

ORIGINAL RESEARCH

STRUCTURAL

Tricuspid Regurgitation Disease Stages and Treatment Outcomes After Transcatheter Tricuspid Valve Repair



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ABSTRACT

BACKGROUND Tricuspid transcatheter edge-to-edge repair (T-TEER) has emerged as a treatment option for patients with severe tricuspid regurgitation (TR). However, randomized trials have not shown a survival benefit, possibly because of the inclusion of patients in an early or too advanced disease stage.

OBJECTIVES The authors sought to investigate the association between disease stage and outcomes following T-TEER.

METHODS In total, 1,885 patients with significant TR were analyzed, including 585 conservatively treated individuals and 1,300 patients who received T-TEER. Patients were evaluated as part of the prospective EuroTR (European Registry of Transcatheter Repair for Tricuspid Regurgitation) registry and grouped into early, intermediate, and advanced disease stage. Disease stage was based on left and right ventricular function, renal function, and natriuretic peptide levels. The stratification was validated in an external cohort. The primary endpoint was 1-year mortality.

RESULTS Overall, 395 patients (21% [395/1,885]) were categorized as early, 1,173 patients (62% [1,173/1,885]) as intermediate, and 317 patients (17% [317/1,885]) as advanced disease stage. In patients with early and advanced disease, mortality did not differ between interventional and conservative treatment (early-stage HR: 0.78; 95% CI: 0.34-1.80; $P = 0.54$; advanced stage HR: 1.06; 95% CI: 0.71-1.60; $P = 0.78$). However, mortality was significantly lower in patients undergoing percutaneous treatment with intermediate disease stage (HR: 0.73; 95% CI: 0.52-0.99; $P = 0.03$).

CONCLUSIONS Compared to medically treated controls, T-TEER was associated with 1-year survival at intermediate stage disease but not at early or advanced disease stages. The timing of T-TEER with regard to disease stages might be crucial to optimize treatment benefits. (JACC Cardiovasc Interv. 2025;18:339-348) © 2025 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

**ABBREVIATIONS
AND ACRONYMS****HF** = heart failure**RCT** = randomized controlled trial**TR** = tricuspid regurgitation**T-TEER** = tricuspid transcatheter edge-to-edge repair

For many decades, tricuspid regurgitation (TR) was considered a relatively benign condition. However, recent evidence indicated that it is associated with high morbidity and mortality.^{1–3} In symptomatic, isolated severe TR, surgical therapy is indicated; however, surgery is infrequently performed because the perioperative morbidity is considerably elevated, pre-existing right ventricular dysfunction remains a major concern, and randomized controlled trial (RCT) data to support surgical treatment do not exist.^{4,5} Tricuspid transcatheter edge-to-edge repair (T-TEER) has recently received guideline recognition for cases in which the heart team deems the surgical risk prohibitive.⁴ However, results from the only RCT (TRILUMINATE Pivotal [Trial to Evaluate Cardiovascular Outcomes in Patients Treated with the Tricuspid Valve Repair System Pivotal; NCT03904147]) that compared T-TEER to conservative therapy did not find that T-TEER affected survival or heart failure (HF) hospitalization but resulted in a relevant symptomatic improvement.⁶ The symptomatic benefit led to an overall positive study result, which was based on a win ratio analysis for the combined endpoint of mortality, need for tricuspid valve surgery, HF hospitalization, and change in quality of life (Kansas City Cardiomyopathy Questionnaire score) at 12 months.

This failure to establish a beneficial effect on HF hospitalization or survival stood in contrast to multiple matched registry analyses that suggested beneficial

effects on these outcomes.^{7–9} Although these analyses may be prone to bias and propensity matching is subject to major limitations, the inconsistent results might stem from differences in the study populations.¹⁰ Of note, the rates of prior HF hospitalization, prevalence of NYHA functional classes III and IV, comorbidities, and mortality were significantly higher in these registry analyses compared to the TRILUMINATE Pivotal trial.^{6,11} Thus, these cohorts might vary in preprocedural risk profiles and TR-associated disease severity, which in turn suggests that treatment effects may be dependent on disease stage. This may be an especially important consideration in TR because it is a progressive disease, and clinical presentation eminently predicts outcome. Ventricular failure, splanchnic volume overload, renal failure, and hepatic congestion significantly contribute to TR-associated morbidity and mortality.^{12–16}

In order to reconcile prior registry and RCT data and to guide patient selection for future clinical trials, this study aimed to stratify TR patients according to disease stage and to compare the outcomes of those who underwent T-TEER with those who were medically managed. Stratification of the patients was performed according to a multiparameter score that took into consideration cardiac and systemic criteria.

METHODS

The study adhered to the principles set forth in the Declaration of Helsinki. Local ethics committee

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

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approvals were obtained, including for retrospective data collection.

STUDY POPULATION AND THE DATA COLLECTION:

T-TEER COHORTS. The EuroTR (European Registry of Transcatheter Repair for Tricuspid Regurgitation; [NCT06307262](#)) registry focused on patients who underwent T-TEER for symptomatic TR between 2016 and 2022 at 12 European study sites. Patients who lacked essential information about TR severity before or after the procedure were not included in the present analysis. Before the T-TEER procedure, all patients remained symptomatic despite being on the maximum tolerated doses of diuretic medications. The decision to pursue an interventional treatment approach was reached after consultations with an interdisciplinary heart team consisting of HF specialists, cardiac surgeons, and interventional cardiologists. Clinical and echocardiographic baseline and follow-up data were retrospectively collected. Clinical follow-up was performed via clinical visits and/or phone consultation.

The bRIGHT EU PAS (An Observational Real-World Study Evaluating Severe Tricuspid Regurgitation Patients Treated With the Abbott TriClip Device; [NCT04483089](#)),¹¹ a prospective, single-arm, open-label, multicenter, postmarket registry that evaluated the performance of T-TEER in a contemporary real-world setting, served as a validation cohort for the TR disease staging. A total of 511 consecutive patients were enrolled at 26 sites in Europe. The study was approved by local ethics committees and the respective health authorities of the participating countries. All subjects provided written informed consent.

STUDY POPULATION: CONSERVATIVELY TREATED TR COHORT.

Patients with severe TR were assessed at Charité Medical University, specifically at Campus Charité Mitte and Benjamin Franklin, from 2010 to 2017, and their data were retrospectively collected for this study. To be included in this study, patients had to have at least severe TR, and their TR had to be of functional origin.

All patients in this cohort study received treatment in accordance with established medical guidelines. Follow-up information was gathered by contacting the relevant local registration offices.

DEVICE AND PROCEDURE. The T-TEER procedure was conducted using either the PASCAL device (Edwards Lifesciences) or the TriClip system (Abbott).

DEFINITIONS. Patients were stratified into 3 disease stages based on a multiparameter score. The score was designed to include multiple TR-related parameters. To this aim, parameters of left and right

ventricular function (left ventricular ejection fraction and tricuspid annular systolic plane excursion, respectively), a marker of end-organ failure as measured by estimated glomerular filtration rate, and markers of heart failure (N-terminal pro-B-type natriuretic peptide or B-type natriuretic peptide) were classified into a 3-tier score ([Central Illustration](#)). A disease severity scoring system was generated, and patients were stratified accordingly. A score of 4 to 6 was classified as early disease, a score of 7 to 9 as intermediate disease, and a score of 10 to 12 as advanced disease ([Central Illustration](#)).

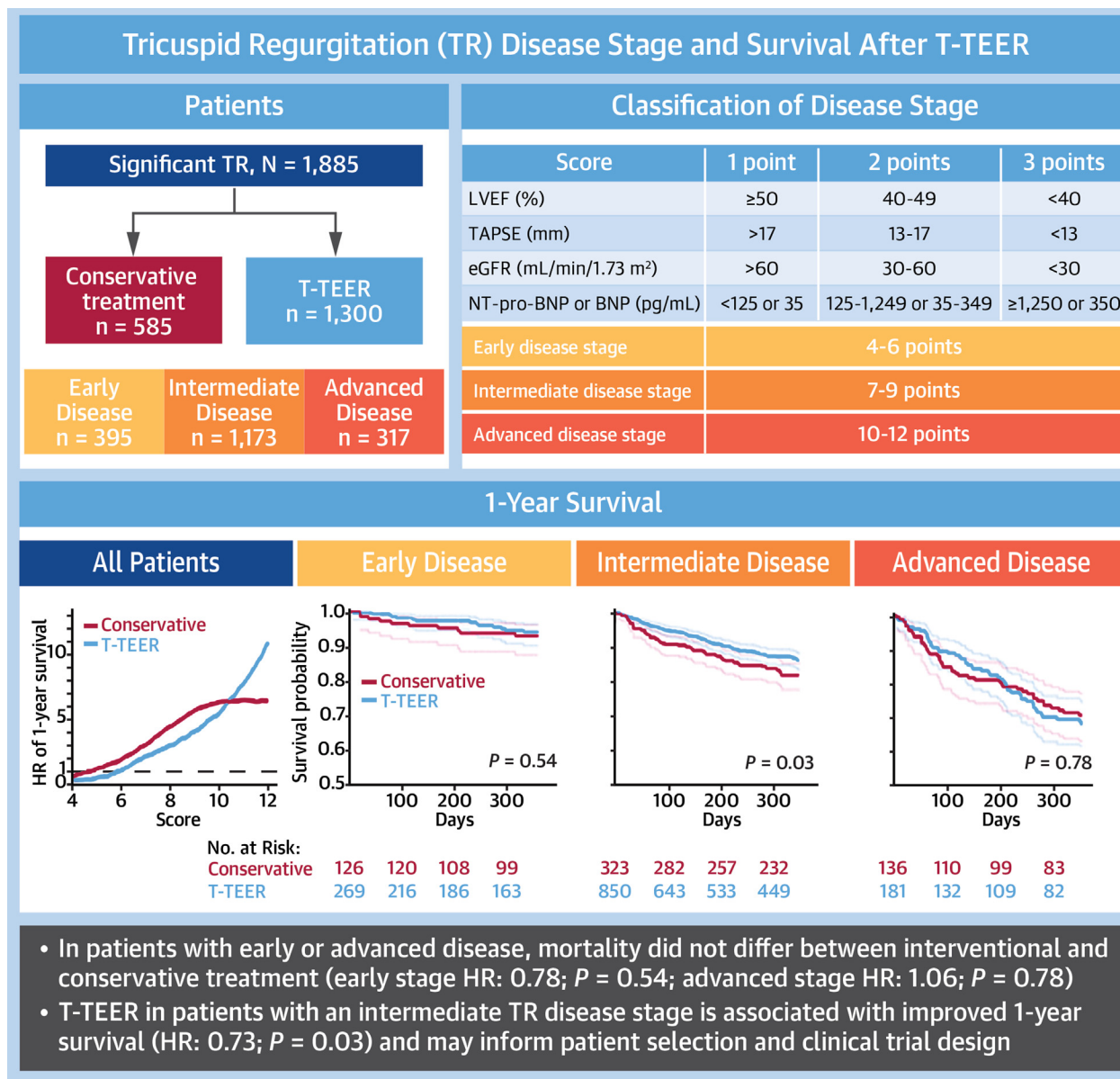
TR severity was assessed using a 5-grade scale: mild (grade 1), moderate (grade 2) severe (grade 3), massive (grade 4), and torrential (grade 5).¹⁷ Procedural success was defined as successful device implantation, delivery system retrieval, and a resultant residual TR grade ≤ 2 . Definitions were consistent with the Tricuspid Valve Academic Research Consortium definitions.¹⁸ Atrial functional TR was defined previously.¹⁹ The primary endpoint was all-cause mortality within 1 year of follow-up.

STATISTICAL ANALYSIS. Continuous data were summarized as mean $\pm$ SD for parametric data or median (IQR) for nonparametric data. To assess normal distribution, the Kolmogorov-Smirnov test was used. Statistical comparisons involved the Mann-Whitney *U* test for 2-group comparisons, whereas multigroup analyses used the chi-square test or Kruskal-Wallis test. For repeated measurements of nonparametric data, the Wilcoxon signed rank test was used.

The primary endpoint and its composites were analyzed using Kaplan-Meier estimates, with group comparisons conducted using the log-rank test. Separate Cox regression analyses were performed to determine HRs for survival when comparing T-TEER with conservative treatment in the disease stages. HRs and their 95% CIs were fitted using cubic nonlinear curves.

Cox regression analyses were conducted to identify predictors for 1-year survival in patients in the intermediate disease stage. The proportionality of hazards assumption was verified for all Cox models. A *P* value <0.05 was considered statistically significant in the multivariable analyses. The Cox proportional hazards models for the intermediate disease stage included the following covariates: atrial fibrillation or flutter, coronary artery disease, systolic pulmonary artery pressure, N-terminal pro-B-type natriuretic peptide or B-type natriuretic peptide, estimated glomerular filtration rate, and the presence of a right ventricular lead.

CENTRAL ILLUSTRATION TR Disease Staging and Post-Treatment Survival



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(Top) Classification of tricuspid regurgitation (TR) severity stage based on a 4-tier scoring system including left and right ventricular parameters (left ventricular ejection fraction [LVEF], tricuspid annular plane systolic excursion [TAPSE]), end organ failure, estimated glomerular filtration rate (eGFR), and markers of heart failure severity (N-terminal pro-B-type natriuretic peptide [NT-pro-BNP]). A sum score classified patients into 3 disease stages: early (score 4-6), intermediate (score 7-9), and advanced disease stage (score 10-12). The association between TR disease score and mortality using a restricted cubic spline regression model. Graphs show HRs for mortality according to the score. (Bottom Left) Kaplan-Meier analyses of 1-year survival after conservative and tricuspid transcatheter edge-to-edge repair (T-TEER) in early, intermediate, and advanced disease stages. *P* for log-rank test.

A restricted cubic spline analysis was conducted. Data were fitted by a restricted cubic spline Cox proportional hazards regression model, and the model was conducted with 4 knots at the 5th, 35th, 65th, and 95th percentiles of score (reference is the 5th percentile). A 2-sided P value <0.05 was considered statistically significant. GraphPad Prism 8.0 (GraphPad Software Inc) and SPSS version 29 (IBM Corp) were used for statistical analyses.

RESULTS

In total, 1,885 patients were included in the analysis. Of these, 585 were treated conservatively, and 1,300 received T-TEER (Supplemental Table 1). Overall, 395 patients (21% [395/1,885]) were categorized as having early disease, 1,173 patients (62% [1173/1,885]) as having intermediate disease, and 317 (17% [317/1,885]) as having advanced disease. In addition to the parameters comprising the disease severity categorization, left ventricular end-diastolic diameter, TR effective regurgitant orifice area, and left atrial volume increased with higher disease severity ($P < 0.05$, respectively) (Supplemental Table 1). The proportion of males, the prevalence of right ventricular leads, coronary artery disease, and NYHA functional class IV increased from early to advanced disease stage ($P < 0.05$) (Table 1, Supplemental Table 1).

Mortality rates increased from early to intermediate and to advanced disease stages in the overall cohort as well as in the conservative and T-TEER subcohorts ($P < 0.01$ for all) (Figure 1A). In the early disease stage, event rates were lowest, averaging a 1-year mortality rate of 6% (24/395). The prognostic performance of the TR disease classification was validated in an external cohort, the BRIGHT cohort, in which 1-year survival gradually decreased from early to intermediate and advanced disease stage (Figure 1B). Interaction analysis revealed a trend for an interaction between treatment modality and TR disease stage ($P = 0.09$). No significant difference was found between conservative treatment and T-TEER in the early disease category (1-year mortality rate of 8% (10/126) and 5% (14/269), respectively; HR: 0.78; 95% CI: 0.34–1.80; $P = 0.53$) (Central Illustration). This observation remained, even when only patients with procedural success were included ($P = 0.24$) (Supplemental Figure 1). In the intermediate disease category, 1-year mortality rates were higher than in the early disease stage (15% [180/1,173] vs 6% [10/126], respectively; $P < 0.01$) (Figure 1A). T-TEER in the intermediate disease cohort was associated with lower 1-year mortality compared with conservatively treated patients (1-year mortality conservative

treatment: 21% [69/323], T-TEER: 13% [111/850]; HR: 0.73; 95% CI: 0.52–0.99; $P = 0.03$) (Central Illustration). Interestingly, in the intermediate category, conservatively treated patients and patients with unsuccessful T-TEER had overlapping survival curves (Supplemental Figure 1). An advanced disease stage was associated with the worst survival (mortality rate: ~31% [99/317]; $P < 0.01$ vs early and intermediate disease stages). One-year survival in the advanced disease category was not significantly different between those treated conservatively and those who had T-TEER (1-year mortality rate conservative treatment: 30% [45/136], T-TEER: 33% [54/181]; HR: 1.06; 95% CI: 0.71–1.60; $P = 0.78$) (Central Illustration). Further analysis revealed a nonlinear relationship between T-TEER and survival, with the intermediate disease stage being associated with lower 1-year mortality compared to conservative treatment (Central Illustration).

To ascertain that the observed difference in outcomes was not caused by differences in baseline characteristics, Cox proportional hazards modeling was performed to adjust for these factors. Cox proportional hazards modeling in the intermediate disease category revealed T-TEER and the presence of coronary artery disease as independent predictors of 1-year survival (Supplemental Table 2). The effect size was similar in an additional model that included procedural success (Supplemental Table 2).

No statistical difference was noted between disease stages for TR effective regurgitant orifice area at baseline in the T-TEER subcohort ($P = 0.81$). Furthermore, no statistical difference was observed for procedural success, as defined by a residual TR $\leq$ grade 2, among the disease categories following T-TEER (early/intermediate/advanced disease stage: 84/83/77%, respectively; $P = 0.14$) (Supplemental Table 3). However, residual postprocedural TR grades after T-TEER differed among the disease stages. There was a gradual decrease of residual TR grade ≤ 1 (early/intermediate/advanced disease stage: 51/43/36%, respectively; $P = 0.02$) (Supplemental Table 3) and an increase of residual TR grade ≥ 3 (16%/17%/23%, respectively; $P = 0.02$) (Supplemental Table 3).

DISCUSSION

With the goal of reconciling incongruent registry and RCT study results, we categorized TR patients from large multicenter registries into 3 different disease stages and assessed, for each stage, the effects of T-TEER as opposed to conservative therapy on 1-year survival. This categorization process took into

TABLE 1 Baseline Clinical and Echocardiographic Parameters of Conservatively Treated and Patients Undergoing T-TEER Stratified by Severity Group

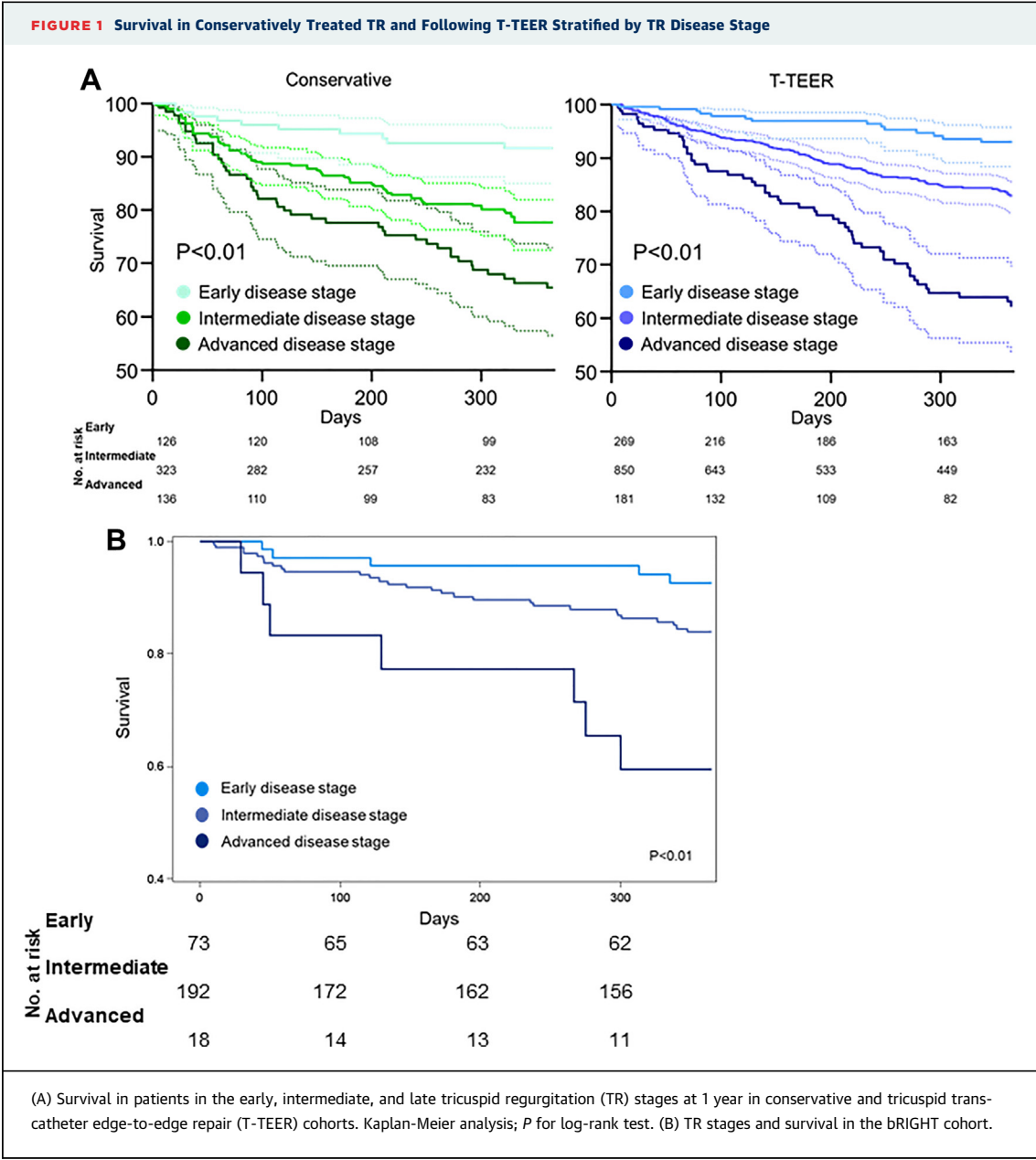
	Overall (N = 1,885)	Early Disease Stage		P Value
		Conservative (n = 126)	T-TEER (n = 269)	
Age, y	79 (74-82)	76 (71-81)	79 (76-82)	<0.01
Males, %	880 (47)	30 (24)	114 (42)	<0.01
BMI, kg/m ²	25.2 (22-29)	24.8 (23-29)	25.3 (23-28)	0.99
RV lead, %	457 (24)	10 (7.9)	43 (16)	0.04
Atrial fibrillation/flutter, %	1,618 (86)	89 (71)	245 (91)	<0.01
Coronary artery disease, %	635 (34)	8 (6.3)	71 (26)	<0.01
NYHA functional class				<0.01
I/II	224 (12)	17 (14)	60 (23)	
III	1251 (67)	90 (71)	190 (71)	
IV	405 (21)	19 (15)	17 (6)	
A-FTR, %	683 (36)	55 (44)	172 (64)	<0.01
LVEF, %	55 (45-60)	60 (55-63)	58 (55-64)	0.04
LVEDD, mm	48 (43-54)	46 (41-50)	47 (43-52)	0.02
LA volume, mL	97 (68-131)	83 (65-125)	94 (68-138)	0.02
TR EROA, cm ²	0.56 (0.40-0.77)	0.59 (0.45-0.76)	0.50 (0.40-0.70)	0.01
TR vena contracta, mm	9.2 (8.0-12.0)	8.6 (7.9-10.0)	9.9 (8.0-13.0)	<0.01
RV base diameter, mm	44 (37-51)	35 (31-42)	48 (43-54)	<0.01
TAPSE, mm	17.0 (14.0-20.0)	21.0 (18.0-24.0)	20.0 (18.0-23.0)	0.02
sPAP, mm Hg	43 (35-55)	45 (36-57)	41 (34-48)	<0.01
eGFR, mL/min/m ²	45 (33-60)	72 (62-83)	64 (50-77)	<0.01
NT-proBNP, pg/mL	2,686 (1,345-5,812)	1,073 (666-2,304)	940 (617-1,254)	0.03

TABLE 1 Continued

	Intermediate Disease Stage			Advanced Disease Stage		
	Conservative (n = 323)	T-TEER (n = 850)	P Value	Conservative (n = 136)	T-TEER (n = 181)	P Value
Age, y	76 (70-82)	80 (76-83)	<0.01	76 (69-81)	78 (73-82)	0.03
Males, %	149 (46)	382 (45)	0.74	92 (68)	111 (61)	0.29
BMI, kg/m ²	25.2 (23-28)	25.3 (23-29)	0.59	24.9 (23-27)	24.9 (23-29)	0.55
RV lead, %	40 (12)	246 (29)	<0.01	40 (29)	77 (43)	0.02
Atrial fibrillation/flutter, %	247 (76)	782 (92)	<0.01	102 (75)	152 (84)	0.05
Coronary artery disease, %	60 (19)	348 (41)	<0.01	44 (32)	104 (57)	<0.01
NYHA functional class			<0.01			<0.01
I/II	21 (7)	107 (13)		1 (1)	18 (10)	
III	183 (57)	612 (72)		58 (43)	118 (65)	
IV	119 (37)	128 (15)		77 (57)	45 (25)	
A-FTR, %	76 (24)	368 (43)	<0.01	4 (3)	8 (4)	0.56
LVEF, %	54 (45-60)	55 (49-60)	<0.01	30 (22-37)	36 (29-43)	<0.01
LVEDD, mm	48 (42-55)	48 (43-53)	0.77	54 (48-63)	56 (47-62)	0.90
LA volume, mL	97 (72-121)	96 (64-135)	0.97	111 (90-133)	103 (74-133)	0.20
TR EROA, cm ²	0.63 (0.48-0.84)	0.50 (0.40-0.74)	<0.01	0.64 (0.55-0.90)	0.52 (0.40-0.77)	<0.01
TR vena contracta, mm	8.7 (7.5-10.0)	10.0 (8.0-13.0)	<0.01	8.5 (7.4-9.4)	11.0 (8.5-13.0)	<0.01
RV base diameter, mm	40 (34-46)	48 (43-54)	<0.01	39 (35-48)	50 (43-56)	<0.01
TAPSE, mm	17.0 (14.0-20.0)	17.0 (14.0-20.0)	0.28	13.0 (11.0-15.0)	12.0 (10.0-14.0)	<0.01
sPAP, mm Hg	50 (38-61)	42 (34-53)	<0.01	47 (36-58)	40 (31-51)	<0.01
eGFR, mL/min/m ²	46 (35-62)	42 (32-53)	<0.01	33 (24-46)	30 (22-45)	0.15
NT-proBNP, pg/mL	3,760 (1,792-8,084)	2,623 (1,652-4,755)	<0.01	9,522 (4,420-17,912)	6,488 (3,337-14,547)	0.06

Values are median (Q1-Q3) or n (%).

A-FTR = atrial functional tricuspid regurgitation; BMI = body mass index; eGFR = estimated glomerular filtration rate; LA = left atrial; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal pro-B-type natriuretic peptide; RV = right ventricular; sPAP = systolic pulmonary artery pressure; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation; TR EROA = tricuspid regurgitant effective orifice area.



consideration parameters of biventricular function, renal failure, and biomarkers of HF. Using this framework for categorization, our main findings were as follows:

- Alongside increasing disease severity, markers of both cardiac and systemic failure tended to increase, with the worst markers of congestion and HF in patients with advanced disease stages.
- Although patients in the early and advanced disease stages did not seem to benefit from T-TEER with respect to 1-year mortality, T-TEER was

associated with an improvement in 1-year survival in patients with intermediate stage disease.

- T-TEER and procedural success served as independent predictors of 1-year mortality in the intermediate disease category.

Although large registries consistently suggested clinical benefit of T-TEER and beneficial effects on survival,^{7,8,14} recent randomized trial data, while reporting a symptomatic benefit, failed to show improvements in survival by T-TEER.⁶ Interestingly, patients in the TRILUMINATE Pivotal trial had relatively low rates of prior HF hospitalization and

appeared to potentially not reflect the full spectrum of patients with TR found in contemporary cohorts.^{6,7,10,20} Various lines of reasoning have been proposed to reconcile the divergent findings in recent studies. First, a learning curve effect could explain the observed differences in that there have been not only procedural refinements in recent years but also improved patient selection and optimization before the procedure. This might explain the observed differences in central venous pressures in TRILUMINATE (~11 mm Hg) compared to registry data (~15 mm Hg²¹). Second, the significant disparity could be attributed to the presence of concomitant left-sided heart diseases in earlier studies. These comorbidities may have significantly contributed to the higher mortality rates observed in those studies. Third, the growing recognition of the negative natural history of TR may have caused a heightened awareness of the dangers of TR progression. This would promote the treatment of TR patients at earlier disease stages, leading to lower midterm event rates. In fact, our data demonstrate a difference in event rates when considering different disease stages. Furthermore, our data suggest that T-TEER associates with higher 1-year survival compared with medically treated patients in intermediate disease stage. Patients in the intermediate disease category are at increased risk of adverse outcome as signified by elevated mortality rates; however, they are not so far advanced as to be beyond “rescue.” Indeed, in the advanced disease category, T-TEER was not associated with beneficial treatment effects, perhaps suggesting that TR-associated sequelae were too advanced and not amendable to interventional therapy. Moreover, for those with advanced disease, unsuccessful T-TEER appears to lead to detrimental outcomes, which highlights the shortcomings of prior studies using procedural failure as a comparator group. In addition, in patients with advanced heart failure, fatal outcomes may be related to ventricular function rather than valvular regurgitation because TR may become an epiphenomenon rather than the primary cause of death.

Residual TR after T-TEER has been identified as a major risk factor for adverse outcomes.²⁰ In our study, we found higher rates of worse residual TR grades after T-TEER in patients who presented with more advanced TR disease. This finding raises an interesting question: Do anatomical or functional conditions in more advanced disease stages hinder TR reduction to lower grades by T-TEER and thereby contribute to elevated rates of adverse events? Although anatomical criteria for procedural

success are well established,²⁰ recently it was suggested that patients who have higher stressed blood volumes might be prone to lower reductions in central venous pressure, even in the context of procedural success, thereby limiting the clinical benefit.¹⁶ The latter of which is also true for patients with a relatively high cardiac output at baseline.¹⁵ Notably, both of these phenotypes were associated with impaired biventricular function and hepatic and renal dysfunction, indicating an advanced disease stage.

Of note 1-year mortality rates in the TRILUMINATE Pivotal trial appear to be comparable to those of patients who were classified as having early disease in our study, suggesting comparable underlying risk. Interestingly, in an analysis using the TRI-SCORE, conservatively treated patients stratified into a low TRI-SCORE category had 1-year mortality rates approximately twice as high as patients from both the TRILUMINATE trial and our early disease stage.¹⁴ Importantly, a 1-year mortality endpoint may be too short to elucidate effects of T-TEER on survival in a low-risk, low-event rate category, and longer-term follow-up may reveal T-TEER effects in patients at low risk.

STUDY LIMITATIONS. Establishing a disease stage definition remains difficult. Here we applied one of multiple potential ways to quantify disease burden; however, it was not an aim of our study to determine the best method to quantify disease burden. Rather, we demonstrate that an intermediate disease stage may represent the optimal window of opportunity to modify the clinical course. Of note, there is no distinct early, intermediate, and advanced disease but rather gradually increased risk. However, categorization into disease stages provides a conceptual framework. The follow-up period was relatively short; therefore, time-sensitive event rates may be too low to detect statistical differences. Group sizes, especially in the early disease stage, were limited and thereby may have lacked statistical power to detect statistically significant differences; however, given the favorable HR for T-TEER in the early disease stage, T-TEER may be clinically advantageous even in the early disease stage. No data were available on follow-up HF hospitalizations in the conservatively treated cohort, thereby reducing the endpoint to survival alone. Parameters reflecting hepatic function were not consistently available. The EuroTR and the conservatively treated cohorts were retrospectively collected and are therefore prone to bias. However,

especially for the T-TEER cohort, consecutive patients from each center were included.

CONCLUSIONS

Classifying TR into disease stages that accounted for cardiac and systemic criteria provided a framework for evaluating which TR patients may receive a survival benefit from T-TEER. Although T-TEER does not seem to associate with short-term survival in patients on the extreme ends of the spectrum of TR disease (ie, early and advanced disease), patients presenting in an intermediate stage may respond favorably to T-TEER in terms of survival as opposed to conservative therapy. Given that our results suggest that disease stage might influence survival outcomes in response to T-TEER and the outcomes of T-TEER registries and a recent RCT conflict, we believe that we have provided a rationale to evaluate T-TEER in a randomized trial that focuses on patients who would fall in an intermediate risk category.

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Dr Stolz has received speaker honoraria from Edwards Lifesciences. Dr Kresoja has received travel expenses from Edwards Lifesciences. Dr Rottbauer has received speaker honoraria from Edwards Lifesciences and Abbott. Dr Denti has served as a consultant for InnovHeart, Picardia, HVR, and Approxima; and has received speaker honoraria from Abbott and Edwards Lifesciences. Dr Rassaf has received speaker honoraria and consulting fees from AstraZeneca, Bayer, Pfizer, and Daiichi-Sankyo. Dr Adamo has received consulting fees in the last 3 years from Abbott Structural Heart and Edwards Lifesciences. Dr von Bardeleben has received institutional grants from Abbott Vascular and Edwards Lifesciences; and has served as a speaker for Abbott Vascular and Edwards Lifesciences. Dr Toggweiler 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, and Daiichi-Sankyo; has received institutional research grants from Edwards Lifesciences, Boston Scientific, Fumedica, Novartis, and Boehringer Ingelheim; and holds equity in Hi-D Imaging. Dr Metra has received consulting fees in the last 3 years from Abbott Structural Heart, AstraZeneca, Bayer, Boehringer Ingelheim, Edwards Lifesciences, and Roche Diagnostics. Dr Geisler has received speaker honoraria/research grants from AstraZeneca, Bayer, Bristol Myers Squibb/Pfizer, Ferrer/Chiesi, Medtronic, and Edwards Lifesciences; none of them was related to this study. Dr Estévez-Loureiro has received speaker fees from Abbott Vascular, Edwards Lifesciences, Boston Scientific, and Venus Medtech. Dr Luedike has received speaker honoraria and consulting fees from AstraZeneca, Bayer, Pfizer, and Edwards Lifesciences; and has received research

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PERSPECTIVES

WHAT IS KNOWN? A symptomatic benefit of T-TEER to treat TR has repeatedly been shown, and large registries suggested a survival benefit for patients undergoing T-TEER; however, RCT data did not suggest an effect on 1-year survival.

WHAT IS NEW? The current analysis reconciles the conflicting registry and RCT data and suggests that the effect on survival may be highest in an intermediate disease stage. Individuals in an intermediate disease stage may receive the most substantial treatment benefit from T-TEER.

WHAT IS NEXT? Our results suggest that TR disease stage may influence survival outcomes following T-TEER, and considering the discrepancies between registry outcomes and a recent RCT, we propose the necessity of a randomized trial to evaluate T-TEER specifically in patients classified as being at intermediate risk.

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KEY WORDS heart failure, right heart, transcatheter repair, tricuspid regurgitation

APPENDIX For supplemental tables and figures as well as a video of the interactive Central Illustration, please see the online version of this paper.