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CLINICAL RESEARCH
Valvular heart disease

Tricuspid regurgitation and outcomes in mitral valve transcatheter edge-to-edge repair

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Abstract

Background and Aims The association between periprocedural change in tricuspid regurgitation (TR) and outcomes in patients undergoing mitral transcatheter edge-to-edge repair (M-TEER) is unclear. This study aimed to examine the prognostic value of TR before and after M-TEER.

Methods Patients in the OCEAN-Mitral registry were divided into four groups according to baseline and post-procedure echocardiographic assessments: no TR/no TR (no TR), no TR/significant TR (new-onset TR), significant TR/no TR (normalized TR), and significant TR/significant TR (residual TR) (all represents before/after M-TEER). Tricuspid regurgitation ≥ moderate was defined as significant. The primary outcome was cardiovascular death or heart failure hospitalization. Tricuspid regurgitation pressure gradient was also evaluated.

Results The numbers of patients in each group were 2103 (no TR), 201 (new-onset TR), 504 (normalized TR), and 858 (residual TR). Baseline assessment for TR and TR pressure gradient was not associated with outcomes after M-TEER. In contrast, patients with new-onset TR had the highest adjusted risk for the primary outcome, followed by those with residual TR [compared with no TR as a reference, hazard ratio 1.83 (95% confidence interval: 1.39–2.40) for new-onset TR, 1.45 (1.23–1.72) for residual TR, and 0.82 (0.65–1.04) for normalized TR]. Similarly, from baseline to post-procedure, TR pressure gradient changes were associated with subsequent outcomes after M-TEER. New-onset and residual TR incidence was commonly associated with dilated tricuspid annulus diameter and atrial fibrillation.

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Conclusions Post-procedural TR, but not baseline TR, was associated with outcomes after M-TEER. Careful TR assessment after the procedure would provide an optimal management for concomitant significant TR in patients undergoing M-TEER.

Structured Graphical Abstract

Key Question

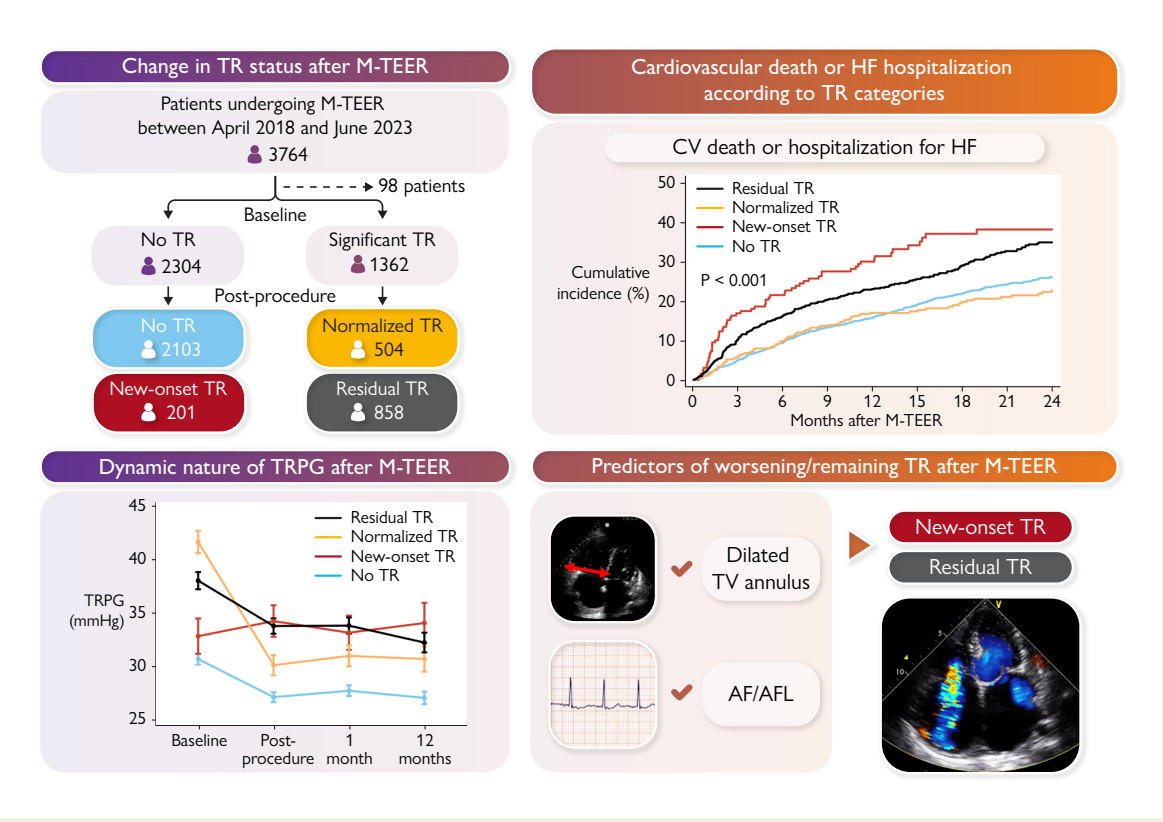
What is the evolution of tricuspid regurgitation (TR) in patients undergoing mitral transcatheter edge-to-edge repair (M-TEER)? Is it related to the subsequent outcomes?

Key Finding

Changes of TR severity between pre- and post-procedure were frequently observed in patients undergoing M-TEER. Post-procedural TR, but not baseline TR, and TR pressure gradient were associated with outcomes after M-TEER. Worsening/unchanged TR was associated with dilated tricuspid annulus diameter and the presence of atrial fibrillation/flutter.

Take Home Message

Careful TR severity monitoring after M-TEER may help guide management in this patient setting.



Change in tricuspid regurgitation and outcome after mitral transcatheter edge-to-edge repair. Change in tricuspid regurgitation pressure gradient was analysed using a linear mixed model, adjusted for the interaction between the four tricuspid regurgitation categories and visit, with a random intercept and slope per patient. AF, atrial fibrillation; AFL, atrial flutter; CV, cardiovascular; HF, heart failure; M-TEER, mitral transcatheter edge-to-edge repair; TR, tricuspid regurgitation; TRPG, tricuspid regurgitation pressure gradient; TV, tricuspid valve.

Keywords Transcatheter edge-to-edge repair • Mitral valve • Mitral regurgitation • Tricuspid regurgitation

Introduction

Tricuspid regurgitation (TR) is highly prevalent in patients with heart failure (HF) and mitral regurgitation (MR) in association with worse outcomes.[1–3] Although TR in the setting of left-sided heart disease was often conservatively managed, current international guidelines recommend more aggressive treatment of TR during mitral valve surgery, as TR does not always improve and can even worsen after surgery, affecting short- and long-term prognosis.[4,5] Additionally, previous studies showed that significant TR at baseline is associated with poor prognosis in patients undergoing mitral transcatheter edge-to-edge repair (M-TEER).[6–8] However, the limited sample size of these studies did not allow comprehensive adjustments for baseline differences to examine clinical outcomes. Moreover, little is known about the dynamic nature of TR in those

undergoing M-TEER, especially the association between periprocedural change in TR and subsequent outcomes. A serial periprocedural assessment of TR may provide a better understanding of the dynamic feature of TR pre- and post-M-TEER and could potentially gain insights regarding the optimal timing for additional intervention for TR if needed.[9]

We hypothesized that serial changes in TR after M-TEER would show a greater association with post-procedural outcomes than with TR status at baseline. Therefore, this study aimed to investigate the association between pre- and post-procedural TR and outcomes in patients undergoing M-TEER.

Methods

Study population

The Optimized CathEter vAlvular iNtervention (OCEAN)-Mitral registry is an ongoing, prospective, investigator-initiated, multicentre observational registry in patients with MR undergoing M-TEER.[10,11] A total of 21 Japanese centres participated in this registry. OCEAN-Mitral operates independently of industrial influence.

This registry enrols patients with both primary and secondary MR, and 3764 patients who underwent M-TEER with the MitraClip (Abbott Vascular Inc., Santa Clara, CA, USA) G2 or G4 system from April 2018 to June 2023 were included. Patient characteristics, procedural details, and clinical outcomes are systematically recorded. Each case was reviewed before M-TEER by a multidisciplinary heart valve team consisting of interventional cardiologists, cardiac surgeons, echocardiologists, and HF specialists. The indication for M-TEER in primary MR was a high surgical risk, while for secondary MR, it was symptomatic status despite optimal medical therapy and, if applicable, cardiac resynchronization therapy. Treatment indications followed Japanese guideline.[12]

In this study, four patient groups based on pre-procedural and post-procedural (i.e. at discharge) significant TR (≥moderate) were compared: no TR, no significant TR at baseline and post-procedure; new-onset TR, no significant TR at baseline but significant TR at post-procedure; normalized TR, significant TR at baseline but no significant TR at post-procedure; and residual TR, significant TR at baseline and post-procedure (*Structured Graphical Abstract*). Patients who did not have their pre- or post-procedural TR status recorded (78 patients) and those in whom edge-to-edge repair was attempted but did not receive it (20 patients) were excluded from this analysis.

Informed consent was obtained from all patients, and the study was approved by the relevant institutional review board and conducted in accordance with the Declaration of Helsinki principles. The study is registered with the University Hospital Medical Information Network (UMIN000023653).

Study visit, data collection, and echocardiographic assessment of mitral and tricuspid regurgitation in the OCEAN-Mitral registry

Transthoracic echocardiographic findings and laboratory data including natriuretic peptides were prospectively collected at all study visits (before and after the procedure, at 1 month and 1 year after the procedure, and every 1 year during the follow-up).

In the OCEAN-Mitral registry, MR and TR were assessed at baseline (pre-procedural), post-procedure (at discharge), 1 month after the procedure, and every 1 year after the procedure. The severity of MR and TR was evaluated based on qualitative and quantitative criteria in line with international guidelines and recent consensuses and classified as 0 (none/trivial), 1+ (mild), 2+ (moderate), 3+ (moderate to severe), or 4+ (≥severe).[13–15] Grade 2+ or higher (from moderate to ≥severe) was considered significant. Left and right heart structures and functions including TR pressure gradient (TRPG), tricuspid valve (TV) annulus diameter, tricuspid annular plane systolic excursion (TAPSE), and right ventricular fractional area change (RVFAC) were also assessed at each time frame. All patients underwent 2D transthoracic echocardiography before and after the procedure and transoesophageal echocardiography during the procedure. Echocardiographic assessments were conducted by experienced echocardiographers.

To further investigate patients with ≥severe TR at baseline ($N = 53$), we conducted a sensitivity analysis and categorized ≥severe TR into three groups according to the criteria using tricuspid vena contracta width (severe TR: 7–13 mm; massive TR: 14–20 mm; and torrential TR: ≥ 21 mm).[13,14,16]

In the OCEAN-Mitral registry, all information was prospectively collected and reported by investigators. Pre-procedural findings were used for baseline characteristics, and the date of the M-TEER procedure was the start of the study follow-up. Estimated glomerular filtration rate was calculated using the Cockcroft–Gault formula. All-cause or cardiovascular death and HF hospitalization were routinely collected, and other adverse events judged significant by local investigators (e.g. events requiring hospitalization) were also reported individually. Further information of the OCEAN-Mitral registry is available in previous studies.[10,11,17]

Outcomes examined

The primary outcome in this study was the composite of cardiovascular death or HF hospitalization. We examined each of the components of the primary outcome and all-cause death.

Statistical analysis

Patient characteristics according to the four TR categories (no TR, new-onset TR, normalized TR, and residual TR) were described using number/percentages (%) for categorical variables and the mean value (± SD) or median value with interquartile range (quartiles 1–3) for continuous variables. Pearson's χ^2 test was used to compare binary variables and analysis of variance and Kruskal–Wallis tests were used for continuous variables. Change in TRPG over time according to the four groups was examined using a linear mixed model for repeated measurements, adjusted for the interaction between the four TR categories and visit, with a random intercept and slope per patient.

Clinical outcomes for the four TR categories were reported as the number of events and rates per 100 person-years. Time-to-first events were examined by the Kaplan–Meier estimator and log-rank test. The outcomes of interest were also evaluated with Cox proportional hazard models to calculate hazard ratios (HRs) with 95% confidence intervals (CIs). Additionally, HRs were reported after adjustments for other prognostic variables including age, sex, clinical frailty scale, body mass index, New York Heart Association functional classification, diabetes mellitus, systolic blood pressure, atrial fibrillation/flutter, degenerative or functional MR, estimated glomerular filtration rate, left ventricular ejection fraction, significant aortic stenosis, significant aortic regurgitation, post-procedural mitral valve gradient, and post-procedural MR ≥ moderate.

The outcomes of interest were plotted based on the estimates from Cox proportional hazard models across TRPG at baseline as a continuous variable, using restricted cubic splines. The association between change in TRPG (as a continuous variable) from baseline to post-procedure, from baseline to 1 month after the procedure, and from baseline to 1 year after the procedure and subsequent outcomes were also examined using restricted cubic splines. The number of knots was set at 3 based on Akaike information criterion for the primary outcome. All analyses using the TRPG at 1 month and 1 year after the procedure were landmark analyses beginning at the 1-month and 1-year post-discharge visits.

To estimate the predictors of new-onset and residual TR after the procedure, the following clinically relevant prognostic variables of new-onset/residual TR were used in univariate and multivariable logistic regression models: atrial fibrillation/flutter, degenerative MR, left ventricular ejection fraction ≥ 40%, left ventricular end-diastolic volume index < 70 mL/m^2, left atrial volume index ≥ 60 mL/m^2, post-procedural MR ≥ moderate, post-procedural mitral valve gradient ≥ 4 mmHg, significant aortic stenosis

or regurgitation (≥moderate), chronic obstructive pulmonary disease, estimated glomerular filtration rate < 45 mL/min/1.73 m^2, the ratio of TAPSE/pulmonary artery systolic pressure (TAPSE/PASP) ≥ 0.42 (median), TV annulus diameter index > 21 mm/m^2, and RVFAC < 35%. Missing values in this multivariable analysis model were addressed by multiple imputation using all baseline variables listed in *Tables 1* and *2* and all outcomes examined. Logistic and multinominal logistic regressions were used to impute missing values for categorical variables, and linear regression was used for categorical variables, with 20 cycles.

As an additional analysis, outcomes according to baseline significant TR (patients without significant TR at baseline vs. patients with significant TR at baseline) were examined. A *P*-value of <.05 was considered statistically significant. All analyses were performed using STATA version 18.0 (StataCorp, College Station, TX, USA).

Results

Among 3764 patients of the OCEAN-Mitral registry, 78 who did not have their pre- or post-procedural TR status recorded and 20 in whom M-TEER was attempted but a clip was not placed were excluded from the current analysis. As a result, 3666 patients undergoing M-TEER and assessed for baseline and post-procedural TR status were included in this analysis. At baseline, significant TR was observed in 1362/3666 (37.2%). New-onset TR after M-TEER was seen in 201/2103 (9.6%) among patients without baseline TR, and residual TR in patients with TR at baseline was observed in 858/1362 (63.0%), respectively (*Structured Graphical Abstract*). Change in TR status (whether significant TR or not) from baseline to 1 year is shown in Supplementary data online, *Figure S1*. The mean (± SD) of TRPG was 34.2 ± 13.5 mmHg at baseline, 29.6 ± 9.9 mmHg at post-procedure, 30.0 ± 10.5 mmHg at 1 month after the procedure, and 28.9 ± 10.8 mmHg at 1 year after the procedure, respectively (see Supplementary data online, *Figure S2*). The median duration of follow-up of this study was 15.3 (11.1–29.2) months.

Baseline characteristics

Table 1 shows baseline characteristics according to TR categories at baseline. Patients with new-onset and residual TR were older and had higher Society of Thoracic Surgeons scores at baseline. Baseline New York Heart Association functional classification and a history of prior HF hospitalization were comparable among TR categories. Although baseline N-terminal pro-B-type natriuretic peptide was higher in patients experiencing new-onset TR and in patients with baseline TR vs. no TR group, left ventricular ejection fraction was highest in the residual TR group, followed by normalized TR and new-onset TR groups, compared with no TR group. Compared with patients in no TR group, those in the other three groups had worse renal function at baseline. A history of atrial fibrillation or flutter was more frequent in patients with residual and new-onset TR, whereas a history of myocardial infarction or angina was more frequent in no TR and normalized TR patients. Loop diuretics were most commonly used in patients in residual TR group, followed by those experiencing new-onset TR and normalized TR, compared with no TR group.

Baseline characteristics according to further categorization for ≥severe TR are shown in Supplementary data online, *Table S1*.

Echocardiographic findings and procedural outcomes

Pre- and post-procedural echocardiographic findings and procedural outcomes are shown in *Table 2*. Patients with baseline TR were more likely to have degenerative MR at baseline. Atrial functional MR was observed more often in patients with residual TR and new-onset TR than in others. Left ventricular size was smaller in patients in new-onset and residual TR groups compared with those in no TR and normalized TR groups, whereas left atrial size was largest in patients experiencing residual TR, followed by those in normalized TR and new-onset TR groups. The severity of MR at baseline was greater in patients with baseline TR, and significant aortic regurgitation was seen more in patients with baseline TR and patients with new-onset TR, compared with no TR group.

Right heart structure and function also differed according to TR categories (*Table 2*). Right ventricular size, including tricuspid annular diameter, was larger in patients who experienced new-onset TR compared with those who did not, and it was larger in patients in residual TR group vs. those in normalized TR group. Right ventricular fractional area change was lower in patients experiencing worsening TR (new-onset TR) compared with those without periprocedural TR and was also lower in patients in residual TR group vs. those in normalized TR group. By contrast, TAPSE was comparable across TR categories.

Acute procedural success, defined as the successful implantation of the device resulting in a MR severity of 2+ or less, was less frequent in patients with residual TR and new-onset TR group. The number of clips tended to be higher in patients with baseline TR compared with those without TR at baseline. Post-procedural mitral valve gradient was comparable among the TR categories, whereas post-procedural MR ≥ moderate was more frequent in patients who experienced new-onset and residual TR than the others. Post-procedural systolic reversal flow was more common in patients with new-onset TR.

Supplementary data online, *Table S2* showed echocardiographic findings and procedural outcomes according to further categorization for ≥severe TR at baseline. Among 53 patients who had ≥severe TR at baseline, 42 (79.2%) were severe TR, 9 (17.0%) were massive, and 2 (3.8%) were torrential TR, respectively. The main aetiology of this ≥severe TR was atrial functional TR (77.4%). Also, a coaptation gap was more common in massive/torrential TR compared with severe TR. Among patients with severe TR (*N* = 42), 23 (54.8%) had ≤moderate severity after the M-TEER procedure, whereas three (27.3%) of those with baseline massive/torrential TR had post-procedural ≤ moderate TR (see Supplementary data online, *Table S2*).

Outcomes according to tricuspid regurgitation categories

Unadjusted and adjusted risks of outcomes examined according to TR categories are shown in *Figure 1* and *Table 3*. Patients experiencing new-onset TR had the highest unadjusted risk of the primary outcome (cardiovascular death or HF hospitalization), followed by those with residual TR [unadjusted HR for the primary outcome was 1.70 (95% CI: 1.32–2.19) in new-onset TR group and 1.47 (95% CI: 1.27–1.70) in residual TR group, compared with no TR group as a reference] (*Table 3*). This was especially seen in HF hospitalization, and a similar trend was also seen in all-cause death (*Figure 1* and *Table 3*). These trends towards a higher risk in patients experiencing new-onset TR and residual TR were maintained after adjustment for baseline prognostic variables [adjusted HR for the primary outcome was 1.83 (95% CI: 1.39–2.40) in new-onset TR group and 1.45 (95% CI: 1.23–1.72) in residual TR group, compared with no TR group as a reference] (*Table 3*). After adjustment, patients in normalized TR group had a comparable risk of the primary outcome, compared with those in no TR group (adjusted HR 0.82, 95% CI: 0.65–1.04) (*Table 3*). Outcomes at 1 year after the procedure

Table 1 Baseline characteristics according to tricuspid regurgitation categories

	Baseline no TR		Baseline TR	
	No TR *N* = 2103	New-onset TR *N* = 201	Normalized TR *N* = 504	Residual TR *N* = 858
Age (years)	77.9 ± 9.9	80.0 ± 8.5	78.6 ± 9.3	80.8 ± 8.6
Age > 70 years	1696 (80.6)	175 (87.1)	414 (82.1)	758 (88.3)
Male	1165 (55.4)	106 (52.7)	271 (53.8)	470 (54.8)
Body surface area (m^2)	1.52 ± 0.20	1.50 ± 0.18	1.50 ± 0.19	1.49 ± 0.18
BMI (kg/m^2)	21.3 ± 3.5	21.1 ± 3.4	21.3 ± 3.6	20.8 ± 3.4
BMI category				
Normal (<25.0)	1798 (85.5)	181 (90.0)	440 (87.3)	766 (89.3)
Overweight (25–29.9)	267 (12.7)	18 (9.0)	49 (9.7)	82 (9.6)
Obesity (30≤)	38 (1.8)	2 (1.0)	15 (3.0)	10 (1.2)
NYHA III or IV	1318 (62.7)	128 (63.7)	315 (62.5)	546 (63.6)
Prior hospitalization for HF	1666 (82.1)	165 (84.2)	400 (83.0)	697 (83.3)
Clinical frailty scale ≥ 4	1051 (51.8)	115 (59.0)	260 (53.3)	513 (62.4)
STS score for mitral valve replacement	8.2 (5.1–12.3)	9.6 (6.2–16.0)	9.8 (6.0–15.3)	10.4 (7.0–15.5)
Heart rate (b.p.m.)	73.4 ± 14.9	75.9 ± 17.1	76.1 ± 16.3	75.5 ± 15.9
Systolic blood pressure (mmHg)	110.6 ± 18.8	113.2 ± 20.4	109.7 ± 18.8	108.6 ± 18.5
Systolic blood pressure < 100 mmHg	621 (29.5)	55 (27.4)	143 (28.4)	293 (34.1)
Diastolic blood pressure (mmHg)	63.9 ± 12.6	65.2 ± 13.7	65.5 ± 12.3	63.6 ± 12.5
LVEF (%)	42.9 ± 16.5	45.4 ± 17.0	45.9 ± 16.4	50.0 ± 15.5
LVEF category				
LVEF < 40%	1086 (51.7)	80 (40.2)	220 (43.7)	259 (30.2)
LVEF 40% to <50%	272 (12.9)	37 (18.6)	71 (14.1)	118 (13.8)
LVEF ≥ 50%	744 (35.4)	82 (41.2)	213 (42.3)	481 (56.1)
eGFR ($mL/min/1.73\ m^2$)	40.2 ± 20.2	37.7 ± 16.9	37.7 ± 19.4	37.9 ± 17.5
eGFR < 60 $mL/min/1.73\ m^2$	1779 (85.0)	183 (91.5)	452 (90.6)	765 (89.6)
eGFR < 45 $mL/min/1.73\ m^2$	1310 (62.6)	138 (69.0)	335 (67.1)	593 (69.4)
NT-proBNP (pg/mL)	2291 (1012–4706)	3061 (1262–5906)	3329 (1346–7441)	3121 (1629–6255)
Medical history				
Diabetes mellitus	590 (28.1)	47 (23.4)	134 (26.6)	192 (22.4)
Hypertension	1378 (65.5)	131 (65.2)	336 (66.7)	548 (63.9)
Myocardial infarction/angina	814 (38.7)	66 (32.8)	184 (36.5)	212 (24.7)
AF/AFL	1091 (51.9)	140 (69.7)	332 (65.9)	690 (80.4)
Ventricular tachycardia/fibrillation	223 (10.6)	14 (7.0)	53 (10.5)	73 (8.5)
Chronic obstructive pulmonary disease	169 (8.0)	22 (10.9)	45 (8.9)	78 (9.1)
Stroke	235 (11.2)	26 (12.9)	60 (11.9)	94 (11.0)
Dialysis	138 (6.6)	10 (5.0)	36 (7.1)	39 (4.5)
Liver cirrhosis	35 (1.7)	4 (2.0)	4 (0.8)	18 (2.1)
Treatment				
ACE-I/ARB/ARNI	1360 (65.4)	129 (64.8)	319 (64.1)	528 (62.0)

Continued

Table 1 *Continued*

	Baseline no TR		Baseline TR	
	No TR N = 2103	New-onset TR N = 201	Normalized TR N = 504	Residual TR N = 858
ACE-I	608 (29.2)	58 (29.1)	149 (29.9)	249 (29.2)
ARB	512 (24.4)	48 (23.9)	105 (20.8)	209 (24.4)
ARNI	251 (11.9)	23 (11.4)	66 (13.1)	75 (8.8)
Beta-blocker	1554 (75.2)	139 (70.2)	371 (74.6)	611 (72.2)
Mineralocorticoid receptor antagonist	1151 (54.9)	103 (51.2)	269 (53.6)	485 (56.6)
SGLT2i	444 (21.1)	43 (21.4)	126 (25.0)	150 (17.5)
Loop diuretics	1629 (77.5)	164 (81.6)	405 (80.4)	736 (85.8)
Digoxin	82 (3.9)	14 (7.0)	29 (5.8)	50 (5.8)
Anticoagulants	1091 (51.9)	134 (66.7)	308 (61.1)	670 (78.1)
Antiplatelets	941 (44.7)	64 (31.8)	187 (37.1)	216 (25.2)

ACE-I, angiotensin-converting enzyme inhibitor; AF/AFL, atrial fibrillation/flutter; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor/neprilysin inhibitor; BMI, body mass index; eGFR, estimated glomerular filtration rate; HF, heart failure; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; SGLT2i, sodium-glucose co-transporter-2 inhibitor; STS, Society of Thoracic Surgeons score.

Table 2 **Pre- and post-procedural echocardiographic findings and procedural outcomes**

	Baseline no TR		Baseline TR		
	No TR N = 2103	New-onset TR N = 201	Normalized TR N = 504	Residual TR N = 858	*P*-value
Pre-procedural findings					
Degenerative mitral regurgitation	592 (28.2)	59 (29.4)	164 (32.5)	280 (32.6)	<.05
Atrial functional mitral regurgitation	219 (10.4)	34 (16.9)	60 (11.9)	201 (23.4)	<.001
Left heart					
LVEF (%)	42.9 ± 16.5	45.4 ± 17.0	45.9 ± 16.4	50.0 ± 15.5	<.001
LVDd (cm)	57.5 ± 10.6	55.7 ± 10.3	56.9 ± 10.0	54.9 ± 9.5	<.001
LVDs (cm)	45.7 ± 13.8	42.9 ± 13.3	43.7 ± 13.3	40.2 ± 11.8	<.001
LVEDV (mL)	154.1 ± 72.1	139.8 ± 67.5	147.8 ± 70.3	129.7 ± 59.5	<.001
LVEDVI (mL/m^2)	100.9 ± 43.5	92.4 ± 39.8	97.1 ± 42.2	86.4 ± 36.5	<.001
LVESV (mL)	98.3 ± 65.4	86.2 ± 61.8	91.3 ± 63.9	72.9 ± 50.6	<.001
LVESVI (mL/m^2)	63.9 ± 40.5	56.3 ± 37.6	59.3 ± 39.3	48.1 ± 31.9	<.001
LAD (mm)	47.5 ± 8.7	49.9 ± 9.1	50.9 ± 9.5	54.0 ± 11.1	<.001
LAV (mL)	113.2 ± 55.5	135.1 ± 75.0	141.4 ± 80.7	170.3 ± 115.6	<.001
LAVI (mL/m^2)	75.0 ± 35.6	90.8 ± 50.3	94.1 ± 52.3	114.4 ± 74.6	<.001
E/A	1.6 ± 1.0	1.8 ± 1.0	2.4 ± 2.4	2.2 ± 1.1	<.001
MR grade at rest					<.001
Trivial–mild	39 (1.8)	9 (4.5)	2 (0.4)	7 (0.8)	
Moderate	295 (14.0)	24 (11.9)	43 (8.5)	58 (6.8)	
Moderate–severe	623 (29.6)	56 (27.9)	111 (22.0)	213 (24.8)	
Severe	1146 (54.5)	112 (55.7)	348 (69.0)	580 (67.6)	
MR volume (mL)	53.7 ± 24.0	51.8 ± 22.0	61.6 ± 39.7	59.6 ± 38.5	<.001
Trace MVA (m^2)	5.1 ± 1.5	5.2 ± 1.9	5.3 ± 1.4	5.5 ± 1.7	<.001
Significant AR	161 (7.7)	22 (10.9)	55 (10.9)	105 (12.2)	<.001

Continued

Table 2 *Continued*

	Baseline no TR		Baseline TR		
	No TR N = 2103	New-onset TR N = 201	Normalized TR N = 504	Residual TR N = 858	P-value
Significant AS	78 (3.9)	6 (3.2)	15 (3.1)	30 (3.7)	.84
Right heart					
RVDd-base (mm)	37.6 ± 7.6	40.4 ± 8.1	41.5 ± 8.7	43.5 ± 8.3	<.001
RVDd-mid (mm)	29.1 ± 6.6	29.9 ± 6.2	30.9 ± 7.1	31.8 ± 6.9	<.001
TV annulus diameter (mm)	31.5 ± 6.2	33.4 ± 5.6	34.1 ± 6.1	36.5 ± 6.3	<.001
TV annulus diameter index (mm/m^2)	21.0 ± 4.2	22.3 ± 3.8	22.9 ± 4.5	24.7 ± 4.2	<.001
TV annulus diameter index > 21 mm/m^2	500 (48.5)	73 (62.4)	180 (62.1)	419 (82.5)	<.001
TR grade at rest					
Moderate			457 (90.7)	531 (61.9)	
Moderate–severe			36 (7.1)	285 (33.2)	
Severe			11 (2.2)	42 (4.9)	
TRPG (mmHg)	30.8 ± 12.3	32.8 ± 10.9	41.6 ± 14.1	38.0 ± 13.7	<.001
PASP (mmHg)	36.4 ± 13.4	37.8 ± 11.6	48.6 ± 15.3	45.6 ± 15.2	<.001
RVFAC (%)	36.8 ± 10.7	38.2 ± 10.2	33.9 ± 10.8	35.9 ± 10.5	<.001
RVFAC < 35%	457 (39.6)	39 (30.7)	152 (50.2)	248 (44.3)	<.001
TAPSE (mm)	16.5 ± 4.8	16.4 ± 5.6	16.7 ± 4.9	16.4 ± 4.9	.71
TAPSE < 17 mm	906 (54.3)	95 (54.9)	231 (55.1)	405 (55.6)	.94
TAPSE/PASP	0.52 ± 0.24	0.48 ± 0.22	0.38 ± 0.18	0.40 ± 0.21	<.001
S' wave (cm/s)	10.0 ± 3.1	10.1 ± 3.2	9.6 ± 2.8	10.0 ± 3.2	.24
Procedural outcome					
Acute procedural success[a]	2038 (96.9)	190 (94.5)	485 (96.2)	801 (93.4)	<.001
Number of clips					<.001
1	1587 (75.5)	148 (73.6)	357 (70.8)	565 (65.9)	
2	500 (23.8)	46 (22.9)	143 (28.4)	276 (32.2)	
3	16 (0.8)	7 (3.5)	4 (0.8)	17 (2.0)	
Post-procedural findings (at discharge)					
Post-procedural MV gradient	2.7 ± 1.4	2.9 ± 1.4	2.6 ± 1.3	2.6 ± 1.3	.13
Post-procedural MR ≥ moderate	233 (11.1)	43 (21.4)	90 (17.9)	187 (21.8)	<.001
Post-procedural PV pattern					<.001
S wave > D wave	1268 (76.5)	100 (61.0)	266 (65.8)	443 (63.5)	
S wave < D wave	363 (21.9)	56 (34.1)	127 (31.4)	235 (33.7)	
Reverse S wave	26 (1.6)	8 (4.9)	11 (2.7)	20 (2.9)	
Post-procedural TR grade					
Moderate		187 (93.0)		598 (69.7)	
Moderate–severe		14 (7.0)		224 (26.1)	
Severe		0		36 (4.2)	

Pearson's χ^2 test was used to compare binary variables and analysis of variance and Kruskal–Wallis tests were used for continuous variables.
AR, aortic regurgitation; AS, aortic stenosis; LAD, left atrial diameter; LAV, left atrial volume; LAVI, left atrial volume index; LVDd, left ventricular diastolic diameter; LVDs, left ventricular systolic diameter; LVEDV, left ventricular end-diastolic volume; LVEDVI, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; LVESVI, left ventricular end-systolic volume index; MR, mitral regurgitation; MV, mitral valve; MVA, mitral valve area; PASP, pulmonary artery systolic pressure; PV, pulmonary venous; RVDd, right ventricular diastolic diameter; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation; TRPG, tricuspid regurgitation pressure gradient; TV, tricuspid valve.
[a]Defined as the successful implantation of the device resulting in an MR severity of 2+ or less.

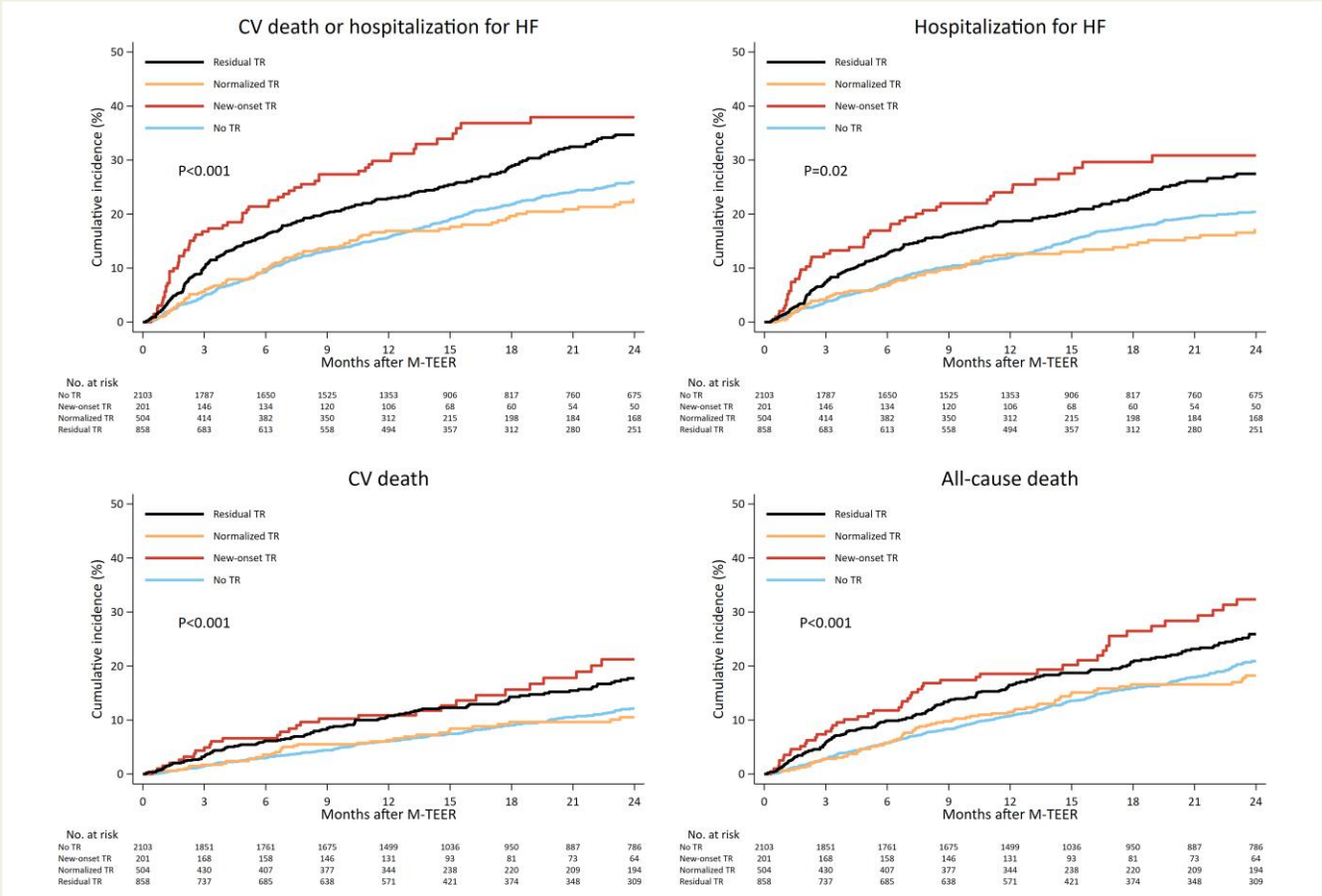


Figure 1 Cumulative incidence of each outcome according to tricuspid regurgitation categories. This figure shows the cumulative incidence of each outcome according to tricuspid regurgitation categories. CV, cardiovascular; HF, heart failure; M-TEER, mitral transcatheter edge-to-edge repair; TR, tricuspid regurgitation

according to TR categories were similar to the main findings (see Supplementary data online, *Table S3*).

By contrast, baseline significant TR was associated with a higher but weaker unadjusted risk of the primary outcome compared with patients without TR [HR 1.18 (95% CI: 1.04–1.35)] (see Supplementary data online, *Table S4* and *Figure S3*). In addition, the risk of the primary outcome was no longer significantly different compared with baseline no TR status after adjustment, and this was also consistent with the other outcomes examined (see Supplementary data online, *Table S4*).

Outcomes according to further categorization for ≥severe TR are shown in Supplementary data online, *Table S5*. Outcomes did not differ between patients with severe and massive/torrential TR at baseline.

Change in tricuspid regurgitation pressure gradient and subsequent outcomes

Structured Graphical Abstract shows the dynamic nature of TRPG after M-TEER. Although baseline TRPG was higher in patients in normalized TR (mean ± SD: 41.6 ± 14.1 mmHg) and residual TR (38.0 ± 13.7 mmHg) groups compared with those without TR at baseline (30.8 ± 12.3 for no TR group and 32.8 ± 10.9 mmHg for new-onset TR group), TRPG significantly decreased after M-TEER in three groups except for patients experiencing new-onset TR [changes from baseline to post-procedure were −3.5 ± 0.2 mmHg for no TR group ($P < .001$), 1.4 ± 0.1 mmHg for new-onset TR group ($P = .03$), −11.5 ± 0.4 mmHg for normalized TR group ($P < .001$), and −4.2 ± 0.3 mmHg for residual TR group ($P < .001$), respectively] (*Structured Graphical Abstract*).

Figure 2 shows the association between each TRPG assessment (at baseline, post-procedure, 1 month, and 1 year) and the subsequent adjusted risk of cardiovascular death or HF hospitalization. The baseline TRPG value was not associated with the adjusted risk of the primary outcome (40 mmHg was the reference). However, at post-procedure, higher TRPG appeared to be associated with a greater adjusted risk of cardiovascular death or HF hospitalization, and similar trends were also observed at 1 month and 1 year after the procedure (*Figure 2*). Similar associations between TRPG and outcomes were seen for the other outcomes, i.e. higher TRPG after M-TEER was associated with worse clinical outcomes, but it was not related to baseline TRPG (Supplementary data online, *Figures S4–S7*).

Supplementary data online, *Figures S8–S10* show the association between the change in TRPG from baseline to post-procedure, 1 month, and 1 year after the procedure and the adjusted risk of subsequent outcomes. A decrease or an increase in TRPG from baseline was associated with a lower or higher adjusted risk of the primary outcome

Table 3 Outcomes according to tricuspid regurgitation categories

	Baseline no TR		Baseline TR	
	No TR *N* = 2103	New-onset TR *N* = 201	Normalized TR *N* = 504	Residual TR *N* = 858
Cardiovascular death or HF hospitalization				
N (%)	497 (23.6)	68 (33.8)	103 (20.4)	274 (31.9)
Event rate per 100 person-years (95% CI)	16.1 (14.7–17.6)	27.8 (21.9–35.3)	14.2 (11.7–17.3)	23.7 (21.0–26.7)
HR (95% CI)	Reference	1.70 (1.32–2.19)	0.89 (0.72–1.10)	1.47 (1.27–1.70)
Adjusted HR (95% CI)[a]	Reference	1.83 (1.39–2.40)	0.82 (0.65–1.04)	1.45 (1.23–1.72)
HF hospitalization				
N (%)	373 (17.7)	53 (26.4)	73 (14.5)	208 (24.2)
Event rate per 100 person-years (95% CI)	12.0 (10.9–13.3)	21.7 (16.6–28.4)	10.1 (8.0–12.7)	17.8 (15.6–20.4)
HR (95% CI)	Reference	1.77 (1.33–2.36)	0.84 (0.65–1.08)	1.48 (1.25–1.76)
Adjusted HR (95% CI)[a]	Reference	1.95 (1.43–2.65)	0.83 (0.64–1.09)	1.48 (1.22–1.80)
Cardiovascular death				
N (%)	247 (11.8)	33 (16.4)	56 (11.1)	153 (17.8)
Event rate per 100 person-years (95% CI)	7.1 (6.3–8.1)	11.0 (7.8–15.5)	7.1 (5.4–9.2)	11.2 (9.6–13.2)
HR (95% CI)	Reference	1.55 (1.08–2.23)	0.99 (0.74–1.33)	1.57 (1.28–1.92)
Adjusted HR (95% CI)[a]	Reference	1.53 (1.04–2.26)	0.85 (0.62–1.16)	1.53 (1.22–1.93)
All-cause death				
N (%)	443 (21.1)	58 (28.9)	94 (18.7)	237 (27.6)
Event rate per 100 person-years (95% CI)	12.8 (11.7–14.1)	19.4 (15.0–25.1)	11.9 (9.7–14.5)	17.3 (15.2–19.6)
HR (95% CI)	Reference	1.52 (1.15–1.99)	0.93 (0.74–1.16)	1.35 (1.15–1.58)
Adjusted HR (95% CI)[a]	Reference	1.36 (1.01–1.84)	0.81 (0.64–1.04)	1.23 (1.02–1.47)

CI, confidence interval; CV, cardiovascular; HF, heart failure; HR, hazard ratio; TR, tricuspid regurgitation.
[a]The Cox models are adjusted for age, sex, clinical frailty scale, body mass index, NYHA, diabetes mellitus, systolic blood pressure, atrial fibrillation/flutter, degenerative mitral regurgitation, estimated glomerular filtration rate, left ventricular ejection fraction, significant aortic stenosis, significant aortic regurgitation, post-procedural mitral valve gradient ≥ 4 mmHg, and post-procedural mitral regurgitation ≥ moderate.

(see Supplementary data online, *Figures S8–S10*). These associations were similar to those seen in the other outcomes.

Prediction of worsening and remaining tricuspid regurgitation after mitral transcatheter edge-to-edge repair

Although the predictors related to the left heart differed between new-onset and residual TR after M-TEER, dilated TV annulus diameter (TV annulus diameter index > 21 mm/m^2) and the presence of atrial fibrillation or flutter appeared to be commonly associated with the incidence of worsening and remaining TR after the procedure (*Table 4*). In patients without TR at baseline, left atrial enlargement and post-procedural MR severity were related to the incidence of new-onset TR. By contrast, left ventricular status (smaller left ventricle and preserved LVEF) and the aetiology of MR were associated with remaining TR after M-TEER in patients with baseline TR (*Table 4*). Tricuspid annular plane systolic excursion/PASP and RVFAC were not independently associated with the incidence of new-onset or residual TR after the procedure.

Discussion

In this large-scale analysis of 3666 patients undergoing M-TEER, the key findings are as follows: (i) significant TR (≥moderate) was common and observed in 37% at baseline in patients undergoing M-TEER; (ii) baseline TR was associated with a higher 'unadjusted' risk of the primary outcome, but it was weak and diminished after a comprehensive adjustment; (iii) 8.7% (201/2304) of patients without significant TR and 63.0% (858/1362) of those with significant TR at baseline experienced new-onset and residual TR after M-TEER, respectively; (iv) the presence of post-procedural TR (i.e. new-onset TR and residual TR) was clearly associated with worse outcomes, especially new-onset TR; (v) TRPG at baseline was not associated with outcomes, whereas post-procedural TRPG and change in TRPG from baseline to post-procedure were associated with higher adjusted risks; and (vi) worsening and remaining TR were commonly linked to dilated TV annulus diameter and the presence of atrial fibrillation/flutter. Left atrial/ventricular dimension, post-procedural MR status, and MR aetiology were also associated with new-onset or residual TR after M-TEER.

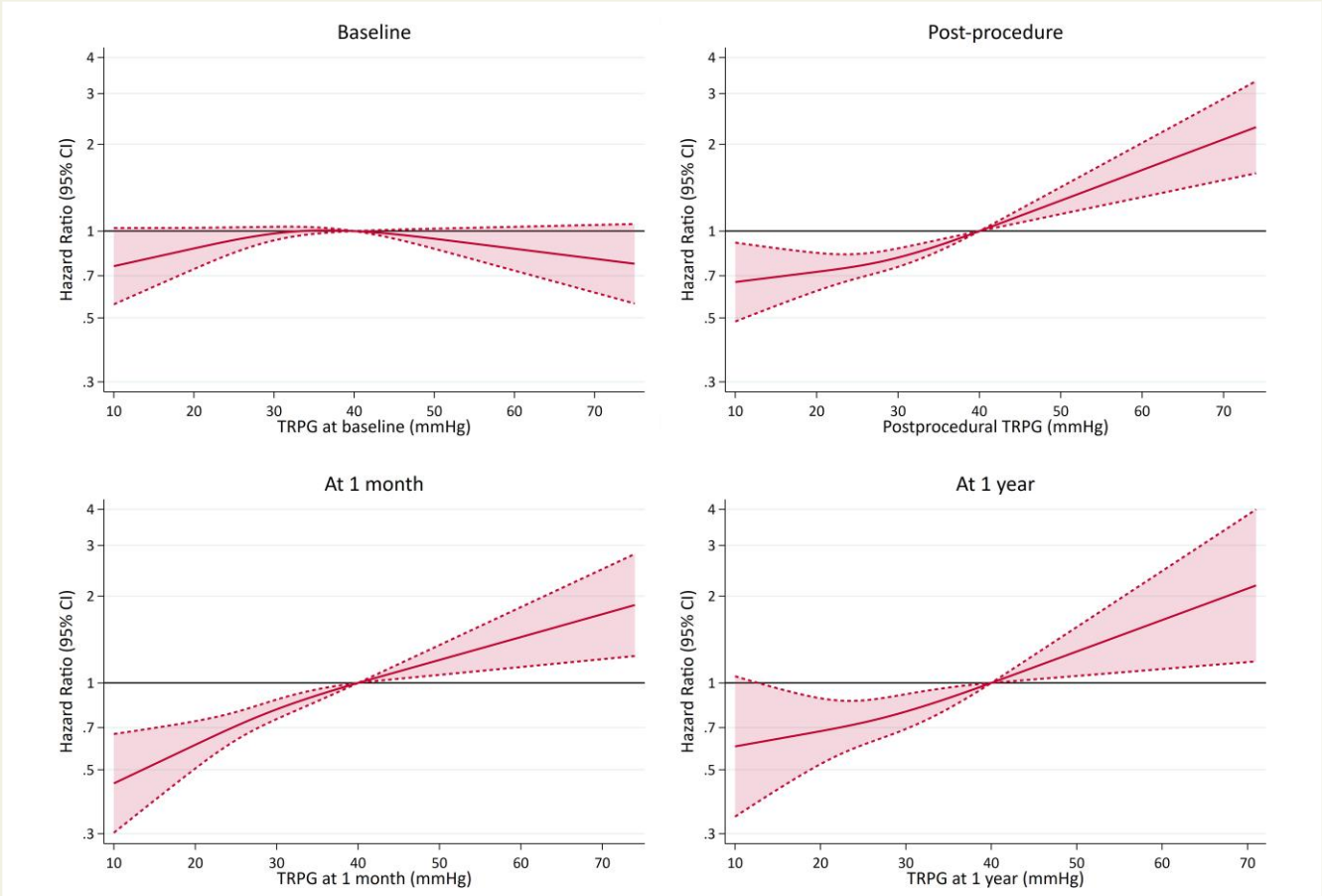


Figure 2 Tricuspid regurgitation pressure gradient assessments and adjusted risk of the primary outcome. This figure shows the association between tricuspid regurgitation pressure gradient value and the adjusted risk of cardiovascular death or heart failure hospitalization, adjusted for age, sex, clinical frailty scale, body mass index, New York Heart Association functional classification, diabetes mellitus, systolic blood pressure, atrial fibrillation/flutter, degenerative or functional mitral regurgitation, estimated glomerular filtration rate, left ventricular ejection fraction, significant aortic stenosis, significant aortic regurgitation, and postoperative significant mitral regurgitation. Analyses using the tricuspid regurgitation pressure gradient at 1 month and 1 year were landmark analyses beginning at the 1-month and 1-year post-procedure visits. TRPG, tricuspid regurgitation pressure gradient

Although several previous studies showed the association between baseline significant TR and worse outcomes after M-TEER,[6–8] they included a limited number of participants (from 139 to 169 patients) to perform a robust adjustment. In this analysis, we demonstrated that baseline TR status was not independently associated with outcomes, and post-procedural TR was more important in predicting subsequent outcomes after M-TEER. This analysis is supported by a previous retrospective study ($N = 503$), which showed the importance of post-procedural TR status to predict future all-cause death.[18] We also found that new-onset TR was more associated with a higher risk of the primary outcome (especially HF hospitalization), than residual TR. Similarly, a decrease or an increase in TRPG from baseline to post-procedure was associated with a lower or higher adjusted risk of the primary outcome.

In this analysis, we also found that the change in TRPG was drastic between before and after M-TEER. Except for the new-onset TR group, patients in the other groups experienced a significant reduction in TRPG after M-TEER, even in patients with residual TR. This finding might explain the higher risk in patients with new-onset TR compared with those with residual TR; i.e. even in those with residual TR, most patients would experience a certain improvement in TR, as MR improved, different from those with new-onset TR. Indeed, the severity of TR improved from baseline to post-procedure in patients with residual TR, and an increase in the proportion of patients with moderate TR was observed (from 61.9% at baseline to 69.7% at post-procedure). In addition, serial assessment of TRPG showed that a substantial reduction after M-TEER, especially seen in the normalized TR group, was maintained until 1 year after the procedure.

Although there is no clear guidance regarding transcatheter intervention for concomitant TR, an additional transcatheter intervention to TR might be beneficial in patients undergoing M-TEER,[19,20] as with intervention to concomitant TR improving outcomes after mitral valve surgery.[4,5] However, given the drastic periprocedural changes in TR status and the unclear association between baseline TR and outcomes, simultaneous intervention without post-procedural TR assessment should not be routinely performed, even if a combined mitral and tricuspid valve transcatheter edge-to-edge repair has a similar procedure risk to M-TEER alone.[19,20] Close monitoring of TR status after the procedure would play an important role in considering the optimal timing and identifying the appropriate target for an additional intervention to concomitant TR in patients undergoing M-TEER.

Table 4 Factors associated with post-procedural new-onset and residual tricuspid regurgitation

	New-onset TR in patients without TR at baseline[a]				Residual TR in patients with TR at baseline[b]			
	Univariate		Multivariable		Univariate		Multivariable	
	Odds ratio	*P*-value	Odds ratio	*P*-value	Odds ratio	*P*-value	Odds ratio	*P*-value
AF/AFL	2.13 (1.56–2.91)	<.001	1.66 (1.19–2.31)	<.01	2.13 (1.66–2.73)	<.001	1.73 (1.32–2.27)	<.001
Functional MR	0.94 (0.69–1.30)	.72	[c]		1.00 (0.79–1.26)	.97	1.42 (1.05–1.91)	.02
LVEF ≥ 50%	1.30 (0.96–1.74)	.09	[c]		1.74 (1.40–2.18)	<.001	1.67 (1.23–2.25)	.001
LVEDVI < 70 mL/m^2	1.25 (0.91–1.72)	.16	[c]		1.70 (1.34–2.17)	<.001	1.43 (1.08–1.90)	.01
LAVI ≥ 60 mL/m^2	2.99 (2.04–4.38)	<.001	2.35 (1.57–3.53)	<.001	1.49 (1.12–1.99)	<.01	[c]	
Post-procedural MR ≥ moderate	2.18 (1.51–3.13)	<.001	1.92 (1.31–2.81)	.001	1.28 (0.97–1.69)	.08	[c]	
Post-procedural MV gradient ≥ 4 mmHg	1.47 (1.05–2.08)	.03	1.45 (1.01–2.08)	.04	0.97 (0.72–1.29)	.83	[c]	
Significant AS or AR at baseline	1.17 (0.75–1.81)	.49	[c]		1.20 (0.88–1.66)	.25	[c]	
Chronic obstructive pulmonary disease	1.41 (0.88–2.25)	.16	[c]		1.02 (0.69–1.50)	.92	[c]	
eGFR < 45 mL/min/1.73 m^2	1.33 (0.97–1.81)	.08	[c]		1.10 (0.87–1.40)	.41	[c]	
TAPSE/PASP ≥ 0.42 (median)	0.70 (0.52–0.96)	.03	[c]		1.27 (0.99–1.62)	.05	[c]	
TV annulus diameter index > 21 mm/m^2	1.99 (1.36–2.90)	<.001	1.72 (1.20–2.46)	<.01	2.36 (1.73–3.22)	<.001	2.35 (1.69–3.27)	<.001
RVFAC < 35%	0.74 (0.51–1.06)	.10	0.65 (0.43–0.99)	.04	0.73 (0.56–0.96)	.02	[c]	

Logistic regression analyses were performed using imputed data.
AF/AFL, atrial fibrillation/flutter; AR, aortic regurgitation; AS, aortic stenosis; DMR, degenerative mitral regurgitation; eGFR, estimated glomerular filtration rate; LAVI, left atrial volume index; LVEDVI, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; MV, mitral valve; RVFAC, right ventricular fractional area change; TAPSE, tricuspid annular plane systolic excursion; TV, tricuspid valve.
[a]Examined in patients without significant TR at baseline.
[b]Examined in patients with significant TR at baseline.
[c]Not statistically significant.

By contrast, the aetiology of TR should be considered in the assessment of concomitant TR because the benefits of additional intervention would differ according to background pathologies.[14,21,22] For instance, only the correction of TR might not improve their outcomes in patients with pre-capillary pulmonary hypertension. To assess the severity of pulmonary hypertension and clarify whether TR is ventricular- or atrial-based TR, other modalities such as right heart catheterization would be important to appropriately manage patients with TR.[14,21,22]

As another novel finding, dilated TV annulus diameter (>21 mm/m^2 for index) was related to the incidence of both new-onset and residual TR, rather than other right heart assessments such as RVFAC and right ventricular pulmonary artery coupling (TAPSE/PASP). Functional TR mainly results from TV annulus dilatation with right atrial and ventricular remodelling, and it is also closely associated with the presence of atrial fibrillation/flutter, the severity of left-sided valve disease, and left atrial enlargement.[23,24] As in patients undergoing mitral valve surgery, right valvular pathology should be carefully assessed in patients undergoing M-TEER, as worsening and remaining TR are associated with worse HF outcomes and impaired functional capacity.[24]

The OCEAN-Mitral registry is a prospective study, whereas this is a *post hoc* analysis. Although we conducted a comprehensive adjustment using baseline prognostic variables, there would still be confounding factors that could influence our results, especially in the analysis of the association between TRPG at 1 month and 1 year after the procedure and subsequent outcomes. Although the echocardiogram and its assessment were performed by experienced echocardiographers, and they were reviewed by experienced certified interventional imagers in each hospital, it should be acknowledged that the echocardiographic findings in this study were not reviewed by an independent core laboratory. Quality-of-life questionnaire specifically designed for patients with cardiovascular disease (e.g. Kansas City Cardiomyopathy Questionnaire score) was not collected in this registry. In the current analysis, outcomes examined did not differ between patients with severe and massive/torrential TR. However, these results might be due to a small number of patients with massive or torrential TR in this study cohort (only 11 patients). Further research is needed to address these limitations.

Baseline significant TR was frequently observed in patients undergoing M-TEER and remained common after the procedure. By contrast, the change in TR was drastic in some patients, with either substantial improvement or significant exacerbation in TR status. Notably, assessment of TR at baseline was not associated with outcomes, but serial changes in TR grade and TRPG after M-TEER were linked to subsequent outcomes. Serial assessment of TR should be performed in patients undergoing M-TEER, especially those with dilated TV annulus diameter and atrial fibrillation/flutter. Our findings would not support routinely performing simultaneous intervention to TR at the same time as M-TEER. Careful, close monitoring after the procedure would provide an optimal management for concomitant TR in patients undergoing M-TEER.

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Supplementary data

Supplementary data are available at *European Heart Journal* online.

Declarations

Disclosure of Interest

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Data Availability

Due to the nature of this research, participants of this study did not agree for their data to be shared publicly; therefore, supporting data are not available.

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Ethical Approval

Informed consent was obtained from all patients, and the study was approved by the relevant institutional review board and conducted in accordance with the Declaration of Helsinki principles.

Pre-registered Clinical Trial Number

The study is registered with the University Hospital Medical Information Network (UMIN000023653).

References

1. Adamo M, Chioncel O, Benson L, Shahim B, Crespo-Leiro MG, Anker SD, *et al.* Prevalence, clinical characteristics and outcomes of heart failure patients with or without isolated or combined mitral and tricuspid regurgitation: an analysis from the ESC-HFA Heart Failure Long-Term Registry. *Eur J Heart Fail* 2023;**25**:1061–71. https://doi.org/10.1002/ejhf.2929
2. Shiran A, Sagie A. Tricuspid regurgitation in mitral valve disease incidence, prognostic implications, mechanism, and management. *J Am Coll Cardiol* 2009;**53**:401–8. https://doi.org/10.1016/j.jacc.2008.09.048
3. Arsalan M, Walther T, Smith RL II, Grayburn PA. Tricuspid regurgitation diagnosis and treatment. *Eur Heart J* 2017;**38**:634–8. https://doi.org/10.1093/eurheartj/ehv487
4. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, *et al.* 2021 ESC/EACTS guidelines for the management of valvular heart disease. *Eur Heart J* 2022;**43**:561–632. https://doi.org/10.1093/eurheartj/ehab395
5. Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP III, Gentile F, *et al.* 2020 ACC/AHA guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. *Circulation* 2021;**143**:e35–71. https://doi.org/10.1161/CIR.0000000000000932
6. Giannini C, Fiorelli F, Colombo A, De Carlo M, Weisz SH, Agricola E, *et al.* Right ventricular evaluation to improve survival outcome in patients with severe functional mitral regurgitation and advanced heart failure undergoing MitraClip therapy. *Int J Cardiol* 2016;**223**:574–80. https://doi.org/10.1016/j.ijcard.2016.08.189
7. Yzeiraj E, Bijuklic K, Tiburtius C, Witt J, Krause K, Steude J, *et al.* Tricuspid regurgitation is a predictor of mortality after percutaneous mitral valve edge-to-edge repair. *EuroIntervention* 2017;**12**:e1817–24. https://doi.org/10.4244/EIJ-D-16-00909
8. Ohno Y, Attizzani GF, Capodanno D, Cannata S, Dipasqua F, Immé S, *et al.* Association of tricuspid regurgitation with clinical and echocardiographic outcomes after percutaneous mitral valve repair with the MitraClip system: 30-day and 12-month follow-up from the GRASP registry. *Eur Heart J Cardiovasc Imaging* 2014;**15**:1246–55. https://doi.org/10.1093/ehjci/jeu114

9. Sisinni A, Taramasso M, Praz F, Metra M, Agricola E, Margonato A, *et al.* Concomitant transcatheter edge-to-edge treatment of secondary tricuspid and mitral regurgitation: an expert opinion. *JACC Cardiovasc Interv* 2023;**16**:127–39. https://doi.org/10.1016/j.jcin.2022.11.022
10. Saji M, Yamamoto M, Kubo S, Asami M, Enta Y, Shirai S, *et al.* Short-term outcomes following transcatheter edge-to-edge repair: insights from the OCEAN-Mitral registry. *JACC Asia* 2023;**3**:766–73. https://doi.org/10.1016/j.jacasi.2023.06.008
11. Kubo S, Yamamoto M, Saji M, Asami M, Enta Y, Nakashima M, *et al.* One-year outcomes and their relationship to residual mitral regurgitation after transcatheter edge-to-edge repair with MitraClip device: insights from the OCEAN-Mitral registry. *J Am Heart Assoc* 2023;**12**:e030747. https://doi.org/10.1161/JAHA.123.030747
12. Izumi C, Eishi K, Ashihara K, Arita T, Otsuji Y, Kunihara T, *et al.* JCS/JSCS/JATS/JSVS 2020 guidelines on the management of valvular heart disease. *Circ J* 2020;**84**:2037–119. https://doi.org/10.1253/circj.CJ-20-0135
13. Zoghbi WA, Adams D, Bonow RO, Enriquez-Sarano M, Foster E, Grayburn PA, *et al.* Recommendations for noninvasive evaluation of native valvular regurgitation: a report from the American Society of Echocardiography developed in collaboration with the Society for Cardiovascular Magnetic Resonance. *J Am Soc Echocardiogr* 2017;**30**:303–71. https://doi.org/10.1016/j.echo.2017.01.007
14. Hahn RT, Badano LP, Bartko PE, Muraru D, Maisano F, Zamorano JL, *et al.* Tricuspid regurgitation: recent advances in understanding pathophysiology, severity grading and outcome. *Eur Heart J Cardiovasc Imaging* 2022;**23**:913–29. https://doi.org/10.1093/ehjci/jeac009
15. Dreyfus J, Lancellotti P, Burwash IG, Messika-Zeitoun D. Refining the grading of tricuspid regurgitation: enhancing outcome prediction and patient management. *Eur Heart J Cardiovasc Imaging* 2024;**25**:1085–6. https://doi.org/10.1093/ehjci/jeae141
16. Hahn RT, Zamorano JL. The need for a new tricuspid regurgitation grading scheme. *Eur Heart J Cardiovasc Imaging* 2017;**18**:1342–3. https://doi.org/10.1093/ehjci/jex139
17. Tokuda T, Yamamoto M, Kagase A, Shimura T, Yamaguchi R, Saji M, *et al.* Clinical impact of baseline frailty status and residual mitral regurgitation after transcatheter edge-to-edge repair: insights from the OCEAN-Mitral registry. *J Am Heart Assoc* 2024;**13**:e035109. https://doi.org/10.1161/JAHA.124.035109
18. Adamo M, Pagnesi M, Ghizzoni G, Estévez-Loureiro R, Raposeiras-Roubin S, Tomasoni D, *et al.* Evolution of tricuspid regurgitation after transcatheter edge-to-edge mitral valve repair for secondary mitral regurgitation and its impact on mortality. *Eur J Heart Fail* 2022;**24**:2175–84. https://doi.org/10.1002/ejhf.2637
19. Besler C, Blazek S, Rommel KP, Noack T, von Roeder M, Luecke C, *et al.* Combined mitral and tricuspid versus isolated mitral valve transcatheter edge-to-edge repair in patients with symptomatic valve regurgitation at high surgical risk. *JACC Cardiovasc Interv* 2018;**11**:1142–51. https://doi.org/10.1016/j.jcin.2018.04.010
20. Mehr M, Karam N, Taramasso M, Ouarrak T, Schneider S, Lurz P, *et al.* Combined tricuspid and mitral versus isolated mitral valve repair for severe MR and TR: an analysis from the TriValve and TRAMI registries. *JACC Cardiovasc Interv* 2020;**13**:543–50. https://doi.org/10.1016/j.jcin.2019.10.023
21. Maisano F, Hahn R, Sorajja P, Praz F, Lurz P. Transcatheter treatment of the tricuspid valve: current status and perspectives. *Eur Heart J* 2024;**45**:876–94. https://doi.org/10.1093/eurheartj/ehae082
22. Hahn RT, Brener MI, Cox ZL, Pinney S, Lindenfeld J. Tricuspid regurgitation management for heart failure. *JACC Heart Fail* 2023;**11**:1084–102. https://doi.org/10.1016/j.jchf.2023.07.020
23. Patel KM, Kumar NS, Neuburger PJ, Desai RG, Krishnan S. Functional tricuspid regurgitation in patients with chronic mitral regurgitation: an evidence-based narrative review. *J Cardiothorac Vasc Anesth* 2022;**36**:1730–40. https://doi.org/10.1053/j.jvca.2021.05.032
24. Dreyfus GD, Martin RP, Chan KM, Dulguerov F, Alexandrescu C. Functional tricuspid regurgitation: a need to revise our understanding. *J Am Coll Cardiol* 2015;**65**:2331–6. https://doi.org/10.1016/j.jacc.2015.04.011