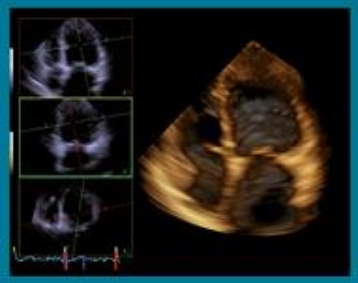


EuroValve

October 24-25, 2014

Université de Liège

Controversies in tricuspid regurgitation: risk marker?

CHU de Liège

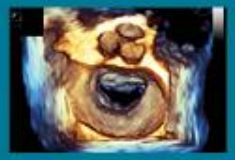
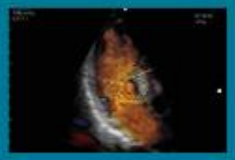
Prof. Patrizio LANCELLOTTI, MD, PhD, FESC

Heart Valve Clinic, Department of Cardiology,

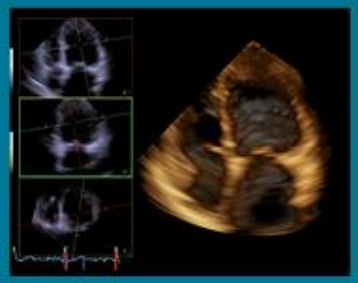
University of Liège, Belgium

GIGA



www.eurovalvecongress.com



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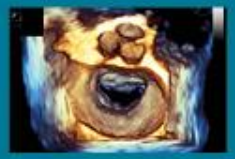
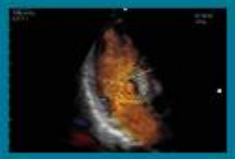
Faculty disclosure

Patrizio Lancellotti

I have **no financial relationships** to disclose



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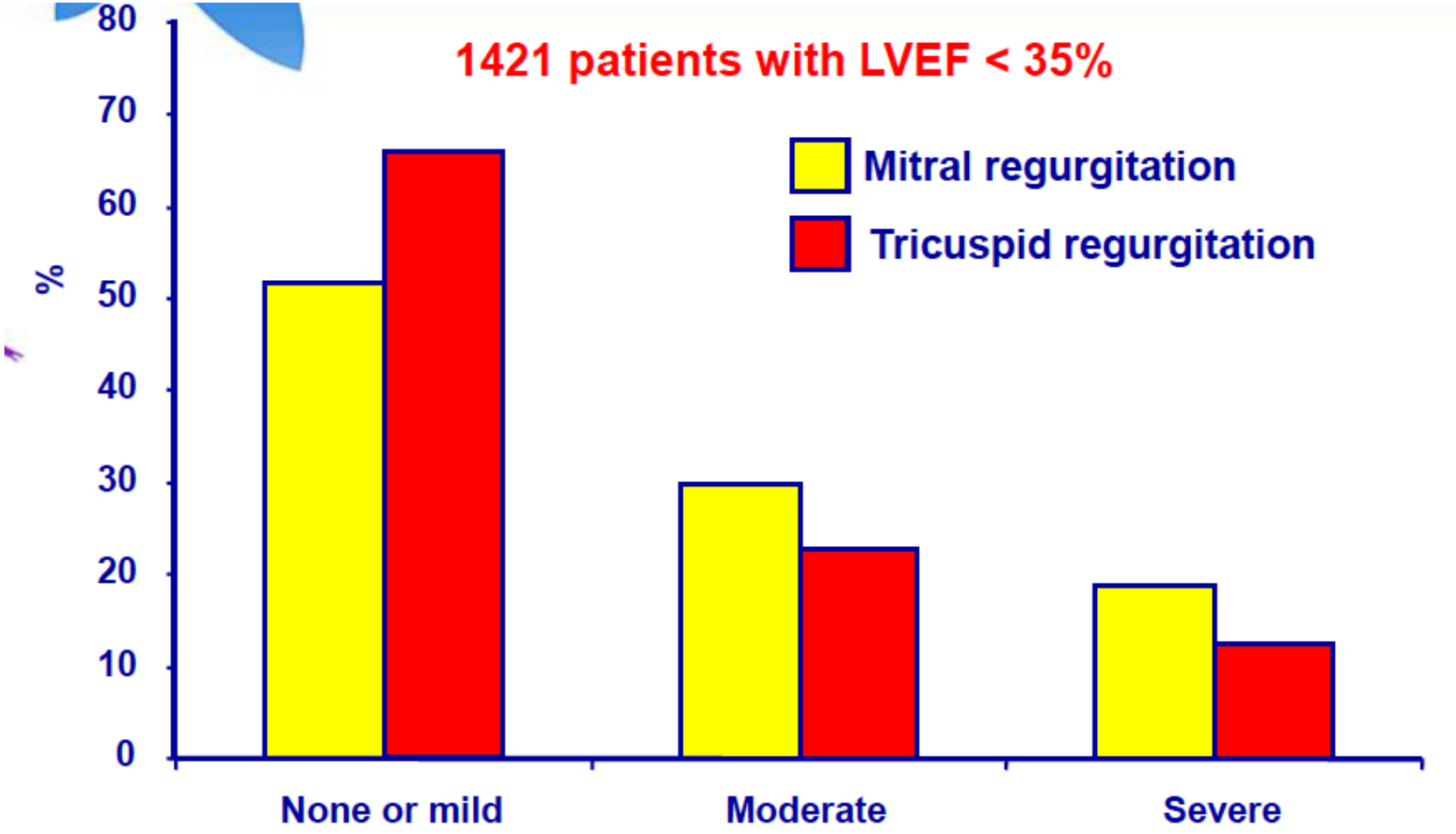
Prevalence of TR in patients with LV dysfunction

TR is a common finding in HF



Koelling Am Heart Journal 2002; 144: 524-9

Tricuspid Regurgitation

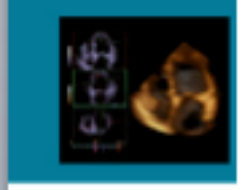
Primary TR

- intrinsec abnormalities of the valve
- rare, 8-10% with severe TR

Secondary TR

- morphologically normal valve
- disease of the right ventricle and right atrium
- the most frequent form of TR requiring surgical intervention

Lancellotti et al. Eur Heart J – Cardiovasc Imag 2013



Left-sided HVD/Cardiomyopathy

Tricuspid annular dilation/Leaflet tethering

RV dilation

Pulmonary Hypertension

Advanced RV dilation

↓

RV failure

↓

↗ RV diastolic pressure

↓

RV septum displacement toward LV

Secondary TR

↗ Risk of atrial fibrillation

↓

↗ Symptoms

↗ LA/RA pressure

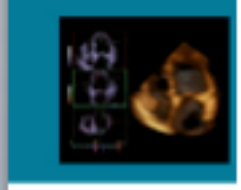
↑

Restricted LV filling

↑

↘ LV cavity size

Lancellotti et al. Eur Heart J 2013



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↓

↗ Symptoms

↗ LA/RA pressure

↑

Restricted LV filling

↑

↘ LV cavity size

Lancellotti et al. Eur Heart J 2013

What is the natural history of secondary TR?

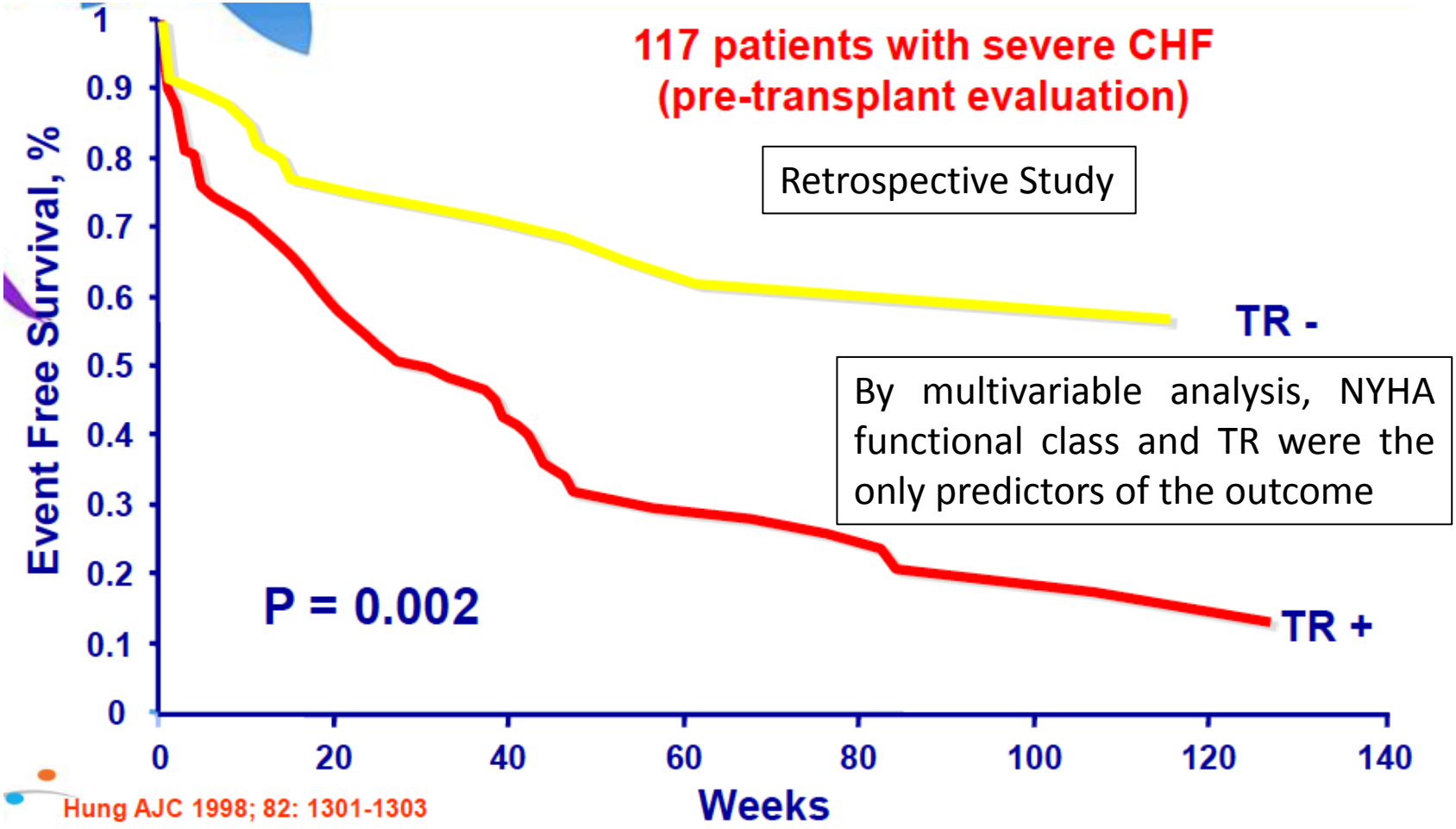
Symptoms are often those of the associated diseases

TR may be well tolerated for many years

TR may lead to irreversible RV dysfunction, HF, and death

Secondary TR and Survival in CHF

TR negatively affects the outcome



Secondary TR and Survival in CHF

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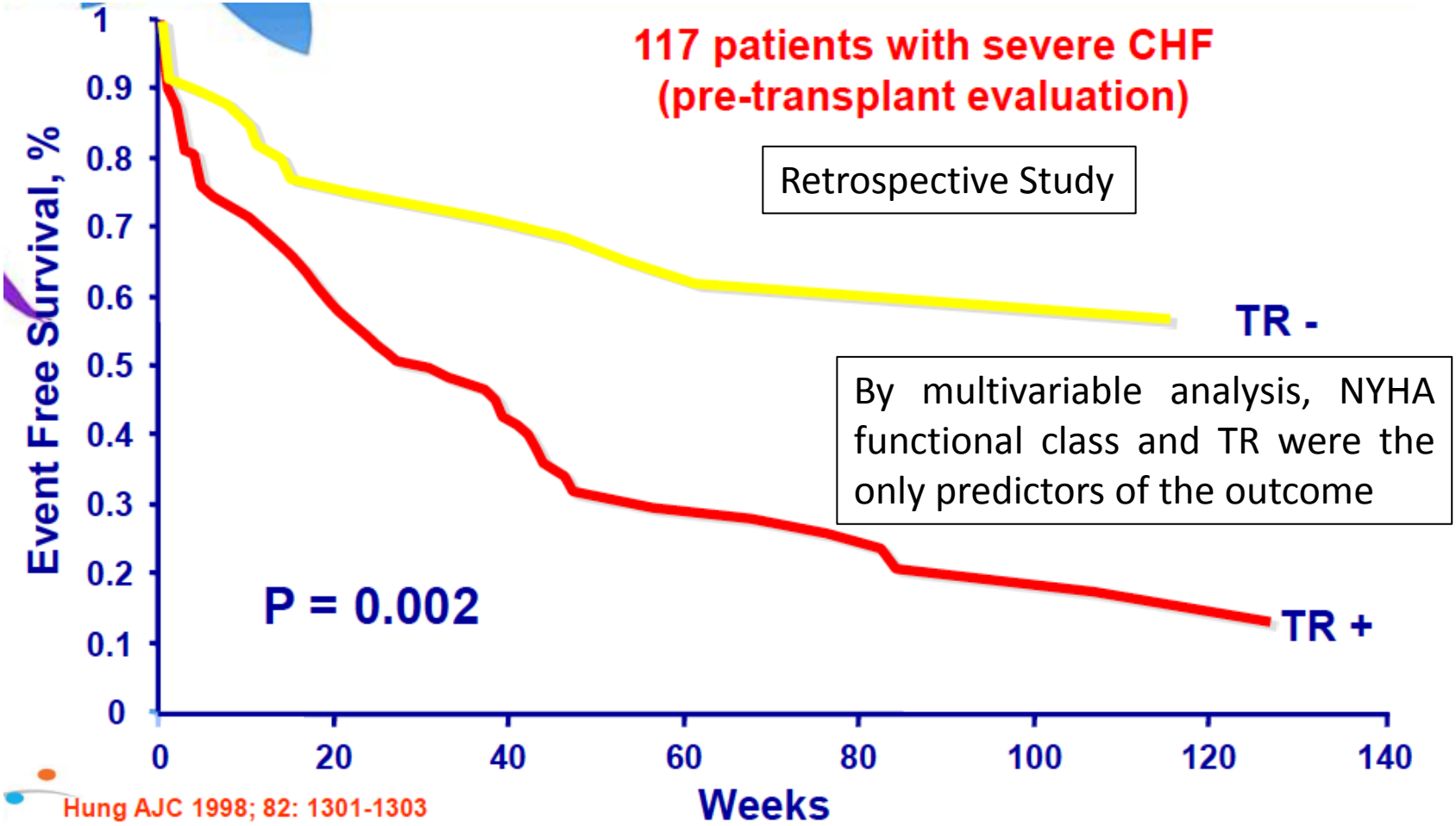
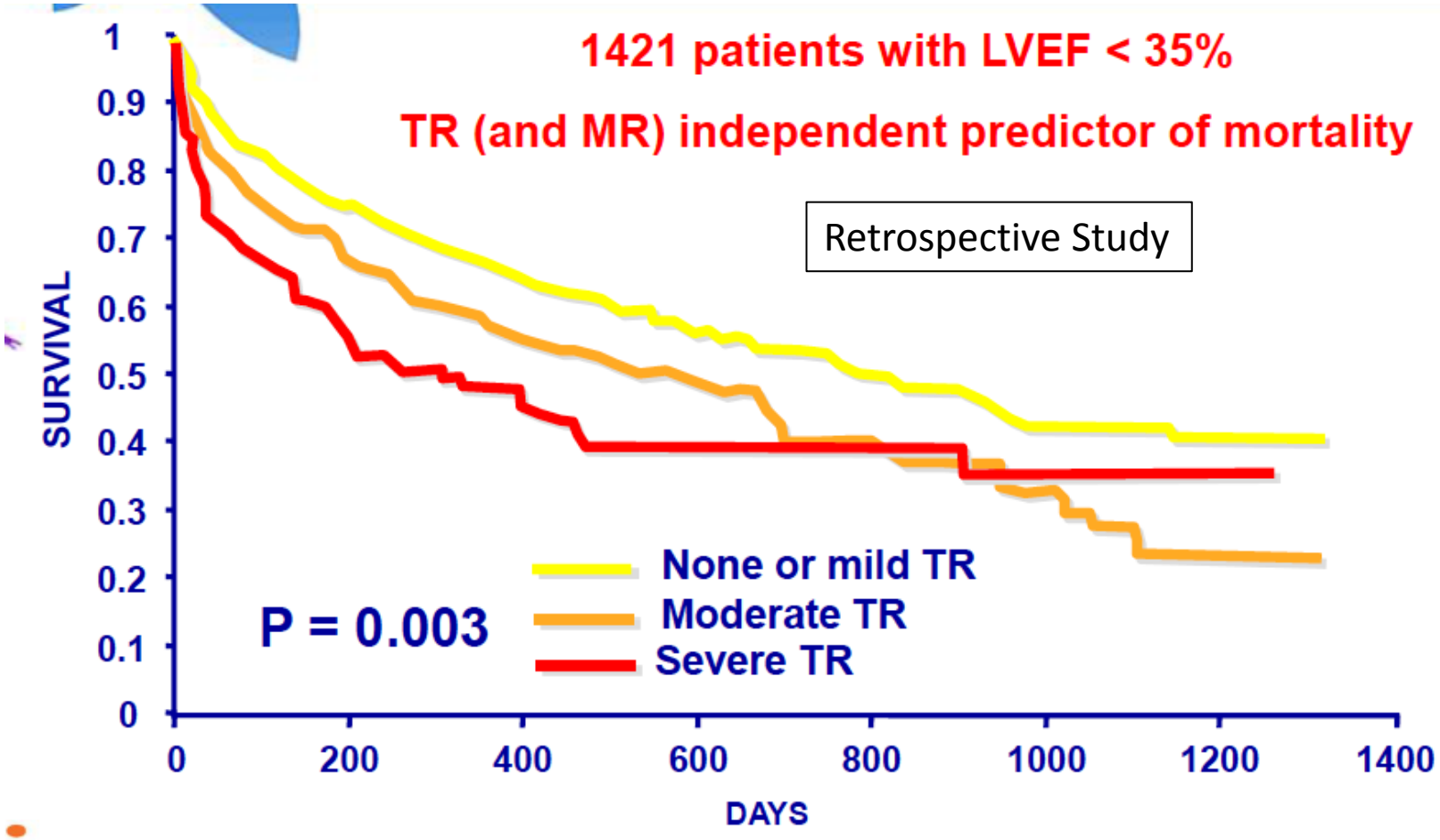


64% of patients had TR and those with TR had significantly larger LV and higher prevalence of concomitant MR

TR grade and Survival in CHF

Moderate to Severe TR negatively affects the outcome

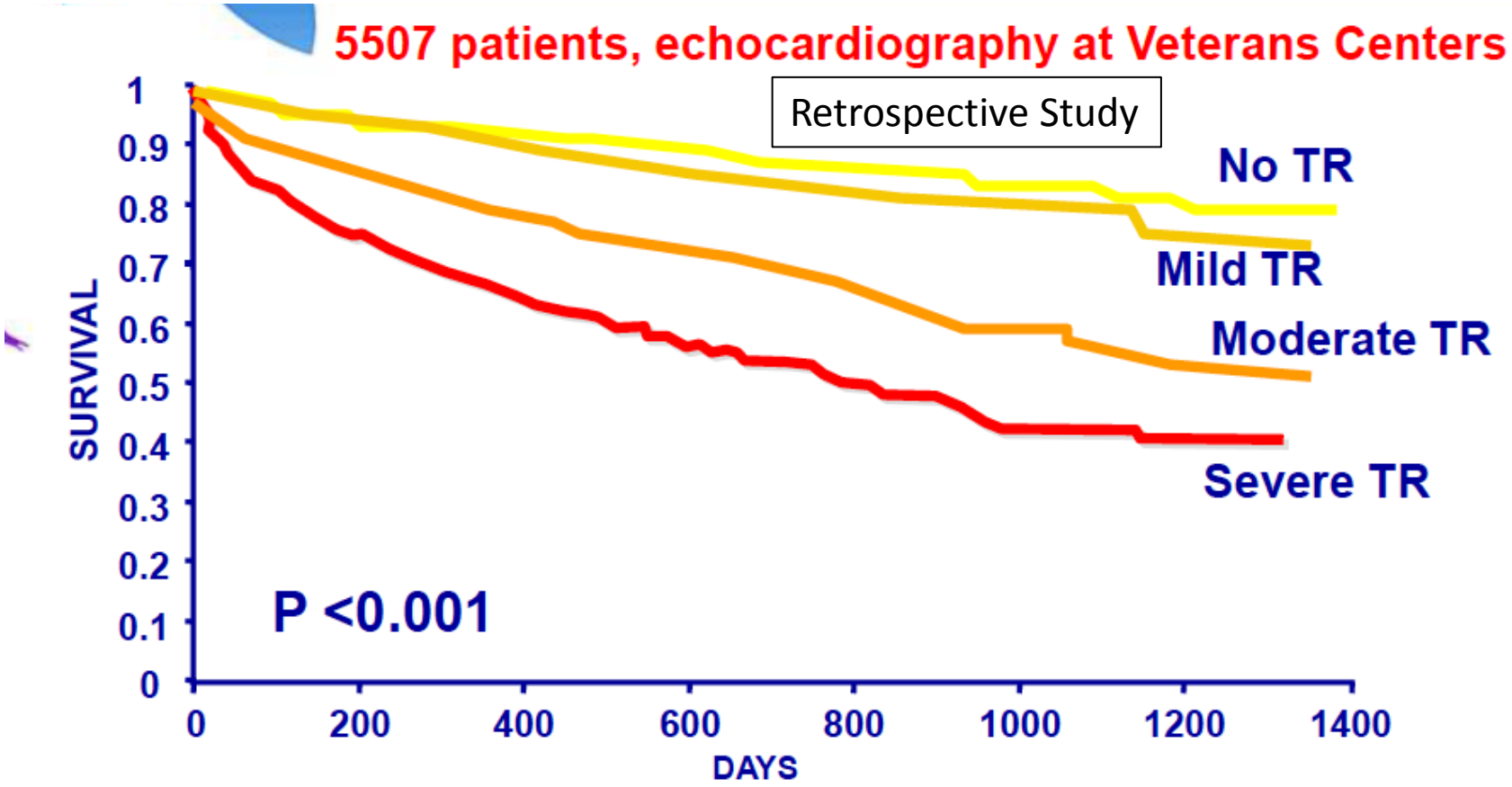


Koelling Am Heart Journal 2002; 144: 524-9

Multivariable predictors of poor outcome included increasing MR and TR grade, [but also cancer, coronary artery disease, LVEF, and heart rate]

TR grade and Survival

> Moderate TR plays a negative impact, irrespective of LVEF and sPAP



After adjustment for age, LVEF, IVC size, RV size and RV function, S-PAP

Nath JACC 2004; 43: 405-9

To summarize ……

data from retrospective studies

Systolic heart failure:

- the simple presence of TR has a negative impact on outcome
- the more severe the TR the lower the event free survival rate

Irrespective of LVEF:

- > moderate TR negatively influences outcome

To summarize ……

data from retrospective studies

Systolic heart failure:

- the simple presence of TR has a negative impact on outcome
- the m… the event fr…

But lacks of information on symptoms, biomarkers, and kidney function

Irrespective of LVEF:

- > moderate TR negatively influences outcome

Secondary TR and Survival in CHF

Data from prospective observational study

576 Pts with CHF, single center study, no AS, no MS

Tertiary care HF clinic

NT-proBNP

Echo
Biology (Creat, …)

Follow-up 69+50 months

CE: death, heart transplantation, or implantation of an LV assist device

Neuhold et al. Eur Heart J 2013

Secondary TR and Survival in CHF

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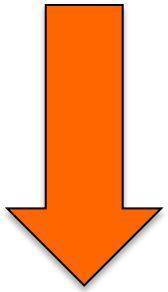


Follow-up 69+50 months

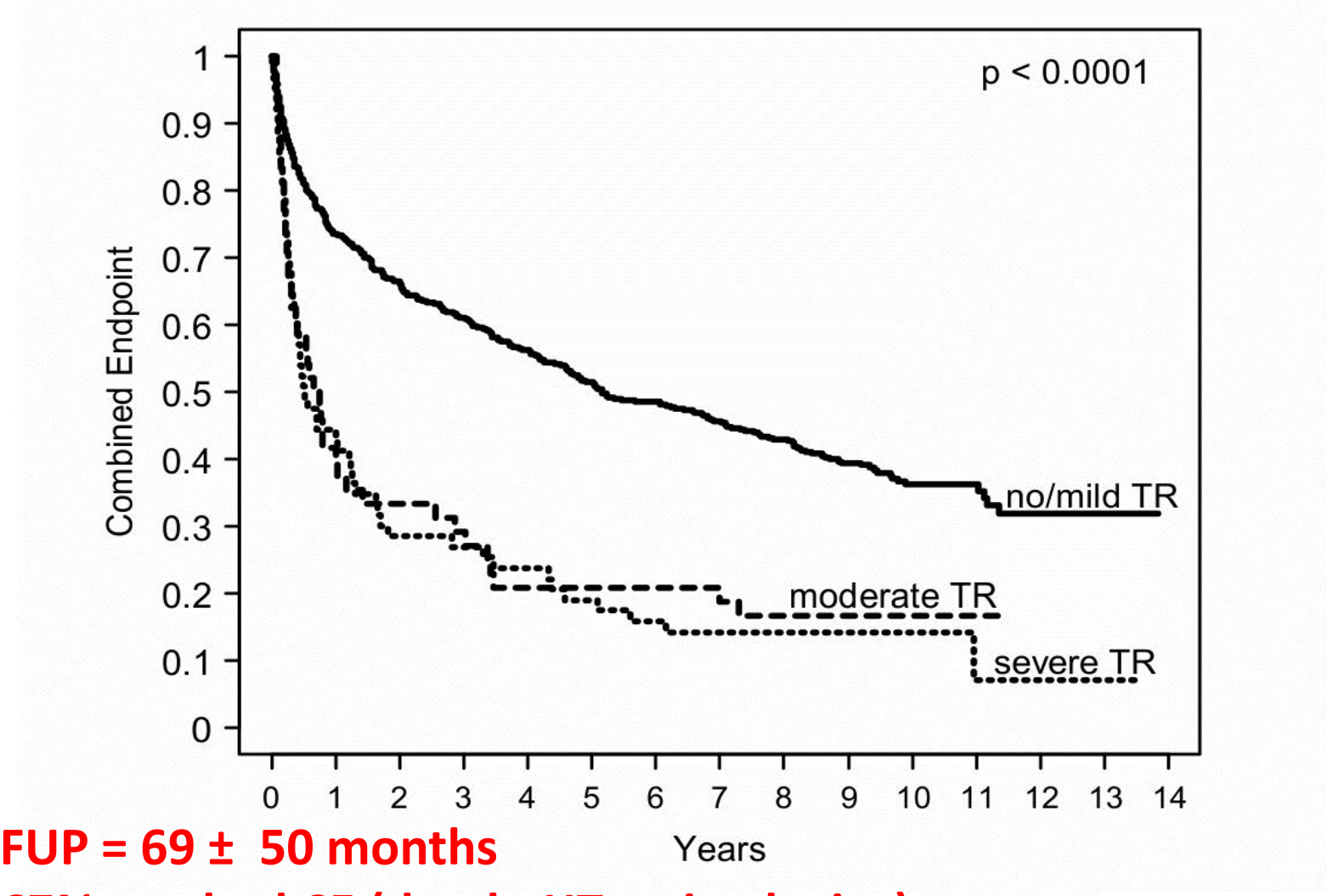
CE: death, heart transplantation, or implantation of an LV assist device

TR No/Mild
Moderate/Severe

Neuhold et al. Eur Heart J 2013

Secondary TR and Survival in CHF

Kaplan-Meier curves for overall survival



FUP = 69 ± 50 months

67% reached CE (death, HT,assist device)

Neuhold. Eur Heart J 2013

Secondary TR and Survival in CHF

Characteristics of patients

Table 1 Baseline characteristics according to tricuspid regurgitation severity

Variable	All patients, $n = 576$	No/mild TR, $n = 465$ (81%)	Moderate/severe TR, $n = 111$ (19%)	*P*-value
Demographic data				
Male (%)	83	82	84	0.723
Age (years)	56.4 ± 11.2	56.3 ± 10.9	56.9 ± 12.4	0.630
BMI (kg/m^2 BSA)	26.6 ± 4.1	26.9 ± 4.2	25.7 ± 3.3	0.002
Clinical data				
Systolic blood pressure (mmHg)	116.2 ± 22.3	118.8 ± 22.2	105.6 ± 19.4	<0.001
Heart rate (b.p.m.)	74.5 ± 16.0	73.9 ± 15.8	77.1 ± 16.9	0.061
Atrial fibrillation (%)	21	19	30	0.009
Coronary artery disease (%)	39	42	27	0.004
Hypertension (%)	49	53	32	<0.001
Diabetes mellitus (%)	23	24	16	0.075
Hyperlipidaemia (%)	41	44	26	0.001
NYHA functional class (%)				<0.001
NYHA I (%)	12	13	6	
NYHA II (%)	26	29	13	
NYHA III (%)	41	42	39	
NYHA IV (%)	21	16	42	
Leg oedema (%)	16	12	31	<0.001
GFR (mg/dL)	77 ± 30	79 ± 30	70 ± 28	0.005
Creatinine (mg/dL)	1.3 ± 0.8	1.3 ± 0.9	1.4 ± 06	0.001[a]
Blood urea nitrogen (mg/dL)	26 ± 15	24 ± 15	31 ± 17	<0.001
Sodium (mmol/L)	139 ± 4	139 ± 4	137 ± 5	<0.001
Potassium (mmol/L)	4.4 ± 0.5	4.4 ± 0.5	4.2 ± 0.6	0.016
NT-proBNP (fmol/mL)	488 ± 645	400 ± 546	858 ± 863	0.004[a]

Neuhold. Eur Heart J 2013

Secondary TR and Survival in CHF

Characteristics of patients

Table 3 Echocardiographic findings according to tricuspid regurgitation severity

Variable	All patients, *n* = 576	No/mild TR, *n* = 465 (81%)	Moderate/severe TR, *n* = 111 (19%)	*P*-value
LVEDD (mm)	64 ± 10	64 ± 11	66 ± 9	0.009
RVEDD (mm)	37 ± 8	35 ± 7	43 ± 7	<0.001
LA (mm)	64 ± 10	63 ± 9	71 ± 8	<0.001
RA (mm)	59 ± 11	58 ± 10	67 ± 11	<0.001
sPAP (mmHg)	47 ± 12	45 ± 12	52 ± 13	<0.001
TAPSE (mm)	19 ± 4	18 ± 4	19 ± 4	0.378
LVEF (%)				<0.001
LVEF >50% (%)	17	19	3	
LVEF 35–50% (%)	27	30	17	
LVEF <35% (%)	56	51	80	
MR (%)				<0.001
No/mild MR (%)	67	75	28	
Moderate MR (%)	23	20	40	
Severe MR (%)	10	5	32	

Neuhold. Eur Heart J 2013

Secondary TR and Survival in CHF

Characteristics according to outcome

Table 2 Baseline characteristics according to outcome

Variable	All patients, *n* = 576	Endpoint, *n* = 386 (67%)	No Endpoint, *n* = 190 (33%)	*P*-value
Demographic data				
Male (%)	83	85	78	0.079
Age (years)	56.4 ± 11.2	57.7 ± 10.8	53.9 ± 11.6	<0.001
BMI ((kg/m^2 BSA)	26.6 ± 4.1	26.5 ± 3.9	26.9 ± 4.5	0.213
Clinical data				
Systolic blood pressure (mmHg)	116.2 ± 22.3	111.2 ± 20.7	124.9 ± 23.0	<0.001
Heart rate (b.p.m.)	74.5 ± 16.0	75.4 ± 15.9	72.7 ± 16.2	0.061
Atrial fibrillation (%)	21	24	13	0.002
Coronary artery disease (%)	39	41	35	0.204
Hypertension (%)	49	48	52	0.376
Diabetes mellitus (%)	23	23	22	0.751
Hyperlipidaemia (%)	41	37	47	0.024
NYHA functional class (%)				<0.001
NYHA I (%)	12	7	20	
NYHA II (%)	26	22	37	
NYHA III (%)	41	42	38	
NYHA IV (%)	21	29	5	
Leg oedema (%)	16	21	6	<0.001
GFR (mg/dL)	77 ± 30	72 ± 28	87 ± 30	<0.001
Creatinine (mg/dL)	1.3 ± 0.8	1.4 ± 0.9	1.2 ± 0.4	<0.001[a]
Blood urea nitrogen (mg/dL)	26 ± 15	28 ± 17	21 ± 9	<0.001
Sodium (mmol/L)	139 ± 4	138 ± 4	140 ± 3	<0.001
Potassium (mmol/L)	4.4 ± 0.5	4.4 ± 0.5	4.4 ± 0.5	0.332
NT-proBNP (fmol/mL)	488 ± 645	615 ± 709	231 ± 378	<0.001[a]

Neuhold. Eur Heart J 2013

Secondary TR and Survival in CHF

Multivariable analysis

Variable	p-value
NT-proBNP	0.0028
LVF	0.0014
Serum-Sodium	<0.0001
NYHA-class	<0.0001
Systolic BP	<0.0001
Right Atrial Size	0.0001
TR	**0.8518**

Neuhold. Eur Heart J 2013

Secondary TR and Survival in CHF

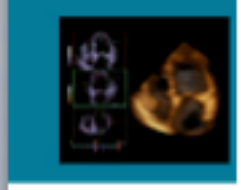
The impact on outcome depends on LVEF

Multivariable Cox Regression, stratified for LVEF

- TR was related to outcome only in patients with LVF EF >35% (p=0.01)
- In patients with severely reduced LVEF <35%:

  TR was not related to outcome (p=0.14)

Neuhold. Eur Heart J 2013



Secondary TR and Survival in CHF

Other factors play a role

In case of severe **LV dysfunction/HF**

Other findings are more reliable to predict the outcome than the TR severity

Secondary TR and Survival in CHF

Other factors play a role

Table 3 Echocardiographic findings according to tricuspid regurgitation severity

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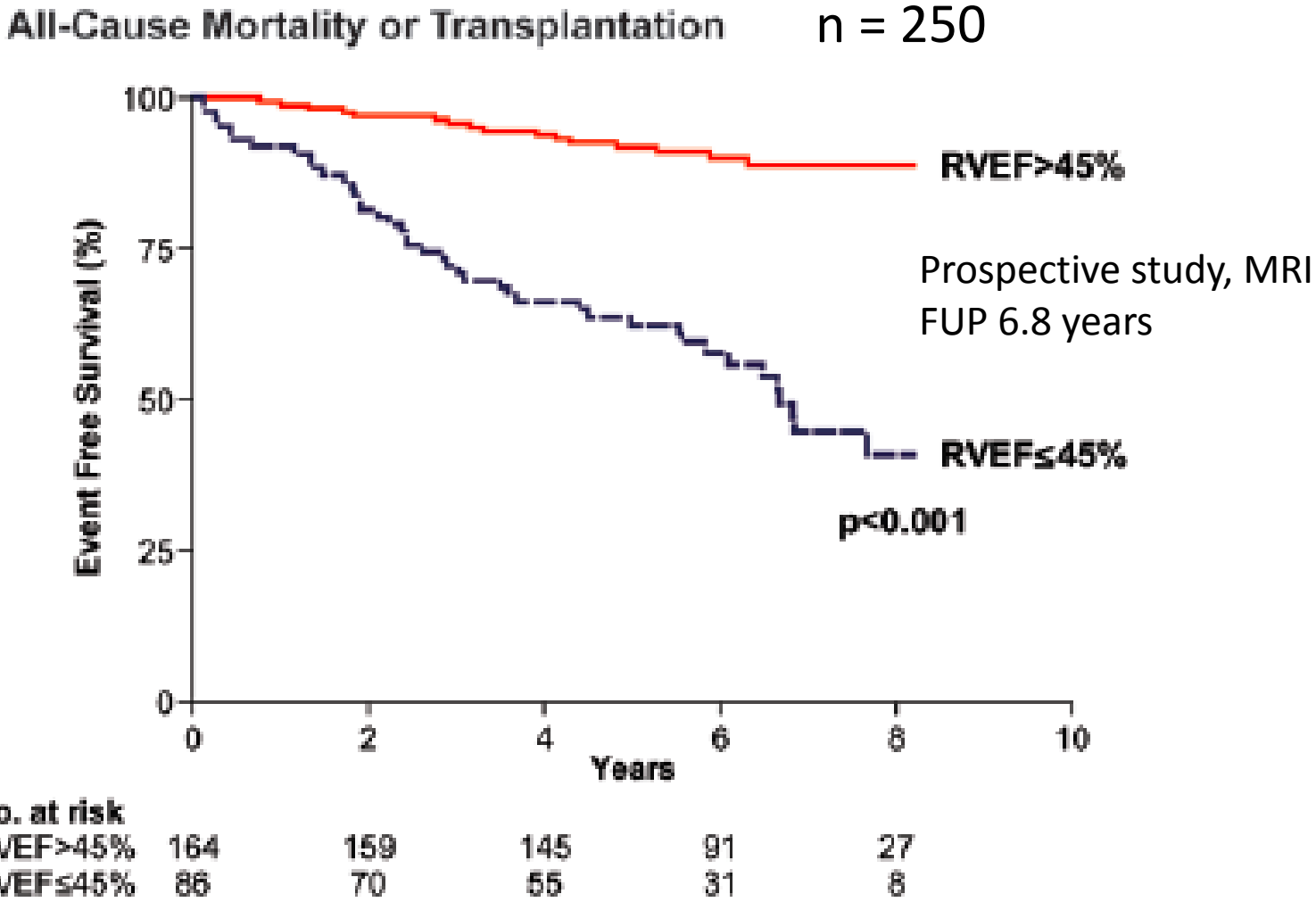
Neuhold. Eur Heart J 2013

Secondary TR and Survival in CHF

RV Dysfunction impaired the outcome in DCM

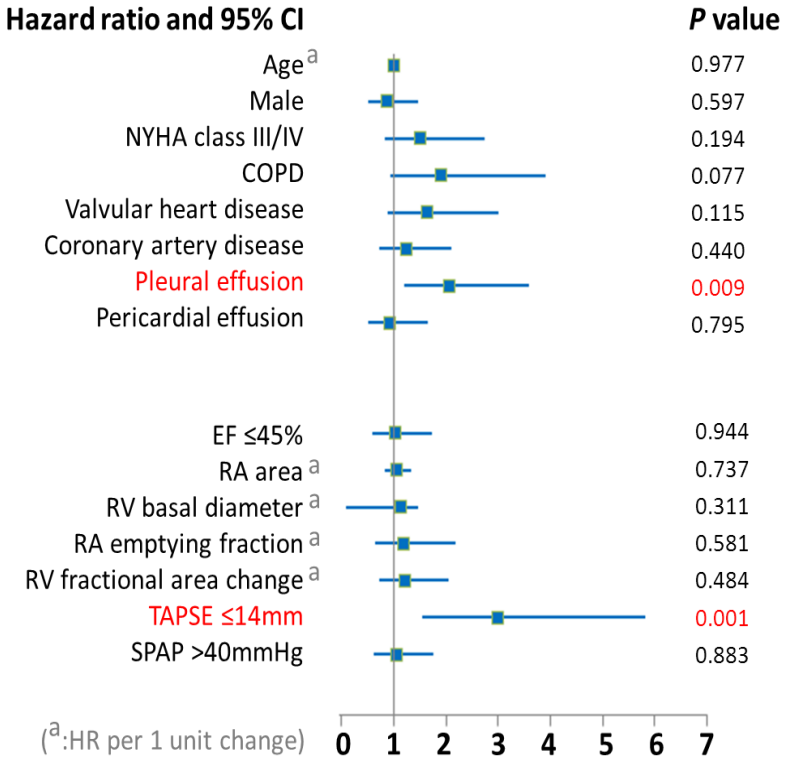


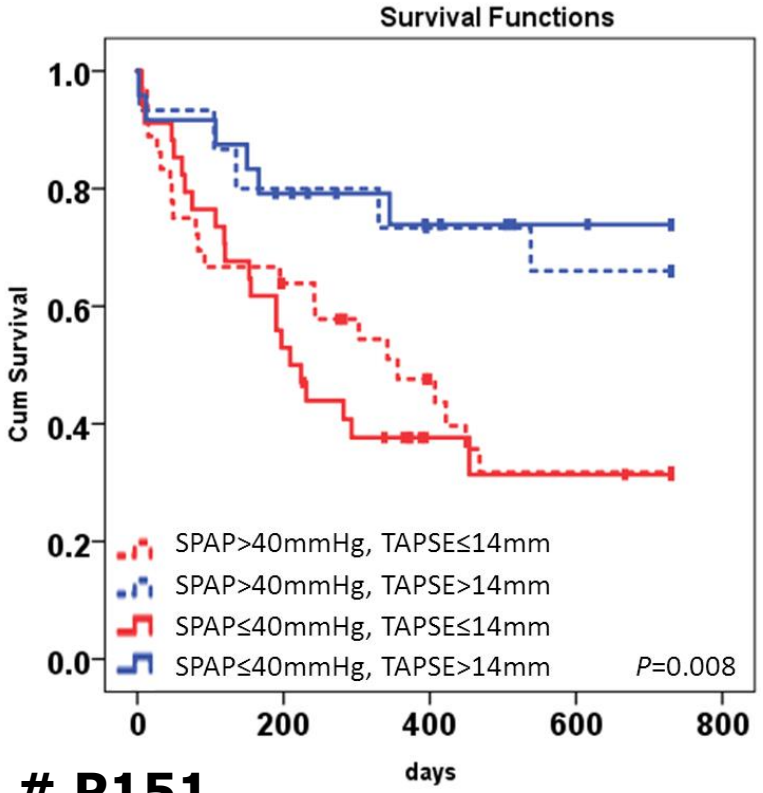
Prospective study, MRI
FUP 6.8 years

Gulati, Circulation 2013

Prognosis and RV Function Assessment in Chronic HF with Severe Tricuspid Regurgitation

- A total of 114 consecutive with clinically diagnosed CHF patients with severe non-organic TR (mean age 77±9 years, 51% male) were enrolled
- Patients were divided into a "low-SPAP" group (≤40mmHg, n=60) and a "high-SPAP" group (>40mmHg, n=54)
- Followed up for 12±9 months by clinical visit or telephone interview

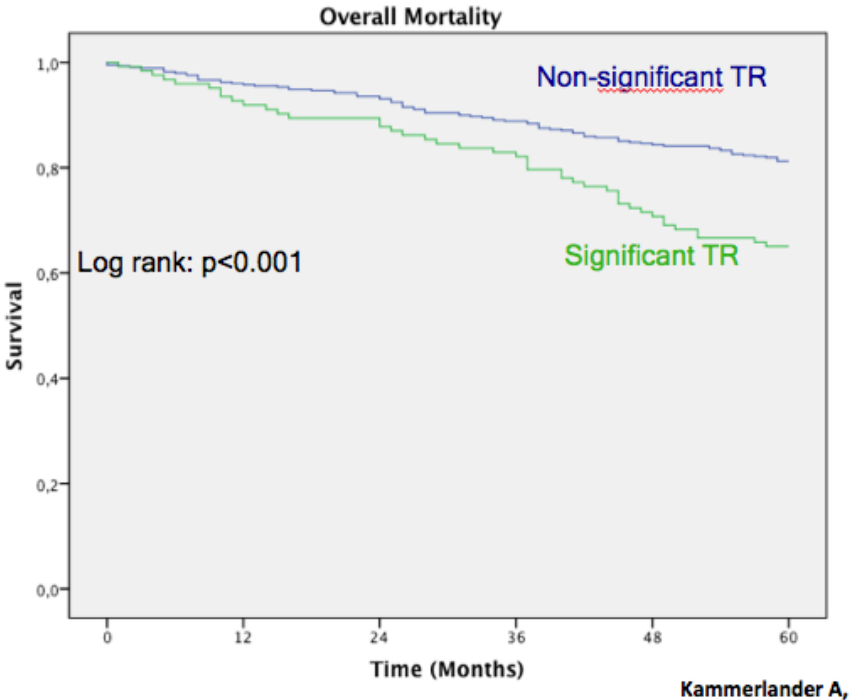




Liu # P151

Is TR Cause or Marker of Poor Prognosis ?

Kaplan Meier Analysis, 571 patients, 50 months after previous left heart valve surgery



Kammerlander A, ESC 2013

Lancellotti et al. Eur Heart J 2013

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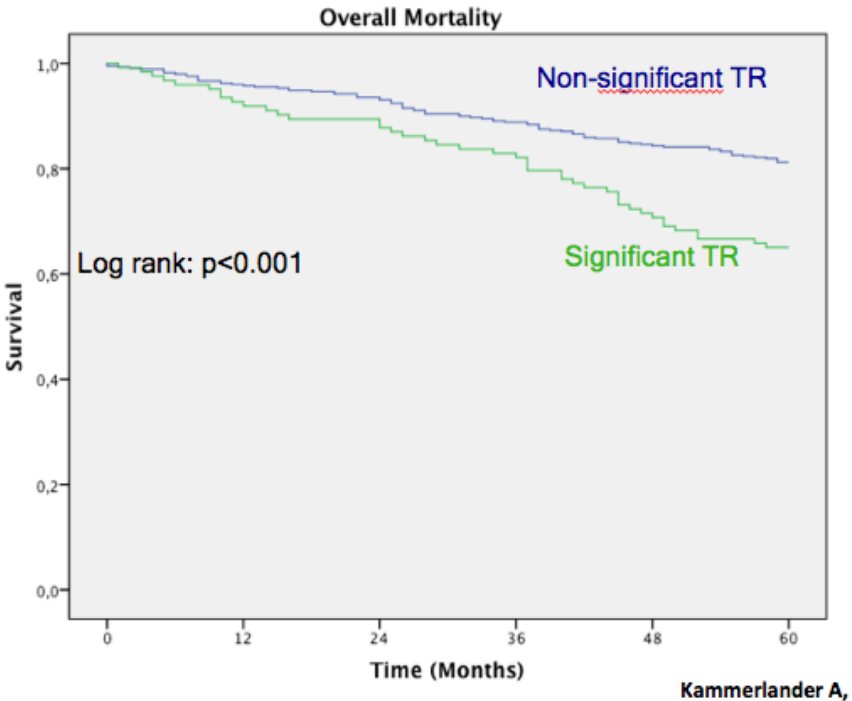


Kammerlander A, ESC 2013

The inclusion of several strong well-established risk factors of mortality in the multivariable model (i.e. LV function, creatinine level, NT-proBNP level, age, and NYHA functional class) may have mitigated the impact of TR on outcome

No definite conclusion

Lancellotti et al. Eur Heart J 2013

Secondary TR and Survival in CHF

Practical Approach

Significant TR and mild LV dysfunction/HF

Consider TVR before the occurrence of:

- Chronic AF
- Severe RV dilatation/dysfunction
- Intractable CHF with renal/liver dysfunction

Secondary TR and Survival in CHF

Practical Approach

Significant TR and severe LV dysfunction/HF

Consider conservative treatment

Indications for Intervention in Secondary TR

Surgery is indicated in patients with severe TR undergoing left-sided valve intervention	IC

Vahanian et al 2012 EHJ

Indications for Intervention in Secondary TR

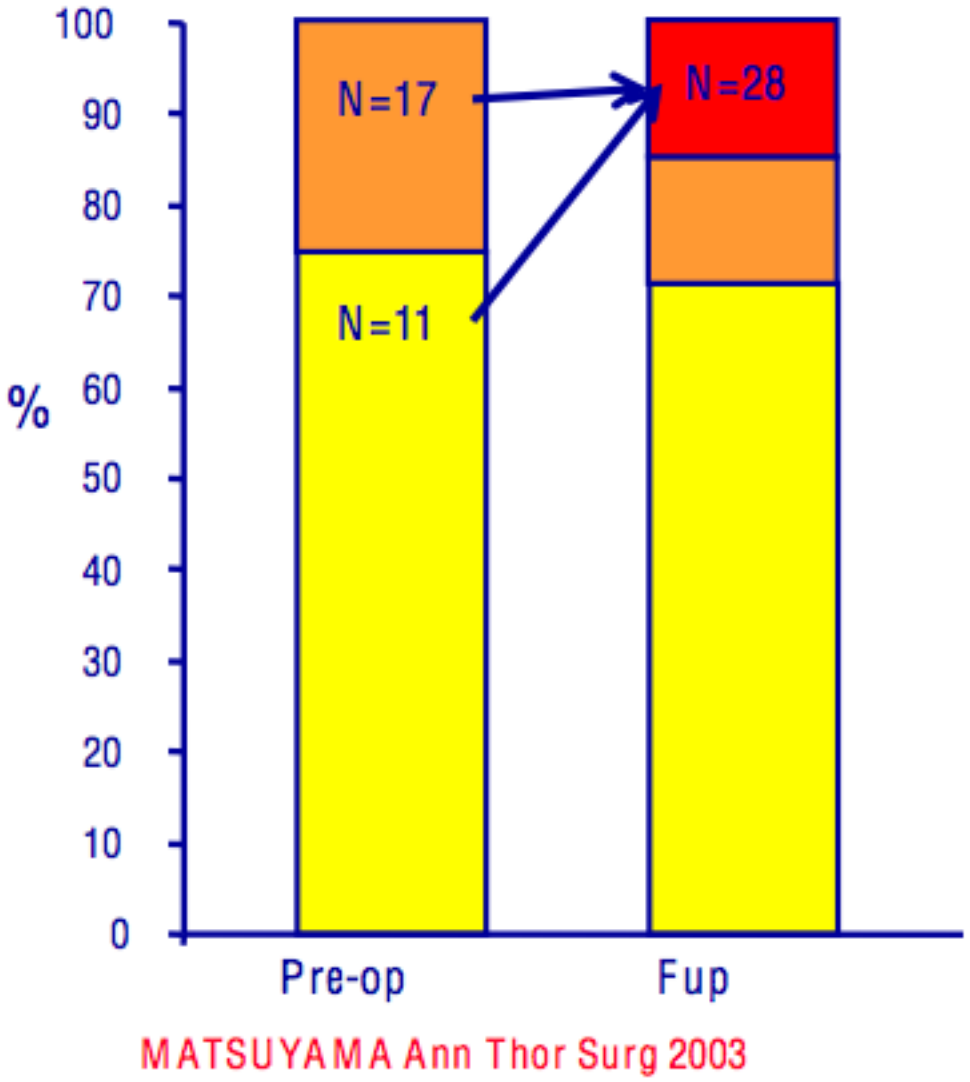
Surgery is indicated in patients with severe TR undergoing left-sided valve intervention	IC
Surgery should be considered in patients with mild or moderate secondary TR with dilated annulus (≥ 40 mm or ≥ 21 mm/m^2) undergoing left-sided valve intervention	IIaC

Vahanian et al 2012 EHJ

TR after MV surgery

174 patients with isolated mitral valve surgery and TR grade ≤ 2/4

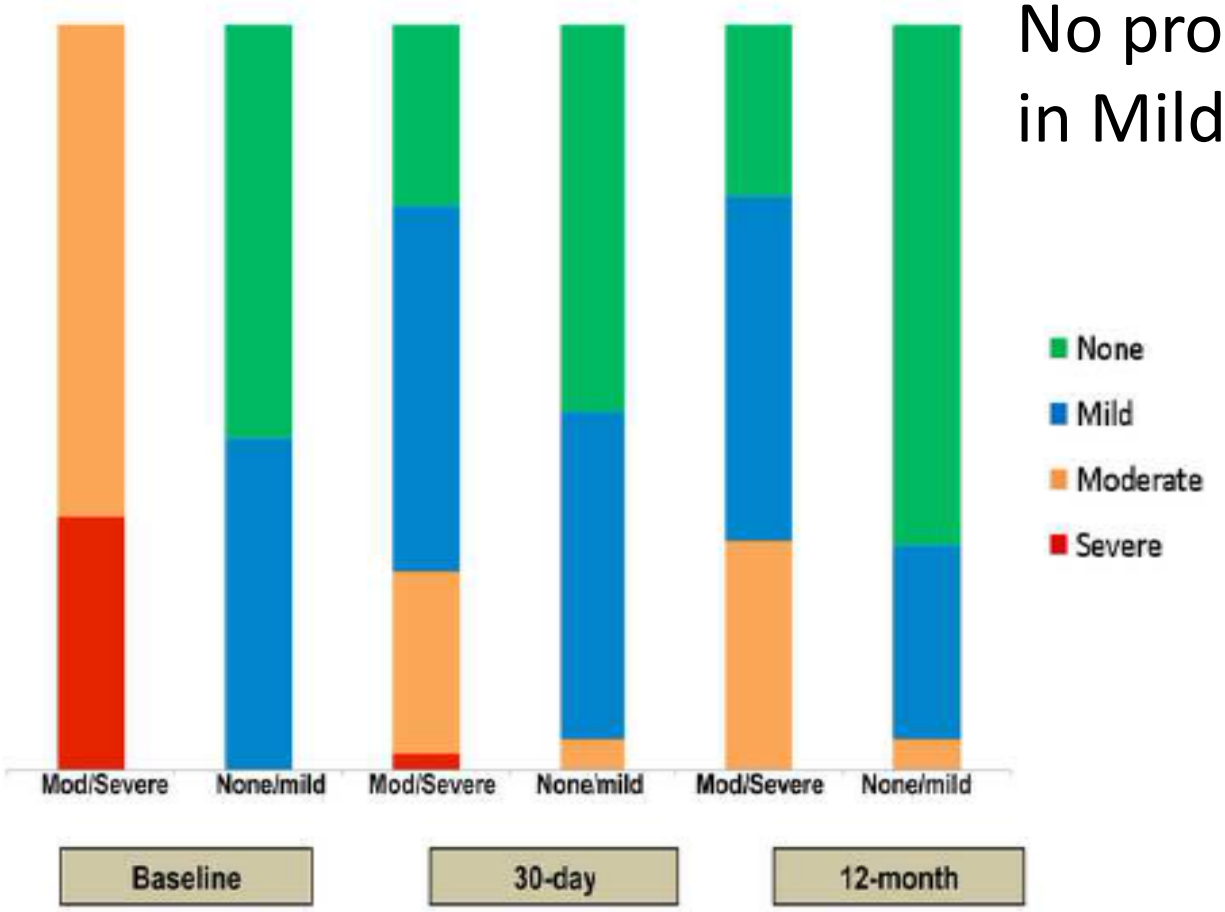
One third of moderate TR developed severe TR



Secondary TR and Survival in MitraClip

TR evolution after MitraClip

146 patients with SMR



No progression in Mild TR ?

EHJ Cardiosvasc Imag 2014

ORIGINAL ARTICLE

Mild-to-moderate functional tricuspid regurgitation in patients undergoing valve replacement for rheumatic mitral disease: the influence of tricuspid valve repair on clinical and echocardiographic outcomes

Joon Bum Kim,[1] Dong Gon Yoo,[2] Gwan Sic Kim,[1] Hyun Song,[3] Sung-Ho Jung,[1] Suk Jung Choo,[1] Cheol Hyun Chung,[1] Jae Won Lee[1]

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ABSTRACT

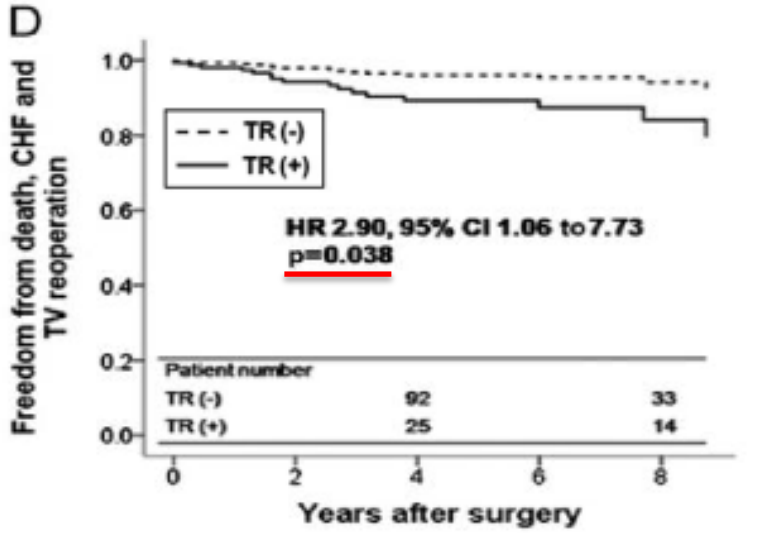
Background The decision to repair mild-to-moderate functional tricuspid regurgitation (TR) during left-side heart surgery remains controversial.

Objectives To avoid heterogeneity in patient population, patients with TR undergoing isolated mechanical mitral valve (MV) replacement for rheumatic mitral diseases were evaluated.

Methods Between 1997 and 2009, 236 patients with mild-to-moderate functional TR underwent first-time isolated mechanical MV replacement for rheumatic mitral diseases with (n=123; repair group) or without (n=113; non-repair group) tricuspid valve (TV) repair. Survival, valve-related complications, and TV function in these two groups were compared after adjustment for baseline characteristics using inverse-probability-of-treatment weighting.

Results Follow-up was complete in 225 patients (95.3%) with a median follow-up of 48.7 months (IQR 20.2—89.5 months), during which time 991 echocardiographic assessments were done. Freedom from moderate-to-severe TR at 5 years was 92.9±2.9% in the repair group and 60.8±6.9% in the non-repair group (p<0.001 and 0.048 in crude and adjusted analyses, respectively). After adjustment, both groups had similar risks of death (HR=0.57, p=0.43), tricuspid reoperation (HR=0.10, p=0.080) and congestive heart failure (HR=1.12, p=0.87). Postoperative moderate-to-severe TR was an independent predictor of poorer event-free survival (HR=2.90, p=0.038).

Conclusions These findings support the strategy of correcting mild-to-moderate functional TR at the time of MV replacement to maintain TV function and improve clinical outcomes.

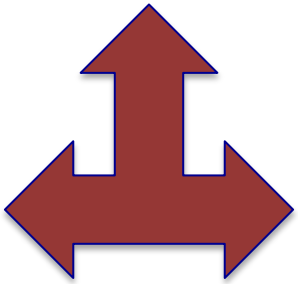


Secondary TR and Survival after prophylactic TVPlasty

TRPlasty is associated with better outcome

44 patients undergoing MVS (repair or replacement)

Moderate (≤+2) TR + TA ≥40 mm at preoperative echo



22 MVS+TVplasty

22 Isolated MVS

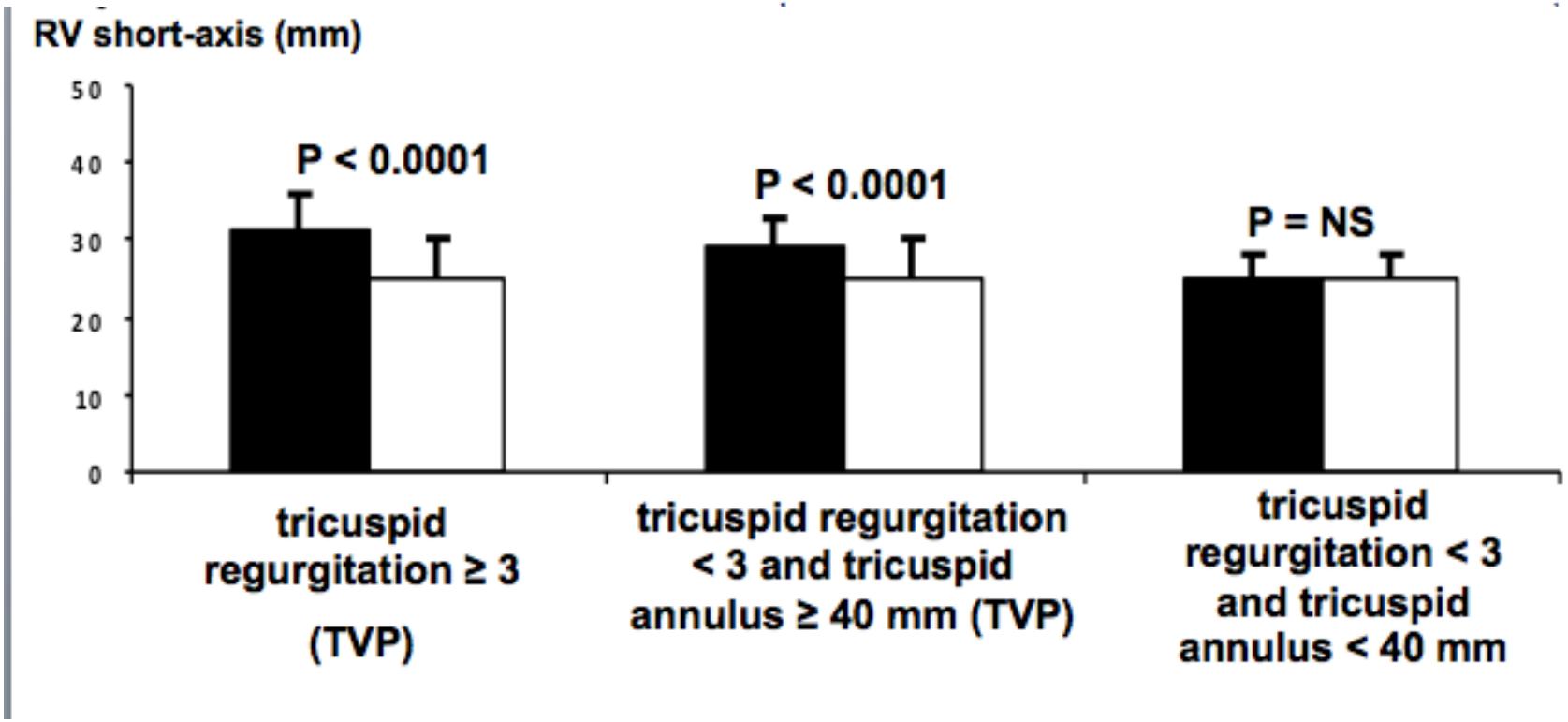
Operative mortality	4.4%		4.4%
At 12 months F-Up			
- Moderate/severe TR	0%	Randomized	28%*
- Reverse RV remodeling	+++		+
- ↗ 6MWT	+++		+

Benedetto U et al. J Thorac Cardiovasc Surg. 2012

Secondary TR and RV remodeling afterTVPlasty

TRPlasty is associated positive RV remodeling

Tricuspid annuloplasty prevents right ventricular dilatation and progression of tricuspid regurgitation in patients with tricuspid annular dilatation undergoing mitral valve repair



Van de Veire et al. J Thorac Cardio Surg 2011

Secondary TR and Survival after TVPlasty

TRPlasty is associated with excess events

175 patients undergoing MV surgery, 89 Tvplasty due to TA > 40 mm or TR > gr II
Similar characteristics between groups at baseline

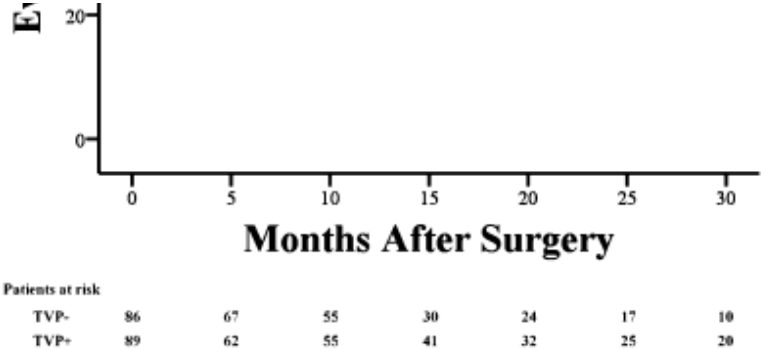
Clinical Outcomes After Tricuspid Valve Annuloplasty in Addition to Mitral Valve Surgery

TVPlasty -

Gille Koppers, MS;[1,2] David Verhaert, MD;[1] Frederik H. Verbrugge, MD;[1,2] Rozette Reyskens, RN;[1] Herbert Gutermann, MD;[3] Chris Van Kerrebroeck, MD, PhD;[3] Pieter Vandervoort, MD;[1,2] W. H. Wilson Tang, MD;[4] Robert Dion, MD, PhD;[2,3] Wilfried Mullens, MD, PhD[1,2]

TVPlasty +

From the Department of Cardiology, Ziekenhuis Oost-Limburg, Genk, Belgium;[1] the Faculty of Medicine and Life Sciences, Hasselt University, Diepenbeek, Belgium;[2] the Department of Cardiovascular Surgery, Ziekenhuis Oost-Limburg, Genk, Belgium;[3] and the Department of Cardiovascular Medicine, Heart and Vascular Institute, Cleveland Clinic, Cleveland, OH[4]



MVP/MVR+CABG+AVR/AVP	8	8	.95
Predicted mortality by the EuroSCORE, %	10	14	.06
Cross clamp time, min	151±57	152±49	.90
CPB time, min	207±76	202±58	.62

Clinical and Echocardiographic Impact of Functional Tricuspid Regurgitation Repair at the Time of Mitral Valve Replacement

Vincent Chan, MD, Ian G. Burwash, MD, B-Khanh Lam, MD, MPH, Titus Auyeung, BS, Anthony Tran, BS, Thierry G. Mesana, MD, PhD, and Marc Ruel, MD, MPH

Divisions of Cardiac Surgery and Cardiology, and Department of Epidemiology and Community Medicine, University of Ottawa, Ottawa, Ontario, Canada

Background. The indications for tricuspid valve repair in the setting of mitral valve disease and concomitant tricuspid regurgitation (TR) remain unclear. We examined patients undergoing mitral valve replacement (MVR) to determine the effect of TR and tricuspid valve repair on survival, functional status, and postoperative TR.

Methods. Between 1990 and 2005, 624 patients underwent MVR. Data included detailed serial echocardiographic tricuspid valve measurements, functional status, and survival data. Preoperative TR exceeded 2+ in 231: 125 received tricuspid repair and MVR, whereas 106 received MVR alone. Clinical and echocardiographic follow-up were complete (average, 6.8 ± 4.8 years). Parametric and semi-parametric tests were used to analyze outcomes.

Results. TR exceeding 2+ at operation was associated with a 53% increase in late death ($p = 0.003$). Tricuspid repair prevented echocardiographic progression of TR and improved congestive heart failure symptoms (both $p < 0.01$). Overall survival did not improve ($p = 0.3$). A trend to worsening TR in patients was noted with a larger tricuspid annulus diameter and without significant (≤ 1+) TR preoperatively (odds ratio, 1.4 per cm increase in annulus diameter; $p = 0.5$), but this was not associated with worse functional or vital outcomes.

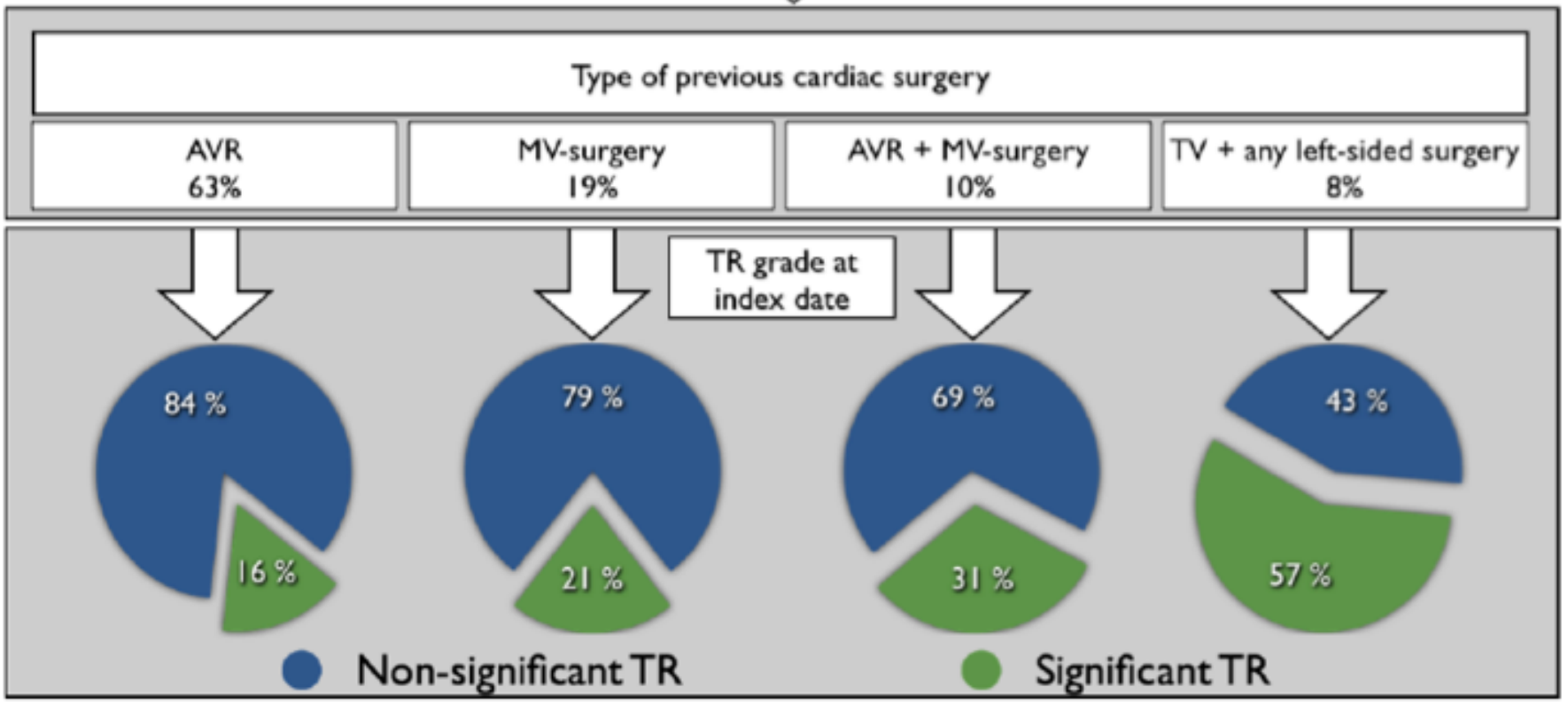
Conclusions. In patients undergoing MVR, tricuspid repair is indicated when TR exceeds 2+ to alleviate heart failure symptoms, but without significantly improving survival in this population. TR of 2+ or less may not require repair. Echocardiographic tricuspid annular dimensions alone, in the absence of significant (≤ 1+) TR preoperatively, should not dictate the performance of tricuspid repair.

(Ann Thorac Surg 2009;88:1209–15)

TR after Left-Sided Valve Surgery: a predictor of outcome?

Study	n	Surgery				Sign. TR	Comment
		AV	MV	AV+MV	add.TV	Late after surgery	
Matsuyama, 2002	174	-	100%	-	-	16%	Retrospective. MV surgery without TR surgery. Impact on survival?
Matsunaga, 2005	70	-	100%	-	13%	49%	Functional TR in pts operated for ischemic MR. Impact on survival?
Dreyfus, 2005	311	-	100%	-	48% dependd annulus size		No impact on survival whether TR was present / repaired
Kwak, 2008	335	22%	52%	26%	4.5%	27%	Poorer event-free survival in patients with TR but only after 10-y
García Fuster, 2011	801	-	100%	-	-	9%	Significant TR had no impact on overall survival but more symptoms of HF

571 patients
49±29 months after left-sided valve surgery



Follow up: 53.4±14.8 months

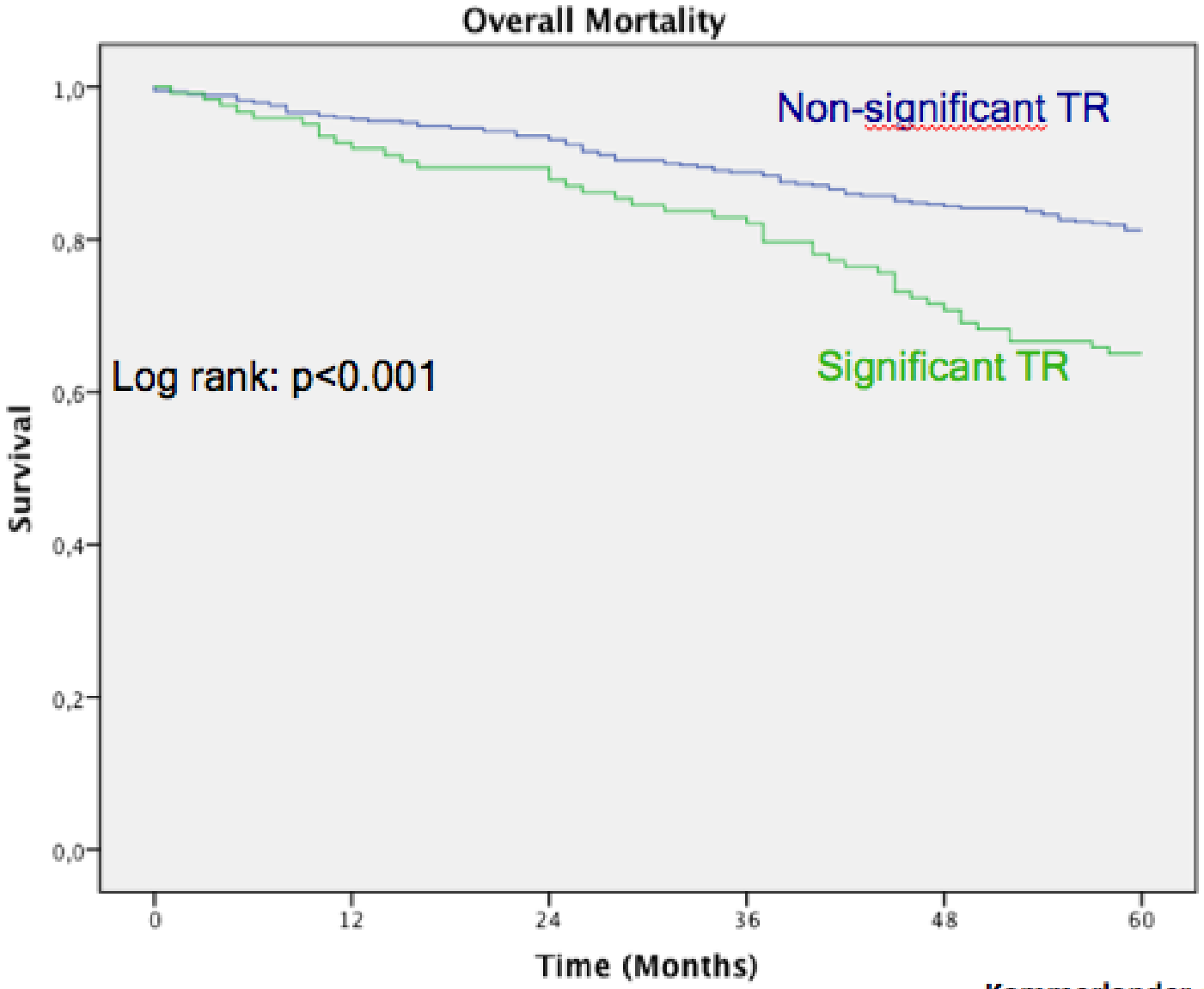
Kammerlander A, ESC 2013

Characteristics of patients with TR

Variable
Age [years]
Additive EuroSCORE
Female [%]
Body Mass Index [kg/m^2]
Number previous valve surgeries
n=1 [%]
n≥2 [%]
Coronary Artery Disease [%]
Atrial Fibrillation [%]
Hypertension [%]
Diabetes [%]
Hypercholesterolemia [%]
COPD [%]
NYHA functional class ≥2 [%]
Creatinine [mg/dl]

Variable
LVEDD [mm]
LVEDD/BSA [mm/m^2]
RVEDD [mm]
RVEDD/BSA [mm/m^2]
LA [mm]
LA/BSA [mm/m^2]
RA [mm]
RA/BSA [mm/m^2]
Reduced (<50%) LVEF [%]
Peak TR velocity [m/s]

Kaplan Meier Analysis, 571 patients, 50 months after previous left heart valve surgery



Kammerlander A, ESC 2013

Multivariable Cox-Regression Overall Mortality

	Parameter Estimate	Standard Error	p-value	Hazard Ratio	95.0% Hazard Ratio Confidence Limits	
Age	0.074	0.013	**<0.001**	1.077	1.050	1.104
Creatinine levels	0.372	0.134	**0.006**	1.451	1.115	1.889
Peak TR velocity	0.698	0.231	**0.003**	2.009	1.278	3.159

Future perspectives

...what are the next steps?

Maybe characterize subgroups of patients who benefit from isolated surgery of tricuspid regurgitation after previous left-sided valve surgery...

Reoperation for severe, isolated TR after left-sided valve surgery is associated with a perioperative mortality rate of 10% to 25%

The treatment of left-sided valve disease only partially cures TR

Indications for Intervention in Secondary TR

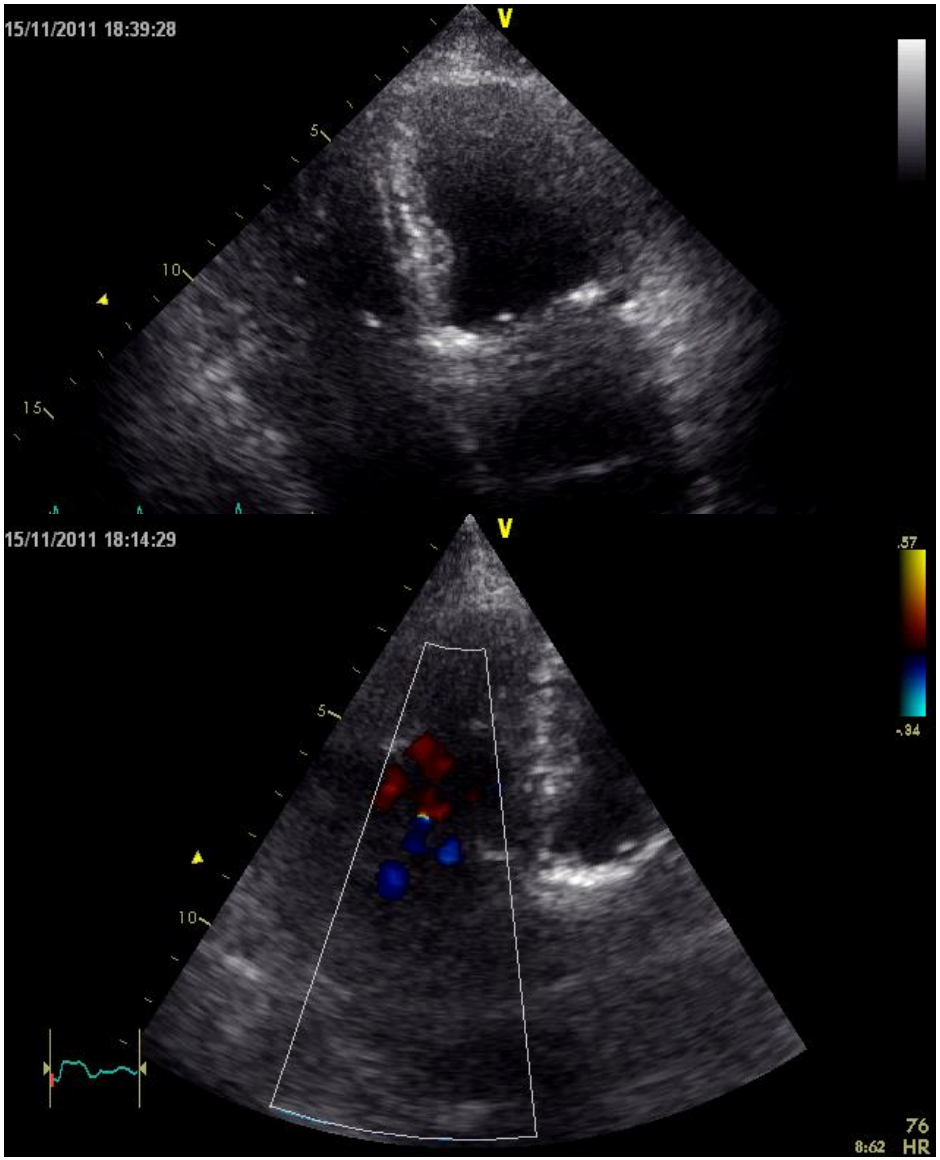
Surgery is indicated in patients with severe TR undergoing left-sided valve intervention	IC
Surgery should be considered in patients with mild or moderate secondary TR with dilated annulus (≥ 40 mm or ≥ 21 mm/m^2) undergoing left-sided valve intervention	IIaC
After left-sided valve surgery, surgery should be considered in patients with severe TR who are symptomatic of have progressive RV dilatation/dysfunction, in the absence of left-sided valve dysfunction, severe RV or LV dysfunction, and severe pulmonary hypertension	IIaC

Vahanian et al 2012 EHJ

Patient with TR, NYHA IV

Women, 75 y

- Left-side Valve surgery 5 years ago
- Isolated Mitral annuloplasty for FED with severe MR
- **Comes with congestive heart failure symptoms**



Conclusions

- Management of TR remains challenging
- TR persistence/occurrence after LSVS portends a poor outcome
- The prognostic benefit of prophylactic TVplasty has to be proven
- Current guidelines underline the urgent need for prospective studies, mostly derived from experts consensus

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