ECHO HAWAII
1/22/2020

Echo beyond 2020: The brave new world of percutaneous treatment of the tricuspid valve

REBECCA T. HAHN, MD, FACC, FESC, FASE
PROFESSOR OF MEDICINE AT COLUMBIA UNIVERSITY MEDICAL COLLEGE
DIRECTOR OF INTERVENTIONAL ECHOCARDIOGRAPHY

1

1

Disclosures

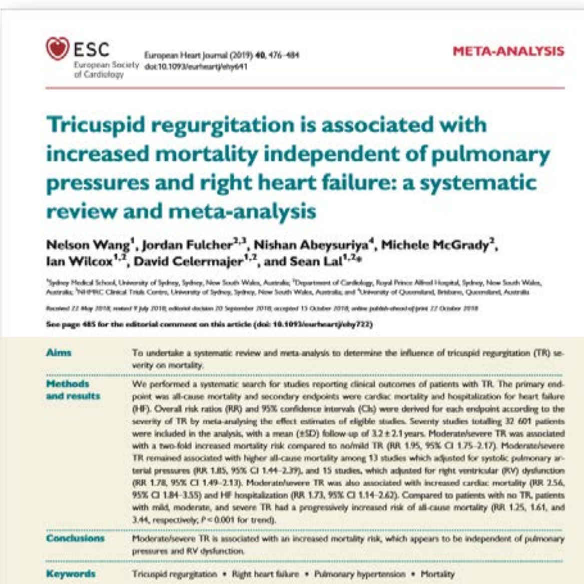
Speakers Bureau: Abbott Vascular, Baylis Medical, Boston Scientific Corporation, Edwards Lifesciences, and Siemens AG;

Consultant: Medtronic, Philips Medical Systems, and Siemens AG

2

Who to Treat: What the Guidelines Tell Us

3


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]*

[1]Sydney Medical School, University of Sydney, Sydney, New South Wales, Australia; [2]Department of Cardiology, Royal Prince Alfred Hospital, Sydney, New South Wales, Australia; [3]NHMRC Clinical Trials Centre, University of Sydney, Sydney, New South Wales, Australia; and [4]University of Queensland, Brisbane, Queensland, Australia

Received 22 May 2018; revised 9 July 2018; editorial decision 20 September 2018; accepted 15 October 2018; online publish-ahead-of-print 22 October 2018

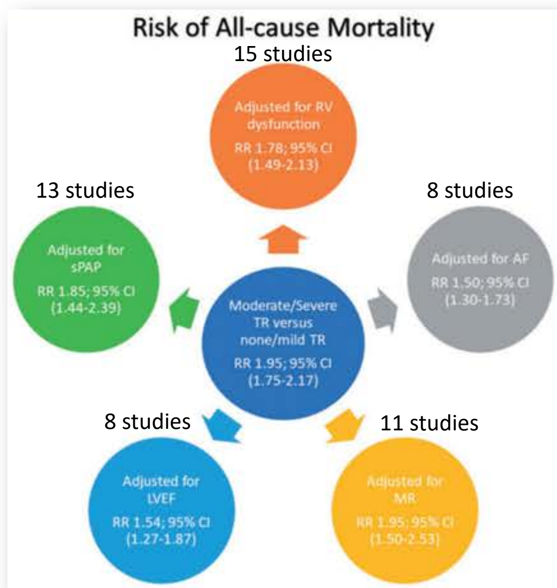
See page 485 for the editorial comment on this article (doi: 10.1093/eurheartj/ehy722)

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 pressures and RV dysfunction.

Keywords Tricuspid regurgitation • Right heart failure • Pulmonary hypertension • Mortality

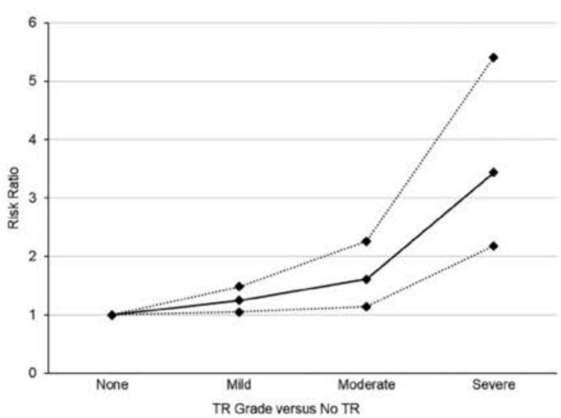


70 studies included in the overall analysis

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

4

Graded relationship between TR severity and impact on mortality



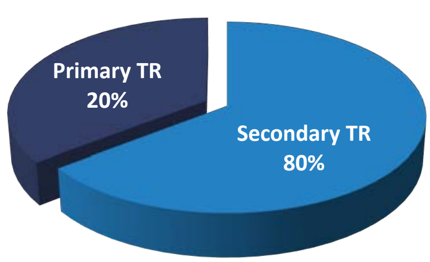
- Compared to patients with no or trivial TR, there was increased mortality associated with every grade of TR:
  - Mild, (RR 1.25, 95% CI 1.05–1.48)
  - Moderate (RR 1.61, 95% CI 1.14–2.26)
  - Severe TR (RR 3.44, 95% CI 2.18–5.41).

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

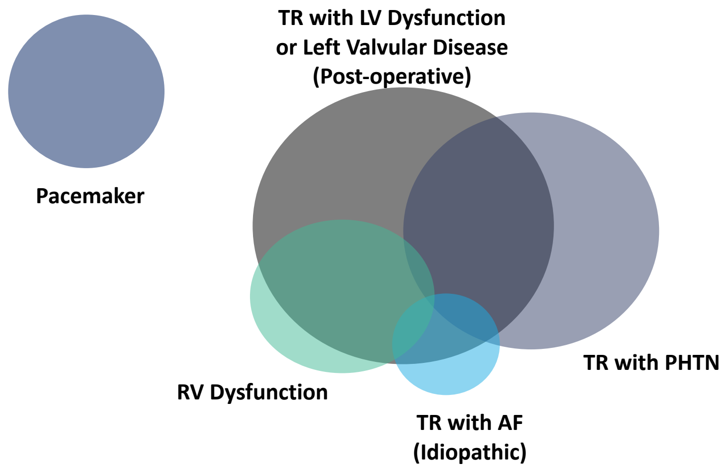
5

Tricuspid regurgitation – patient segmentation

PRIMARY AND SECONDARY TR

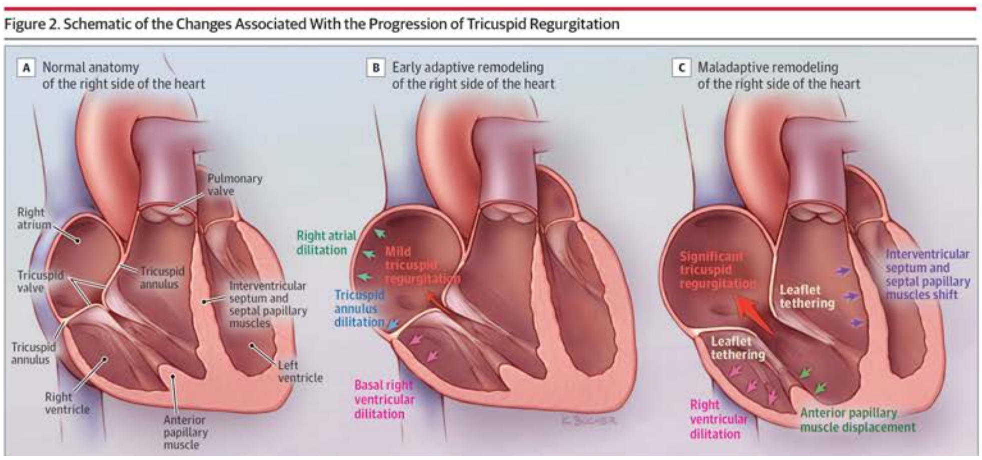


Secondary TR



6

6



Early	**Progressive**	**Late**
Initial Right Ventricular (RV) dilatation results in Tricuspid Annulus (TA) dilatation	**Progressive RV and TA dilatation results in lack of leaflets coaptation**	**Progressive RV distortion (±PHTN) results in further tethering of the leaflets**

Hahn RT et al. JAMA Cardiol. doi:10.1001/jamacardio.2019.0535 Published online April 17, 2019

7

Tricuspid Regurgitation Pathophysiology

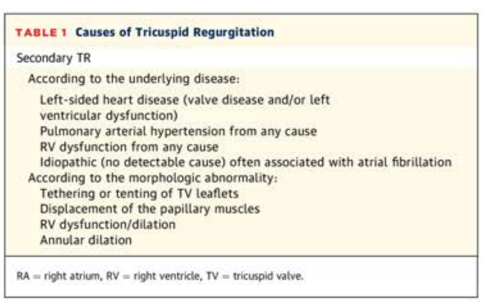


TABLE 1 Causes of Tricuspid Regurgitation

Secondary TR
- According to the underlying disease:
  - Left-sided heart disease (valve disease and/or left ventricular dysfunction)
  - Pulmonary arterial hypertension from any cause
  - RV dysfunction from any cause
  - Idiopathic (no detectable cause) often associated with atrial fibrillation
- According to the morphologic abnormality:
  - Tethering or tenting of TV leaflets
  - Displacement of the papillary muscles
  - RV dysfunction/dilation
  - Annular dilation

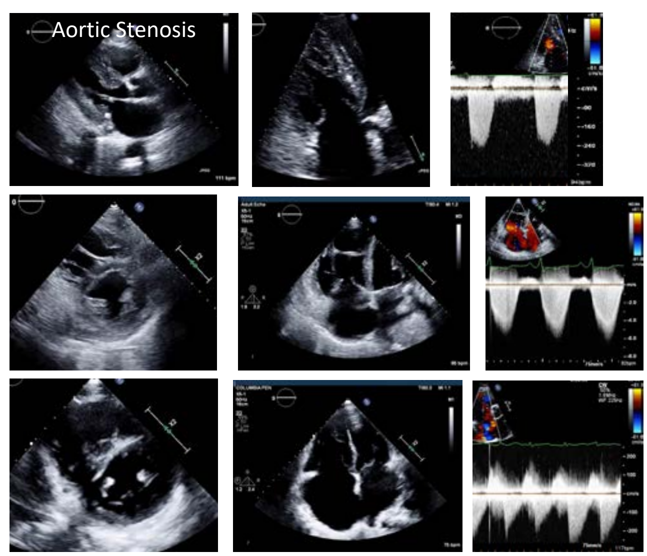
RA = right atrium, RV = right ventricle, TV = tricuspid valve.

Causes of Secondary TR:
1. Underlying Disease
2. Morphology

Left-sided Valve Dis

Pulmonary HTN

Idiopathic

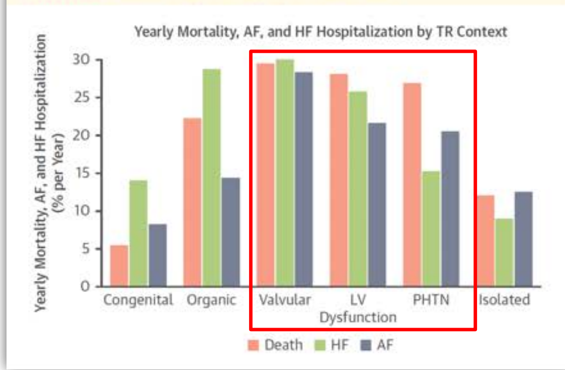


Dahou A et al. J Am Coll Cardiol Img 2019;12:458–68

8

TR Mortality

FIGURE 4 Linearized Yearly Mortality by TR Clinical Context



Topilsky Y et al. J Am Coll Cardiol Img 2019;12:433–42

Table 1 Univariable and multivariable correlates of all-cause mortality in patients with significant TR

Variables	Univariable analysis			Multivariable analysis		
	Hazard ratio	95% CI	P-value	Hazard ratio	95% CI	P-value
Age (years)	1.03	1.02–1.04	**<0.001**	1.03	1.02–1.04	**<0.001**
Sex (female)	1.23	0.93–1.36	0.229	—	—	—
Diabetes mellitus	1.64	1.29–2.07	**<0.001**	—	—	—
History of coronary artery disease	1.65	1.36–2.00	**<0.001**	—	—	—
History of atrial fibrillation	0.90	0.73–1.10	0.288	—	—	—
Lung disease	1.43	1.17–1.75	**<0.001**	—	—	—
Functional TR vs. organic TR	0.96	0.56–1.63	0.875	—	—	—
Severe TR vs. moderate TR	1.07	0.91–1.28	0.421	—	—	—
Presence of pacemaker or defibrillator lead	1.13	0.94–1.38	0.200	—	—	—
eGFR (mL/min/1.73 m^2)	0.98	0.97–0.99	**<0.001**	—	—	—
TAPSE (each 1-mm decrease)	1.05	1.03–1.07	**<0.001**	1.04	1.02–1.06	**<0.001**
LVEF (each 1% decrease)	1.02	1.01–1.02	**<0.001**	1.02	1.01–1.02	**<0.001**
RV systolic pressure (mmHg)	1.02	1.01–1.02	**<0.001**	1.02	1.01–1.02	**<0.001**
Isolated CABG[a]	1.18	0.78–1.79	0.426	—	—	—
Left-sided valvular intervention[a]	0.90	0.69–1.80	0.442	—	—	—
Tricuspid annuloplasty[a]	0.74	0.50–1.10	0.134	—	—	—
Time-to-development of significant TR (years)	1.09	1.07–1.12	**<0.001**	1.09	1.06–1.11	**<0.001**

CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; RV, right ventricular; TAPSE, tricuspid annulus planar systolic excursion; TR, tricuspid regurgitation.
[a]After index echocardiography.

Fastest development of significant TR (≤1.2 years) were **older,** more frequently **female** and showed more **RV** dilation and dysfunction as compared to patients with slowest development of TR (≥9.0 years).

Prihadi EA et al. Eur Heart J. 2018 Oct 14;39(39):3574-3581.

9

Guidelines Regarding Tricuspid Regurgitation

PRACTICE GUIDELINE

2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the American Association for Thoracic Surgery, American Society of Echocardiography, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons

Writing Committee Members*

Rick A. Nishimura, MD, MACC, FAHA, *Co-Chair*†
Catherine M. Otto, MD, FACC, FAHA, *Co-Chair*†

Robert O. Bonow, MD, MACC, FAHA†
Blase A. Carabello, MD, FACC*†
John P. Erwin III, MD, FACC, FAHA‡
Robert A. Guyton, MD, FACC*§
Patrick T. O'Gara, MD, FACC, FAHA†
Carlos E. Ruiz, MD, PhD, FACC†
Nikolaos J. Skubas, MD, FASE¶
Paul Sorajja, MD, FACC, FAHA#
Thoralf M. Sundt III, MD*,**††
James D. Thomas, MD, FASE, FACC, FAHA‡‡

*Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry and other entities may apply; see Appendix 1 for recusal information. †ACC/AHA representative. ‡ACC/AHA Task Force on Performance Measures liaison. §ACC/AHA Task Force on Practice Guidelines liaison. ¶Society of Cardiovascular Anesthesiologists representative. #Society for Cardiovascular Angiography and Interventions representative. **American Association for Thoracic Surgery representative. ††Society of Thoracic Surgeons representative. ‡‡American Society of Echocardiography representative.

Nishimura, RA et al JAmCollCardiol 2014 Jun 10;63(22):2438-88

European Heart Journal (2012) 33, 2451–2496
doi:10.1093/eurheartj/ehs109

ESC/EACTS GUIDELINES

Guidelines on the management of valvular heart disease (version 2012)

The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Authors/Task Force Members: Alec Vahanian (Chairperson) (France)*, Ottavio Alfieri (Chairperson)* (Italy), Felicita Andreotti (Italy), Manuel J. Antunes (Portugal), Gonzalo Barón-Esquivias (Spain), Helmut Baumgartner (Germany), Michael Andrew Borger (Germany), Thierry P. Carrel (Switzerland), Michele De Bonis (Italy), Arturo Evangelista (Spain), Volkmar Falk (Switzerland), Bernard Iung (France), Patrizio Lancellotti (Belgium), Luc Pierard (Belgium), Susanna Price (UK), Hans-Joachim Schäfers (Germany), Gerhard Schuler (Germany), Janina Stepinska (Poland), Karl Swedberg (Sweden), Johanna Takkenberg (The Netherlands), Ulrich Otto Von Oppell (UK), Stephan Windecker (Switzerland), Jose Luis Zamorano (Spain), Marian Zembala (Poland)

Vahanian, A et al. European Heart Journal (2012) 33, 2451–2496

NOTE: The guidelines are based on small retrospective studies as well as on expert consensus, and prospective randomized trials on the benefit of tricuspid valve surgery on outcome are lacking.

10

Nishimura, RA et al JAmCollCardiol 2014 Jun 10;63(22):2438-88

8.2.2. Medical Therapy

CLASS IIa

1. Diuretics can be useful for patients with severe TR and signs of right-sided HF (stage D). (Level of Evidence: C)

CLASS IIb

1. Medical therapies to reduce elevated pulmonary artery pressures and/or pulmonary vascular resistance might be considered in patients with severe functional TR (stages C and D). (Level of Evidence: C)

11

Guidelines for Tricuspid Regurgitation	**ESC/ EACTS**	**AHA/ ACC**
Primary TR		
Symptomatic isolated severe TR without severe RV dysfunction	I	IIa
Severe TR **undergoing left-side surgery**	I	I
Moderate TR **undergoing left-side surgery**	IIa	NM
Asymptomatic isolated mild or moderate TR and progressive RV dilatation or RV function deterioration	IIa	IIb (only for severe TR)
Secondary TR		
Severe TR **undergoing left-side surgery**	I	I
Mild or moderate TR **at the time of left-side surgery** with either dilated annulus (≥40 mm or >21 mm/m²) or prior evidence of right heart failure	IIa/IIb[a]	IIa
Moderate TR and PH **undergoing left-side surgery**	NM	IIb
After left-side surgery, severe TR with **symptoms OR progressive RV dilatation/dysfunction but without severe RV or LV dysfunction, left-sided valve dysfunction and severe PH**	IIa	IIb[b]

Abbreviations: ACC, American College of Cardiology; AHA, American Heart Association; EACTS, European Association for Cardio-Thoracic Surgery; ESC, European Society of Cardiology; NM, not mentioned; PH, pulmonary hypertension; RV, right ventricle; TR, tricuspid regurgitation.

[a] IIa indication with dilated annulus, IIb indication for prior right heart failure

[b] IIb indication only for persistent symptoms (no mention of progressive RV dilatation or dysfunction)

12

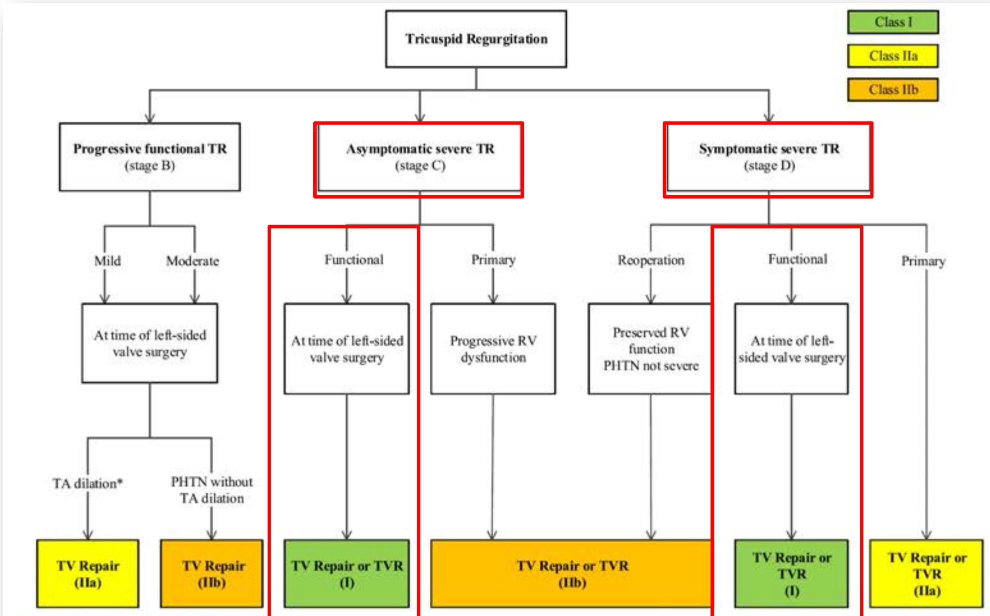


Figure 5. Indications for Surgery

Nishimura, RA et al JAmCollCardiol 2014 Jun 10;63(22):2438-88

13

Who to Treat: Where the Guidelines Fail

14

Stages of TR

Table 17. Stages of TR

Stage	Definition	Valve Anatomy	Valve Hemodynamics*	Hemodynamic Consequences	Symptoms
A	At risk of TR	**Primary** • Mild rheumatic change • Mild prolapse • Other (e.g., IE with vegetation, early carcinoid deposition,	• No or trace TR	• None	• None or in relation to other left heart or pulmonary/pulmonary vascular disease
			blunting		
C	Asymptomatic severe TR	**Primary** • Flail or grossly distorted leaflets **Functional** • Severe annular dilation (>40 mm or 21 mm/m²) • Marked leaflet tethering	• Central jet area >10.0 cm² • Vena contracta width >0.7 cm • CW jet density and contour: dense, triangular with early peak • Hepatic vein flow: systolic reversal	• RV/RA/IVC dilated with decreased IVC respirophasic variation • Elevated RA pressure with "c-V" wave • Diastolic interventricular septal flattening may be present	• None, or in relation to other left heart or pulmonary/pulmonary vascular disease
D	Symptomatic severe TR	**Primary** • Flail or grossly distorted leaflets **Functional** • Severe annular dilation (>40 mm or >21 mm/m²) • Marked leaflet tethering	• Central jet area >10.0 cm² • Vena contracta width >0.70 cm • CW jet density and contour: dense, triangular with early peak • Hepatic vein flow: systolic reversal	• RV/RA/IVC dilated with decreased IVC respirophasic variation • Elevated RA pressure with "c-V" wave • Diastolic interventricular septal flattening • Reduced RV systolic function in late phase	• Fatigue, palpitations, dyspnea, abdominal bloating, anorexia, edema

*Several valve hemodynamic criteria are provided for assessment of severity of TR, but not all criteria for each category will necessarily be present in every patient. Categorization of severity of TR as mild, moderate, or severe also depends on image quality and integration of these parameters with clinical findings.

CW indicates continuous wave; ICD, implantable cardioverter-defibrillator; IE, infective endocarditis; IVC, inferior vena cava; RA, right atrium; RV, right ventricle; and TR, tricuspid regurgitation.

Table 17. Stages of TR

Stage	Definition	Valve Anatomy	Valve Hemodynamics*	Hemodynamic Consequences	Symptoms
D	Symptomatic severe TR	**Primary** • Flail or grossly distorted leaflets **Functional** • Severe annular dilation (>40 mm or >21 mm/m²) • Marked leaflet tethering	• Central jet area >10.0 cm² • Vena contracta width >0.70 cm • CW jet density and contour: dense, triangular with early peak • Hepatic vein flow: systolic reversal	• RV/RA/IVC dilated with decreased IVC respirophasic variation • Elevated RA pressure with "c-V" wave • Diastolic interventricular septal flattening • Reduced RV systolic function in late phase	• Fatigue, palpitations, dyspnea, abdominal bloating, anorexia, edema

1. Valve Anatomy
2. Severity of Disease
3. Hemodynamic consequences
4. Symptoms

15

Limitations of Guidelines: Tricuspid Annulus Parameters

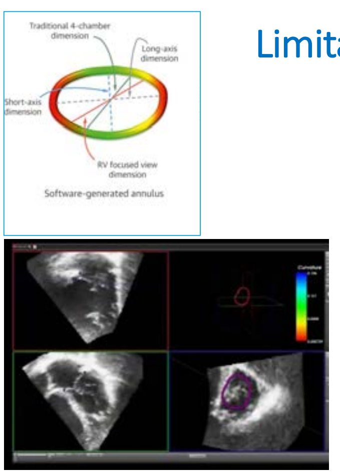


TABLE 4 Tricuspid Annulus Parameters in Men and Women

3DE Parameters	End Diastole		Mid-Systole		End Systole		Late Diastole	
Nonindexed	Men	Women	Men	Women	Men	Women	Men	Women
Area, cm²	9.5 ± 1.9	7.8 ± 1.6*	8.6 ± 1.6	6.8 ± 1.4*	8.5 ± 1.7	6.8 ± 1.5*	11.6 ± 2.5	9.9 ± 2.3*
Perimeter, cm	11.1 ± 1.2	10.1 ± 1.0*	10.5 ± 1.0	9.4 ± 1.0*	10.5 ± 1.0	9.4 ± 1.0*	12.3 ± 1.3	11.4 ± 1.3*
Long axis, mm	37.8 ± 4.4	34.7 ± 3.7*	35.5 ± 3.9	31.9 ± 3.4*	35.67 ± 4.0	32.2 ± 3.8*	41.6 ± 4.8	38.7 ± 4.4*
Short axis, mm	31.7 ± 4.5	28.4 ± 3.8*	30.7 ± 3.8	27.1 ± 3.7*	30.4 ± 3.8	26.9 ± 3.8*	35.5 ± 5.3	31.6 ± 4.3*
Circularity	0.84 ± 0.10	0.82 ± 0.09	087 ± 0.09	085 ± 0.09	0.86 ± 0.09	0.83 ± 0.09	0.86 ± 0.10	0.82 ± 0.10*
Indexed (to BSA)	Men	Women	Men	Women	Men	Women	Men	Women
Area, cm²/m²	4.9 ± 0.9	4.7 ± 0.9*	4.5 ± 0.8	4.1 ± 0.8*	4.4 ± 0.8	4.1 ± 0.8*	6.0 ± 1.2	5.9 ± 1.3
Perimeter, cm/m²	5.8 ± 0.6	6.1 ± 0.7*	5.5 ± 0.5	5.6 ± 0.7*	5.5 ± 0.6	5.6 ± 0.7*	6.4 ± 0.7	6.9 ± 0.9*
Long axis, mm/m²	19.7 ± 2.2	20.8 ± 2.6*	18.5 ± 2.0	19.1 ± 2.4*	18.6 ± 2.1	19.3 ± 2.4*	21.6 ± 2.4	23.2 ± 3.0*
Short axis, mm/m²	16.5 ± 2.2	17.0 ± 2.4	16.0 ± 1.9	16.2 ± 2.3	15.8 ± 2.0	16.0 ± 2.4	18.5 ± 2.7	18.9 ± 2.7

Values are mean ± SD. *p ≤ 0.05 men versus women.
Abbreviations as in Tables 1 and 2.

- Cardiac cycle timing is an important determinant of TA size and function
- Sex is an important determinant of TA size and function.
  - After indexing to BSA, women were found to have larger TA perimeters and longer long-axis dimensions than men.
  - Fractional changes in area, perimeter, and long-axis dimensions were larger in women than in men

Karima Addetia et al. J Am Coll Cardiol Img 2019;12:401–12

16

Stages of TR

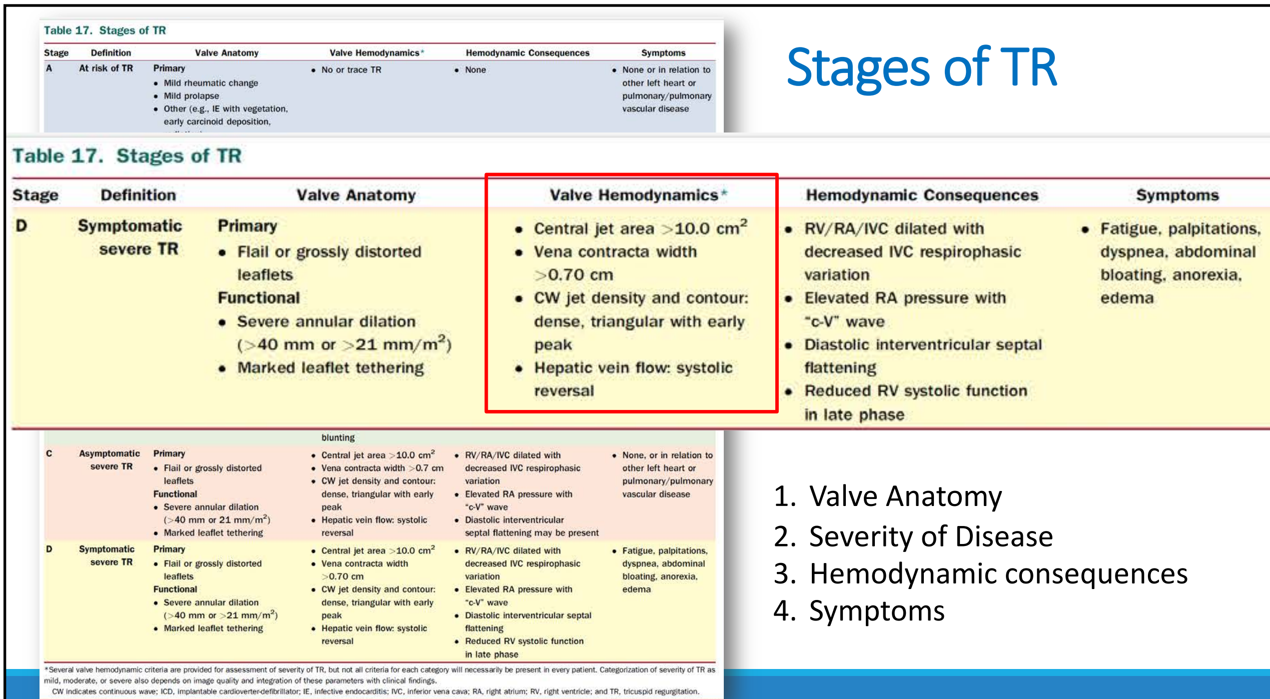


Table 17. Stages of TR

Stage	Definition	Valve Anatomy	Valve Hemodynamics*	Hemodynamic Consequences	Symptoms
A	At risk of TR	**Primary** • Mild rheumatic change • Mild prolapse • Other (e.g., IE with vegetation, early carcinoid deposition,	• No or trace TR	• None	• None or in relation to other left heart or pulmonary/pulmonary vascular disease
			blunting		
C	Asymptomatic severe TR	**Primary** • Flail or grossly distorted leaflets **Functional** • Severe annular dilation (>40 mm or 21 mm/m^2) • Marked leaflet tethering	• Central jet area >10.0 cm^2 • Vena contracta width >0.7 cm • CW jet density and contour: dense, triangular with early peak • Hepatic vein flow: systolic reversal	• RV/RA/IVC dilated with decreased IVC respirophasic variation • Elevated RA pressure with "c-V" wave • Diastolic interventricular septal flattening may be present	• None, or in relation to other left heart or pulmonary/pulmonary vascular disease
D	Symptomatic severe TR	**Primary** • Flail or grossly distorted leaflets **Functional** • Severe annular dilation (>40 mm or >21 mm/m^2) • Marked leaflet tethering	• Central jet area >10.0 cm^2 • Vena contracta width >0.70 cm • CW jet density and contour: dense, triangular with early peak • Hepatic vein flow: systolic reversal	• RV/RA/IVC dilated with decreased IVC respirophasic variation • Elevated RA pressure with "c-V" wave • Diastolic interventricular septal flattening • Reduced RV systolic function in late phase	• Fatigue, palpitations, dyspnea, abdominal bloating, anorexia, edema

*Several valve hemodynamic criteria are provided for assessment of severity of TR, but not all criteria for each category will necessarily be present in every patient. Categorization of severity of TR as mild, moderate, or severe also depends on image quality and integration of these parameters with clinical findings.

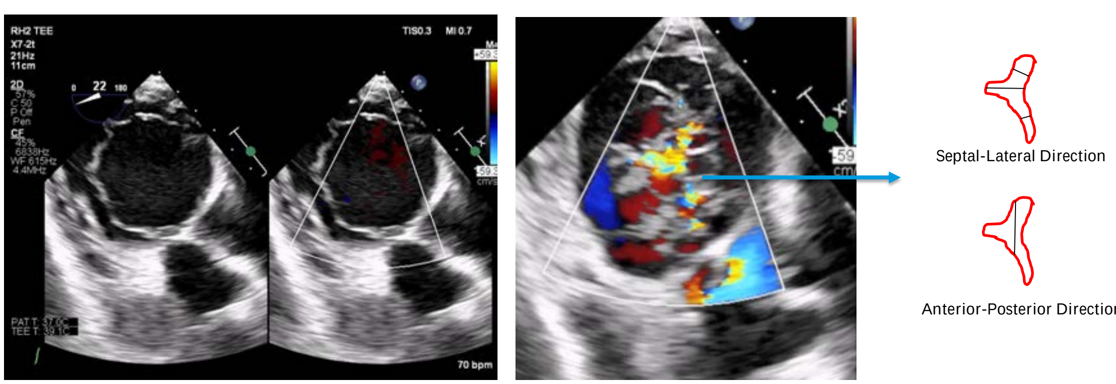
CW indicates continuous wave; ICD, implantable cardioverter-defibrillator; IE, infective endocarditis; IVC, inferior vena cava; RA, right atrium; RV, right ventricle; and TR, tricuspid regurgitation.

1. Valve Anatomy
2. Severity of Disease
3. Hemodynamic consequences
4. Symptoms

17

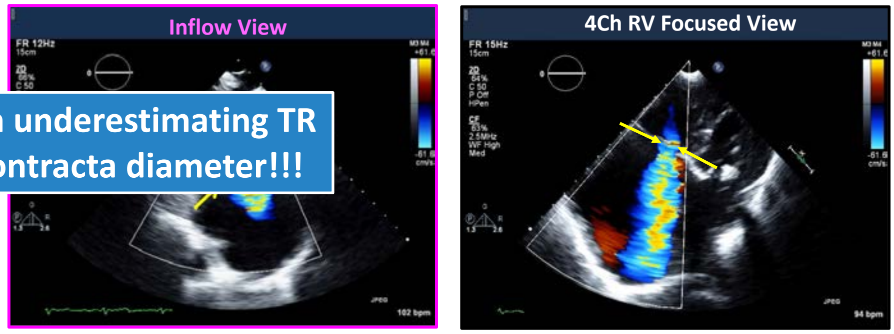
Current guidelines – Vena contracta width (and PISA)

VC Width – can be measured in multiple locations, and the regurgitant orifice is not generally symmetric



18

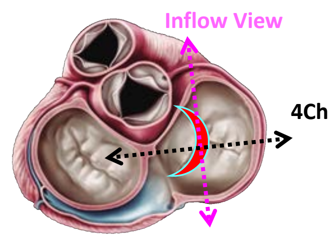
Current guidelines – Vena contracta width



We have been underestimating TR using vena contracta diameter!!!

Limitations:

1. FTR jets are most frequently elliptical or crescent-shaped
   - Usually the "maximum dimension is an inflow view
   - **Usually the "minimum" dimension is a 4Ch view**
2. Imaging of the Convergence Zone difficult
   - High variability in patient anatomy – number and size of leaflets



19

Current guidelines – Color flow jet area

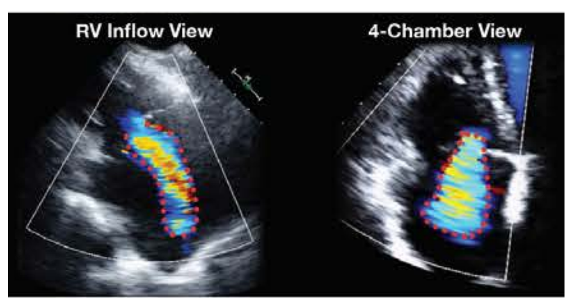
- *"Severe, wide-open TR may have low velocity, without aliasing or turbulence, and thus may be difficult to see as a distinct jet by color Doppler"* - Zoghbi 2017

Limitations:

- ❖ Direction and shape of jet may overestimate (central) or underestimate (eccentric, wall-impinging) jet area
- ❖ Jet flow (and thus color Doppler jet area) is governed mainly by conservation of momentum:

  Flow (Q) = A x v

  Momentum (M) = Q x v



We have been underestimating TR using color Doppler jet area!!!

- ❖ *For the same effective regurgitant orifice area (A), a 2.5 m/s jet (i.e. tricuspid regurgitant jet) will have 1/4x the color jet area as a 5.0 m/s jet (i.e. mitral regurgitant jet)*

20


Circulation

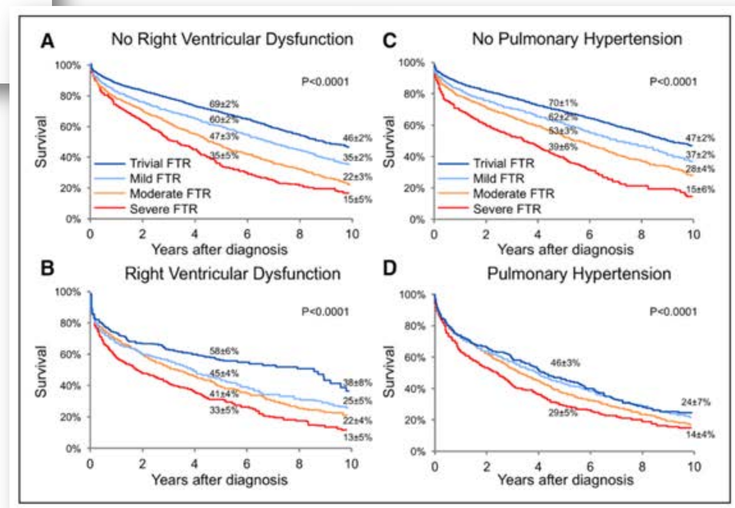
ORIGINAL RESEARCH ARTICLE

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

Quantitative measurements should be performed!

- The addition of grading by quantitative improved the model prediction (p < 0.001 for survival and p . 0.02 for cardiac events).
- **The 10-year survival rate was lower with an ERO ≥40 mm²** versus <40 mm² (38±7% vs. 70±6%; p < 0.0001).



Benfari G et al. Circulation. 2019;140:196–206.

21

TR Grading: Work in Progress

Quantitation Method	Measurements Required	Example	Calculation
PISA	1. PISA radius [r] 2. PISA aliasing velocity [v] (approximately 28 cm/s) 3. TR peak velocity [v_0] 4. TR velocity time integral [TR_{VTI}]		$Q = 2\pi r^2 v$ $ROA = Q/v_0$ Reg Vol = ROA x TR_{VTI}
Quantitative Doppler	1. TV velocity time integral [TV_{VTI}] • PW Doppler sample volume at the annulus		Diastolic Stroke Volume = $TV_{annulus}$ Area x TV_{VTI} RegVol = Diastolic Stroke Volume – Forward Stroke Volume
	2. Diastolic $TV_{annulus}$ Area • 3D annular area OR • Biplane annular area		ROA = RegVol ÷ TR_{VTI} Note: Forward stroke volume may be either the left ventricular or right ventricular stroke volume
3D color Doppler	1. 3D Color Doppler planimetered vena contracta area [VC_{area}] 2. TR velocity time integral [TR_{VTI}]		ROA = Vc_{area} RegVol = VC_{area} x TR_{VTI}

Abbreviations: PISA = proximal isovelocity surface area, TR = tricuspid regurgitation, Q = flow, ROA = regurgitant orifice area, TV = tricuspid valve, PW = pulsed wave, 3D = three dimensional, RegVol = regurgitant volume, VC = vena contracta

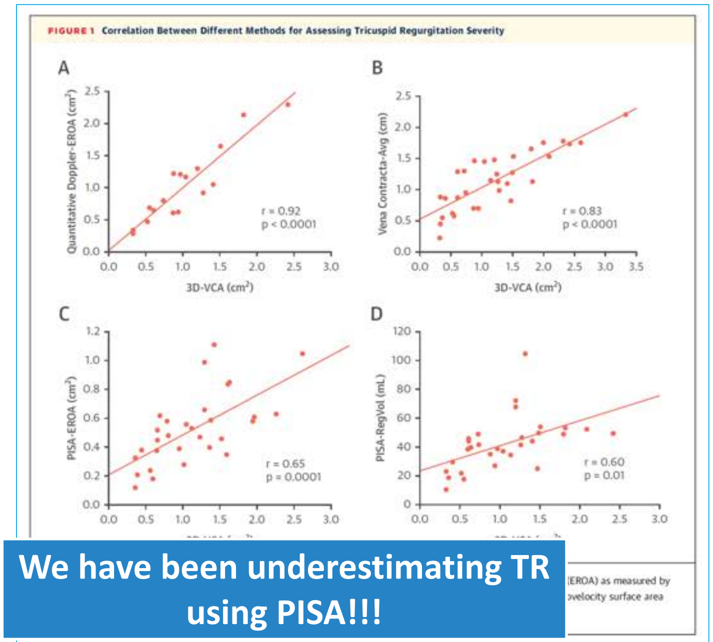
Quantifies EROA
Calculates Regurgitant Volume

Quantifies Regurgitant Volume
Calculates EROA

Quantifies EROA
Calculates Regurgitant Volume

Hahn RT. *Circ Cardiovasc Imaging*. 2016 Dec;9(12)

22



We have been underestimating TR using PISA!!!

160 cases

The PISA method showed better correlation with the 3D-VCA method in less elliptical regurgitant orifices (VCmax/VCmin < 1.6)

- PISA-EROA and 3D VCA (r = 0.87; p = 0.001
- PISA-RegVol and 3D-RegVol (r = 0.75; p = 0.01)

PISA-EROA and PISA-RegVol were significantly lower than quantitative Doppler and 3D methods.

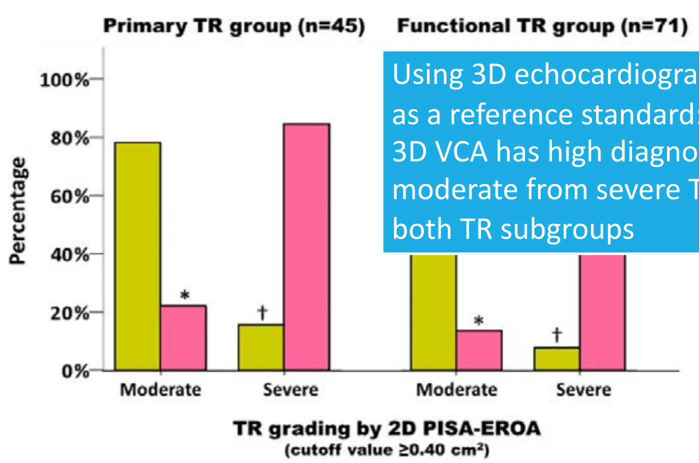
Using Youden's index, the best cutoff value for severe TR

- **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%),**
- **VC_{avg} cutoff was ≥9 mm (sensitivity: 85%; specificity: 97%).**

Dahou A. ….Hahn RT. Quantifying Tricuspid Regurgitation Severity. DOI: 10.1016/j.jcmg.2018.11.015

23

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



Using 3D echocardiography–derived RVol (>45 mL) as a reference standard:
3D VCA has high diagnostic value for separating moderate from severe TR (**cutoff >0.61 mm^2**) in both TR subgroups

The *asterisks* and *daggers* represent percentages of patients in whom TR severity was under- and overestimated by 2D PISA-EROA, respectively, compared with 3D VCA.

TR classification according to 3D VCA– and 2D PISA-EROA–based TR grading. Overall, 17 patients (14.7%) were misclassified when 2D PISA-EROA alone was used for TR grading.

Utsunomiya, H. et al. J Am Soc Echocardiogr 2019;32:1526-37.

24

Imaging Assessment of Tricuspid Regurgitation Severity

Rebecca T. Hahn, MD,[a] James D. Thomas, MD,[b] Omar K. Khalique, MD,[a] João L. Cavalcante, MD,[c] Fabien Praz, MD,[a,d] William A. Zoghbi, MD[e]

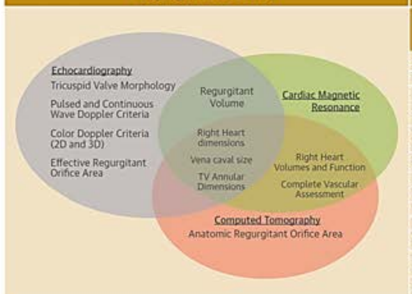
SUMMARY

Assessing the severity of tricuspid regurgitation remains a challenging task, and
choice, significant limitations of the current recommendations exist. Newer met
transcatheter devices and may improve our understanding of the disease process.
computed tomography angiography may play significant roles as adjunctive ima
imaging modalities currently used to quantify tricuspid regurgitation severity. (
© 2019 by the American College of Cardiology Foundation.

Hahn RT et al. J Am Coll Cardiol Img 2019;12:469–90

CENTRAL ILLUSTRATION Multimodality Imaging for the Assessment of Tricuspid Regurgitation

Multi-modality Imaging for Assessment of Tricuspid Regurgitation Severity



Relative Utility of Each Imaging Modality

Parameters	Echocardiography (TTE or TEE) 2D/Doppler	Echocardiography (TTE or TEE) 3D/Color	Cardiac Magnetic Resonance	Computed Tomography Angiography
Structural Parameters				
TV Morphology	+++	+++	++	++
RV and RA size	++	+++	+++	+++
SVC and IVC Size	+++ (proximal cavae only)	+++	+++	+++
Comprehensive vascular assessment	-	-	+++	+++
Semi-Quantitative parameters				
Jet Area	+++	+++	++	-
Vena Contracta Width	+++	+++	++	-
Vena Contracta Area	-	+++	++	-
Anatomic Orifice Area	-	+	++	+++
Quantitative Parameters				
Effective Regurgitant Orifice Area	++ (PISA and Doppler SV)	- (see VCA)	-	-
Regurgitant Volume	++ (PISA and Doppler SV)	++ (from VCA)	++	-

Hahn, R.T. et al. J Am Coll Cardiol Img. 2019;12(3):469-90.

Although echocardiography remains the diagnostic modality of choice for the initial evaluation of the right heart and tricuspid valve, the Venn diagram illustrates the utility and complementary nature of the imaging modalities for certain parameters important in the assessment of tricuspid regurgitation severity. The table shows the relative strengths of each modality for the evaluation of specific parameters. IVC = inferior vena cava; PISA = proximal isovelocity surface area; RA = right atrium; RV = right ventricle; SV = stroke volume; SVC = superior vena cava; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography; TV = tricuspid valve; VCA = vena contracta area.

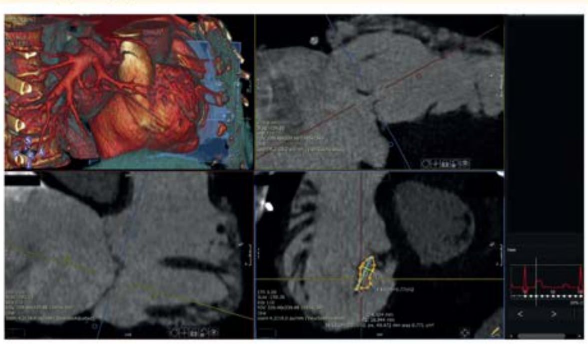
Multi-modality Imaging may be helpful!

25

Multi-modality Imaging for TR Assessment

Computed Tomography

FIGURE 15 Computed Tomography Measurement of AROA

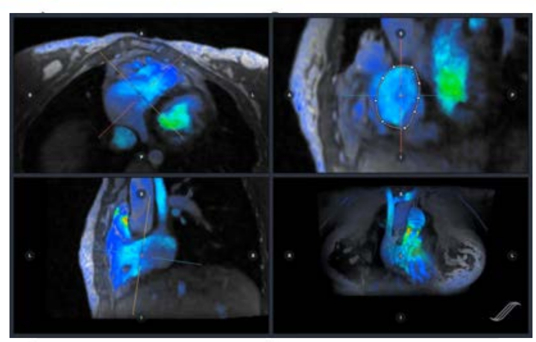


Multiplanar reconstruction planes are aligned at the tips of tricuspid valve leaflet at mid-peak systole (20% to 40% of the R-R interval). TR AROA is then traced using cubic spline interpolation, yielding an area of 0.77 cm^2, which is consistent with severe TR. AROA = anatomical regurgitant orifice area; other abbreviations as in Figure 1.

Hahn RT et al. J Am Coll Cardiol Img 2019;12:469–90

Magnetic Resonance Imaging

FIGURE 12 Cardiac Magnetic Resonance 4D Flow Imaging Assessment of TR



A multiplanar reconstruction still frame from a 4D CMR velocity-encoded acquisition is shown with retrospective valve tracking (see Video 1). In this systolic frame, high-velocity TR flow is represented by a **bright green color**. The crosshairs can be manipulated in the long-axis images **(A and C)** to align flow, which can then be measured in the short-axis through-plane of the TR jet **(B)**. Valve tracking **(B, polygon)** allows semiautomated adjustment of through-plane motion for more accurate assessment of flow. CMR = cardiac magnetic resonance; other abbreviation as in Figure 1. Figure was supplied courtesy of Melany Atkins, MD.

26

Stages of TR

Table 17. Stages of TR

Stage	Definition	Valve Anatomy	Valve Hemodynamics*	Hemodynamic Consequences	Symptoms
A	At risk of TR	**Primary** • Mild rheumatic change • Mild prolapse • Other (e.g., IE with vegetation, early carcinoid deposition,	• No or trace TR	• None	• None or in relation to other left heart or pulmonary/pulmonary vascular disease
			blunting		
C	Asymptomatic severe TR	**Primary** • Flail or grossly distorted leaflets **Functional** • Severe annular dilation (>40 mm or 21 mm/m²) • Marked leaflet tethering	• Central jet area >10.0 cm² • Vena contracta width >0.7 cm • CW jet density and contour: dense, triangular with early peak • Hepatic vein flow: systolic reversal	• RV/RA/IVC dilated with decreased IVC respirophasic variation • Elevated RA pressure with "c-V" wave • Diastolic interventricular septal flattening may be present	• None, or in relation to other left heart or pulmonary/pulmonary vascular disease
D	Symptomatic severe TR	**Primary** • Flail or grossly distorted leaflets **Functional** • Severe annular dilation (>40 mm or >21 mm/m²) • Marked leaflet tethering	• Central jet area >10.0 cm² • Vena contracta width >0.70 cm • CW jet density and contour: dense, triangular with early peak • Hepatic vein flow: systolic reversal	• RV/RA/IVC dilated with decreased IVC respirophasic variation • Elevated RA pressure with "c-V" wave • Diastolic interventricular septal flattening • Reduced RV systolic function in late phase	• Fatigue, palpitations, dyspnea, abdominal bloating, anorexia, edema

*Several valve hemodynamic criteria are provided for assessment of severity of TR, but not all criteria for each category will necessarily be present in every patient. Categorization of severity of TR as mild, moderate, or severe also depends on image quality and integration of these parameters with clinical findings.

CW indicates continuous wave; ICD, implantable cardioverter-defibrillator; IE, infective endocarditis; IVC, inferior vena cava; RA, right atrium; RV, right ventricle; and TR, tricuspid regurgitation.

1. Valve Anatomy
2. Severity of Disease
3. Hemodynamic consequences
4. Symptoms

27

Problem with TR

Volume overload is well-tolerated for years

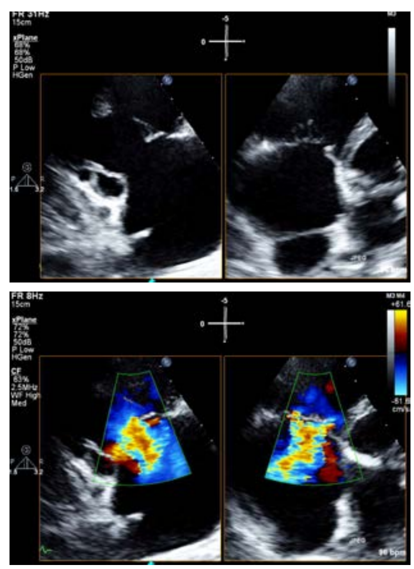
- No reduction in RV function
- Few symptoms of insidious onset

No prior interventional therapy available except surgical TVR/repair

- GDMT = diuretic (Class IIa)

Poor understanding about grading the severity of TR on Echo

- Patients present LATE!!



EROA > 2 cm2
Regurgitant volumes >100 cc

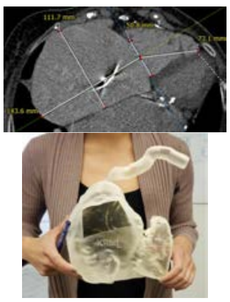
28

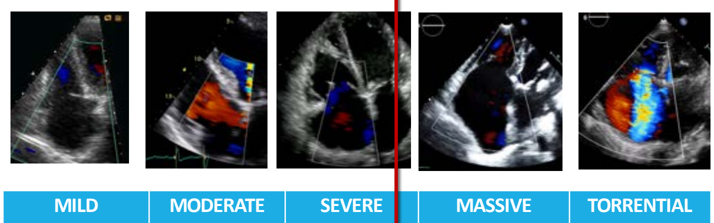
Extended Grading Scheme

Table 1 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	60–79 mm^2	≥80 mm^2
3D VCA or quantitative EROA[a]			75–94 mm	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. European Heart J (2017) 00, 1–2. doi:10.1093/ehjci/jex139

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

29

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]*

Santoro C et al. European Heart Journal - Cardiovascular Imaging (2019) 0, 1–8

Outcomes according to new grading scheme for TR severity assessment.

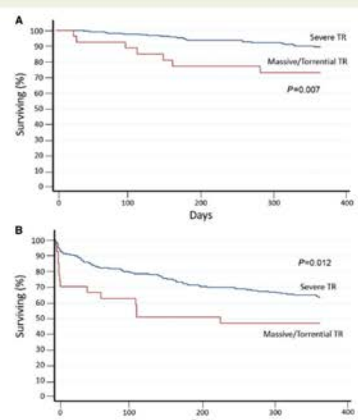


Figure 2 A 1-year follow-up survival curve according to the new classification scheme for TR severity. (A) Kaplan–Meier survival curves for cardiovascular mortality (P < 0.007 for log-rank) and (B) of the combined endpoint for cardiovascular mortality and re-hospitalization (P < 0.012 for log rank) according to new grading scheme for TR severity assessment.

(A) Kaplan–Meier survival curves for cardiovascular mortality (P< 0.007 for log-rank)
(B) Kaplan–Meier survival curves for the combined endpoint for cardiovascular mortality and re-hospitalization (P<0.012 for log rank)

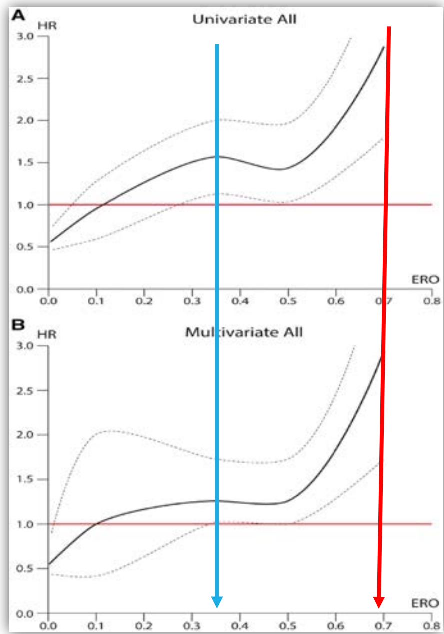
30

Quantitative assessment of effective regurgitant orifice: impact on risk stratification, and cut-off for severe and torrential tricuspid 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]*

European Heart Journal - Cardiovascular Imaging (2019)

- The optimal cut-off value to separation survival between severe vs. lesser degree of TR was 0.35 cm^2 [$P < 0.0001$, HR =2.0 (1.5–2.7)].
- The optimal threshold to separation survival between severe vs. 'torrential' [**massive in the Hahn/Zamorano grading scheme**] TR was 0.7 cm^2 [$P = 0.005$, HR =2.6 (1.2–5.1)].



31

31

Stages of TR

Table 17. Stages of TR

Stage	Definition	Valve Anatomy	Valve Hemodynamics*	Hemodynamic Consequences	Symptoms
D	Symptomatic severe TR	**Primary** • Flail or grossly distorted leaflets **Functional** • Severe annular dilation (>40 mm or >21 mm/m^2) • Marked leaflet tethering	• Central jet area >10.0 cm^2 • Vena contracta width >0.70 cm • CW jet density and contour: dense, triangular with early peak • Hepatic vein flow: systolic reversal	• RV/RA/IVC dilated with decreased IVC respirophasic variation • Elevated RA pressure with "c-V" wave • Diastolic interventricular septal flattening • Reduced RV systolic function in late phase	• Fatigue, palpitations, dyspnea, abdominal bloating, anorexia, edema

Table 17. Stages of TR

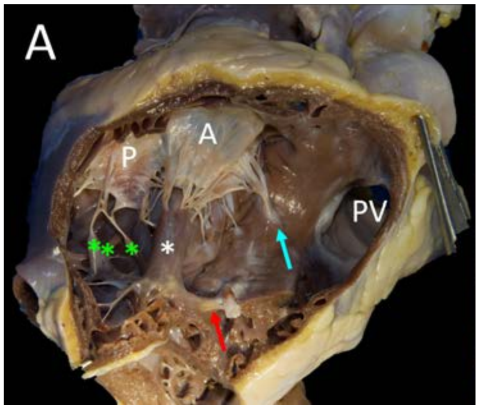
Stage	Definition	Valve Anatomy	Valve Hemodynamics*	Hemodynamic Consequences	Symptoms
A	At risk of TR	**Primary** • Mild rheumatic change • Mild prolapse • Other (e.g., IE with vegetation, early carcinoid deposition,	• No or trace TR	• None	• None or in relation to other left heart or pulmonary/pulmonary vascular disease
			blunting		
C	Asymptomatic severe TR	**Primary** • Flail or grossly distorted leaflets **Functional** • Severe annular dilation (>40 mm or 21 mm/m^2) • Marked leaflet tethering	• Central jet area >10.0 cm^2 • Vena contracta width >0.7 cm • CW jet density and contour: dense, triangular with early peak • Hepatic vein flow: systolic reversal	• RV/RA/IVC dilated with decreased IVC respirophasic variation • Elevated RA pressure with "c-V" wave • Diastolic interventricular septal flattening may be present	• None, or in relation to other left heart or pulmonary/pulmonary vascular disease
D	Symptomatic severe TR	**Primary** • Flail or grossly distorted leaflets **Functional** • Severe annular dilation (>40 mm or >21 mm/m^2) • Marked leaflet tethering	• Central jet area >10.0 cm^2 • Vena contracta width >0.70 cm • CW jet density and contour: dense, triangular with early peak • Hepatic vein flow: systolic reversal	• RV/RA/IVC dilated with decreased IVC respirophasic variation • Elevated RA pressure with "c-V" wave • Diastolic interventricular septal flattening • Reduced RV systolic function in late phase	• Fatigue, palpitations, dyspnea, abdominal bloating, anorexia, edema

*Several valve hemodynamic criteria are provided for assessment of severity of TR, but not all criteria for each category will necessarily be present in every patient. Categorization of severity of TR as mild, moderate, or severe also depends on image quality and integration of these parameters with clinical findings.

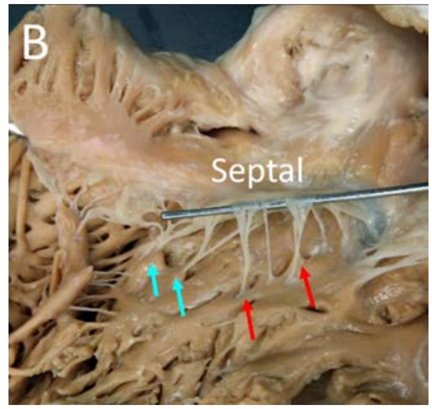
CW indicates continuous wave; ICD, implantable cardioverter-defibrillator; IE, infective endocarditis; IVC, inferior vena cava; RA, right atrium; RV, right ventricle; and TR, tricuspid regurgitation.

1. Valve Anatomy
2. Severity of Disease
3. Hemodynamic consequences
4. Symptoms

32



Two leaflets (anterior and posterior) are dependent upon a large anterior papillary muscle attached to the antero-lateral RV wall.

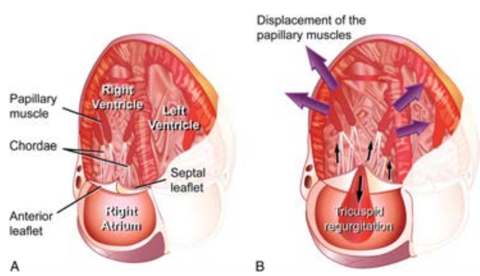


Two TV leaflets (septal and anterior) are connected to the intraventricular septum (via chordal attachment to the septal papillary muscle or directly to the septum)

Dahou A et al. J Am Coll Cardiol Img 2019;12:458–68

33

Tenting and Papillary Muscle Displacement

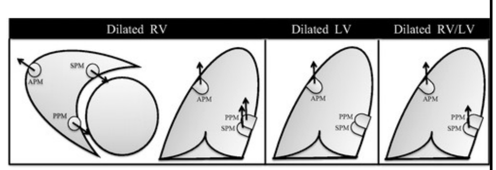


Julia Mascherbauer, Gerald Maurer. Eur Heart J. 2010;31(23):2841-2843.

- (*A*) Normal tricuspid valve.
- (*B*) Functional tricuspid regurgitation: enlargement of th right ventricle results in displacement of the papillary muscles and tethering of the tricuspid leaflets. In additio there is dilatation of the tricuspid annulus.

Spinner E et al. Circ Cardiovasc Imaging. 2012;5:43-50

- **Patients with a dilated right ventricle had significant displacement of all papillary muscles away from the center of the right ventricle, as well as apically.**
- **Patients with a dilated left ventricle had significant displacement of the anterior papillary muscle toward the apex.**
- **Patients with both right ventricle and left ventricle dilatation had significant displacement of the anterior papillary muscle and posterior papillary muscle apically.**

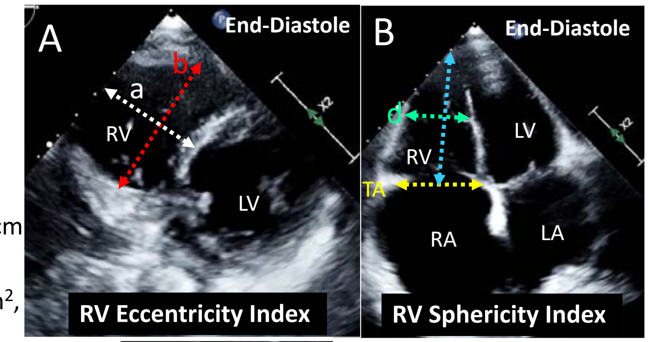


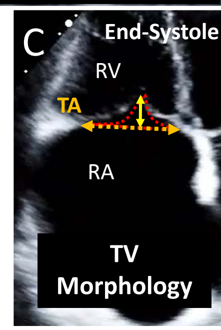
34

Predictors of TR Progression

Predictors of TR progression on serial echo studies include:

1. Tricuspid annular dilatation (4.0 ± 0.7 to 4.6 ± 0.7 cm, P < 0.0001),
2. Increased TV tenting area (2.0 ± 0.7 to 2.5 ± 1.0 cm^2, P = 0.0003).
3. An increase in pulmonary artery systolic pressure (sPAP, 62 ± 22 to 92 ± 23 mmHg, P < 0.0001),
4. RV enlargement, mainly at mid-ventricular level (RV mid diastolic, 2.0 ± 0.5 to 2.5 ± 0.5 cm^2, P < 0.0001; RV mid systolic, 1.8±0.5 to 2.3±0.59 cm, P < 0.0001),
5. Increased RV sphericity (6.1 ± 1.7 to 6.9 ± 1.8, P = 0.004),



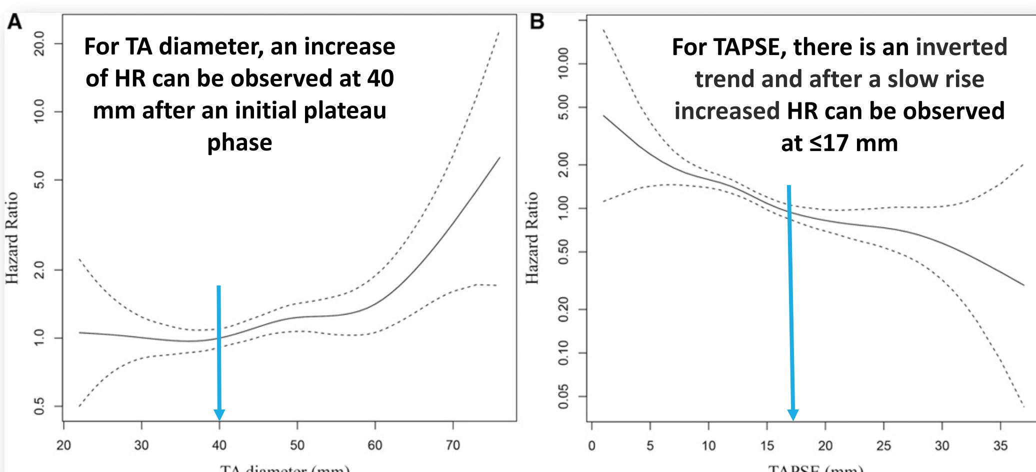


Echocardiographic measurements of RV and TV morphology

After Kim YJ, Kwon DA, Kim HK et al. Circulation 2009;120:1672-8.

Medvedofsky D, et al. European heart journal cardiovascular Imaging 2017;18:86-94.

35



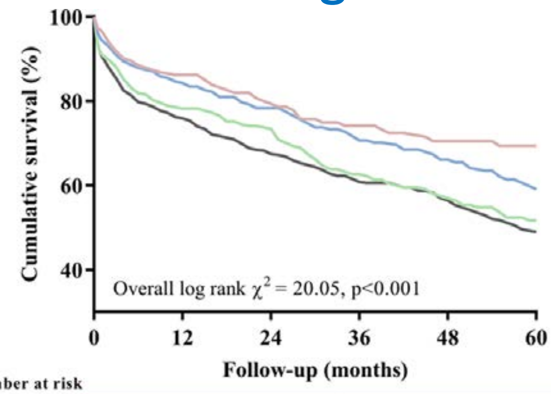
Note: No independent association was observed between RV FAC and all-cause mortality.

Dietz MF et al. Circulation. 2019;140:836–845

36

Outcomes Associated with RV Remodeling

- KM Analysis: **lower survival rates in patients with more advanced patterns of RV remodeling** (log-rank [chi]^2 20.05; *P*<0.001).
- **Patterns 3 and 4 RV remodeling were associated with significantly lower 5-year survival rates** than patterns 1 or 2 (p<0.01)
- **RV dysfunction** (defined as TAPSE<17mm), had **significantly worse survival than patients with normal RV function** (log-rank [chi]^2 17.95; *P*<0.001)



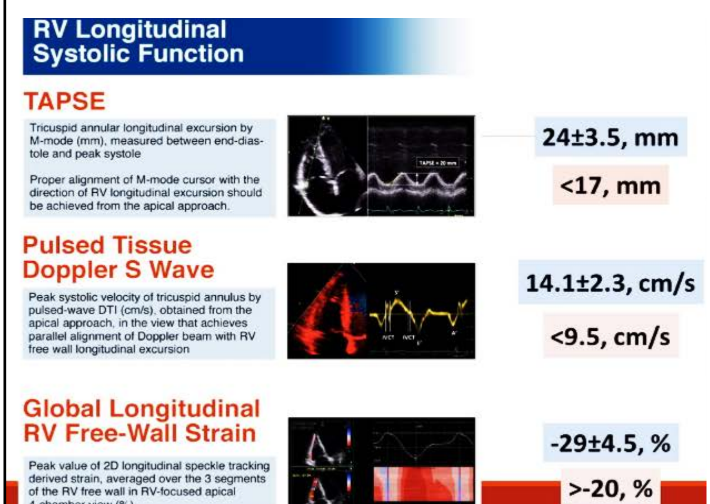
Number at risk

	0	12	24	36	48	60
Pattern 1	183	154	119	91	71	59
Pattern 2	256	211	179	137	107	78
Pattern 3	304	239	203	153	109	77
Pattern 4	549	415	329	253	200	156

Dietz MF et al. Circulation. 2019;140:836–845

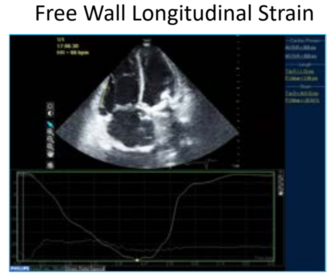
37

Right Ventricular Function: ASE Guidelines

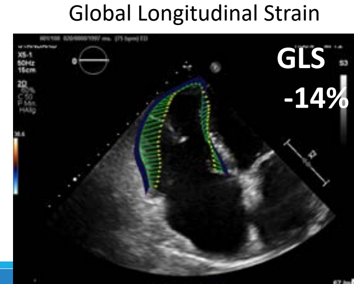


Lang et al. J Am Soc Echocardiogr 2012;25:3-46

Free Wall Longitudinal Strain



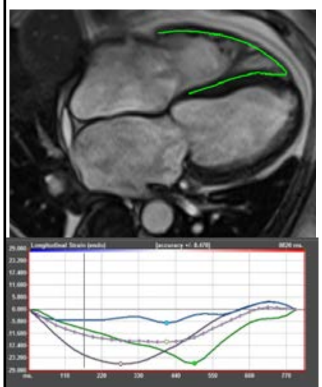
Global Longitudinal Strain



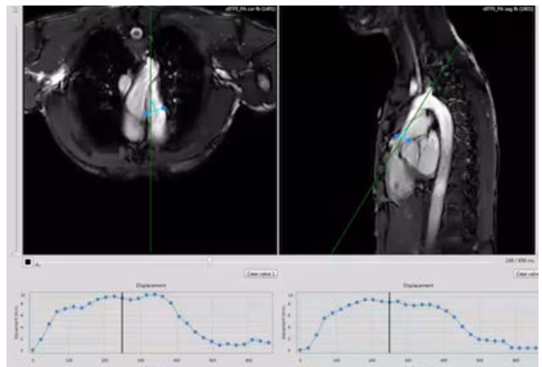
38

Going Beyond RVEF…

CMR RV strain

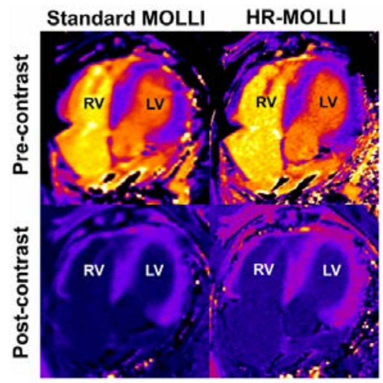


4D Flow



Courtesy of Gaston Voegel (CASS/Pie Medical)

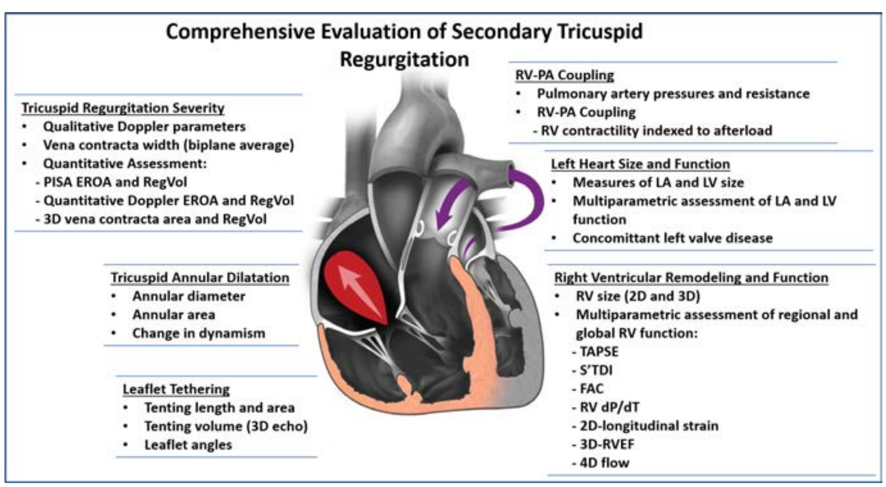
RV Fibrosis



39

When to Intervene will depend on our ability to accurately measure:

1. **TR severity and TV morphology**
2. **Right heart function and RV-PA coupling**



When to Intervene will depend on our ability to accurately predict outcomes

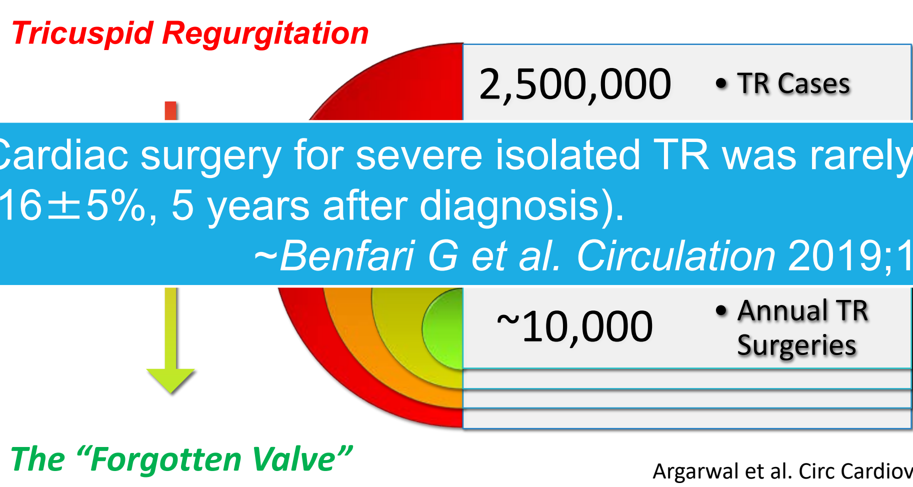
Hahn RT et al JACC Cardiovasc Imaging 2019 https://doi.org/10.1016/j.jcmg.2018.11.016

40

How to Treat: What the Guidelines Tell Us

41

Tricuspid Valve Disease – The "Forgotten Valve"



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

~*Benfari G et al. Circulation* 2019;140:196–206.

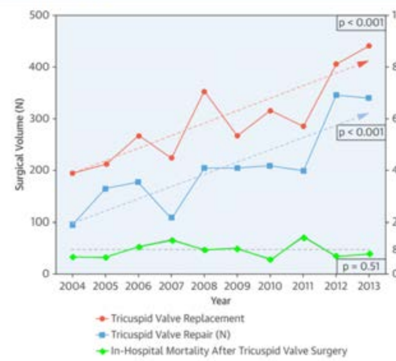
Argarwal et al. Circ Cardiovasc Interv 2009;2:565-573
Stuge O, Liddicoat J. J Thorac Cardiovasc Surg. 2006 Dec;132(6):1258-61

42

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]

CENTRAL ILLUSTRATION Temporal Trends in Surgical Volume and Mortality for Isolated Tricuspid Valve Surgery



Zack, C.J. et al. J Am Coll Cardiol. 2017;70(24):2953-60.

From 2004 to 2013, there was a significant increase in the number of isolated tricuspid valve repair and replacement surgeries performed annually in the United States (p < 0.001 for trend). Isolated valve replacement was performed more frequently than valve repair. In-hospital mortality was 8.8% and remained unchanged despite increasing surgical volumes (p = 0.51 for trend).

- **TV replacement was performed in 59.2% of patients, whereas TV repair was performed in 40.8%.**
- **From 2004 to 2013, the proportion of TV replacements significantly decreased from 67.2% to 57.1% (p = 0.003).**

- **In-hospital mortality = 8.8% and did not vary across the study period**

Zack CJ et al. J Am Coll Cardiol 2017;70:2953–60

43

449 consecutive patients (152 men, aged 56.2±12. 3 years) who underwent TV surgery (397 repairs and 52 replacements) due to severe TR between 1997 and 2010.

Cox-regression analysis revealed independent determinants of mortality:

- Age (HR=1.03; 95% CI 1.01 to 1.05)
- Male gender (HR=1.96; 95% CI 1.29 to 2.99)
- NYHA functional class IV (HR=2.08; 95% CI 1.31 to 3.30)
- Liver cirrhosis (HR=2.51; 95% CI 1.11 to 5.68)
- Preoperative levels of hemoglobin (HR=0.89; 95% CI 0.80 to 0.99)
- Albumin (HR=0.52; 95% CI 0.33 to 0.81)
- GFR (HR=0.86; 95% CI 0.78 to 0.95)

WE OPERATE TOO LATE!!

Kim JB, Jung S-H, Choo SJ, et al. Heart 2013;99:181–187.

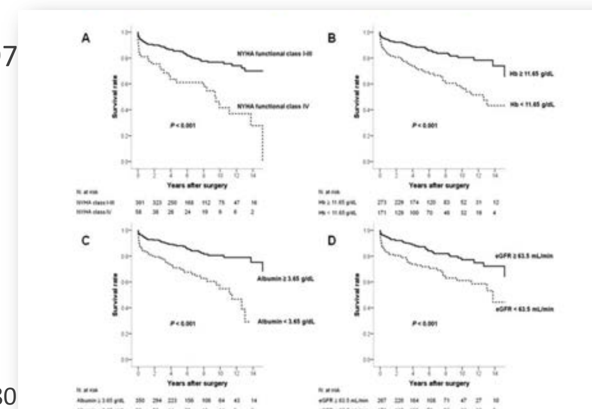


Figure 2 Survival curves according to (A) NYHA functional class and initial levels of (B) haemoglobin, (C) albumin and (D) eGFR. eGFR, estimated glomerular filtration rate; NYHA, New York Heart Association.

Procedural type was not predictive of mortality (p=0.58) or causes of TR (p=0.97)

44

How to Treat: Novel Transcatheter Options

45

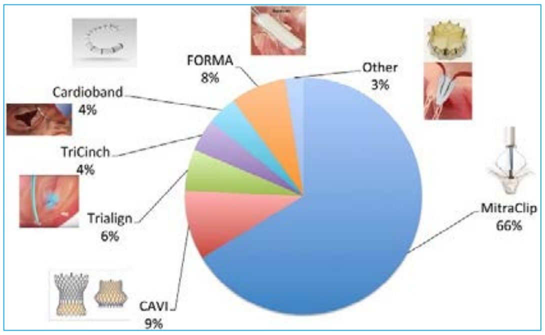
New tricuspid therapies

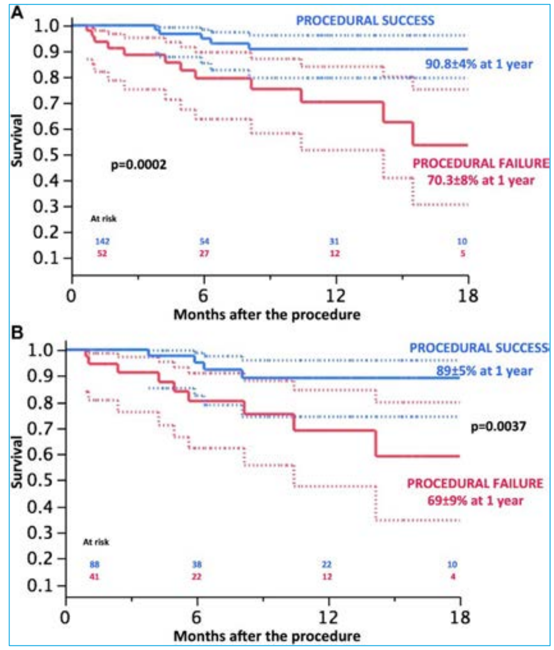
TRANSCATHETER TECHNOLOGIES

Mechanism	New Technologies
Annuloplasty (Direct and Indirect) Device	TriAlign, Cardioband, 4Tech, Millepede, Pasta, Cardiac Implants, MIA PolyCor Anchors
Leaflet Device	Forma, MitraClip, PASCAL, Mistral
Heterotopic Valve (in IVC/SVC)	Trinity /Sapien, TriCentro, SAPIEN in IVC
Orthotopic Valve Replacement	Navigate, Trisol, LUX, Tri-Cares, Intrepid, EVOQUE (Edwards)

46

International TriValve Registry (312 patients, 18 centers)



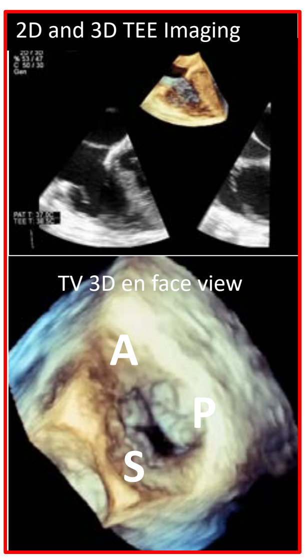


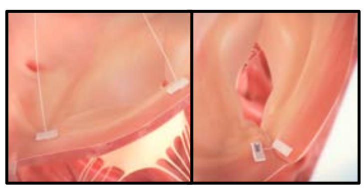
Greater coaptation depth (odds ratio: 24.1; p = 0.002) an independent predictor of reduced procedural success: depth >1 cm best cutoff to predict failure. 30d mortality 3.6%, significantly lower with procedural success (1.9% vs. 6.9%; p = 0.04);

Taramasso, M et al. J Am Coll Cardiol Intv 2019 https://doi.org/10.1016/j.jcin.2018.10.022

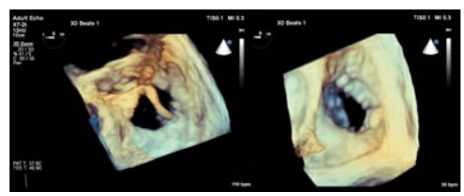
47

Intra-procedural Imaging for Tricuspid Valve Interventions

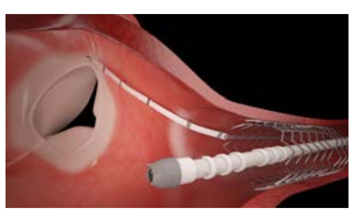




Trialign™



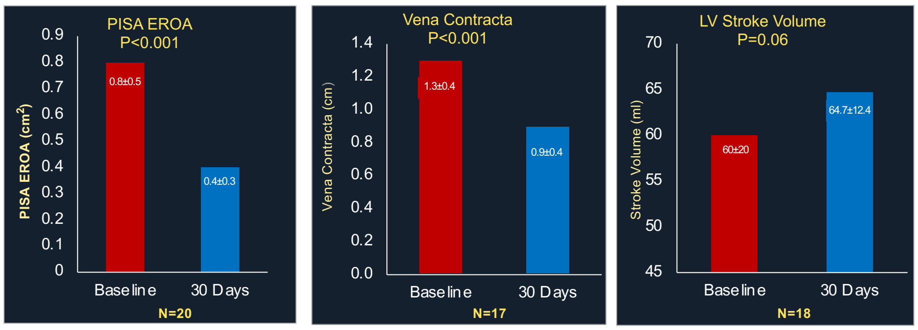
Cardioband™



4Tech TriCinch™ Coil System

48

Edwards TRI-REPAIR Study
50% reduction in PISA EROA, 31% reduction in vena contracta, and 7% improvement in stroke volume by core lab at 30 days

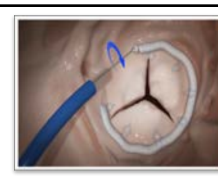


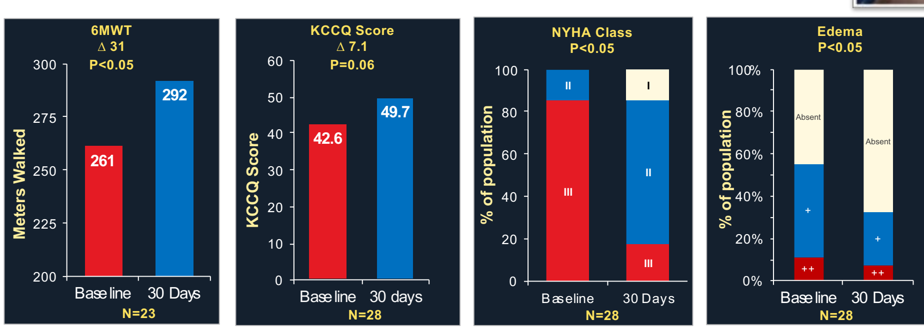
- Large proportion of patients treated with “torrential TR”
- Improvements resulted in most patients achieving lower severity or moderate TR at 30 days.

Data not fully monitored, subject to change

49

Edwards TRI-REPAIR Study
Functional improvement at 30 days





- NYHA functional status and KCCQ QoL scores are left-sided Heart failure clinical endpoints
- Further study needed to understand clinically important endpoints for patients with right-sided heart dysfunction

Data not fully monitored, subject to change

50

Univariable Predictors of <1Grade Reduction

(Severe TR at 1 month FU)

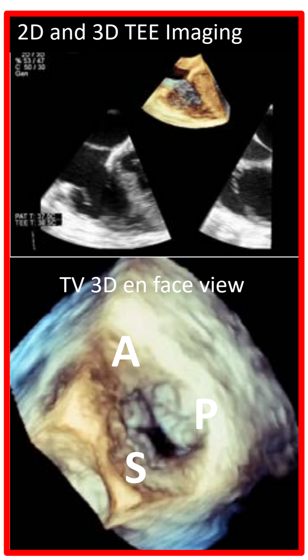
Variable	Beta coefficient	Standard error	P-value	Best Cutoff	Ss	Sp	AUC
PISA-EROA	1.74	0.97	**0.05**	0.77	78	80	**0.78**
TR VC Min	6.86	3.25	**0.0008**	1.0	70	93	**0.84**
TR VC Max	4.15	1.71	**0.0005**	1.6	82	87	**0.87**
RV End-diast Diameter (Base)	1.43	0.74	**0.03**	5.2	83	56	0.72
RV End-diast Diameter (Mid)	2.06	0.94	**0.008**	3.9	83	75	**0.76**
RV End-diastolic Area, cm2	0.23	0.09	**0.005**	28	67	81	**0.78**
RV End-systolic Area, cm2	0.25	0.13	**0.038**	18	67	75	0.72
TA diameter (End-diast), cm			0.09				
Tethering Volume	0.48	0.26	**0.045**	2.30	82	73	0.72
RA Volume	0.02	0.01	**0.016**	102	100	50	0.73

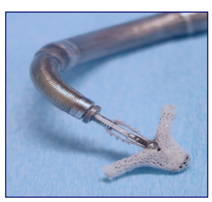
tct2019

Cardiovascular® Research Foundation

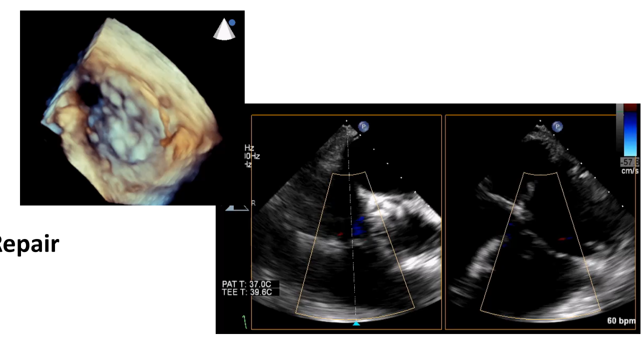
51

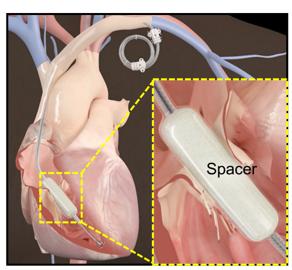
Intra-procedural Imaging for Tricuspid Valve Interventions



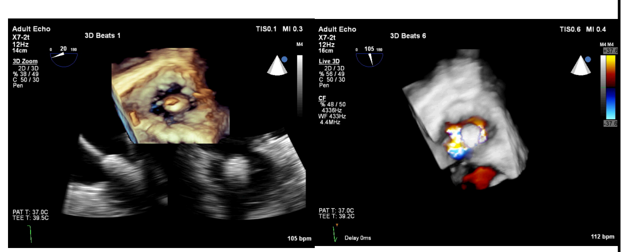


Edge-to-edge Repair





FORMA System

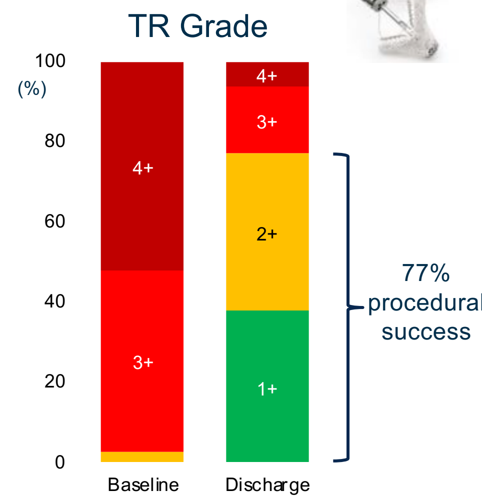


52

Procedural Results Tricuspid Edge-to-Edge Repair

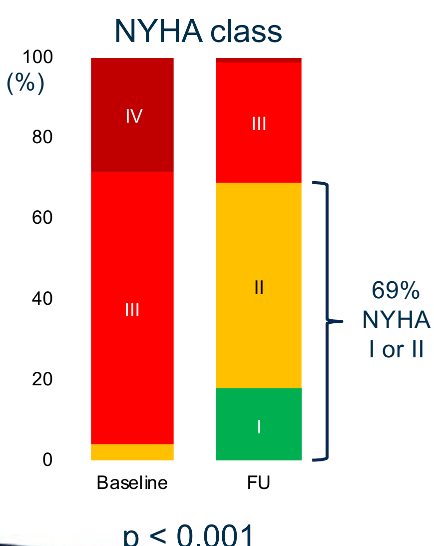
(249 patients)

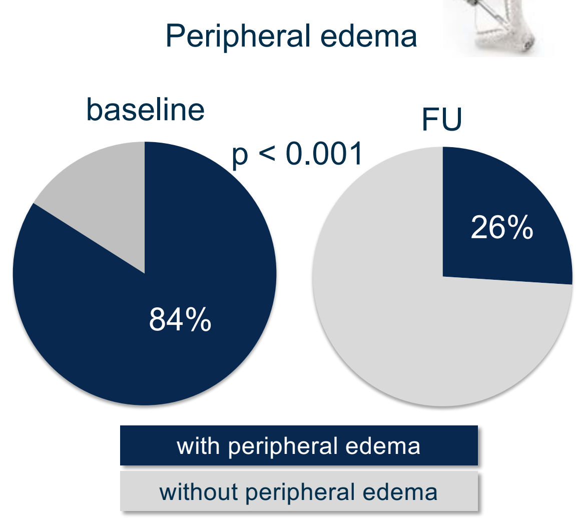
Number of clips	2 ± 1 (range: 0 - 5)
Clip location, n (%)	
Antero-septal	162 (65.1%)
Antero-septal + postero-septal	52 (20.9%)
Other	35 (14.0%)
Duration of TR procedure, min	136 ±62
Reduction of ≥1 TR grade, n (%)	222 (89.2%)
Concomitant MR treatment, n (%)	129 (51.8%)



53

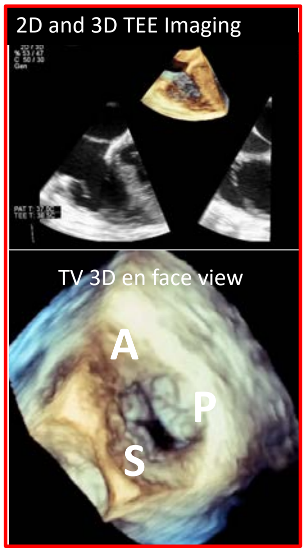
Clinical Improvement



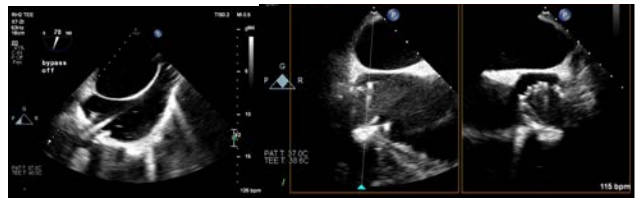


54

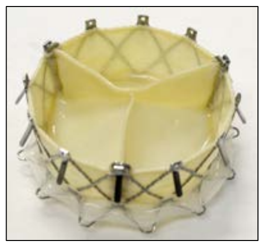
Intra-procedural Imaging for Tricuspid Valve Interventions



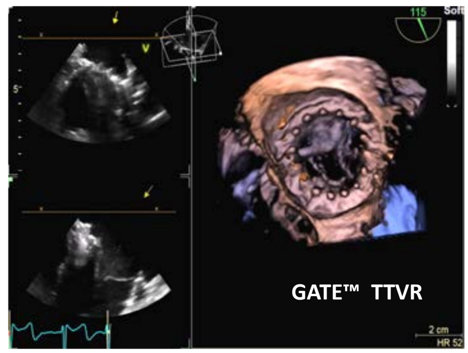
CAVI



SAPIEN 3 in IVC



GATE™ TTVR



55

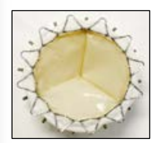
TABLE 3 Baseline and Follow-Up Echocardiographic Parameters

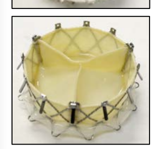
Baseline Echo Parameters	Case #1	Case #2	Case #3	Case #4	Case #5
LVIDD (cm)	4.4	3.6	3.9	5.8	3.3
LVIDS (cm)	3.2	2.3	2.8	4.9	2.8

TAPSE (cm)	0.8	1.4	1.1	1.0	1.2
Fractional area change (%)	41	43	26	29	38
RV systolic TDI (cm/s)	13	12	7	9	9
Global longitudinal strain (RV, %)	−28	−19	−16	−12	−19
RV dP/dT (mm Hg/s)	543	583	300	240	501
In-hospital outcomes					
Significant bleeding	No	No	Yes (chest wall)	Yes (chest wall)	Yes (esophageal, chest wall)
Stroke	No	No	No	No	No
Myocardial infarction	No	No	No	No	No
Other complications	None	None	Temporary pacer for bradycardia	CVVH	None
ICU stay (days)	5	2	28	28	3
Length of stay (days)	13	5	43	Expired 28	8

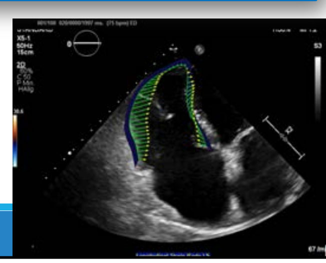
Minimum/maximum diameters (cm)	4.3 × 4.9	4.7 × 5.0	42.1 × 5.7	4.2 × 4.4	3.9 × 5.1
Annular area–derived diameter (cm)	4.4	4.8	5.0	4.3	4.5
Implanted GATE valve size	48	48	52	44	44
Intraprocedural, post-device TEE					
Peak transtricuspid gradient	1.4	1.5	0.8	2.5	1.0
Mean transtricuspid gradient	0.8	0.5	0.3	0.8	0.5
Tricuspid valve area (by CE, in cm^2)	3.5	3.1	3.1	2.7	2.2
Tricuspid regurgitation (total)	Mild–moderate	Trace	Mild	Mild	Trace
Central	Mild	Trace	Mild	None	None
Paravalvular	Mild (posterior)	Trace (septal)	None	Mild (lateral and at wire)	Trace (anterior)

2D = 2-dimensional; 4Ch = 4 chamber; dP/dT = change in pressure divided by the change in time; CE = continuity equation; CT = computed tomography; EROA = effective regurgitation orifice area; LVEF = left ventricular ejection fraction; LVIDD = left ventricular internal dimension in diastole; LVIDS = left ventricular internal dimension in systole; LVOT = left ventricular outflow tract; PASP = pulmonary artery systolic pressure; PISA = proximal isovelocity surface area; RA = right atrium; RV = right ventricular; TAPSE = tricuspid annular plane systolic excursion; TDI = tissue Doppler imaging; TEE = transesophageal echocardiography; TR = tricuspid regurgitation.





Navigate



Hahn RT et al. JAm Coll Cardiol Img 2019;12:416–29

56

Journal of the American College of Cardiology
Available online 27 September 2019
In Press, Journal Pre-proof

Transcatheter versus medical treatment of symptomatic severe tricuspid regurgitation

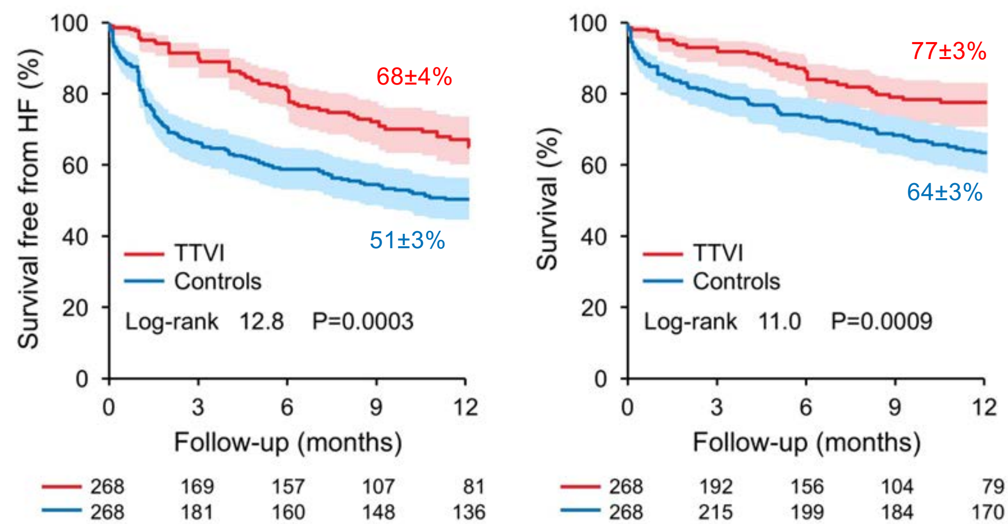
Maurizio Taramasso MD PhD [1], Giovanni Benfari MD [2], Pieter van der Bijl MD [3], Hannes Alessandrini MD [4], Adrian Attinger-Toller MD [5], Luigi Biasco MD [6], Philipp Lurz MD PhD [7], Daniel Braun MD [8], Eric Brochet MD [9], Kim A. Connelly MD [10], Sabine de Bruijn MD [11], Paolo Denti MD [12], Florian Deuschl MD [13], Rodrigo Estevez-Loureiro MD PhD [14], Neil Fam MD [10], Christian Frerker MD [4, 15], Mara Gavazzoni MD [1], Jo¨rg Hausleiter MD [8] ...

https://doi.org/10.1016/j.jacc.2019.09.028

- TriValve (Transcatheter Tricuspid Valve Therapies) registry collected 472 patients from 22 European and North American centers, who underwent TTVI from 2016 to 2018.
- A control cohort formed by two large retrospective registries enrolling medically managed patients with ≥moderate TR in Europe and North America (1179 pts) were propensity score 1:1 matched (distance ± 0.2 SD) using age, Euroscore II, and systolic pulmonary artery pressure.

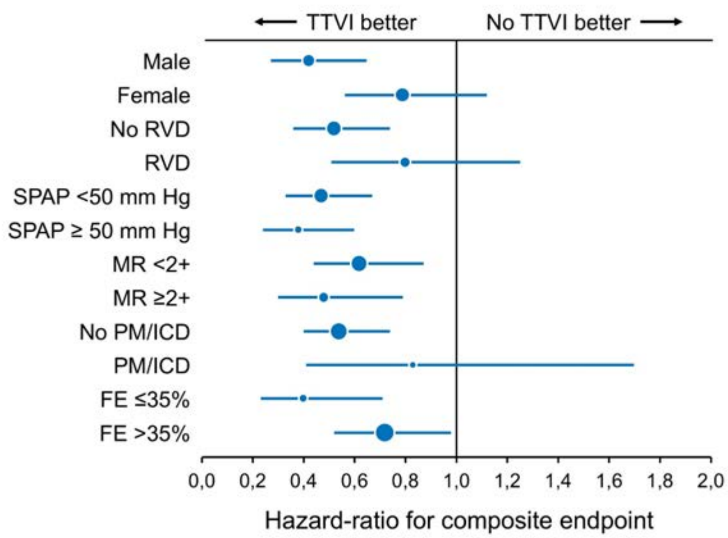
57

Results: Primary and secondary endpoint



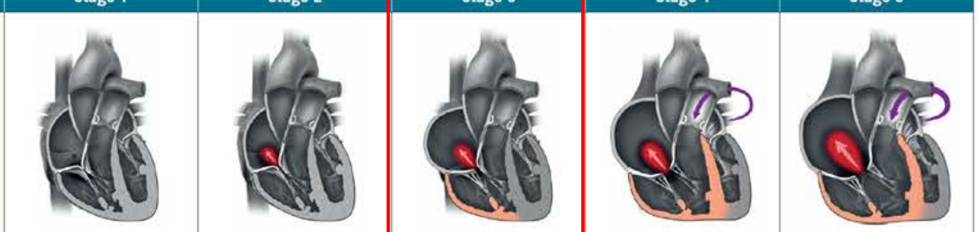
58

Results: subgroup analysis



59

Table 4. A proposed classification of patients presenting with FTR and potential treatment options.



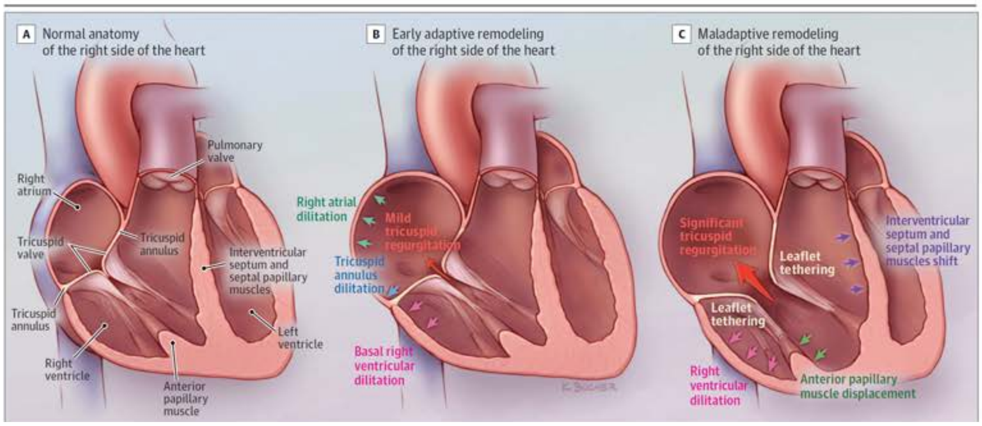
	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
Symptoms	None	None*	None-vague*	Current or previous episodes of RHF	Overt RHF and/or end-organ damage due to chronic RV volume overload#
TR grade	Less than moderate	>Moderate	Severe	Severe	Torrential
Annular remodelling	Normal	Normal or mildly remodelled	Present	Moderate-severe	Severe
Leaflet coaptation	Normal	Mildly abnormal	Abnormal	Coaptation gap	Large coaptation gap
Tethering	None	None or mildly abnormal (<8 mm)	Abnormal (usually <8 mm)	Significantly abnormal with varying degree of tethering	Significantly abnormal (usually >8 mm)
RV function and remodelling	Normal	Normal function Absent or mild remodelling	Mild RV dysfunction and/or remodelling	>Moderate dysfunction and remodelling	Severe RV dysfunction and remodelling

Recent studies suggest that in the presence or absence of PH, tricuspid annular dilation and right/left atrial enlargement are early events associated with mild functional TR and that RV dilation occurs late and is associated with severe TR.

A. Latib, F. Grigioni, RT Hahn. Euro**Intervention** 2018;14:**AB101-AB111**

60

Figure 2. Schematic of the Changes Associated With the Progression of Tricuspid Regurgitation



Early	Progressive	Late
Initial Right Ventricular (RV) dilatation results in Tricuspid Annulus (TA) dilatation	Progressive RV and TA dilatation results in lack of leaflets coaptation	Progressive RV distortion (±PHTN) results in further tethering of the leaflets
Annular Device Leaflet Device Replacement Device	± Annular Device Leaflet Device Replacement Device	± Leaflet Device Palliative Caval/FORMA Device Replacement Device (?RV Fx)

Hahn RT et al. JAMA Cardiol. doi:10.1001/jamacardio.2019.0535 Published online April 17, 2019

61

Heart Team Discussion on Who and How to Treat

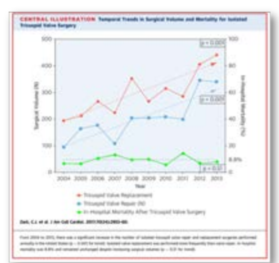
When to intervene and when not to intervene in tricuspid regurgitation is a "work in progress"

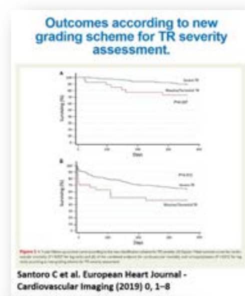
1. **Earlier in the disease process**
2. **Patient-specific anatomy**

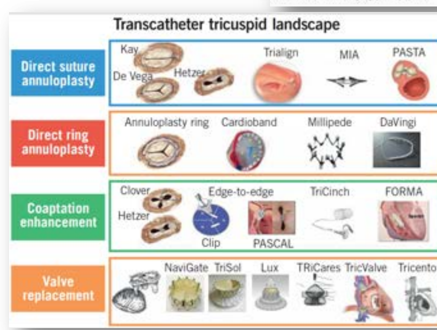
Which Device:

1. **High Safety profile**
2. **High Efficacy**
3. **Improved outcomes**

@hahn_rt







62