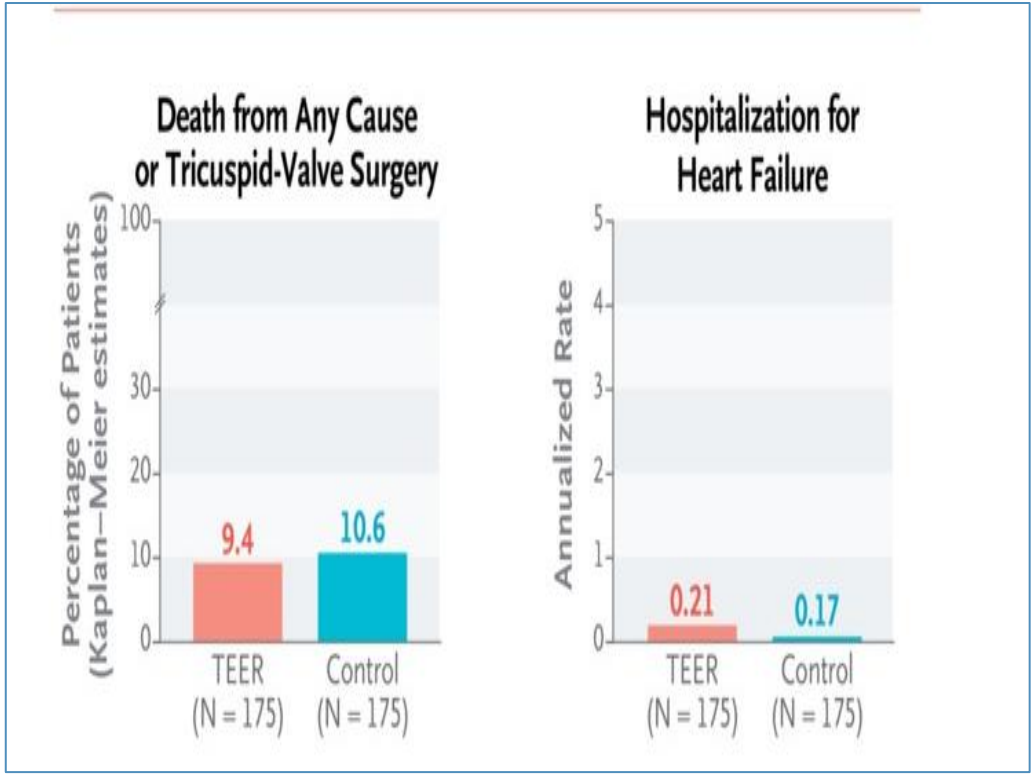






CONCLUSIONS

In patients with symptomatic, severe tricuspid regurgitation, TEER was safe and was associated with a greater improvement in quality of life than medical therapy alone.



N Engl J Med
Volume 388(20):1833-1842
May 18, 2023

Trans-catheter Repair for Patients with Tricuspid Regurgitation

STATISTICAL ANALYSIS

Under the assumption of a 1-year incidence of death or tricuspid-valve surgery of 20% in the control group

Possible reasons for the relatively good outcome in the TRILUMINATE control arm

- Selection “clinical bias”- low clinical risk?
- Optimal medical management?
- Selection “anatomic” bias- predilection for “atrial functional”?

Selection clinical bias?

Enrollment, Randomization, and Follow-up

Patients were eligible:

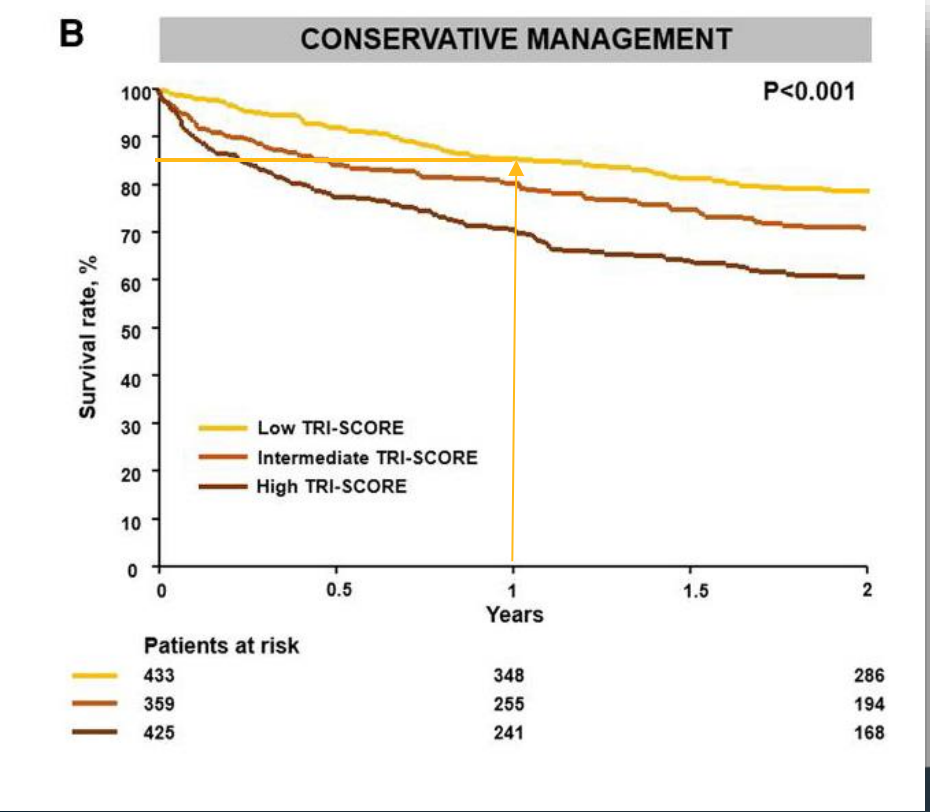
- **Tricuspid regurgitation confirmed as severe**
- **Symptomatic (NYHA II, III, or IVa)**
- **Pulmonary artery systolic pressure <70 mm Hg**
- **No other cardiovascular conditions (severe AS or MR)**
- **Intermediate or greater surgical risk**

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	TEER Group (N=175)	Control Group (N=175)
Age — yr	78.0±7.4	77.8±7.2
Female sex — no. (%)	98 (56.0)	94 (53.7)
New York Heart Association class III or IV — no. (%)	104 (59.4)	97 (55.4)
Atrial fibrillation — no. (%)	153 (87.4)	162 (92.6)
Kidney disease — no. (%)	62 (35.4)	62 (35.4)
Liver disease — no. (%)	11 (6.3)	16 (9.1)
Chronic obstructive pulmonary disease — no. (%)	19 (10.9)	24 (13.7)
Glomerular filtration rate — ml/min/1.73 m²**	54.1±20.4	56.9±20.0
Medications — no. (%)		
β-receptor antagonist	114 (65.1)	115 (65.7)
ACE-I, ARB, or ARNI	68 (38.9)	66 (37.7)
Vasodilator	14 (8.0)	17 (9.7)
Diuretic	152 (86.9)	161 (92.0)

Figure 1b Survival rate according to the TRI-SCORE in the conservative group

The average patient in TRILUMINATE had TRISCORE 2-3 (Low)



Optimal medical management

Optimal medical management

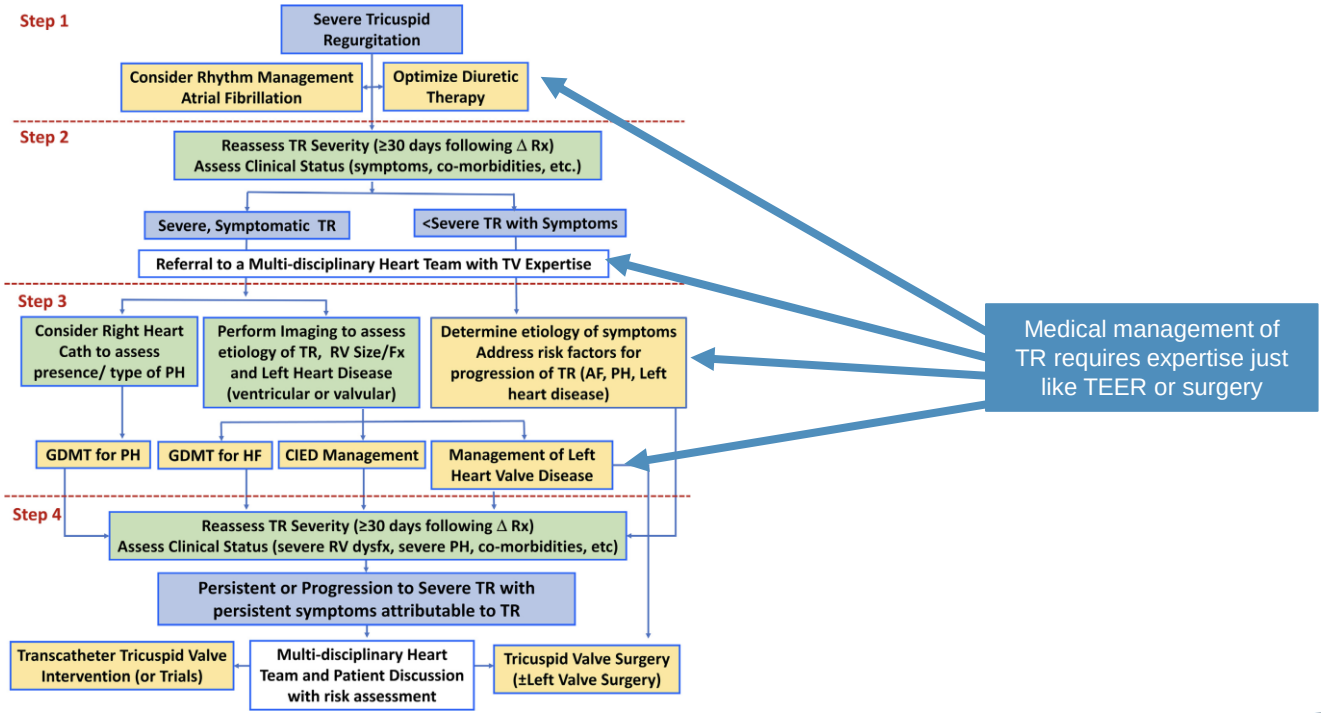
In the Triluminate trial introduction the medical therapy for tricuspid regurgitation is “dismissed” as:

“Largely limited to diuretic agents, which can lead to abatement of symptoms in some patients”.

A gross under appreciation of the required expertise

Tricuspid Regurgitation Management for Heart Failure

Rebecca T. Hahn, MD, Michael I. Brener, MD, MS, Zachary L. Cox, PHARMD, Sean Pinney, MD, JoAnn Lindenfeld, MD



Tricuspid Regurgitation Management for Heart Failure

Rebecca T. Hahn, MD, Michael I. Brener, MD, MS, Zachary L. Cox, PHARMD, Sean Pinney, MD, JoAnn Lindenfeld, MD

DIURETICS

Significant TR leads to diuretic resistance through altered oral diuretic intestinal absorption and intra-renal venous congestion

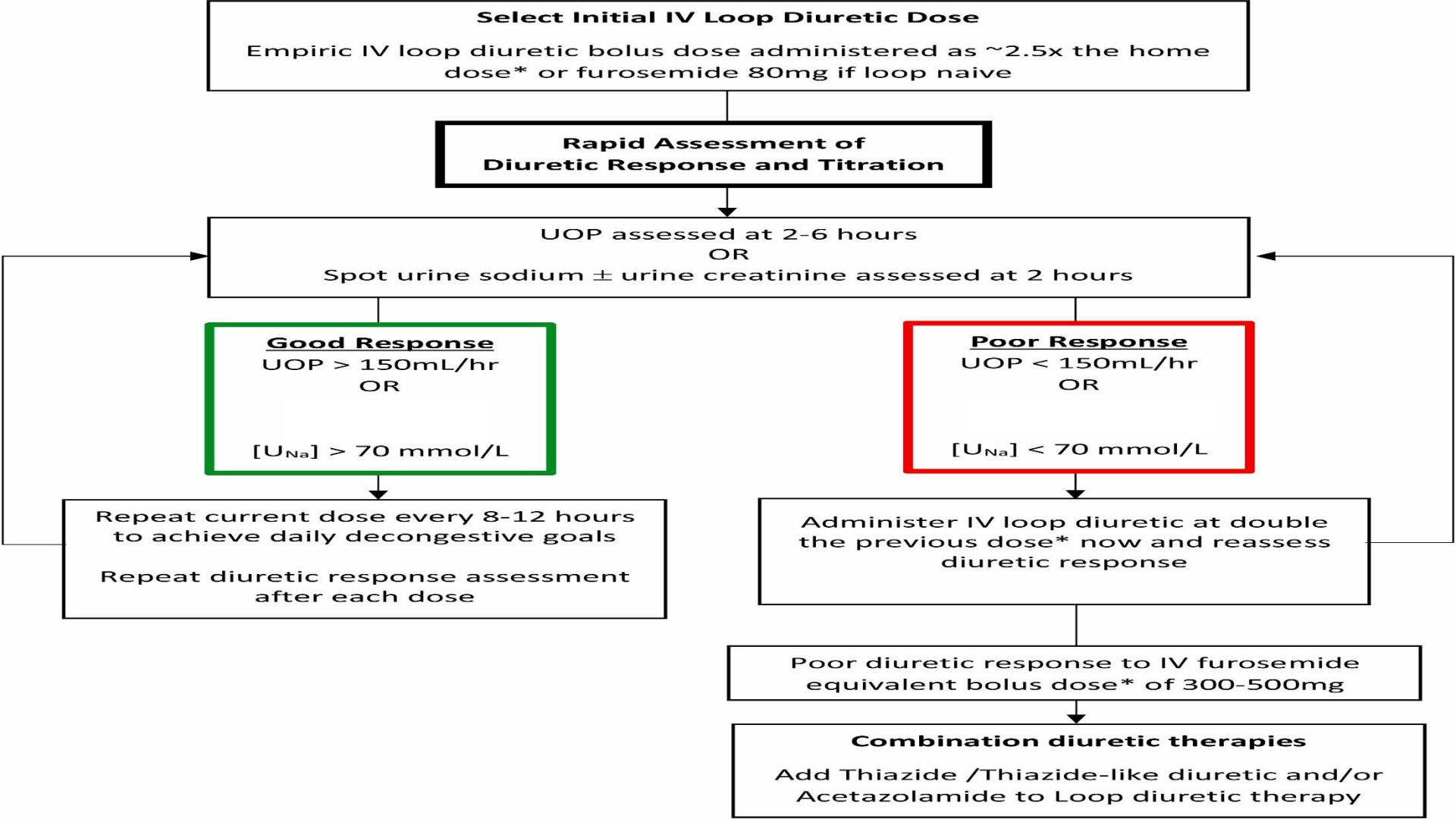
Optimal diuretic therapy may need intermittent intravenous treatment.

Loop diuretics are the primary but not the only decongestive therapy

SGLT-2 inhibitors, mineralocorticoid antagonists.

The ideal RV preload in TR is a normal RA pressure (reduces septal shifting which limits both RV and LV contractility/compliance)

Normalizing RA pressure may require tolerating mild to moderate increases in serum creatinine.


Select Initial IV Loop Diuretic Dose
Empiric IV loop diuretic bolus dose administered as ~2.5x the home dose* or furosemide 80mg if loop naive
Rapid Assessment of Diuretic Response and Titration
UOP assessed at 2-6 hours
OR
Spot urine sodium ± urine creatinine assessed at 2 hours
Good Response
UOP > 150mL/hr
OR
[UNa] > 70 mmol/L
Poor Response
UOP < 150mL/hr
OR
[UNa] < 70 mmol/L
Repeat current dose every 8-12 hours to achieve daily decongestive goals
Repeat diuretic response assessment after each dose
Administer IV loop diuretic at double the previous dose* now and reassess diuretic response
Poor diuretic response to IV furosemide equivalent bolus dose* of 300-500mg
Combination diuretic therapies
Add Thiazide /Thiazide-like diuretic and/or Acetazolamide to Loop diuretic therapy

Tricuspid Regurgitation Management for Heart Failure

Rebecca T. Hahn, MD, Michael I. Brener, MD, MS, Zachary L. Cox, PHARMD, Sean Pinney, MD, JoAnn Lindenfeld, MD

OTHER MEDICAL THERAPY

The LV contributes 20% to 40% of RV stroke volume from systolic ventricular interdependence and septal contraction.

Improvement in LV function may directly improve RV function, as well as indirectly by reducing mitral regurgitation, lowering LA/LV filling pressures, improving pulmonary vascular compliance, and reducing RV afterload

Patients with TR and left sided HF (HFrEF, HFmrEF, HFpEF) should receive guideline-directed medical therapy.

Limited data suggests beta-blockers, *aldosterone system inhibitors* and SGLT2 inhibitors may improve RV function and TR (conflicting data for renin *angiotensin system inhibitors)*

Digoxin may be useful in patients with secondary ventricular TR.

Pulmonary vasodilators are indicated in pre-capillary (group 1) pulmonary arterial hypertension.

Medical management in the TRILUMINATE Trial

Supplementary

- Follow-up at 1, 6, and 12 months with ECG, Labs, Echo, 6 minute walk.
- Control subjects seen by HF specialist.
- Neuro-hormonal antagonists were not changed (GDMT)
- Diuretic therapy was individually tailored throughout FU

Selection “anatomic” bias- “atrial functional”?

Supplementary Appendix Page 14
Anatomic eligibility for TriClip

Echocardiographic images were reviewed to determine if anatomically suitable for the TriClip

Only patients judged to have a high likelihood of achieving ≤moderate residual TR after TEER were randomized to either TEER or Medical therapy

Optimal TEER candidates

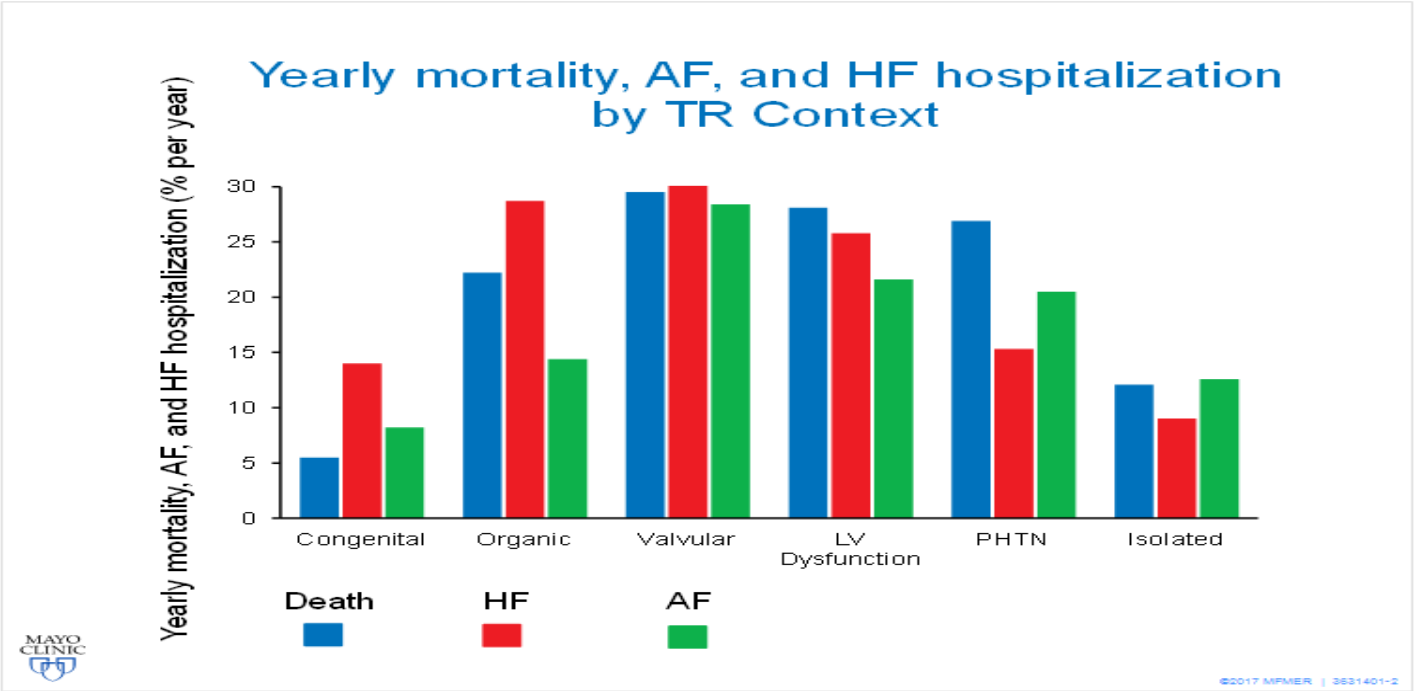
Table 3. Anatomical criteria for device selection.

Strategy	Favourable anatomy	Feasible anatomy	Unfavourable anatomy
Leaflet approximation	Small septolateral gap ≤7 mm[10] Anteroseptal jet location Confined prolapse or flail Trileaflet morphology	Septolateral coaptation gap >7 but ≤8.5 mm[65] Posteroseptal jet location Non-trileaflet morphology Incidental CIED RV lead (i.e., without leaflet impingement)	Large septolateral coaptation gap >8.5 mm[65] Leaflet thickening/shortening (rheumatic, carcinoid)/perforation Dense chordae with marked leaflet tethering Anteroposterior jet location Poor echocardiographic leaflet visualisation CIED RV lead leaflet impingement Unfavourable device angle of approach

Burden of Tricuspid Regurgitation in Patients Diagnosed in the Community Setting

JACC: CARDIOVASCULAR IMAGING

Yan Topilsky, MD,[a] Simon Maltais, MD,[b] Jose Medina Inojosa, MD,[c] Didem Oguz, MD,[c] Hector Michelena, MD,[c] Joseph Maalouf, MD,[c] Douglas W. Mahoney, MSc,[d] Maurice Enriquez-Sarano, MD[c]

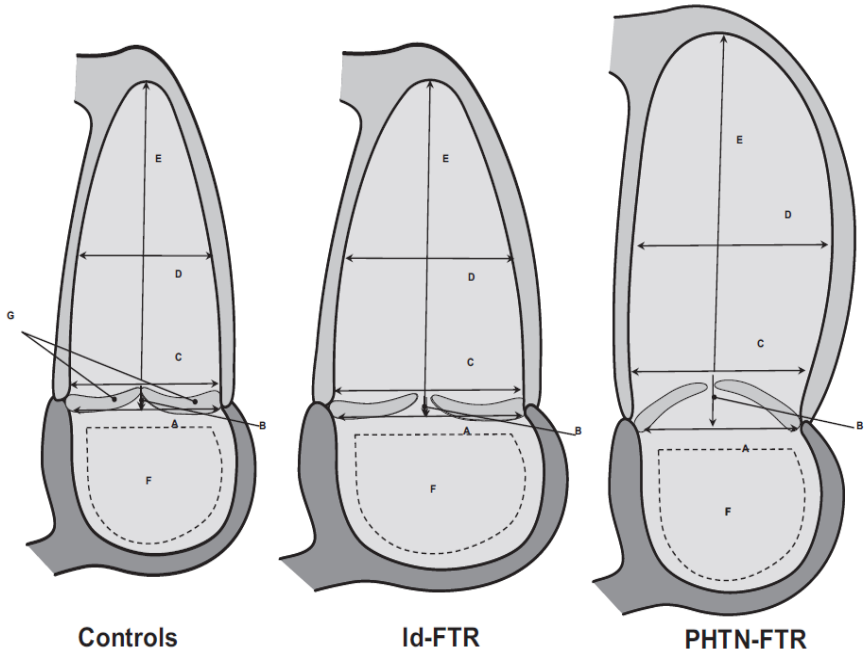


New Classification of Tricuspid Regurgitation

Functional Tricuspid Regurgitation

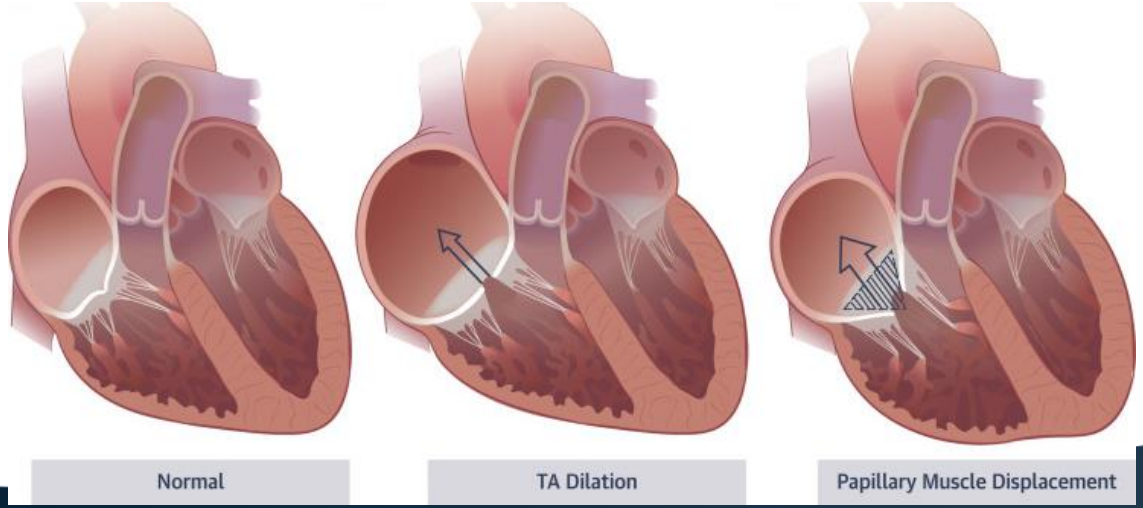
- *RV lengthening (elliptical RV)*
- *Less annular dilation*
- *TV leaflet tethering and tenting*

Wide TV annulus and RV base



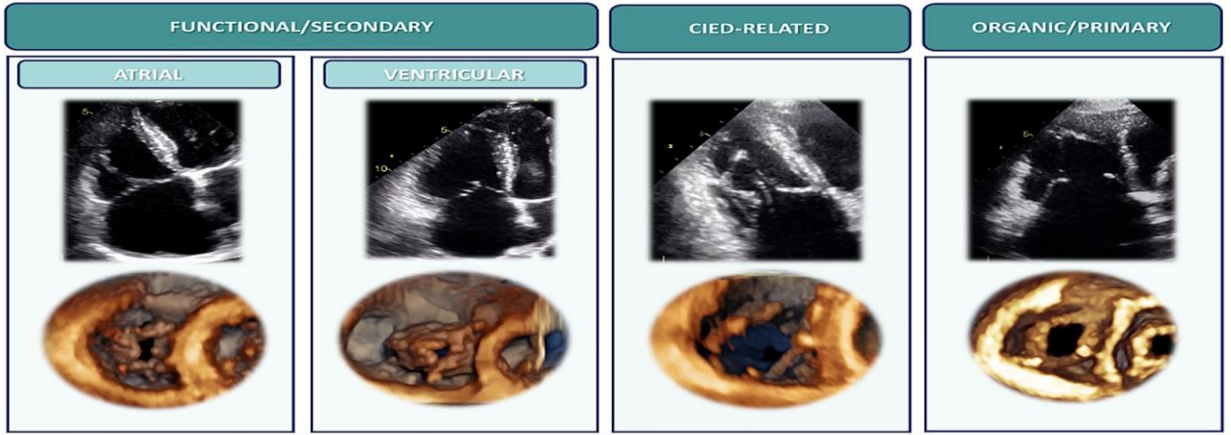
Functional Tricuspid Regurgitation

- ***Right ventricular remodeling***
  - *Papillary muscle displacement*
  - *Leaflet tenting and tethering*
- ***Annulus dilatation***



Eur Heart J Cardiovasc Imaging, Volume 23, Issue 7, July 2022, Pages 913–929

Current Classification

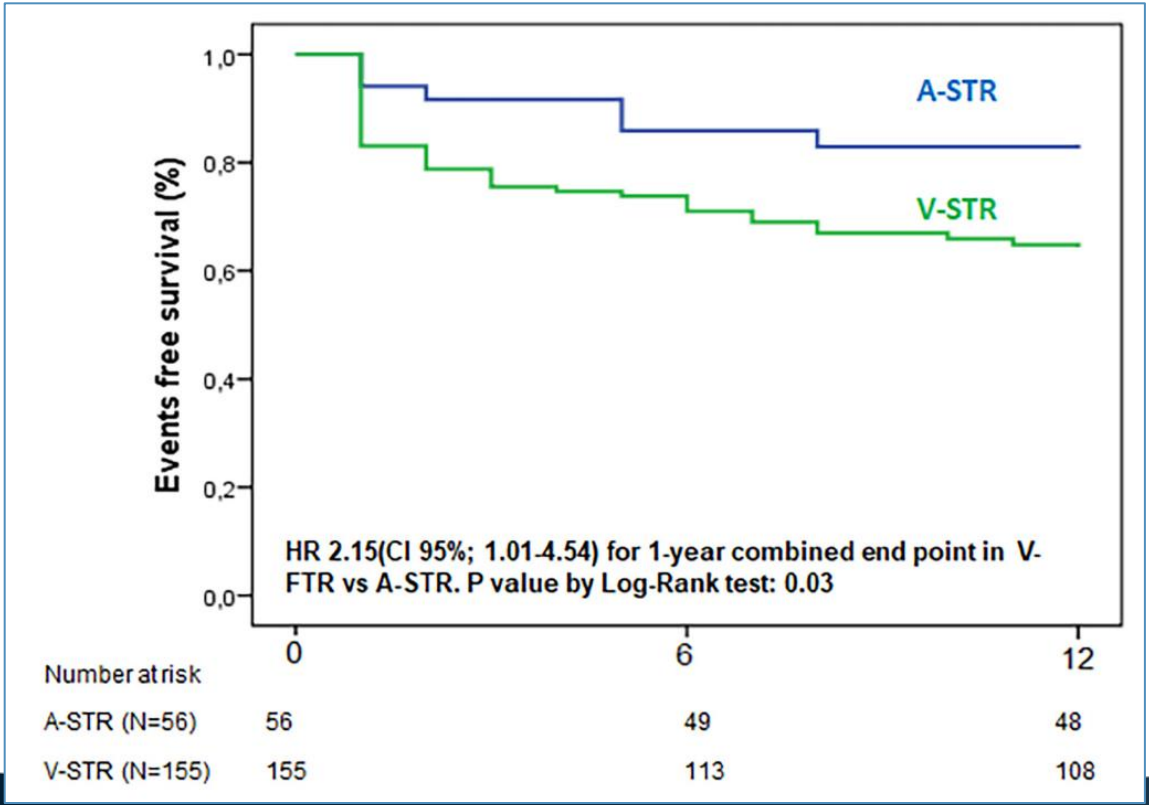


Parameter	Atrial FTR	Ventricular FTR	CIED-Related	Primary TR	
				Prolapse (I)	RHD (IIIA)
Leaflet Tethering	-	+++	++	-	-
Leaflet Restriction	-	Systole	Systole/Diastole	-	Diastole
RA/TA Dilatation	+++	++	+/-	++	++
RV Dilatation	+/-	+++	+/-	+/-	+/-
RV Dysfunction	+/-	+++	+/-	+/-	+/-

Table S4. Baseline echo data

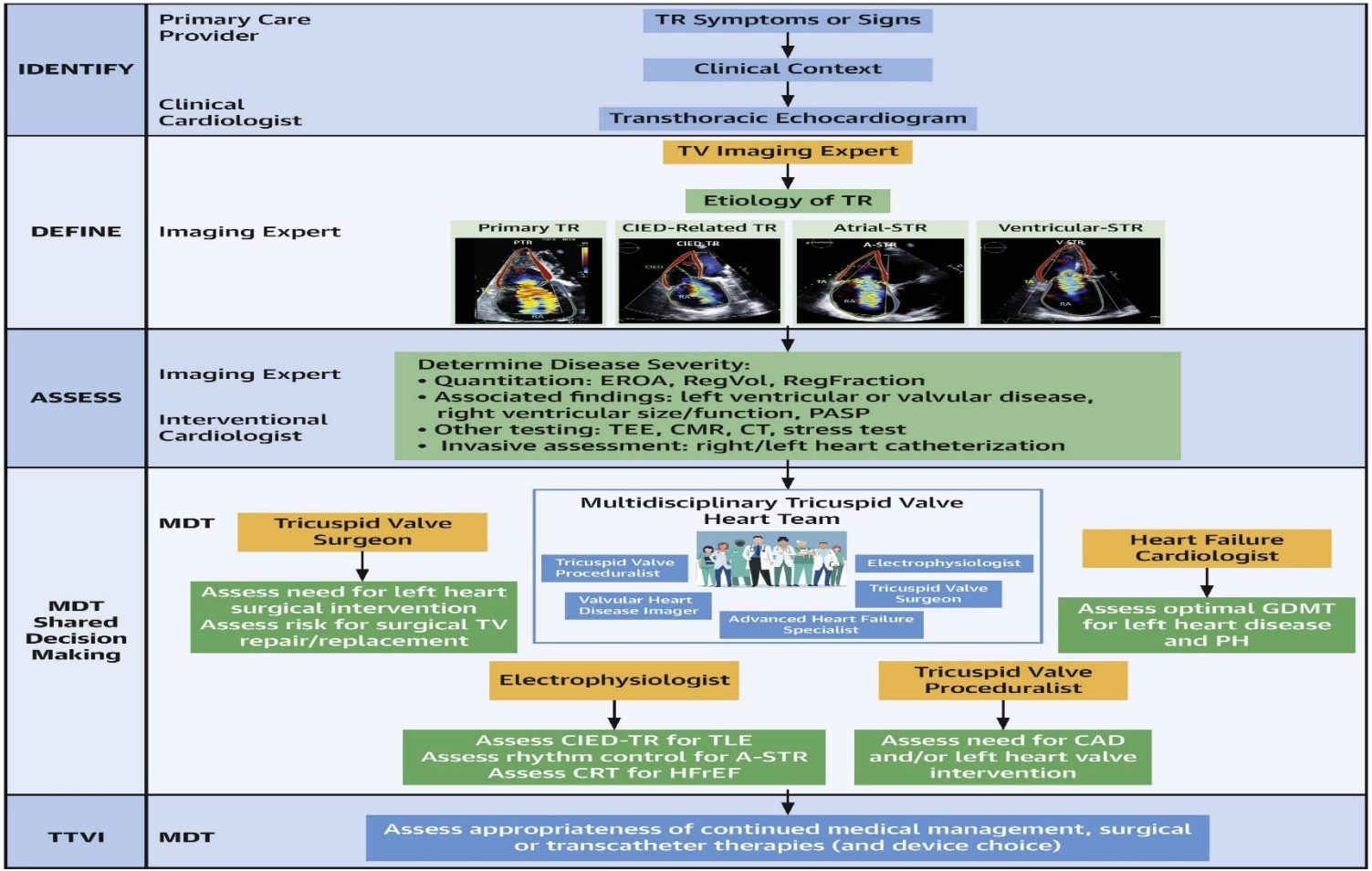
Echocardiographic parameter	TEER Group	Control Group
Ejection Fraction %	59.3±9.3	58.7±10.5
Ejection Fraction<50% n, (%)	23 (14)	21 (14)
Functional etiology n, (%)	165 (94.8%)	158 (92.9%)
Coaptation gap mm	5.5±1.8	5.2±1.7
TAPSE ≤1.7cm n, (%)	83 (48.0%)	68 (41.2%)
Right atrial volume mL	143.2±85.4	153.2±83.2
Tricuspid annulus diameter cm	4.3±0.7	4.5±0.8
Pulmonary systolic pressure mmHg	39.7±9.2	40.1±10.1

Atrial secondary tricuspid regurgitation is associated to more favorable outcome than the ventricular phenotype



Mara Gavazzoni et al. Front Cardiovasc Med. 2022; 9: 1022755

CENTRAL ILLUSTRATION: Clinical Approach to TR



Hahn RT, et al. J Am Coll Cardiol HF. 2023;11(8):1084–1102.

In summary

- TR adversely affects prognosis
- Natural history is affected by severity, etiology and mechanism
- Atrial functional TR is associated with lower mortality
- Proper medical heart failure therapy may decrease mortality
- Future trials should assess the effectiveness of personalized medical regimens tailored by echocardiographic and right heart catheterization data.