TRI-SCORE: a single-centre validation study

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Word count: 3772

Abstract

Background and Aims: The TRI-SCORE is a recently published risk score for predicting in-hospital mortality in patients undergoing isolated tricuspid valve surgery (ITVS). The aim of this study is to externally validate the ability of the TRI-SCORE in predicting in-hospital and long-term mortality following ITVS.

Methods: A retrospective review of our institutional database was carried out to identify all patients undergoing isolated tricuspid valve repair or replacement from March 1997 to March 2021. The TRI-SCORE was calculated for all patients. Discrimination of the TRI-SCORE was assessed using receiver operating characteristic curves. Accuracy of the models was tested calculating the Brier score. Finally, a COX regression was employed to evaluate the relationship between the TRI-SCORE value and long-term mortality.

Results: A total of 176 patients were identified and the median TRI-SCORE was 3 (1-5). The cut-off value identified for increased risk of isolated ITVS was 5. Regarding in-hospital outcomes, the TRI-SCORE showed high discrimination (area under the curve 0.82), and high accuracy (Brier score 0.054). This score showed also very good performance in predicting long-term mortality (at 10 years HR: 1.47, 95% CI [1.31-1.66], p<0.001), with high discrimination (area under the curve >0.80 at 1-5 and 10 years) and high accuracy values (Brier score 0.179).

Conclusions: This external validation confirm the good performance of the TRI-SCORE in predicting in-hospital mortality. Moreover, the score showed also very good performance in predicting the long-term mortality.

Key Words: TRI-SCORE, risk scores, isolated tricuspid valve surgery, tricuspid regurgitation, tricuspid valve disease

Abbreviations:

AUC: area under the curve

ITVS: isolated tricuspid valve surgery

ROC: receiver operating characteristic

TR: tricuspid regurgitation

TV: tricuspid valve

TVr: tricuspid valve repair

TVR: tricuspid valve replacement

Introduction

Isolated tricuspid valve regurgitation (TR) has gained increasing recognition in recent years. Initially considered benign, isolated severe TR has been found to be a strong predictor of poor prognosis (1,2). If left untreated, isolated TR significantly decrease survival at short and long-term (3–5). Despite such dismal prognosis, treatment of patients with severe isolated TR remains controversial, with reported high in-hospital mortality rates and great uncertainty regarding long-term outcomes (6–8). For these reasons surgical treatment is often delayed or even rejected (9). Therefore, a very low percentage of patients are currently receiving surgical treatment, resulting in undertreatment of the disease (5,9).

Patient selection and correct timing have emerged as key factors in determining favorable outcome following TR treatment (10). However, the most commonly available surgical scores do not reliably predict outcomes of patients undergoing isolated tricuspid valve surgery (ITVS) (11). Recently, a dedicated risk score, named the TRI-SCORE, was specifically developed to predict in-hospital mortality in patients undergoing ITVS (12). Even though results are extremely interesting and the usefulness is evident, this new score still lacks external validation. The aim of this study is to validate the discriminatory ability of the TRI-SCORE in predicting in-hospital mortality following ITVS. Furthermore, we sought to evaluate the ability of the score to predict long-term results following ITVS.

Materials and Methods

Ethics Statement

The Ethical Committee of our Institution approved the Study and waived individual informed consent for this retrospective analysis.

Study Population and follow-up

A retrospective review of our institutional database was carried out to find all patients who underwent ITVS in our department from March 1997 to March 2021. 199 patients fulfilled the inclusion criteria and were initially included in the study cohort. Charts were analyzed to identify preoperative characteristics, laboratory values, and echocardiographic parameters in order to determine the TRI-SCORE value. Postoperative results and echocardiographic data were also analyzed, and all data were inserted within a second dedicated database. Survival and echocardiographic follow-ups were carried out using the informatics hospital system for outpatient clinic visits and echocardiographic examinations. If follow-up information was not retrieved through the hospital system, patients, or their referring cardiologists, were reached via telephone calls and asked to provide recent laboratory and echocardiographic data (<6 months). Cause of death was determined by death certificates or information from family members or referring physicians. Clinical follow-up was 94% complete.

Statistical analyses

Statistical analyses were performed using Stata Software (Statacorp, LLC; TX, USA; version 15). Analyses were exploratory in nature. Categorical variables were expressed as absolute number and percentages. Normal distribution of continuous variables was assessed with the Shapiro-Wilk test. Continuous normal distributed variables were expressed as mean± standard deviation (SD), whereas continuous not-normal variables were reported as median [25th percentile; 75th percentile].

Discrimination of a test indicates the extent to which the model distinguishes between patients who will die or survive in the perioperative period. Discrimination was assessed with receiver operating characteristic (ROC) curves. ROC area under the curve (AUC) values vary between 0.5 and 1, where 0.5 denotes a bad diagnostic test and 1 denotes an excellent diagnostic test (13,14). In the literature, a value of 0.8 is considered the cut-off indicating a good performance of a score. Another index used to evaluate the discrimination was the Somers' D_{xy} rank correlation between predicted probabilities and observed responses. When $D_{xy} = 0$, the model is making random prediction, when $D_{xy} = 1$, the prediction is perfect (15). The accuracy of the models was tested calculating the Brier score (quadratic difference between predicted probability and observed outcome for each patient); when the prediction of the model is perfect, the Brier score is 0.

A Cox regression model was employed to evaluate the relationship between the TRI-SCORE value and long-term mortality. Finally, ROC curves for the TRI-SCORE, EuroSCORE II and Society of Thoracic Surgeons (STS) scores were compared using timeROC package (16).

Results

Out of the 199 patients who underwent ITVS at our center during the study period, 23 were excluded due to lack of sufficient preoperative data and, therefore, inability of calculating the risk score. The main parameters that were lacking were specific echocardiographic data regarding right ventricular function and specific laboratory values. A total of 176 patients have been considered for the purpose of this study, among which 131 (74.4%) underwent isolated TV replacement (ITVR) and 45 (25.6%) underwent TV repair (ITVr).

Baseline clinical and echocardiographic parameters of the study cohort are summarized in **Table 1**. Median TRI-SCORE at baseline was 3 [interquartile range (IQR) 1-5]. In-hospital mortality was 6.3%. Death was due to low cardiac output syndrome (LCOS) leading to multiorgan failure in 7 patients, septic shock in 1 patient, cerebral hemorrhage in 1 patient and other causes in the remaining 2 patients. Intraoperative variables and post-operative complications are listed in **Table 2**.

The TRI-SCORE value emerged as a significant predictor of in-hospital mortality ($p<0.001$), with an exponential growth of the risk of in-hospital mortality as the TRI-SCORE increases above the value 5 (**Fig.1**). The TRI-SCORE showed high discrimination with an area under the ROC curve of 0.82 (**Fig.2**). The Somers' D_{xy} index was 0.639. The Brier score was 0.054 indicating high accuracy in predicting in-hospital mortality.

There were 33 late deaths at 10 years follow-up (20%). Overall survival was 96.7$\pm$1.43% at 1 year, 81$\pm$3.72% at 5 years and 60$\pm$6.63% at 10 years (**Fig. 3**). Finally, and most importantly, the TRI-SCORE showed very good performance in predicting mortality during follow-up (Hazard Ratio: 1.47. 95% confidence interval [1.31-1.66], $p<0.001$). The time-dependent area under the ROC curve was >0.80 in all stages of follow-up, as shown in **Fig. 4**. Furthermore, the Brier score was 0.179. These values indicate a high discrimination and high accuracy of the TRI-SCORE not only for in-hospital mortality but also for predicting mortality at 10-years following ITVS.

A comparison between TRI-SCORE, EuroSCORE II and STS scores was performed, in order to evaluate performance of the currently available scores in predicting both in-hospital mortality and long-term outcomes. No statistically significant difference was found; however, analyses highlighted that the EuroSCORE II does not reliably predict outcomes, with an AUC always below 0.8 (**Fig. 5 and 6**).

Discussion

Prediction models and risk scores play an extremely important role in current cardiac surgery practice. The most commonly available surgical risk scores are capable of predicting outcomes in patients undergoing ITVS, as shown also by our analyses, however, they were not designed specifically for this population of patients. In an era of great fervor for the surgical and transcatheter treatment of isolated TV disease, the need of a dedicated risk score has become evident.

The main findings of our study are the following:

- in patients undergoing ITVS the TRI-SCORE shows high discrimination (AUC 0.82) and high accuracy (Brier score 0.054) for predicting in-hospital mortality.
- The TRI-SCORE also shows very good discrimination (AUC >0.80) and high accuracy (Brier score 0.179) in predicting mid- and long-term outcomes.
- Based on our experience, a TRI-SCORE value of 5 was identified as the cut-off for an increased risk in ITVS.

Recent studies have paved the way to the idea that ITVS can be performed with a reasonable surgical risk and good long-term outcomes in selected patients (17–19). Particularly, whenever surgical correction of isolated TR is performed early in the disease course, mainly before the occurrence of overt symptomatology, of RV dilation or dysfunction, and of end-organ involvement, it is associated with no in-hospital mortality, fewer postoperative complications and shorter postoperative lengths-of-stay (20,21). Moreover, patients at early stages of the disease, following TR treatment, experience 100% survival at 5 years and no further hospitalizations for right heart failure (22). These findings are in strong contrast with the ingrained belief that ITVS is always associated with high in-hospital mortality and uncertain long-term outcomes (23–25). Therefore, it has become evident that adequate patient selection and correct timing are of paramount importance in order to obtain good surgical results (20,22).

Although some risk scores for ITVS have been proposed, they are very rarely used in daily clinical practice (26,27). Furthermore, the most commonly utilized scores (EuroSCORE II and STS), despite being fairly capable of predicting both short and long-term outcomes, are not specific for tricuspid valve surgery and lack the evaluation of those precise parameters that should help guide the decision-making process of “who” and “when” to treat these patients. The TRI-SCORE, on the other hand, is a novel surgical risk score that aims at predicting in-hospital mortality of patients undergoing ITVS. It was developed analyzing a cohort of 466 patients operated on in 12 French centers. The score is an additive score, based on eight easy to ascertain parameters related to right and left ventricular function, end-organ involvement, medical therapy and clinical status. More specifically the variables used to calculate the score are: age ≥70 years, New York Heart Association (NYHA) class≥ III, presence of right heart failure signs (severe jugular venous distension, ascites and/or marked peripheral edema), daily dose of furosemide ≥125mg, glomerular filtration rate <30ml/min, elevated total bilirubin, left ventricular ejection fraction <60% and moderate/severe right ventricular dysfunction (tricuspid annular plane systolic excursion (TAPSE) <17mm and/or a tissue doppler imaging (TDI) <9.5cm/sec) (12). Observed and predicted in-hospital mortality rates increased from 0% to 60% and from 1% to 65% respectively, as the score increased from 0 up to ≥9 points (12). Despite the promising results and the extreme simplicity in the calculation of the score, external validation of a risk model is crucial in order to effectively assess its validity. Moreover, the performance of the score in predicting the long-term mortality was not evaluated, and to the best of our knowledge this is the first report analyzing this aspect. Furthermore, among the findings of our study, a TRI-SCORE cut-off value of 5 is in-line with results of the French group, as the predicted in-hospital mortality grows exponentially when the score points go from 5 to ≥9 (12). But probably the main finding of our study is the very good performance of the score also in predicting mortality at mid- and long-term follow-up after surgery.

Up to now, management of patients with isolated TV disease was controversial and, despite recent guidelines (28) support the idea of early referral and treatment, the questions of “who” and “how” to treat this population remains. In this light, the external validation of the TRI-SCORE and its good performance also in predicting long term outcomes could increase its value in the daily clinical practice.

Finally, the TRI-SCORE could have an important role in the decisions whether a patient should be considered for surgical correction, or whether the surgical risk is too high and an alternative trans-catheter approach should be pursued (29). It would be interesting to assess the performance of the TRI-SCORE in patients undergoing transcatheter interventions. This step could be crucial in the future and dedicated studies are warranted in this respect.

Limitations

The main limitation of the study is the retrospective, single-centre nature of the design, which may have led to selection bias. Also, only patients treated surgically were considered within the study, while patients deemed “inoperable” were not considered, limiting findings of the study. Furthermore, the sample size is relatively small due to the few isolated TV surgeries performed.

Conclusions

Our report externally validates the TRI-SCORE performance in predicting 30-day mortality with an overall good performance with high discrimination and high accuracy. Furthermore, this scoring model also showed very good performance in predicting mortality at mid- and long-term follow-up with high discrimination and high accuracy.

Acknowledgements

The Alfieri Heart Foundation provided support for data collection and analysis of this research.

Funding

No funding was received for this study.

Conflicts of Interest

No conflicts of interest to declare.

Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

Figures

Central Image. Receiver operative characteristic curve regarding mortality at 10 years following isolated tricuspid valve surgery, showing good performance of the TRI-SCORE, with an AUC>0.8.

Figure 1. Predicted probability of in-hospital mortality. This figure highlights the exponential growth of the risk of in-hospital mortality as the TRI-SCORE increases above the value 5.

Figure 2. Receiver operating characteristic curves for patients undergoing isolated tricuspid valve surgery. The value of the area under the curve was 0.82 indicating a high discrimination of the TRI-SCORE in these patients. AUC: area under the curve.

Figure 3. Kaplan Meier curve for all-cause death at follow-up in patients undergoing isolated tricuspid valve surgery.

Figure 4. Receiver operating characteristic curves regarding mortality at follow-up in patients undergoing isolated tricuspid valve surgery. The area under the curve was >0.8 at all time-frames indicating high discrimination of the TRI-SCORE also at mid- and long-term follow-up.

Figure 5. Comparison between TRI-SCORE, EuroSCORE II and STS scores. Receiver operating characteristic curve regarding in-hospital mortality.

Figure 6. Comparison between TRI-SCORE, EuroSCORE II and STS scores. Receiver operating characteristic curve regarding long-term outcome. The performance of the TRI-SCORE was excellent, with an AUC constantly above 0.80, particularly the AUC was 0.84, 0.86, 0.85, 0.86 and 0.83 at 2-4-6-8-10 years, respectively. The performance of the EuroSCORE II was worse with an AUC constantly below 0.8, particularly the AUC was 0.74, 0.79, 0.79, 0.75 and 0.75 at 2-4-6-8-10 years, respectively. Finally, the performance of the STS was better compared to the EuroSCORE II but worse compared to the TRI-SCORE, with an AUC of 0.79, 0.79, 0.80, 0.84 and 0.85 at 2-4-6-8-10 years, respectively.

The 6th panel describes the AUC over time.

Tables

Table 1. Baseline clinical and echocardiographic parameters

	N=176
CLINICAL	
• Age (years)	67.5 [56-74.5]
• Sex (M)	62 (35.2%)
• EuroSCORE II (%)	5.5 [2.1-10.4]
• NYHA III-IV	110 (62.5%)
• AFib	120 (68.2%)
• Permanent Pacemaker	32 (18.2%)
• Insulin-dependent diabetes	25 (14.2%)
• eGFR (ml/min)	63.8 [47-84.5]
• Total bilirubin (mg/dL)	1 [0.6-1.4]
• REDO	103 (58.5%)
• REDO > 1	29 (16.5%)
• Diuretics dose (mg)	50 [0-100]
• Ascites	38 (21.6%)
• Previous RHF	60 (34.1%)
ECHOCARDIOGRAPHIC	
• TR 3-4+	176 (100%)
• LVEF (%)	60 [55-60]
• Basal RVEDD (mm)	46.6±8.48
• sPAP (mmHg)	40 [35-48]
• TAPSE (mm)	20.1±5.39
• S'TDI (cm/s)	10 [9-13]
TRI-SCORE	3 [1-5]

AFib: atrial fibrillation; eGFR: estimated glomerular filtration rate; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; RHF: right heart failure; RVEDD: right ventricular end diastolic diameter; sPAP: systolic pulmonary artery pressure; s'TDI: peak systolic velocity tissue doppler imaging; TAPSE: tricuspid annular plane systolic excursion; TR: tricuspid regurgitation

Table 2. Intraoperative characteristics and postoperative complications

	N=176
Beating Heart	114 (64.8%)
CPB time (min)	57 [47-75]
Cross-clamp time (min)	0 [0-30]
Low cardiac output syndrome	24 (13.6%)
Acute Kidney Injury	40 (22.7%)
Re-exploration for bleeding	19 (10.8%)
New permanent pacemaker	19 (10.8%)
Permanent neurologic damage	14 (8%)
Length-of-stay (days)	8 [6-15]
In-hospital mortality	11 (6.3%)

CPB: cardiopulmonary bypass

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Figure 1

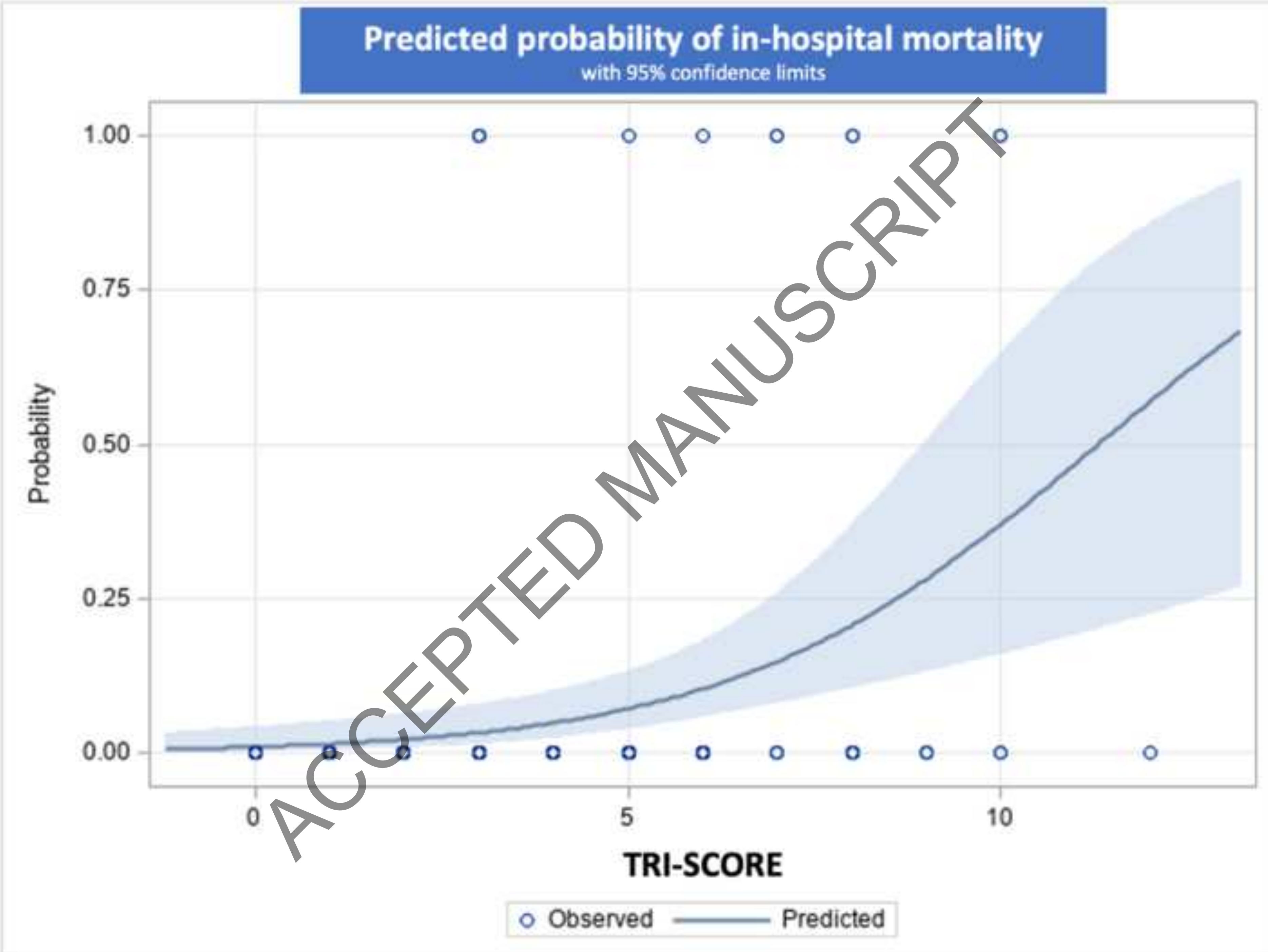

Predicted probability of in-hospital mortality
with 95% confidence limits
1.00
0.75
0.50
0.25
0.00
Probability
0
5
10
TRI-SCORE
Observed
Predicted

Figure 2

Click here to access/download;Figure;Figure 2.jpg

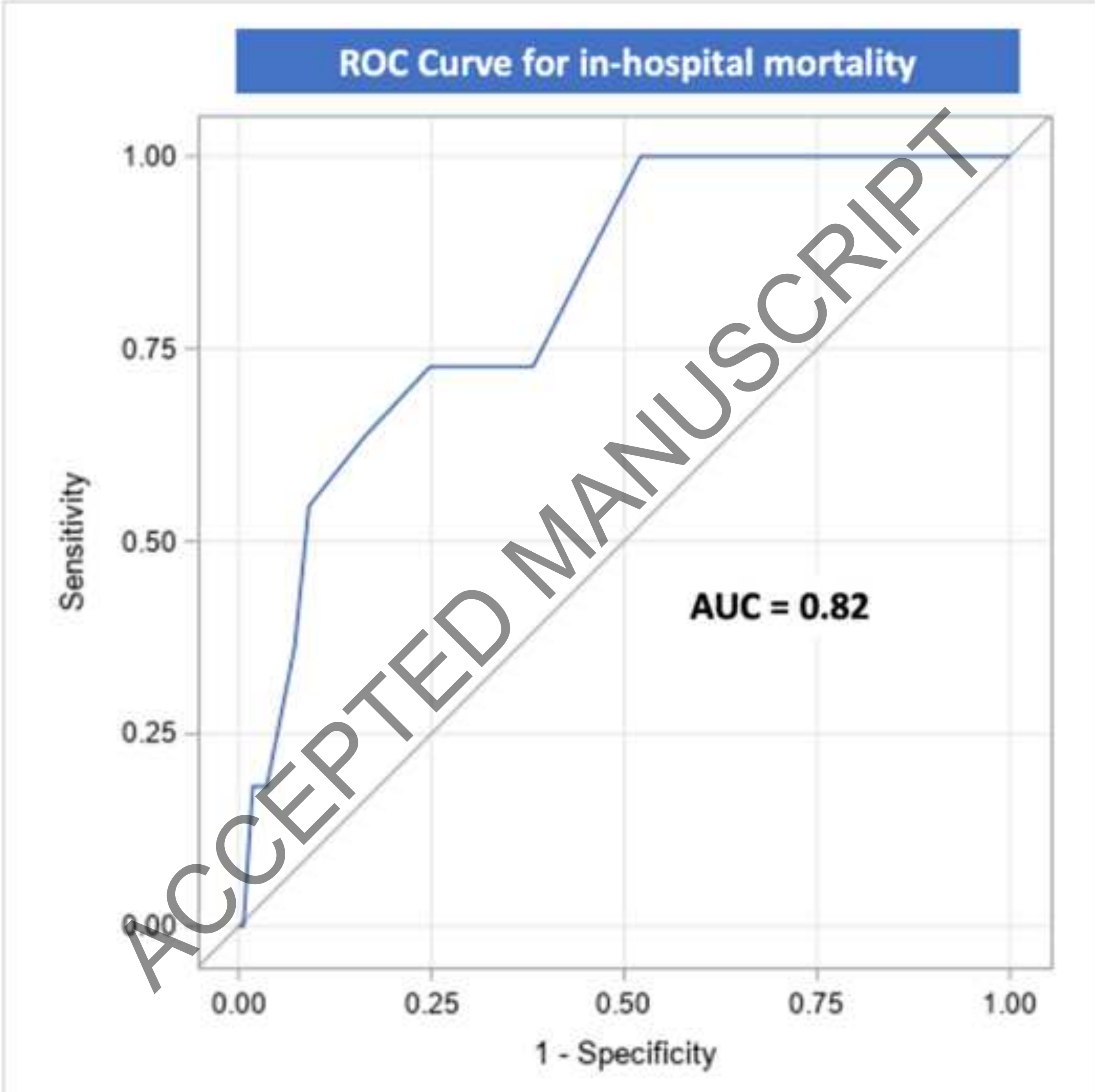


Figure 3

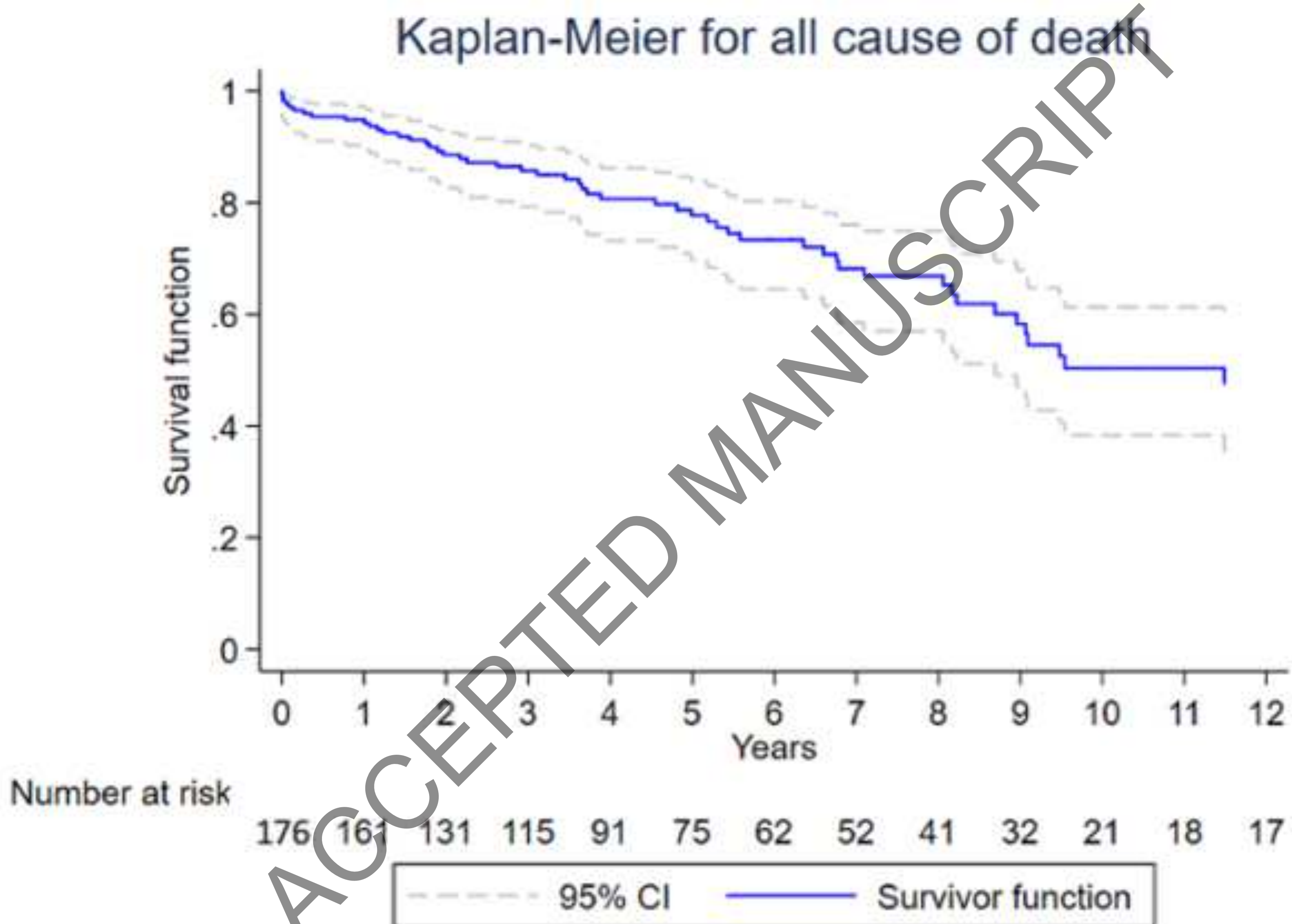

Kaplan-Meier for all cause of death
Survival function
1
.8
.6
.4
.2
0
0 1 2 3 4 5 6 7 8 9 10 11 12
Years
Number at risk
176 161 131 115 91 75 62 52 41 32 21 18 17
95% CI
Survivor function

Figure 4

Click here to access/download;Figure;Figure 4.jpg

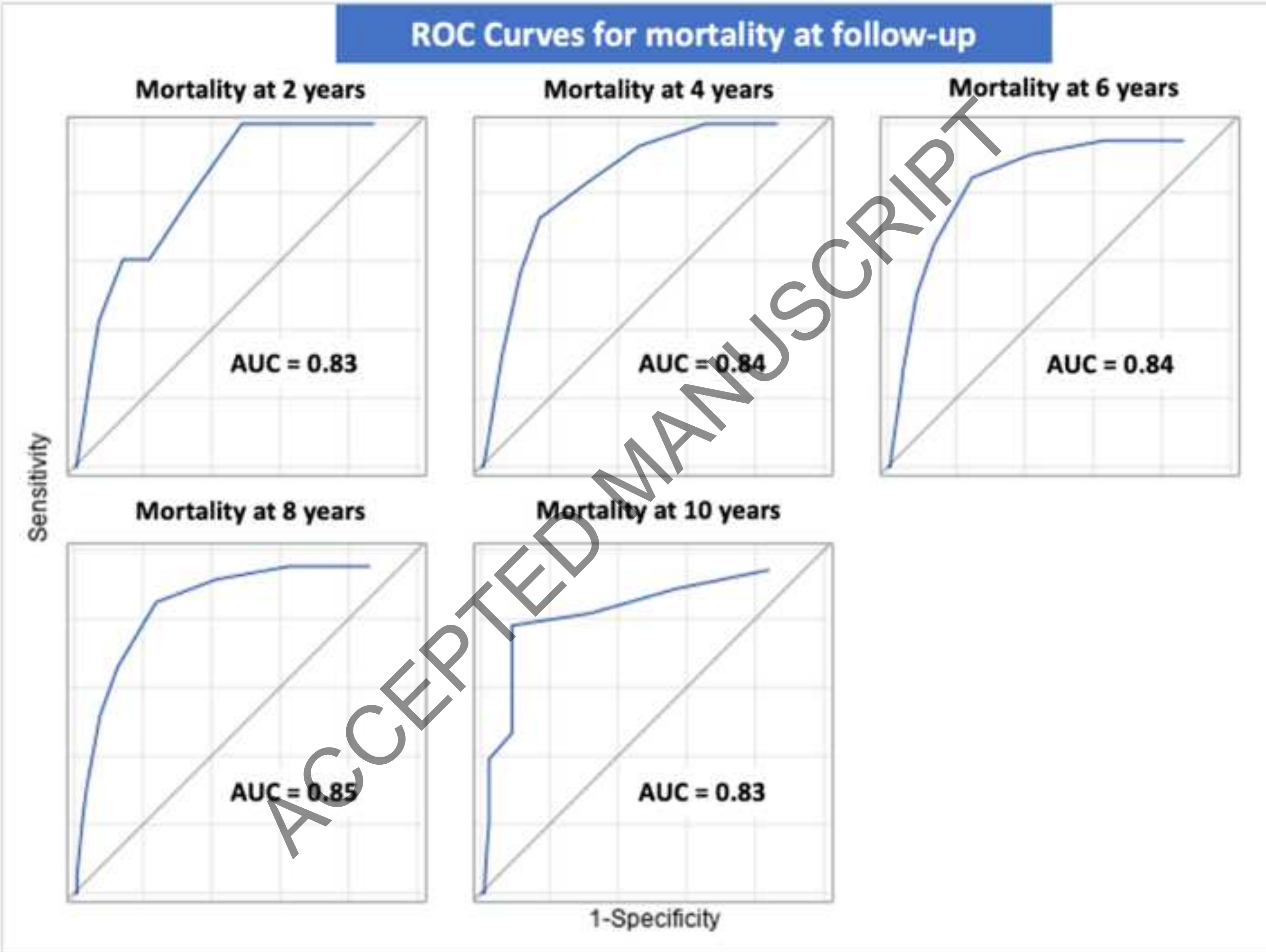


Figure 5

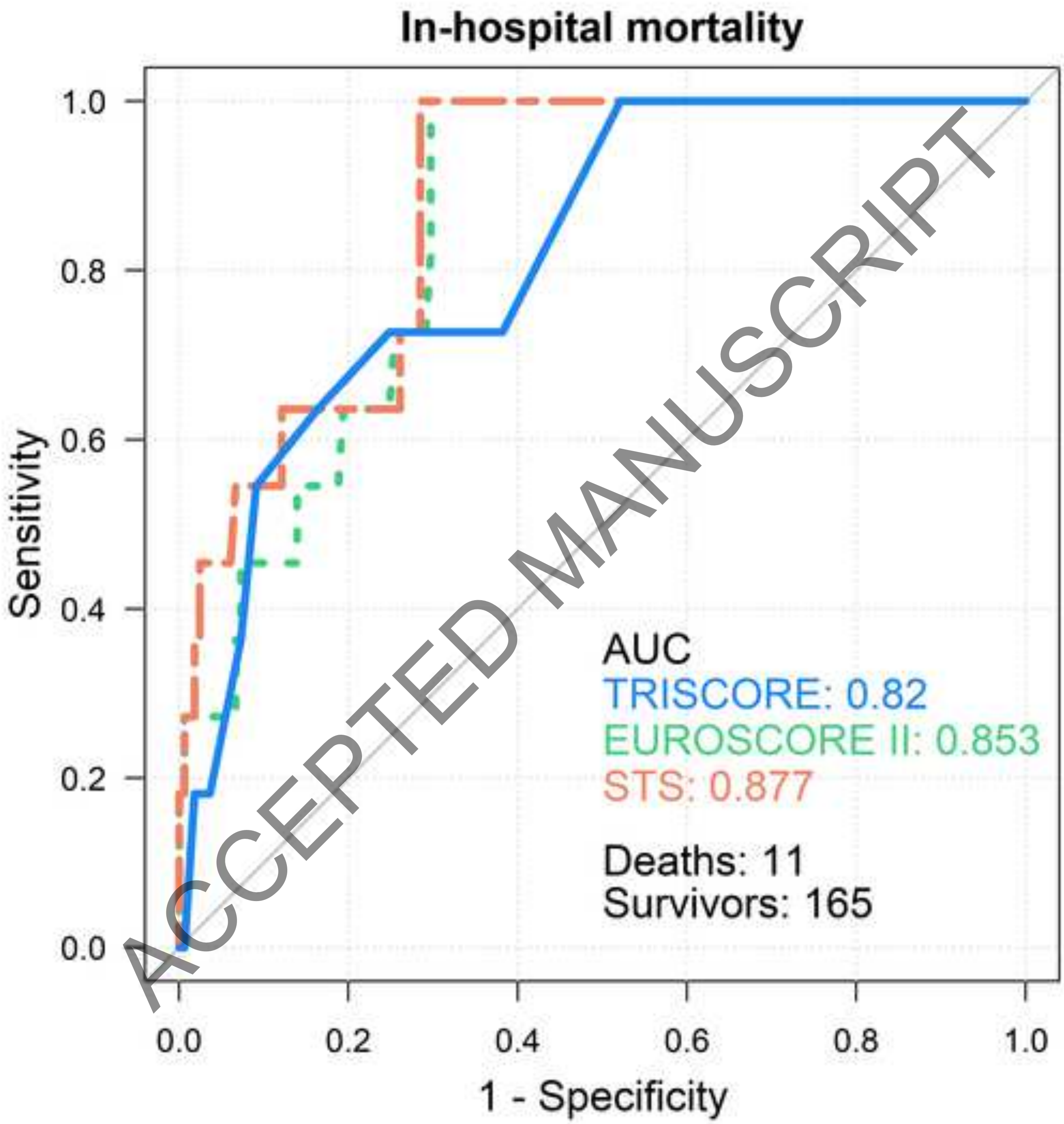
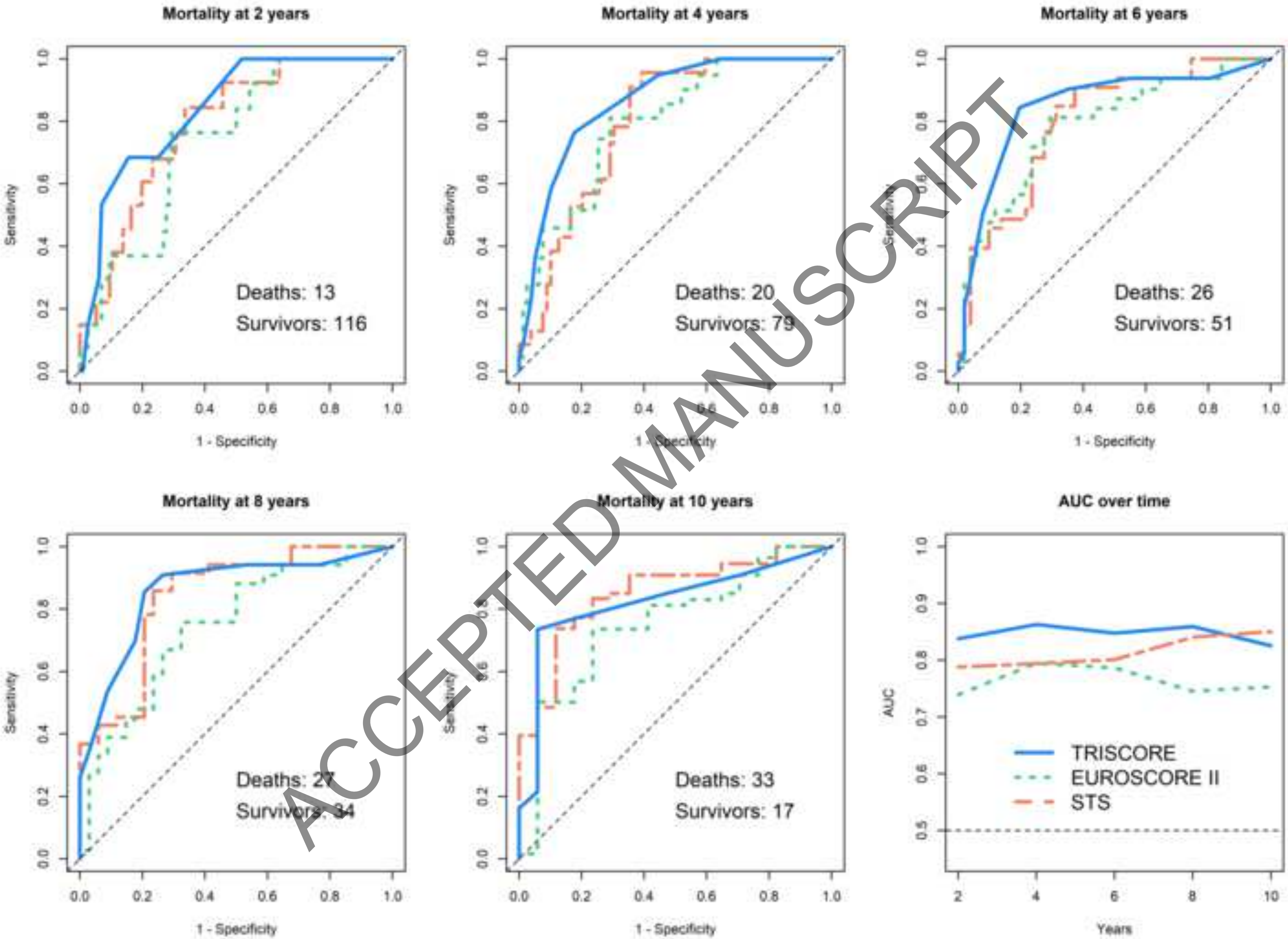

In-hospital mortality
1.0
0.8
0.6
0.4
0.2
0.0
Sensitivity
0.0
0.2
0.4
0.6
0.8
1.0
1 - Specificity
AUC
TRISCORE: 0.82
EUROSCORE II: 0.853
STS: 0.877
Deaths: 11
Survivors: 165

Figure 6



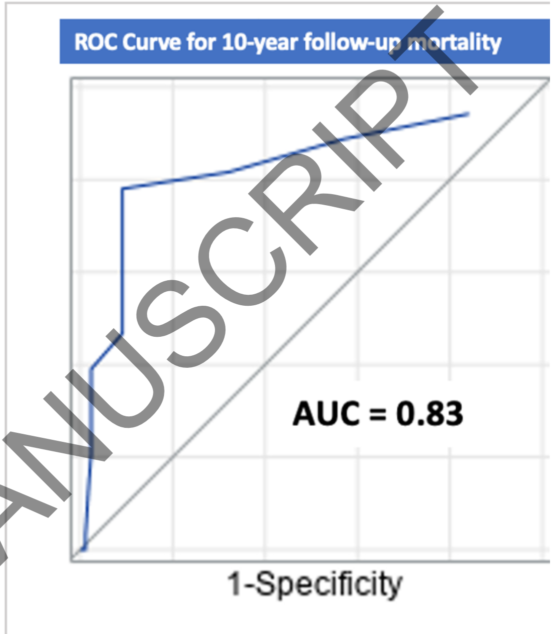
Mortality at 2 years
Deaths: 13
Survivors: 116
Mortality at 4 years
Deaths: 20
Survivors: 79
Mortality at 6 years
Deaths: 26
Survivors: 51
Mortality at 8 years
Deaths: 27
Survivors: 34
Mortality at 10 years
Deaths: 33
Survivors: 17
AUC over time
TRISCORE
EUROSCORE II
STS
Sensitivity
1 - Specificity
AUC
Years

Central image

Is TRI-SCORE a reliable tool for predicting in-hospital and long-term mortality in patients undergoing ITVS?

Summary

In this retrospective study on 176 patients undergoing ITV repair or replacement, the TRI-SCORE showed high discrimination and high accuracy both at short and long-term follow-up, reliably predicting both in-hospital and 10-year mortality.



Legend: AUC: area under curve; ITVS: isolated tricuspid valve surgery; ROC: receiver operating curves