Diagnostic and Classification Strategies – and Pitfalls – in TR

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  - Edwards Lifescience
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ESC European Society of Cardiology
European Heart Journal (2019) **40**, 476–484
doi:10.1093/eurheartj/ehy641

META-ANALYSIS

Tricuspid regurgitation is associated with increased mortality independent of pulmonary pressures and right heart failure: a systematic review and meta-analysis

Nelson Wang[1], Jordan Fulcher[2,3], Nishan Abeysuriya[4], Michele McGrady[2], Ian Wilcox[1,2], David Celermajer[1,2], and Sean Lal[1,2]*

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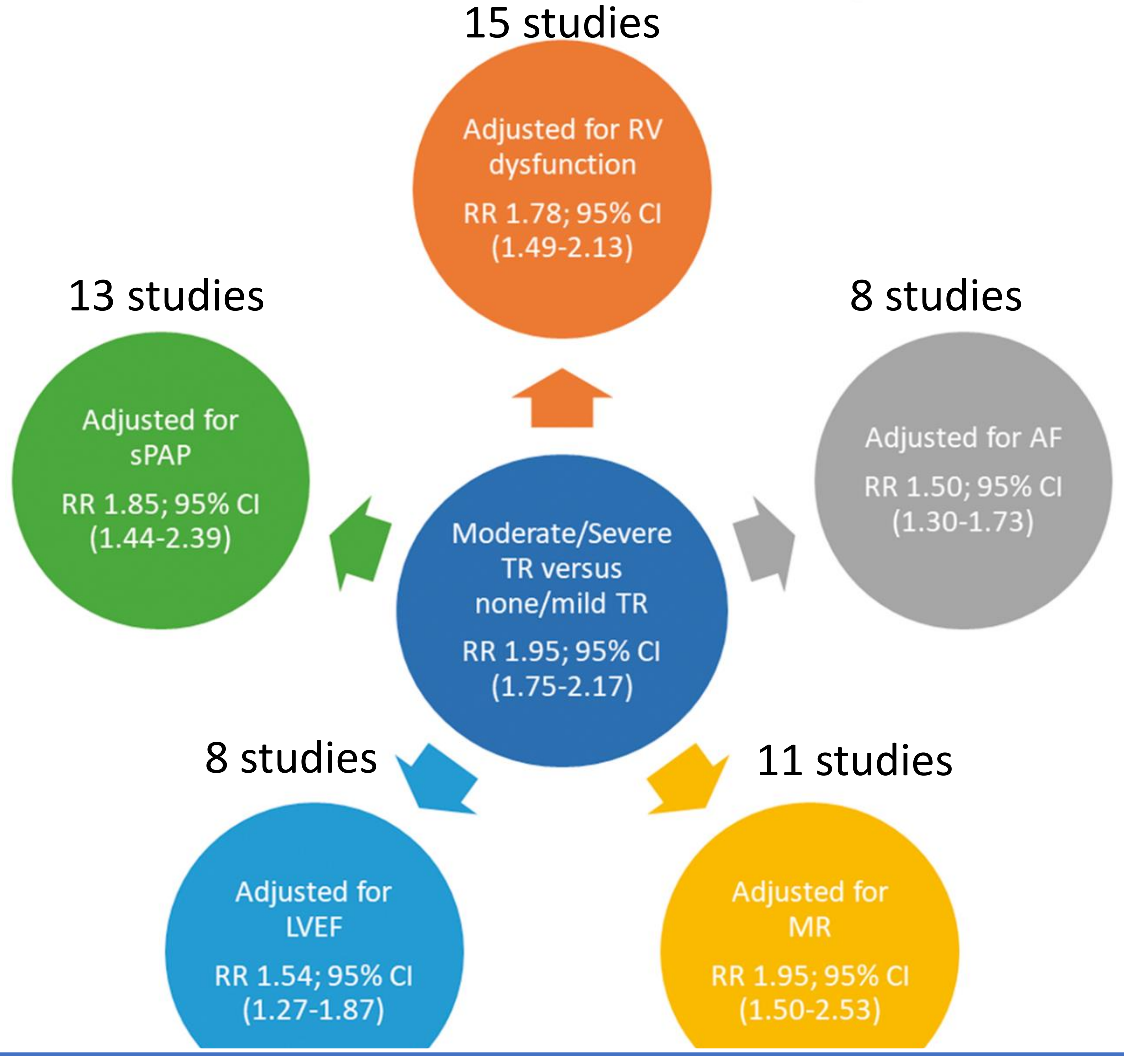
See page 485 for the editorial comment on this article (doi: 10.1093/eurheartj/ehy722)

Aims To undertake a systematic review and meta-analysis to determine the influence of tricuspid regurgitation (TR) severity on mortality.

Methods and results We performed a systematic search for studies reporting clinical outcomes of patients with TR. The primary endpoint was all-cause mortality and secondary endpoints were cardiac mortality and hospitalization for heart failure (HF). Overall risk ratios (RR) and 95% confidence intervals (CIs) were derived for each endpoint according to the severity of TR by meta-analysing the effect estimates of eligible studies. Seventy studies totalling 32 601 patients were included in the analysis, with a mean (±SD) follow-up of 3.2 ± 2.1 years. Moderate/severe TR was associated with a two-fold increased mortality risk compared to no/mild TR (RR 1.95, 95% CI 1.75–2.17). Moderate/severe TR remained associated with higher all-cause mortality among 13 studies which adjusted for systolic pulmonary arterial pressures (RR 1.85, 95% CI 1.44–2.39), and 15 studies, which adjusted for right ventricular (RV) dysfunction (RR 1.78, 95% CI 1.49–2.13). Moderate/severe TR was also associated with increased cardiac mortality (RR 2.56, 95% CI 1.84–3.55) and HF hospitalization (RR 1.73, 95% CI 1.14–2.62). Compared to patients with no TR, patients with mild, moderate, and severe TR had a progressively increased risk of all-cause mortality (RR 1.25, 1.61, and 3.44, respectively; $P < 0.001$ for trend).

Conclusions Moderate/severe TR is associated with an increased mortality risk, which appears to be independent of pulmonary

Risk of All-cause Mortality



Tricuspid Regurgitation is not an "Innocent Bystander"…

Wang N et al. European Heart Journal (2019) 40, 476–484

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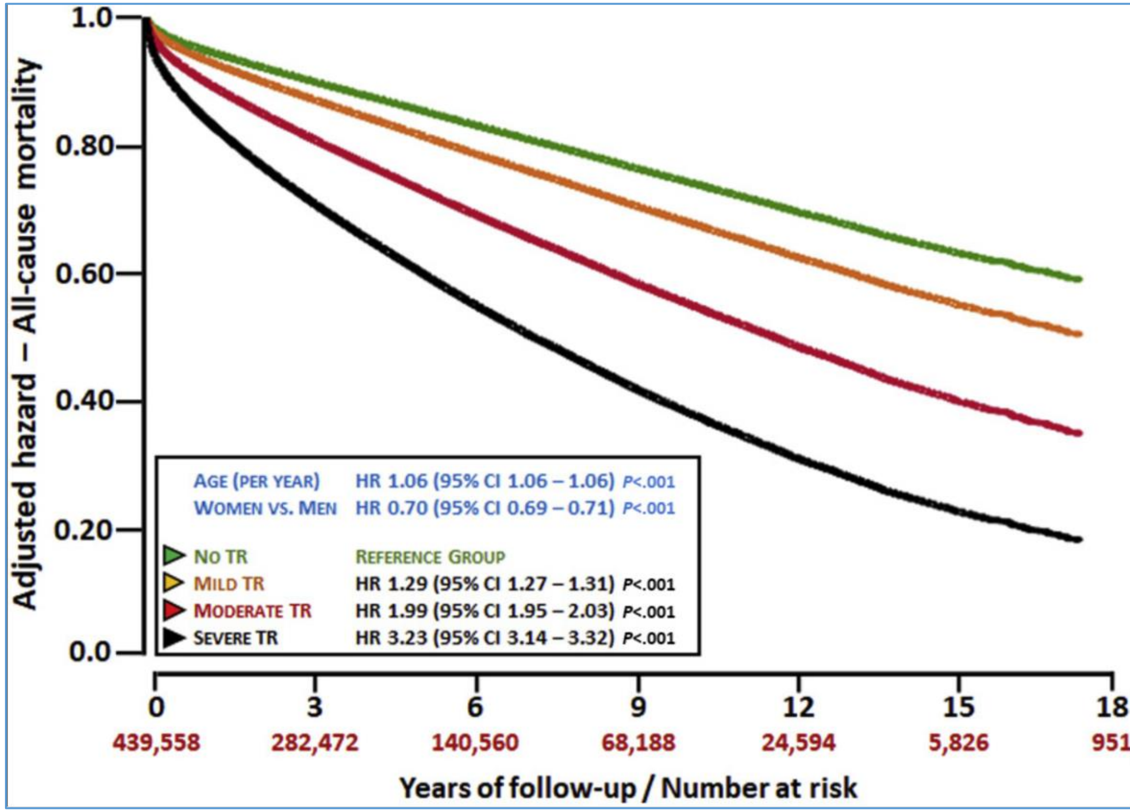
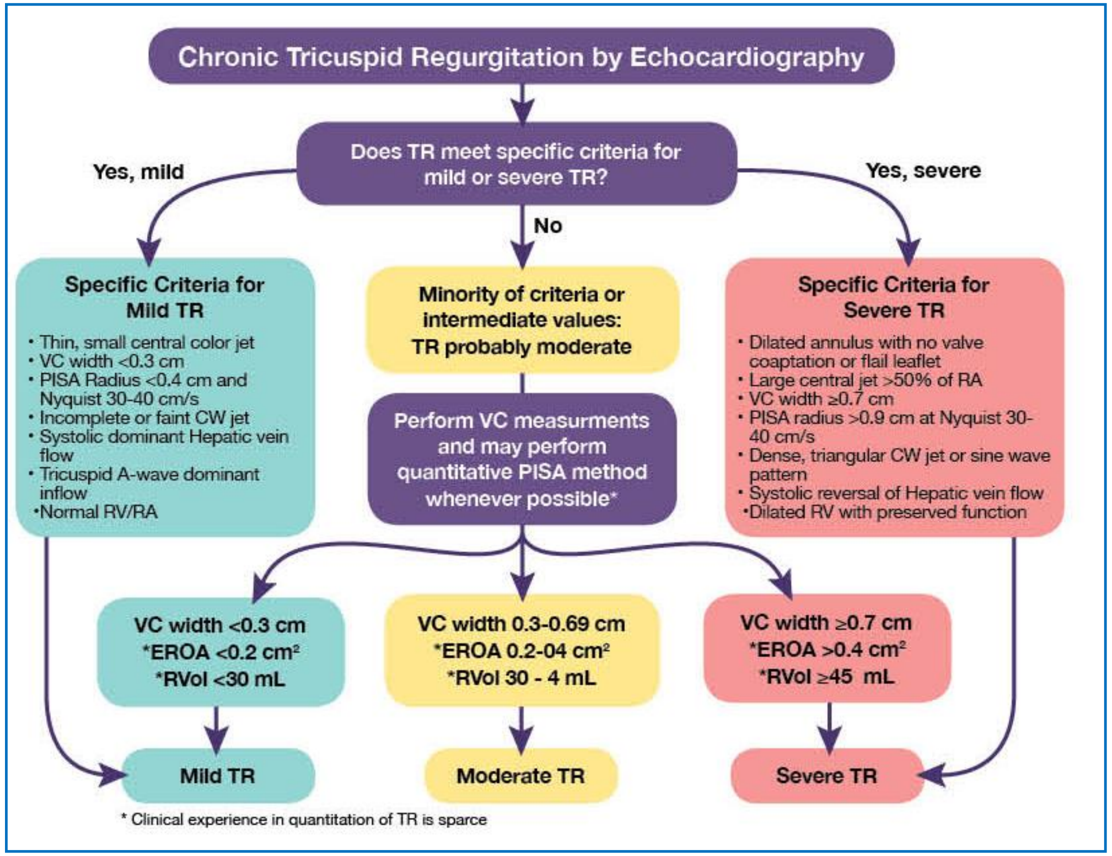
Long-term, all-cause mortality, according to TR severity (adjusted for age and sex)

- **TR severity was analyzed in 439,558 adults (mean age, 62.1 ± 17.8 years; 51.5% men) from 2000 to 2019, by 25 centers contributing to the National Echocardiography Database of Australia.**
- Long-term, all-cause mortality, according to TR severity and adjusted for age and sex.
    - Adjusted HR per grade increase in TR severity above None/Trace
        - **Mild: 1.29 (95% CI, 1.27–1.31; *P* < .001)**
        - **Moderate: 1.99 (95% CI, 1.95–2.03; *P* < .001)**
        - **Severe: 3.23 (95% CI, 3.14–3.32; *P* < .001)**



Assessment of TR Severity

Quantifying Severity of Tricuspid Regurgitation



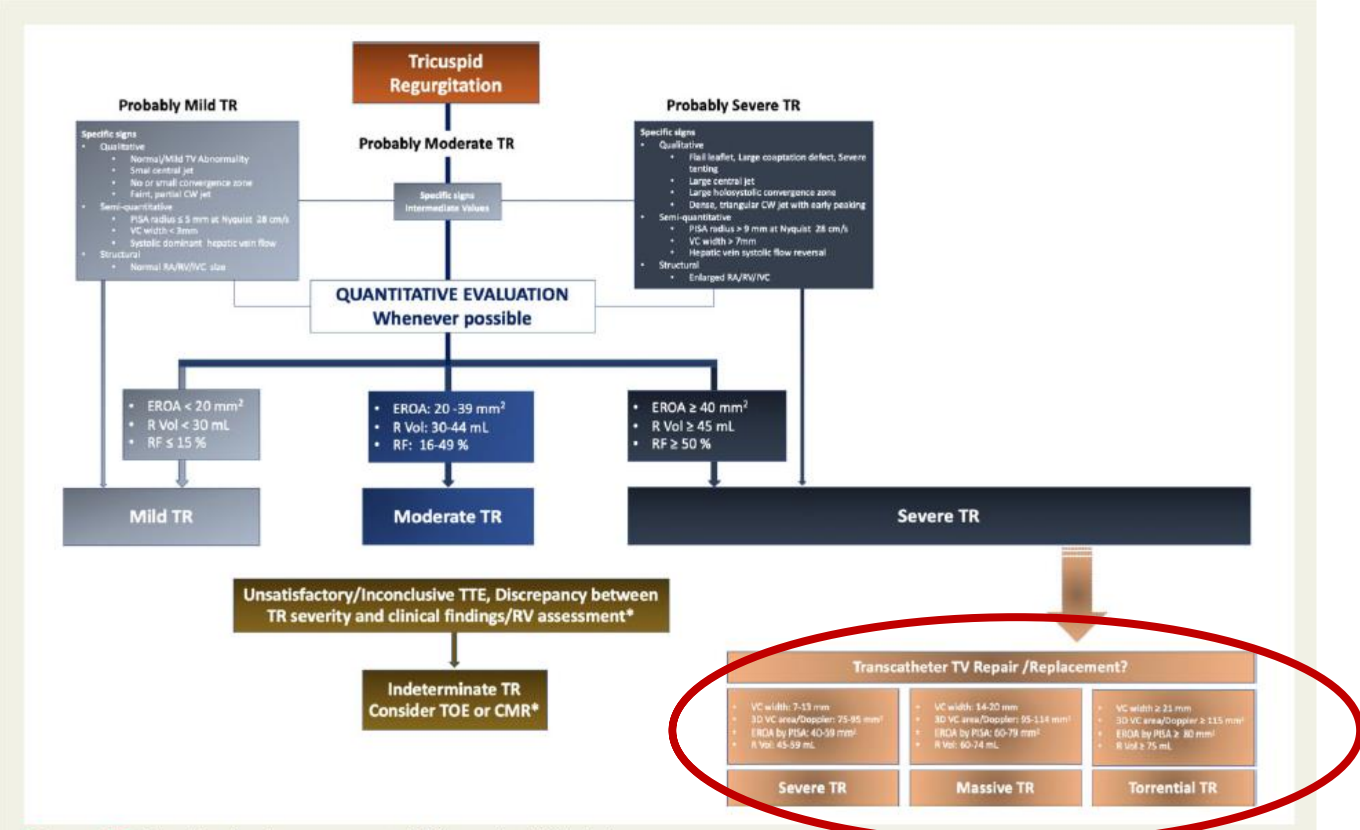
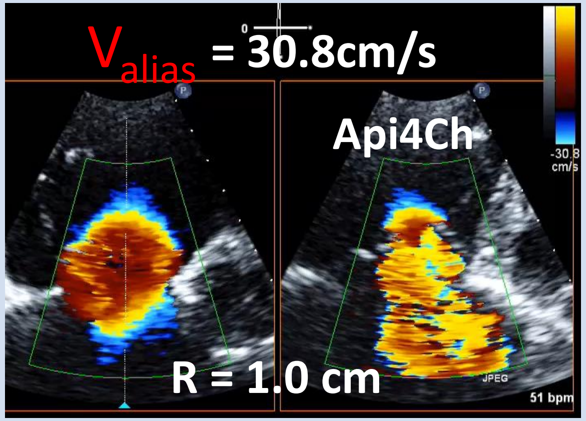
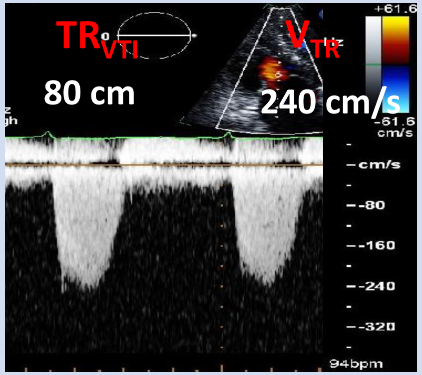


Figure 54 Algorithm for the assessment of TR severity. IVC, inferior vena cava.

Zoghbi WA et al. J Am Soc Echocardiogr 2017; 30: 303-37.

Lancellotti P, et al. Eur Heart J Cardiovasc Imaging. 2022 Apr 18;23(5):e171-e232

Quantitation by PISA

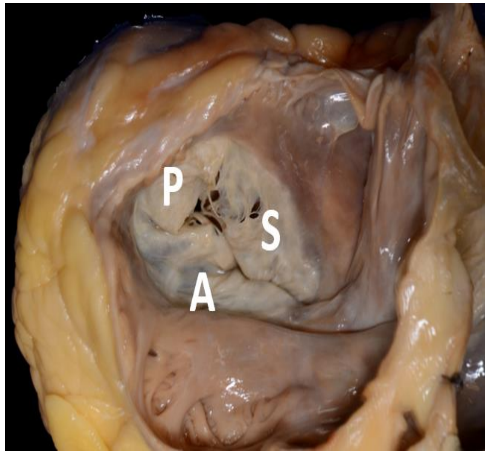
Proximal Isovelocity Surface Area	Measurements Required	Example	Calculation
Proximal Isovelocity Surface Area (PISA)	**Aliasing velocity (V_{Alias})** Color Doppler with baseline shift in the direction of regurgitant jet **Radius of PISA (r)** **TR peak velocity (V_{TR})** CW of the TR jet **TR velocity time integral (TR_{VTI})** CW of the TR jet	 	**PISA EROA:** EROA = $2\pi r^2(V_{Alias}) \div V_{TR}$ **TR Regurgitation Volume** = EROA X TR_{VTI} EROA = (6.282 x 1.0 x 30.8 cm/s) ÷ 240 cm/s = 0.87 cm^2 Reg Vol = 0.87 cm^2 X 80cm = 70 ml* *Note: Underestimates true EROA and Regurtiant volume given the elliptical orifice

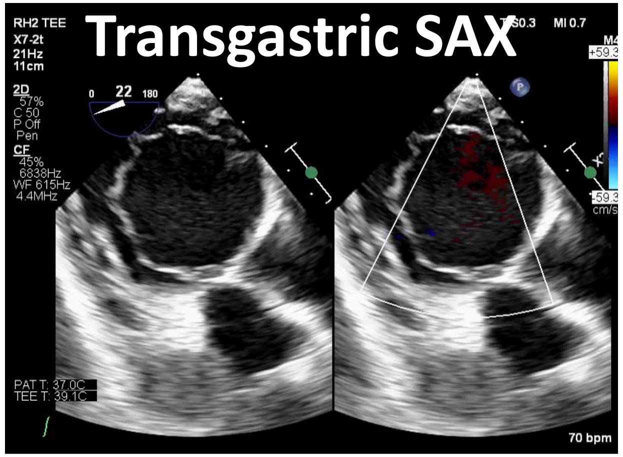
PISA Advantages:

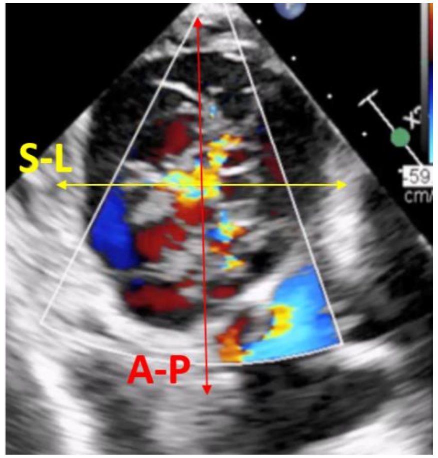
1. Easy to measure
2. Outcomes data

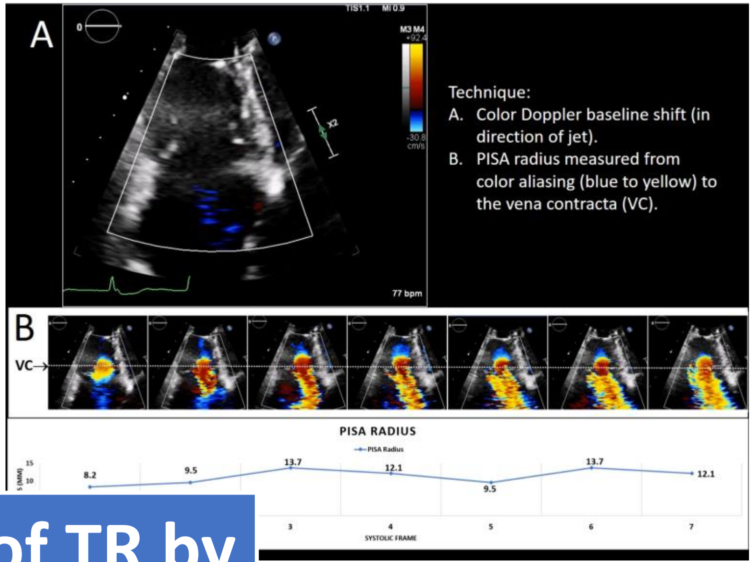
Zoghbi WA et al. J Am Soc Echocardiogr 2017; 30: 303-371.

Limitations of PISA Assumptions

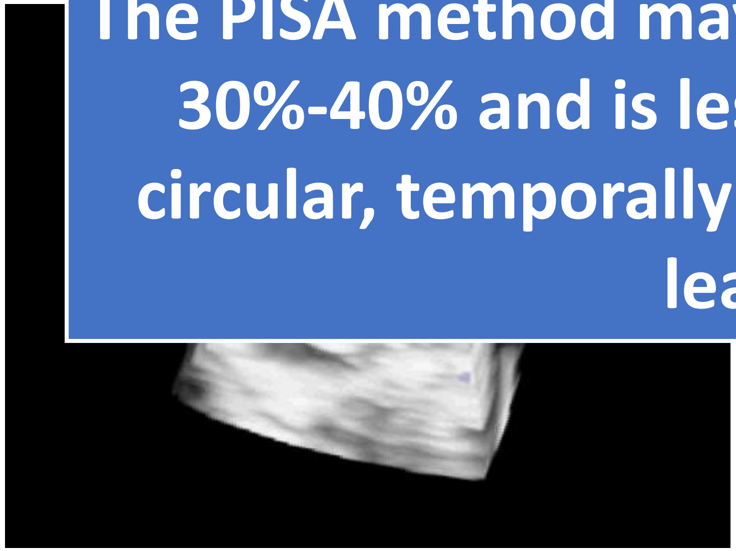


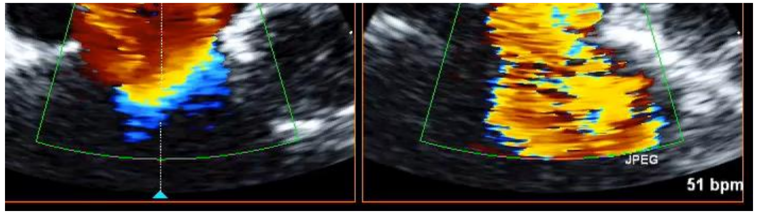






The PISA method may underestimate the severity of TR by 30%-40% and is less accurate with jets that are: non-circular, temporally variable, eccentric or with tethered leaflets, multiple jets





ns of PISA
Hole/Hemispheric
onvergence

2. Flat Surface
3. No temporal variability

PISA EROA and Outcomes

JACC: CARDIOVASCULAR IMAGING
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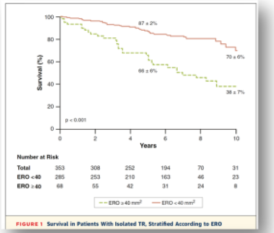
ISSN 1936-878X/$36.00
http://dx.doi.org/10.1016/j.jcmg.2014.07.018

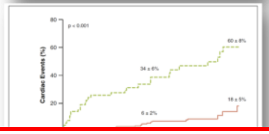
ORIGINAL RESEARCH

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†

Survival rates (± SE) at 5 and 10 years.





- Severe isolated TR independently predicted higher mortality:
  - Adjusted HR = 1.78 [95% confidence interval (CI): 1.10 to 2.82], p = 0.02 for qu
    definition
  - **Adjusted HR = 2.67 [95% CI: 1.6**
    an ERO ≥40 mm², p < 0.0001).

Topilsky Y et al. J Am Coll Cardiol Img 2014;7

Circulation

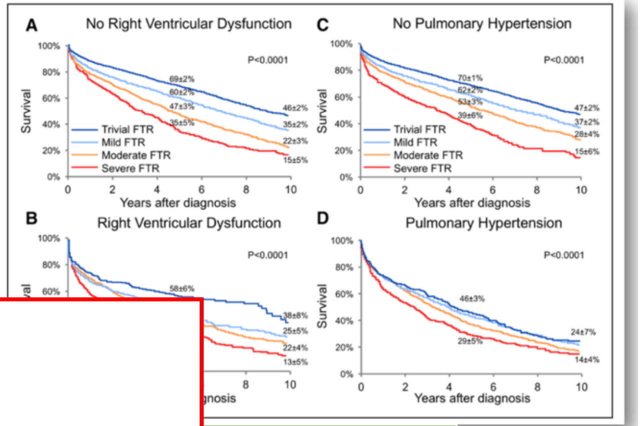
ORIGINAL RESEARCH ARTICLE

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

- The addition of grading by quantitative improved the model prediction (p < 0.001 for survival and p . 0.02 for cardiac events).

Quantitative measurements of TR severity are predictive of outcomes



Note: Corrected PISA

Key Points:

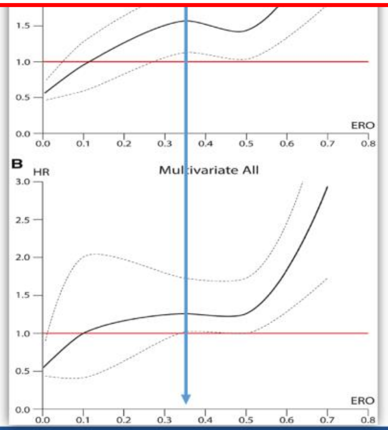
1. **Quantify all patients by PISA**
2. **When PISA EROA 30-35 mm² (uncorrected), refer to a Level 1 Valvular Heart Center for further evaluation**

Quantitative assessment of effective regurgitant orifice: impact on risk stratifi and cut-off for severe and torrential tricu regurgitation grade

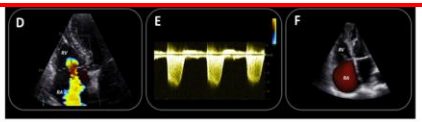
Yogev Peri[1], Ben Sadeh[1], Chen Sherez[1], Aviram Hochstadt[1], Simon Biner[1], Galit Aviram[2], Meirav Ingbir[1], Ido Nachmany[3], Guy Topaz[4], Nir Flint[1], Gad Keren[1], and Yan Topilsky[1]*

- **Using PISA EROA**
- The optimal cut-off value to separation survival between **severe vs. lesser degree of TR was 0.35 cm²** [$P < 0.0001$, HR =2.0 (1.5–2.7)].

Note: Uncorrected PISA (?)



Peri Y et al. Eur Heart J Cardiovasc Imaging. 2020 Jul 1;21(7):768-776.



PISA to calculate EROA and regurgitant volume
3D RV Volumes to calculate regurgitant fraction

Table 4. Outcome-based cut-off values for the quantitative parameters used to grade tricuspid regurgitation severity by Dopplerechocardiography.

	Low risk	Intermediate risk	High risk
VC_{avg} (mm)	<3	3–6	>6
EROA (cm²)	<0.15	0.15–0.30	>0.30
RegVol (mL)	<15	15–30	>30
RegFr (%)	<25	25–45	>45

EROA, effective regurgitant orifice area; RegFr, regurgitant fraction; RegVol, regurgitant volume; VC_{avg}, vena contracta width.

k PISA EROA >0.3 cm²

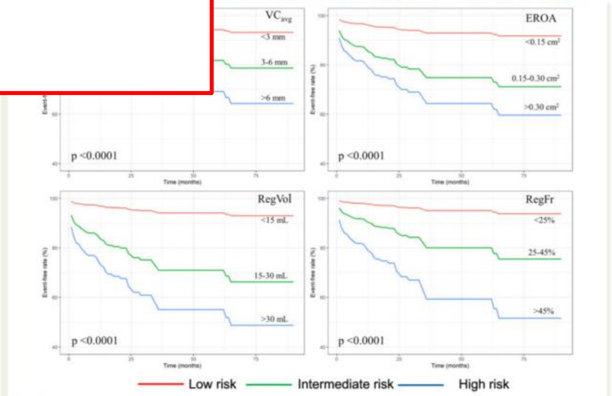


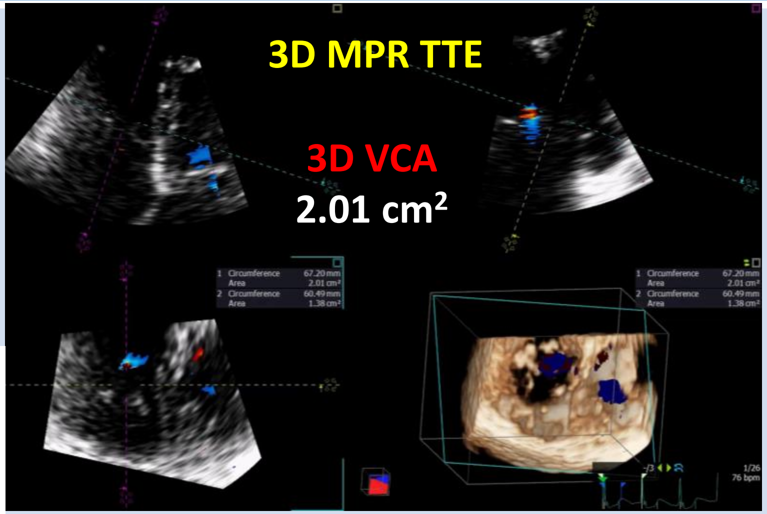
Figure 5. Cox-models derived survival curves for the composite endpoint of death and hospitalization for congestive heart failure. The relative hazard has been stratified by mild, moderate, and severe tricuspid regurgitation (TR), using the derived cut-offs for vena contracta width (VCavg), effective regurgitant orifice area (EROA), regurgitant volume (RegVol), and regurgitant fraction (RegFr), as quantitative parameters used to assess TR severity.

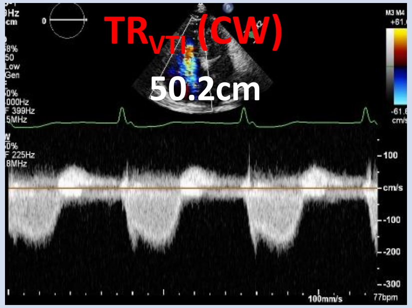
Note: Uncorrected PISA

Muraru, D et al. Eur Heart J Cardiovasc Imaging. 2021 Jan 22;22(2):155-165

3D Vena Contracta Area

3D Color Doppler	Measurements Required	Example	Calculation
3D Vena Contracta Area (VCA)	3D Color Doppler planimetry of the VCA TR velocity time		EROA ≅ VCA TR Regurgitation Volume = VCA X TR_{VTI} **Example:** 3D VCA = $2.01cm^2$ Reg Vol = $2.01cm^2$ X 50.2cm = 100.9ml



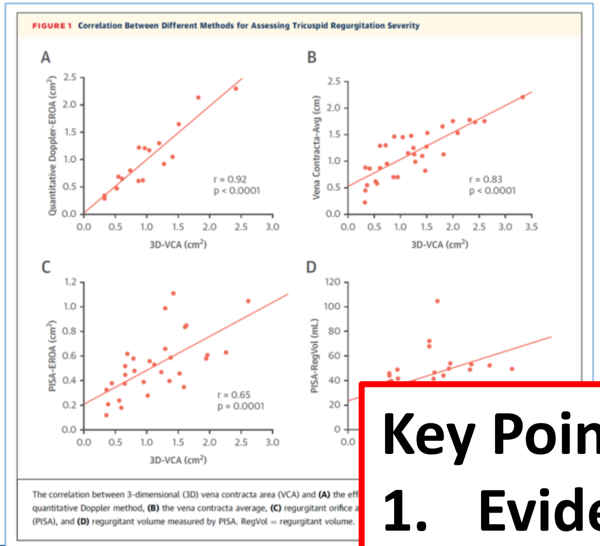


Advantages:
1. Direct measurement of the vena contracta area with no geometric assumptions
2. Can be used following device placement!

Disadvantages:
1. Limitations of 3D color line density and frame rates
2. Non-planar orifice
3. Time varying jets (planimetry should be performed on each [mid] systolic frame)

Caveat: Integrated PISA and 3D VCA should typically be performed

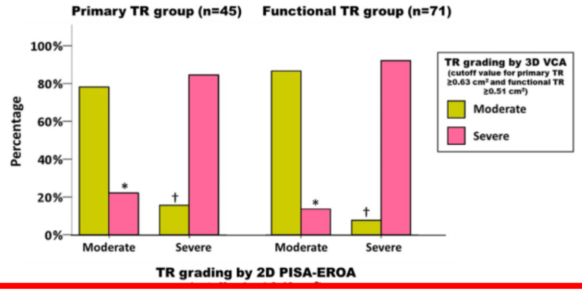
Validations of PISA EROA and 3D VCA



The correlation between 3-dimensional (3D) vena contracta area (VCA) and (A) the eff... quantitative Doppler method, (B) the vena contracta average, (C) regurgitant orifice a... (PISA), and (D) regurgitant volume measured by PISA. RegVol = regurgitant volume.

- PISA-EROA and PISA-RegVol were significantly lower than quantitative Doppler and 3D methods.
- **Using Youden's index, the best cutoff value for severe TR**
  - **PISA-EROA was ≥0.34 cm2 (sensitivity: 89%; specificity: 90%)**
  - **3D-VCA, this cutoff was ≥0.60 cm2 (sensitivity: 92%; specificity: 75%)**
  - **Doppler-EROA cutoff was ≥ 0.65 cm2** (sensitivity: 82%; specificity 94%)

Discordant TR Severity Grading between 2D PISA-EROA and 3D-VCA



Using 3D echocardiography–derived RVol (>45 mL) as a reference standard:

- **Underestimation of 2D PISA-EROA by a mean of 40%**
- **3D VCA has high diagnostic value for separating moderate from severe TR (cutoff >0.61 cm²)**
- **3D VCA has independent and incremental value to grade TR severity**

Dahou A. et al. JACC Cardi... ;32:1526-37.

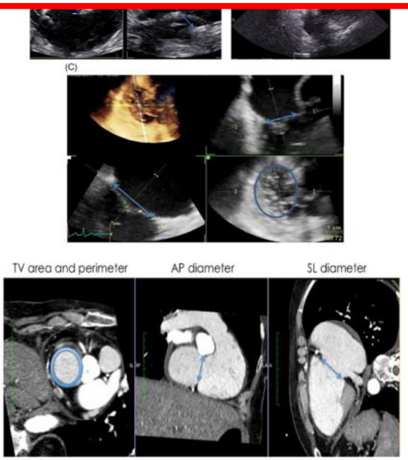
Key Points:

1. **Evidence for clinical utility of 3D VCA is growing.**
2. **Guidelines advocate use of the method when feasible.**

In more elliptical orific... there was greater underestimation of 3D VCA or volumetric EROA by PISA EROA

...imaging modalities

- 40 patients, single site
- MSCT and 3D-TEE showed a **strong correlation for determination of TV annulus area** (r = 0.94, 95% CI: 0.57-0.98, P = .002; ICC = 0.95, P = .4), **perimeter** (r = 0.9, 95% CI: 0.6-0.98, P = .002; ICC = 0.97, P = .3) and **diameters** (AP-Diameter: r = 0.73, 95% CI: 0.06-0.94, P = .03; ICC = 0.83, P = .09; SL-Diameter: r = 0.86, 95% CI: 0.47-0.97, P = .02; ICC = 0.95, P = .1).
- Significant differences between the 2D-TEE-based calculated EROAs according to method:
  - Semi-quantitative **PISA-method (0.49 ± 0.4 cm²)**
  - **3D color vena contracta area (0.67 ± 0.17 cm²**, P = .05; r = 0.93, 95% CI: 0.5-0.99, P = .006).



Öztürk C, et al. Health Sci Rep. 2020 Apr 23;3(2):e159.

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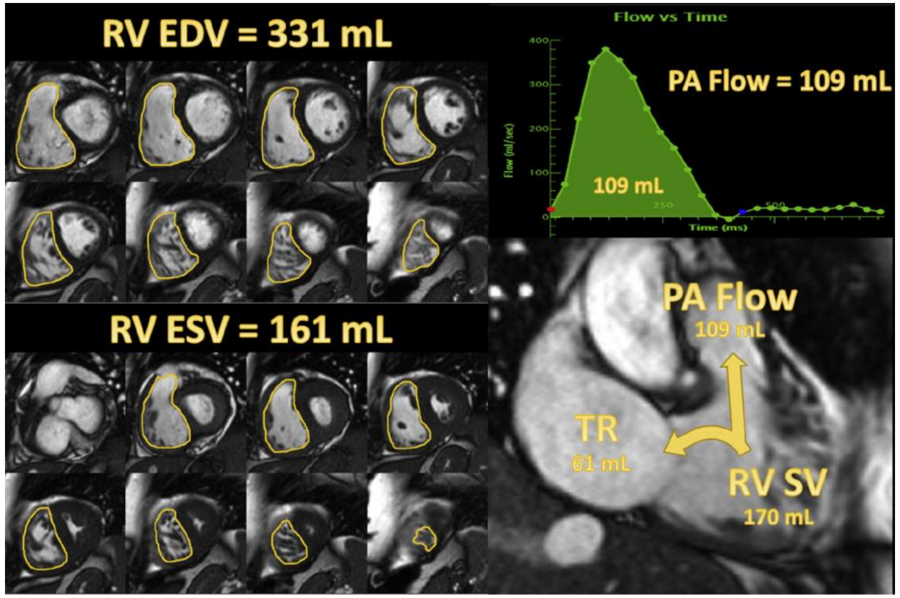
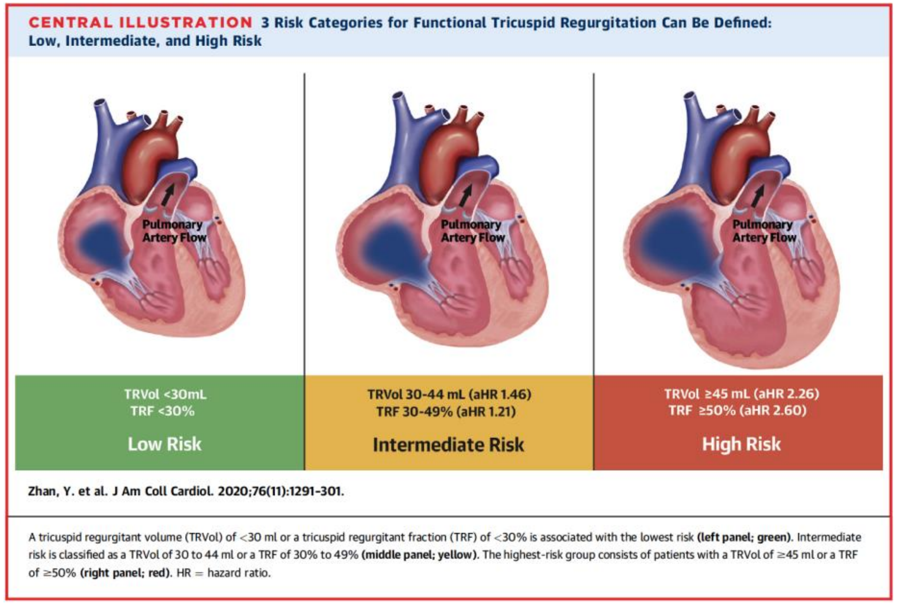
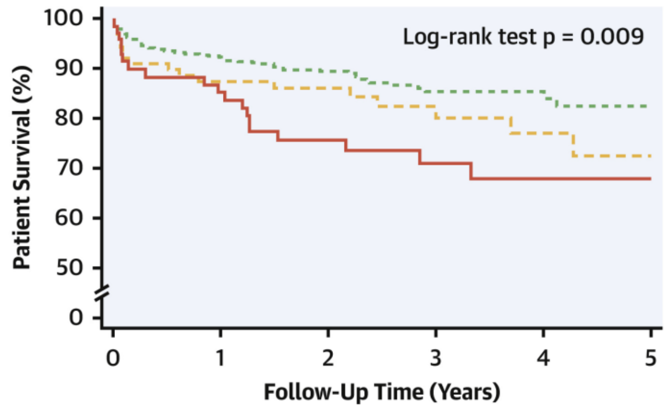
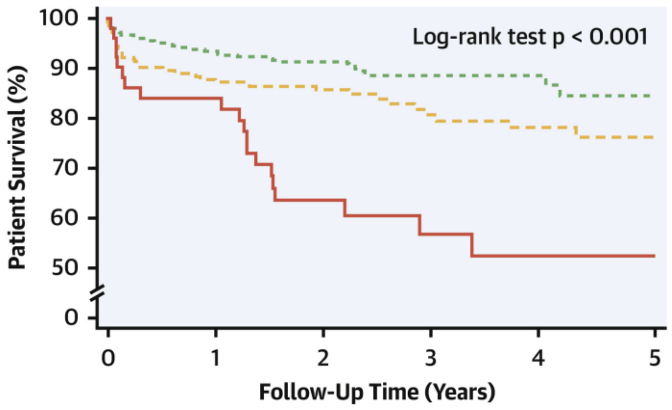
Prognosis based on MRI quantification







TRV (ml)	0	1	2	3	4	5
<30	384	350	257	108	60	45
30-44	88	74	54	35	21	14
≥45	75	54	38	25	20	15



TRF (%)	0	1	2	3	4	5
<30	325	303	219	87	44	34
30-49	166	137	109	67	48	33
≥50	56	38	21	14	9	7

547 patients with functional TR

Consider CMR when echocardiographic quantitation is not possible

Zhan Y et al. J Am Coll Cardiol. 2020 Sep 15;76(11):1291-1301

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Table 15 Grading the severity of TR

TR Severity classes	Mild	Moderate	Severe
Qualitative parameters			
Tricuspid valve morphology	Normal or mildly abnormal leaflets	Moderately abnormal leaflets	Severe valve lesions/**flail/large coaptation defect//severe tenting**
Colour flow TR jet[a]	Small, narrow, central	Moderate central	**Large central jet** or eccentric wall impinging jet of variable size
Flow convergence zone	Not visible, transient or small	Intermediate in size and duration	**Large throughout systole**
CW signal of TR jet	Faint/partial/parabolic	Dense/parabolic, or triangular	**Dense/often triangular with early peaking** (peak <2 m/s in massive TR)
Semi-quantitative parameters			
Hepatic vein flow[b]	Systolic dominance	Systolic blunting	**Systolic flow reversal**
Tricuspid inflow	A-wave dominant	Variable	E wave dominant (≥1 m/s)[e]
PISA radius (mm)[c]	≤5	6-9	**>9**
VC width (mm)[a,d]	<3	3–6.9	**>7**
3D VC area or quantitative Doppler EROA (mm^2)			75–94
Quantitative parameters			
EROA (mm^2)	<20	20–39	≥40
R Vol (mL)	<30	30–44	≥ 45
RF (%)	≤15	16–49	≥50
CMR parameters			
RF (%)	≤15	16–49	≥50
Structural parameters			
RV, RA, IVC size[e]	Usually normal	Normal of mild dilation	Usually dilated

Standard Clinical Grading Scheme

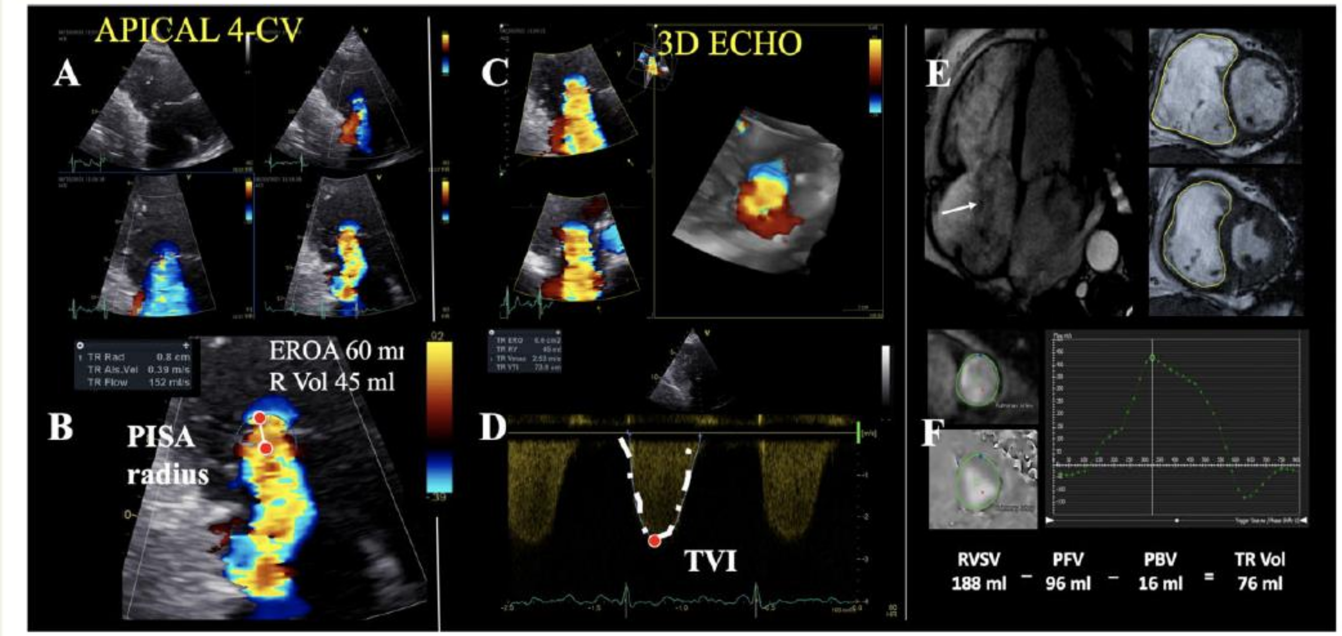

Figure 52 Quantitative assessment of TR severity using the PISA method (*A–D*) and the indirect CMR method (*E* and *F*). White arrow: extent of the signal loss on cine CMR. (*E*) Assessment of LV volumes using cine images. (*I*) Phase-contrast velocity mapping at the aortic root level and flow-time curves computing forward aortic flow.

"Quantify whenever possible….."

Lancellotti P, et al. Eur J Echocardiogr. 2010 May;11(4):307-321

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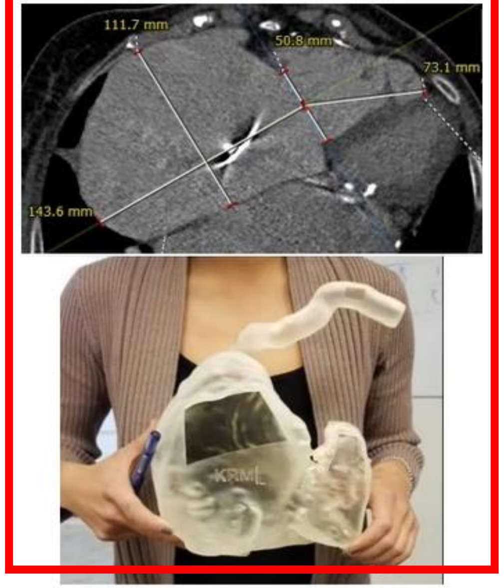
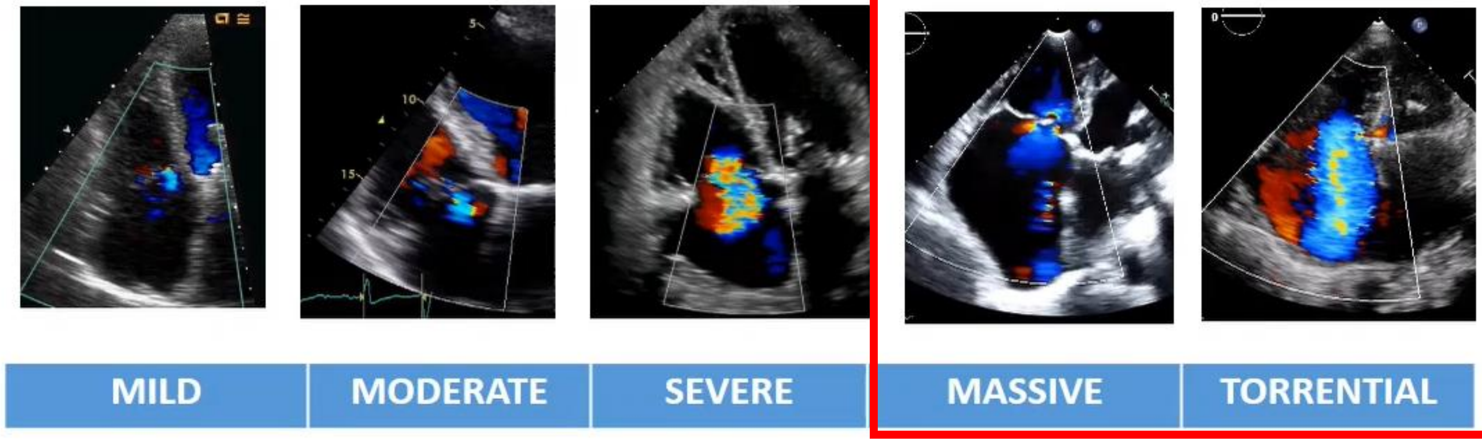
NEW GRADING SCHEME

Table I Proposed expansion of the 'Severe' grade

Variable	Mild	Moderate	Severe	Massive	Torrential
VC (biplane)	<3 mm	3-6.9 mm	7–13 mm	14–20 mm	≥21 mm
EROA (PISA)	<20 mm^2	20–39 mm^2	40–59 mm^2	60–79 mm^2	≥80 mm^2
3D VCA or quantitative EROA[a]			75–94 mm^2	95–114 mm^2	≥115 mm^2

VC, vena contracta; EROA, effective regurgitant orifice area; 3D VCA, three-dimensional vena contracta area.
[a]3D VCA and quantitative Doppler EROA cut-offs may be larger than PISA EROA.





RT Hahn and JL Zamorano. Europ
(2017) 00, 1–2. doi:10.1093/ehjci/je

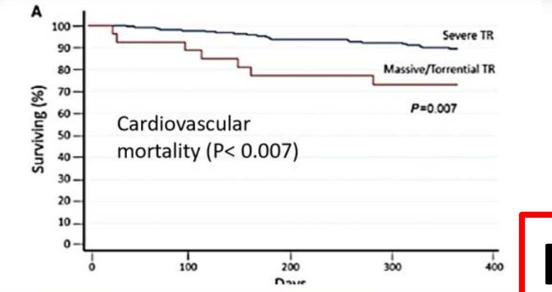
Range of TR Severity with signs and symptoms of "right heart failure"

ESC European Society of Cardiology
European Heart Journal - Cardiovascular Imaging (2019) 0, 1–8
doi:10.1093/ehjci/jez024

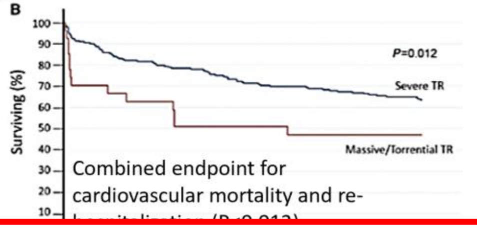
Mid-term outcome of severe tricuspid regurgitation: are there any differences according to mechanism and severity?

Ciro Santoro[1,2], Alvaro Marco del Castillo[1,2], Ariana González-Gómez[1,2], Juan Manuel Monteagudo[1,2], Rocio Hinojar[1,2], Alvaro Lorente[1,2], María Abellás[1,2], Jose Maria Vieitez[1,2], Ana Garcia Martin[1,2], Eduardo Casas Rojo[1,2], Soledad Ruíz[1,2], Vivencio Barrios[1,2], Jose Luis Moya[1,2], Jose Julio Jimenez-Nacher[1,2], Jose Luis Zamorano Gomez[1,2], and Covadonga Fernández-Golfin[1,2]*

Vena Contracta Average Diameter



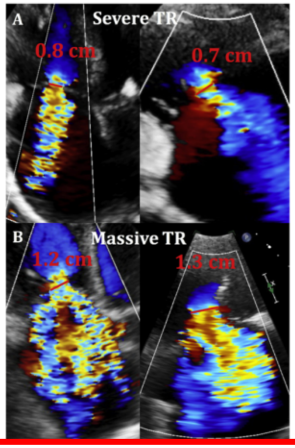
Cardiovascular mortality (P< 0.007)

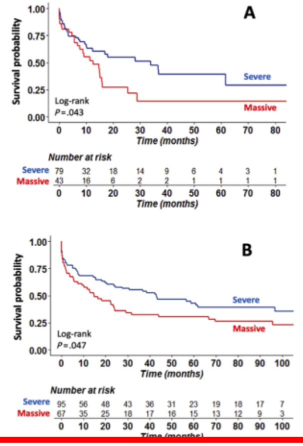


Combined endpoint for cardiovascular mortality and re-

Santoro C et al. Eur Heart J Cardiovasc Imag

Vena Contracta Average Diameter





Refining Severe Tricuspid Regurgitation Definition by Echocardiography with a New Outcomes-Based "Massive" Grade

Kalie Y. Kebed, MD, Karima Addetia, MD, Michael Henry, MD, Megan Yamat, RDCS, Lynn Weinert, RDCS, Stephanie A. Besser, MSAS, MSA, MACJC, Victor Mor-Avi, PhD, and Roberto M. Lang, MD, *Chicago, Illinois*

- In the study cohort, VC > 0.92 cm (massive TR) was associated with TA and RV size, and optimally associated with worse survival.
- **In the independent validation cohort, VC > 0.92 also correlated with increased mortality in the massive group (log-rank P < .05).**

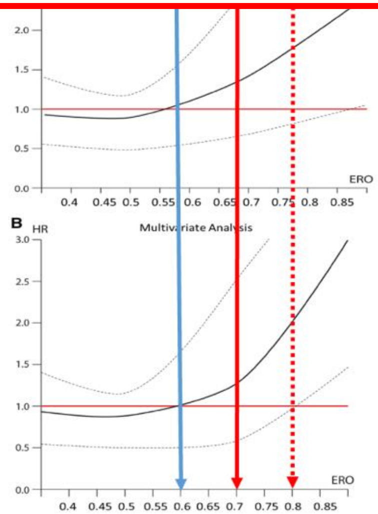
Key Points:

1. **Evidence for Outcomes associated with extended grading scheme…in native TR…**

Patients with ≥Severe TR (ER

- ERO negatively impacted survival, even when including only the subgroup of patients with severe TR [HR 1.5 (1.01–2.3); *P* = 0.04].
- The risk of death increases even further when ERO >0.7 cm².
  - The optimal threshold to separation survival between **severe vs. 'torrential' TR was 0.7 cm²** [*P* = 0.005, HR =2.6 (1.2–5.1)].

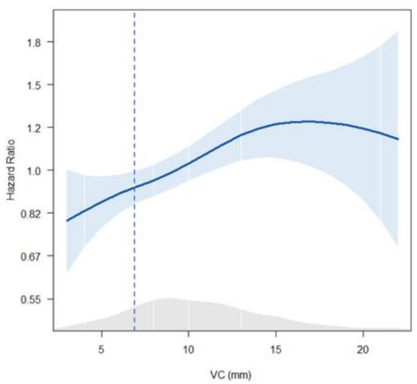
NOTE: Hahn Scheme cutoffs: Massive = 0.6 cm² and Torrential = 0.8 cm²



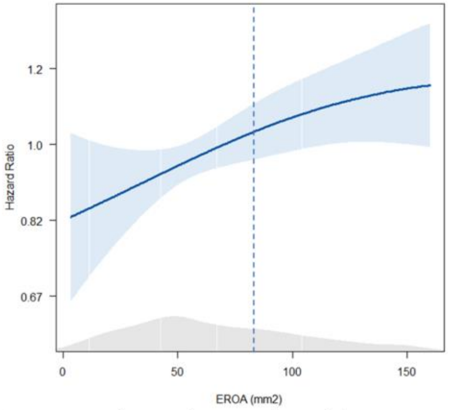
Peri Y et al. Eur Heart J Cardiovasc Imaging. 2020 Jul 1;21(7):768-776.

B) vs all-cause mortality

wise integration of VC width and EROA into the novel algorithm because the risk for all-cause mortality:

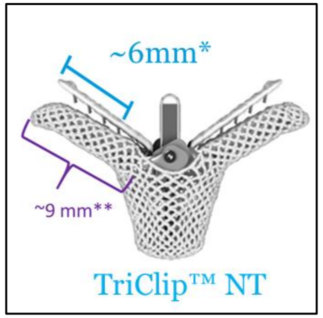


- Increased until it reached a peak, followed by a plateau for VC width



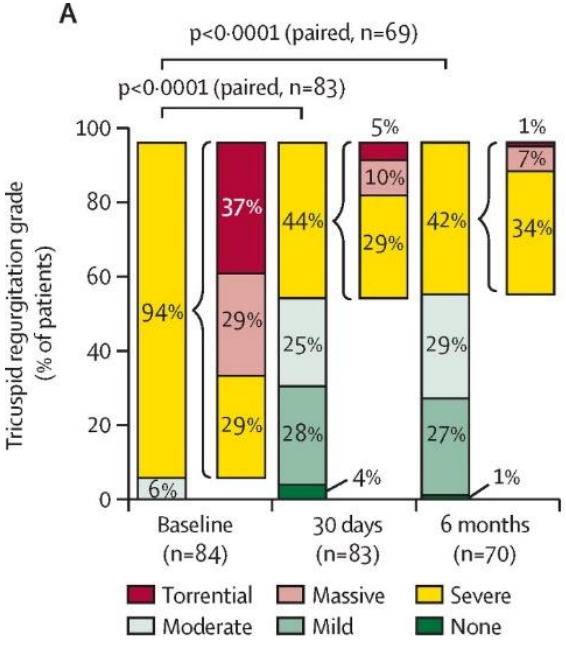
- Increased continuously without any plateau phase for higher values of EROA.

Fortuni F. et al. *J Am Coll Cardiol Cardiovasc Imaging* 2021

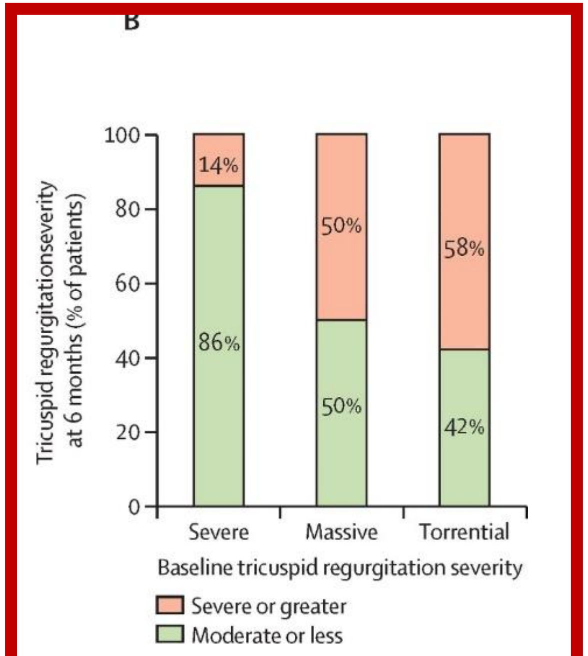


Transcatheter edge-to-edge repair for reduction of tricuspid regurgitation: 6-month outcomes of the TRILUMINATE single-arm study

Georg Nickenig*, Marcel Weber*, Philipp Lurz, Ralph Stephan von Bardeleben, Marta Sitges, Paul Sorajja, Jörg Hausleiter, Paolo Denti, Jean-Noël Trochu, Michael Näbauer, Abdellaziz Dahou, Rebecca T Hahn

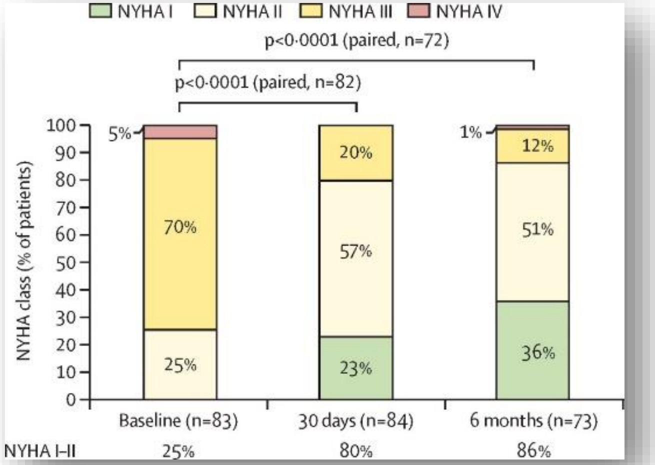


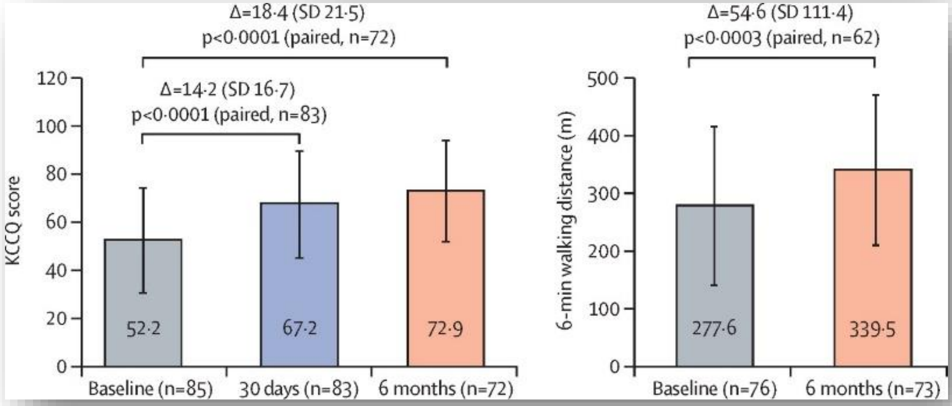
(A) Severity of tricuspid regurgitation at baseline, 30 days and 6 months



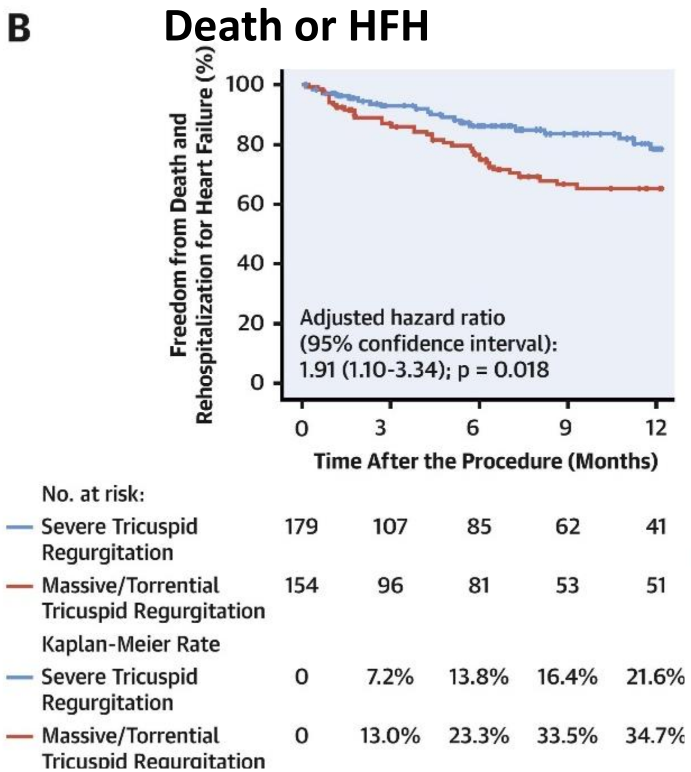
(B) Proportion of patients with reduced tricuspid regurgitation severity by baseline severity status.

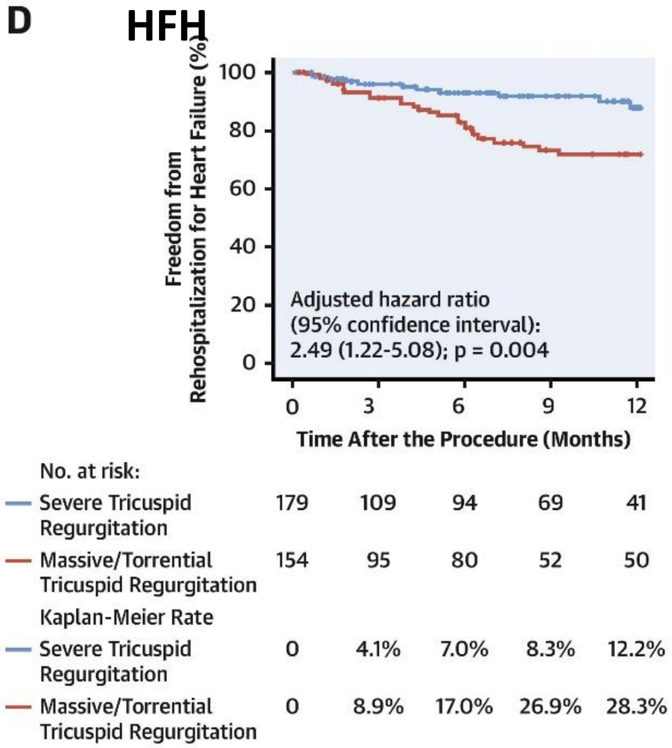
The TriClip system appears to be safe and effective at reducing tricuspid regurgitation by at least one grade. This reduction could translate to significant clinical improvement at 6 months post procedure.

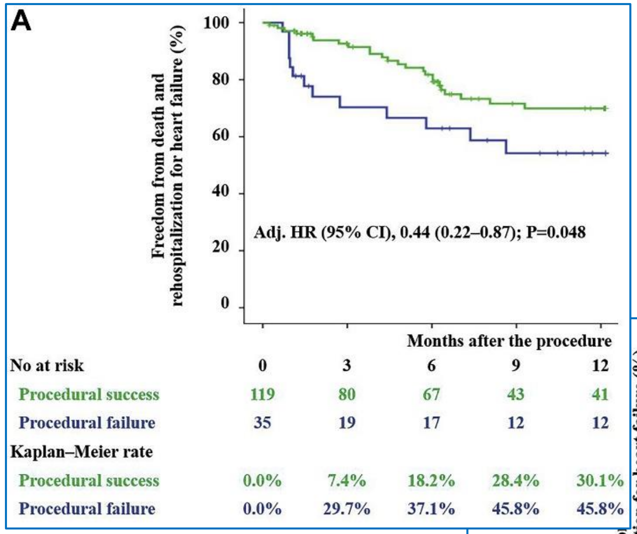




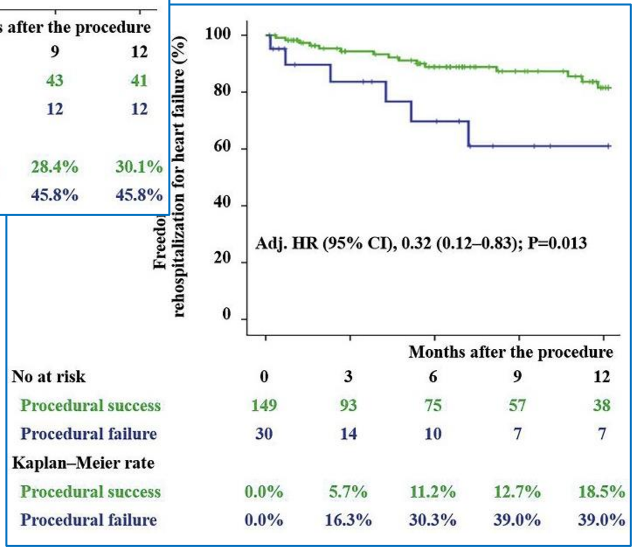
TriValve Investigators: Impact of Massive or Torrential Tricuspid Regurgitation in Patients Undergoing Transcatheter TV Intervention







Massive



Torrential

- **Baseline massive or torrential TR is associated with an increased risk for all-cause mortality and rehospitalization for heart failure 1 year after TTVI.**

Procedural success (TR ≤2+) is associated with improved outcomes, even in with baseline massive or torrential TR.

Trialign Tricuspid Annular Repair

SCOUT I & II Pooled Cohort

Safety and Technical Success

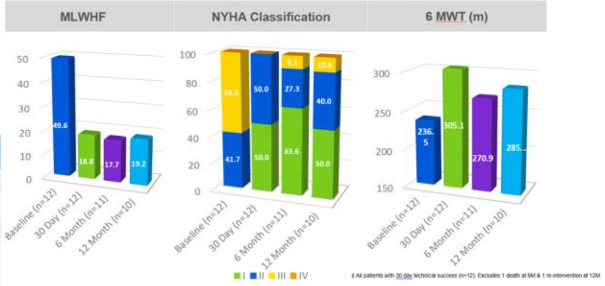
30-Day Outcome	(n/N) %
Freedom from mortality within 30-days	51/51 (100%)
Procedural Success (Successful access, delivery & retrieval of the system)	50/51 (98.0%)
No unplanned or emergency surgery or re-intervention related to the device or access procedure within 30 days	50/51 (98.0%)

	Baseline◊	1 Month	p-value*
TV annular diameter (cm)	4.0 ± 0.6 (41)	3.8 ± 0.6 (42)	0.005
TV area (2D) (cm2)	12.66 ± 2.67 (43)	11.25 ± 2.3 (42)	<0.001
PISA EROA (cm2)	0.5 ± 0.18 (42)	0.4 ± 0.21 (38)	0.035
TV area-derived diameter (cm)	3.99 ± 0.42 (43)	3.77 ± 0.38 (42)	<0.001

Safe and "Effective"

Intermediate Follow-up

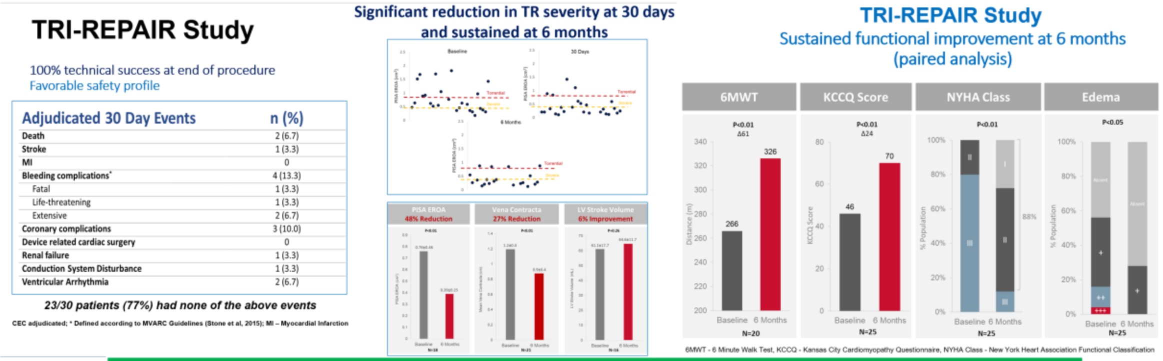
Per Protocol‡



Improved Function and QoL

Hahn RT et al. J Am Coll Cardiol. 2017 Apr 11;69(14):1795-1806

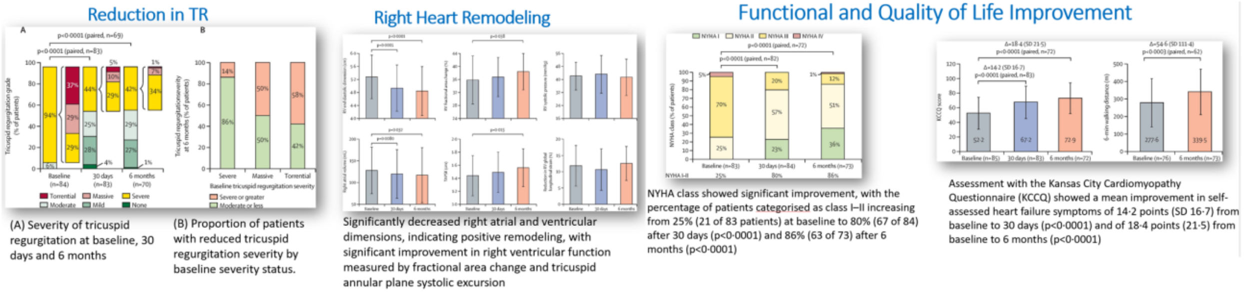
Cardioband Tricuspid Annuloplasty Device



April 30, 2018—Edwards Lifesciences announced that it has received European CE Mark approval for its Cardioband tricuspid valve reconstruction system for the treatment of tricuspid regurgitation.

Nickenig G et al. . J Am Coll Cardiol. 2019 Apr 23;73(15):1905-1915.

TRILUMINATE Early Feasibility Trial Transcatheter Edge-to-Edge Repair (TEER) with Triclip Device



(A) Severity of tricuspid regurgitation at baseline, 30 days and 6 months

(B) Proportion of patients with reduced tricuspid regurgitation severity by baseline severity status.

Significantly decreased right atrial and ventricular dimensions, indicating positive remodeling, with significant improvement in right ventricular function measured by fractional area change and tricuspid annular plane systolic excursion

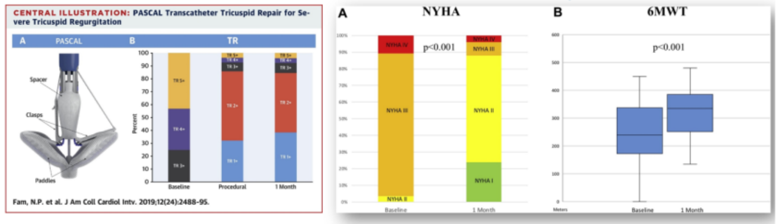
NYHA class showed significant improvement, with the percentage of patients categorised as class I–II increasing from 25% (21 of 83 patients) at baseline to 80% (67 of 84) after 30 days (p<0·0001) and 86% (63 of 73) after 6 months (p<0·0001)

Assessment with the Kansas City Cardiomyopathy Questionnaire (KCCQ) showed a mean improvement in self-assessed heart failure symptoms of 14·2 points (SD 16·7) from baseline to 30 days (p<0·0001) and of 18·4 points (21·5) from baseline to 6 months (p<0·0001)

April 9, 2020 -- Abbot announced that its TriClip™ Transcatheter Tricuspid Valve Repair System has received CE Mark

Nickenig G et al. Lancet. 2019 Nov 30;394(10213):2002-2011

Compassionate Use and CLASP TR Early Feasibility Trial for PASCAL TEER Device

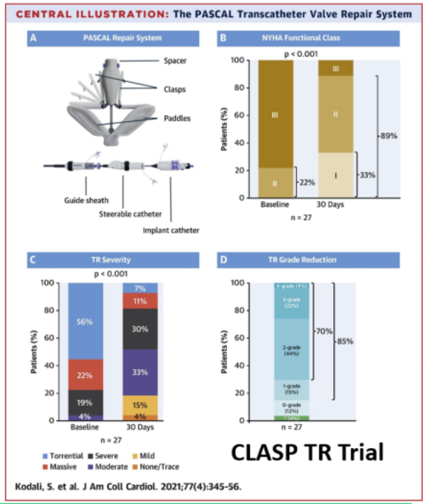


The presence of a TR grade ≥3+ was reduced from 100% (28 of 28 patients) before the procedure to 15% (4 of 26 patients) at 30-day follow-up ($p < 0.001$)

➢88% of patients were in New York Heart Association functional class I or II, with TR grades≤2+ in 85%.

➢Six-min walk distance improved from 240 m(interquartile range: 172 to 337 m) to 335 m (interquartile range: 251 to 385 m) (p<0.001)

Compassionate Use



CLASP TR Trial

May 18, 2020 — Edwards Lifesciences announced that it received CE Mark approval for its Pascal transcatheter valve repair system for treating tricuspid valve regurgitation

Kodali S et al. J Am Coll Cardiol. 2021 Feb 2;77(4):345-356.

ORIGINAL ARTICLE

Transcatheter Repair for Patients with Tricuspid Regurgitation

Paul Sorajja, M.D., Brian Whisenant, M.D., Nadira Hamid, M.I
Hursh Naik, M.D., Raj Makkar, M.D., Peter Tadros, M.D., Matthew J. P
Gagan Singh, M.D., Neil Fam, M.D., Saibal Kar, M.D.,
Jonathan G. Schwartz, M.D., Shamir Mehta, M.D., Richard Bae, M
Nishant Sekaran, M.D., Travis Warner, M.D., Moody Makar, M.
George Zorn, M.D., Erin M. Spinner, Ph.D., Phillip M. Trusty, Ph
Raymond Benza, M.D., Ulrich Jorde, M.D., Patrick McCarthy, M
Vinod Thourani, M.D., Gilbert H.L. Tang, M.D., Rebecca T. Hahn,
and David H. Adams, M.D., for the TRILUMINATE Pivotal Investig

Table 2. Primary and Secondary End Points.*

End Point	TEER Group (N=175)	Control Group (N=175)	Difference (95% CI	
Primary				
Hierarchical composite of death from any cause or tricuspid-valve surgery; hospitalization for heart failure; and improvement of ≥15 points in KCCQ score at 1 yr — no. of wins†	11,348	7643	1.48 (1.06 to 2.13)	
Secondary, listed in hierarchical order				
Kaplan–Meier estimate of percentage of patients with freedom from major adverse events through 30 days after the procedure (lower 95% confidence limit)‡	98.3 (96.3)	—	—	<0.001
Change in KCCQ score from baseline to 1 yr — points§	12.3±1.8	0.6±1.8	11.7 (6.8 to 16.6)	<0.001
Tricuspid regurgitation of no greater than moderate severity at 30-day follow-up — no. of patients/total no. (%)¶	140/161 (87.0)	7/146 (4.8)	—	<0.001
Change in 6-min walk distance from baseline to 1 yr — m‖	−8.1±10.5	−25.2±10.3	17.1 (−12.0 to 46.1)	0.25

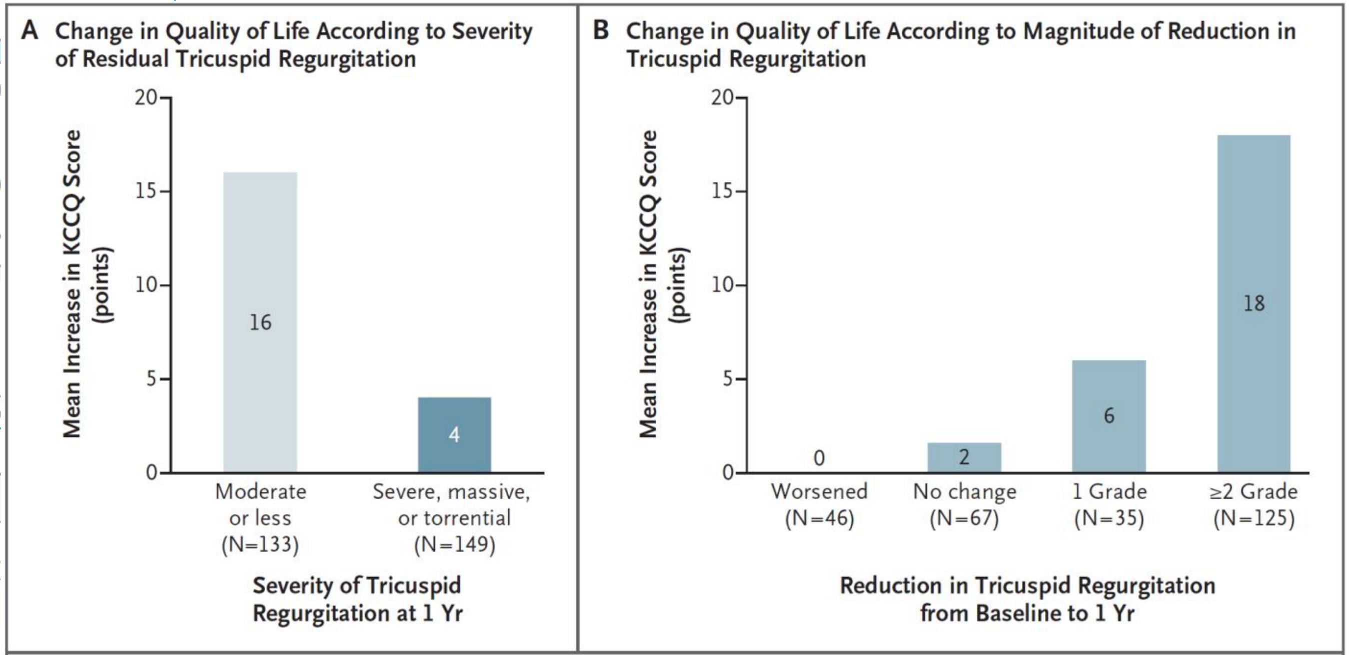


Figure 2. Changes in Quality of Life from Baseline to 1 Year, Stratified According to the Severity of Residual Tricuspid Regurgitation and the Magnitude of the Reduction in Tricuspid Regurgitation.

Sorajja P, et al. N Engl J Med. 2023 Mar 4.

@hahn_rt

ESC European Society of Cardiology
European Heart Journal (2021) 00, 1–72
doi:10.1093/eurheartj/ehab395
ESC/EACTS GUIDELINES

2021 ESC/EACTS Guidelines for the management of valvular heart disease

Developed by the Task Force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Echocardiographic evaluation of tricuspid regurgitation severity is based on an integrative approach considering multiple qualitative and quantitative parameters (*Table* 9). Due to the non-circular and non-planar shape of the regurgitant orifice, biplane vena contracta width should be considered in addition to the conventional 2D measurement.[402] Similarly, underestimation of tricuspid regurgitation severity by the PISA method may occur.[403] In case of inconsistent findings, the 3D vena contracta area may be evaluated, although diverging cut-offs have been reported.[402,404–406] Recently, a new grading scheme including two additional grades ('massive' and 'torrential') has been proposed[407] and used in clinical studies on transcatheter interventions.[408,409] Studies showed an incremental prognostic value of the two additional grades (massive and torrential) in terms of mortality and rehospitalization for heart failure in patients with advanced disease.[410–412]

Vahanian A, et al. Eur Heart J. 2022 Feb 12;43(7):561-632

ESC European Society of Cardiology
European Heart Journal - Cardiovascular Imaging (2022) 00, 1–62
https://doi.org/10.1093/ehjci/jeab253
EACVI DOCUMENT

Multi-modality imaging assessment of native valvular regurgitation: an EACVI and ESC council of valvular heart disease position paper

Key point: When feasible, the PISA method is the best to quantify the TR severity. A TR PISA radius >9 mm at a Nyquist limit of 28 cm/s indicates severe TR. An EROA ≥40 mm² and/or a R Vol ≥45 mL indicates severe TR. When severe, TR can be subcategorized into severe, massive and torrential, which is of clinical interest in patients referred for transcatheter intervention.

Lancellotti P et al. Eur Heart J Cardiovasc Imaging. 2022 Mar 16

Table 16 Grading the severity of TR in the context of transcatheter TV repair/replacement

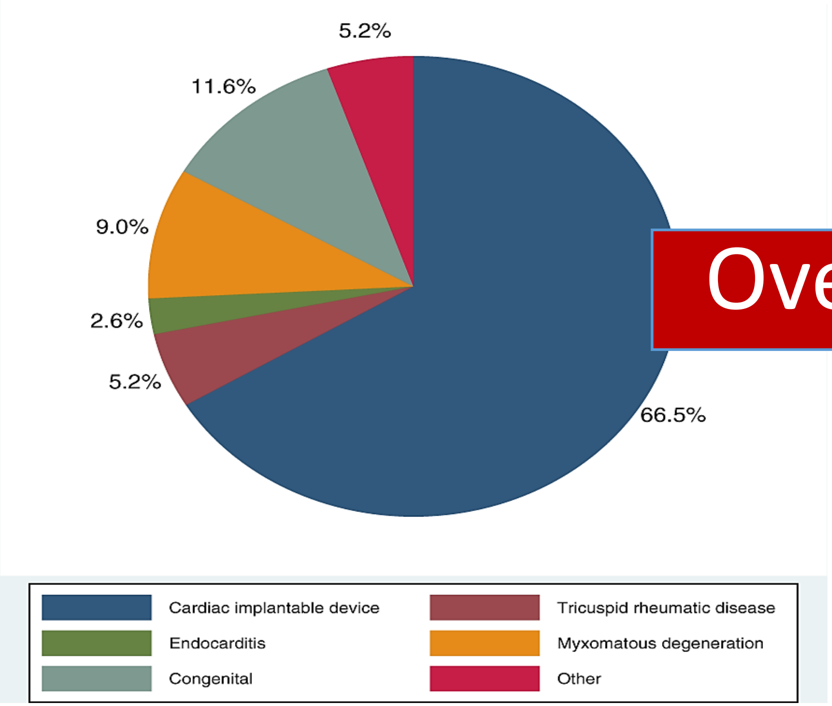
	Severe	Massive	Torrential
Semi-quantitative parameters			
VC width (mm)[a]	7–13	14–20	≥21
3D VC area or quantitative Doppler EROA (mm^2)	75–94	95–114	≥115
Quantitative parameters			
EROA by PISA (mm^2)[b]	40–59	60–79	≥80
R Vol (mL)	40–59	60–74	≥75

EROA, effective regurgitant orifice area; RF, regurgitant fraction; R Vol, regurgitant volume.
[a]At a Nyquist limit of 50–60 cm/s.
[b]Baseline Nyquist limit shift of 28 cm/s.

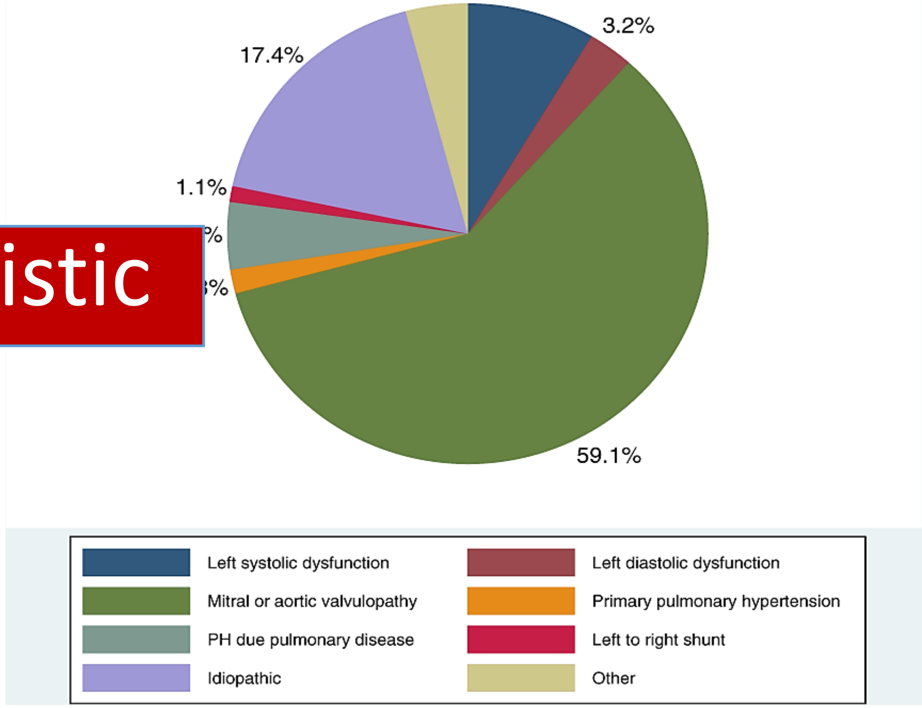
Assessment of TR Etiology

Etiology of the Tricuspid Valve

- **Ten Spanish centres participated in this study.**
- **Significant TR was present in 2121 of the 35 088 (6.0%) consecutive echocardiographic studies performed.**



Overly simplistic

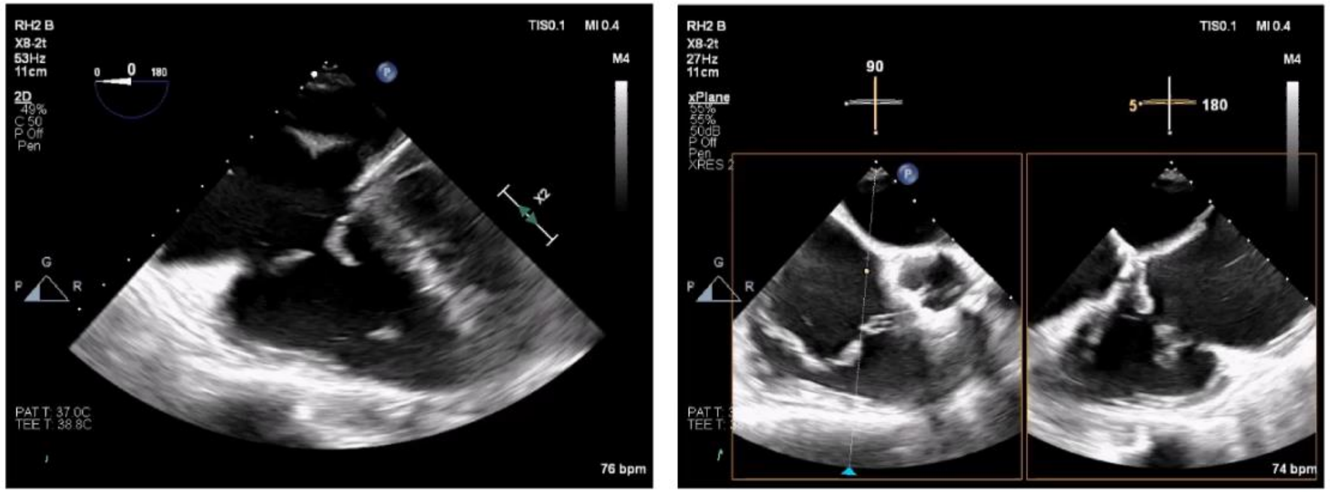


- **Primary TR was present only in 7.4% (n = 157)**
- In the group of primary TR, the **most frequent etiology was Cardiac Implantable Devices (66.5%),** representing 5% of all TR.

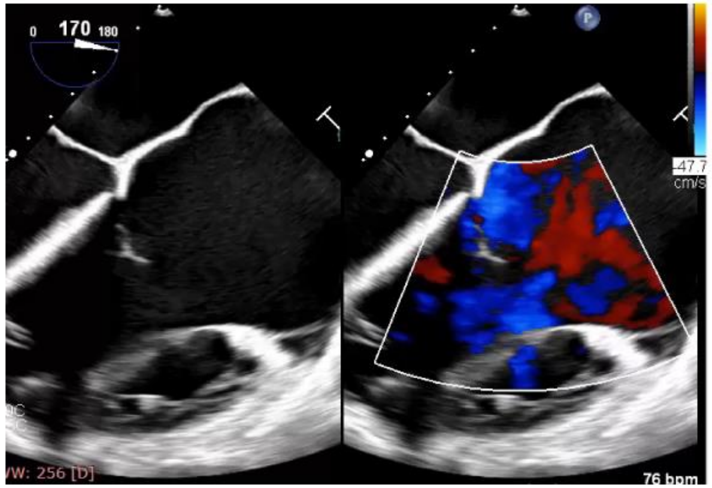
- **Secondary TR was present in 92.6% (n= 1964)**
- Most common etiology **was mitral or aortic valvulopathy** (59.1%) with MR representing >50% of associated VHD
- **Isolated TR was the second most common** etiology (17.4%)

Primary

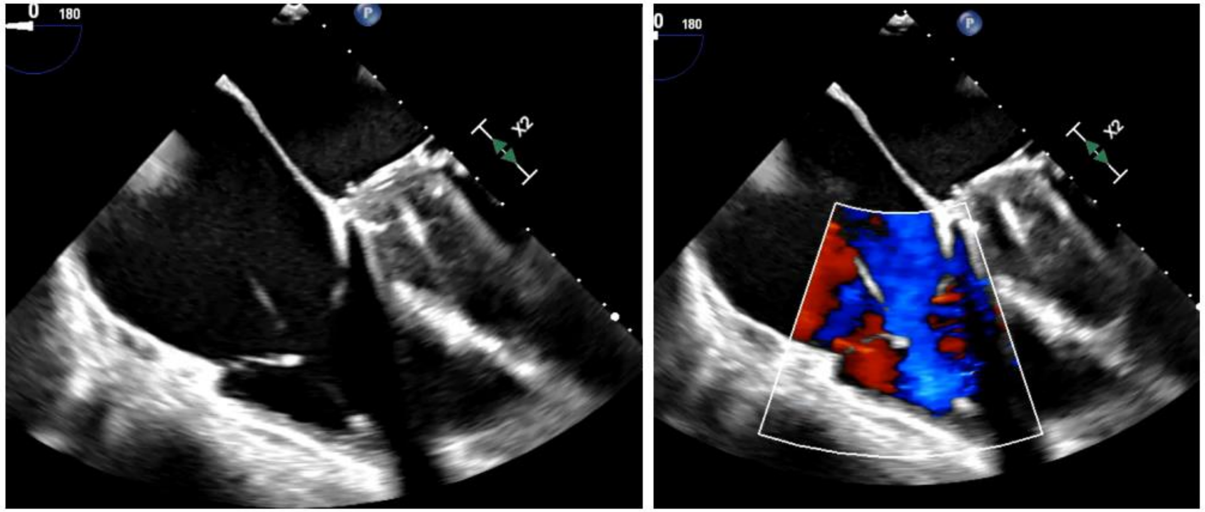
Prolapse



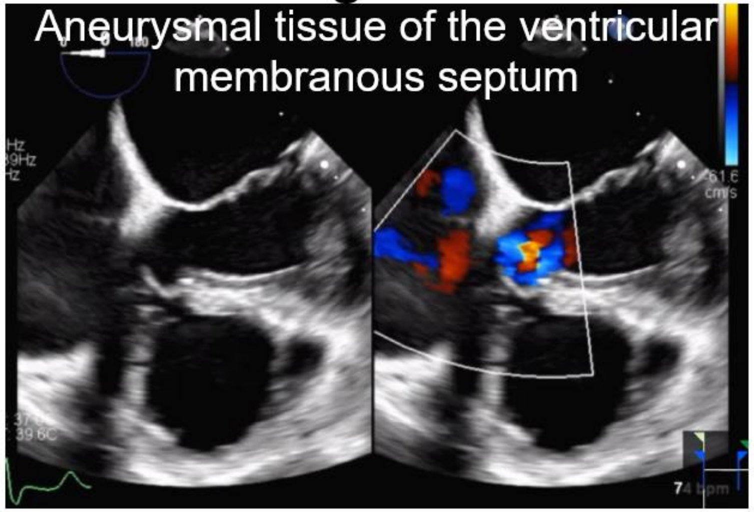
Flail Septal Leaflet



Rheumatic



Congenital



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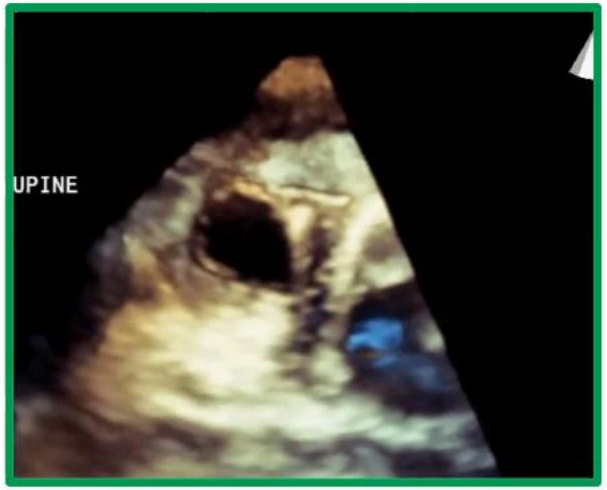
Primary or Secondary Disease?

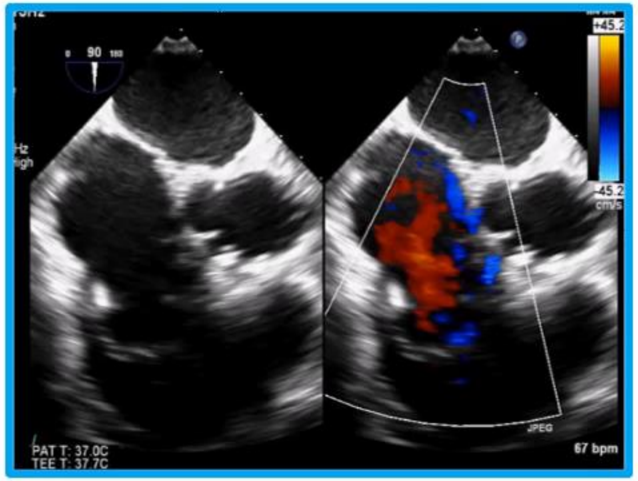
Transthoracic Echo

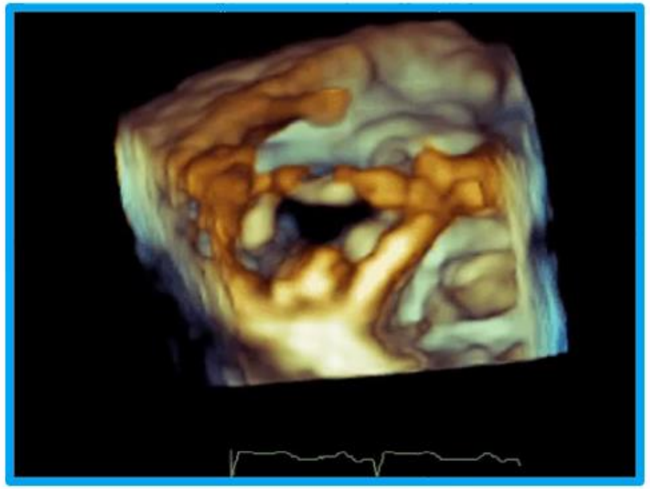
Anterior leaflet impingement

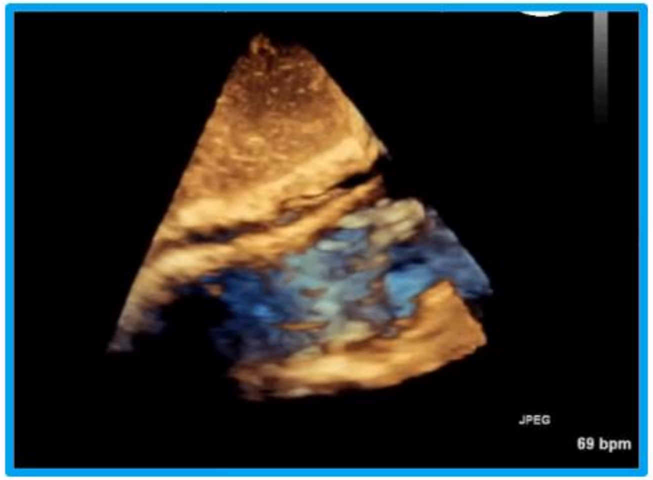


TEE

Posterior leaflet impingement







Not the same as incidental TR with a pacemaker!

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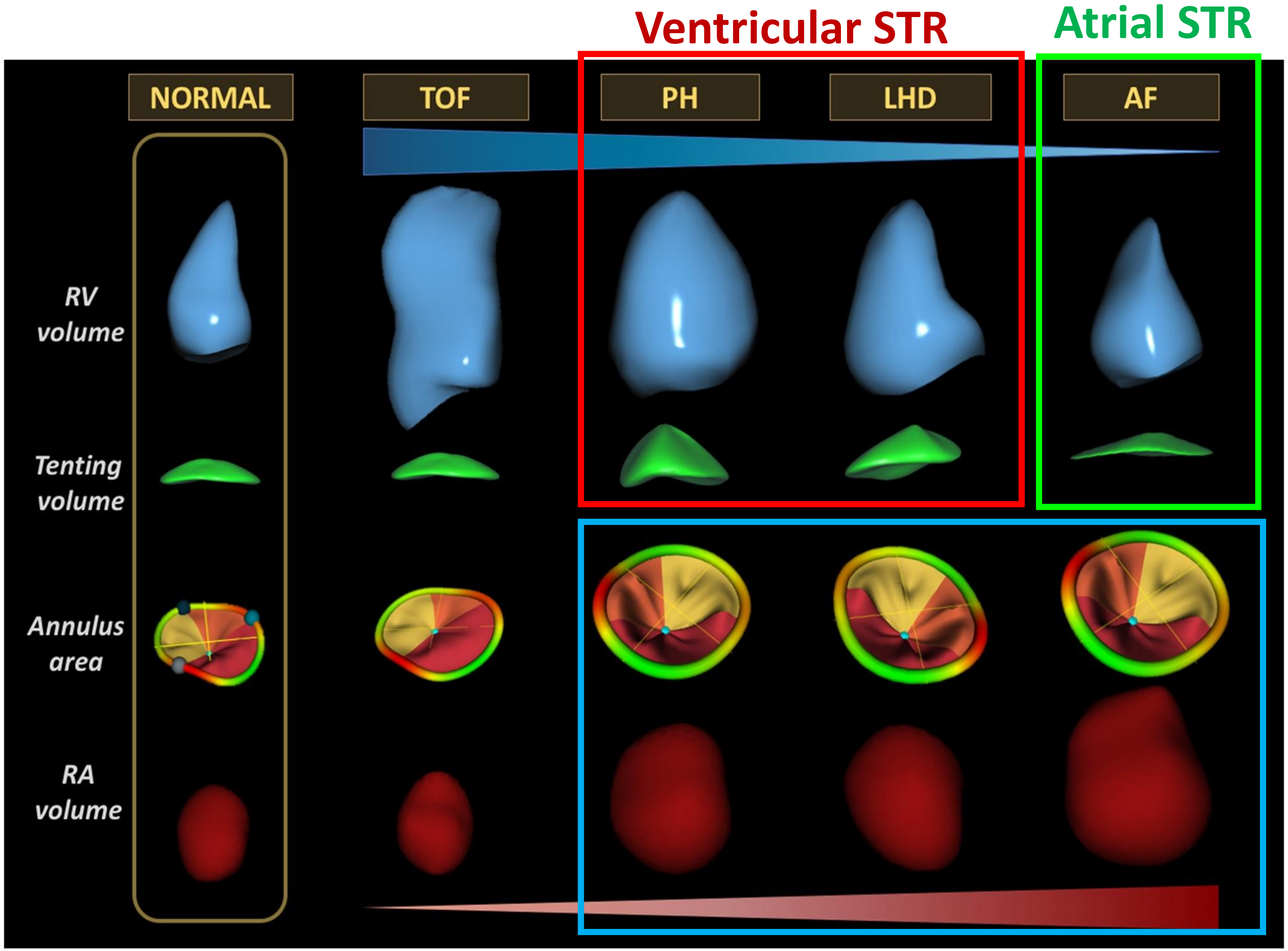
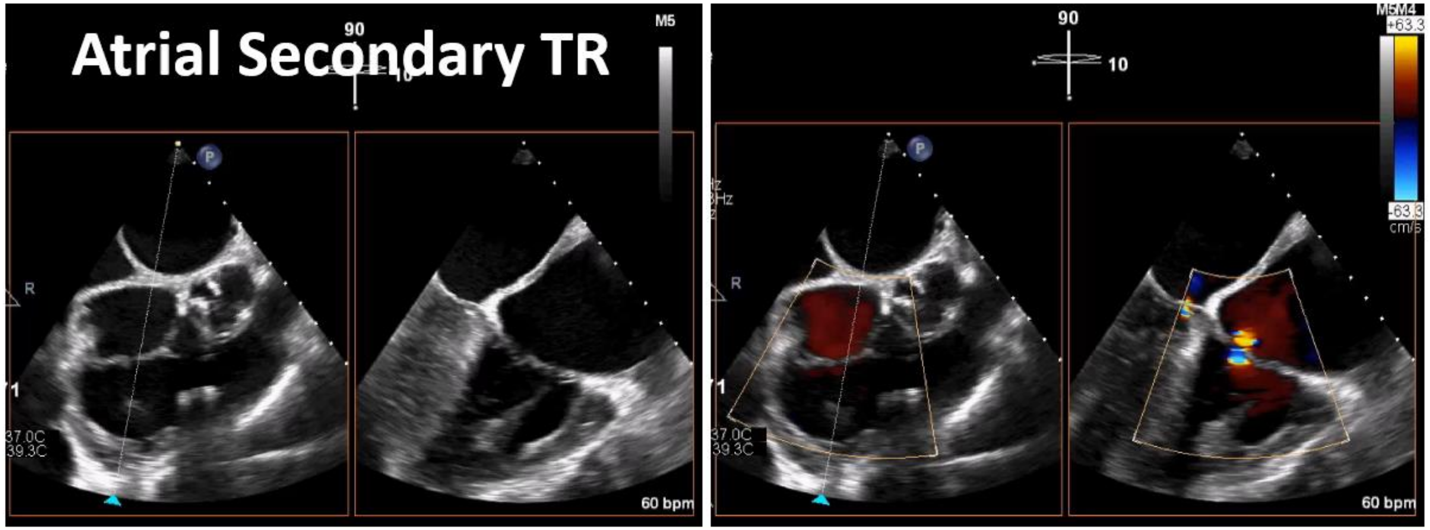


Three-dimensional echocardiographic study of Functional TR

- **RAVmax (AUC = 0.81) and TAA (AUC = 0.78)** had a greater ability than RVEDV (AUC = 0.72) to **predict severe FTR** (*P* < 0.05).

Muraru D et al. Eur Heart J Cardiovasc Imaging. 2021 May 10;22(6):660-669.

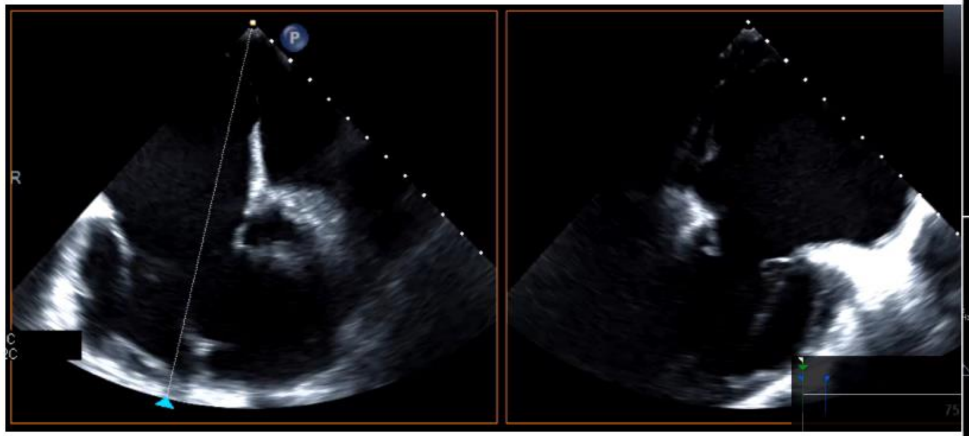
Atrial Secondary TR

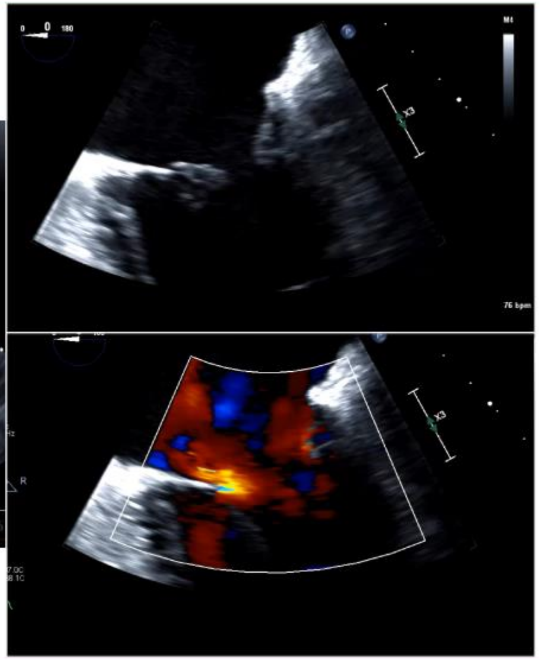


A-STR Criteria (ACC/AHA Guidelines):

- Atrial fibrillation
- Left ventricular ejection fraction > 60%,
- Pulmonary artery systolic pressure (PASP) <50 mmHg,
- No left-sided valve disease,
- Normal appearing tricuspid valve leaflets.

Ventricular Secondary TR



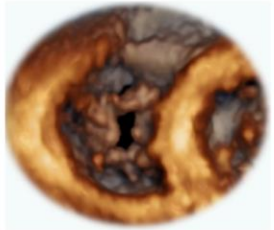
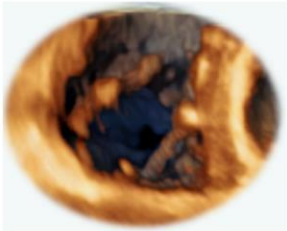
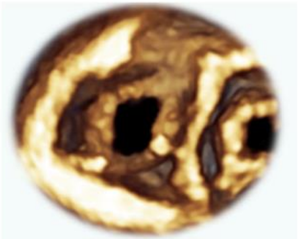


V-STR possible Criteria:

- Left ventricular ejection fraction ±reduced (≤50%)
- Tricuspid valve tenting height >10 mm
- Midventricular right ventricular diameter >38 mm

Novel Classification of TR by Valve/Right Heart Morphology

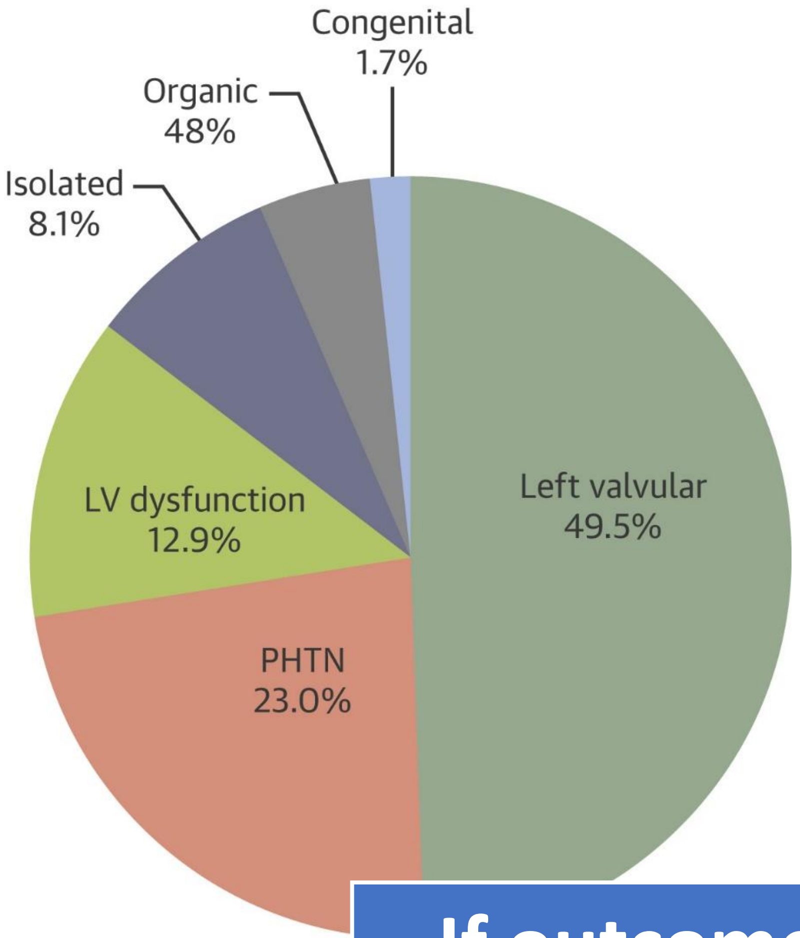
Adopted by the 2022 ESC/EACTS VHD Guidelines and the 2022 EACVI/ESC Multimodality Imaging Guidelines

	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	+++	+/-	+/-	+/-	+/-

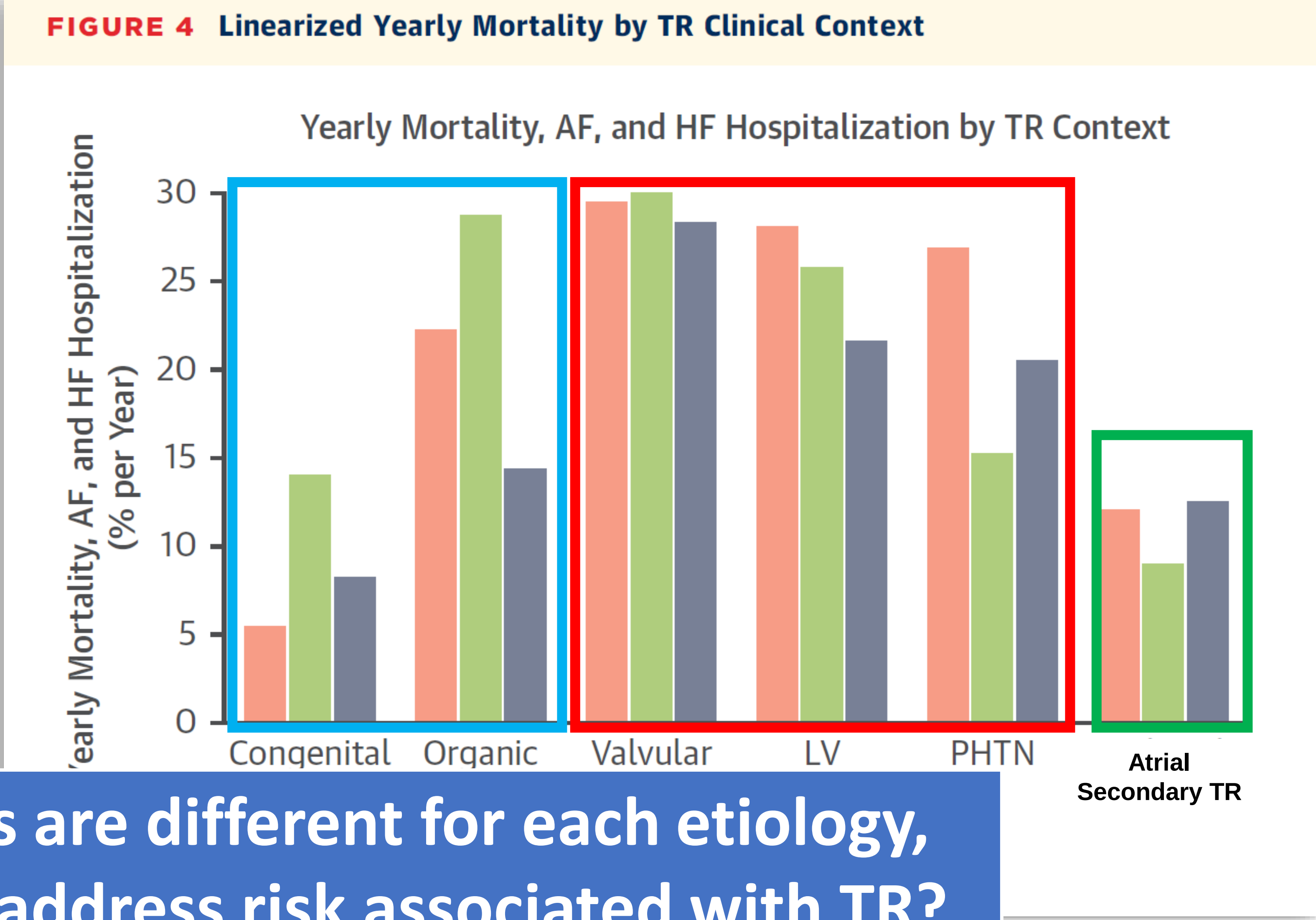
https://bit.ly/Update_TR

Hahn RT et al. Eur Heart J Cardiovasc Imaging. 2022 Feb 14:jeac009

Outcomes by Etiology in Secondary TR



Relativ



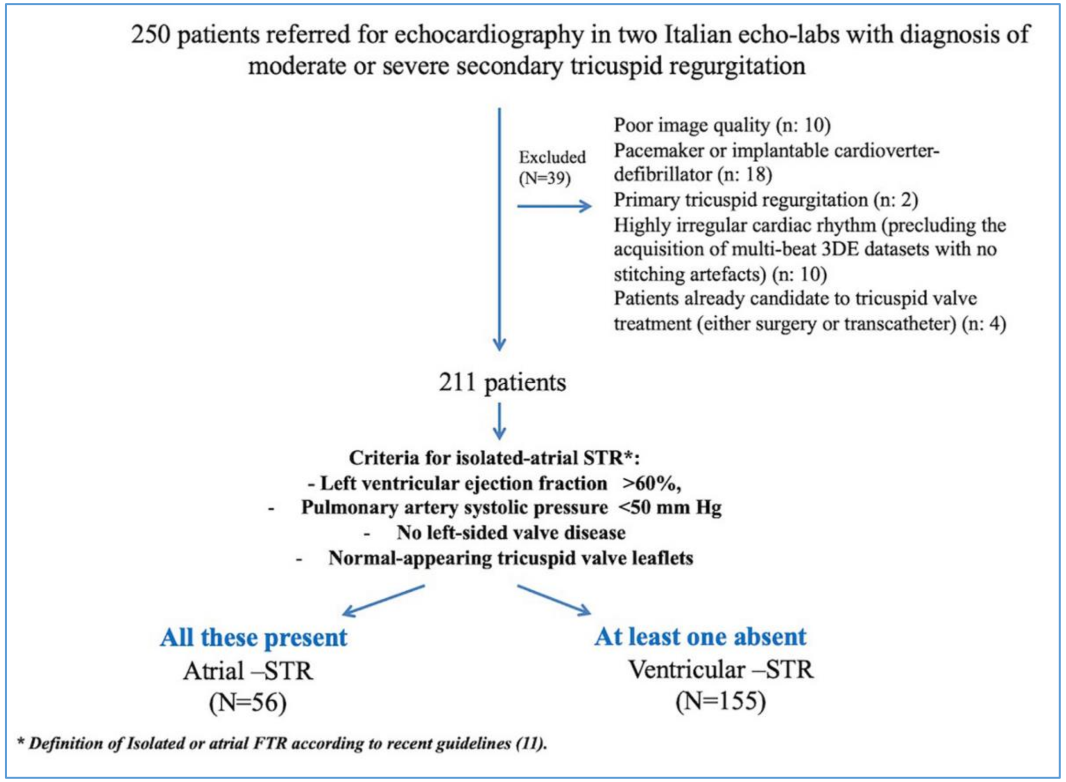
If outcomes are different for each etiology, how do we address risk associated with TR?

Assessing Risk Associated with TR

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

Mara Gavazzoni[1,2], Francesca Heilbron[1], Luigi P. Badano[1,2]*, Noela Radu[2,3], Andrea Cascella[2], Michele Tomaselli[1,2], Francesco Perelli[2], Sergio Caravita[1,4], Claudia Baratto[1,2], Gianfranco Parati[1] and Denisa Muraru[1,2]

[1]Department of Cardiology, Istituto Auxologico Italiano, IRCCS, Milan, Italy, [2]Department of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy, [3]Emergency University Hospital Bucharest, University of Medicine and Pharmacy Carol Davila Bucharest, Bucharest, Romania, [4]Department of Management, Information, and Production Engineering, University of Bergamo, Dalmine, Italy



The primary endpoint of the study was the occurrence of death for any cause and/or hospitalization for heart failure

- **A-STR Criteria (ACC/AHA Guidelines):**
  - **Atrial fibrillation**
  - **Left ventricular ejection fraction > 60%,**
  - **Pulmonary artery systolic pressure (PASP) < 50 mmhg,**
  - **No left-sided valve disease,**
  - **Normal appearing tricuspid valve leaflets.**

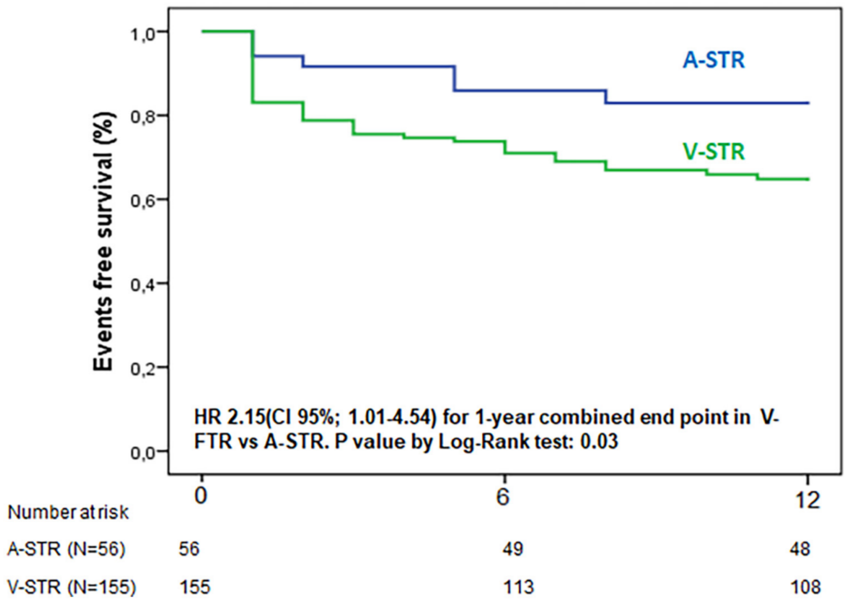


FIGURE 3
Kaplan-Meier curves for 1 year combined endpoint of all-cause death and hospitalization for heart failure. A-STR, atrial-secondary tricuspid regurgitation; HR, hazard Ratio; V-STR, ventricular secondary tricuspid regurgitation.

- There was a 2.15-fold significantly higher risk of 1-year combined endpoint (death and hospitalization for HF) for V-STR patients than A-STR

Multivariable Predictors of Outcomes (Medically Managed)

- A-STR
  - TR severity (HR: 5.8, CI 95%: 1.4–25, P = 0.019).
- V-STR
  - TR severity (HR 2.9, CI 95% 1.4–6.3, P = 0.005 for TR severe),
  - RVEF (HR: 0.97, CI 95%: 0.94–0.99, P = 0.044),
  - RVFWLS (HR: 0.93, CI 95%: 0.85–0.98, P = 0.009)

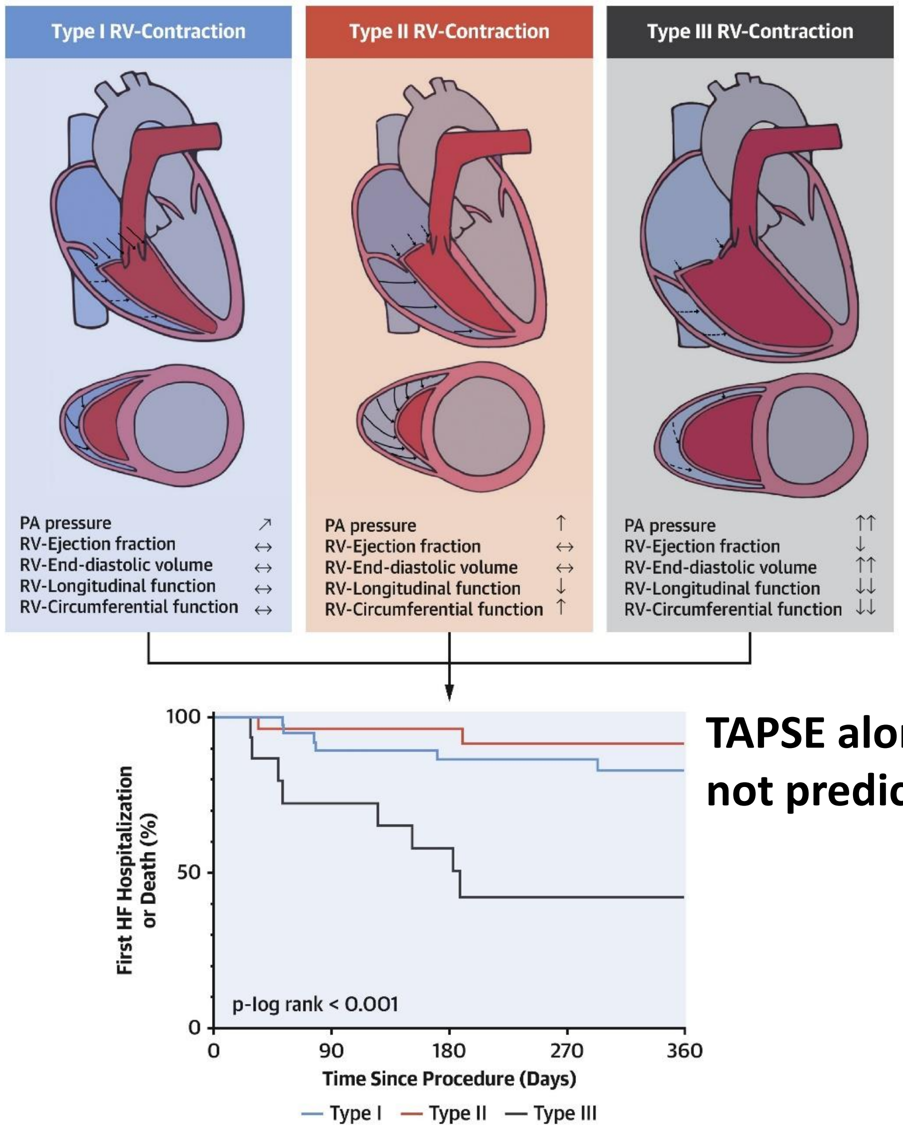
While STR severity is the only parameter independently associated with prognosis in A-STR, RV function (in addition to STR severity) had prognostic relevance in V-STR.

RVEF (CMR) and TAPSE (TTE) in patients undergoing TTVR

- Global RV dysfunction was defined as **CMR-derived RVEF ≤45%** and longitudinal RV dysfunction was defined as **TAPSE <17 mm** on echo.
- Patients were stratified into 3 types of RV contraction:
  - Type I, TAPSE ≥17 and RVEF >45%;
  - Type II, TAPSE <17 and RVEF >45%; and
  - **Type III, TAPSE <17 and RVEF ≤45%.**

Tricuspid regurgitation patients in which a loss of longitudinal function can be compensated by increasing circumferential function (preserving RVEF) had favorable outcomes.

CENTRAL ILLUSTRATION: Features and Prognostic Implications of RV Contraction Patterns in Patients Undergoing Transcatheter Tricuspid Valve Repair



TAPSE alone not predictive

Kresoja, K.-P. et al. J Am Coll Cardiol Intv. 2021;14(14):1551-61.

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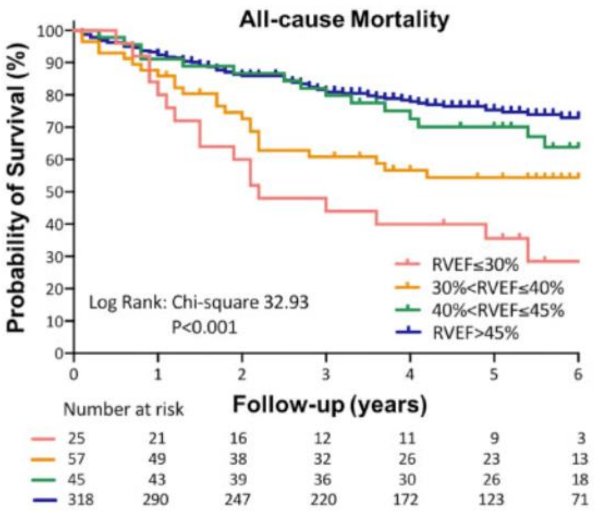
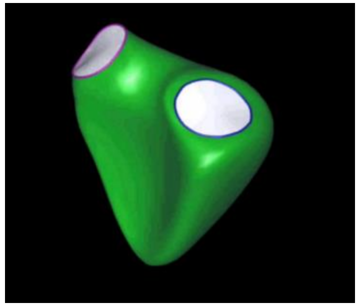
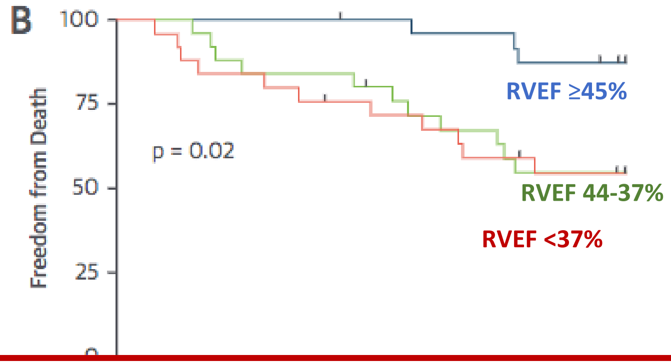
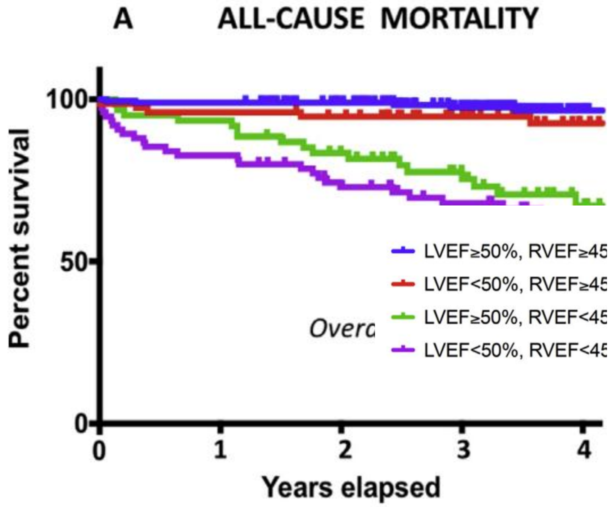
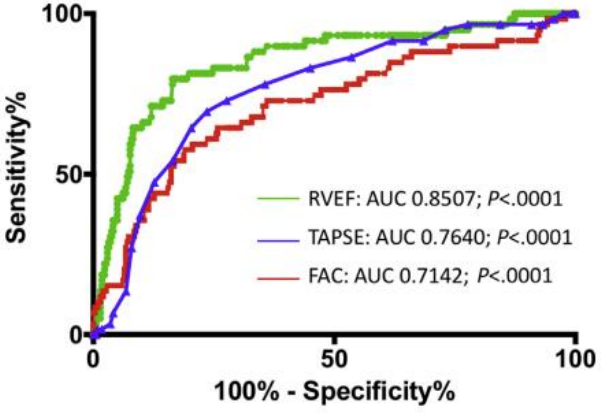
RVEF by 3D Echocardiography in Unselected and TTVR Patients











- ***RVEF <45% by 3DE** is a better outcome predictor than TAPSE and FAC*
- *Impairment of RVEF carried a significantly higher risk of mortality **independent of LVEF.***
- ***Impaired preprocedural RVEF by 3DE** was associated with **mortality after TTVR***

- **Orban M, …Hausleiter J. JACC Cardiovasc Imaging. 2021 doi: 10.1016/j.jcmg.2021.06.026**
- **Muraru D, Badano L et al. Eur Heart J Cardiovasc Imaging. 2020 doi: 10.1093/ehjci/jez233**
- **Surkova E, Muraru D, …Badano LP. J Am Soc Echocardiogr. 2019 doi: 10.1016/j.echo.2019.06.009.**

Slide developed for PCR Tricuspid Focus Group

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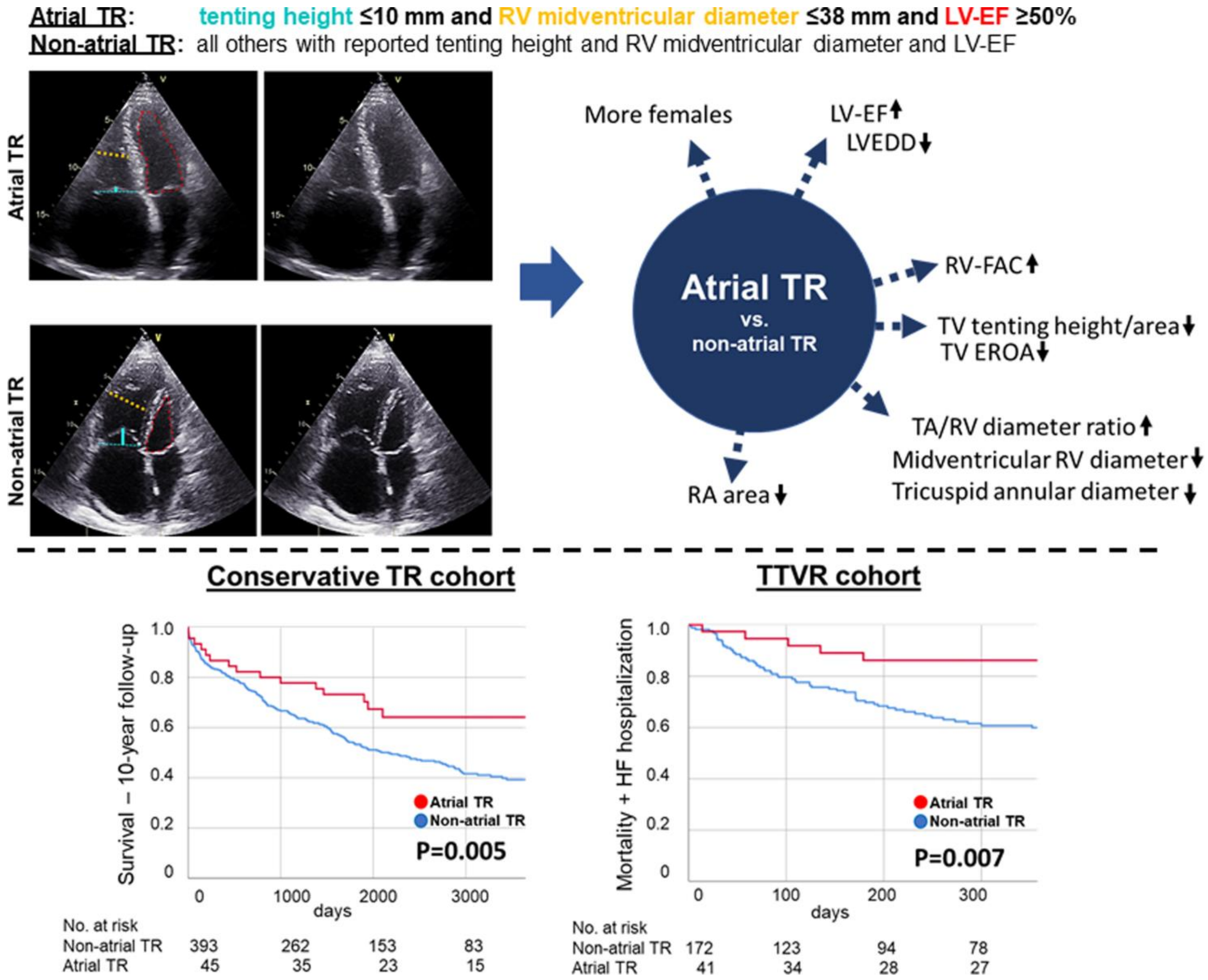
Atrial and Ventricular Secondary Tricuspid Regurgitation following TTVI

Based on a clustering approach, atrial TR was defined as:

- Tricuspid valve tenting height ≤10 mm,
- Midventricular right ventricular diameter ≤38 mm,
- Left ventricular ejection fraction ≥50%.



Schlotter F, et al. Circ Cardiovasc Interv. 2022 Sep;15(9):e011958

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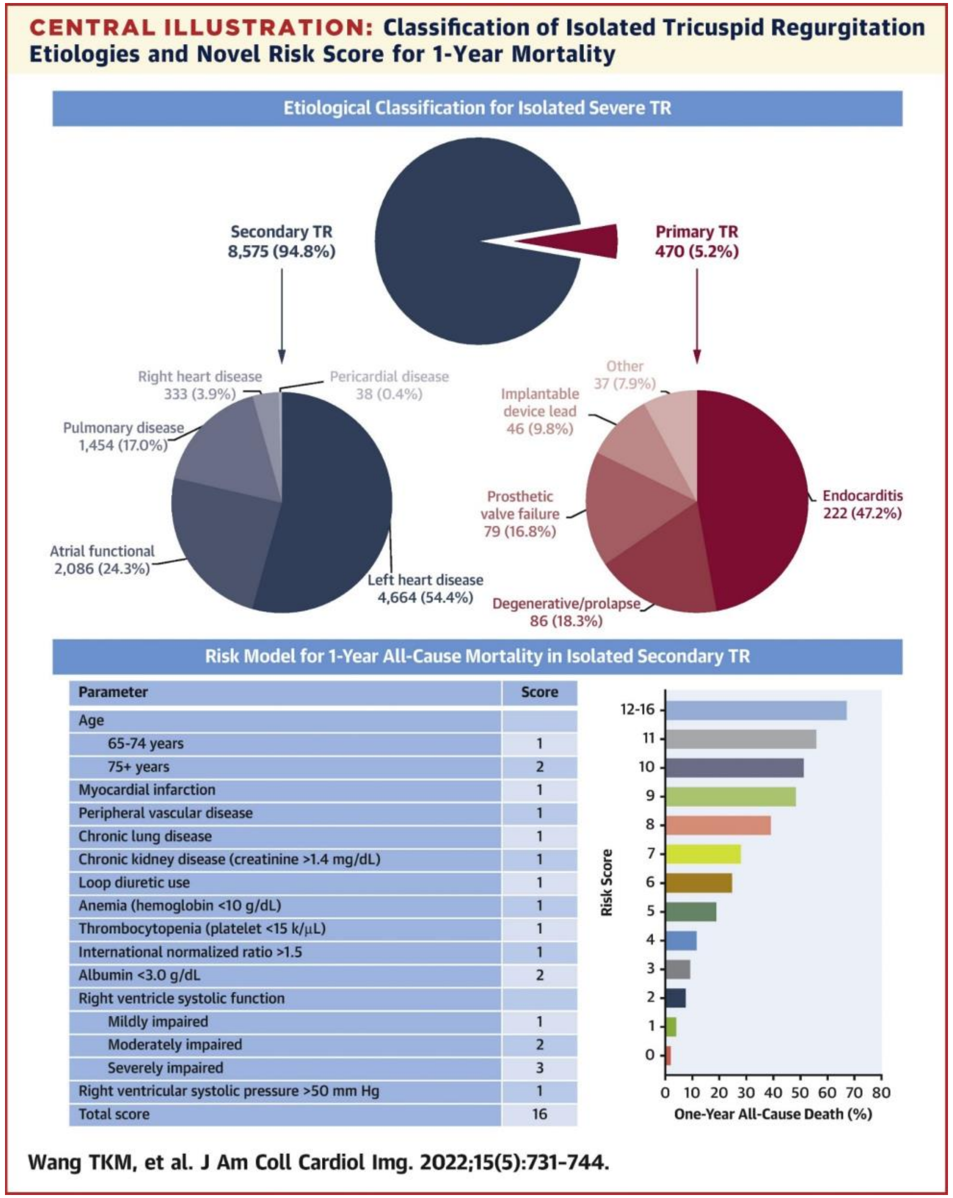
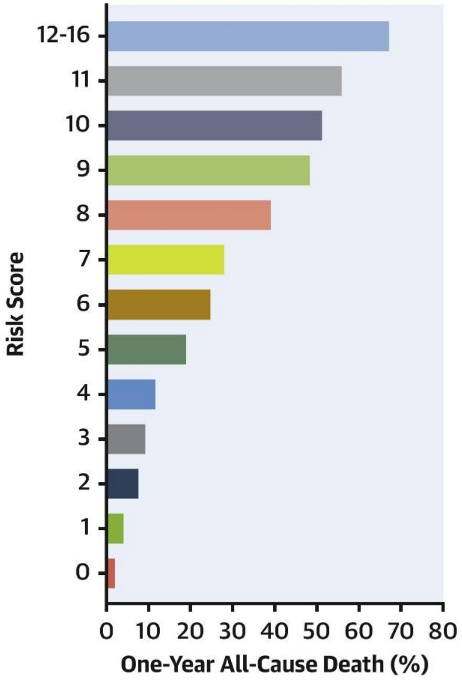


Risk Model for 1-Year All-Cause Mortality in Isolated Secondary TR

Parameter	Score
Age	
65-74 years	1
75+ years	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 (hemoglobin <10 g/dL)	1
Thrombocytopenia (platelet <15 k/μL)	1
International normalized ratio >1.5	1
Albumin <3.0 g/dL	2
Right ventricle systolic function	
Mildly impaired	1
Moderately impaired	2
Severely impaired	3
Right ventricular systolic pressure >50 mm Hg	1
Total score	16



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

- Secondary TR constituted conferred worse survival than primary TR in unadjusted but not adjusted analyses.
- A novel risk score stratifies the risk for 1-year death

The 5 Phenotypes of Tricuspid Regurgitation

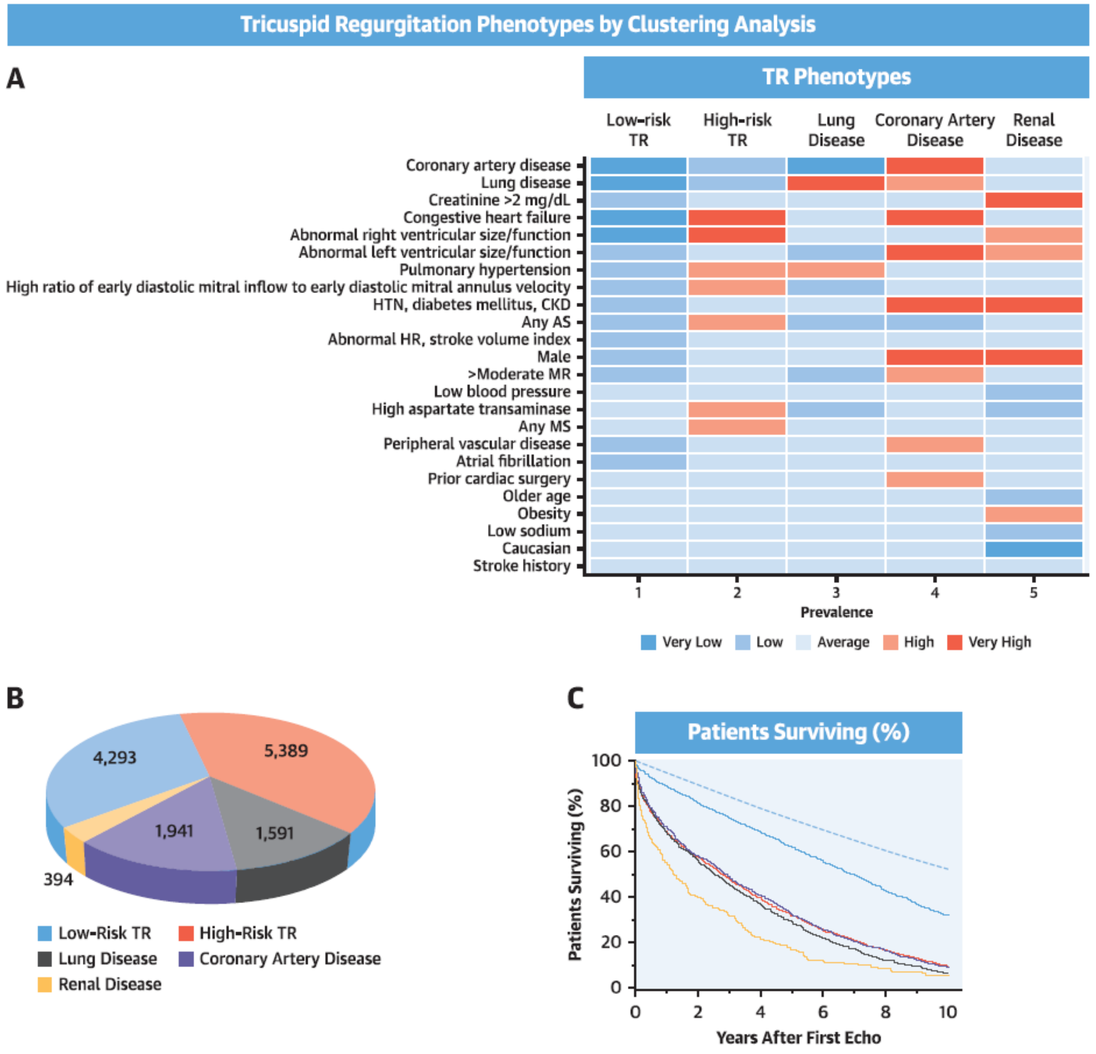
Insight From Cluster Analysis of Clinical and Echocardiographic Variables

Vidhu Anand, MBBS,[a] Christopher G. Scott, MS,[b] Meredith C. Hyun,[b] Kyla Lara-Breitinger, MD,[a] Vuyisile T. Nkomo, MD, MPH,[a] Garvan C. Kane, MD, PhD,[a] Cristina Pislaru, MD,[a] Kathleen F. Kopeck
Phillip J. Schulte, PhD,[c] Sorin V. Pislaru, MD, PhD[a]

Progressively worse prognosis:

1. Low-risk TR cluster (**few comorbidities and lesser severity of TR**) had the lowest mortality
2. High-risk TR cluster (m**ore severe TR, more comorbidities**, larger RV size, and more congestive heart failure),
3. TR associated with **ischemic cardiomyopathy** (a high prevalence of coronary artery disease and LV dysfunction),
4. TR associated with **lung disease** (a higher proportion of pulmonary hypertension),
5. **TR associated with chronic kidney disease.**

CENTRAL ILLUSTRATION Tricuspid Regurgitation Phenotypes and Survival



Anand V, et al. J Am Coll Cardiol Intv. 2023;16(2):156–165.

(A) Heat map results of the cluster analysis showing the relative prevalence of the different variables in each cluster. The **color bar** indicates the range of relative prevalence. **(B)** A pie chart showing different clusters and number of patients in each cluster. **(C)** Kaplan-Meier survival curves for all-cause mortality by clusters. Cluster 1 had the lowest mortality (but higher than the expected survival for the age- and sex-matched general population) followed by clusters 2 (HR: 2.22 [95% CI: 2.1–2.35]; $P < 0.0001$); 4 (HR: 2.19 [95% CI: 2.04–2.35]; $P < 0.0001$); 3 (HR: 2.45 [95% CI: 2.27–2.65]; $P < 0.0001$); and, lastly, cluster 5, which had the highest mortality (HR: 3.48 [95% CI: 3.07–3.95]; $P < 0.0001$). AS = aortic stenosis; CKD = chronic kidney disease; DM = diabetes mellitus; HR = heart rate; HTN = hypertension; LV = left ventricular; MR = mitral regurgitation; TR = tricuspid regurgitation.

JACC Cardiovasc Interv. 2023 Jan 23;16(2):156-165

ESC European Society of Cardiology
European Heart Journal (2023) 00, 1–15
https://doi.org/10.1093/eurheartj/ehad133
CLINICAL RESEARCH
Valvular heart disease

Long-term outcomes of phenoclusters in severe tricuspid regurgitation

Vishal N. Rao [1,2], Anna Giczewska[2], Karen Chiswell[2], G. Michael Felker [1,2], Andrew Wang [1], Donald D. Glower[3], Jeffrey G. Gaca[3], Kishan S. Parikh[1,2], and Sreekanth Vemulapalli [1]*

[1]Division of Cardiology, Duke University Medical Center, 2301 Erwin Road, Durham, NC 27710, USA; [2]Duke Clinical Research Institute, Duke University School of Medicine, 300 W Morgan Street, Durham, NC 27701, USA; and [3]Division of Cardiovascular and Thoracic Surgery, Department of Surgery, Duke University Medical Center, 2301 Erwin Road, Durham, NC 27710, USA

- Unfortunately, the present analysis was unsuccessful in identifying distinct phenoclusters despite application
- The lack of identifiable patterns among clinical characteristics at the time of severe TR diagnosis further **underscores the continuum and diversity of co-morbidities found in this condition** and may explain in part similar prognoses observed across TR etiology groups.

Key Question

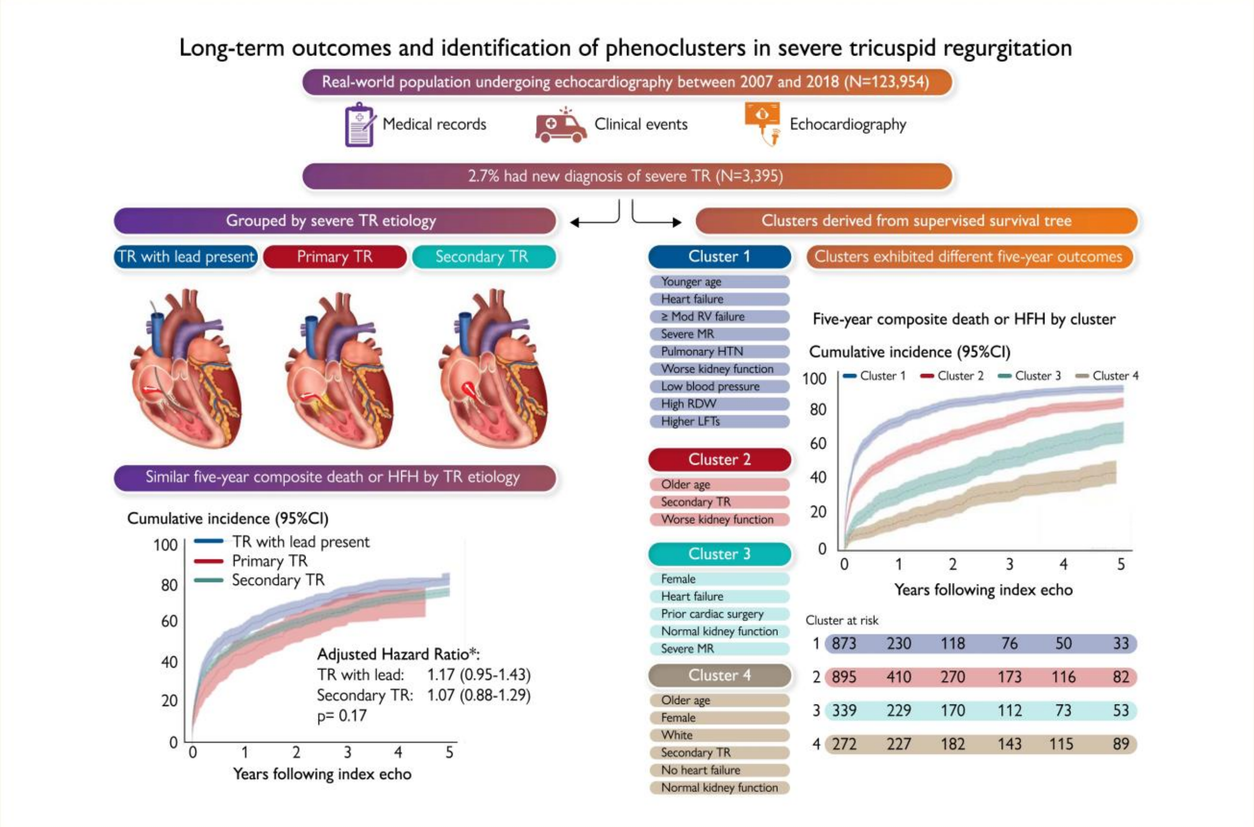
How do cardiovascular outcomes differ across a population with newly diagnosed severe tricuspid valve regurgitation (TR) when grouped by etiology or by clinical risk profiles identified by machine learning?

Key Finding

Severe TR categorized by etiology was associated with indistinguishably high 5-year risk of death and composite death or heart failure hospitalization. Outcome-driven recursive partitioning (survival tree models) yielded phenoclusters with distinct clinical risk profiles for both outcomes.

Take Home Message

Classifying severe TR by etiology alone is insufficient in discriminating clinical risk. The identified subgroups exhibiting differential characteristics and outcomes may aid in clinical risk / benefit analysis for TR interventions and inform selection and enrichment for future clinical research in TR.



Outcomes of ITVS

Isolated Tricuspid Valve Surgery on Native Valve (N=466)

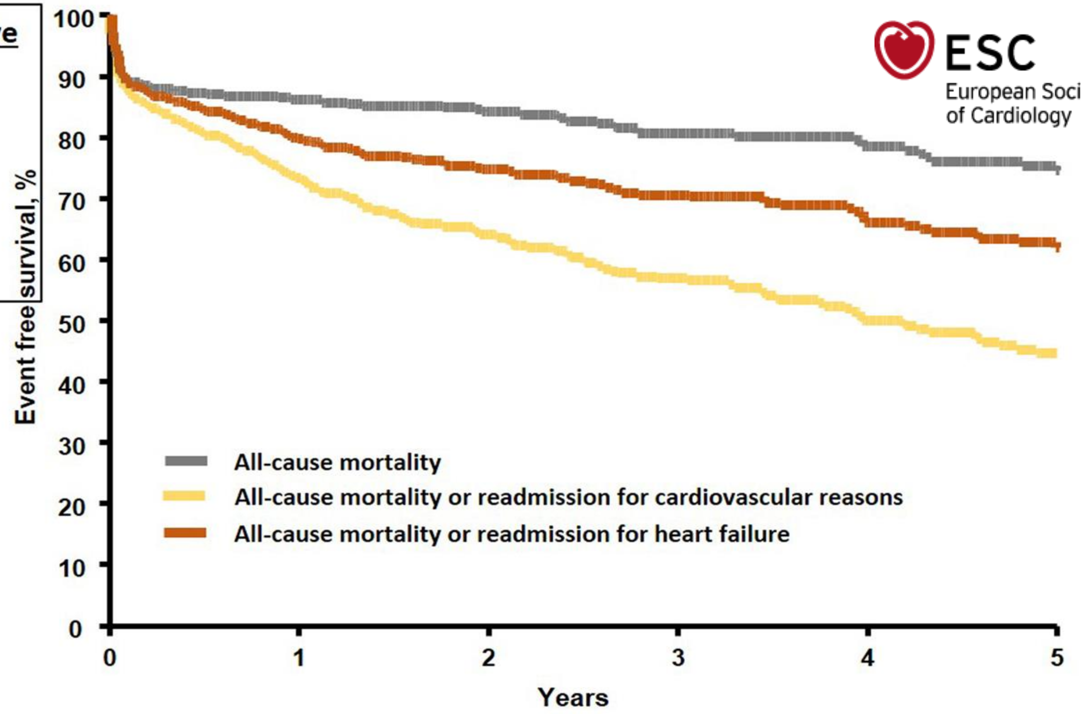
- **Functional tricuspid regurgitation (N=229)**
  - Prior left-sided heart valve surgery (N=101)
  - Isolated (N=128)
- **Organic tricuspid regurgitation (N=237)**
  - Infective endocarditis (N=142)
  - Other (N=95)

Pre-operative presentation

- **Clinical** (NYHA class III/IV, right heart failure signs)
- **Biological** (lower prothrombin time, lower glomerular filtration rate)
- **Echocardiography** (moderate/severe RV dysfunction or dilatation)

Outcome

- **In-hospital death: 10%**
- **In-hospital major complications: 31%**
- **Overall survival, survival free of cardiovascular readmission and survival free of heart failure readmission at 5 years were 75%, 44% and 62%.**



Isolated tricuspid valve surgery is associated with high mortality and morbidity, both in-hospital and during follow-up, predicted by the severity of the pre-operative clinical, biological and echocardiographic presentation but not by etiology or the regurgitation mechanism

ESC European Society of Cardiology

In multivariate analysis, independent determinants of in-hospital death were:

- **NYHA Class III/IV [OR = 2.7 (1.2–6.1), P = 0.01],**
- **Moderate/severe RV dysfunction [OR = 2.6 (1.2–5.8), P = 0.02],**
- **Lower prothrombin time [OR = 0.98 (0.96–0.99), P= 0.008],**
- **Borderline statistical significance**
  - **Presence of right CHF signs [OR = 2.4 (0.9– 6.5), P= 0.06]**
  - **Systolic pulmonary artery pressure >_50 mmHg [OR = 2.5 (0.9–7.0), P = 0.08]**

WE INTERVENE TOO LATE!!

Dreyfus J et al. Eur Heart J. 2020 Dec 1;41(45):4304-4317.

@hahn_rt

Comparison of Risk Scores for Isolated TVS

EuroSCORE

Table 1
EuroSCORE risk factors, their additive weights and beta coefficients

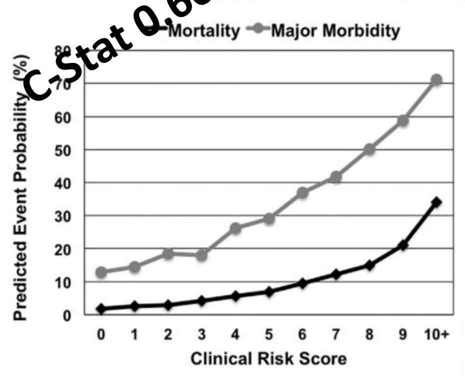
Variable	Additive weight	β coefficient
Age (continuous)	1 per 5 years (or part) >60	0.0666354
Female	1	0.3304052
Serum creatinine > 200 μmol/l	2	0.6521653
Extracardiac arteriopathy	2	0.6558917
Pulmonary disease	1	0.4931341
Neurological dysfunction	2	0.841626
Previous cardiac surgery	3	1.002625
Active endocarditis	3	1.101265
Critical preoperative state	3	0.9058132
Unstable angina	2	0.5677075
LVEF 30–50%	1	0.4191643
LVEF <30%	3	1.094443
Recent myocardial infarct	2	0.5460218
Systolic PA pressure >60 mmHg	2	0.7676924
Emergency operation	2	0.7127953
Ventricular septal rupture	4	1.462009
Other than isolated CABG	2	0.5420364
Thoracic aortic surgery	3	1.159787

LVEF, left ventricular ejection fraction; PA, pulmonary artery; full definition of these variables are published [1] and can be seen on-line (http://www.euroscore.org).

C-Stat 0.83 (0.74–0.93)

STS-TVS

Patient Factor	Mortality CRS	Major Morbidity CRS	Example Case
Age (years)			73 yo, female, moderate lung disease, NYHA Class III
50-59	0	1	
60-69	2	2	Total Mortality CRS: 3 + 1 + 1+ 2 = 7
70+	3	2	
Sex (Female)	1	1	
Stroke	2	1	Total Major Morbidity CRS: 2 + 1 + 1 + 2 = 6
Hemodialysis	4	1	
Chronic Lung Disease			
Moderate	1	1	Predicted Mortality = 12% (from graph below)
Severe	3	1	
Ejection Fraction < 55%	0	2	Predicted Major Morbidity = 37% (from graph below)
NYHA Class			
Class III	2	2	
Class IV	3	3	
Reoperation	2	3	
Status			
Emergent	[illegible]	[illegible]	



C-Stat 0.60 (0.45–0.75)

MELD Score

MELD = 3.78 x $\log_e$ serum bilirubin (mg/dL) +
11.20 x $\log_e$ INR +
9.57 x $\log_e$ serum creatinine (mg/dL) +
6.43 (constant for liver disease etiology)

NOTES:
If the patient has been dialyzed twice within the last 7 days, then the value for serum creatinine used should be 4.0

Any value less than one is given a value of 1 (i.e. if bilirubin is 0.8, a value of 1.0 is used) to prevent the occurrence of scores below 0 (the natural logarithm of 1 is 0, and any value below 1 would yield a negative result)

C-Stat 0.74 (0.58–0.89)

Hepatorenal Score

- **EuroSCORE II to perform bast** in terms of predicting operative mortality, including both primary and secondary etiologies subgroups, and similar in terms of calibration to STS-TVR score in isolated TVS.
- **MELD score had intermediate performance.**
- **STS TVR score performed the worst** (compared to EuroSCORE II and MELD scores) to predict other postoperative complications.
- **All three scores were associated with mortality during follow-up and discriminated most postoperative complications.**

www.tri-score.com

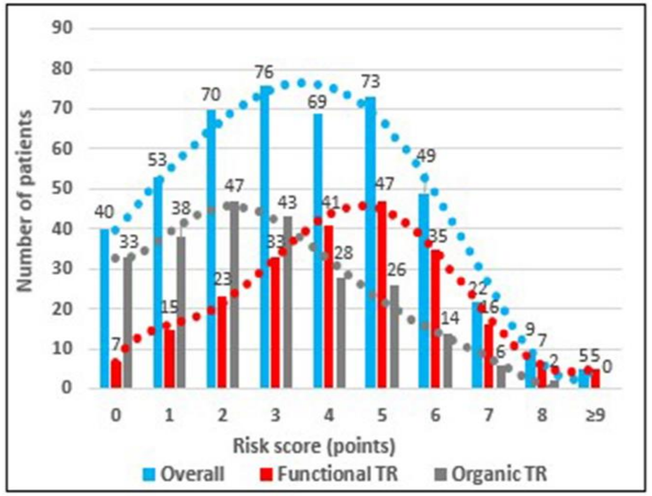
- **The final risk score (0 to 12) included eight parameters:**
  1. Age >_70 years
  2. NYHA Class III–IV
  3. Right-sided heart failure signs
  4. Daily dose of furosemide ≥125 mg
  5. eGFR<30 mL/min
  6. Elevated total bilirubin
  7. Left ventricular EF <60%
  8. Moderate/severe RV dysfunction

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)

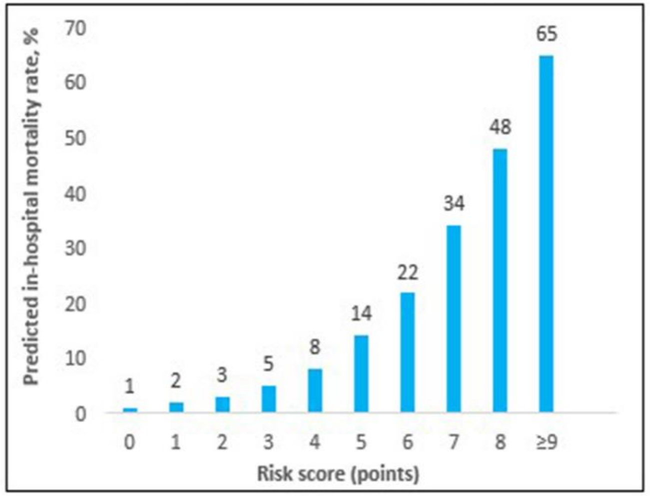
Risk factors and scoring system for in-hospital mortality after isolated tricuspid valve surgery

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

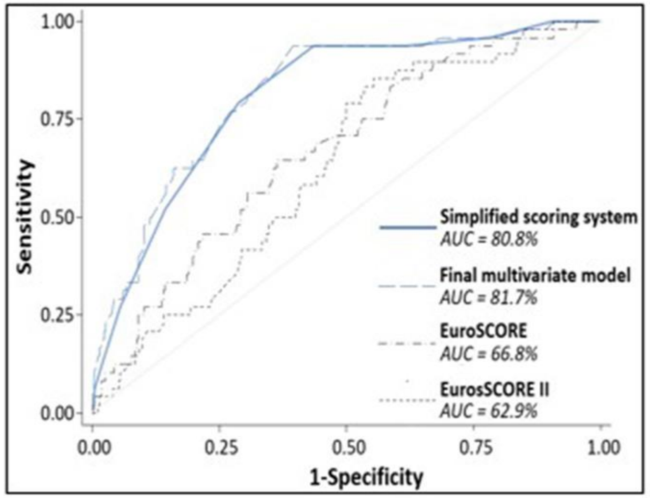
Number of patients presenting with each score value and trends



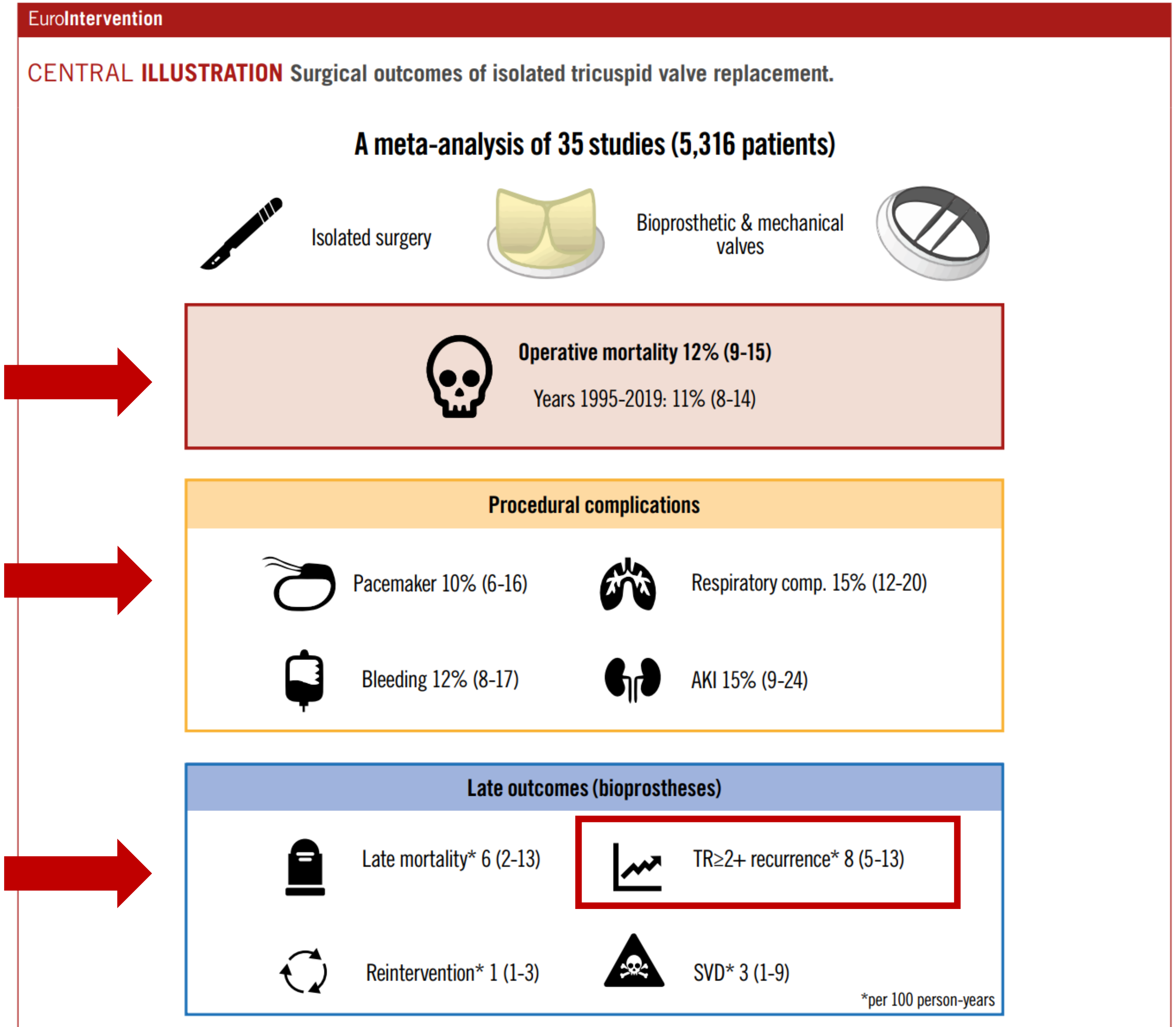
Predicted in-hospital mortality rate according to the final risk score model



Receiver operating characteristic curves



Outcomes of isolated tricuspid valve replacement



The 35 included studies investigated isolated surgical tricuspid valve replacement. The pooled outcomes for 5,316 patients are reported as proportions and incidence rates (late) with confidence intervals. AKI: acute kidney injury; SVD: structural valve deterioration; TR: tricuspid regurgitation

Higher mortality for patients who were operated on before 1995, who had prior cardiac surgeries, or who had liver disease (RV fx not collected).

Scotti A et al. EuroIntervention. 2022 Nov 18;18(10):840-851.

What the Surgeon Knows!!

TABLE 5 Risk Factors Associated With Tricuspid Regurgitation Recurrence After Tricuspid Annuloplasty

	Risk Factors for Recurrence of Significant TR After Repair	Impact on Early TR Recurrence	Impact Late TR Recurrence
Morphologic Predictors	Echocardiographic predictors		
	Pre-operative TR severity	++	+
	Larger annular diameter	+	–
	Advanced leaflet tethering	+++	+++
	Presence and persistence of severe pulmonary hypertension after TV repair	+	++
	Reduced LV function (<40%) …and dilated RV, reduced RV Fx	+	++
Clinical Predictors	Clinical predictors		
	Female gender	+	+
	Chronic atrial fibrillation	+	++
	Presence of ischemic coronary disease	+	+
	Presence of intra-annular pacemaker leads	–	+++
	Kidney dysfunction	+	+++
	Concomitant chronic obstructive pulmonary disease …and recurrent MR	+	+
Surgical Predictors	Surgical/procedural predictors		
	Repair technique (suture vs. ring annuloplasty, flexible vs. rigid or semirigid ring)	+	+++
	Concomitant mitral valve replacement rather than repair	+	+

How to address TR and TR recurrence?
Which procedure and for which anatomy ?

Taramasso M et al. J Am Coll Cardiol Img 2019;12:605–21

New Methods of Quantifying and Grading TR

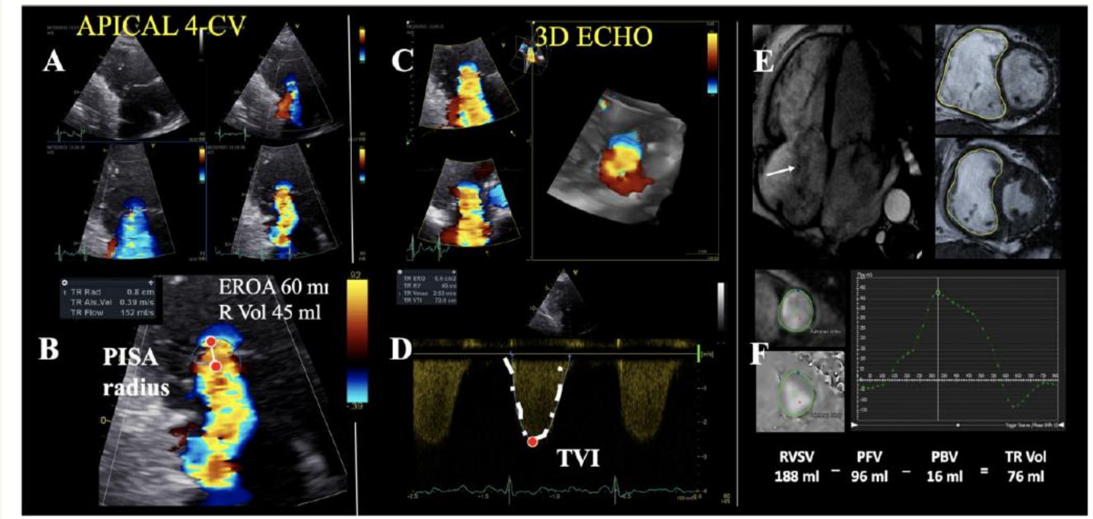
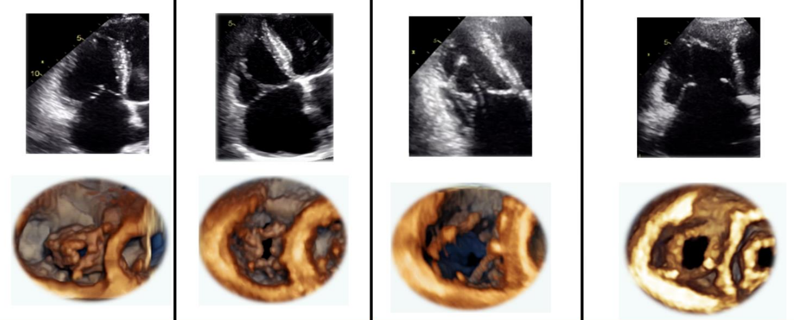


Figure 52 Quantitative assessment of TR severity using the PISA method (*A–D*) and the indirect CMR method (*E* and *F*). White arrow: extent of the signal loss on cine CMR. (*E*) Assessment of LV volumes using cine images. (*I*) Phase-contrast velocity mapping at the aortic root level and flow-time curves computing forward aortic flow.

Lancellotti P, et al. Eur Heart J Cardiovasc Imaging. 2022 Apr 18;23(5):e171-e232

New Classification of TR

	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 RT et al. Eur Ht J CVImg. 2022 Feb

New Ways of Assessing Risk

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
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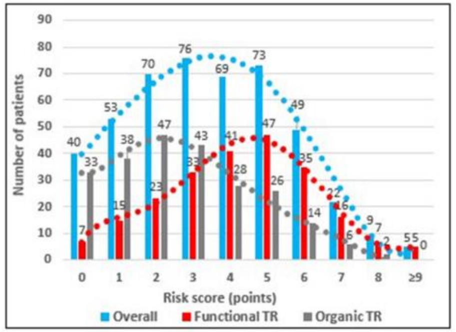

Dreyfus J et al. Eur Heart J. 2021 Sep 29:ehab679

Thank you!