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TRI-SCORE and benefit of intervention in patients with severe tricuspid regurgitation

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Introduction

Tricuspid regurgitation (TR) is highly prevalent in the general population and is associated with an increased mortality and morbidity.^{1–4} In patients with isolated severe TR, North American and European Societies of Cardiology and Cardiac Surgery guidelines recommend tricuspid valve surgery when patients are symptomatic or present with right ventricular dilatation in the absence of severe right ventricular dysfunction.^{5,6} However, the level of evidence is limited, and most patients are conservatively managed, left with diuretics to relieve symptoms, while a surgical correction for isolated severe TR is seldom performed even in the recent era.^{7–9} Reluctance to refer patients for isolated tricuspid valve surgery is due on the one hand to the belief that TR is benign and on the other hand to the high post-operative mortality and to the uncertainties regarding the benefit of TR correction.^{10,11} Transcatheter intervention has emerged as a less invasive alternative to surgery and is nowadays the dominant mode of TR correction in several countries.^{12,13} However, the recent TRILUMINATE trial comparing transcatheter tricuspid edge-to-edge therapy to medical management failed to show any impact on mortality or heart failure admissions in patients with isolated TR at one year.¹⁴

A key element, often overlooked, is the progressive nature of the disease and its long-term effects on cardiac and extra-cardiac function. Clinical presentation is the main driver of the post-operative outcome,^{15–17} and a late intervention after the development of right ventricular remodelling, or renal and hepatic dysfunction contributes to the 10% in-hospital mortality rate reported after isolated tricuspid valve surgery. We recently developed the TRI-SCORE, based on eight clinical, biological, and echocardiographic parameters (age, New York Heart Association functional class, right-sided heart failure signs, daily dose of furosemide, glomerular filtration rate, total bilirubin level, left ventricular ejection fraction, and right ventricular function), to predict in-hospital mortality after isolated tricuspid valve surgery^{18,19} (see [Supplementary data online, Figure S1](#)). The TRI-SCORE is ideally suited to stage TR populations and to evaluate whether the benefit of an intervention and its modality vary according to a TR disease stage. To answer this question, we developed TRIGISTRY, a large multicentre international registry of patients with severe isolated functional TR and we aimed to compare mortality rates after isolated tricuspid valve surgery and transcatheter correction to conservative management according to the TR clinical stage as assessed using the TRI-SCORE.

Methods

Study design

The TRIGISTRY is a multinational registry across 10 countries (Austria, Canada, France, Germany, Israel, Italy, the Netherlands, Spain, Switzerland, and the USA) and 33 centres aiming to compare outcomes of adult patients with severe isolated functional TR on native valve either conservatively managed, who underwent an isolated tricuspid valve surgery or a transcatheter tricuspid valve intervention. The list of participating centres and investigators is provided in the [Supplementary data online, Appendix](#). Clinical, laboratory, echocardiographic, and outcomes information were collected locally by each centre and centralized in a unique depository anonymized database at the University of Ottawa Heart Institute.

The first and last authors designed the study protocol and were responsible for the study coordination. All the investigators were responsible for data collection and vouched for the completeness and accuracy of the data. All the authors reviewed and approved the manuscript written by the first and last authors. Data analyses 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. There was no dedicated funding for this study.

Study population

TRIGISTRY retrospectively enrolled patients with severe isolated functional TR on native valve. Functional TR was defined by structurally normal tricuspid valve. TR severity was assessed using an integrative multiparametric approach.^{20,21} Patients with prior tricuspid valve intervention or patients with moderate or greater concomitant left-sided valvular heart disease were excluded. Patients who underwent an aortic or mitral valve intervention (either surgical or transcatheter) within 3 months prior to the tricuspid valve intervention were also excluded. Patients with congenital heart disease were excluded. The study population was divided based on treatment modality (conservative management, surgery, and transcatheter intervention). In the surgical group, only patients who underwent an isolated tricuspid valve surgery (repair or replacement) were included (i.e. no concomitant intervention such as mitral or aortic valve surgery, or coronary artery bypass graft). We included all transcatheter tricuspid valve repair techniques and excluded transcatheter valve replacements. For patients under loop diuretics treatments other than furosemide, 10 mg of torasemide or 1 mg of bumetamide were considered equivalent to 40 mg of furosemide. Patients for whom the eight mandatory parameters to calculate the TRI-SCORE could not be collected were excluded. The TRI-SCORE ranges from 0 to 12 points, and the population was divided into three subsets based on previously validated TRI-SCORE risk categories and predicted post-operative mortality (low risk: ≤ 3 points, intermediate risk: 4–5 points, and high risk: ≥ 6 points).¹⁸

Follow-up and primary endpoint

All-cause death (in-hospital or during follow-up) at 2 years after the initial evaluation in the conservative management group and after the intervention in patients who underwent a surgical or transcatheter intervention was collected. Length of stay after surgical or transcatheter interventions was calculated as the time duration between the admission and hospital discharge. Tricuspid regurgitation grade at discharge after surgery or transcatheter intervention was semi-quantitatively assessed by transthoracic echocardiography, and a successful correction was defined as a mild to moderate (2+) or lower TR degree based on a four grades scale.

Statistical analysis

Variables were expressed as mean \pm standard deviation or median [25th–75th percentile] for continuous variables and number of patients (percentage) for categorical variables. Comparisons of baseline characteristics between the treatment groups were performed using ANOVA, χ^2 , Student's *t*-test or non-parametric Wilcoxon test as appropriate in the overall population and in each TRI-SCORE risk category. Survival rates were presented using the Kaplan–Meier method and compared using log-rank test up to 2 years including in-hospital mortality (follow-up censored at 2 years). A Cox proportional hazards regression model was performed to compare mortality according to treatment modality at 2 years after adjustment for age (as a continuous variable), sex, atrial fibrillation, and comorbidities (diabetes, chronic lung disease, coronary artery disease, and prior left heart valve intervention). Comparisons were performed between the different groups overall and for the surgical and transcatheter groups using conservative management as reference with adjusted hazard ratios (HR) and 95% confidence intervals. For analyses comparing the treatment groups, a treatment by logtime interaction term was used to assess the proportionality assumption. Analyses were repeated subdividing the transcatheter group based on procedural results (residual TR at discharge \leq mild to moderate, or \geq moderate). Analyses were performed at the two-tailed $P < .05$ level, using SAS statistical software version 9.4 (SAS Institute Inc., Cary, NC).

Table 1 Baseline characteristics of the population overall and according to treatment modality

Characteristics	Overall (n = 2413)	Conservative management (n = 1217)	Isolated tricuspid valve surgery (n = 551)	Transcatheter tricuspid valve repair (n = 645)	P-value
Clinical					
Age—years	72 ± 12	71 ± 13	68 ± 11	77 ± 8	<.001
Age ≥ 70 years—no. (%) ^a	1618 (67)	769 (63)	283 (51)	566 (88)	<.001
Female sex—no. (%)	1270 (53)	535 (44)	348 (63)	387 (60)	<.001
Diabetes mellitus—no./total no. (%)	619/2410 (26)	339 (28)	118 (21)	162/642 (25)	.003
Chronic lung disease—no./total no. (%)	466/2412 (19)	241 (20)	90 (16)	135/644 (21)	.002
Coronary artery disease—no. (%)	917 (38)	529 (43)	132 (24)	256 (40)	<.001
Permanent pacemaker—no./total no. (%)	651/2406 (27)	319 (26)	145/544 (27)	187 (29)	.43
Prior left heart valve intervention—no./total no. (%)	633/2412 (26)	157/1216 (13)	257 (47)	219 (34)	<.001
New York Heart Association functional class III–IV—no. (%) ^a	1562 (65)	637 (52)	366 (66)	559 (87)	<.001
Right-sided heart failure signs—no. (%) ^a	1431 (59)	660 (54)	364 (66)	407 (63)	<.001
Daily dose of loop diuretics—mg	50 [40–80]	40 [30–80]	60 [40–120]	60 [40–120]	<.001
Daily dose of loop diuretics ≥ 125 mg—no. (%) ^a	401 (17)	145 (12)	129 (23)	127 (20)	<.001
Atrial fibrillation—no./total no. (%)	1532/2317 (66)	685/1204 (57)	367 (67)	480/562 (85)	<.001
Laboratory					
Haemoglobin—g/dL	11.7 ± 2.4	12.1 ± 2.2	12.2 ± 1.9	10.4 ± 2.6	<.001
Creatinine—μmol/L	124 ± 78	129 ± 90	112 ± 63	124 ± 59	<.001
Glomerular filtration rate—mL/min	62 ± 33	67 ± 39	64 ± 29	51 ± 21	<.001
Glomerular filtration rate < 30 mL/min—no. (%) ^a	266 (11)	148 (12)	37 (7)	81 (13)	.009
Elevated total bilirubin—no. (%) ^a	688 (29)	373 (31)	169 (31)	146 (23)	<.001
Echocardiographic					
Left ventricle ejection fraction—%	51 ± 14	45 ± 15	57 ± 10	54 ± 11	<.001
Left ventricle ejection fraction < 60%—no. (%) ^a	1605 (66)	871 (72)	265 (48)	468 (73)	<.001
Moderate/severe RV dilatation—no./total no. (%)	1471/2336 (63)	594/1217 (49)	442 (80)	435/568 (77)	<.001
Moderate/severe right ventricular dysfunction—no. (%) ^a	1001 (41)	657 (54)	173 (31)	171 (27)	<.001
Systolic pulmonary artery pressure—mmHg	49 ± 18	54 ± 19	42 ± 11	43 ± 16	<.001
TRI-SCORE					
≤ 3—no. (%)	764 (32)	433 (36)	183 (33)	148 (23)	<.001
4–5—no. (%)	800 (33)	359 (29)	185 (34)	256 (40)	<.001
≥ 6—no. (%)	849 (35)	425 (35)	183 (33)	241 (37)	.31

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

^aThe eight parameters included in the TRI-SCORE.

Results

Population characteristics

We enrolled 2413 adult patients with severe isolated functional TR on native valve; 1217 (50%) patients were conservatively managed, 551 (23%) underwent an isolated tricuspid valve surgery, and 645 (27%) a transcatheter tricuspid valve intervention. Mean age was

72 ± 12 years, and 53% were women. A permanent pacemaker was present in 27% and 26% had a prior left-sided valvular heart disease intervention. Most patients were severely symptomatic (65% in New York Heart Association class III–IV, 59% presented with overt heart failure) and 66% had atrial fibrillation. Characteristics of the population overall and according to treatment modality are presented in [Table 1](#).

Table 2 Distribution of TRI-SCORE parameters according to TRI-SCORE category

Characteristics	Low TRI-SCORE (n = 764)	Intermediate TRI-SCORE (n = 800)	High TRI-SCORE (n = 849)	P-value
Age ≥ 70years—no. (%)	441 (58)	549 (69)	628 (74)	<.001
New York Heart Association functional class III–IV—no. (%)	258 (34)	567 (71)	737 (87)	<.001
Right-sided heart failure signs—no. (%)	114 (15)	547 (68)	770 (91)	<.001
Daily dose of loop diuretics ≥ 125 mg—no. (%)	20 (3)	75 (9)	306 (36)	<.001
Glomerular filtration rate < 30 mL/min—no. (%)	10 (1)	54 (7)	202 (24)	<.001
Elevated total bilirubin—no. (%)	33 (4)	158 (20)	497 (59)	<.001
Left ventricle ejection fraction < 60%—no. (%)	407 (53)	526 (66)	672 (79)	<.001
Moderate/severe right ventricular dysfunction—no. (%)	195 (26)	300 (38)	506 (60)	<.001

Values are number of patients (percentage).

Patients in the transcatheter group were older, presented more frequently with comorbidities such as diabetes, coronary artery disease, or lung disease than their counterpart who underwent a tricuspid valve surgery but presence of overt heart failure signs, dose of diuretics, or rate of right ventricular dysfunction were similar between the two intervention groups and distribution according to TRI-SCORE category was only mildly different although statistically significant. Among the patients who underwent a transcatheter or surgical tricuspid valve intervention, only 28% were considered at low surgical risk according to the TRI-SCORE.

Distribution of each TRI-SCORE parameters according to TRI-SCORE category is presented in Table 2. Prevalence of each parameter increased with TRI-SCORE category. In the low TRI-SCORE category, few patients presented with overt heart failure, high dose of diuretics, kidney or liver dysfunction and only 26% presented with moderate/severe right ventricular dysfunction.

In-hospital outcome after tricuspid valve intervention

A surgical tricuspid valve repair was performed in 200 patients (36%) and a replacement in 351 patients (64%), of whom 91% received a bioprosthetic valve. A new permanent pacemaker was implanted in 11% of patients. The length of stay was 13 [8–22] days. In-hospital mortality rate was 9.6%. At discharge, residual TR degree was mild to moderate or less in 97% of patients.

In the transcatheter group, 509 patients (79%) were treated with tricuspid edge-to-edge repair [MitraClip® or TriClip® system (Abbott Structural Heart, Santa Clara, CA, USA)], or PASCAL system® (Edwards Lifesciences, Irvine, CA, USA). The remaining were treated with annuloplasty [CardioBand system® (Edwards Lifesciences, Irvine, CA, USA)] or other techniques [Trialign® (Mitralign, Inc., Boston, MA, USA), Trichinch® (4Tech Cardio Ltd, Galway, Ireland)]. In-hospital length of stay was 7 [5–10] days. A new permanent pacemaker was implanted in 0.4% of patients. In-hospital mortality rate was 2.5%. At discharge, residual TR was mild to moderate or less in 65% of patients.

Survival according to TRI-SCORE

The TRI-SCORE was low in 32%, intermediate in 33%, and high in 35%. Follow-up was available in 98% of patients [median 1.7 years (0.46–2)].

Survival rates decreased with TRI-SCORE category overall (83%, 74%, and 59% in the low, intermediate, and high categories, respectively, $P < .0001$) and in each treatment group (79%, 71%, and 61%, respectively, $P < .001$ in the conservative management group; 93%, 80%, and 58% $P < .001$ in the surgical group, respectively, and 87%, 71%, and 56%, respectively, $P < .001$ in the transcatheter group) (Figure 1). Results remained unchanged after adjustment for age, sex, atrial fibrillation, and comorbidities (all $P < .001$).

Survival according to treatment modality and TRI-SCORE category

Overall

There were 556 deaths within 2 years, 327 in the conservative management group, 111 in the surgical group, and 118 in the transcatheter valve repair group. At 2 years, survival rates were not different between groups (71%, 77%, and 69% in the conservative management, surgical, and transcatheter groups, respectively, $P = .10$) (Figure 2A). The similar mortality rates between treatment modalities persisted after adjustment for age, sex, atrial fibrillation, and comorbidities ($P = .23$).

Low TRI-SCORE

In-hospital mortality in the surgical and transcatheter groups was 2.7% and 0.7%, respectively. At 2 years, survival rates were significantly different between groups (79%, 93%, and 87% in the conservative management, surgical, and transcatheter groups, respectively, $P = .0002$) (Figure 2B). After adjustment for age, sex, atrial fibrillation, and comorbidities, results remained unchanged ($P = .006$). Compared to the conservative management group, survival was significantly higher in the surgical group [adjusted HR 0.35 (0.18–0.69), $P = .002$] but not in the transcatheter valve repair group [adjusted HR 0.65 (0.32–1.31), $P = .23$].

Intermediate TRI-SCORE

Compared to the low TRI-SCORE subset, in-hospital mortality rate was significantly higher in the surgical group (9.2% vs. 2.7%, $P = .009$) but the difference did not reach statistical significance in the transcatheter group (2.0% vs. 0.7%, $P = .27$). Survival rates at 2 years were not significantly different between groups (71% in the conservative management group, 80% in the surgical group, and 71% in the transcatheter

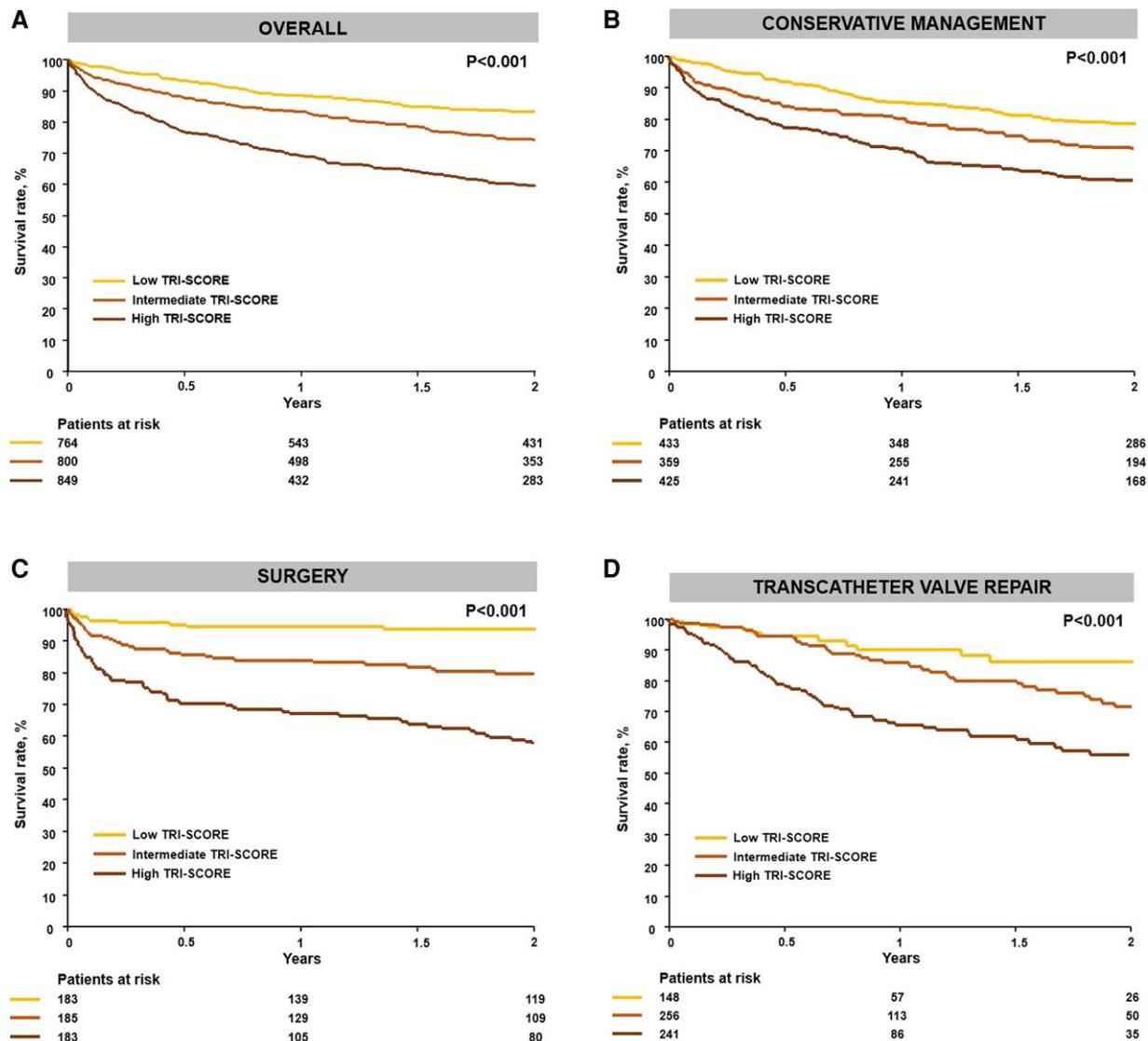


Figure 1 Survival rate according to the TRI-SCORE. The figure displays Kaplan–Meier curves of the survival of (A) the overall population, (B) the conservative management group, (C) the surgical group, and (D) the transcatheter valve repair group according to the TRI-SCORE risk category (low: ≤ 3 points, intermediate: 4–5 points, and high: ≥ 6 points).

group, $P = .13$) (Figure 2C). Similar mortality rates were also observed after adjustment for age, sex, atrial fibrillation, and comorbidities ($P = .15$). Compared to the conservative management group, survival rates in the surgical group [adjusted HR 0.73 (0.47, 1.15), $P = .14$] and the transcatheter group [adjusted HR 0.69 (0.44–1.09), $P = .11$] were not statistically different.

High TRI-SCORE

Compared to the low and intermediate risk category, in-hospital mortality rates markedly increased in the surgical group (16.9%, $P < .001$) and to a lesser extent in the transcatheter group but did not reach statistical significance (4.3%, $P = .06$). At 2 years, survival rates were not different between groups (61%, 58%, and 56% in the conservative management, surgical, and transcatheter groups, respectively, $P = .66$) (Figure 2D). Results remained unchanged after adjustment for age,

sex, atrial fibrillation, and comorbidities ($P = .48$). When compared to the conservative management group, survival was similar in the surgical [adjusted HR 1.21 (0.87–1.70), $P = .26$] and transcatheter groups [adjusted HR 0.98 (0.68–1.43), $P = .90$].

Impact of residual tricuspid regurgitation post-intervention

Overall

Impact of residual TR was only assessed in the transcatheter group since a suboptimal correction was only observed in 3% (15 patients) after surgery. At 2 years, survival rates were 71% in the conservative management group, 77% in the surgical group, 79% in transcatheter group with successful correction, and 51% in transcatheter group with suboptimal correction ($P < .0001$) (Figure 3A).

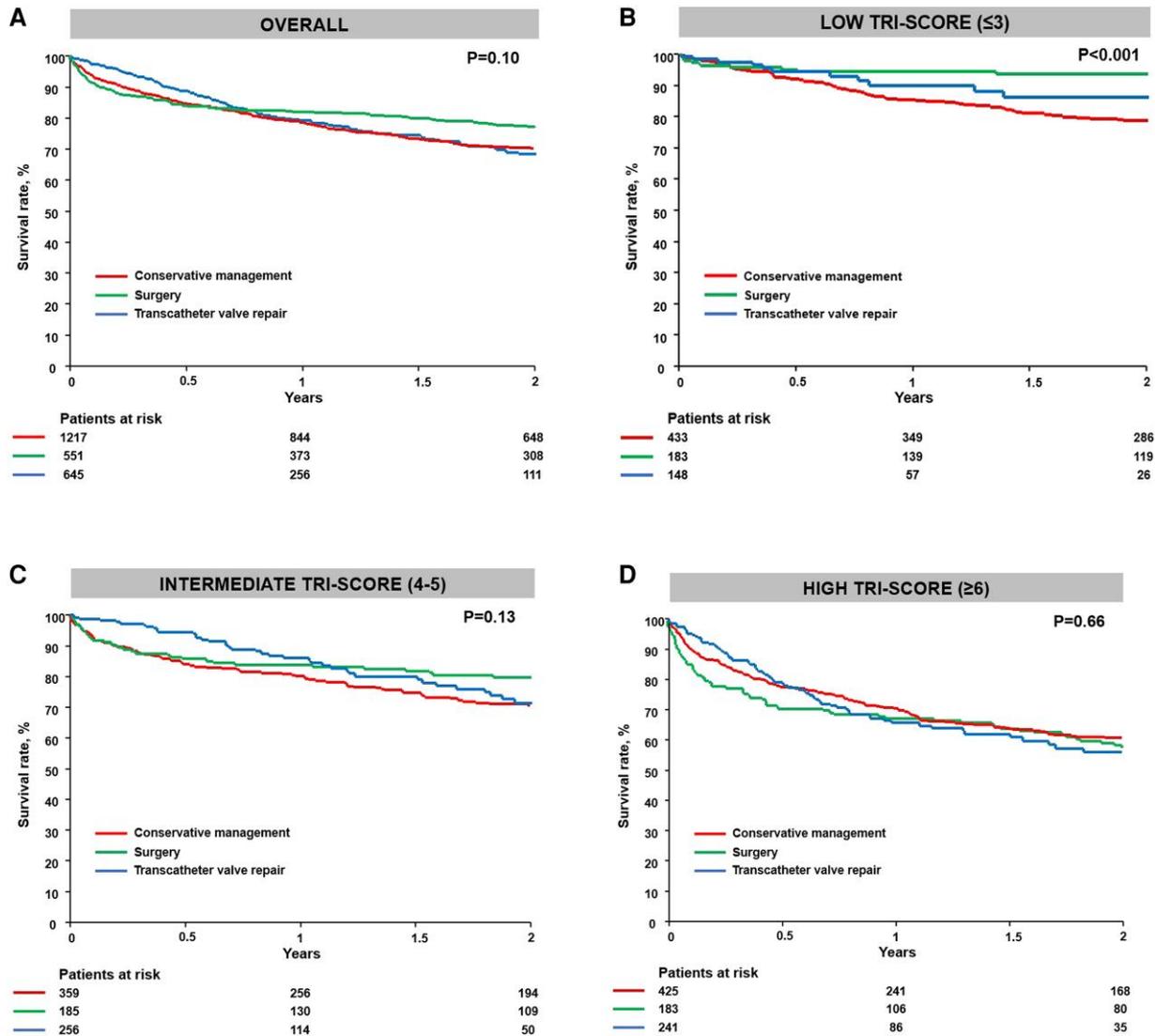


Figure 2 Survival rate according to treatment modality and TRI-SCORE category. The figure displays Kaplan–Meier curves of the survival of the conservative management, surgical, and transcatheter valve repair groups at 2 years, (A) overall and according to the TRI-SCORE category (B) low TRI-SCORE, (C) intermediate TRI-SCORE, and (D) high TRI-SCORE.

Low TRI-SCORE

Survival rates at 2 years were significantly different between the four groups (79%, 93%, 92%, and 76% in the conservative management, surgical, transcatheter with successful correction, and transcatheter with suboptimal correction groups, respectively, $P = .0001$) (Figure 3B). Results remained unchanged after adjustment for age, sex, atrial fibrillation, and comorbidities ($P = .004$). Compared to the conservative management group, survival almost reached statistical significance in the transcatheter intervention group with successful correction [adjusted HR 0.36 (0.13–1.02), $P = .055$].

Intermediate TRI-SCORE

Survival rates at 2 years were also significantly different between the four groups [71%, 80%, 81%, and 54% in the conservative management, surgical, transcatheter with successful correction, and transcatheter with suboptimal correction groups, respectively (Figure 3C)]. Results

remained unchanged after adjustment for age, sex, atrial fibrillation, and comorbidities ($P = .02$). Compared to the conservative management group, survival rates were significantly higher in the transcatheter group with successful correction [adjusted HR 0.46 (0.25–0.85), $P = .01$] and not different in the transcatheter group with suboptimal correction [adjusted HR 1.26 (0.70–2.25), $P = .44$].

High TRI-SCORE

In univariate analysis, survival rates were significantly different between the four groups (58%, 61%, 68%, and 40% in the conservative management, surgical, transcatheter with successful correction, and transcatheter with suboptimal correction groups, respectively, $P = .006$) (Figure 3D) but not after adjustment for age, sex, atrial fibrillation, and comorbidities ($P = .13$). Compared to the conservative management group, survival rate in the transcatheter with successful correction was not significantly better [adjusted HR 0.71 (0.43–1.19),

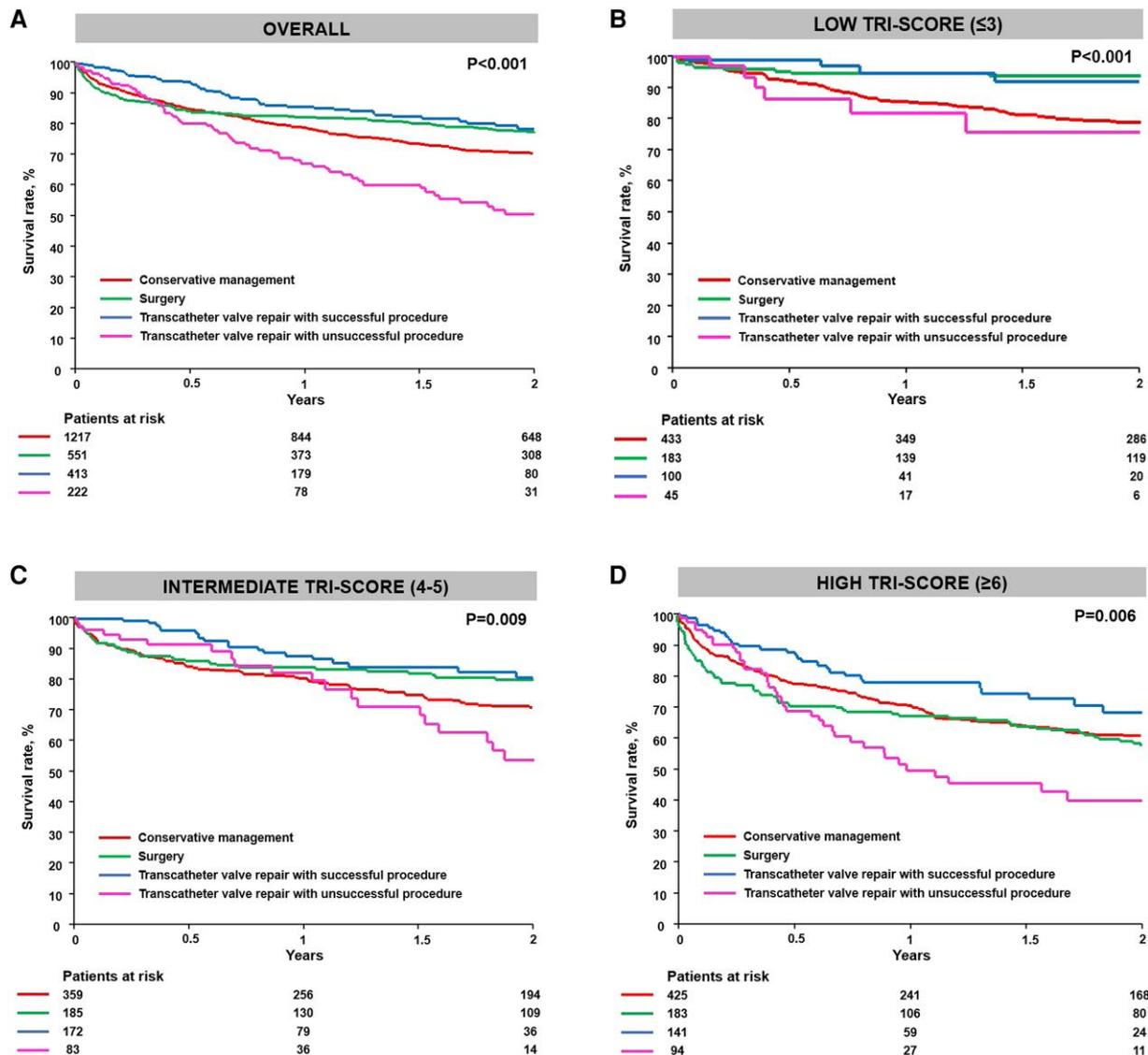


Figure 3 Survival rate according to treatment modality, procedural success, and TRI-Score category. The figure displays Kaplan–Meier curves of the survival of the conservative management, surgical, transcatheter valve repair with successful correction of the tricuspid regurgitation, and transcatheter valve repair with suboptimal correction of the tricuspid regurgitation groups at 2 years, (A) overall and according to the TRI-Score category (B) low TRI-Score, (C) intermediate TRI-Score, and (D) high TRI-Score.

$P = .18$] nor survival was significantly worse in the transcatheter group with suboptimal correction [adjusted HR 1.35 (0.83–2.20), $P = .22$].

Discussion

In this large multicentre international registry of patients with severe isolated functional TR, we evaluated the interaction between treatment modality and clinical presentation as assessed by the TRI-Score. First, we confirmed the poor prognosis associated with severe TR in patients with an advanced disease stage and extended the predictive value of the TRI-Score not only for the post-operative mortality but also at 2 years irrespective of treatment modality with nearly 40% of the patients deceased within 2 years in the high TRI-Score category. Second, we observed a beneficial impact of an intervention, whether surgical or

transcatheter, on survival compared to conservative management in the low and, to a lesser extent, in the intermediate TRI-Score category, while survival was similar irrespective of the treatment group in the high TRI-Score category. Finally, we showed the deleterious effect of suboptimal TR correction on survival (*Structured Graphical Abstract*).

Tricuspid regurgitation, including in the absence of any other structural abnormalities as in isolated functional atrial TR, is associated with an increased risk of mortality and morbidity increasing with TR severity. The main drivers of the outcome are the severity of the clinical presentation and TR consequences on the right ventricle, kidneys, and liver.²² These parameters are captured into the TRI-Score, which provides a simple and accurate method to predict post-operative mortality and to guide the management of patients with TR. The predictive value of the TRI-Score has been recently externally validated^{23,24} and

also extended to patients referred for transcatheter tricuspid valve intervention.²⁵ The present study confirms and extends these findings. Irrespective of the treatment group and modality, post-operative mortality and 2-year mortality gradually increased with the TRI-SCORE. A clinical stage is therefore critical to consider when designing randomized controlled trials and evaluating the potential benefit of interventions.

In contrast to the robust evidence linking TR and outcome, formal proof of the beneficial impact of TR correction has remained so far elusive. Observational studies are suffering from limited sample size, lack of comparator groups, or if present, patients were matched without considering the main determinants of outcomes as those included in the TRI-SCORE. Only one randomized study, TRILUMINATE, has been reported and shows an improvement of the quality of life in the transcatheter arm compared to the conservative management arm but no benefit on mortality, admission for heart failure, or on the 6-minute walk distance at one year. The disease stage of the patients enrolled in TRILUMINATE, as in most observational studies, is unclear as no TRI-SCORE is provided and might explain contradictory results previously reported. It is worth noting that there was no difference in mortality rates between the three treatment modalities overall even after adjustment for age, sex, atrial fibrillation, and comorbidities. Therefore, when analysing the benefit of a tricuspid valve intervention, it is critical to account for the heterogeneity of the TR population and to carefully phenotype the population. To assess the interaction between clinical presentation and potential benefit of tricuspid valve interventions, we developed TRIGISTRY, a large multicentre international registry across 10 countries and 33 centres. In addition to its unmatched size, TRIGISTRY is constituted exclusively of patients with severe isolated functional TR, fully characterized and staged based on the TRI-SCORE, a multiparametric adjustment parameter specific for the TR population. TRIGISTRY was well powered and uniquely enrolled patients conservatively managed, who underwent an isolated tricuspid valve surgery or an isolated transcatheter tricuspid valve repair, with sizeable populations in all treatment modalities and all TRI-SCORE category subsets followed up to 2 years.

The present study shows that the benefit of TR correction is not uniform but varies according to the disease stage. A significant benefit was observed in patients in the low TRI-SCORE category and, to a lower extent, in the intermediate category, while we did not observe any survival benefit in the high TRI-SCORE category with either surgery or transcatheter therapies. In patients with a low TRI-SCORE, surgery and transcatheter repair provided excellent outcomes at 2 years. It is worth noting that in the low TRI-SCORE category, in-hospital mortality rate for isolated tricuspid valve surgery was low (2.7%) and in line with predicted. Therefore, paradigm should be shifted, the 10% in-hospital mortality reported in most series (including in TRIGISTRY when all TRI-SCORE categories were combined) is not intrinsically due to the complexity of the tricuspid valve surgery but is due to the late referral of patients and to the 'wait and see until too late' attitude that has prevailed for a long time. The current results stress the importance of a careful risk-stratification of TR patients, and to consider an intervention earlier in the course of the disease. At the extreme end of the spectrum, in patients with high TRI-SCORE, survival was similar in the conservative management, transcatheter, and surgical groups, suggesting that no benefit on survival is likely to be expected at an advanced disease stage.

TRIGISTRY also highlights the importance of a successful TR correction. In the low and intermediate TRI-SCORE categories, survival curves of the surgical and transcatheter groups with successful

correction were superimposable. These results, besides reinforcing the evidence that TR correction improves outcome, show that more than the technique itself, an efficient TR correction is critical to achieve good outcomes. In TRIGISTRY, approximately one-third of the transcatheter population presented a significant residual TR likely preventing any benefit on survival. These real-life results are in line with those reported in other real-life registries¹¹ and might explain at least partially the neutral effect of transcatheter correction in TRILUMINATE.¹⁴ Therefore, a decrease of one or two TR grades, especially from torrential or massive to severe, should not be considered as a satisfactory result and transcatheter correction should aim for mild to moderate or even lower TR degree. Our results also highlight the need to improve the results of transcatheter tricuspid valve repair.

The present study is not without limitations. First, inherent bias associated to its retrospective design cannot be excluded. However, our population was derived from consecutive collection of TR patients at each centre. In addition, comparisons between groups were performed according to TRI-SCORE categories, avoiding complex and often inaccurate adjustment, and reducing the risk of confounders. Second, prescription and dose of mineralocorticoid receptor antagonists were not collected. Third, the TRI-SCORE was only calculated at one time point, and we could not evaluate the prognostic impact of its change over time. Fourth, data collection including echocardiographic parameters was collected locally at the centre level with no centralized evaluation. The worse outcome of patients with significant residual TR can be considered as a *post hoc* validation of the overall quality of TR grading. Fifth, 26% had a previous left-sided intervention. We did not collect the type of intervention and its time interval with the enrolment in registry but a delay of at least 3 months was required and patients with moderate or greater concomitant left-sided valvular heart disease on native or prosthetic valve were excluded. Sixth, both transcatheter (and to a lower extent surgical) technology and operator's expertise improved over time. Importantly, 80% of transcatheter interventions were performed after 2018, and analyses were repeated according to transcatheter procedural success. It is worth noting that such sub-analysis was not performed in the surgical group as a successful TR correction was not achieved in only 3% of the patients. Finally, 2 years may seem a relatively short follow-up duration. However, transcatheter interventions are relatively novel, and our follow-up duration in this group is one of the longest to date. Importantly, our follow-up was long enough to overcome the excess immediate mortality intrinsically associated with surgery and to fairly compare the three strategies.

Conclusion

TRIGISTRY confirmed and extended the predictive value of the TRI-SCORE and showed that a tricuspid valve intervention, irrespective of the modality as long as enabling a successful TR correction, was associated with significantly better survival rates than conservative management in the low and, to a lower extent, intermediate TRI-SCORE categories while survival was similar across groups in the high TRI-SCORE category. Our result better defines the optimal timing to treat patients with severe TR promoting a curative intervention at an earlier disease stage as assessed by the TRI-SCORE and will guide the design of future randomized controlled trials.

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Supplementary data

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

Declarations

Disclosure 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. Philipp Bartko received speaker fees from Abbott Vascular. Manuel Carnero-Alacazar received consulting fees from Edwards-Lifesciences, and for lectures and proctoring from Abbott Vascular and Atricure. Augustin Coisne received speaker fees from Abbott Vascular and GE Healthcare. Juan Crestanello received consulting fees from Medtronic. 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 Abbott Vascular, Edwards-Lifescience and Philips Healthcare. Jörg Hausleiter received grant and consulting fees from Edwards-Lifesciences. Christos Iliadis received consulting fees from Abbott Vascular and Edwards-Lifesciences. Francesco Maisano received Grant and/or Research Institutional Support from Abbott, Medtronic, Edwards Lifesciences, Biotronik, Boston Scientific Corporation, NVT, Terumo, Venus, 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, 4Tech and Perifect. David Messika-Zeitoun received research grants from Edwards. Thomas Modine received speaker or consulting fees from Abbott, Edwards-Lifesciences, Medtronic, Microport and GE. Mohammed Nejari received proctoring fees from Abbott Vascular. Luis Nombela-Franco received consulting or speaker fees from Abbott Vascular, Edwards-Lifesciences and Products and Features. Jean-François Obadia received consulting or speaker fees from Abbott Delacroix Chevalier and Medtronic. Volker Rudolph received consulting or speaker fees from Abbott Vascular and Edwards-Lifesciences. Gilbert H. L. Tang is a physician proctor, consultant and advisory board member for Medtronic, a consultant and physician advisory board member for Abbott Structural Heart, a consultant for NeoChord, a physician advisory board member for Boston Scientific and JenaValve and has received speakers honoraria from Siemens Healthineers and East End Medical. Maurizio Taramasso received consulting or speaker fees from Abbott, Edwards Lifesciences. Boston Scientific, Medtronic, Shenqi Medical, PiCardia, CardioValve, Coremedic, ReCross, CorQuest, VentriMend and Simulands. Christophe Tribouilloy received speaker fees from Novartis and Sanofi. Ralph Stephan von Bardeleben received consulting or speaker fees from Abbott Vascular, Edwards-Lifesciences, Medtronic, Philips and Siemens. Jose Luis Zamorano received consulting or speaker fees from Novartis, Novonordisk, Bayer, Pfizer, Daichii and Medtronic. All other authors have no relationship to declare.

Data Availability

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

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Ethical Approval

Ethical Approval was not required.

Pre-registered Clinical Trial Number

TRIGISTRY ClinicalTrials.gov, NCT05825898.

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