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RESEARCH ARTICLE

Residual tricuspid regurgitation after tricuspid transcatheter edge-to-edge repair: Insights into the EuroTR registry

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Aims Data on the prognostic impact of residual tricuspid regurgitation (TR) after tricuspid transcatheter edge-to-edge repair (T-TEER) are scarce. The aim of this analysis was to evaluate 2-year survival and symptomatic outcomes of patients in relation to residual TR after T-TEER.

Methods and results Using the large European Registry of Transcatheter Repair for Tricuspid Regurgitation (EuroTR registry) we investigated the impact of residual TR on 2-year all-cause mortality and New York Heart Association (NYHA) functional

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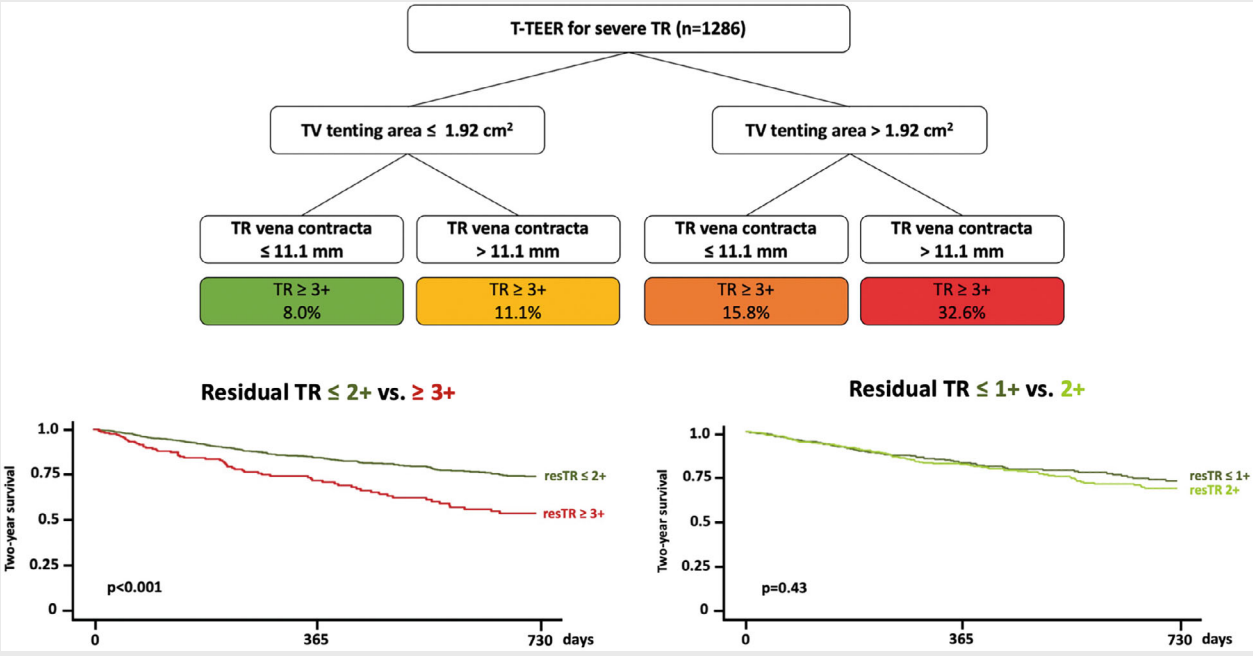
class at follow-up. The study further identified predictors for residual TR ≥3+ using a logistic regression model. The study included a total of 1286 T-TEER patients (mean age 78.0 ± 8.9 years, 53.6% female). TR was successfully reduced to ≤1+ in 42.4%, 2+ in 40.0% and 3+ in 14.9% of patients at discharge, while 2.8% remained with TR ≥4+ after the procedure. Residual TR ≥3+ was an independent multivariable predictor of 2-year all-cause mortality (hazard ratio 2.06, 95% confidence interval 1.30–3.26, $p = 0.002$). The prevalence of residual TR ≥3+ was four times higher in patients with higher baseline TR (vena contracta >11.1 mm) and more severe tricuspid valve tenting (tenting area >1.92 cm^2). Of note, no survival difference was observed in patients with residual TR ≤1+ versus 2+ (76.2% vs. 73.1%, $p = 0.461$). The rate of NYHA functional class ≥III at follow-up was significantly higher in patients with residual TR ≥3+ (52.4% vs. 40.5%, $p < 0.001$). Of note, the degree of TR reduction significantly correlated with the extent of symptomatic improvement ($p = 0.012$).

Conclusions T-TEER effectively reduced TR severity in the majority of patients. While residual TR ≥3+ was associated with worse outcomes, no differences were observed for residual TR 1+ versus 2+. Symptomatic improvement correlated with the degree of TR reduction.

Graphical Abstract



Impact of residual tricuspid regurgitation (TR) after tricuspid transcatheter edge-to-edge repair (T-TEER) ($n = 1286$). TV, tricuspid valve.

Keywords Tricuspid regurgitation • Residual tricuspid regurgitation • Tricuspid regurgitation reduction • Procedural success

Introduction

Tricuspid regurgitation (TR) is a substantial health burden due to high rates of morbidity, mortality, and hospitalizations for heart failure.[1–3] In the past, a lack of low-risk therapeutic options led to scientific under-recognition of TR and right ventricular (RV) function. The rapid evolvement of transcatheter repair techniques enabled the treatment of TR even in patients with advanced or prohibitive surgical risk.[4] Retrospective data reported high rates of procedural success and substantial symptomatic improvement

for patients undergoing tricuspid transcatheter edge-to-edge repair (T-TEER).[5–7] Recently, results of the randomized controlled TRILUMINATE Pivotal trial (Trial to Evaluate Cardiovascular Outcomes in Patients Treated with the Tricuspid Valve Repair System Pivotal) confirmed effective and safe TR reduction and an improvement in quality of life beyond optimal medical therapy.[8] For patients undergoing mitral valve transcatheter edge-to-edge repair (M-TEER), previous studies have shown that reducing mitral regurgitation (MR) severity to ≤1+ is associated with superior survival prognosis compared to residual MR 2+ especially in patients with preserved left ventricular dimensions and RV function.[9]

Until today, data on the prognostic impact of procedural TR reduction and residual TR in T-TEER patients are scarce. Most retrospective analyses that aimed at identifying predictors for procedural success used TR reduction to ≤2+ as a primary endpoint.[7,10] Residual TR ≥3+ has been shown to be associated with increased 2-year all-cause mortality in multivariable prediction models.[10,11]

The aim of the present study was to assess predictors for residual TR ≥3+ after T-TEER and its impact on symptomatic and survival outcomes after T-TEER using the large European Registry of Transcatheter Repair for Tricuspid Regurgitation (EuroTR registry).

Methods

Study cohort and procedural technique

The EuroTR registry included patients who underwent T-TEER for symptomatic TR from 2016 to 2022. Concomitant M-TEER or missing information on pre- or post-procedural TR severity led to exclusion from the present analysis. Characteristics of included and excluded patients are presented in online supplementary *Table S1*. Prior to the procedure, all patients remained symptomatic despite the application of maximum tolerated diuretic medication dosages. After discussion in an interdisciplinary heart team usually consisting of heart failure specialists, cardiac surgeons, and interventional cardiologists, the decision in favour of an interventional treatment approach was made. T-TEER was performed as previously described[12] using either the PASCAL device (Edwards Lifesciences, Irvine, CA, USA) or the MitraClip/TriClip system (Abbott, Santa Clara, CA, USA). This study adheres to the principles outlined in the Declaration of Helsinki and received proper ethical oversight (NCT06307262).

Study variables and endpoint

Clinical baseline characteristics included age, sex, comorbidities (arterial hypertension, myocardial infarction, coronary artery disease, stroke, diabetes mellitus), heart failure symptoms (dyspnoea according to New York Heart Association [NYHA] functional class, oedema, ascites, jugular venous distension, pleural effusion), as well as renal and hepatic function. Echocardiographic evaluation was performed in line with current guidelines[13] and comprised left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD), RV fractional area change, tricuspid annular plane systolic excursion (TAPSE), tricuspid annular diameter, RV end-systolic and diastolic area, right atrial area, TR effective regurgitant orifice area (EROA), TR regurgitant volume (RegVol) and echocardiographically estimated systolic pulmonary artery pressure. TR vena contracta was measured biplane if eligible. Tricuspid valve (TV) tenting area was derived from a RV focused apical four-chamber view (*Figure 1*). TR severity was assessed using a five-grade scale[14]: mild (1+), moderate (2+), severe (3+), massive (4+), and torrential (5+). The primary study endpoint was 2-year survival. Secondary endpoints were survival free from heart failure hospitalization and changes in NYHA functional class at latest available clinical follow-up.

Statistical analysis

Data were reported using means and standard deviation or median with interquartile range as appropriate. Differences between two independent samples were evaluated using the Mann–Whitney U test. Dependent samples were compared by applying the Wilcoxon test. Survival differences were depicted using Kaplan–Meier charts. A Cox regression model was built in order to identify predictors for 2-year all-cause mortality. Predictors for residual TR ≥3+ were analysed using a logistic regression model. Parameters with a p-value <0.05 in the univariable analysis were included into the respective multivariable models. Results were displayed as hazard or odds ratio (HR/OR) with 95% confidence interval (CI) and p-value. Receiver operating characteristic charts and calculation of Youden's J identified cut-offs for optimized prediction of TR ≥3+. The level of statistical significance was set to a two-sided p-value <0.05. All analyses were performed using R (version 4.0.4) and SPSS (version 25, IBM Corp., Armonk, NY, USA).

Results

Baseline characteristics and overall outcomes

The present study included 1286 patients with a mean age of 78.0 ± 8.9 years (53.6% female). TR aetiology was primary in 7.6%, secondary in 84.1%, and mixed primary/secondary in 8.3% of patients. A transtricuspid pacing lead was present in 28.2% of patients. Overall, left ventricular dimensions and function were preserved (LVEDD 48.3 ± 8.0 mm; LVEF 53.5 ± 11.2%). A total of 889 patients (72.0%) presented with heart failure with preserved ejection fraction, 204 patients (16.5%) with heart failure with mildly reduced ejection fraction, and 141 patients (11.4%) with heart failure with reduced ejection fraction. RV dysfunction according to TAPSE <17 mm was present in 46.2% of patients. TR severity was 5+ in 17.3%, 4+ in 33.4%, 3+ in 47.0%, and 2+ in 2.4% of patients with a mean EROA and RegVol of 0.67 ± 0.51 cm^2 and 51.6 ± 32.9 ml, respectively. *Table 1* provides a detailed summary of clinical and echocardiographic baseline characteristics within the study cohort. Residual TR after T-TEER was ≤1+ in 42.4%, 2+ in 40.0%, 3+ in 14.9%, and ≥4+ in 2.6% of patients at discharge (*Table 2*). Overall, 51.2% of patients were treated using the TriClip and 48.7% using the PASCAL device.

Predictors for residual tricuspid regurgitation

To predict residual TR (≥3+) after T-TEER, a multivariable logistic regression model was used. The later identified TR vena contracta

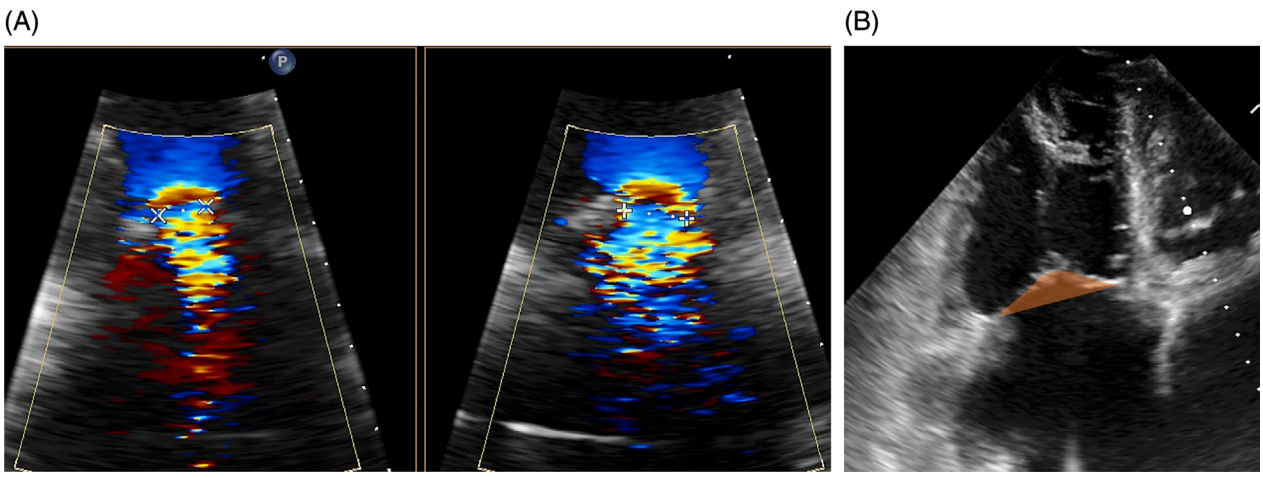


Figure 1 Example of a patient with high probability of residual tricuspid regurgitation ≥3+ after tricuspid transcatheter edge-to-edge repair. Tricuspid regurgitation vena contracta and tricuspid valve tenting area were measured in a right ventricular focused apical four-chamber view. (*A*) Measurement of biplane vena contracta, and (*B*) measurement of tricuspid valve tenting area.

(OR 1.08, 95% CI 1.02–1.14, $p = 0.005$), and TV tenting area (OR 1.50, 95% CI 1.24–1.82, $p < 0.001$) to be independently associated with residual TR ≥3+ after T-TEER (*Table 3*, online supplementary *Table S2*). Using sensitivity analyses, we identified optimized cut-offs for TR vena contracta (11.1 mm) and TV tenting area (1.92 cm^2) in terms of residual TR. Residual TR ≥3+ at discharge was significantly more common in patients with TV vena contracta >11.1 mm (26.7% vs. 11.1%) and TV tenting area >1.92 cm^2 (24.8% vs. 9.9%). In patients who presented with favourable anatomic parameters (TV vena contracta <11.1 mm and TV tenting area <1.92 cm^2) residual TR ≥3+ was observed in 8% of patients, while the prevalence increased four-fold to 32.6% in patients with TR vena contracta >11.1 mm and TV tenting area >1.92 cm^2 (*Figures 1* and *2*). Mean follow-up duration was 1102 ± 299 days. Median 1- and 2-year survival rates were 82.5% and 70.8%, respectively. NYHA functional class at latest available follow-up was ≤II in 57.5% of patients versus 15.9% at baseline ($p < 0.001$). NYHA functional class at follow-up was available in 612 patients (47%) at a median time of 203 (71–409) days.

Online supplementary *Figure S1.* depicts TR reduction in patients with primary, secondary, and mixed primary-secondary TR. Of note, TR aetiology (secondary vs. primary/mixed) was not an independent predictor for residual TR (OR 1.224, 95% CI 0.801–1.851, $p = 0.337$). The presence of a transtricuspid lead was a uni- but no multivariate predictor for residual TR (online supplementary *Figure S2* and *Table S2*).

Impact of residual tricuspid regurgitation on 2-year all-cause mortality and symptomatic outcome

Figures 3 and *4* illustrate the impact of residual TR and the absolute degree of TR reduction on 2-year survival after T-TEER. Residual TR ≥3+ after T-TEER was associated with reduced 2-year survival probability (54.2% vs. 74.4% in patients with residual TR ≤2+, $p < 0.001$; *Figure 3A*). Of note, reducing TR severity to ≤1+ did not lead to significantly higher survival rates compared to residual TR 2+ (76.2% in patients with TR ≤1+ vs. 73.1% in patients with TR 2+, $p = 0.461$; *Figure 3B*). While patients without TR reduction presented with worse 2-year survival (57.5%), we observed a trend towards better survival with an increasing degree of TR improvement (1-grade improvement achieved in 25.4% of patients: 68.8%; 2-grade improvement achieved in 48.1% of patients: 74.0%; 3-grade improvement achieved in 16.6% of patients: 70.2%; 4-grade improvement achieved in 3.3% of patients: 80.3%; *Figure 4*). A multivariable Cox regression model identified residual TR ≥3+ (HR 2.06, 95% CI 1.30–3.26, $p = 0.002$), NYHA functional class IV (HR 2.39, 95% CI 1.54–3.72, $p < 0.001$), RV mid diameter (HR 1.03, 95% CI 1.01–1.06, $p = 0.010$) and TAPSE per 1 mm reduction (HR 1.08, 95% CI 1.02–1.12, $p = 0.003$) to be independently associated with reduced 2-year survival after T-TEER (*Table 4*, online supplementary *Table S1.*). Comparable results were observed for survival free from HHF (online supplementary *Figure S1.*).

Although NYHA functional class significantly improved from baseline to follow-up, the rate of NYHA class ≥III at follow-up was significantly higher in patients with residual TR ≥3+ (52.4% vs. 40.5%, $p < 0.001$; *Figure 5*). Of note, the degree of symptomatic improvement as assessed by NYHA functional class correlated with the degree of TR reduction ($p = 0.012$, *Figure 6*).

Discussion

With more than 1200 patients the EuroTR registry represents the largest patient cohort treated exclusively with edge-to-edge repair for relevant TR. Alternative treatment approaches like annuloplasty or patients who underwent concomitant M-TEER were excluded

Table 1 Patient baseline characteristics

	All patients ($n = 1286$)	Residual TR ≤2+ ($n = 1060$)	Residual TR ≥3+ ($n = 226$)	*p*-value
Age, years	78.0 ± 8.9	78.1 ± 9.1	77.7 ± 7.9	0.314
Female sex, *n* (%)	689 (53.6)	592 (55.8)	129 (57.1)	**<0.001**
BMI, kg/m^2	26.1 ± 4.9	26.1 ± 5.0	26.2 ± 4.7	0.559
EuroSCORE II, %	6.5 ± 5.8	6.3 ± 5.6	7.0 ± 6.5	0.075
AHT, *n* (%)	903 (79.6)	739 (79.9)	164 (78.5)	0.645
Dyslipidaemia, *n* (%)	507 (48.0)	426 (48.7)	81 (44.5)	0.305
Peripheral oedema, *n* (%)	732 (66.0)	593 (64.7)	139 (72.0)	0.052
Ascites, *n* (%)	164 (14.8)	127 (13.9)	37 (19.2)	0.062
Jugular vein distension, *n* (%)	97 (20.8)	75 (19.3)	22 (28.2)	0.067
Prior MI, *n* (%)	141 (11.0)	108 (10.2)	33 (14.6)	0.055
COPD, *n* (%)	228 (17.7)	181 (17.1)	33 (47)	0.184
DM, *n* (%)	297 (26.1)	246 (23.2)	51 (24.4)	0.526
Prior stroke, *n* (%)	93 (11.6)	71 (10.9)	22 (14.7)	0.193
TV lead, *n* (%)	392 (28.2)	283 (26.8)	79 (35.0)	**0.013**
Afib/flutter, *n* (%)	1159 (90.3)	956 (90.4)	203 (89.8)	0.805
CAD, *n* (%)	507 (39.5)	405 (38.3)	102 (45.1)	0.057
LVEF, %	53.5 ± 11.2	53.8 ± 11.3	52.3 ± 11.1	**0.016**
LVEDD, mm	48.3 ± 8.0	48.2 ± 8.1	49.2 ± 7.8	**0.030**
TR EROA, cm^2	0.67 ± 0.51	0.62 ± 0.50	0.89 ± 0.57	**<0.001**
TR RegVol, ml	51.6 ± 32.9	48.7 ± 26.5	66.0 ± 51.9	**<0.001**
TR VC, mm	11.3 ± 4.3	10.8 ± 4.1	13.3 ± 4.7	**<0.001**
RV FAC, %	39.2 ± 11.3	39.5 ± 11.1	37.9 ± 11.9	**0.143**
RV EDA, cm^2	29.1 ± 13.9	28.3 ± 13.6	33.4 ± 15.1	**<0.001**
RV ESA, cm^2	18.4 ± 8.8	17.8 ± 8.3	21.8 ± 10.2	**<0.001**
RV mid-ventricular diameter, mm	41.2 ± 8.6	40.5 ± 8.4	44.4 ± 9.1	**<0.001**
RV basal diameter, mm	48.9 ± 9.6	48.2 ± 9.6	52.1 ± 8.7	**<0.001**
RV length, mm	71.2 ± 11.8	70.2 ± 11.2	76.0 ± 13.7	**<0.001**
TV annulus diameter, mm	45.2 ± 8.4	44.7 ± 8.4	47.6 ± 7.9	**<0.001**
RAA, cm^2	37.3 ± 14.0	36.6 ± 14.0	40.8 ± 13.4	**<0.001**
TAPSE, mm	17.1 ± 4.5	17.3 ± 4.5	16.5 ± 4.6	**0.020**
Echo sPAP, mmHg	43.2 ± 14.6	43.6 ± 14.5	41.4 ± 14.9	**0.012**
Coaptation gap, mm	6.3 ± 3.1	6.0 ± 2.9	7.6 ± 3.5	**<0.001**
Tenting height, mm	8.2 ± 3.4	8.0 ± 3.3	9.1 ± 3.8	**0.006**
Tenting area, cm^2	2.2 ± 1.3	2.0 ± 1.2	2.8 ± 1.5	**<0.001**
eGFR, ml/min	46.8 ± 24.1	46.8 ± 20.3	46.6 ± 37.2	0.104
NT-proBNP, pg/ml	4699 ± 9264	4261 ± 7518	6811 ± 14 934	0.055
MRA, *n* (%)	550 (42.8)	438 (41.4)	112 (49.6)	**0.025**
Loop diuretic, *n* (%)	1194 (92.8)	978 (92.3)	216 (95.6)	0.080
Thiazide diuretic, *n* (%)	133 (17.1)	104 (16.2)	29 (21.3)	0.147
Beta-blocker, *n* (%)	1088 (84.6)	887 (83.7)	201 (88.9)	**0.047**
RASI, *n* (%)	400 (42.1)	337 (43.0)	63 (37.7)	0.207
NYHA functional class, *n* (%)				0.357
I	14 (1.1)	13 (1.2)	1 (0.4)	
II	189 (14.8)	146 (13.8)	43 (19.1)	
III	902 (70.5)	753 (71.4)	149 (66.2)	
IV	175 (13.7)	143 (13.6)	32 (14.2)	
TR severity, *n* (%)				**<0.001**
2+	31 (2.4)	31 (2.9)	0 (0.0)	
3+	604 (47.0)	550 (51.9)	54 (23.9)	
4+	429 (33.4)	352 (33.2)	77 (34.1)	
5+	222 (17.3)	127 (12.0)	95 (42.0)	
TR aetiology, *n* (%)				**<0.001**
Primary	96 (7.6)	88 (8.5)	8 (3.6)	
Secondary	1063 (84.1)	869 (83.6)	194 (86.2)	
Mixed	105 (8.3)	82 (7.9)	23 (10.2)	

Values are mean ± standard deviation, unless otherwise indicated.

Afib, atrial fibrillation; AHT, arterial hypertension; BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; EDA, end-diastolic area; eGFR, estimated glomerular filtration rate; ESA, end-systolic area; EROA, effective regurgitant orifice area; FAC, fractional area change; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N-terminal pro-B-type natriuretic peptide; RAA, right atrial area; RASI, renin–angiotensin system inhibitor; RegVol, regurgitant volume; RV, right ventricular; sPAP, systolic pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation; TV, tricuspid valve; VC, vena contracta.

Bold values indicate statistical significance ($p < 0.05$).

Table 2 Procedural data and study outcomes

	All patients ($n = 885$)	Residual TR ≤2+	Residual TR ≥3+	*p*-value
Residual TR severity, *n* (%)				**<0.001**
1+	545 (42.4)	545 (51.4)	0 (0.0)	
2+	515 (40.0)	515 (48.6)	0 (0.0)	
3+	192 (14.9)	0 (0.0)	192 (85.0)	
4+	25 (1.9)	0 (0.0)	25 (11.1)	
5+	9 (0.7)	0 (0.0)	9 (4.0)	
TR reduction, grades, *n* (%)				**<0.001**
0	73 (5.7)	2 (0.2)	71 (31.4)	
1	327 (25.4)	246 (23.2)	81 (35.8)	
2	618 (48.1)	544 (51.3)	74 (32.7)	
3	226 (17.6)	226 (21.3)	0 (0.0)	
4	42 (3.3)	42 (4.0)	0 (0.0)	
NYHA class at follow-up, *n* (%)				**0.034**
I	69 (11.2)	61 (11.9)	8 (7.9)	
II	284 (46.3)	244 (47.6)	40 (39.6)	
III	221 (36.0)	175 (34.1)	46 (45.5)	
IV	40 (6.5)	33 (6.4)	7 (6.9)	

NYHA, New York Heart Association; TR, tricuspid regurgitation.
Bold values indicate statistical significance ($p < 0.05$).

Table 3 Multivariable logistic regression model for residual tricuspid regurgitation ≥3+

	Univariable			Multivariable		
	Odds ratio	95% CI	*p*-value	Odds ratio	95% CI	*p*-value
TR vena contracta, mm	1.130	1.093–1.168	<0.001	1.078	1.023–1.135	0.005
Tenting area, cm^2	1.491	1.260–1.766	<0.001	1.501	1.240–1.818	<0.001

CI, confidence interval; TR, tricuspid regurgitation.

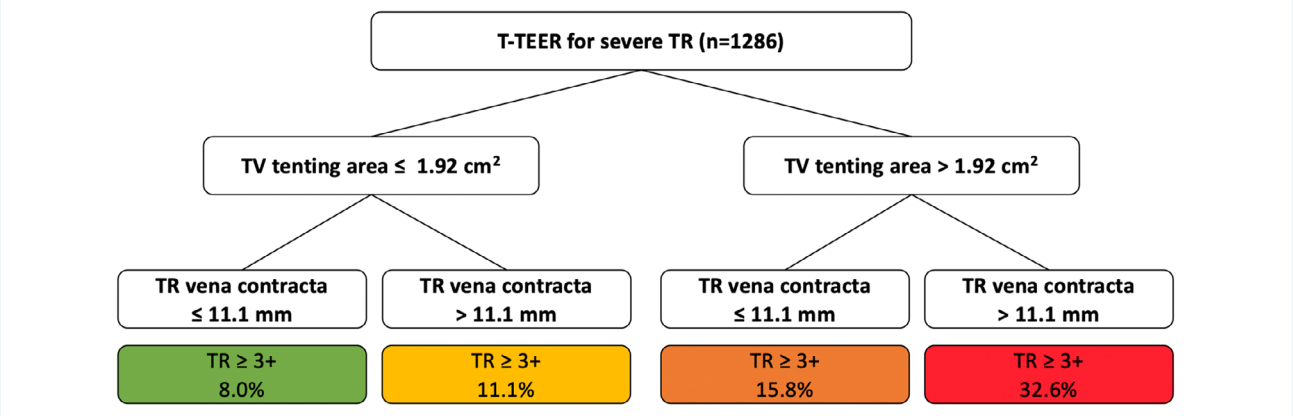


Figure 2 Flow-chart for the prediction of residual tricuspid regurgitation (TR) ≥3+ after tricuspid transcatheter edge-to-edge repair (T-TEER). Residual TR ≥3+ after T-TEER is more frequently observed in patients with large tricuspid valve (TV) tenting area and vena contracta.

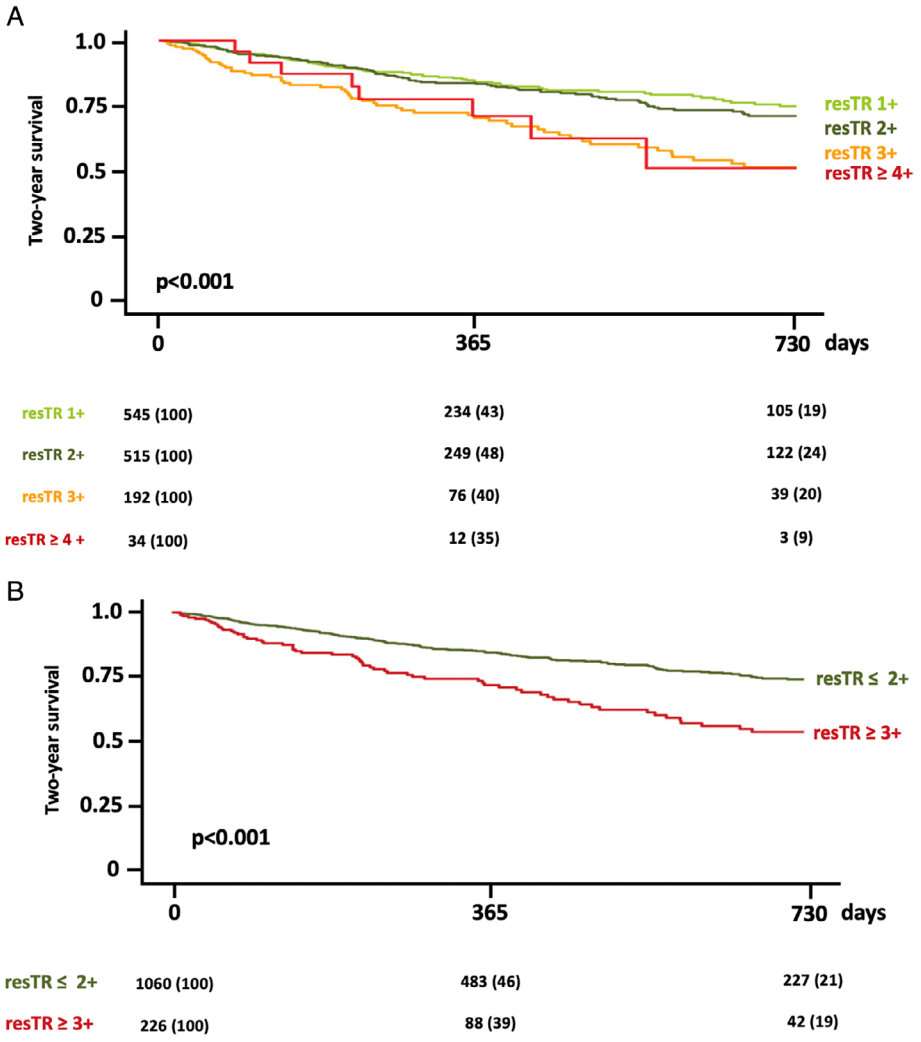


Figure 3 Two-year survival after tricuspid transcatheter edge-to-edge repair stratified by residual postprocedural tricuspid regurgitation (TR). Residual TR ≥3+ was associated with significantly reduced 2-year survival rates following tricuspid transcatheter edge-to-edge repair for relevant TR. (*A*) Detailed survival curves for each grade of postprocedural TR severity. (*B*) Patients with residual TR ≤2+ versus ≥3+.

from this analysis. The majority of patients included in the EuroTR registry suffered from secondary TR with 72% of patients presenting with preserved left ventricular function and 53.8% presenting with preserved RV function. We focused on investigating the impact of residual TR and the magnitude of TR reduction on survival and symptomatic outcomes after T-TEER. The main findings include: (i) TR was effectively reduced to ≤2+ in 82% of patients by T-TEER; (ii) baseline TR vena contracta and TV tenting area were major predictors for residual TR ≥3+; (iii) residual TR ≥3+ was associated with significantly reduced 2-year survival while no significant survival difference was observed in patients with residual TR ≤1+ and TR 2+; (iv) residual TR ≥3+ was associated with more severe heart failure symptoms at follow-up; and (v) the degree of TR reduction correlated with the degree of symptomatic improvement (*Graphical Abstract*).

Procedural tricuspid regurgitation reduction and its impact on prognosis

Among a total of 1286 included real-world patients, T-TEER reduced TR to ≤2+ in 82% of patients, a considerably higher percentage compared to results of the earlier real-world TriValve registry ($n = 249$, 77%) which captured patients in the beginning of tricuspid transcatheter therapies and which also included different treatment modalities like annuloplasty.[6] On the other hand, the TRILUMINATE trial achieved even higher TR reduction rates to ≤2+ in a randomized controlled setting (90% at 30-day follow-up),[8] which might be explained by a rigorous patient selection.[7] Besides advanced heart failure with dyspnoea at rest (NYHA class IV), RV dysfunction (decreasing TAPSE), RV dilatation (increasing RV diameters), and residual TR ≥3+ were independently associated with significantly impaired 2-year survival rates after T-TEER in

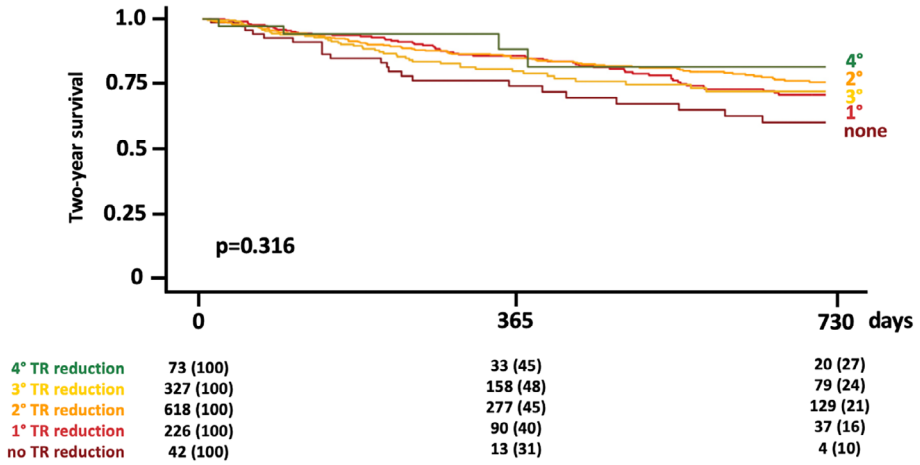


Figure 4 Two-year survival after tricuspid transcatheter edge-to-edge repair stratified by the absolute degree of tricuspid regurgitation (TR) reduction. There was a trend towards better survival with an increasing degree of TR improvement (1-grade improvement achieved in 25.4% of patients: 68.8%; 2-grade improvement achieved in 48.1% of patients: 74.0%; 3-grade improvement achieved in 16.6% of patients: 70.2%; 4-grade improvement achieved in 3.3% of patients: 80.3%).

Table 4 Multivariable Cox regression model (2-year all-cause mortality)

	Univariable			Multivariable		
	Hazard ratio	95% CI	*p*-value	Hazard ratio	95% CI	*p*-value
RV mid-ventricular diameter, mm	1.022	1.004–1.040	0.016	1.031	1.007–1.056	0.010
TAPSE per 1 mm reduction	1.087	1.052–1.121	<0.001	1.073	1.024–1.124	0.003
NYHA class IV	2.265	1.662–3.078	<0.001	2.392	1.537–3.722	<0.001
Residual TR ≥3+	2.074	1.550–2.773	<0.001	2.061	1.304–3.258	0.002

CI, confidence interval; NYHA, New York Heart Association; RV, right ventricular; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation.

the present cohort. Although this study cannot prove a causal survival benefit of T-TEER treatment due to its retrospective nature and the lack of a conservatively treated control group, our results suggest that an adequate degree of TR reduction likely impacts outcomes of patients with significant symptomatic TR. Remarkably, whether TR was reduced to 2+ or ≤1+ did not affect 2-year survival. Nevertheless, this result needs to be interpretated with caution. From studies focusing on the natural course of TR we learned that mild and moderate non-severe TR influences survival prognosis especially in the long term.[3] Due to the lack of long-term data, we currently cannot draw conclusions on a potential impact of TR 1+ on survival beyond 2 years after T-TEER. Beyond that, we were able to show that the degree of procedural TR reduction significantly correlated with the degree of symptomatic improvement as assessed by NYHA functional class (*Figure 6*). This emphasizes the importance of optimizing procedural T-TEER results. Interestingly, we observed improvement in NYHA functional class in a subset of patients without effective TR reduction. Possible explanations therefore might be more regular doctor visits, a certain degree of placebo effect and haemodynamic improvement despite absence of visual reduction of TR and underestimation of TR reduction.

In this large multicentre registry, TR vena contracta and TV tenting area were identified as main predictors for relevant residual TR at discharge. Patients with TR vena contracta >11.1 mm and TV tenting area >1.92 cm^2 presented with residual TR ≥3+ in 32.6% (vs. 8% in case of TR vena contracta ≤11.1 mm and TV tenting area ≤1.92 cm^2). A previous study with a smaller sample size identified jet location and coaptation gap sizes as independent predictors for procedural success.[15] Using a larger population of T-TEER patients, the present analysis did not confirm an independent predictive value of jet localization. Though, tenting area became an important parameter in this larger EuroTR cohort in terms of predicting residual TR. Of note, pulmonary hypertension was not an independent predictor for residual TR after T-TEER.

Transcatheter tricuspid valve replacement and residual tricuspid regurgitation

The field of transcatheter TV replacement (TTVR) has made rapid progress, allowing for almost complete elimination of TR.[16–19] This

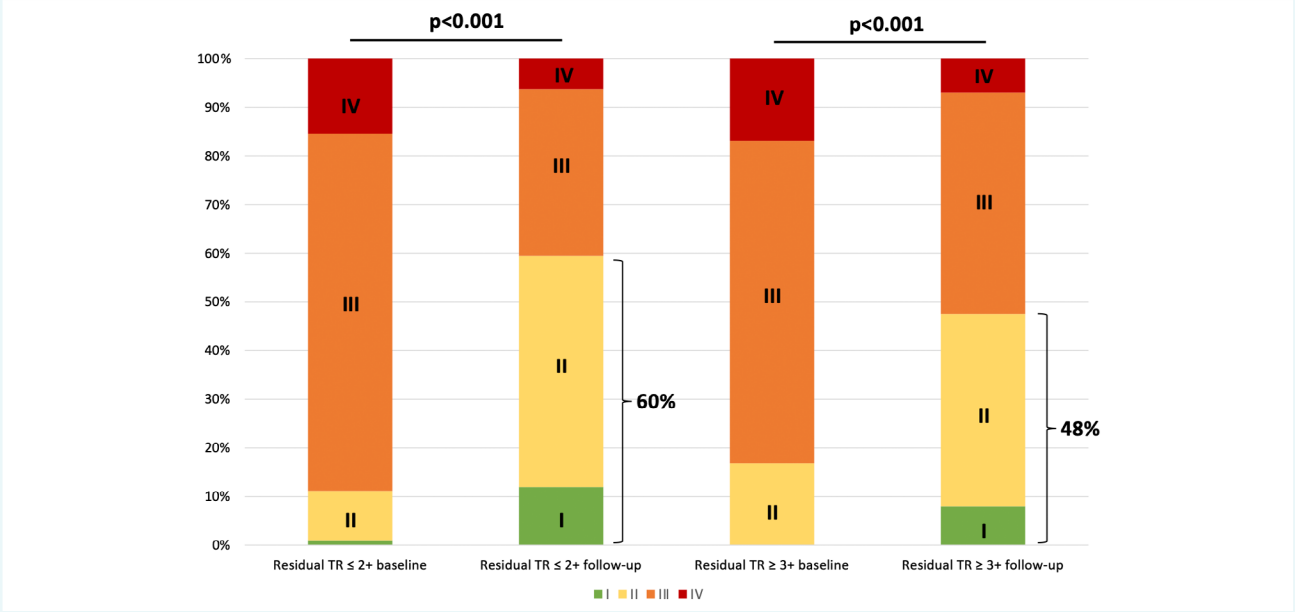


Figure 5 New York Heart Association functional class development stratified by residual tricuspid regurgitation (TR). While class was comparable irrespective of residual TR severity at follow-up, TR ≥3+ after tricuspid transcatheter edge-to-edge repair was associated with more severe heart failure symptoms.

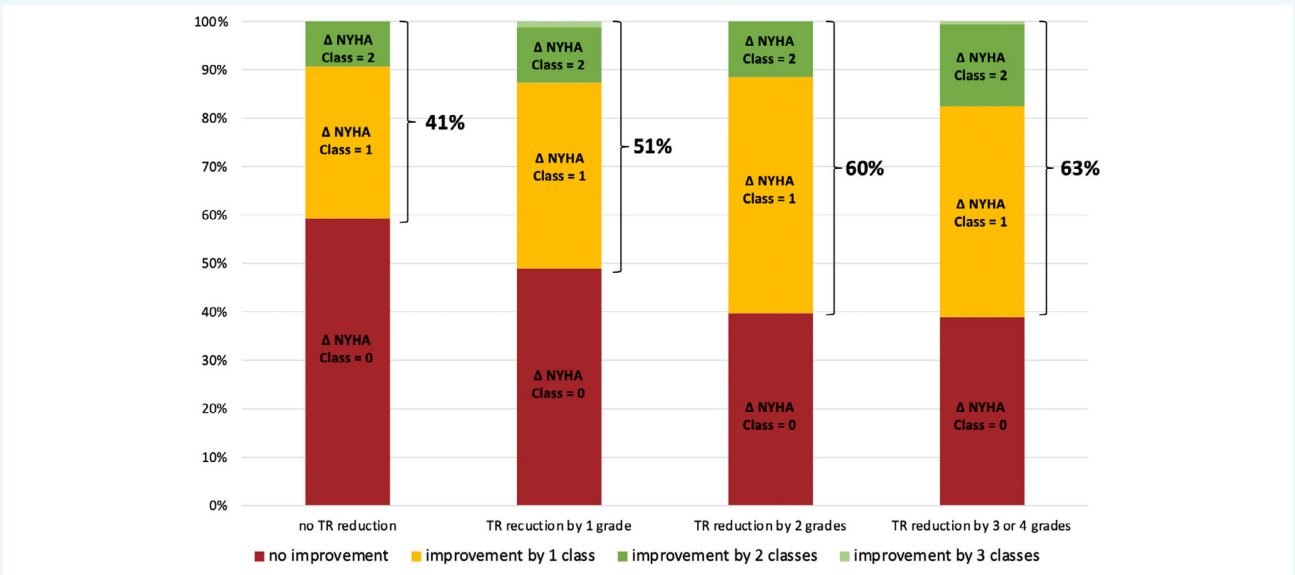


Figure 6 Correlation of tricuspid regurgitation (TR) reduction and symptomatic improvement by New York Heart Association (NYHA) class. The degree of symptomatic improvement as assessed by NYHA functional class correlated with the degree of TR reduction.

progress will provide valuable information on the significance of residual TR after transcatheter TV interventions. Results of the randomized controlled TRISCEND II study (NCT04482062) are highly anticipated to gain further insight into the importance of TR reduction and residual TR. It has been established that reducing regurgitant blood flow through the TV effectively unloads the right ventricle.[19,20] However, the necessary degree of TR reduction for sufficient volume unloading or even structural RV reverse remodelling, which may lead to favourable outcomes over a longer follow-up period, remains unclear.

However, as TTVR is currently used mainly in different patient populations with torrential TR and massive coaptation gaps (often ineligible for T-TEER),[4] direct comparisons between T-TEER and TTVR will be limited until randomized head-to-head

comparisons become available. In the near future, this may change after the EVOQUE device, which showed promising results in a non-randomized setting, recently received its CE mark and Food and Drug Administration approval.[21,22] Given the four-fold increase in residual TR ≥3+ in patients with large vena contracta and tenting areas, it could be speculated that TTVR may be a more effective treatment option than T-TEER for such patients.

Limitations

The main limitations of this study are due to its retrospective nature. Although echocardiographic analyses were not subject to core laboratory supervision, all evaluations were performed by highly experienced specialists at each centre. No information regarding the contribution of transvalvular tricuspid leads to TR were available. The EuroTR registry did not collect information regarding single leaflet device attachment or postprocedural TV inflow gradients. Even though we chose a 2-year survival follow-up, median clinical follow-up was 203 (71–409) days.

Conclusions

Tricuspid transcatheter edge-to-edge repair is effective in reducing TR severity in the majority of patients. Residual TR ≥3+ was associated with worse outcomes, while no significant differences were observed for residual TR 1+ versus 2+.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Conflict of interest: L.S. received speaker honoraria from Edwards Lifesciences. K.P.K. reports travel expenses from Edwards Lifesciences. J.v.S. received lecture honoraria from Edwards Lifesciences. W.R. received speaker honoraria from Edwards and Abbott. P.D. served as consultant for InnovHeart, Picardia, HVR, Approxima and received speaker honoraria from Abbott and Edwards. T.R. received speaker honoraria and consulting fees from AstraZeneca, Bayer, Pfizer, Daiichi Sankyo. M.B.P. received speaker fees from Abbott Vascular, Edwards Lifesciences and Venus Medtech. M.A. received consulting fees in the last 3 years from Abbott Structural Heart and Edwards Lifesciences. R.S.v.B. has received institutional grants and served as speaker to Abbott Vascular and Edwards Lifesciences. S.T. has received personal honoraria from Medtronic, Boston Scientific, Biosensors, Abbott Vascular, Medira, Shockwave, Teleflex, atHeart Medical, Cardiac Dimensions, Polares Medical, Amarin, Sanofi, AstraZeneca, ReCor Medical, Daiichi Sankyo, has received institutional research grants from Edwards Lifesciences, Boston Scientific, Fumedica, Novartis, Boehringer Ingelheim, and holds equity in Hi-D Imaging. M.M. received consulting fees in the last 3 years from Abbott Structural Heart, AstraZeneca, Bayer, Boehringer Ingelheim, Edwards Lifesciences, Roche Diagnostics. T.G. received speaker honoraria/research grants from AstraZeneca, Bayer, Bristol Myers Squibb/Pfizer, Ferrer/Chiesi, Medtronic and Edwards Lifesciences, none related to this study. R.E.L. received speaker fees from Abbott Vascular, Edwards Lifesciences, Boston Scientific and Venus Medtech. P.L. received speaker honoraria and consulting fees from AstraZeneca, Bayer, Pfizer, Edwards Lifesciences, and research honoraria from Edwards Lifesciences. F.M. received grant and/or research institutional support from Abbott, Medtronic, Edwards Lifesciences, Biotronik, Boston Scientific Corporation, NVT, Terumo, Venus, and consulting fees, honoraria personal and institutional from Abbott, Medtronic, Edwards Lifesciences, Xeltis, Cardiovalve, Occlufit, Simulands, Mtex, Venus, Squadra, Valgen Royalty Income/IP Rights Edwards Lifesciences, and is shareholder (including share options) of Magenta, Transseptalsolutions, 4Tech. F.P. received travel expenses from Edwards Lifesciences, Abbott Vascular, Polares Medical, Medira, and Siemens Healthineers. M.K. received speaker honoraria from Edwards and Abbott. D.K. has received personal fees from Abbott Medical, Edwards Lifesciences, Pi-Cardia Ltd and Medtronic Inc. V.R. received research grants from Abbott Medical, Boston Scientific, and Edwards Lifesciences. C.I. received consultant fees and travel expenses from Abbott Medical and Edwards Lifesciences. P.L. received institutional grants from Edwards Lifesciences and honoraria from Innoventrics. J.H. reports research grant support and speaker honoraria from Edwards Lifesciences. All other authors have nothing to disclose.

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Carsten Salomon[9]
Harald Lapp[9]
Tania Puscas[11]
Alain Berrebi[11]
Amir Abbas Mahabadi[12]
Florian Schindhelm[12]
Berenice Caneiro-Queija[13]
Julio C. Echarte[13]
Jürgen Schreieck[16]
Andreas Goldschmied[16]
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Natacha Rousse[18]
Samy Aghezzaf[18]
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