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### ► To cite this version:

Julien Dreyfus, Maurizio Taramasso, Karl-Patrik Kresoja, Hazem Omran, Christos Iliadis, et al.. Prognostic Implications of Residual Tricuspid Regurgitation Grading After Transcatheter Tricuspid Valve Repair. JACC: Cardiovascular Interventions, 2024, 17 (12), pp.1485-1495. 10.1016/j.jcin.2024.04.023 . hal-04595102

HAL Id: hal-04595102

<https://u-picardie.hal.science/hal-04595102v1>

Submitted on 3 Jul 2024

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**Prognostic implications of residual tricuspid regurgitation grading after transcatheter  
tricuspid valve repair**

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Running Title: Impact of residual tricuspid regurgitation

Word Count:

Text (Introduction to conclusion)	3206 words
Number of tables	2
Number of figures	2
Abstract	249 words

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**TWEET:**

Data from TRIGISTRY: Residual tricuspid regurgitation grade following transcatheter tricuspid valve interventions significantly impacts survival. Procedural success should be defined as a mild-to-moderate or lower tricuspid regurgitation grade at discharge.

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**FUNDING**

None

**CONFLICT OF INTEREST**

- Luigi Badano received consulting or speaker fees from Edwards-Lifesciences, GE Healthcare and Philips Medical Systems.
- Jeroen Bax received Lecture fees from Abbott and Edwards Lifesciences.
- Julien Dreyfus received speaker or proctoring fees from Abbott.
- Rodrigo Estevez-Loureiro received speaker fees from Abbott Vascular, Edwards-Lifesciences, Boston Scientific and Venus Medtech.
- Rebecca T. Hahn received speaker fees from Boston Scientific, Edwards-Lifescience and Philips Healthcare.

- Jörg Hausleiter received grant and consulting fees from Edwards-Lifesciences.
- Dominique Himbert received proctoring fees from Edwards-Lifesciences and Abbott Vascular.
- Christos Iliadis received consulting fees from Abbott Vascular and Edwards-Lifesciences.
- Karl-Patrik Kresoja received consulting fees from Edwards-Lifesciences.
- Alexander Lauten received speaker fees from Boehringer Ingelheim, Medtronic, Amgen, Bayer, Novartis, Sanofi, Chiesi, Astra Zeneca, and is shareholder of Devie Medical Drug Eluting Valve for Endocarditis Treatment.
- Philipp Lurz received consulting fees from Abbott Medical, Innoventric and Edwards-Lifesciences.
- Francesco Maisano received Grant and/or Research Institutional Support from Abbott, Medtronic, Edwards Lifesciences, Biotronik, Boston Scientific Corporation, NVT, Terumo, Venus, 3 mensio, consulting fees, Honoraria personal and Institutional from Abbott, Medtronic, Edwards Lifesciences, Xeltis, Cardiovalve, Occlufit, Simulands, Mtex, Venus, Squadra, Royalty Income/IP Rights from Edwards Lifesciences and is shareholder (including share options) of Cardiogard, Cardiovalve, Magenta, SwissVortex, Transseptalsolutions, and 4Tech.
- David Messika-Zeitoun received research grants from Edwards Lifesciences.
- Thomas Modine received speaker or consulting fees from Abbott, Edwards Lifesciences, Medtronic, Microport and GE
- Mohammed Nejari received consulting or speaker fees from Abbott vascular, Medtronic, Edwards, Boston Scientific, Robocath.
- Luis Nombela-Franco received consulting or speaker fees from Abbott Vascular, Edwards-Lifesciences and Products and Features.
- Josep Rodés-Cabau received consulting or speaker fees from Abbott Vascular, Edwards-

Lifesciences and Medtronic.

- Volker Rudolph received consulting or speaker fees from Abbott Vascular and Edwards-Lifesciences.
- Lukas Stolz received consulting or speaker fees from Edwards-Lifesciences.
- Gilbert H. L. Tang has received speaker's honoraria and served as a physician proctor, consultant, advisory board member, TAVR publications committee member, APOLLO trial screening committee member and IMPACT MR steering committee member for Medtronic, has received speaker's honoraria and served as a physician proctor, consultant, advisory board member and TRILUMINATE trial anatomic eligibility and publications committee member for Abbott Structural Heart, has served as an advisory board member for Boston Scientific and JenaValve, a consultant and physician screening committee member for Shockwave Medical, a consultant for NeoChord, Peija Medical and Shenqi Medical Technology, and has received speaker's honoraria from Siemens Healthineers.
- Maurizio Taramasso received consulting or speaker fees from Abbott Vascular, Edwards Lifesciences, Medtronic, Boston Scientific, Shenqi Medical, PiCardia, CoreMedic, VentriMend, MEDIRA, CoreQuest, HiD Imaging.
- Ralph Stephan von Bardeleben received consulting or speaker fees from Abbott Vascular, Edwards-Lifesciences, Medtronic, Philips and Siemens.
- Stephan Windecker reports research, travel or educational grants to the institution without personal remuneration from Abbott, Abiomed, Amgen, Astra Zeneca, Bayer, Braun, Biotronik, Boehringer Ingelheim, Boston Scientific, Bristol Myers Squibb, Cardinal Health, CardioValve, Cordis Medical, Corflow Therapeutics, CSL Behring, Daiichi Sankyo, Edwards Lifesciences, Farapulse Inc. Fumedica, Guerbet, Idorsia, Inari Medical, InfraRedx, Janssen-Cilag, Johnson

& Johnson, Medalliance, Medicure, Medtronic, Merck Sharp & Dohm, Miracor Medical, MonarQ, Novartis, Novo Nordisk, Organon, OrPha Suisse, Pharming Tech. Pfizer, Polares, Regeneron, Sanofi-Aventis, Servier, Sinomed, Terumo, Vifor, V-Wave; and served as advisory board member and/or member of the steering/executive group of trials funded by Abbott, Abiomed, Amgen, Astra Zeneca, Bayer, Boston Scientific, Biotronik, Bristol Myers Squibb, Edwards Lifesciences, MedAlliance, Medtronic, Novartis, Polares, Recardio, Sinomed, Terumo, and V-Wave with payments to the institution but no personal payments. He is also member of the steering/executive committee group of several investigator-initiated trials that receive funding by industry without impact on his personal remuneration.

- John Webb received consulting fees from Edwards Lifesciences and research funding from Medtronic, Abbott, Boston Scientific, Edwards Lifesciences.
- Jose Luis Zamorano received consulting or speaker fees from Novartis, Bayer and Pfizer.
- All other authors have no relationship to declare.



**ABSTRACT**

**Background.** The safety profile of transcatheter tricuspid valve (TTV) repair techniques is well established but residual tricuspid regurgitation (TR) remains a concern.

**Objectives.** We sought to assess the impact of residual TR severity post-TTV repair on survival.

**Methods.** We evaluated the survival rate at 2 years of 613 patients with severe isolated functional TR who underwent a TTV repair in TRIGISTRY according to the severity of residual TR at discharge assessed using a 3-grade (mild, moderate, severe) or 4-grade scheme (mild, mild-to-moderate, moderate-to-severe, severe).

**Results.** Residual TR was none/mild in 33%, moderate in 52% and severe in 15%. Two-year adjusted survival rates significantly differed between the three groups (85%, 70% and 44%, respectively, restricted mean survival time (RMST)  $P=0.0001$ ). When the 319 patients with moderate residual TR were subdivided into mild-to-moderate ( $N=201$ , 33%) and moderate-to-severe ( $N=118$ , 19%), adjusted survival rate was also significantly different between groups (85%, 80%, 55% and 44% respectively, RMST  $P=0.001$ ). Survival was significantly lower in patients with moderate-to-severe residual TR compared to patients with mild-to-moderate residual TR ( $P=0.006$ ). No difference in survival rates was observed between patients with no/mild and mild-to-moderate residual TR ( $P=0.67$ ) and between patients with moderate-to-severe and severe residual TR ( $P=0.96$ ).

**Conclusion.** The moderate residual TR group was heterogeneous and encompassed patients with markedly different clinical outcomes. Refining TR grade classification with a more granular 4-grade scheme improved outcome prediction. Our results highlight the importance of achieving mild-to-moderate or lower residual TR grade during TTV repair which could define a successful intervention.

**Keywords:** tricuspid regurgitation, transcatheter intervention, survival.

**CONDENSED ABSTRACT**

In TRIGISTRY, survival rate at 2 years of 613 patients who underwent a transcatheter tricuspid valve (TTV) repair was significantly different between groups defined based on the grade of residual tricuspid regurgitation (TR) at discharge either assessed using a 3-grade (mild, moderate, severe) or a 4-grade scheme (mild, mild-to-moderate, moderate-to-severe, severe). More importantly, survival rate was significantly lower in patients with moderate-to-severe than in patients with mild-to-moderate residual TR. Our results support the use of a more granular TR classification and highlight the importance of achieving mild-to-moderate or lower residual TR grade during TTV repair.

**ABBREVIATIONS**

CI = Confidence Interval

RMST = Restricted Mean Survival Time

RV = Right Ventricular

TR = Tricuspid Regurgitation

TTV = Transcatheter Tricuspid Valve

TV = Tricuspid Valve

## INTRODUCTION

Tricuspid regurgitation (TR) is one of the most common valvular heart diseases in Western countries. Its prevalence is estimated to be similar to that of aortic stenosis and is expected to further increase as the population ages.(1) TR is associated with an excess mortality and morbidity that increases with the severity of the regurgitation.(2-8) The high mortality rates associated with isolated tricuspid valve (TV) surgery have led to the development of transcatheter tricuspid valve (TTV) interventions.(9-12) Although still under investigation, TTV interventions have emerged as a less invasive alternative to surgery and are nowadays the dominant treatment modality in several countries. The safety of TTV repair is well documented, but significant residual TR observed in up to one third of patients post procedures remains an important issue.(13-16)

We and others have shown that significant residual TR post TTV repair was associated with a poor outcome.(13,16) Interestingly, the current 3-grade scheme (mild, moderate, and severe) recommended for the assessment of TR severity before and after interventions by the European and North American Societies of Cardiology (17,18) contrasts with the 4-grade scheme routinely used for mitral regurgitation (mild, mild-to-moderate, moderate-to-severe and severe).(17) We hypothesized that a more granular grading classification, similar to that of mitral regurgitation, may better define the prognosis of patients undergoing TTV interventions and more specifically that the current moderate TR grade encompasses patients experiencing markedly different outcomes, shedding new lights on the relatively neutral effect of TTV repair compared to guidelines directed medical therapy recently reported in the TRILUMINATE trial.(15)

In patients who underwent a TTV repair in TRIGISTRY, a large international multicenter registry, we aimed to evaluate the impact of residual TR severity on all-cause mortality rates at 2 years, and more specifically to compare mortality rates according to the degree of residual TR at

discharge assessed using the currently recommended 3-grade scheme(17,18) or using a 4-grade scheme subdividing moderate TR into mild-to-moderate and moderate-to-severe residual TR.

## **METHODS**

### **Study design**

TRIGISTRY is a retrospective international multicenter registry across 10 countries (Austria, Canada, France, Germany, Israel, Italy, Netherlands, Spain, Switzerland, and the USA) and 33 centers including adult patients with severe isolated functional TR on native valve who were either conservatively/medically managed, who underwent an isolated TV surgery or who underwent a TTV repair. Inclusion and exclusion criteria have been previously reported.(16) Patients with moderate or greater concomitant left-sided valvular heart disease were excluded as well as patients who underwent an aortic or mitral valve intervention (either surgical or transcatheter) within 3 months prior to the tricuspid valve intervention. In the present study, we identified all patients who underwent an isolated TTV repair, with no concomitant interventions, who were discharged alive post intervention, and had their degree of residual TR assessed at discharge. Clinical, laboratory, echocardiographic and outcomes information were collected locally by each center and centralized in a unique depository anonymized database at the University of Ottawa Heart Institute (echocardiographic methodology is presented with more details elsewhere).(16,19) Data analyzes were performed by the Cardiovascular Research Methods Center at the University of Ottawa Heart Institute. The study was conducted in accordance with local institutional policies and was approved by each local institutional review board.

### **Follow-up and outcome**

Post TTV repair, residual TR grade was semi-quantitatively assessed at discharge locally at each center level by experienced dedicated echocardiographers using transthoracic echocardiography and graded using a 4-grade scheme (no or mild, mild-to-moderate, moderate-to-severe, and severe) similar to mitral regurgitation, based on a multi-parametric approach integrating jet extension into the right atrium, vena contracta, diameter of the flow convergence, residual gap width and mechanism of the residual regurgitation. We then aggregated the "mild-to-moderate" and "moderate-to-severe" categories into a single "moderate" TR grade to obtain a 3-grade scheme (mild, moderate, and severe) as recommended by current guidelines.(17,18,20) Study endpoint was all cause death at 2 years.

### **Statistical analysis**

Variables were expressed as mean  $\pm$  standard-deviation or median [25%-75% percentile] for continuous variables and number of patients (percentage) for categorical variables. Comparisons of baseline characteristics between groups were performed using ANOVA, Chi-square, Student's t-test or non-parametric Wilcoxon test as appropriate. Actuarial survival rates were calculated and presented using the Kaplan-Meier method. As the proportional hazards assumption was violated, the restricted mean survival time (RMST) method was used to compare the survival experience between groups and expressed using RMST difference and 95% confidence interval (CI). We performed univariable and multivariable analyzes adjusted for age (as a continuous variable), sex, atrial fibrillation, diabetes, chronic lung disease, coronary artery disease, prior left-sided heart valve intervention and for the TRI-SCORE (model 1).(19) Multivariable analyzes were also repeated after adjustment for age, sex, atrial fibrillation, diabetes, chronic lung disease, coronary artery disease, prior left-sided heart valve intervention and for each of the individual components of the TRI-SCORE (age  $\geq$ 70 years, NYHA functional Class III-IV, right-

sided heart failure signs, daily dose of furosemide  $\geq 125$  mg, glomerular filtration rate  $< 30$  ml/min, elevated total bilirubin, left ventricular ejection fraction  $< 60\%$ , moderate/severe right ventricular (RV) dysfunction) (model 2). Two by two comparisons were also performed using the RMST method. Analyses were performed at the two-tailed  $P < 0.05$  level, using SAS statistical software version 9.4 (SAS Institute Inc, Cary, NC).

## RESULTS

### Population

In TRIGISTRY, 645 adult patients underwent a TTV repair for severe isolated functional TR on native tricuspid valve; 509 patients (79%) were treated with tricuspid edge-to-edge repair system (MitraClip® or TriClip® system (Abbott Structural Heart, Santa Clara, CA, USA), or PASCAL system® (Edwards Lifesciences, Irvine, CA, USA), 125 patients (19%) with an annuloplasty (CardioBand system® (Edwards Lifesciences, Irvine, CA, USA)) and 11 patients (1%) with other techniques (Trialign® (Mitralign, Inc., Boston, MA, USA), Trichinch® (4Tech Cardio Ltd., Galway, Ireland)). Our study population consisted of 613 patients after exclusion of 16 patients who died after the intervention during the same hospitalization and 16 patients in whom TR residual severity was not documented at discharge. Baseline characteristics of the study population are presented in **Table 1**. Briefly, mean age was  $78 \pm 8$  years and 60% were women. A permanent pacemaker was present in 29% and 33% had prior left-sided valvular heart disease interventions. Most patients were severely symptomatic (86% were in New-York Heart Association class III-IV, 63% presented with overt heart failure), 86% had atrial fibrillation and mean TRI-SCORE was  $5 \pm 2$  (median 5[4-6]). TTV interventions consisted of an edge-to-edge repair in 492 patients (80%) and annuloplasty in 115 (19%).

### Survival according to residual TR using the 3-grade scheme

Among the 613 patients considered in this study, 203 patients had no/mild residual TR (33%), 319 had moderate residual TR (52%), and 91 had severe residual TR (15%) at discharge. Comparisons of baseline characteristics according to residual TR severity using the 3-grade scheme are presented in **Table 1**. Groups differed with regards to age, daily dose of loop diuretics, creatinine, hemoglobin and total bilirubin level, presence of moderate/severe RV dilatation, systolic pulmonary pressure, and TRI-SCORE categories (**Table 1**). Differences in terms of prior history of coronary artery disease, prior left-sided heart valve intervention and permanent pacemaker were of borderline statistical difference.

Overall, the median follow-up was 0.74 [0.27;1.77] year and the survival rate, available in 98% of the population, was 71% at 2 years. As shown in **Figure 1**, survival was markedly different between patients with no/mild, moderate, and severe residual TR (85%, 70% and 44%, respectively,  $P=0.0001$ ). After adjustment for age, sex, atrial fibrillation, diabetes, chronic lung disease, coronary artery disease, prior left-sided heart valve intervention and the TRI-SCORE (model 1), residual TR grade remained significantly associated with survival ( $P=0.01$ ). Survivals of patients with no/mild residual and with moderate TR were both significantly better than the survival of patients with severe TR (RMST difference = 0.27, 95% CI [0.09, 0.46],  $P=0.004$  and RMST difference = 0.10, 95% CI [0.01, 0.38],  $P=0.04$ , respectively). Importantly, survival of patients with moderate residual TR was not significantly different than the survival of patients with no/mild residual TR (RMST difference = -0.08, 95% CI [-0.21, 0.06],  $P=0.25$ ). Adjusting for each of the component of the TRI-SCORE instead of the TRI-SCORE (model 2) only marginally changed our results with a persistent significant difference in survival between groups overall ( $P=0.02$ ), the lack of difference in survival between patients with no/mild and moderate residual



TR ( $P=0.27$ ), a significant difference between patients with no/mild and severe residual TR ( $P=0.006$ ), but a difference in survival between patients with moderate and severe residual TR of borderline statistical significance ( $P=0.06$ ).

### Survival according to residual TR using the 4-grade scheme

Among the 319 patients with moderate TR at discharge, 201 had a mild-to-moderate residual TR (33% of the overall study population), and 118 had a moderate-to-severe residual TR (19%). Comparisons between residual TR groups using the 4-grade scheme are presented in **Table 2**. There were several differences between groups as regard to daily dose of diuretics, hemoglobin and bilirubin level, presence of RV dilatation and TRI-SCORE.

Two-year survival was markedly different between the 4 groups (85%, 80%, 55% and 44% in patients with no/mild, mild-to-moderate, moderate-to-severe, and severe residual TR respectively) in univariate and multivariate analyzes ( $P=0.001$ , **Figure 2**). Adjusted survival was also significantly better in patients with mild-to-moderate residual TR than in patients with moderate-to-severe residual TR (RMST difference = 0.27, 95% CI [0.07, 0.47],  $P=0.006$ ). Adjusted survival of patients with mild-to-moderate residual TR and no/mild TR was not different (RMST difference = 0.03, 95% CI [-0.12, 0.17],  $P=0.67$ ) as was adjusted survival of patients with moderate-to-severe residual TR and severe residual TR (RMST difference = 0.01, 95% CI [-0.24, 0.25],  $P=0.96$ ). Adjusting for each component of the TRI-SCORE provided very similar results for the overall and two-by-two comparisons.

Results remained grossly unchanged when analyzes were repeated in the transcatheter edge-to-edge repair ( $P<0.0001$ ) and transcatheter non-edge-to-edge repair subsets, although did not reach statistical in the later ( $P=0.10$ ) likely due to the limited number of patients in each TR grade category in this subset (**Figure S1A and B**).

## DISCUSSION

In this large multicenter international registry of patients with severe isolated functional TR who underwent a transcatheter tricuspid valve repair, we assessed the impact of residual TR severity evaluated at discharge on mortality and observed that 2-year survival decreased with increasing residual TR grade (**Central Illustration**). More importantly, we observed an important heterogeneity in the outcome of patients with moderate residual TR, which accounted for approximately half of the population. Survival rates of patients with mild-to-moderate and moderate-to-severe were markedly different showing that a more granular 4-grade scheme further refines the prognosis of these patients. Conversely, survival of patients with no/mild and mild-to-moderate residual TR was not different, while patients with moderate-to-severe residual TR experienced a survival akin to those with severe residual TR.

Transcatheter treatment of severe mostly functional TR has gained a substantial momentum, with repair techniques being nowadays widely adopted globally. Despite the excellent safety profile of these interventions, residual TR post-TTV repair is common and represents an important limitation. TRIGISTRY encompassed 613 patients who underwent a TTV repair; 33% presented with no/mild residual TR, while 52% and 15% exhibited moderate or severe residual TR at discharge, respectively. These proportions mirror those reported in the TRILUMINATE randomized trial, where 175 patients underwent a TTV edge-to-edge repair.<sup>(15)</sup> The multiparametric and centralized evaluation of TR severity in TRILUMINATE revealed that 38% had moderate residual TR and 13% had severe residual TR at 30 days. Additionally, findings from the bRIGHT prospective multicenter registry, featuring 511 patients who underwent a TTV edge-

to-edge repair, demonstrated that 23% and 20% of patients had a moderate residual TR and severe residual TR at 30 days respectively. (14) The alignment between TRIGISTRY and other studies which included a centralized echocardiographic evaluation regarding residual TR rates emphasizes the magnitude of the problem and the relevance of our findings.

Building on our previous findings that procedural success, defined based on the degree of residual TR at discharge, correlated with 2-year mortality rates,(16) we aimed in the present study to delve deeper into the association between residual TR severity and survival rates. Using first the recommended 3-grades scheme, we observed a decrease in survival rates as residual TR grade increased. This association was observed in univariate analysis as well as using multiple adjustments and modelling, reinforcing the strength of the association between the degree of residual TR and mortality. Importantly, we adjusted for the TRI-SCORE, which has been specifically developed to predict in-hospital mortality after isolated tricuspid valve surgery.(19) The TRI-SCORE is dedicated to TV interventions and specifically capture the clinical presentation and sequelae of TR on the right ventricle, kidney, and liver. It is noteworthy that in TRIGISTRY, the survival of patients with significant residual TR after TTV repair was comparable to the survival of patients conservatively managed (medical therapy) while a successful procedure demonstrated a benefit compared to conservative management in the subsets of patients with low ( $\leq 3$ ) and, to a lesser extent, intermediate TRI-SCORE categories (4-5).

A major result of the present study is to highlight the limitations of the current 3-grade scheme for the assessment of TR severity. TR severity is a continuum, and it has been suggested to add at the right hand of the spectrum 2 additional grades – massive and torrential (5-grade scheme).(21,22) We show that the left hand of the spectrum also deserves a more precise assessment of the severity of the regurgitation as routinely performed for mitral regurgitation.

Indeed, moderate TR encompasses a wide range of TR severity with patients experiencing different outcomes and subdividing the moderate grade into mild-to-moderate and moderate-to-severe as for mitral regurgitation further refined the prognosis of these patients (4-grade or 6-grade scheme when also considering massive and torrential). Thus, patients with mild-to-moderate residual TR experienced a significantly better 2-year survival than patients with moderate-to-severe residual TR (80% and 55% respectively,  $P=0.006$ ). While others are still ongoing, TRILUMINATE is the only randomized controlled study reported so far with a TTV repair arm.<sup>(15)</sup> TRILUMINATE showed an improvement in the quality of life of patients in the transcatheter edge-to-edge TV repair arm compared to the conservative management arm but no benefit on mortality or admission for heart failure at one year. As above mentioned, 38% of patients presented a moderate residual TR and 13% a severe residual TR at 30 days. Assuming a similar subdivision of patients with moderate residual TR as in TRIGISTRY (2/3 mild-to-moderate and 1/3 moderate-to-severe), 25% of the patients exhibited an unsuccessful intervention in TRILUMINATE, which might explain, at least partially, the absence of benefit of the intervention on hard endpoints.

**Clinical implications and perspectives.** Our results advocate for a shift towards a more nuanced four-grade scheme for the assessment of TR severity, subdividing the moderate TR category into mild-to-moderate and moderate-to-severe. Notably, patients with mild-to-moderate TR exhibited survival rates comparable to those with no/mild TR, emphasizing the importance of achieving mild-to-moderate or less residual TR grade and not considering moderate residual TR uniformly as a conclusive measure of successful TTV interventions. As transcatheter techniques continue to evolve and more technology becomes available, the choice between repair and replacement strategies will be crucial. Balancing safety, efficacy, durability, and predictability of procedural results will be imperative. Our results underscore the need for directing effort toward

technological advancements and operator expertise to optimize the procedural results of TTV repair.

**Study limitations.** First, TRIGISTRY is a retrospective, observational registry with inherent bias related to its design. However, TRIGISTRY is a large, homogenous, multicenter international registry with patients consecutively enrolled at each center. In addition, only patients with isolated functional severe TR were enrolled. Second, the assessment of residual TR degree, which may be difficult, particularly after edge-to repair, was semi-quantitative and conducted locally by each center, without a centralized assessment and no precise quantitative thresholds. However, the echocardiographic assessment was performed by experienced dedicated echocardiographers, and the large number of participating centers mitigate the risk of systematic under or overestimation of TR severity. The similar distribution of TR grades between TRIGISTRY and other studies is also very reassuring. Nevertheless, we show that real-life assessment of residual TR severity by centers and more granular grading predict survival. Providing definition for mild-to-moderate and moderate-to-severe TR is outside the scope of the present study but should definitively be part of future objectives under the guidance of Scientific Societies. Third, TR grade was only assessed at discharge, and we were unable to evaluate the prognostic impact of changes in TR severity over time. Similarly, changes in diuretic doses were not captured. Fourth, survival rates of patients with mild-to-moderate and no/mild residual TR were not statically different although numerically lower (80% vs 85% respectively) as survival rates between patients with moderate-to-severe and severe residual TR (55% vs 44% respectively). These results deserve validation in future studies, but we cannot exclude that the lack of difference observed in the present study was not due to lack of statistical power. Fifth, although TTV interventions are relatively recent and a learning curve is expected, 80% of the transcatheter

interventions were performed after 2018. In addition, different devices were used in TRIGISTRY. Transcatheter edge-to-edge repair was performed in 80% of the population but impact of residual TR was consistent across the types of interventions (transcatheter edge-to-edge repair vs. transcatheter non-edge-to-edge repair, **Figure S1A and B**). Although the rate of moderate-to-severe or severe residual TR might decrease with experience and advances in technology, it does not affect our main finding, i.e. the impact of residual TR on survival and the need for a more granular evaluation of TR severity. Sixth, determinants of residual TR are likely complex and the combination of patients' characteristics, tricuspid valve anatomy as gap width and experience of the operators. Lack of precise anatomical evaluation in our registry precluded performing relevant analysis regarding the determinants of residual TR. Seventh, we defined isolated TR, as TR occurring in the absence of other concomitant significant valvular disease but did not exclude patients with prior left-sided interventions (which accounted to one-third of our population). In addition, we were not able to differentiate between atrial and ventricular functional TR. Eighth, echocardiographic evaluation of the right ventricular systolic pulmonary pressure in patients with severe TR is often inaccurate, especially when TR is laminar, explaining why it was not an independent determinant of outcome and not part of the TRI-SCORE. Hemodynamic assessment of the right ventricular systolic pulmonary pressure would have been of interest but was not collected in TRIGISTRY. Eighth, the cause of death was not collected and we only reported all-cause death. Finally, our findings deserve further validation in other observational studies and in subgroup analyzes of randomized controlled studies showing a potential benefit of TTV intervention only in patients with mild-to-moderate or lower residual TR.

## CONCLUSION

We have evaluated the impact of the degree of residual TR after transcatheter tricuspid valve repair in TRIGISTRY and showed that survival rates decreased with the grade of residual TR. We also showed that the outcome of patients with moderate residual TR grade was heterogenous and that subdividing the moderate TR grade into mild-to-moderate and moderate-to-severe TR grades refined the prognosis of these patients. Our results support the use of a more granular 4-grade scheme and highlight the importance of achieving optimal procedural results defined as a mild-to-moderate or lower residual TR instead of a moderate or lower residual TR grade. These findings deserve further confirmation in other studies and critically in randomized controlled studies.

**CLINICAL PERSPECTIVES****What's known?**

Significant residual tricuspid regurgitation (TR) is common after transcatheter tricuspid valve repair (TTVR).

**What's new?**

Residual TR grade following TTVR significantly impacts survival. Procedural success should be defined as a mild-to-moderate or lower TR grade at discharge.

**What's next?**

Future recommendations should aim to refine TR grade assessment by adopting a four-grade scheme that subdivides moderate TR into mild-to-moderate and moderate-to-severe TR and efforts should be directed toward achieving mild-to-moderate or lower residual tricuspid regurgitation grade after TTVR.



## **ACKNOWLEDGEMENTS**

We thank Dr. George Wells and Jordan Bernick for their help with the statistical analysis. We also deeply thank all the investigators of TRIGISTRY for their active participation and support.

## **DATA AVAILABILITY STATEMENT**

Data sharing with qualified researchers may be considered after submission of a proposal to Doctor Julien Dreyfus.

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**LEGEND OF FIGURES****FIGURE 1. Impact of residual tricuspid regurgitation on survival – 3-grade scheme.**

The figure displays Kaplan-Meier curves showing survival at 2 years after transcatheter tricuspid valve repair according to the degree of residual tricuspid regurgitation (TR) at discharge assessed based on a 3-grade scheme (no/mild in green, moderate in blue, and severe residual TR in red). The adjusted mean restricted survival time P value is provided.

**FIGURE 2. Impact of residual tricuspid regurgitation on survival – 4-grade scheme.**

The figure displays Kaplan-Meier curves showing survival at 2 years after transcatheter tricuspid valve repair according to the degree of residual tricuspid regurgitation (TR) at discharge assessed based on a 4-grade scheme (no/mild in green, mild-to-moderate in light blue, moderate-to-severe in dark blue, and severe TR in red). The adjusted mean restricted survival time P value is provided.

**CENTRAL ILLUSTRATION. Impact on mortality of residual TR grade after transcatheter tricuspid valve repair.**

We evaluated the survival rates up to 2 years of 613 TRIGISTRY patients who underwent a transcatheter tricuspid valve repair (TTVR) according to the degree of residual tricuspid regurgitation (TR) at discharge, assessed using either a 3-grade scheme (no/mild, moderate and severe) or a 4-grade scheme subdividing moderate TR into mild-to-moderate and moderate-to-severe. Residual TR grade was semi-quantitatively assessed using transthoracic echocardiography, based on a multi-parametric approach. There was a significant difference between groups using both the 3 and 4 grades classifications (adjusted  $P=0.01$  and  $P=0.001$  respectively) but noteworthy, survival was significantly different between patients with mild-to-moderate and moderate-to-

severe residual TR, suggesting that a more granular grading scheme improves outcome prediction.

**TABLE 1:** Baseline characteristics overall and according to residual TR grade at discharge – 3-grade scheme.

Characteristics	Overall (N=613)	No/mild TR (N=203)	Moderate TR (N=319)	Severe TR (N=91)	P- Value
<b>Clinical</b>					
Age – years	78±8	78±7	77±8	77±7	0.11
Age ≥70years – no. (%) *	542 (88%)	188 (93%)	277 (87%)	77 (85%)	<b>0.05</b>
Female sex – no. (%)	366 (60%)	126 (62%)	186 (58%)	54 (59%)	0.69
Body surface area – m <sup>2</sup>	1.86±0.22	1.86±0.22	1.86±0.23	1.85±0.19	0.88
Body mass index – kg/m <sup>2</sup>	26±5	27±5	26±5	26±5	0.39
Diabetes mellitus – no./total no. (%)	155/610 (25%)	51/201 (25%)	85/318 (27%)	19/91 (21%)	0.53
Chronic lung disease – no. (%)	130 (21%)	34 (17%)	76 (24%)	20 (22%)	0.15
Coronary artery disease – no. (%)	246 (40%)	74 (36%)	126 (40%)	46 (51%)	0.07
Permanent pacemaker – no. (%)	178 (29%)	47 (23%)	102 (31%)	29 (32%)	0.08
Prior left-sided heart valve intervention – no. (%)	204 (33%)	62 (31%)	103 (32%)	39 (43%)	0.10
New York Heart Association functional class III-IV – no. (%) *	528 (86%)	175 (86%)	273 (86%)	80 (88%)	0.85
Right-sided heart failure signs – no. (%) *	390 (63%)	127 (63%)	210 (66%)	53 (58%)	0.38
Daily dose of loop diuretics – mg	60 [40-120]	40 [20-80]	60 [40-120]	80 [40-120]	<b>0.013</b>
Daily dose of loop diuretics ≥125mg – no. (%) *	116 (19%)	21 (10%)	74 (23%)	21 (23%)	<b>&lt;0.001</b>
Atrial fibrillation – no./total no. (%)	461/533 (86%)	167/194 (86%)	215/253 (85%)	79/86 (92%)	0.27
<b>Laboratory</b>					
Hemoglobin – g/dl	10.4±2.6	10.7±2.6	10.1±2.7	11.1±2	<b>&lt;0.001</b>
Creatinine – μmol/l	125±59	115±46	128±63	131±61	<b>0.03</b>
Glomerular filtration rate – ml/min	52±22	53±20	52±23	48±19	0.19
Glomerular filtration rate <30ml/min – no. (%) *	74 (12%)	21 (10%)	40 (13%)	13 (14%)	0.59
Elevated total bilirubin – no. (%) *	133 (22%)	41 (20%)	60 (19%)	32 (35%)	<b>0.003</b>
NT-proBNP – pg/mL	1980 [1135-3783]	1697 [1052-3673]	1980 [1133-3539]	2486 [1630-4988]	<b>0.004</b>
<b>Echocardiographic</b>					
Left Ventricle ejection fraction – %	54±11	54±11	54±11	53±11	0.98
Left Ventricle ejection fraction <60% – no. (%) *	446 (73%)	145 (71%)	235 (74%)	66 (73%)	0.85
Tricuspid annulus diameter in apical 4-chamber view – mm	45±7	44±6	46±7	48±9	<b>0.0003</b>
Moderate/severe right ventricular dilatation – no./total no. (%)	420/541 (78%)	119/181 (66%)	229/282 (81%)	72/78 (92%)	<b>&lt;0.001</b>
Moderate/severe right ventricular dysfunction – no. (%) *	160 (26%)	47 (23%)	83 (26%)	30 (33%)	0.21
Systolic pulmonary artery pressure – mmHg	44±16	45±15	45±16	39±16	<b>0.02</b>
<b>TRI-SCORE</b>	5 [4-6]	5 [3-6]	5 [4-6]	5 [4-7]	<b>0.05</b>
≤3 – no. (%)	144 (23%)	56 (28%)	69 (22%)	19 (21%)	-
4-5 – no. (%)	245 (40%)	84 (41%)	128 (40%)	33 (36%)	-
≥6 – no. (%)	224 (37%)	63 (31%)	122 (38%)	39 (43%)	-

Values are number of patients (percentage), mean ± standard deviation or median [inter-quartiles].

\* The eight parameters included in the TRI-SCORE.

**TABLE 2:** Baseline characteristics according to residual TR grade at discharge – 4-grade scheme.

Characteristics	No/mild TR (N=203)	Mild-to-moderate TR (N=201)	Moderate-to-severe TR (N=118)	Severe TR (N=91)	P-Value
<b>Clinical</b>					
Age – years	78±7	76.8±8	77.5±9	77±7	0.17
Age ≥70years – no. (%) *	188 (93%)	174 (87%)	103 (87%)	77 (85%)	0.13
Female sex – no. (%)	126 (62%)	123 (61%)	63 (53%)	54 (59%)	0.45
Body surface area – m <sup>2</sup>	1.86±0.22	1.85±0.22	1.89±0.23	1.85±0.19	0.42
Body mass index – kg/m <sup>2</sup>	27±5	26±5	26±5	26±5	0.53
Diabetes mellitus – no./total no. (%)	51/201 (25%)	53 (26%)	32/117 (27%)	19/91 (21%)	0.75
Chronic lung disease – no./total no. (%)	34 (17%)	51 (25%)	25 (21%)	20 (22%)	0.21
Coronary artery disease – no. (%)	74 (36%)	73 (36%)	53 (45%)	46 (51%)	0.06
Permanent pacemaker – no./total no. (%)	47 (23%)	63 (31%)	39 (33%)	29 (32%)	0.16
Prior left-sided heart valve intervention – no./total no. (%)	62 (31%)	66 (33%)	37 (31%)	39 (43%)	0.20
New York Heart Association functional class III-IV – no. (%) *	175 (86%)	174 (87%)	99 (84%)	80 (88%)	0.86
Right-sided heart failure signs – no. (%) *	127 (63%)	134 (67%)	76 (64%)	53 (58%)	0.56
Daily dose of loop diuretics – mg	40 [20-80]	60 [30-120]	70 [40-160]	80 [40-120]	<b>0.02</b>
Daily dose of loop diuretics ≥125mg – no. (%) *	21 (10%)	42 (21%)	32 (27%)	21 (23%)	<b>&lt;0.001</b>
Atrial fibrillation – no./total no. (%)	167/194 (86%)	138/163 (85%)	77/90 (86%)	79/86 (92%)	0.44
<b>Laboratory</b>					
Hemoglobin – g/dl	10.7±2.6	10±2.7	10.2±2.8	11.1±2	<b>0.002</b>
Creatinine – μmol/l	115±46	127±66	130±59	131±61	0.08
Glomerular filtration rate – ml/min	53±20	54±22	51±24	48±19	0.30
Glomerular filtration rate <30ml/min – no. (%) *	21 (10%)	21 (10%)	19 (16%)	13 (14%)	0.35
Elevated total bilirubin – no. (%) *	41 (20%)	34 (17%)	26 (22%)	32 (35%)	<b>0.005</b>
NT-proBNP – pg/mL	1697 [1052-3673]	1930 [1100-3050]	2156 [1172-4214]	2486 [1630-4988]	<b>0.006</b>
<b>Echocardiographic</b>					
Left Ventricle ejection fraction – %	54±11	53.85±10.4	53.2±11.1	53±11	0.96
Left Ventricle ejection fraction <60% – no. (%) *	145 (71%)	149 (74%)	86 (73%)	66 (73%)	0.95
Moderate/severe right ventricular dilatation – no./total no. (%)	119/181 (66%)	137/165 (83%)	92/117 (79%)	72/78 (92%)	<b>0.0001</b>
Tricuspid annulus diameter in apical 4-chamber view – mm	44±6	46±6	47±7	48±9	<b>0.006</b>
Moderate/severe right ventricular dysfunction – no. (%) *	47 (23%)	57 (28%)	26 (22%)	30 (33%)	0.20
Systolic pulmonary artery pressure – mmHg	45±15	47±16	42±16 §	39±16	<b>0.003</b>
<b>TRI-SCORE</b>					
≤3 – no. (%)	5 [3-6]	5 [4-6]	5 [4-6]	5 [4-7]	<b>0.03</b>
4-5 – no. (%)	56 (28%)	44 (22%)	25 (21%)	19 (21%)	-
4-5 – no. (%)	84 (41%)	84 (42%)	44 (37%)	33 (36%)	-
≥6 – no. (%)	63 (31%)	73 (36%)	49 (42%)	39 (43%)	-

Values are number of patients (percentage), mean ± standard deviation or median [inter-quartiles].

\* The eight parameters included in the TRI-SCORE.

§ P<0.05 between moderate-to-severe and mild-to-moderate TR.

Figure 1.

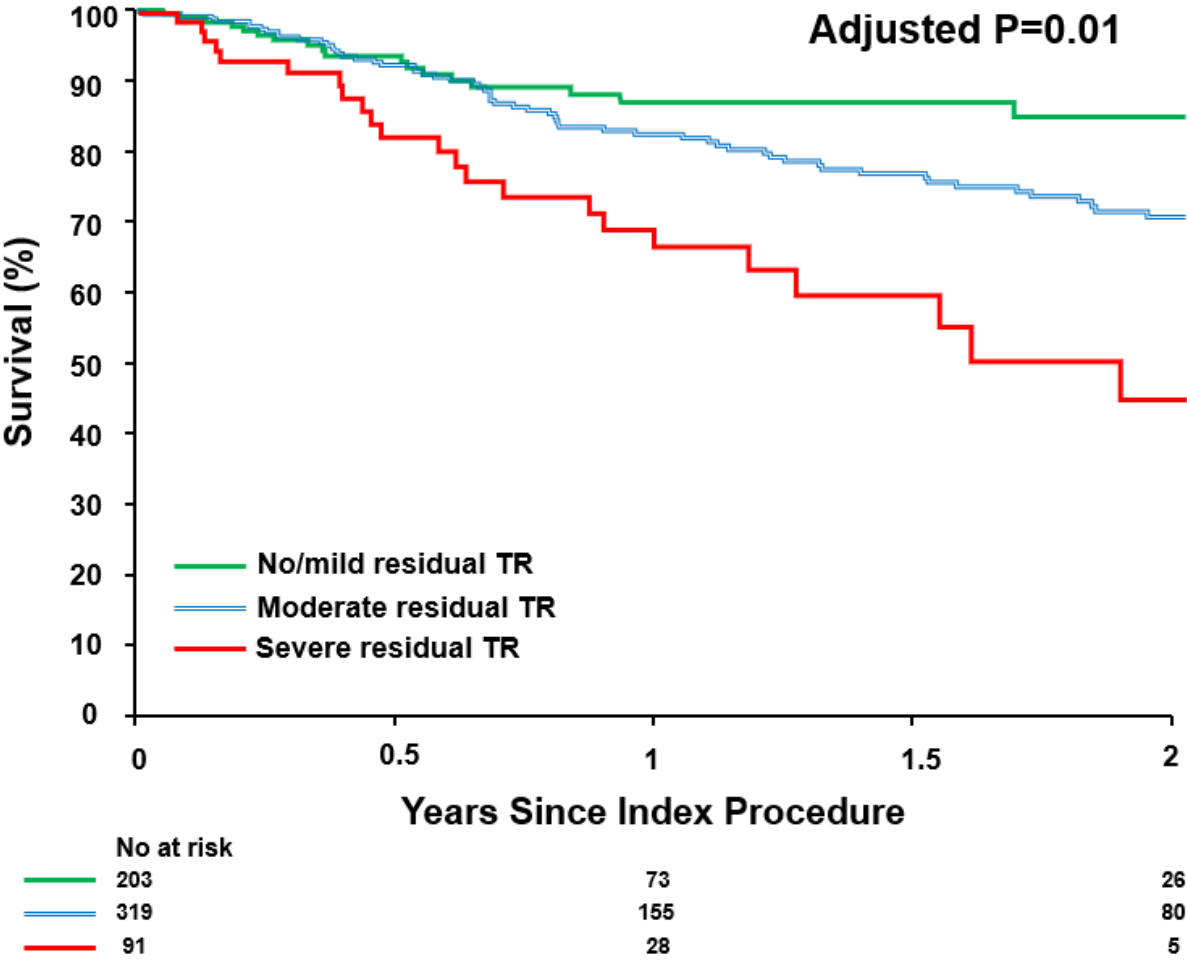
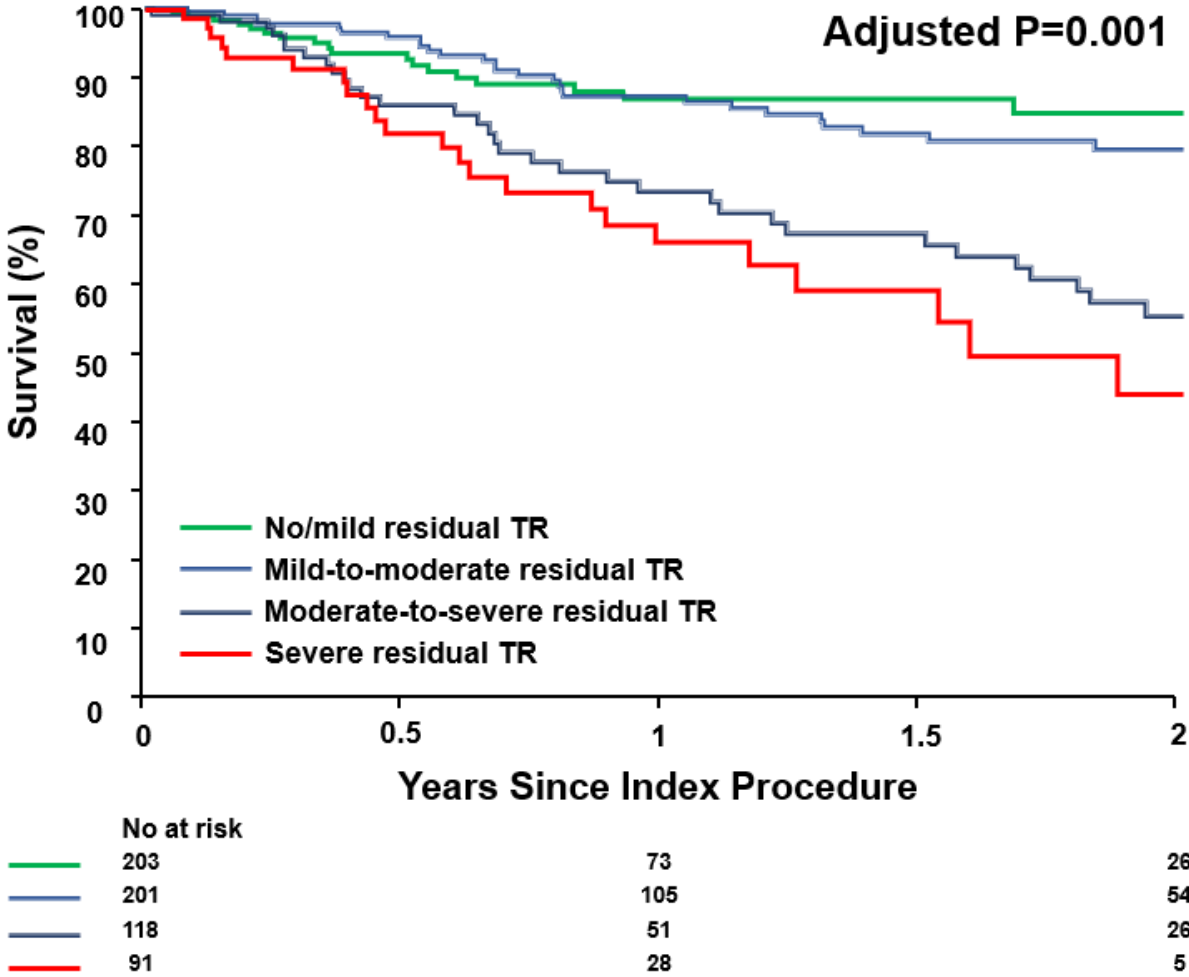




Figure 2.



## CENTRAL ILLUSTRATION.

