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ORIGINAL ARTICLE

Massive transfusion prediction in patients with multiple trauma by decision tree: a retrospective analysis

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Abstract Early initial massive transfusion protocol and blood transfusion can reduce patient mortality, however accurately identifying the risk of massive transfusion (MT) remains a major challenge in severe trauma patient therapy. We retrospectively analyzed clinical data of severe trauma patients with and without MT. Based on analysis results, we established a MT prediction model of clinical and laboratory data by using the decision tree algorithm in patients with multiple trauma. Our results demonstrate that shock index, injury severity score, international normalized ratio, and pelvis fracture were the most significant risk factors of MT. These four indexes were incorporated into the prediction model, and the model was validated by using the testing dataset. Moreover, the sensitivity, specificity, accuracy and area under curve values of prediction model for MT risk prediction were 60%, 92%, 90% and 0.85. Our study provides an easy and understandable classification rules for identifying risk factors associated with MT that may be useful for promoting trauma management.

Keywords Massive hemorrhage · Multiple trauma · Massive transfusion · Decision tree · Algorithm

Introduction

Trauma is a major global public problem and the leading cause of death [1–4]. About 50% of trauma deaths occur as a result of uncontrolled hemorrhage within the first 48 h after trauma [3, 4]. In recent years, with the clinical progress of damage control resuscitation (DCR) and massive transfusion protocol (MTP), the mortality of trauma patient has reduced [5, 6]; however, the mortality of trauma patients with massive hemorrhage remains high.

Previous studies have shown that the mortality of trauma patients was associated with an increase of blood transfusion; furthermore, the mortality of massive transfusion (MT) patients is significantly higher than non-MT patients [7–9]. For massive hemorrhage in trauma patients, MTP plays an important role in early DCR and improved survival [6, 10, 11]. MTP is defined as rapid hemorrhage control through early administration of blood products in a balanced ratio for the prevention and immediate correction of coagulopathy, and to minimize occurrence of increased use of crystalloid fluids [12–14]. Studies have shown that early start MTP could reduce the risk of MT and related complications. They have also been shown to improve outcomes [12–14]. However, it is still difficult to identify the MT risk early and accurately.

Decision tree (DT) is a machine learning method used as a powerful solution to classify and predict problems [15]. Several studies have demonstrated that the DT algorithm can classify and predict diseases or outcomes with high accuracy, sensitivity, and specificity [16–22]. However, so far, the DT algorithm has not been used to predict MT risk in multiple trauma patients. Thus, to define the variables that could identify individuals at a risk for MT among patients with multiple trauma, we aimed to construct a model for MT prediction using the DT algorithm. This

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established model may be useful to determine patients with a high MT risk, and help to improve clinical decision-making in the case of patients with multiple trauma.

Materials and Methods

Study Population

The present study is a retrospective study of patients treated from 1 January 2013 through 30 June 2017. Patients diagnosed with multiple trauma who were consecutively admitted to the First Affiliated Hospital of Nanchang University were enrolled in this study. The inclusion criteria were as follows: all patients diagnosed as multiple trauma and adult patients with age $\geq$ 18 years. The exclusion criteria were as follows: pregnant woman; diagnosed with traumatic brain injury; diagnosed with serious cardiovascular and cerebrovascular diseases; or diagnosed with serious hematologic disorders.

Base Characteristics and Clinical Data Collection

Of the 670 identified patients with multiple trauma, 478 patients were eligible for inclusion and were included in this study, which included 435 who did not receiving MT ($\geq$ 10 units of packed red blood cells (RBCs) in 24 h or $>$ 4 units RBCs 1 h with anticipation of continued need) and 43 who receiving MT. Clinical data of enrolled patients were obtained through review of medical records. The following data were selected for the decision tree analysis: sex; age; injury causes; injury type; vital signs, including body temperature, systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), shock index (SI); injury severity score (ISS); fracture, including rib fracture and pelvis fracture; Glasgow coma score (GCS); and levels of hemoglobin (Hb), platelets, prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (APTT). The clinical outcomes related to in-hospital mortality, 24 h mortality, complications (including infection, multiple organs dysfunction syndromes (MODS), and acute kidney failure), hospital length of stay (LOS), intensive care unit (ICU) LOS, and duration of mechanical ventilation.

Decision Tree Development and Internal Validation

Enrolled patients were randomly divided into a training dataset and a testing dataset with a ratio of 7:3. Of the 478 patients with multiple trauma, 332 and 146 patients were assigned to the training dataset and the testing dataset, respectively. The training dataset was used for predictor discovery and supervised classification to generate a plausible model. The testing dataset was used to test the performance of the model, which was generated in the training sample.

Statistical Analysis

Statistical analyses were performed using R-program (version 3.5.1, The R Foundation for Statistical Computing). All tests were two-sided, and a p-value less than 0.05 was considered statistically significant. Continuous variables are presented as mean $\pm$ standard deviation or medians and quartiles, Data were analyzed with t-test or Mann-Whitney U-test, as appropriate. Categorical variables are presented as frequency and percentages and were analyzed with Chi-squared test or Fisher's exact test, as appropriate. The DT model was performed using classification and regression trees (CART) [23], based on the Gini impurity index using the *rpart package* in the R-program.

Results

Base Characteristics and Outcomes of Patients with Multiple Trauma

As shown in Table 1, the MT group had significantly higher in-hospital mortality, 24 h mortality, LOS, ICU LOS, duration of mechanical ventilation, and incidence of complications. No significant differences in sex, age, causes of injury, rib fracture, or body temperature were observed between the MT and non-MT group. In addition, the MT group had a significantly higher ISS, HR, SI, PT, APTT, and INR, but it had a lower GCS, SBP, DBP, and Hb levels compared with the non-MT group (Table 1).

Establishment Decision Tree Model

In this model, a decision tree was built on training dataset (332 records). Testing datasets (146 records) were used to evaluate the model. There were no differences in clinical characteristics between the training dataset and testing dataset (Table 2). The algorithm used the Gini index to select the variables. In the training model, 12 variables were used as input variables. The INR, SBP, ISS, and injury type remained in the model. The final decision tree is shown in Fig. 1.

Evaluation of the Decision Tree Model

The evaluation of the model was undertaken using a confusion matrix on a training and testing dataset and is shown in Tables 3 and 4. The present decision tree model had an accuracy of 90%. Of the 136 individuals without MT in

Table 1 Patient characteristics and outcomes of patients with massive transfusion (MT) and non-massive transfusion (non-MT) groups

Variables	Overall (n = 478)	Non-MT group (n = 435)	MT group (n = 43)	*p* value
Male (n, %)	356 (74.5)	328 (75.4)	28 (65.1)	0.196
Age (years)	45.21 ± 13.82	45.15 ± 13.85	45.84 ± 13.64	0.756
Injury cause (n, %)				0.561
Traffic injury	265 (55.4)	242 (55.6)	23 (53.5)	
Mechanical injury	4 (0.8)	4 (0.9)	0 (0.0)	
Sharp injury	34 (7.1)	29 (6.7)	5 (11.6)	
Falling injury	146 (30.6)	135 (31.0)	11 (25.6)	
Others	29 (6.1)	25 (5.8)	4 (9.3)	
Injury type (n, %)				< 0.001
Blunt injury	328 (68.6)	311 (71.5)	17 (39.5)	
Penetrating injury	150 (31.4)	124 (28.5)	26 (60.5)	
Rib fracture (n, %)	154 (32.2)	142 (32.6)	12 (27.9)	0.643
Pelvis fracture (n, %)	61 (12.8)	46 (10.6)	15 (34.9)	< 0.001
ISS	16.00 (9.00, 22.00)	14.00 (9.00, 22.00)	22.00 (17.00, 27.00)	< 0.001
GCS	14.40 ± 2.11	14.46 ± 2.05	13.81 ± 2.60	0.058
Body temperature (°C)	36.82 ± 0.56	36.82 ± 0.56	36.75 ± 0.62	0.418
HR (beats/min)	93.29 ± 18.45	91.44 ± 17.22	112.07 ± 20.13	< 0.001
SBP (mmHg)	118.17 ± 19.77	120.27 ± 18.22	96.88 ± 22.32	< 0.001
SI	0.82 ± 0.28	0.78 ± 0.22	1.23 ± 0.44	< 0.001
DBP (mmHg)	71.87 ± 13.47	73.16 ± 12.58	58.84 ± 15.29	< 0.001
Hb (g/L)	106.35 ± 30.79	110.43 ± 28.61	65.05 ± 19.74	< 0.001
PT (s)	11.90 (11.20, 13.50)	11.80 (11.10, 13.00)	16.20 (14.60, 18.00)	< 0.001
APTT (s)	28.60 (24.20, 34.95)	27.90 (23.95, 32.40)	52.60 (39.45, 69.10)	< 0.001
INR	1.07 (1.00, 1.19)	1.05 (0.99, 1.15)	1.47 (1.31, 1.69)	< 0.001
RBC transfusion (U)	0.00 (0.00, 2.00)	0.00 (0.00, 0.00)	10.00 (8.00, 13.50)	< 0.001
Plasma transfusion (mL)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	950.00 (600.00, 1325.00)	< 0.001
Complication (n, %)				< 0.001
Infections	62 (13.0)	50 (11.5)	12 (27.9)	
MODS	10 (2.1)	4 (0.9)	6 (14.0)	
Acute kidney failure	2 (0.4)	1 (0.2)	1 (2.3)	
Duration of mechanical ventilation (days)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	1.00 (0.00, 6.00)	< 0.001
ICU LOS(days)	0.00 (0.00, 4.00)	0.00 (0.00, 3.00)	5.00 (2.00, 12.50)	< 0.001
Hospital LOS (days)	18.00 (11.00, 28.75)	18.00 (10.00, 27.00)	32.00 (16.00, 50.00)	< 0.001
24 h mortality (n, %)	9 (1.9)	5 (1.1)	4 (9.3)	0.002
Hospital mortality (n,%)	19 (4.0)	11 (2.5)	8 (18.6)	< 0.001

Data are present as mean ± standard deviation or median (quartile)

ISS injury severity score, *GCS* glasgow coma score, *HR* heart rate, *SBP* systolic blood pressure, *SI* shock index, *DBP* diastolic blood pressure, *Hb* hemoglobin, *PT* prothrombin time, *APTT* activated partial thromboplastin time, *INR* international normalized ratio, *RBC* red blood cells, *MODS* multiple organs dysfunction syndromes, length of stay *LOS*, *ICU* intensive care unit

testing datasets, 122 were classified correctly using the decision-tree, with a specificity of 90%. For the 10 cases of MT in the testing dataset, the decision tree correctly classified 8 individuals with a sensitivity of 80%.

A ROC curve was obtained by applying the decision tree to test the dataset model that is shown in Fig. 2. The sensitivity, specificity, accuracy and area under the ROC curve (AUC) values for model were 80%, 90%, 89% and 0.86, respectively, for the testing dataset. We also repeated the analysis for the dataset when there was a partition of 50% in the training dataset and 50% in the testing dataset, or a partition of 80% in the training dataset and 20% in the testing dataset. The confusion matrix outcomes are shown in Table 5.

Table 2 Patient characteristics and outcomes of patients in training dataset and testing dataset

Variables	Training dataset (n = 332)	Testing dataset (n = 146)	*p* value
Male (n, %)	241 (72.6)	115 (78.8)	0.189
Age (years)	44.82 ± 13.30	46.10 ± 14.94	0.350
Injury cause (n, %)			0.992
Traffic injury	183 (55.1)	82 (56.2)	
Mechanical injury	3 (0.9)	1 (0.7)	
Sharp injury	23 (6.9)	11 (7.5)	
Falling injury	102 (30.8)	44 (30.1)	
Others	21 (6.3)	8 (5.5)	
Injury type (n, %)			0.999
Penetrating injury	104 (31.3)	46 (31.5)	
Blunt injury	228 (68.7)	100 (68.5)	
Rib fracture (n, %)	106 (31.9)	48 (32.9)	0.922
Pelvis fracture (n, %)	47 (14.2)	14 (9.6)	0.219
ISS	15.00 (9.00, 22.00)	17.00 (9.00, 22.00)	0.568
GCS	14.35 ± 2.22	14.51 ± 1.84	0.426
Body temperature (°C)	36.85 ± 0.58	36.74 ± 0.51	0.068
HR (beats/min)	93.92 ± 18.47	91.86 ± 18.39	0.262
SBP (mmHg)	117.79 ± 19.84	119.04 ± 19.65	0.523
SI	0.83 ± 0.29	0.80 ± 0.25	0.260
DBP (mmHg)	71.93 ± 13.59	71.73 ± 13.24	0.879
HB (g/L)	104.70 ± 31.92	110.10 ± 27.80	0.077
PT (s)	12.00 (11.30, 13.62)	11.80 (11.20, 13.20)	0.199
APTT (s)	28.70 (24.50, 35.15)	28.15 (23.63, 34.22)	0.294
INR	1.08 (1.00, 1.21)	1.05 (0.99, 1.18)	0.366
RBC transfusion (U)	0.00 (0.00, 2.00)	0.00 (0.00, 0.00)	0.252
Plasma transfusion (mL)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.274
Massive transfusion (n,%)	33 (9.9)	10 (6.8)	0.361
Complication (n, %)			0.700
Infections	44 (13.2)	18 (12.3)	
MODS	8 (2.4)	2 (1.4)	
Acute kidney failure	2 (0.6)	0 (0.0)	
Duration of mechanical ventilation (days)	0.00 (0.00, 0.00)	0.00 (0.00, 1.00)	0.823
ICU LOS(days)	0.00 (0.00, 4.25)	1.00 (0.00, 4.00)	0.565
Hospital LOS (days)	18.00 (11.00, 28.00)	19.00 (10.25, 29.00)	0.975
24 h mortality (n, %)	7 (2.1)	2 (1.4)	0.856
Hospital mortality (n,%)	13 (3.9)	6 (4.1)	0.999

Data are present as mean ± standard deviation or median (quartile)

ISS injury severity score, *GCS* glasgow coma score, *HR* heart rate, *SBP* systolic blood pressure, *SI* shock index, *DBP* diastolic blood pressure, *Hb* hemoglobin, *PT* prothrombin time, *APTT* activated partial thromboplastin time, *INR* international normalized ratio, *RBC* red blood cells, *MODS* multiple organs dysfunction syndromes, length of stay *LOS*, *ICU* intensive care unit

Discussion

Massive hemorrhage is a major potential preventable cause of deaths [3, 24]. Recent studies have suggested that an improvement of survival in trauma patients can be achieved by implementing MTP and by resuscitating with a balanced proportion of platelets, plasma, and packed red blood cells [12, 14, 25, 26]. Early and accurate prediction for trauma patients who required MT is necessary to increase the mortality benefits of early administration of blood transfusion. However, one of the major challenges of improving the outcome of trauma patients is the early identification of patients in need of MT. Several scoring systems [27–30], including the trauma associated severe

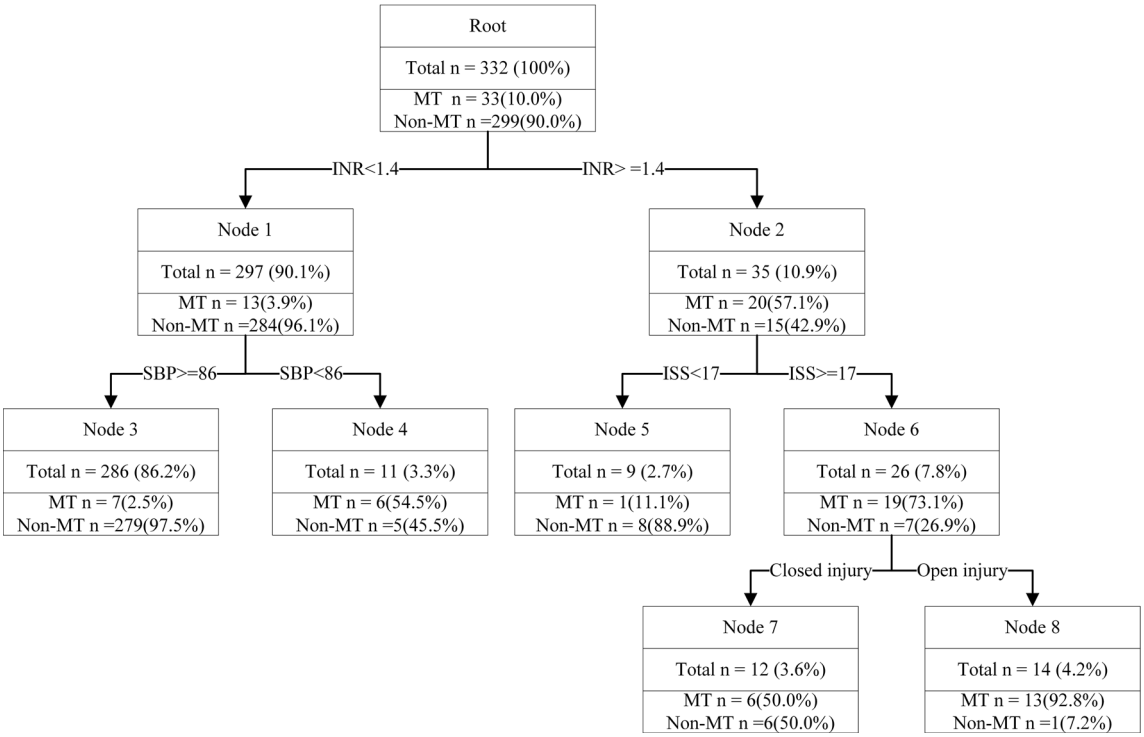

Fig. 1 Decision tree model for the occurrence of MT with training dataset. MT: massive transfusion; INR: international normalized ratio; SBP: systolic blood pressure; ISS: injury severity score

Table 3 The confusion matrix obtained as a result of training the rpart decision tree

	Predicted	
	MT	Non-MT
Actual		
MT	28	5
Non-MT	8	291

MT massive transfusion

Table 4 The confusion matrix obtained as a result of testing the rpart decision tree

	Predicted	
	MT	Non-MT
Actual		
MT	8	2
Non-MT	14	122

MT massive transfusion

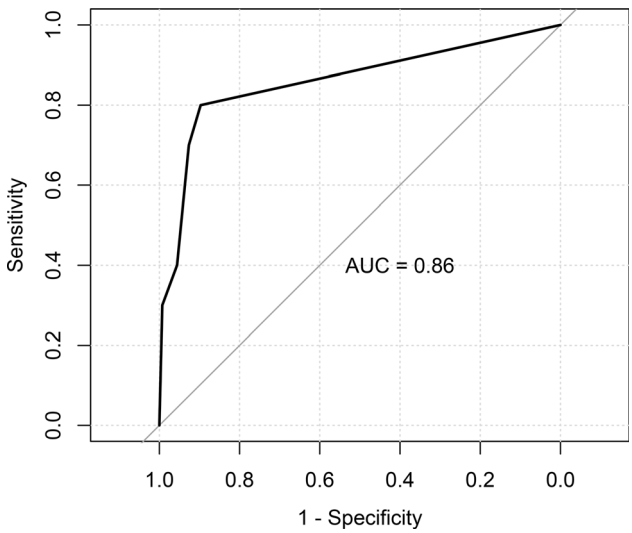

Fig. 2 Roc curve of the decision tree model in testing dataset

hemorrhage (TASH), prince of wales hospital (PWH) and assessment of blood consumption (ABC) score, have been introduced to predict the risk of MT in trauma patients. Brockamp et al. [31] validated 6 scoring systems and algorithms related to calculating the risk of MT and concluded that the TASH score was the highest (AUC of 0.889).

In the present study, the decision tree (DT) algorithm was used to screen the risk factors related to MT and constructed a prediction model in the training dataset and we further validated the testing dataset. The variables of INR, SBP, ISS, and injury type were entered in the prediction model. Wang et al. [32] set up an early blood transfusion needs score and Nunez et al. [28] set up an ABC score; both concluded that penetrating injury and SBP were independent risk factors of massive transfusion in trauma patients. Lui et al. [33] incorporated INR to the dynamic MBT score, and found that ISS and INR differed

Table 5 The confusion matrix obtained as a result of testing the rpart decision tree

	Predicted (using 50% as testing dataset)		Predicted (using 20% as testing dataset)	
	MT	Non-MT	MT	Non-MT
Actual				
MT	12	10	4	2
Non-MT	12	198	6	81

MT massive transfusion

from MT and non-MT. The results obtained from our model were similar to the results of other studies [28, 32, 33].

Our MT prediction model demonstrated an 80% sensitivity, 90% specificity, and 89% accuracy. A major strength of the present study was the application of the decision tree for investigating predictors associated with MT in multiple trauma. The study presented may provide a new insight into exploring MT risk prediction with trauma patients.

Despite our promising findings, there are still some certain limitations in our study. Firstly, the small sample size of this single-center retrospective study is the major limitation. This MT prediction model has not been validated in a prospective study. Secondly, this study did not use other machine learning algorithms such as a support vector machine (SVM), random forest (RF) for analysis. The best machine learning prediction model is still worth further exploring. In future studies, multi-center and larger-scale researches still need to be performed to develop a machine learning prediction model with greater sensitivity and specificity, which can be used to more accurately determine the risk of MT.

Conclusion

A MT prediction model is established using the decision tree algorithm and evidently has a good predictive performance. This study provides an easy and understandable classification of rules that helps to identify risk factors associated with MT that may be useful to develop programs for trauma management.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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