Development and Validation of a Risk Prediction Tool for In-hospital Mortality After Thoracic Endovascular Repair in Patients with Blunt Thoracic Aortic Injury Using the Aortic Trauma Foundation Registry

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Background: The objective of our present effort was to use an international blunt thoracic aortic injury (BTAI) registry to create a prediction model identifying important preoperative and intraoperative factors associated with postoperative mortality, and to develop and validate a simple risk prediction tool that could assist with patient selection and risk stratification in this patient population.

Methods: For the purpose of the present study, all patients undergoing thoracic endovascular aortic repair (TEVAR) for BTAI and registered in the Aortic Trauma Foundation (ATF) database from January 2016 as of June 2022 were identified. Patients undergoing medical management or open repair were excluded. The primary outcome was binary in-hospital all-cause mortality. Two predictive models were generated: a preoperative model (i.e. only including variables before TEVAR or intention-to-treat) and a full model (i.e. also including variables after TEVAR or per-protocol).

Results: Out of a total of 944 cases included in the ATF registry until June 2022, 448 underwent TEVAR and were included in the study population. TEVAR for BTAI was associated with an 8.5% in-hospital all-cause mortality in the ATF dataset. These study subjects were subsequently divided using 3:1 random sampling in a derivation cohort (336; 75.0%) and a validation cohort (112; 25.0%). The median age was 38 years, and the majority of patients were male (350; 78%). A total of 38 variables were included in the final analysis. Of these, 17 variables were considered in the preoperative model, 9 variables were integrated in the full model, and 12

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variables were excluded owing to either extremely low variance or strong correlation with other variables. The calibration graphs showed how both models from the ATF dataset tended to underestimate risk, mainly in intermediate-risk cases. The discriminative capacity was moderate in all models; the best performing model was the full model from the ATF dataset, as evident from both the Receiver Operating Characteristic curve (Area Under the Curve 0.84; 95% CI 0.74–0.91) and from the density graph.

Conclusions: In this study, we developed and validated a contemporary risk prediction model, which incorporates several preoperative and postoperative variables and is strongly predictive of early mortality. While this model can reasonably predict in-hospital all-cause mortality, thereby assisting physicians with risk-stratification as well as inform patients and their caregivers, its intrinsic limitations must be taken into account and it should only be considered an adjunctive tool that may complement clinical judgment and shared decision-making.

INTRODUCTION

Traumatic injuries to the thoracic aorta are associated with high mortality and are the second most common cause of death in patients with blunt trauma.[1] Over the past 2 decades, thoracic endovascular aortic repair (TEVAR) has become the preferred treatment modality in these patients. Although TEVAR offers significantly improved outcomes over open repair for blunt thoracic aortic injury (BTAI), there remains a substantial risk of perioperative morbidity and mortality in patients undergoing TEVAR in the setting of trauma.[2,3] The development of tools or algorithms capable of more accurately predicting these adverse outcomes has, however, proven elusive. To date, there exists only a singular attempt to develop a specific prediction tool to estimate the risk of in-hospital mortality following TEVAR for BTAI, made by Mohapatra et al. using data from the Society for Vascular Surgery - Vascular Quality Initiative.[4] The development of a new, simple, reproducible and accurate model could be clinically relevant to aid physicians with decision-making as well as to inform patients and their caregivers.[5]

The objective of our present effort was to use an international BTAI registry to create a prediction model identifying important preoperative and intraoperative factors associated with postoperative all-cause mortality, and to develop and validate a simple risk prediction tool that could assist with patient selection and risk stratification in this patient population.

METHODS

Data Sources

The Aortic Trauma Foundation (ATF) is an international prospective multicenter registry, established in 2014, designed to capture the diagnosis, management, surveillance, and outcomes of patients with BTAI. At present, >900 patients have been enrolled from >40 centers across the globe.[6,7] Each participating institution was required to obtain local IRB approval to participate and was provided with specific data collection tools to capture and record information on patients demographics, comorbidities, mechanism of injury, admission physiology, initial imaging and laboratory information, associated injuries, Injury Severity Score, BTAI grade, management approach, interventions, complications, and outcomes (in-hospital and after discharge). A total of 369 variables are recorded in the ATF database and the overall number of cases and centers participating in the ATF registry has increased steadily until 2022. (Supplementary Figure 1). All centers participating in the ATF registry are asked to contribute consecutive BTAI cases, irrespective of treatment modalities.

Study Design

For the purpose of the present study, all patients undergoing TEVAR for BTAI and registered in the ATF database from January 2016 as of June 2022 were identified. A complex endovascular procedure was defined as any endovascular procedure that required the concomitant use of parallel grafts, branched devices, or in-situ fenestration. Patients undergoing medical management or open repair were excluded. The study population was randomly divided in a 3: 1 fashion into a derivation cohort and a validation cohort. The primary outcome was binary in-hospital all-cause mortality.

Statistical Analysis

Selection of variables was carried out through the alternation of operator-dependent and operator-independent selections. The operator-dependent selections involved two investigators (M.D. and M.P.), who selected independently the variables considered relevant and developed a list of derived variables (e.g. transformed, combined) where appropriate. A third investigator (S.L.) was consulted to achieve consensus in case of disagreement. The operator-independent selections was based on thresholds for the number of missing values and/or the *P* value as calculated on the primary outcome in the training population. The established thresholds were set as follows: *P* value for univariate analyses less than or equal to 0.20; variables with missing values less than 10% percent.

Univariate analyses were performed using inferential tests: Fisher's exact test for factorial variables and Wilcoxon-Mann-Whitney test for numeric variables. The odds ratio (OR) with 95% confidence intervals (95% CIs) of each variable was calculated by means of binary logistic regression. The predictive models were generated by Least Absolute Shrinkage and Selection Operator (LASSO) regulated logistic regression (glmnet) and were two: a preoperative model (i.e. only including variables before TEVAR or intention-to-treat) and a full model (i.e. also including variables after TEVAR or per-protocol). The LASSO allows to apply a penalty to the coefficients coming from the logistic regression to provide better control for the risk of overfitting; it also allows to remove the coefficients of those variables that have a low correlation toward the outcome, thus reducing the complexity of the resulting model. The penalty parameter was selected by evaluating the Area Under the Curve (AUC) performance for different penalties in 50 different patient samples generated by random bootstrapping.

All inferential values were calculated on the derivation cohort only. In relation to the low frequency (<10%) of the primary outcome, the OR values provide a reliable estimate of the relative risk. External validation was performed through the fraction of patients (testing set) that was not used to derive the models. The same testing set of patients was also used to perform the external validation of the model by Mohapatra et al. both in its original (plain) version and in the simplified (score) version. The diagnostic accuracy was evaluated by means of Receiver Operating Characteristic curves and density plot for all models that were analyzed. The AUC, or C-statistic, was used as objective measure of the models' discriminative ability. The calibration of the models was represented graphically by means of calibration plots. All statistical analyses were carried out using the tidyverse package (v1.3.0; Wickham et al., 2019) and R (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Study Cohort

Out of a total of 944 cases included in the ATF registry until June 2022, 448 underwent TEVAR and were included in the study population. Of these, 382 patients (85%) received TEVAR at institutions located in the United States while 66 patients (15%) received TEVAR at institutions located outside of the United States. The study cohort was subsequently divided using 3:1 random sampling in a derivation cohort (336; 75.0%) and a validation cohort (112; 25.0%). Baseline characteristics of the study cohort are summarized in Table I. The median age was 38 years, and the majority of patients were male (350; 78%). Overall, 90% of patients were treated at Level 1 trauma centers, and motor vehicle injuries accounted for nearly 90% of all trauma mechanisms. Grade 3 BTAI were most common (321; 73%), while grade IV were less frequent (57; 13%). Left subclavian artery coverage was performed in almost one-third of cases. The Glasgow Coma Scale score was abnormal (<15) in approximately one-half of patients at presentation, and <8 in about 28%. The median length of hospital stay was 13 days and the average stay in intensive care unit was 7 days. The overall rate of in-hospital death was 8.5%, with 38 death events recorded before hospital discharge.

Model Development

Based on the before-mentioned combined application of operator-dependent and operator-independent algorithms, a total of 38 variables were included in the final analysis, as listed in Table II. Of these, 17 variables were considered in the preoperative model, 9 variables were integrated in the full model, and 12 variables were excluded owing to either extremely low variance or strong correlation with other variables. The OR coefficients of the multivariate models are shown in Figure 1, while Table III lists all the variables for which the logistic regression regularized with LASSO returned coefficients greater than 0 both for the preoperative model and for the full model. For the preoperative model, the variables with the strongest positive association to the outcome were the need for a complex endovascular procedure (OR 2.91) and BTAI grade IV (OR 2.16). On the other hand, hemoglobin had the strongest negative association with the outcome both in the preoperative model and in the full model. In the former model, the increase in hemoglobin by one standard deviation (2.3 g/dl) above 12.5 g/dl was associated with a reduction

Table I. Baseline characteristics of the entire study cohort and details of traumatic injury

Variable	Median [IQR], or percentage	
	Outcome	
	Yes	No
Preoperative & Intraoperative		
Age	48 (29, 65.8)	38 (28, 54)
Gender		
Male	(32, 84%)	(318, 78%)
Female	(6, 16%)	(92, 22%)
Coronary artery disease	4, 10.5%	14, 3.4%
Congestive heart failure	2, 5.3%	4, 1.0%
Smoker	4, 10.5%	80, 19.5%
Dialysis dependent renal failure	1, 2.6%	1, 0.2%
Previous surgery	3, 7.9%	15, 3.7%
Trauma center designation		
Level 1	(34, 89%)	(385, 95.8%)
Level 2	(4, 11%)	(12, 3.0%)
Level 3	(0, 0%)	(5, 1.2%)
Trauma mechanism		
Other	(2, 5.3%)	(20, 4.9%)
Fall	(4, 10.5%)	(26, 6.4%)
Motorcycle accident	(10, 26.3%)	(56, 13.7%)
Auto vs. pedestrian	(5, 13.2%)	(43, 10.5%)
Motor vehicle collision	(17, 44.7%)	(264, 64.5%)
Injury severity score	44.5 (36, 50)	32.5 (24, 41)
Intracranial hemorrhage or contusion	21, 55.3%	87, 21.2%
Facial fractures	10, 26.3%	84, 20.5%
Cervical spinal fracture	11, 28.9%	39, 9.5%
Severe thorax injury	11, 28.9%	78, 19.0%
Severe abdominal injury	26, 68.4%	245, 59.8%
Severe pelvic injury	16, 42.1%	145, 35.4%
Long bone fracture	17, 44.7%	176, 42.9%
BTAI		
Grade I	(2, 5.3%)	(11, 2.7%)
Grade II	(8, 21.1%)	(41, 10.2%)
Grade III	(18, 47.4%)	(303, 75.4%)
Grade IV	(10, 26.3%)	(47, 11.7%)
Systolic blood pressure	98 (78, 128)	113 (95, 132)
Heart rate	100 (85, 120)	98.5 (84.2, 116)
Hemoglobin	11.1 (9.5, 13.3)	12.9 (11.4, 14.2)
Creatinine	1.3 (1.1, 1.7)	1.1 (0.9, 1.4)
Lactate	5 (3.5, 8.1)	3.5 (2.2, 4.6)
Glasgow coma scale	5 (3, 13.8)	14 (6, 15)
Craniotomy or craniectomy	7, 18.4%	5, 1.2%
Laparotomy	16, 42.1%	90, 22.0%
Pneumothorax	15, 39.5%	116, 28.3%
Complex endovascular procedure	2, 5.3%	10, 2.4%
Left SCA covered	12, 38.7%	126, 32.8%
Postoperative		
Units packed red blood cells	6 (3.2, 8.8)	2 (0, 5.8)
Vasopressors	18, 64.3%	64, 17.6%
Failure of endovascular procedure	3, 7.9%	4, 1.0%
Endoleak	2, 5.3%	11, 2.7%
Intestinal ischemia	1, 2.6%	0, 0.0%
Paraperesis or paraplegia	3, 7.9%	8, 2.0%
Dysrythmia other than sinus tachycardia	6, 15.8%	9, 2.2%

(*Continued*)

Table I. Continued

Variable	Median [IQR], or percentage	
	Outcome	
	Yes	No
Acute renal failure	6, 15.8%	20, 4.9%
Stroke	0, 0.0%	0, 0.0%
Acute respiratory distress syndrome	6, 15.8%	19, 4.6%
Sepsis	7, 18.4%	25, 6.1%
Intensive care unit length of stay	4.5 (2, 7)	7 (3, 16)
Hospital length of stay	5 (2, 7)	14 (8, 25)

IQR, interquartile range; SCA, subclavian artery.

in the risk of death during hospitalization of approximately 0.60; the same degree of hemoglobin increase was associated with a reduction in the risk of in-hospital death of approximately 0.69 in the latter model. A spreadsheet for quick and easy calculation of the mortality risk according to the ATF-derived predictive models is presented in Supplementary Table I.

Calibration & Validation

The preoperative model and the full model were validated in the validation cohort (consisting of 112 patients of which 10 died during their index hospitalization). The risk models from Mohapatra et al. were also validated in the same cohort, to perform a comparison with other models in the literature. The calibration graphs (Fig. 2A) showed how both models from the ATF dataset tended to underestimate risk, mainly in intermediate-risk cases (0.20). On the other hand, the models from Mohapatra et al. tended to underestimate risk in low-risk patients and overestimate risk in high-risk patients, thus demonstrating weak calibration. As shown in Figure 2B, the discriminative capacity was moderate in all models with AUC ranging between 0.86 and 0.76. The best performing model was the full model from the ATF dataset, as evident from both the Receiver Operating Characteristic curve (AUC 0.84; 95% CI 0.74–0.91) and from the density graph displayed in Figure 3.

In Table IV the number of people at risk, number of events, specificity, sensitivity, and predictive values (positive and negative) of the full model at different risk thresholds are displayed. Risk thresholds are displayed as two equivalent forms: probability and OR. The latter (in its mathematical form of 1:X) displays the expected number of false positives per each true positive at any threshold value. For instance, at a risk threshold of 14.3% (OR1:6), 15 patients are recognized as being at high-risk for in-hospital death. Of these, 6 will be true positives, while 4 positive cases are not identified. The Aortic Trauma Foundation Registry full model has better discriminative ability at low threshold risks as it is able to recognize a significant proportion of patients who will develop the outcome (true positives) but at the cost of a mislabeling some as false positives. These same limitations are shared by all the other models (Aortic Trauma Foundation Registry preoperative model, Mohapatra et al. plain model, Mohapatra et al. score model), as shown in Supplementary Table II.

DISCUSSION

It is well acknowledged that BTAI remains one of the leading causes of death from blunt trauma and a clinical challenge of modern trauma care. Indeed, BTAI commonly occurs in the context of high-energy traumas with associated multiple system injuries that may contribute to early mortality, but the potential impact of adverse aortic events is an ever-present danger in the setting of BTAI.[5] Since the introduction of TEVAR for BTAI, outcomes following endovascular treatment have been reported for over 2 decades[6] and show significantly lower morbidity and mortality than conventional open surgery, thereby leading to clinical practice guidelines recommending TEVAR as first-line treatment option for most BTAI cases.[7]

Despite these improvements, there remains a need to define optimal utilization of TEVAR in the trauma setting, particularly as it relates to timing of intervention, the optimal indication in specific subset of individuals and proper resources utilization, as well as providing patients and their caregivers with reliable expectations on postoperative outcomes. In this study, we aimed to identify risk factors for in-hospital all-cause mortality after TEVAR for BTAI after leveraging data from a

Table II. List of predictive variables that were identified by combination of operator-dependent and operator-independent algorithms, with comparison of patients with versus without the outcome of interest (i.e. in-hospital mortality) in the derivation cohort

	Variable	OR (95% CI)	*P* Value	NA (%)
Preoperative model				
1	Glasgow coma scale	0.5 (0.3, 0.7)	<0.001	2.4%
2	Age	1.6 (1.1, 2.3)	0.042	0.0%
3	Hemoglobin	0.4 (0.3, 0.6)	<0.001	3.6%
4	Heart rate	1 (0.6, 1.4)	0.061	3.0%
5	Systolic blood pressure	0.5 (0.3, 0.7)	0.009	1.8%
6	Injury severity score	2.3 (1.5, 3.5)	<0.001	16.1%
7	Creatinine	1.2 (0.9, 1.5)	0.005	3.6%
8	Lactate	1.8 (1.3, 2.7)	<0.001	22.0%
9	Intracranial hemorrhage or contusion	4.2 (1.9, 9.3)	<0.001	0.0%
10	Cervical spinal fracture	3.6 (1.4, 8.6)	0.009	0.0%
11	Patient intubated at time of Glasgow coma score assessment	2.6 (1.2, 5.9)	0.018	1.8%
12	Trauma mechanism		0.056	0.3%
	Fall	1 (0.1, 8.6)		
	Motorcycle accident	1.2 (0.3, 8.7)		
	Auto vs. Pedestrian	0.7 (0.1, 5.7)		
	Motor vehicle collision	0.4 (0.1, 2.5)		
13	BTAI greater than III grade	2.5 (0.9, 6)	0.071	1.5%
14	Laparotomy	2 (0.9, 4.4)	0.111	0.0%
15	Left SCA covered	2 (0.8, 4.6)	0.165	7.1%
16	Complex endovascular procedure	3.3 (0.5, 14.5)	0.167	0.0%
17	Pneumothorax	1.8 (0.8, 3.9)	0.197	0.0%
Full model addition				
1	Postoperative heart rate	0.9 (0.6, 1.4)	<0.001	7.7%
2	Vasopressors	9.9 (3.9, 27.4)	<0.001	10.4%
3	Units packed red blood cells	1.6 (1.2, 2.3)	<0.001	12.2%
4	Stroke	8.1 (2.6, 24.1)	<0.001	0.0%
5	Dysrythmia other than sinus tachycardia	8.4 (2, 31.4)	0.006	0.0%
6	Paraperesis or Paraplegia	4.5 (0.9, 16.7)	0.054	0.0%
7	Acute renal failure	2.9 (0.8, 8.5)	0.086	0.0%
8	Sepsis	2.9 (0.8, 8.5)	0.086	0.0%
9	Acute respiratory distress syndrome	2.7 (0.6, 9.2)	0.139	0.0%
Not selected				
1	Postoperative blood pressure	0.5 (0.3, 0.8)	<0.001	7.4%
2	Postoperative hemoglobin	0.8 (0.5, 1.2)	0.080	8.0%
3	Postoperative creatinine	1.3 (1, 1.7)	<0.001	8.3%
4	Craniotomy or craniectomy	20.7 (5.5, 86.4)	<0.001	0.0%
5	Failure of endovascular procedure	12.2 (2.2, 69)	0.009	0.0%
6	*N*. of trauma patients admitted per year		0.015	1.8%
	1,000−2,000	10.8 (1.8, 209.6)		
	2,000−3,000	3.7 (0.7, 69.1)		
	Greater than 3,000	2.2 (0.4, 41.2)		
7	Trauma center designation		0.029	1.8%
	Level	25.4 (1.4, 17.8)		
	Level	3 0		
8	BTAI		0.068	1.5%
	Grade.II	1.8 (0.2, 36)		
	Grade.III	0.7 (0.1, 13.8)		
	Grade.IV	2.1 (0.3, 42.3)		
9	Intestinal ischemia		0.083	0.0%
10	Coronary artery disease	3.6 (0.8, 12.6)	0.084	0.0%
11	Dialysis dependent renal failure	11.4 (0.4, 293)	0.160	0.0%
12	Endoleak	3.3 (0.5, 14.5)	0.167	0.0%

SCA, subclavian artery.

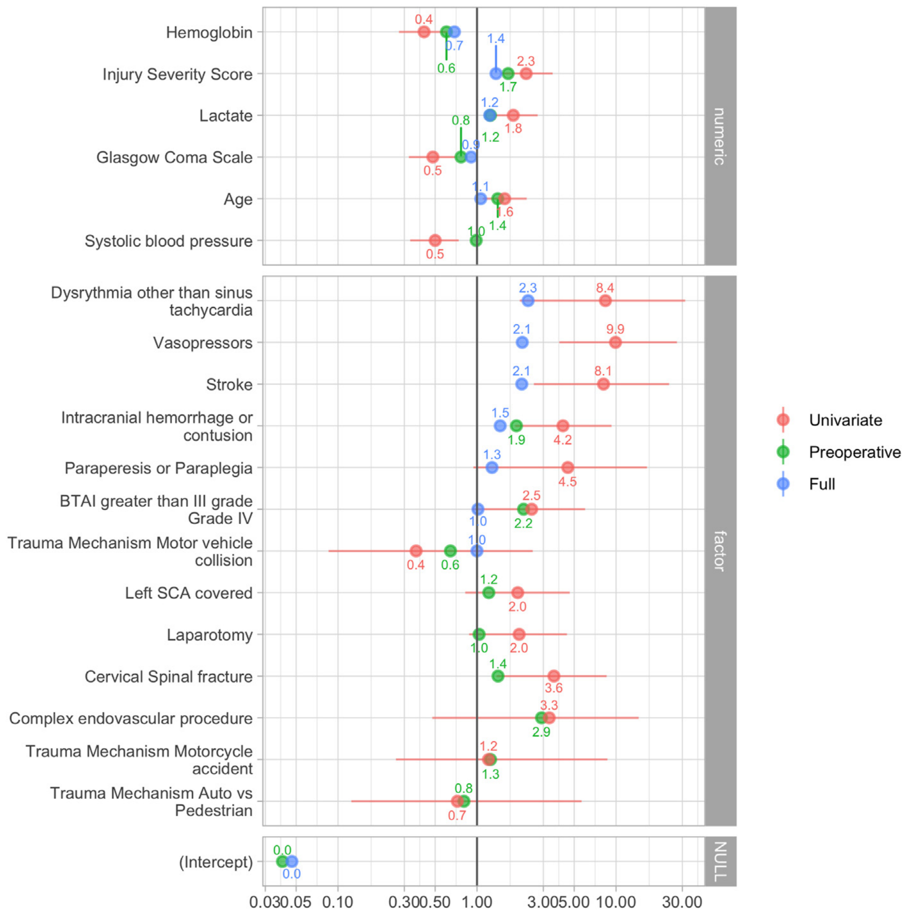

Fig. 1. Odds Ratio coefficients of univariate and multivariate models.

large contemporary international prospective multicentric registry, and to develop a simple but reliable prediction tool that could aid with risk stratification in this critically ill patient population. We found that several variables were all independent predictors of early mortality in the TEVAR-treated BTAI population. Based on these factors, we were able to create two scoring systems that could predict which patients were at greatest risk for postoperative mortality: an intention-to-treat model, mainly focused on risk assessment before TEVAR, and a per-protocol model, which also incorporates postoperative adverse events to optimize the prognostic assessment after the intervention.

The model devised in the present study may provide patients and their families or caregivers with useful prognostic information both before and after the operation, thereby potentially creating a common understanding of the risk profile associated with BTAI among the various stakeholders that are engaged in the care of these severely polytraumatized individuals. In order for this tool to be clinically useful, it will have to be easy and quick to implement during the decision-making process and at the bedside. The calculator provided may be easily translated into an app-based software and assist physicians as a complementary instrument to their clinical judgment. However, some notable limitations remain to our study (including for instance that it does not account for the risk/benefit ratio of other alternatives such as medical management or open surgery), although these would be similarly shared in the previous work by Mohapatra et al.

Indeed, BTAI patients who survive until hospital presentation typically have a number of concomitant injuries that can influence the overall prognosis and may affect the decision on whether or not to proceed with TEVAR; this further complicates any study on all-cause mortality in this population. Nonetheless, it is also undoubted that, especially for most severe BTAI forms, attempts at conservative management would invariably result in aorta-related mortality. In our internationally representative sample of patients, we found an 8.5% overall

Table III. Multivariable predictors of in-hospital mortality following TEVAR for BTAI in the two models (preoperative model and full model)

				Normalization	
Variable	Sign	Beta	OR	Mean	SD
Preoperative model					
(Intercept)	Neg	3.222	0.04		
Complex endovascular procedure	Pos	1.069	2.91		
BTAI grade IV	Pos	0.771	2.16		
Intracranial hemorrhage or contusion	Pos	0.653	1.92		
Injury severity score	Pos	0.515	1.67	32.9	13.6
Hemoglobin	Neg	0.506	0.60	12.5	2.3
Trauma mechanism motor vehicle collision	Neg	0.440	0.64		
Cervical spinal fracture	Pos	0.348	1.42		
Age	Pos	0.343	1.41	41.9	17.1
Glasgow coma scale	Neg	0.265	0.77	11.0	5.0
Trauma mechanism motorcycle accident	Pos	0.224	1.25		
Lactate	Pos	0.223	1.25	3.9	2.7
Trauma mechanism auto vs pedestrian	Neg	0.217	0.81		
Left SCA covered	Pos	0.195	1.22		
Laparotomy	Pos	0.035	1.04		
Systolic blood pressure	Neg	0.014	0.99	111.7	30.6
Full model addition					
(Intercept)	Neg	3.067	0.05		
Dysrythmia other than sinus tachycardia	Pos	0.846	2.33		
Vasopressors	Pos	0.749	2.12		
Stroke	Pos	0.742	2.10		
Intracranial hemorrhage or contusion	Pos	0.384	1.47		
Hemoglobin	Neg	0.374	0.69	12.5	2.3
Injury severity score	Pos	0.315	1.37	32.9	13.6
Paraperesis or paraplegia	Pos	0.248	1.28		
Lactate	Pos	0.210	1.23	3.9	2.7
Glasgow coma scale	Neg	0.098	0.91	11.0	5.0
Age	Pos	0.061	1.06	41.9	17.1
BTAI grade IV	Pos	0.016	1.02		
Trauma mechanism motor vehicle collision	Neg	0.001	1.00		

SD, standard deviation.

in-hospital mortality, a figure that is fairly consistent with the rates observed in other studies.[4] While it is reasonable to assume that any of these deaths may have been related to the overall burden of traumatic insults and not just the aortic injury itself, the intention-to-treat model may still assist physicians with preoperative risk stratification in order to assess potential futility of care. Furthermore, the developed model could be useful for quality improvement initiatives, with the aim of enabling cross-comparison of outcomes observed with those predicted at institutions treating such cases, through external validation using independent datasets.

For the above reasons, we felt it was important to limit the risk factors to those that could be prospectively evaluated when approaching a trauma patient for possible TEVAR or during hospital admission after the intervention itself. Each of the components of the risk prediction model are, therefore, easily obtainable and either patient-related or procedure-related. For instance, the need for coverage of the left subclavian artery can usually be judged preoperatively based on imaging, although we do acknowledge that in a minority of cases intraoperative findings may not be entirely congruent with what was projected during preoperative assessment. Therefore, by limiting the intention-to-treat model components to those that can be evaluated preoperatively, we believe the clinical utility of this risk prediction model mainly lies in patient prognosis prior to performing the TEVAR, which can be useful in the consenting process with patients and their families, as well as to allocate resources.

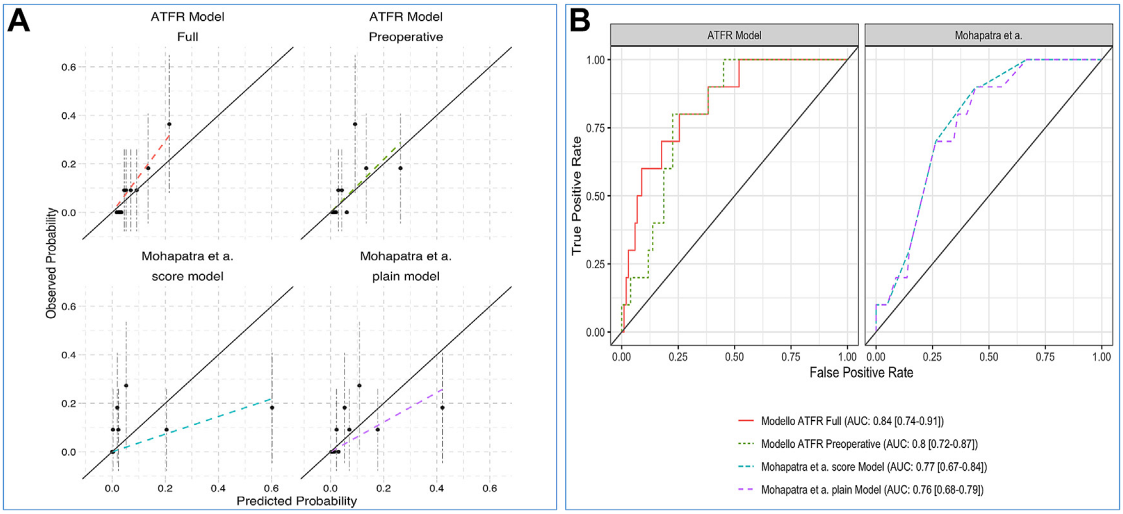

Fig. 2. (A) Calibration plots for all validated models in the testing set of patients. **(B)** Comparison of receiver operating characteristic (ROC) curves for all validated models. The Area Under Curve (AUC) with 95% Confidence Intervals (95% CIs) is shown in the legend.

In that sense, similar to other surgical operations, there is a threshold of operative risk above which TEVAR may not be appropriate, but the threshold at which the expected benefits of the intervention may be outweighed by overall poor prognosis in practice is subjective and may vary between clinical providers. Many variables will need to be taken into consideration in clinical practice when deciding which ''threshold'' of risk physicians, patients, and policy-makers may be willing to accept. In fact, it may well be that different stakeholders would accept or pursue different thresholds based on their perceived risk-to-benefit ratios. Furthermore, costs (both direct and indirect) may vary widely based on health-care systems so risk prediction models should only be judiciously implemented into a larger decision-making process. Nonetheless, the intention-to-treat model may provide an objective measure of operative risk thereby aiding in this decision-making process. At the same time, the per-protocol model may have other important implications for care of BTAI patients, as it could be especially useful to identify adjunctive risk factors (some of which may be modifiable or could be intervened upon) that influence the risk of mortality in TEVAR, thereby providing a refined assessment after the intervention has taken place. Furthermore, although the indication for TEVAR was left to the treating physicians' discretion, it should be borne in mind that endovascular repair represents nowadays the first-line approach for BTAI, with medical management reserved for very mild cases and open surgery for those few not amenable to TEVAR.

Although a specific threshold of mortality high enough to withhold potentially life-saving operations or terminate life-support in critically ill patients may be impractical to ascertain, it is certainly clinically relevant to implement risk prediction tools to warrant counseling of patients and their families, to have an informed discussion about the expected mortality even with prompt treatment, and ultimately optimize resource utilization.[8] In that sense, our prediction model could be easily translated into a nomogram or web-based interactive tool with which physicians may easily calculate the estimates of early deaths for their patients and balance those against the overall clinical picture. It is important to recognize that trauma victims who sustain BTAI have usually endured high-energy traumas, which may often result in severe multisystem injuries and these can critically contribute to the ultimate outcome. In that sense, the inability to ascertain the actual cause of death from the ATF dataset could represent a potential limitation to the analyses. Nonetheless, the risk prediction model included several variables not directly or causally linked to BTAI/TEVAR, thereby reflecting the systemic nature of the traumatic injury and the overall effect of several concomitant factors.

Endovascular stent-grafting of the thoracic aorta in BTAI patients can also be challenging owing to some peculiar anatomic features in this population (as compared with subjects receiving treatment for aneurysms or dissection). Indeed, BTAI patients are often younger, have smaller and sometimes angulated aortas, with more focal pathology from

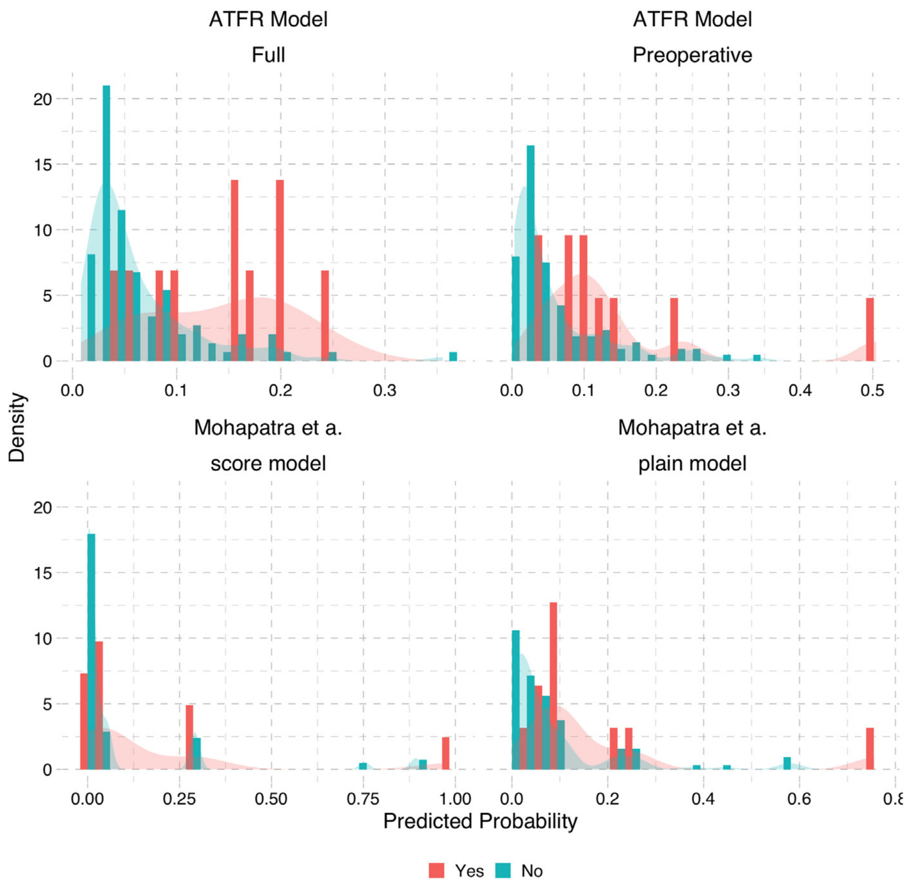

Fig. 3. Density plot and histograms showing distribution of patients with and without the outcome of interest (i.e. in-hospital mortality) between different predicted probabilities in all validated models.

the traumatic injury. In the setting of hypovolemic shock, there might also be further challenges with achieving appropriate sizing of the device(s).[9] While it is undoubted that enormous advancements have occurred in endografts technology over the last 2 decades, whether specific devices might achieve superior outcomes in the setting of BTAI and how this could affect the preoperative decision-making also in terms of risk stratification remains to be fully elucidated.[10]

Study limitations

There are a number of limitations to this study, which largely reflect the nature of ATF data. Indeed, data are collected by center-specific processes that are heterogeneous throughout the registry. As a result, some variables (such as the severity of a concomitant traumatic injury) may be inconsistently applied across centers. In addition, some data were incomplete; although we tried to address this issue with multiple imputation methods, there remains the possibility that some data were not missing at random which may introduce bias into our results. Also, we were unable to account for selection bias with regard to which patients reach hospital and receive care; therefore, our all-cause mortality estimate reflects the mortality of those receiving treatment, rather than all patients with BTAI. Most centers participating in the ATF registry were Level 1 Trauma Centers located mainly in North America or Europe; therefore, whether findings from this study may be easily generalized to different health-care settings remains beyond the merits of the current analysis. Another shortcoming of this study may be identified in the relatively low number of death events, which may have limited the available statistical power. For that reason, we have refrained from deriving a simplified point-based score which would require further loss of statistical power. Some technical aspects of the repair, such as improper oversizing or poor positioning of

Table IV. Diagnostic outcomes of the Aortic Trauma Foundation Registry full model on varying risk thresholds

		No of people at risk		No of events			Performances			
Probability	Odds_ratio	High_risk	Low_risk	Identified(tp)	Not identified(fn)	True positive beyond chance	Sens	Spec	Ppv	Npv
6.2%	1:15	42	70	8	2	4.2	80%	67%	19%	97%
7.7%	1:12	35	77	8	2	4.9	80%	74%	23%	97%
9.1%	1:10	28	84	7	3	4.5	70%	79%	25%	96%
10.0%	1:9	25	87	7	3	4.8	70%	82%	28%	97%
11.1%	1:8	21	91	6	4	4.1	60%	85%	29%	96%
12.5%	1:7	17	95	6	4	4.5	60%	89%	35%	96%
14.3%	1:6	16	96	6	4	4.6	60%	90%	38%	96%
16.7%	1:5	10	102	4	6	3.1	40%	94%	40%	94%
20.0%	1:4	5	107	2	8	1.6	20%	97%	40%	93%
25.0%	1:3	1	111	0	10	−0.1	0%	99%	0%	91%
33.3%	1:2	1	111	0	10	−0.1	0%	99%	0%	91%
50.0%	1:1	0	112	0	10	0.0	0%	100%	NA	91%
55.6%	1:0.8	0	112	0	10	0.0	0%	100%	NA	91%
66.7%	1:0.5	0	112	0	10	0.0	0%	100%	NA	91%

the proximal and distal stents, which may also contribute to clinical failure, could not be studied from the available dataset and will require further assessment. Lastly, this model remains to be further externally validated (and compared against other models such as the one by Mohapatra et al.) in a different dataset to investigate whether these predictors hold true in a distinct group of patients. In addition, any case in which the treating physician(s) assessed TEVAR to be futile would not have been captured in the ATF registry database. The full list of participating centers is available in Supplementary Table III.

CONCLUSIONS

TEVAR for BTAI was associated with an 8.5% in-hospital mortality in the ATF dataset. In this study, we developed and validated a contemporary risk prediction model, which incorporates several preoperative and postoperative variables and is strongly predictive of early mortality. While this model can reasonably predict in-hospital mortality, thereby assisting physicians with risk-stratification as well as inform patients and their caregivers, its intrinsic limitations must be taken into account and it should only be considered an adjunctive tool that may complement clinical judgment and shared decision-making.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at doi: 10.1016/j.avsg.2023.09.076.

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