EuroValve 2018 | Palermo, Italy

Trans-catheter TV repair

Leaflet or Annuloplasty Techniques

Corrado Tamburino, MD, PhD

Full Professor, University of Catania

Division of Cardiology, CAST

University Policlinic, Catania

FACTS ON TRICUSPID REGURGITATION

The tricuspid valve (TV) has traditionally been considered as the forgotten valve and often neglected by clinicians.

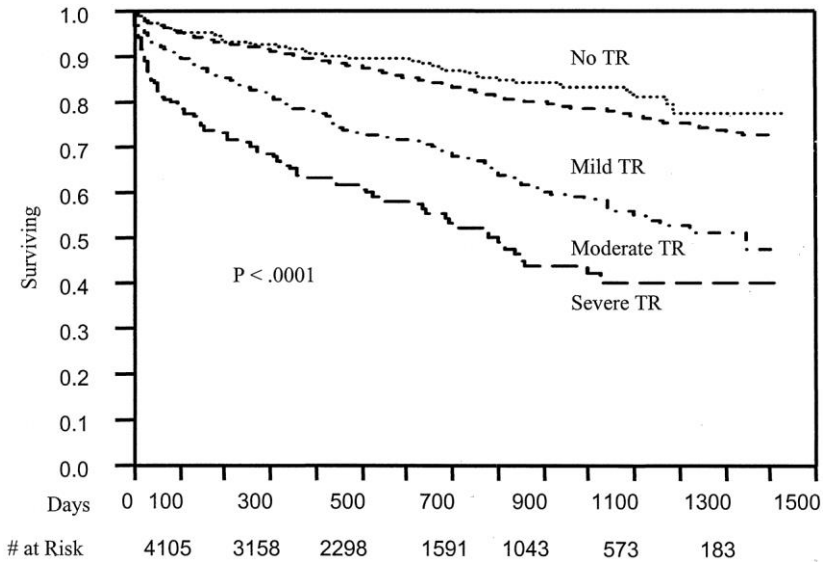
- Tricuspid regurgitation (TR) is a common finding in patients with left-sided valvular heart disease[1]
- It is independently associated with increased mortality rates[1]
- The prognostic benefit of isolated TR repair is unclear and medical treatment of decompensated right heart failure alone does not prevent progression of disease[1]

1. Hammerstingl et al. European Heart Journal 2016; 37, 849–853

2. Stuge et al. J Thorac Cardiovasc Surg 2006;132:1258–61

FACTS ON TRICUSPID REGURGITATION

Severe TR is associated with a poor prognosis, independent of age, biventricular systolic function, RV size, and dilation of the inferior vena cava.



Nath J et al. J Am Coll Cardiol. 2004;43(3):405-409

Table 1. Prevalence of TR Among Different Populations

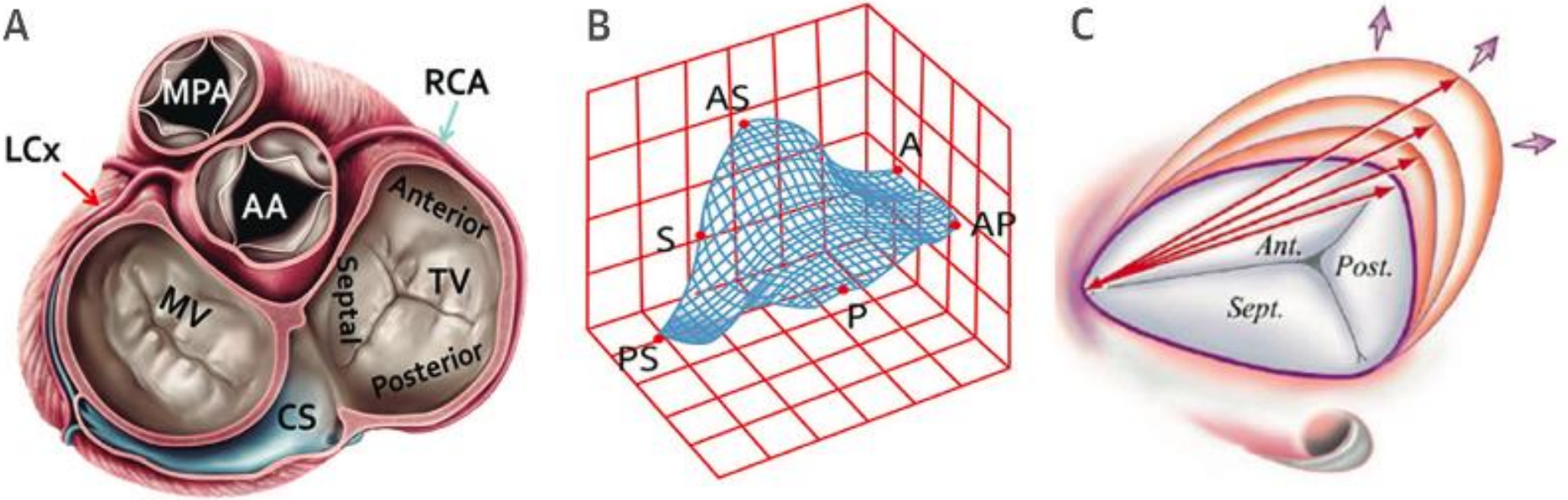
Study	Population	FU	TR Severity	No. of Patients	TR Patients (%)
Ohno et al	MitraClip	1 y	Moderate to severe	99	11 (11)
Barbanti et al	TAVI	30 d	Moderate to severe	518	109 (21)
Lindman et al	TAVI	1 y	Moderate to severe	542	89 (16)
Jeong et al	SAVR	4.4 y	Mild to severe	324	70 (21)
Lee et al	Valvuloplasty for rheumatic MS	12 y	Moderate to severe	299	56 (19)
Rajbanshi et al	MV surgery for degenerative MV disease	>5 y	Severe	163	10 (6)
De Bonis et al	MV repair in dilated cardiomyopathy	7.3 y	Moderate to severe	84	17 (20)

FACTS ON TRICUSPID REGURGITATION

Etiology of Tricuspid Regurgitation		
Morphologic Classification	Disease Subgroup	Specific Abnormality
Primary Leaflet Abnormality - 25%	Acquired Disease	Degenerative myxomatous Rheumatic Endocarditis Carcinoid Endomyocardial fibrosis Toxins Trauma Iatrogenic (Pacing leads, RV biopsy) Other (eg. Ischemic papillary muscle rupture)
	Congenital	Ebstein's anomaly Tricuspid valve tethering associated with perimembranous VSD and VSA Other (Giant right atrium)

Etiology of Tricuspid Regurgitation		
Morphologic Classification	Disease Subgroup	Specific Abnormality
Secondary ('Functional") - 75%	Left heart disease	LV dysfunction or valve disease
	Right ventricular dysfunction	RV ischemia RV volume overload RV cardiomyopathy (eg. ARVD)
	Pulmonary Hypertension	Chronic lung disease Pulmonary thromboembolism Lleft-to-right shunt)
	Right atrial abnormalities	Atrial fibrillation
Other	Post-operative	Recurrent TR post-surgical intervention

Tricuspid Anatomy



Rodés-Cabau et al. JACC 2016; 67:1829-45

Heart Team players

Diagnosis

The AV valves patient

The echocardiographist

The HF specialist

Echocardiographic parameters of severe TR

Parameters	Mild	Moderate	Severe
Qualitative			
TV morphology	Mildly abnormal leaflets (e.g. mild rheumatic thickening, limited prolapse)	Moderately abnormal leaflets (e.g. moderate thickening or prolapse)	**Severe valve lesions (e.g. Flail leaflet, ruptured papillary muscle, severe retraction, large perforation or vegetation)**
Interventricular septal motion	Normal	Typically normal	Paradoxical/ volume overload pattern
Color flow TR jet [Note: not recommended for sole grading of severity]	**Small RA penetration or not holosystolic**	Moderate RA penetration or large penetration and late systolic	Deep RA penetration and holosystolic jet
Flow convergence zone	**Not visible, transient or small**	Intermediate in size and duration	**Large throughout systole**
CW signal TR jet	Faint/parabolic or partial contour	Dense, variable contour	Dense, triangular with early peaking contour (peak <2 m/s in very severe TR)
IVC diameter	Normal	2.1 -2.5 cm	>2.5 cm
Semi-quantitative			
Color flow jet area (cm^2) [Central Jet][a]	<5	5-10	> 10
Color jet area:RA area (%)	10-20	10-33	>33
Vena contracta (cm)	<0.3	<0.6	**≥ 0.7**
PISA Radius (cm)[b]	≤0.5	0.6-0.9	> 0. 9
Hepatic vein flow	Systolic dominance	Systolic blunting[c]	**Systolic flow reversal**
Tricuspid inflow	E-wave < 1 m/sec or A-wave dominant	Variable	E-wave ≥1.0 m/sec
Quantitative			
EROA (mm^2) [by PISA]	<20	20-39[d]	≥40
EROA (mm^2) [by 3D]	Unknown	Unknown	>75
Regurgitant volume(mL) [by PISA]	<30	30-45[d]	≥45
RV and RA size	Usually normal	Usually normal or mild dilatation	Usually dilated[e]

CW = continuous wave; EROA = effective regurgitant orifice area; RA = right atrium; RV = right ventricular; TR = tricuspid regurgitation; TV = tricuspid valve valve

Bolded qualitative and semi-quantitative signs are considered specific of their TR grade

^ There may be uncertainty between mild and moderate or between moderate and severe; consider further evaluation (eg cardiac magnetic resonance imaging, exercise echocardiography, right and left heart cath) to clarify, if clinically indicated or needed for clinical trial classification.

aWith Nyquist limit >50-60 cm/s

b With Baseline Nyquist limit shift of 28 cm/s.

c Signs are non-specific and are influenced by many other factors (RV diastolic function, atrial fibrillation, RA pressure). A cutoff of 18

d-There is little data to support further separation of these values.

e RV and RA can be within the "normal" range for patients with acute severe TR or with chronic severe TR associated with restrictive cardiomyopathy

Heart Team players

Risk Assessment

The interventionalist

The AV valves patient

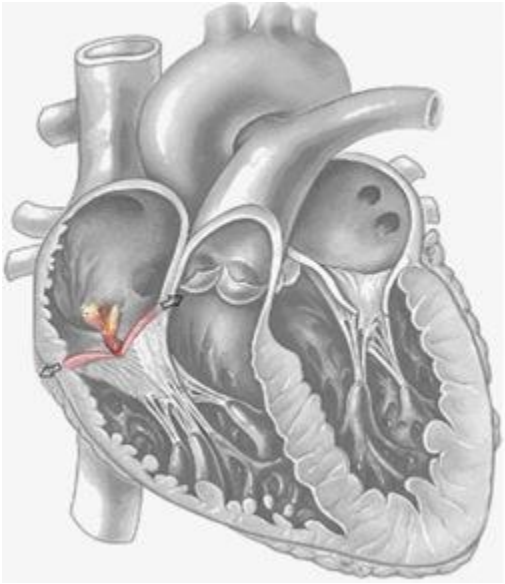
The cardiac surgeon

The anesthesiologist

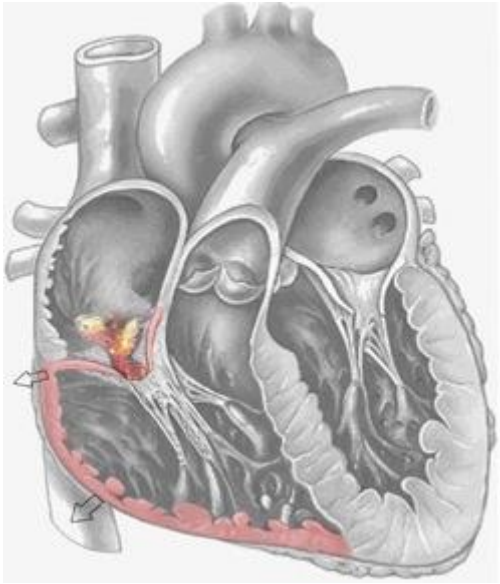
In 1967, Braunwald advised a conservative approach to TR. It was thought that appropriate correction of the left-sided valve disease would probably result in a decrease or even abolition of functional TR.

Braunwald NS, Ross J Jr, Morrow AG. Conservative management of TR in patients undergoing mitral valve replacement. Circulation 1967

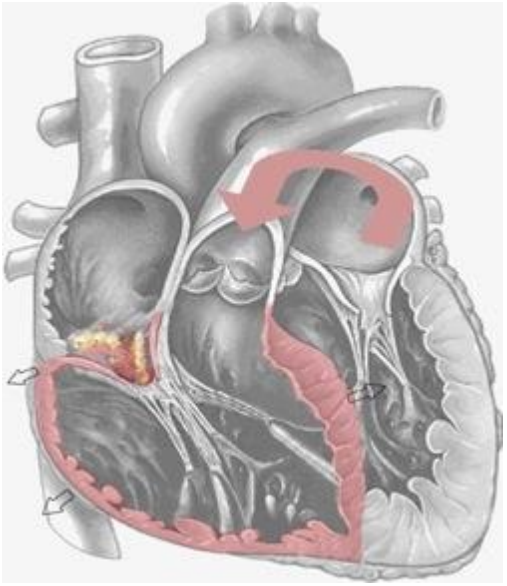
TR: When should we treat ?



Phase I
Initial dilation of RV
results in TA dilation

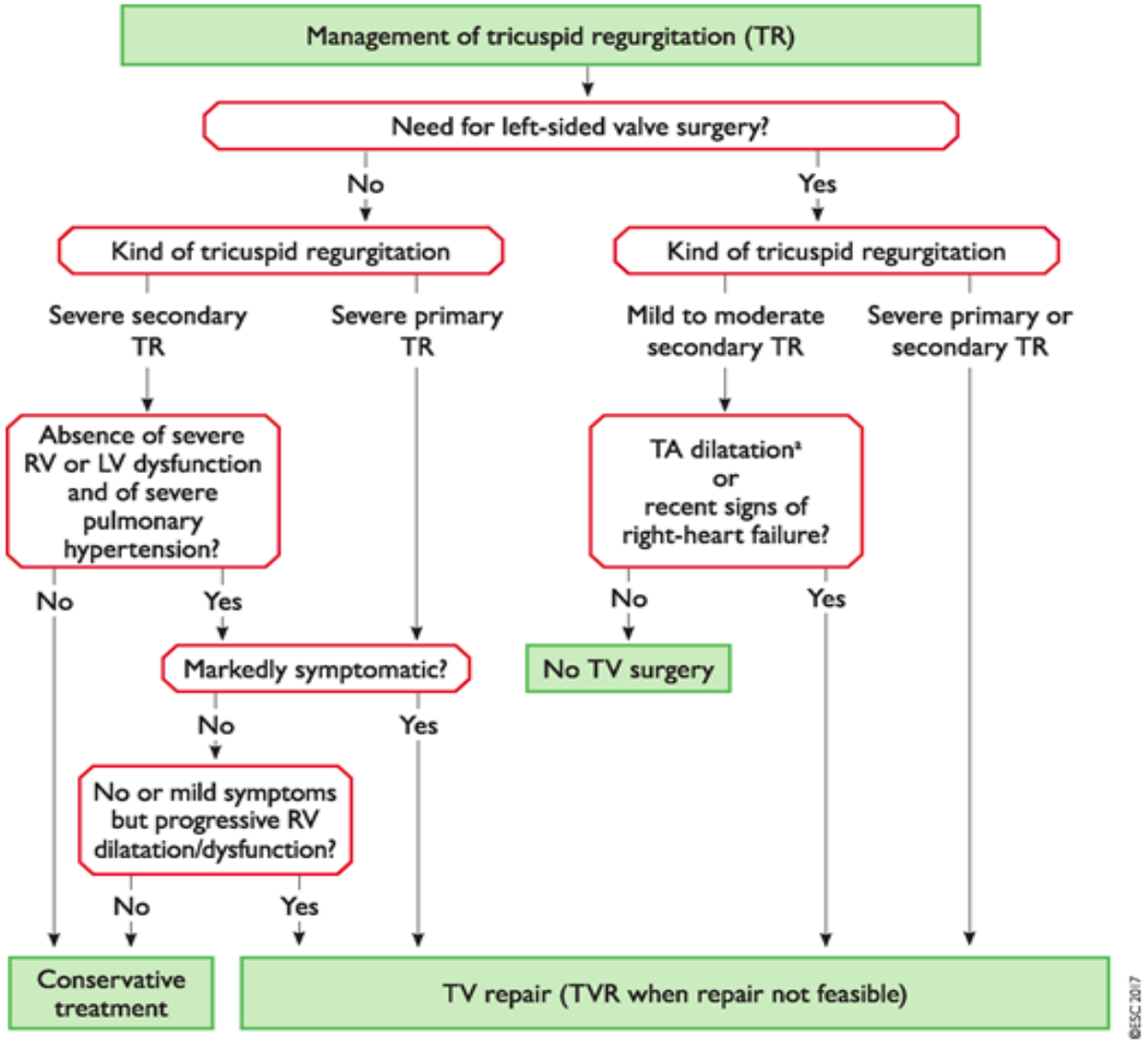


Phase II
Progressive RV
and TA dilation
results in lack of coaptation



Phase III
Progressive RV distortion
tethering of the leaflets,
TA dilation, pulm hypertension

ESC 2017 TR indication for Surgery



In patients undergoing left-sided valve surgery, the guidelines recommend concomitant TV repair when the tricuspid annulus is dilated, even if TR severity is mild . This algorithm is designed to prevent evolution to severe TR and eventual RV dysfunction

If possible, valve repair is preferable to valve replacement

Percutaneous repair techniques are in their infancy and must be further evaluated before any recommendations can be made.

TV repair

The Kay procedure essentially consists of bicuspidization of the TV through plication of the posterior leaflet, but does not address the tendency of the anterior annulus to dilate and creates a hypofunctional posterior leaflet.

The De Vega technique is based on suturing the annulus surrounding the anterior and the posterior leaflets, whose functionality is preserved but this technique is limited by suture dehiscence because of the frequent presence of friable tissue.

Ring annuloplasty consists of the implantation of a prosthetic annuloplasty ring that restores both the original annular dimensions and the tridimensional shape of the annulus. Partial bands and rings avoid sutures in the region of the conduction system, thus minimizing the risk of permanent pacemaker implantation. In contrast, they do not prevent annular dilatation in the septal part of the valve and therefore may be associated with TR recurrence. An advantage of rigid rings over the flexible bands is that the dimension of the septal annulus is better stabilized, thus reducing the recurrence of regurgitation. However, there is some evidence to suggest that annuloplasty ring dehiscence might be more common with rigid rings. Thus, a semirigid device may be the optimal choice.

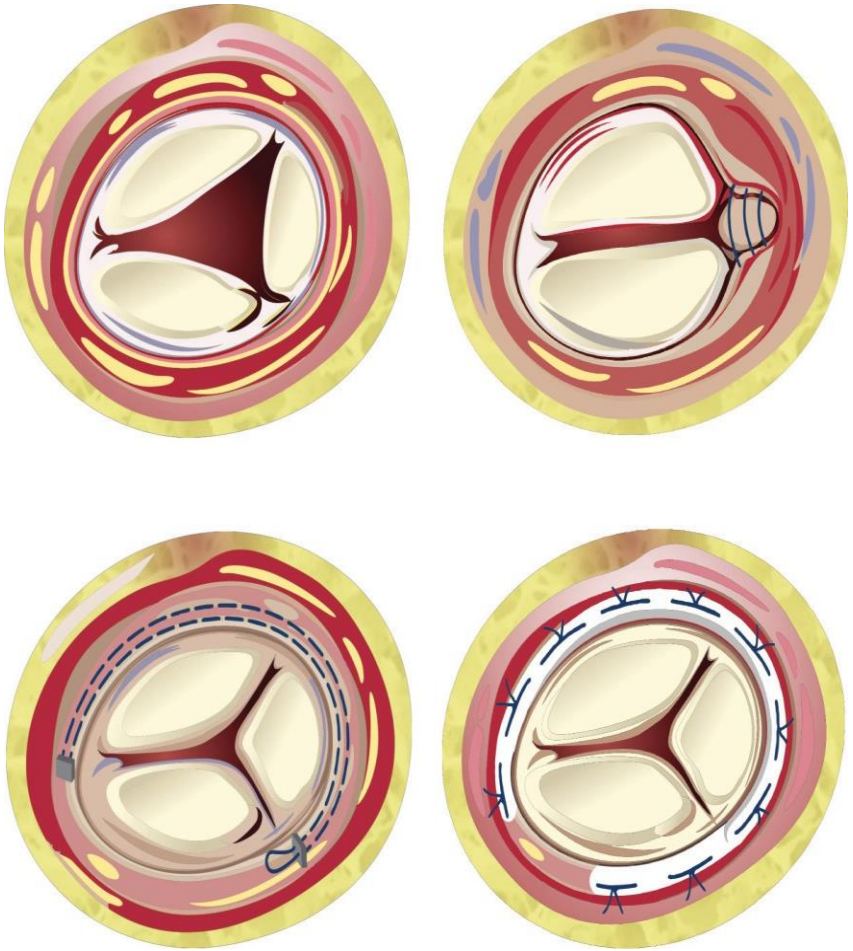


Figure 1. **Tricuspid annuloplasty repair techniques**
(A) Tricuspid valve before surgical intervention. (B) Surgical plication of the posterior leaflet (Kay bicuspidisation repair). (C) De Vega suture repair, which allows reduction of the annular area and increases leaflet coaptation.
(D) Ring annuloplasty with use of an incomplete semirigid prosthetic ring.

A

TV repair

Most of the published studies, both randomized and observational, have demonstrated that ring annuloplasty repairs are more durable than suture annuloplasty, particularly in patients with severe tricuspid annular dilation or pulmonary hypertension.

Besides being more durable, ring repairs also provide better long-term survival and event-free survival up to 15 years after surgery compared with suture annuloplasty and therefore are considered the gold standard of therapy.

Study	Year	No. of Patients	Treatment	Mean Follow-Up	TR Recurrence
Guenther et al	2013	717	Use of ring: 433 patients	10 y	2% in the ring group, 13% in the no-ring group
			No ring: 225 patients		
Tang et al	2010	702	Use of ring: 209 patients	5.7 y	30% in the ring group, 36% in the no-ring group
			No ring use: 493 patients		
Roshanali et al	2009	105	Use of ring: 53 patients	1 y	14% in the ring group, 28% in the no-ring group
			No use of ring: 52 patients		
Rivera et al	1985	159	Use of ring: 76 patients	5.3 y	10% in the ring group, 34% in the no-ring group
			No use of ring: 83 patients		
McCarthy et al	2004	256	Use of ring: 139 patients	5 y	17% in the ring group, 33% in the no-ring group
			No use of ring: 116 patients		

Table 2. Different Rates of TR Recurrence at Follow-Up in Surgical Patients Treated With or Without Annuloplasty

The AV valves patient

The interventionalist

The echocardiographist

The cardiac surgeon

Radiologist

Challenges of TR percutaneous treatment

Large tricuspid annulus size
Nonplanar and elliptical annulus shape
Fragility of tricuspid annular tissue and narrower annular shelf in comparison to mitral annulus
Noncalcified annulus in secondary tricuspid regurgitation
Angulation in relation to superior and inferior vena cava
Trabeculated right ventricle, muscular bands and chordae tendinae
Thin right ventricular free wall
Proximity of AV node and right His bundle branch
Proximity of the right coronary artery to annulus and risk of coronary injury
Risk of occlusion of coronary sinus, vena cava or outflow tract
Slow-flow in right ventricle
Patients with pacemaker or defibrillator leads

Heart Team players

Percutaneous procedure

The interventionalist

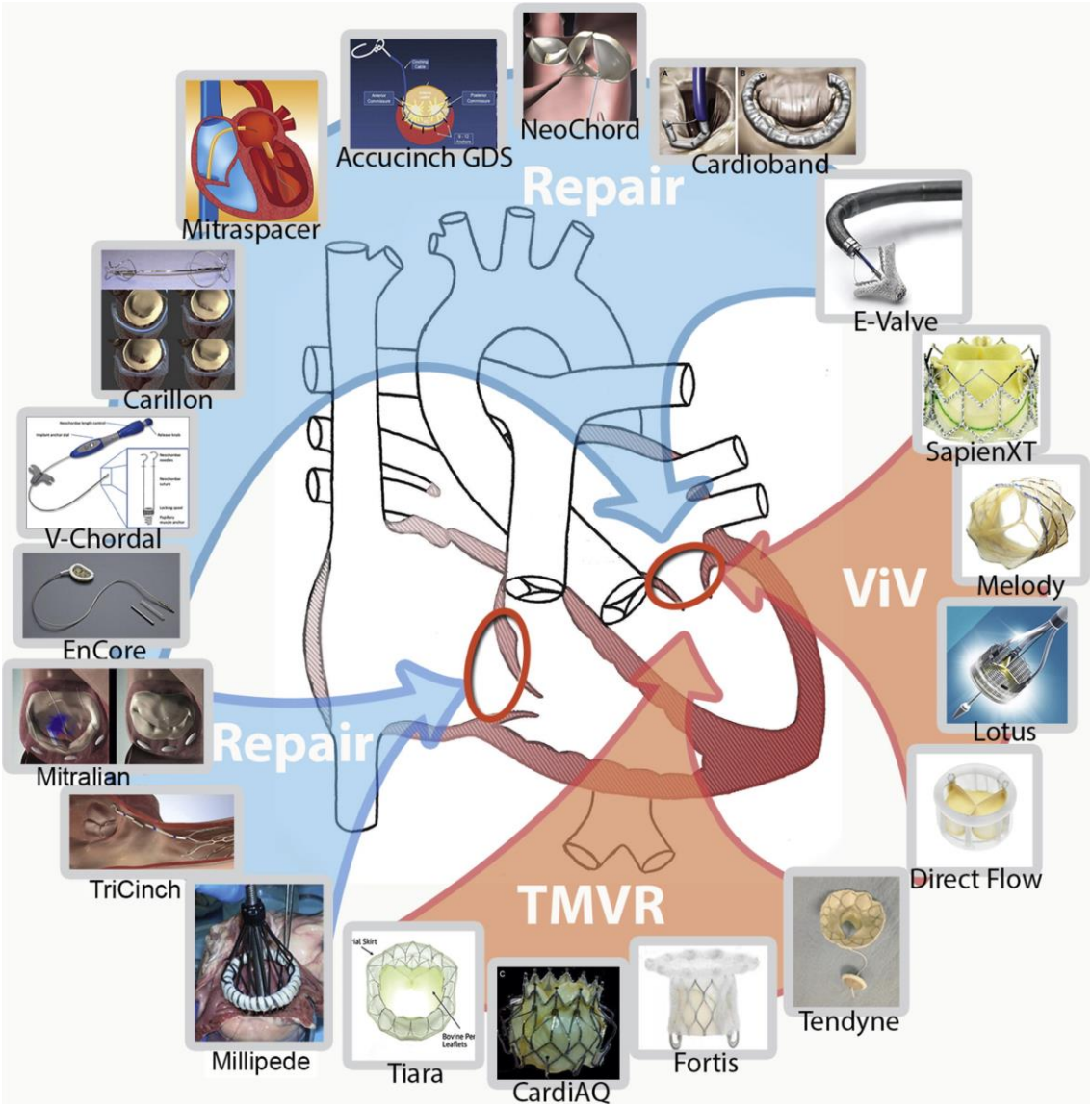
The cardiac surgeon

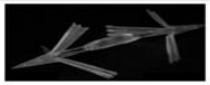
The AV valves patient

The echocardiographist

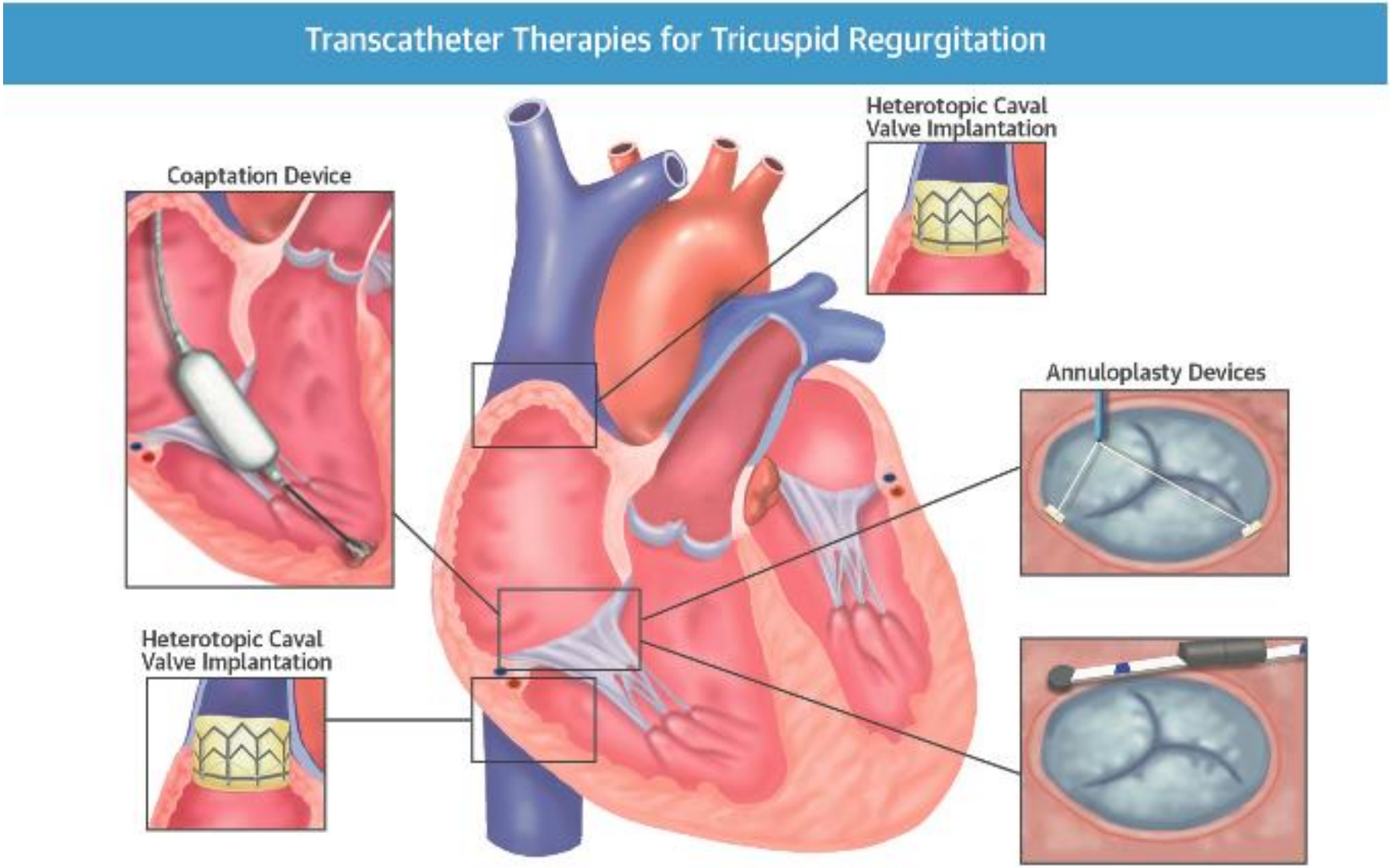
The anesthesiologist

Mitral & Tricuspid Valve



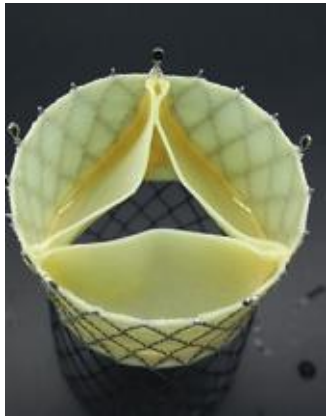
Structure	Device name and typology	Description	Summary	Current clinical experience
	**TRAIPTA** (Trans-Atrial Intra-Pericardial Tricuspid Annuloplasty) [54] *Annuloplasty system*	A delivery device is used to position a suture circumferentially in the atrio-ventricular groove and to deploy a semirigid device, in order to apply direct compression to the tricuspid annulus.	- Good preclinical results - Increase in leaflet coaptation - Challenging procedure with need of pericardial space - Risk of coronary injury	Only preclinical implants performed.
	**Trialign**: system for tricuspid bicuspidization [55] *Annuloplasty system*	Delivery of polyester pledgets via the right ventricle through the tricuspid annulus. Pledgets are plicated and locked directly on the annulus. The system is advanced through a transjugular route.	- Risk of mid-term failure (incomplete plasty) which can be mitigated by implanting 2 pairs of pledgets	15 patients (SCOUT trial) 1. Acute implant success in 100%; 2. Reduced annular dimensions, annular area and EROA; 3. Three late pledget detachments and one right coronary artery damage occurred
	**TriCinch**: catheter-based device to perform tricuspid annular cinching [56] *Annuloplasty system*	The system consists of a corkscrew anchor, a self-expanding stent, and a Dacron band connecting both. Once anchored, the stent is released in the inferior vein cava and tension is applied through the Dacron band.	- Potential risk of leaflet or coronary damage - Single anchor with risk of anchor detachment - Incomplete plasty with risk of TR recurrence	24 patients (PREVENT trial): 1. Successful procedure in 85% patients patients (2 haemopericardium) 2. four late anchor detachments and one right coronary artery damage occurred occurred
	**Millipede**: repositionable and retrievable tricuspid ring [57] *Annuloplasty system*	Collapsible nitinol ring with individually controlled collars. Corkscrew-shaped anchors attach the ring to the annulus. The implant is then contracted, reducing the dilated annulus to a physiological size.	- Complete annuloplasty with potential reduced risk of TR recurrence - Risk of atrio-ventricular block	2 patients (surgical implant): 1. Immediate reduction in tricuspid diameter; 2. Abolishment of TR 3.Positive remodeling of both ventricles.
	**Cardioband**: adjustable, sutureless annuloplasty band [58] *Annuloplasty system*	A flexible implant delivered through a flexible catheter. Anchors are attached to the annulus. Once all anchors are fixed, tension can be applied reducing the annular diameters.	- Complete annuloplasty with potential reduced risk of TR recurrence - It could be effective in the reduction of the annular diameters - Risk of anchor detachment & coronary injury	5 patients (compassionate use): 1. Reduction in TR grade, septo-lateral and antero-posterior diameter; 2. Reduction in EROA, PISA radius, and VC.
	**FORMA**: spacer anchored at the right ventricular apex [59] *Coaptation device*	A foam-filled polymer balloon and rail that is anchored at the right ventricular apex. The device is advanced via left axillary vein access and is fully retrievable.	- Large device not addressing the anatomical changes that occur in functional TR - May have impact on RV pacing lead insertion	Cohort of 18 patients: 1. Implantation success in 89%, with no operative mortality. 2. Less than severe TR grade in 71% at 6-month follow-up; 3. Improvement in NYHA functional class and clinical outcomes at 1-year follow-up.
	**Caval valve implantation**: valve implantation in inferior and superior vein cava.	The *TricValve* device consists of 3 leaflets of bovine pericardium mounted on a self-expandable nitinol frame. The size ranges from 28 to 43 mm.	- Not technically challenging but sizing is an issue - Ventricularization of the right atrium - Optimal relief of symptoms and signs of heart failure in advance patients	4 patients: 1. Technical success in 75% of patients; 2. Clinical improvement at 7-month follow-up.
	**MitraClip**: a v-shaped clip which can grasp contiguous leaflets together [60] *Leaflet plasty device*	A 4-mm-wide cobalt-chromium polyester-covered implant with 2 arms that can grasp 2 leaflets. The delivery system can be advanced through a transjugular or transfemoral access.	- Large interventional experience - Operators are confident with the device - MitraClip does not target the annular dilation - Risk of leaflet detachment, leaflet injury and chordal entanglement	64 patients (compassionate use): 1. Significant reduction in TR grade, EROA, regurgitant volume, septo-lateral diameter; 2. Improvement of clinical outcomes at 9-month follow-up.
	**MIA device:** two Polycor anchors connected by MyoLast elastomer *Annuloplasty system*	The annular reduction is achieved without sutures or other intervention due to the compliant, self-tensioning MIA implant incorporating the PolyCor anchors and MyoLastTM implantable elastomer.	- Replicates the surgical sutures - Encouraging pre clinical data - Reliable and rapid deployment	1. the 2 first-in-man experiences have been successful with proven safety and reduction in annular valve are. 2. In the first 2 patients 9 and 8 MIAs were implanted in a 270-degree ring pattern
	**NAVIGATE valve:** Nitinol tapered stent with a truncated cone configuration and annular winglets for secure anchoring of annulus and tricuspid valve leaflets. *Transcatheter valve prosthesis*	The winglets engage the annulus from both atrial and ventricular sides. The truncated cone enables low height profile	- The valve replacement can virtually minimize the risk of residual regurgitation - The valve replacement can reach a wider patient population with different anatomies and etiologies - Valve replacement can shorter procedural times	1. the first compassionate use was performed with procedural success and no events at short-term follow-up.

Rodés-Cabau et al. JACC 2016; 67:1829-45



Caval valve implantation (CAVI) :

The procedure addresses the regurgitation of blood into the caval veins, a condition found often in patients with severe, long- standing TR and RV enlargement, but does not address TR per se.



TRIC VALVE: (…) Compassionate clinical use has confirmed the technical feasibility of CAVI, as well as the immediate and sustained hemodynamic improvement from the reduction of IVC and SVC backflow

Preliminary studies: 5 patients

EDWARDS SAPIEN: Caval implantations of balloon-expandable valves normally used to treat aortic stenosis (29 mm Edwards Sapien XT or Sapien 3) have also been used off-label for the treating severe TR. (HOVER trial and the TRICAVAL trial)

A total of **10 patients** have been treated to date under a compassionate clinical use program.

Rodés-Cabau et al. JACC 2016; 67:1829-45

Coaptation device

This device acts as a coaptation device, with the objective of reducing the TR grade in patients with significant TR secondary to annular dilation.

The FORMA Repair System: It is composed of a rail, which is anchored at the apex of the RV, and a spacer, which serves as the coaptation element (i.e., increases the coaptation surface in order to improve leaflet malcoaptation). (SPACER study)

Cohort of 18 patients:

1. Implant success in 89% with no operative mortality
2. Less than severe TR grade in 71 % at 6-month follow-up
3. Improvement in NYHA functional class and clinical outcomes at 1 year follow-up

Percutaneous Annuloplasty

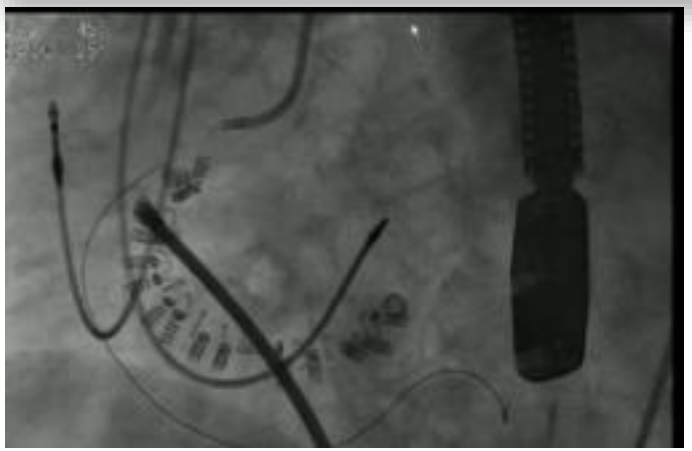
Trialign device: is a percutaneous annuloplasty system that reproduces the Kay surgical procedure, which converts an incompetent TV into a competent bicuspid valve by plication of both the anterior and posterior tricuspid annulus.
(SCOUT TRIAL: 15 patients

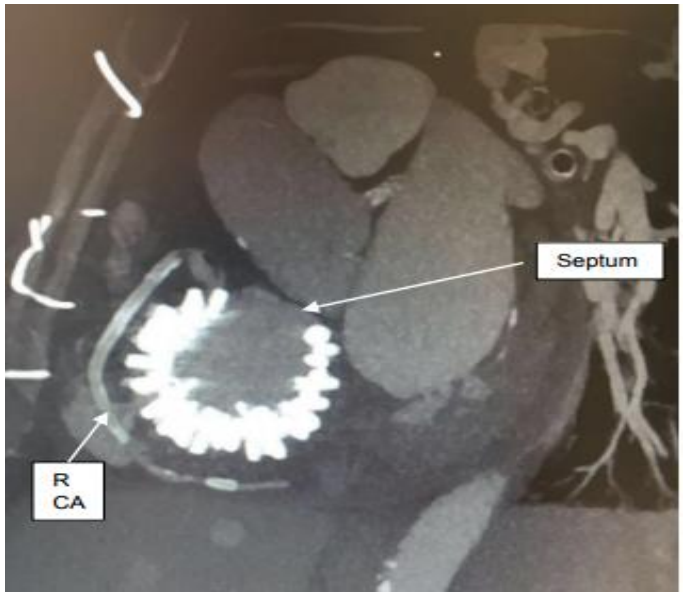
TriCinch system: is a percutaneous annuloplasty device designed for functional TR repair. This device system consists of a corkscrew anchor, a self-expanding stent, and a Dacron band connecting both. The self-expanding nitinol stent is deployed in the IVC.
The device is currently being evaluated in an ongoing feasibility trial, the PREVENT study (24 patients)

Edwards Cardioband Tricuspid Repair System: Dedicated technology to treat tricuspid regurgitation with same concept and implant technique used with Cardioband for mitral valve repair
TRI-REPAIR: single arm, multi-center (Germany, France, Italy) prospective study

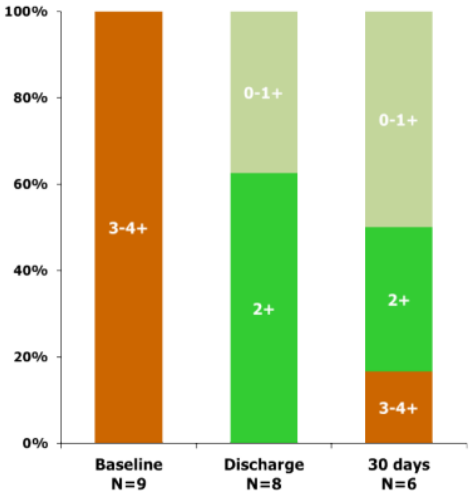
Rodés-Cabau et al. JACC 2016; 67:1829-45

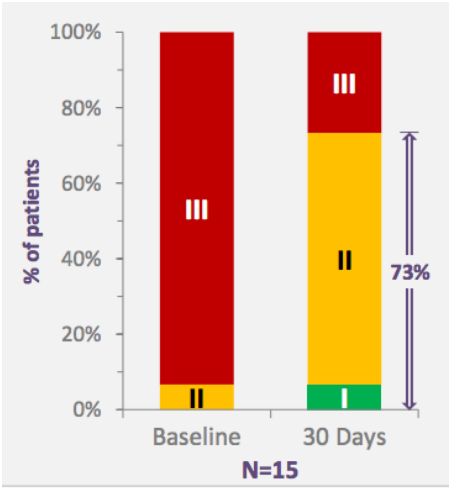
Percutaneous Annuloplasty: The Cardioband



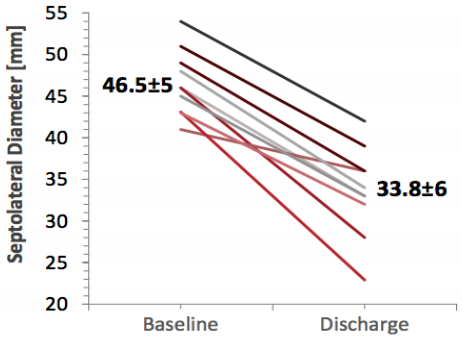


TR severity and NYHA Class from baseline to 1 month follow-up





- N = 10 patients



From Von Bardeleben, JIM 2017 and EuroPCR 2017

Percutaneous Leaflet Repair

The MitraClip System

EHJ 2016

Transcatheter treatment of severe tricuspid regurgitation with the MitraClip system

Christoph Hammerstingl*†, Robert Schueler†, Margarita Malasa, Nikos Werner, and Georg Nickenig

JACC 2016

Transcatheter Repair of Primary Tricuspid Valve Regurgitation Using the MitraClip System

Daniel Braun, MD,[a] Michael Nabauer, MD,[a] Steffen Massberg, MD,[a,b] Jörg Hausleiter, MD[a]

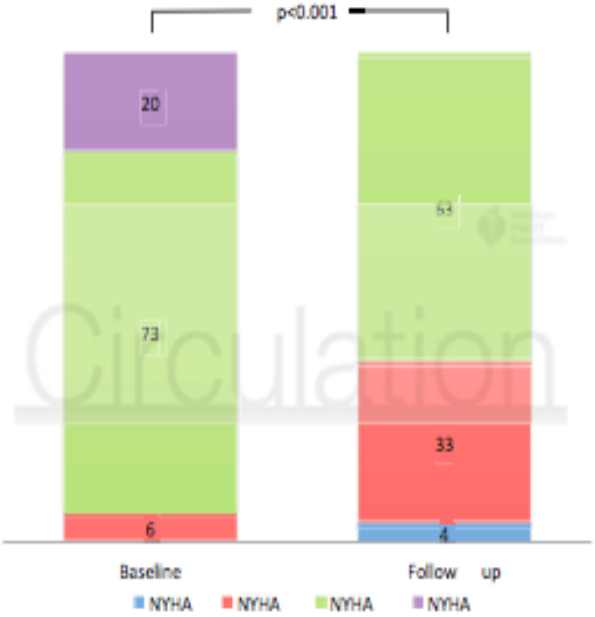
TRILUMINATE trial will study efficacy and safety of a new transcatheter clip-based repair system for tricuspid valve disease

Transcatheter repair of tricuspid regurgitation: MitraClip System

64 patients with severe TR were recruited from 10 international centers.

The procedures were performed both with transjugular approach

	N	All patients (n=64)
Length of stay, days	59/64	12.6 ± 14 (1 – 92)
Procedure duration, min	46/64	143.4 ± 91.6 (20 – 390)
Concomitant mitral clip, n (%)	64/64	22 (34)
In-hospital mortality, n (%)	62/64	3 (5)
Myocardial infarction, n (%)	62/64	0 (0)
Cardiac Tamponade, n (%)	62/64	0 (0)
Acute renal failure, n (%)	62/64	2 (3)
New dialysis, n (%)	62/64	0 (0)
Emergent procedure related surgery/ intervention, n (%)	62/64	0 (0)
Bleeding requiring transfusion, n (%)	62/64	3 (5)
Device migration, n (%)	62/64	0 (0)
Vascular complication requiring surgery, n (%)	62/64	0 (0)
New arrhythmias, n (%)	62/64	3 (5)
Stroke/TIA, n (%)	62/64	0 (0)
Device successfully deployed, n (%)	64/64	62 (97)
Inability to reduce TR, n (%)	62/64	6 (9)



Nickenig, et al. (2017), Circulation

Representative Case

Female, 64 years old

Co-morbidities

- Hypertension; Obesity (**body mass index 37 kg/m^2**); Chronic kidney disease with Glomerular Filtration Rate of 48 ml/min/1.73 m^2.
- Logistic EuroSCORE I: **5.35%** ;
- Logistic EuroSCORE II: **1.23%**

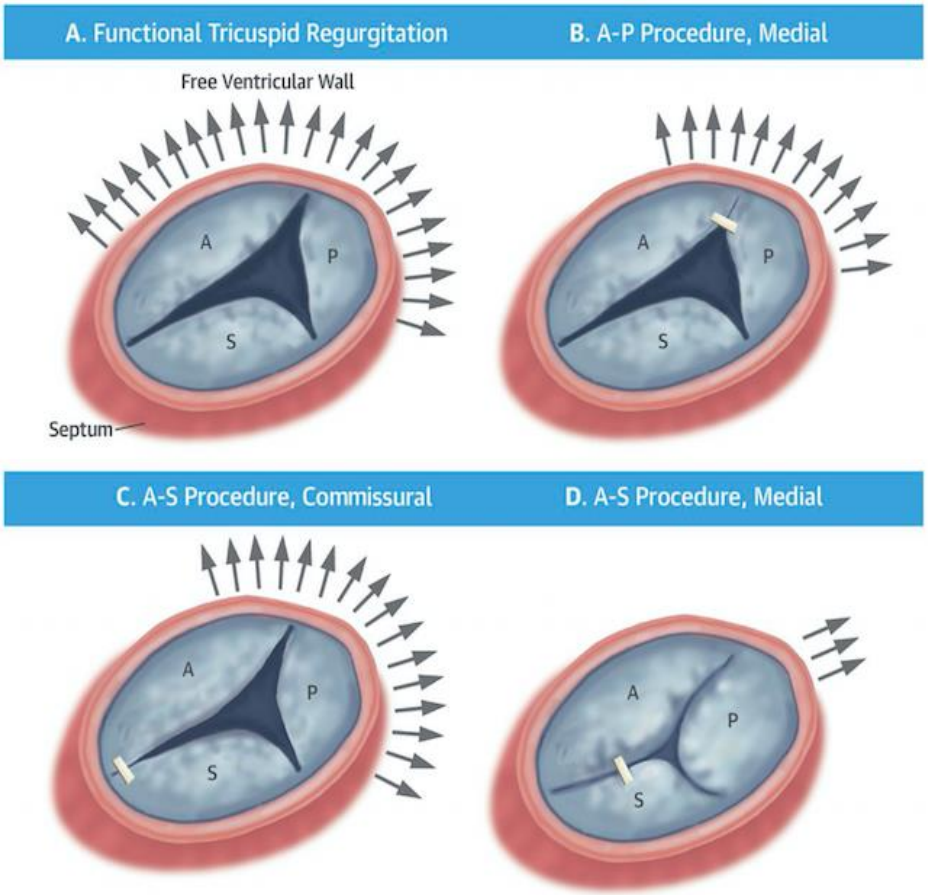
Clinical presentation (March 2017)

- Symptomatic dyspnea (**NYHA IV**) and fatigue requiring hospitalization.
- April 2017 admission at our Institute

- **FE**: 55%
- **LVEDD/LVESD: 55/34 mm**
- **LVEDV/LVESV: 120/60 ml**
- **RAA: 23 cm^2**
- **RV: 40 mm**
- **TAPSE: 30 mm**
- **MR moderate**
- **TR severe**
- **sPAP: 73 mmHg**

Interventional Strategy

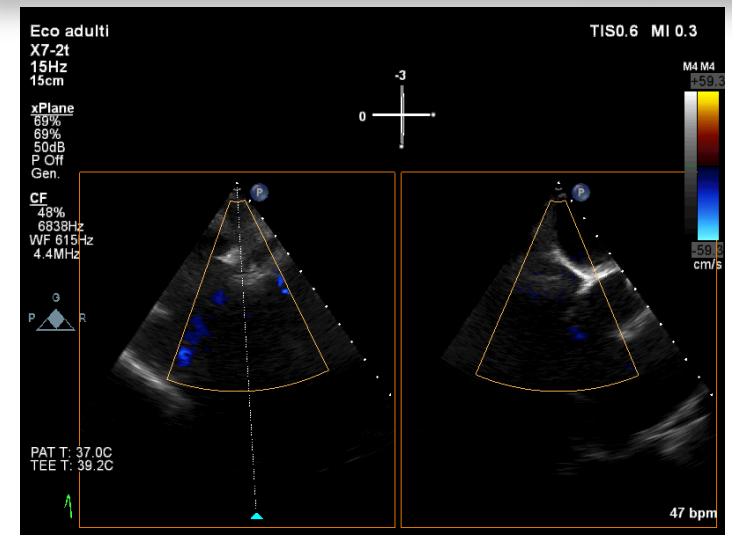
Vismara et al. JACC, 2016; 68:1024-1033
Transcatheter Edge-to-Edge Treatment of Functional Tricuspid Regurgitation in an Ex Vivo Pulsatile Heart Model

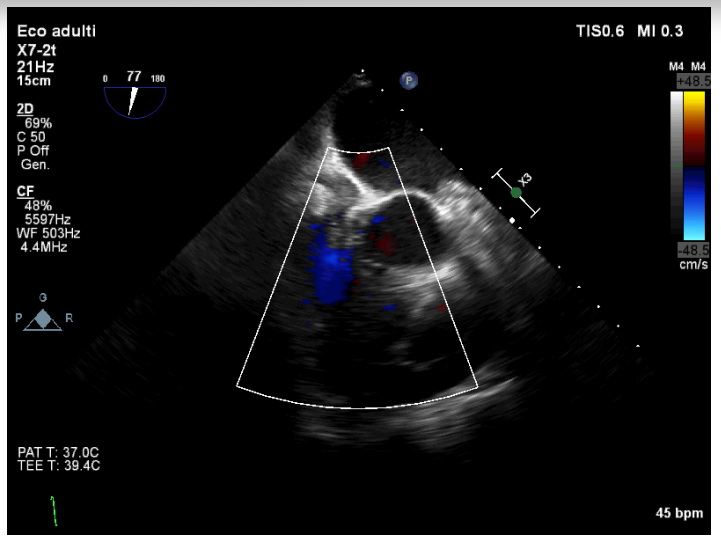


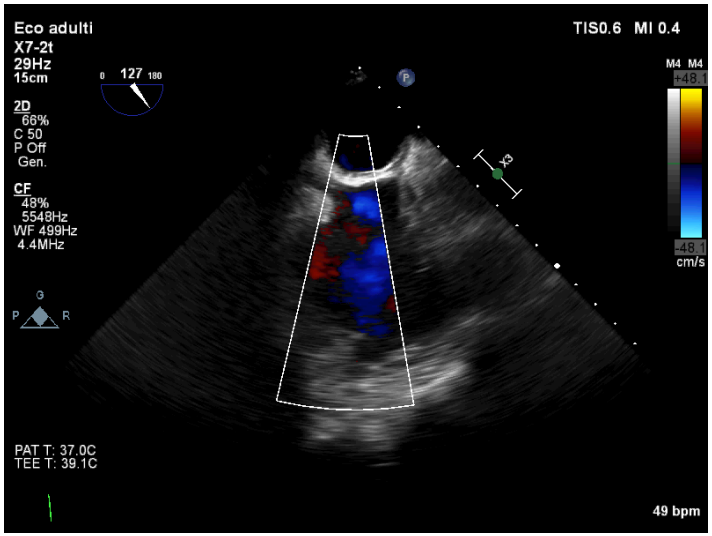
- **Single-clip treatment**: grasping leaflet pairs in the medial or commissural position (6 combinations).
- **Two-clip treatments:** 15 combinations of leaflet pairs and medial/commissural grasping.

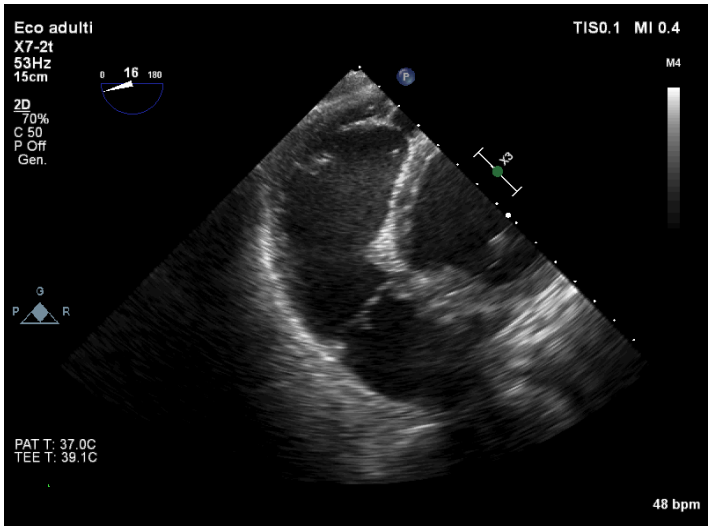
Grasping the **septal** and **anterior** leaflets allowed for the best post-procedural outcome, ensuring a complete re-establishment of physiological-like hemodynamics. **Septal** and **posterior** grasping induced a significant recovery from FTR, although less marked. Conversely, grasping the anterior and posterior leaflets did not reduce FTR, and was detrimental in some specific cases.

Baseline TEE Assessment

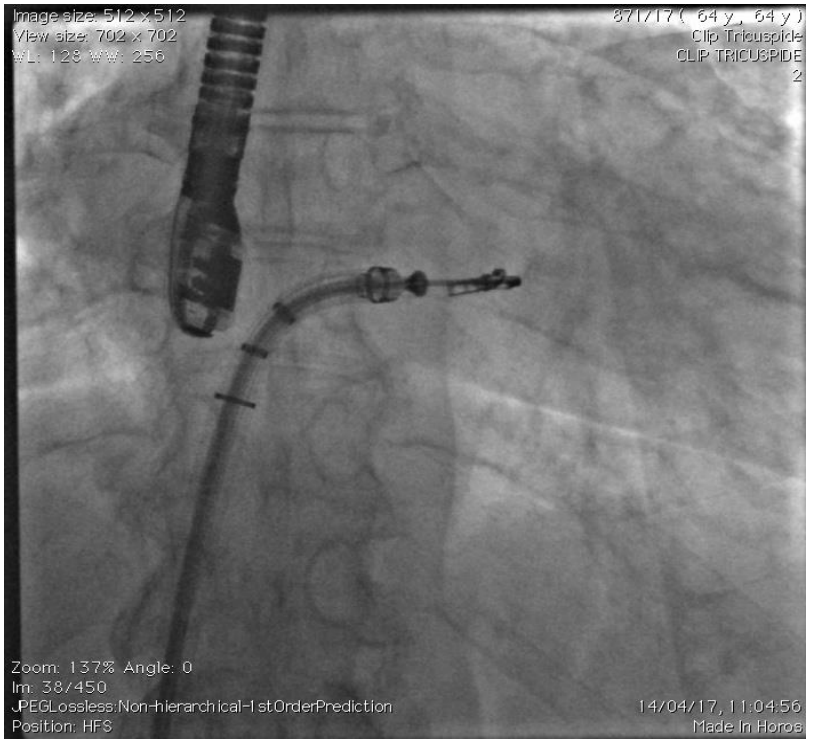




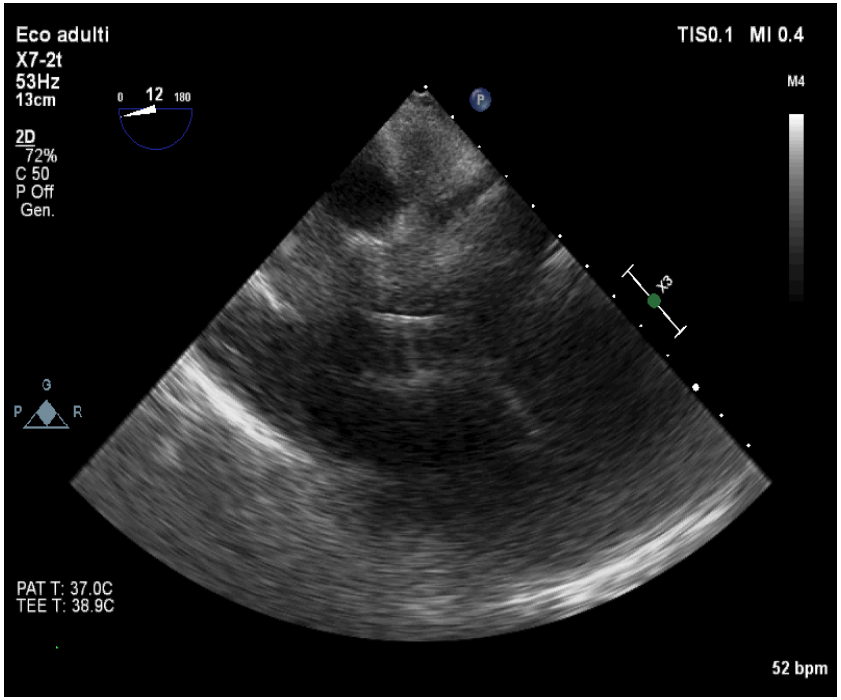


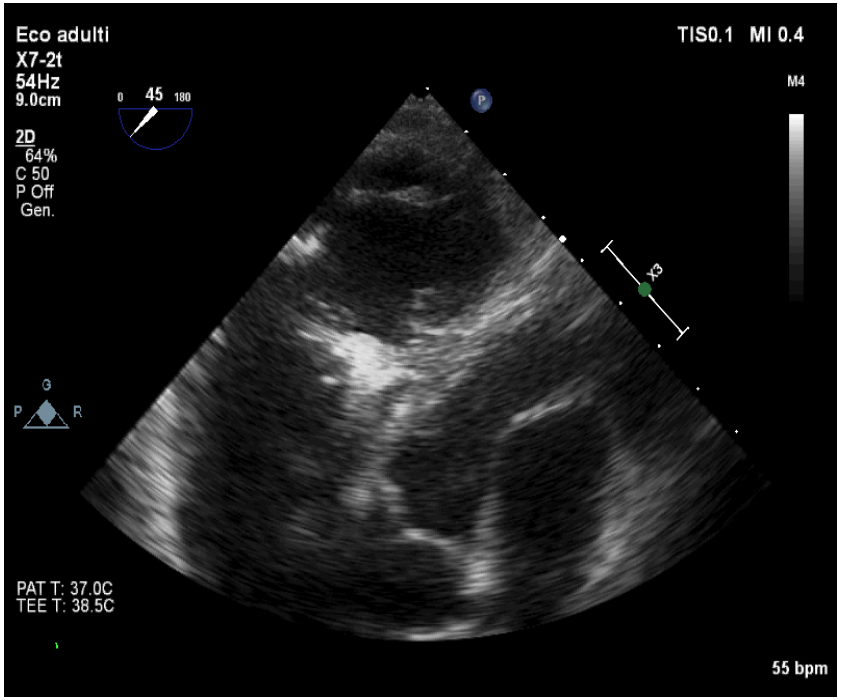


NT- MitraClip™ - first grasping

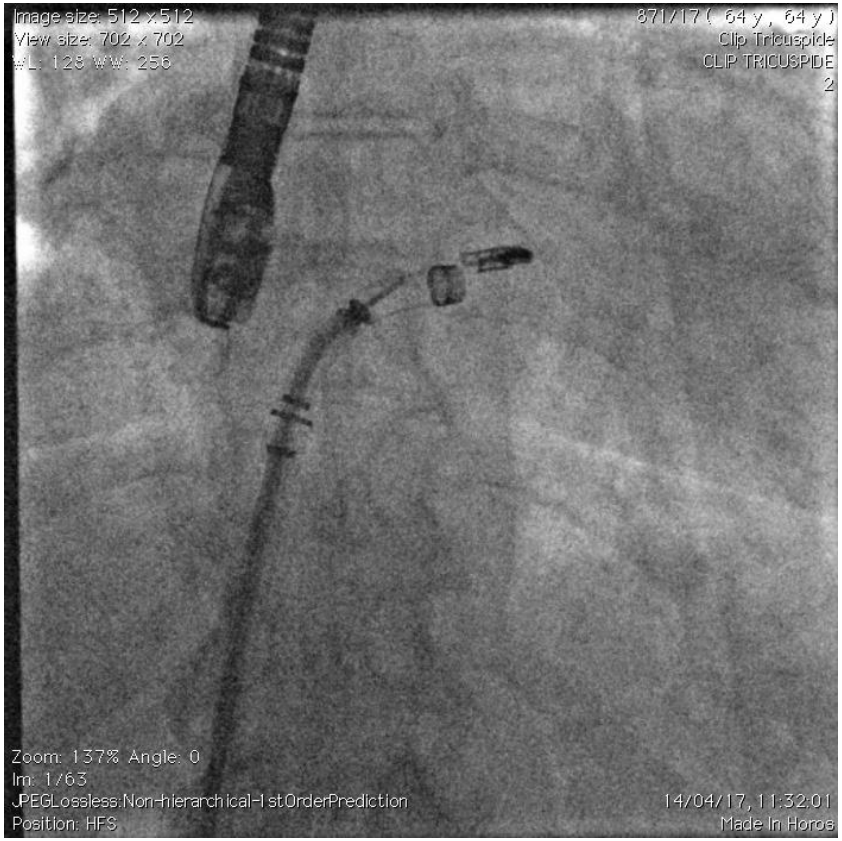


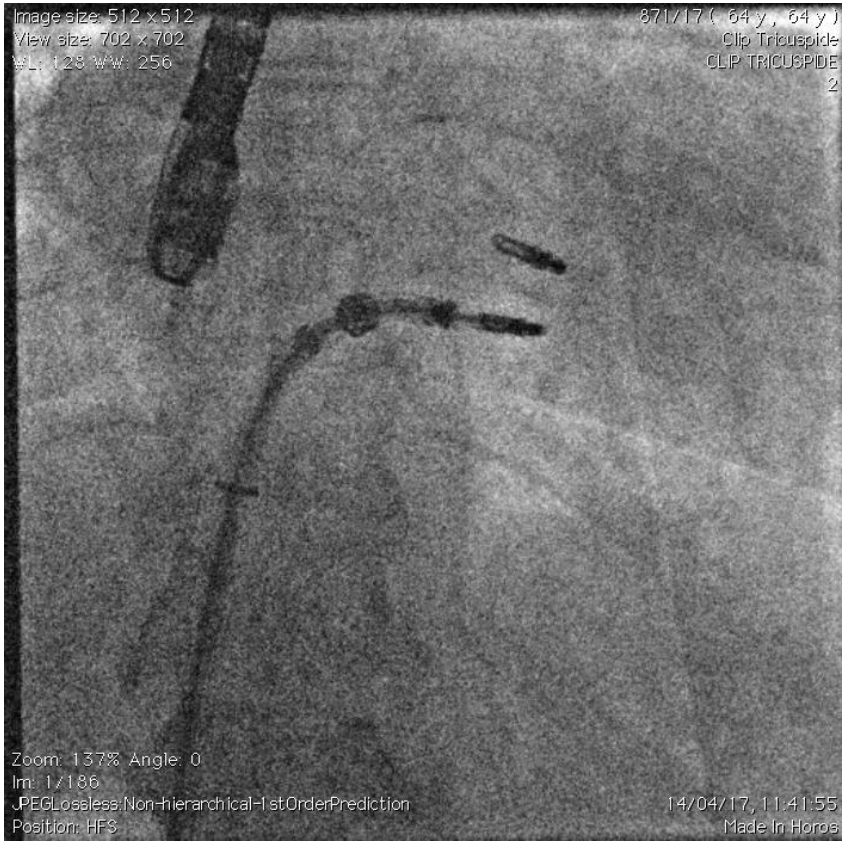
Intraprocedural TEE Assessment
First grasping



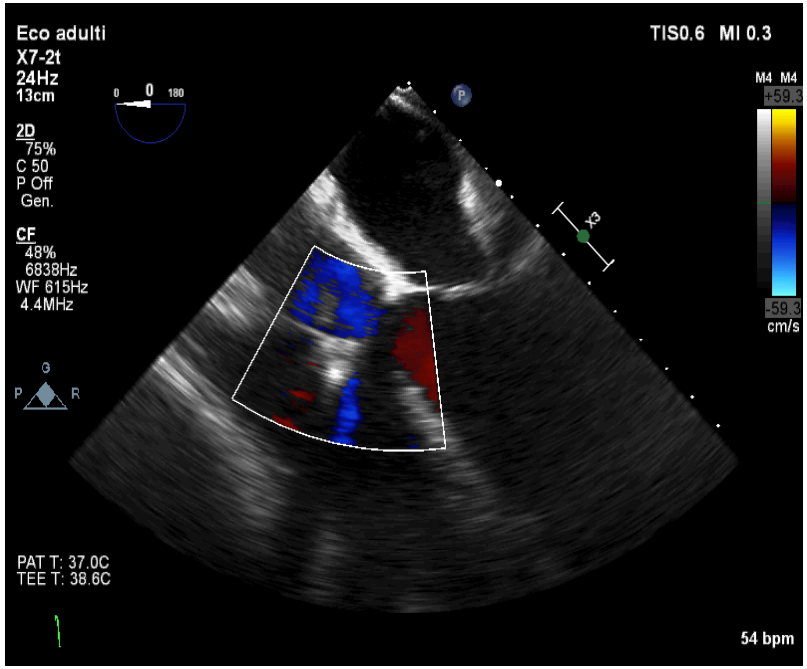


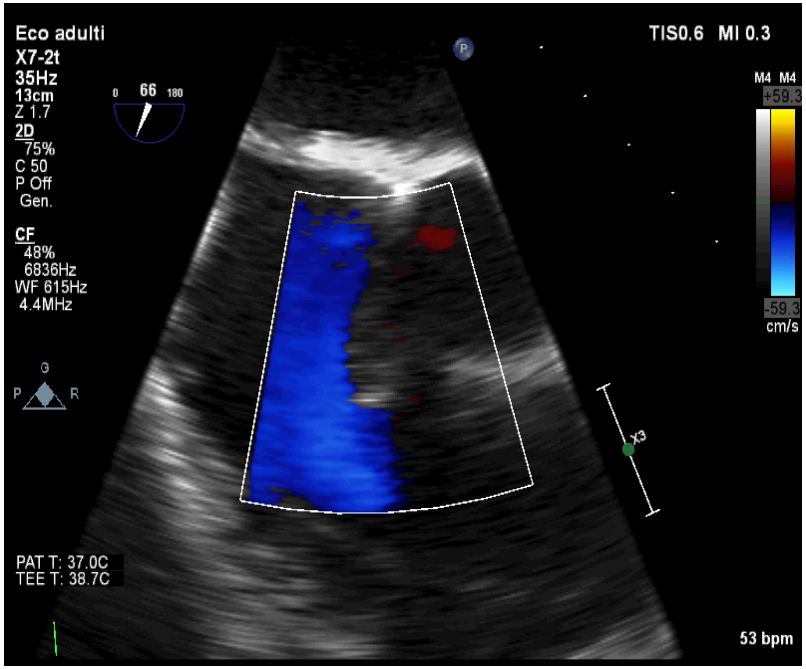
NT- MitraClip™
first clip release and second grasping





Intraprocedural TEE Assessment
Second grasping





Final result with 2 clips on the antero-septal leaflets with moderate residual TR.
Gmed 1.5 mmHg. sPAP 45 mmHg

Post-Procedure course

- ❑ Transferred to Coronary Intensive Care Unit
- ❑ Discharged after 5 days

- ❑ Echocardiogram at discharge
- ❑ Mean tricuspid gradient 2 mmHg
- ❑ Moderate residual tricuspid regurgitation
- ❑ sPAP 35 mmHg

Heart Team players

Follow-up

The AV valves patient

The echocardiographist

The HF specialist

Conclusions

- Tricuspid regurgitation is a very common condition in patients with heart failure, left heart valve and/or myocardial disease, with significant impact on survival and quality of life.

- Current guidelines recommend surgical treatment for isolated symptomatic TR or for mild TR associated to severe left heart valve disease.

- The implementation of less invasive therapies has a significant role for all the high risk patients who are denied surgery.

- Different devices are now available for the transcatheter treatment of TR, although these treatments are still in the early stages.

- Further single-center, multi-center and trial investigations will shade light on this field.