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Original Article

Development and internal validation of a nomogram to predict massive blood transfusions in neurosurgical operations

Kanisorn Sungkaro[1], Chin Taweesomboonyat[1], Anukoon Kaewborisutsakul[1]

[1]Department of Surgery, Division of Neurosurgery, Prince of Songkla University, Songkhla, Thailand.

ABSTRACT

Objectives: A massive blood transfusion (MBT) is an unexpected event that may impact mortality. Neurosurgical operations are a major operation involving the vital structures and risk to bleeding. The aims of the present research were (1) to develop a nomogram to predict MBT and (2) to estimate the association between MBT and mortality in neurosurgical operations.

Material and Method: We conducted a retrospective cohort study including 3660 patients who had undergone neurosurgical operations. Univariate and multivariate logistic regression analyses were used to test the association between clinical factors, pre-operative hematological laboratories, and MBT. A nomogram was developed based on the independent predictors.

Results: The predictive model comprised five predictors as follows: Age group, traumatic brain injury, craniectomy operation, pre-operative hematocrit, and pre-operative international normalized ratio and the good calibration were observed in the predictive model. The concordance statistic index was 0.703. Therefore, the optimism-corrected c-index values of cross-validation and bootstrapping were 0.703 and 0.703, respectively.

Conclusion: MBT is an unexpectedly fatal event that should be considered for appropriate preparation blood components. Further, this nomogram can be implemented for allocation in limited-resource situations in the future.

Keywords: Nomogram, Prediction, Massive transfusions, Neurosurgical operations

INTRODUCTION

Massive blood transfusion (MBT) occurs in several situations including for severely injured trauma victims,[1] uncontrolled blood loss,[2,3] and intraoperative incidental injury to major vessels.[4] The incidence of MBT ranges from 1.8% to 5.0%,[1-3] and the common situations that lead to MBT include trauma, cardiac surgery, liver transplantation, ruptured abdominal aortic aneurysm, gastrointestinal hemorrhage, and postpartum hemorrhage.[2,3] However, the association between MBT and mortality remains inconclusive. O'Keeffe *et al*. studied 8799 patients who had undergone revascularization of the lower extremity and found that MBT was significantly associated with both increased 30-day mortality and complications.[5] However, the study of Rangarajan *et al*. reported that MBT was not associated with mortality in traumatic patients.[6] In addition, Reppucci *et al*. reported that MBT did not impact mortality in massively transfused pediatric trauma patients.[7]

Neurosurgical operations usually involve the critical anatomy, meaning there is risk of injury to major vascular structures and unexpected intraoperative bleeding.[8,9] However, there is a lack of evidence mentioned concerning the factors influencing MBT in neurosurgical operation from the literature review.

At present, a nomogram is one of the clinical prediction tools (CPT) widely used to predict outcomes in several fields.[10-12] Several risk factors can be combined to predict and visualize an outcome as a two-dimensional figure or web-based application.[13] Hence, this study aimed to develop a nomogram to predict MBT in neurosurgical operations. In addition, the secondary objective was to estimate the association between MBT and mortality in neurosurgical operations.

MATERIALS AND METHODS

Study design and study population

The present study was a retrospective study design by including patients who had undergone neurosurgical

***Corresponding author:** Kanisorn Sungkaro, Department of Surgery, Division of Neurosurgery, Prince of Songkla University, Songkhla, Thailand. kanisorn7640@gmail.com

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operations at our institute from January 1, 2014, to October 31, 2019. Exclusion criteria were patients who were dead on arrival or who did not have data for cross-match and transfusion. Therefore, various clinical characteristics were reviewed and collected. Therefore, the outcome was an event of massive packed red cell (PRC) transfusion for each patient as the binary classifiers. In addition, massive PRC transfusion was defined as a transfusion using more than 4 units of PRC within 1 h or more than 10 units of PRC within 24 h.[14,15]

Sample size estimation was performed using receiver operating characteristics (ROC) with the area under the ROC curve (AUC) formula.[16] Based on an AUC of 0.850 from the study of Huang *et al*.[17] with a 0.05 margin of error, a minimum of 302 patients from the testing data would be needed to evaluate the predictability.

Ethical considerations

The present study was approved by a Human Research Ethics Committee (REC 65-052-10-1). The present study did not require informed consent from patients because it employed a retrospective study design. However, patients' identification numbers were encoded before analysis.

Statistical analysis

Clinical characteristics and imaging findings were calculated from descriptive statistics. Continuous variables were presented as mean ± standard deviation for normally distributed data and median with interquartile range for non-normally distributed data. For categorical data, the percentages were used for description.

To construct a predictive model, several factors were assessed using binary logistic regression analysis both univariate analysis and multivariable analysis. The *P*-values that were reported as being <0.05 were considered to be statistically significant.

The evaluation of the nomogram's predictability contained two domains including calibration and discrimination. The Hosmer-Lemeshow goodness-of-fit (GOF) test and a GOF test *P*-value of 0.05 or higher indicated good calibration of the model.[18] Therefore, the discrimination ability of the nomogram was estimated by the concordance statistic index (c-index) that equaled the AUC in the prediction of binary outcome.[19-21] Thus, internal validation was achieved to detect the overfitting problems of the model. In the present study, both 5-cross-validation and 1000 bootstrapping methods were used for internal validation. The results of internal validation were described as the optimism-corrected c-index for both methods.[20,21] Consequently, a two-dimensional nomogram was used to display the prediction model. Statistical analyses were performed using the R version 4.4.0 software (R Foundation, Vienna, Austria).

RESULTS

Characteristics of patients

A total of 3660 patients underwent neurosurgical operations between January 2014 and October 2019; the baseline characteristics of patients are shown in [Table 1]. The patients comprised 1903 males and 1757 females with a mean age of 46.48 ± 20.55 years. Moreover, the average body mass index was 22.99 ± 4.41 kg/m^2. The leading neurosurgical conditions included brain tumor (45.7%), traumatic brain injury (TBI) (15.2%), and cerebral aneurysm (13.8%). The major neurosurgical operations included craniotomy, craniectomy, and burr hole at 36.7%, 11.7%, and 8.7%, respectively. In addition, emergency surgery was observed in 48.0% of the present cohort.

For pre-operative hematologic laboratory, the mean hematocrit of the present cohort was 12.60 ± 2.08 g/dL, and average hematocrit was 37.83 ± 5.87%. Moreover, mean international normalized ratio (INR) was 1.06 ± 0.17. Pre-operative antiplatelet usage was observed in 3.5%, while pre-operative warfarin usage was found in 0.8%. As a result, average intraoperative blood loss was 600.80 ± 918.18 ml, and the blood transfusion rate in the present cohort was 41.1%. For those who were transfused, MBT was observed in 3.9%. In addition, 83 patients (2.3%) in the overall cohort were dead at hospital discharge. For hospital-discharge mortality according to MBT, 69.8% (58/83) of mortality cases in the MBT group. Moreover, MBT was significantly associated with increased mortality with odds ratio (OR) 95.31, 95% confidence interval (CI) 56.89–159.66.

Independent risk factors for MBT

Twelve variables with $P < 0.1$ in the univariate analysis were included as follows: Age group (<15 years = reference group, >15–60 years = OR 2.08 [95%CI 0.95–4.53], >60 years = OR 2.93 [95%CI 1.31–6.54]), pre-operative warfarin usage (OR 4.18 [95%CI 1.43–12.23]), body mass index (OR 1.03 [95%CI 0.97–1.07]), TBI (OR 2.51 [95%CI 1.74–3.64]), craniectomy operation (OR 3.38, [95%CI 2.32–4.92]), emergency operation (OR 3.38 [95%CI 2.32–4.92]), surgical infection operation (OR 0.19, [95%CI 0.02–1.37]), pre-operative hematocrit level (OR 0.85 [95%CI 0.79–0.92]), pre-operative white blood cell count (OR 1.03, [95%CI 1.01–1.06]), pre-operative platelet count (OR 0.998 [95%CI 0.996–0.999]), pre-operative prothrombin time ratio (OR 4.40, [95%CI 2.15–9.01]), and INR (OR 5.53 [95%CI 2.53–12.08]).

Subsequently, multivariable analysis with the backward elimination procedure demonstrated that age group (<15 years = reference group, >15–60 years = OR 2.10 [0.95–4.68], >60 years = OR 2.68 [95%CI 1.19–6.04]), TBI (OR 1.82 [95%CI 1.23–2.70]), craniectomy operation (OR 2.45 [95%CI 1.63–3.67]), pre-operative hematocrit level (OR 0.95

Table 1: Baseline characteristics of patients by red cell transfusion (n=3,660).

Characteristics	Non-massive blood transfusion (n=3517)	Massive blood transfusion (n=143)	Total (%)
Gender			
Male	1837 (52.2)	66 (46.2)	1903 (52.0)
Female	1680 (47.8)	77 (53.8)	1757 (48.0)
Age-year			
<=15	376 (10.7)	7 (4.9)	383 (10.5)
>15–60	2245 (63.8)	87 (60.8)	2332 (63.7)
>60	896 (25.5)	49 (34.3)	945 (25.8)
Mean Age-year (SD)			46.48 (20.55)
Comorbid			
Hypertension	1059 (30.1)	42 (29.4)	1101 (30.1)
Diabetes mellitus	388 (11.0)	16 (11.2)	404 (11.0)
Dyslipidemia	521 (14.8)	20 (14.0)	541 (14.8)
Liver disease	115 (3.3)	7 (4.9)	122 (3.3)
Renal failure	161 (4.6)	9 (6.3)	170 (4.6)
Pre-operative current medication			
Antiplatelet	122 (3.5)	7 (4.9)	129 (3.5)
Clexane	11 (0.3)	1 (0.7)	12 (0.3)
Warfarin	24 (0.7)	4 (2.8)	28 (0.8)
Neurosurgical condition			
Tumor	1602 (45.6)	69 (48.3)	1671 (45.7)
Traumatic brain injury	513 (14.6)	43 (30.1)	556 (15.2)
Aneurysm	488 (13.9)	18 (12.6)	506 (13.8)
Non-aneurysm cerebrovascular disease	301 (8.6)	9 (6.3)	310 (8.5)
Spinal operation-tumor	188 (5.3)	3 (2.1)	191 (5.2)
Spinal operation-trauma	137 (3.9)	0	137 (3.7)
Spinal operation-degenerative disease	38 (1.1)	1 (0.7)	39 (1.1)
Spinal operation-infection	13 (0.4)	0	13 (0.4)
Congenital disease-brain	93 (2.6)	0	93 (2.5)
Congenital disease-spine	32 (0.9)	0	32 (0.9)
Infection (non-surgical site infection)	100 (2.8)	0	100 (2.7)
Normal pressure hydrocephalus	12 (0.3)	0	12 (0.3)
American Society of Anesthesiologists classification			
1	2 (0.1)	1 (0.7)	3 (0.1)
2	211 (6.0)	3 (2.1)	214 (5.8)
3	3275 (93.1)	132 (92.3)	3407 (93.1)
4	29 (0.8)	7 (4.9)	36 (1.0)
Mean body mass index-kg/m^2 (SD)	22.9 (4.4)	23.6 (3.6)	22.9 (4.4)
Neurosurgical operation			
Craniotomy	1249 (35.5)	93 (65.0)	1342 (36.7)
Craniectomy	385 (10.9)	42 (29.4)	427 (11.7)
Suboccipital or rectosigmoid approach	210 (6.0)	3 (2.1)	213 (5.8)
Endoscopic approach with tumor removal	173 (4.9)	1 (0.7)	174 (4.8)
Cranioplasty	42 (1.2)	0	42 (1.1)
Burr hole with biopsy/aspiration/irrigation	320 (9.1)	0	320 (8.7)
Spinal operation with instrumentation	204 (5.8)	1 (0.7)	205 (5.6)
Spinal operation without instrumentation	168 (4.8)	3 (2.1)	171 (4.7)
Spinal operation in congenital condition	29 (0.8)	0	29 (0.8)
Ventriculostomy insertion	181 (5.1)	0	181 (4.9)
Shunt insertion	299 (7.3)	0	299 (8.2)
Other	257 (7.3)	0	257 (7.0)
Emergency operation	1679 (47.7)	79 (55.2)	1758 (48.0)
Surgical infection operation	125 (3.6)	1 (0.7)	126 (3.4)
Packed red cell transfusion	1361 (38.7)	143 (100.0)	1504 (41.1)

(Contd...)

Table 1: *(Continued).*

Characteristics	Non-massive blood transfusion (*n*=3517)	Massive blood transfusion (*n*=143)	Total (%)
Pre-operative hematologic laboratories			
Hematocrit -%	37.9 (5.8)	35.6 (6.5)	37.8 (5.8)
Hemoglobin g/dL	12.6 (2.0)	11.9 (2.2)	12.6 (2.0)
White blood cell count -×103/µL	11.2 (5.4)	12.5 (6.0)	11.3 (5.4)
Neutrophil l-%	68.3 (16.5)	69.0 (17.3)	68.3 (16.5)
Lymphocyte-%	22.8 (13.6)	22.3 (15.1)	22.8 (13.7)
Neutrophil-to-lymphocyte ratio	6.1 (9.3)	7.4 (12.0)	6.1 (9.5)
Platelet count-×103/µL	298.3 (123.4)	268.9 (111.8)	297.2 (123.1)
Prothrombin time ratio	0.9 (0.1)	1.0 (0.3)	0.9 (0.1)
International normalized ratio	1.0 (0.1)	1.1(0.5)	1.06 (0.17)
Mean intraoperative blood loss-ml	489.3 (564.7)	3342.4 (2439.0)	600.8 (918.1)
Hospital-discharge mortality	25 (0.7)	58 (40.6)	83 (2.3)

[95%CI 0.92–0.97]), and pre-operative INR (OR 2.55 [95%CI 1.33–4.86]) were independent predictors of MBT.

Development and internal validation of a nomogram

The predictive model with five predictors was estimated in terms of model performance and internal validation. For calibration, the results of the Hosmer-Lemeshow GOF test gave a *P*-value of 0.11, which revealed good calibration. Hence, the model discrimination had a c-index value of 0.703, as shown in [Figure 1]. Therefore, the overfitting of the model was evaluated by 5-cross-validation techniques and 1000 bootstrapping. The optimism-corrected c-index values of cross-validation and bootstrapping were 0.703 and 0.703, respectively. Therefore, the nomogram is presented in [Figure 2].

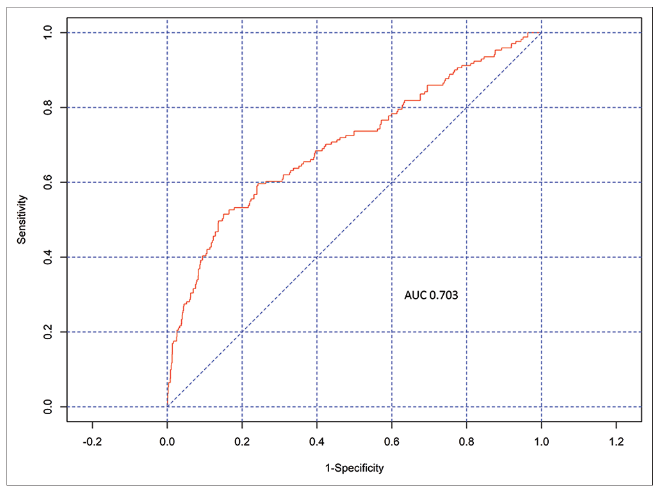

Figure 1: Receiver operating characteristics curve with the area under the curve (c-index) for discrimination.

DISCUSSION

In the present study, the incidence of MBT was 3.9%, concordant with prior studies that have been reported in a range from 1.8% to 5.0%.[1-3] MBT can occur unexpectedly as an event, which is important to consider because such an event significantly increased mortality in the present study. This finding is similar to what was previously shown in a study by O'Keeffe *et al.*, which demonstrated that MBT was significantly associated with 30-day mortality.[5] However, the association between MBT and mortality continues to be debated. Other previous studies did not find that MBT influenced mortality.[6,7]

The factors associated with MBT comprised age group, TBI, craniectomy operation, pre-operative hematocrit, and pre-operative INR following multivariable analysis. Older patients had a higher risk for MBT than younger patients. Similarly, our results are in concordant with prior studies.[22,23] Akaraborworn *et al.* studied 867 patients with trauma and found that those aged >60 years were more associated with MBT.[23] In the present study, patients suffering from TBI and craniectomy operation showed predictors influencing MBT, which was a novel finding in terms of the authors' knowledge. Moreover, pre-operative anemia and coagulopathy have been reported as predictors of MBT. These associations among predictors may be explained by traumatic-induced coagulopathy caused by tissue factor release from severe tissue damage and tissue hypoperfusion following trauma.[24,25] Therefore, the vicious cycle between coagulopathy and vigorous bleeding is promoted and needs appropriate resuscitation and treatment strategies.[26] Hence, severe brain damage can develop brain swelling intraoperatively, thus leading to performance of decompressive craniectomy.

The nomogram in the present study was developed based on various predictors from multivariable analysis. Hence, the predictability of the nomogram for MBT had a c-index of 0.703, which was acceptable in the range of 0.7–0.8.[27] After optimism correction, the c-index values

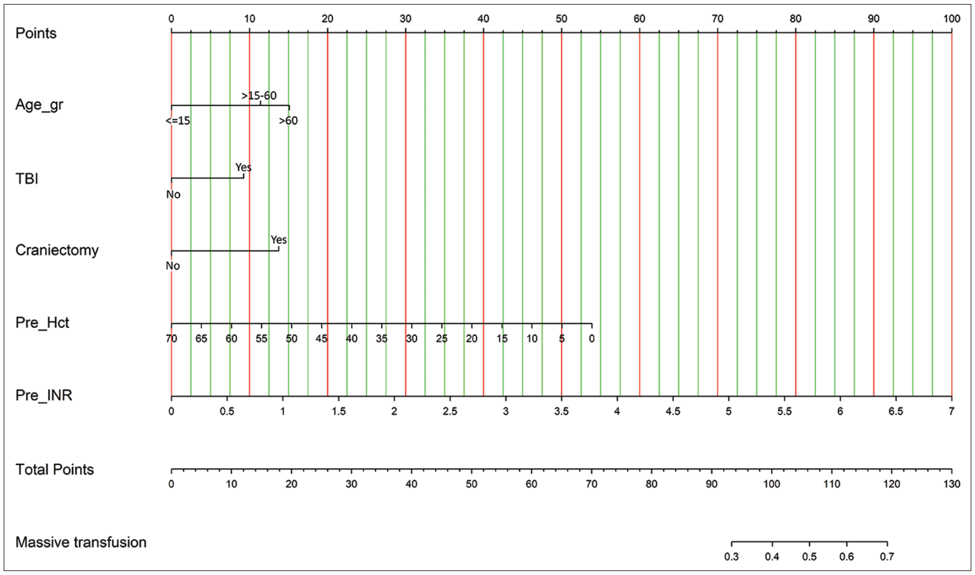

Figure 2: Nomogram predicting massive blood transfusion.

of internal validation did not drop, meaning no overfitting performance.[20,21] From prior studies, Kang *et al*. developed a scoring model for predicting MBT in placenta previa. They found that the c-index of the model was 0.922.[28] Moreover, Chico-Fernández studied the scoring systems for MBT in trauma patients and reported that the Assessment of Blood Consumption score had the highest c-index at 0.779.[29]

The nomogram and other prediction scores should be estimated with the unseen dataset to ensure generalizability in the future.[21] At present, machine learning is proposed to predict various clinical outcomes as the CPT. For intraoperative transfusion, Chang *et al*.[30] used the support vector machine algorithm to forecast intraoperative transfusions in orthopedic operations with an AUC of 0.707, while Mitterecker *et al*.[31] reported AUC of transfusion prediction using the gradient boosting, neural network, and random forest algorithms at 0.966, 0.966, and 0.963, respectively. Therefore, comparison of predictability between nomogram and various machine learning algorithms is challenged to perform. Tunthanathip *et al*.[13] compared the predictability of intracranial injury in pediatric TBI between nomogram and machine learning-based algorithms. Therefore, the best performance of the CPT can be implicated in real-world practice.

To the best of the authors' knowledge, this study is the first to reveal the acceptable performance of a nomogram for predicting MBT in neurosurgery. Besides, the limitations of the present study are considered. First, MBT is an uncommon event and incidence reported in <10% of cases; multicenter trials should be conducted in the future using a large number of MBT. Second, the study design was a retrospective approach that could have led to selection and information bias. However, the authors attempted to use multivariable analysis to mitigate this limitation.[32-34] Finally, this prediction tool needs to be validated externally with unseen data before implementation in real-world practice.[35]

CONCLUSION

MBT is an unexpectedly fatal event that should be considered for appropriate preparation blood component. Further, this nomogram can be implemented for allocation in limited-resource situations in the future.

Transparency declaration

This research was a part of a retrospective and cohort study that will be published elsewhere, whereas this study focused on nomogram predicting MBT.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Akaraborworn O, Chaiwat O, Chatmongkolchart S, Kitsiripant C, Chittawatanarat K, Morakul S, *et al*. Prediction of massive transfusion in trauma patients in the surgical intensive care units (THAI-SICU study). Chin J Traumatol

2019;22:219-22.
2. Dzik WS, Ziman A, Cohen C, Pai M, Lozano M, Kaufman RM, *et al*. Survival after ultramassive transfusion: A review of 1360 cases. Transfusion 2016;56:558-63.
3. Halmin M, Chiesa F, Vasan SK, Wikman A, Norda R, Rostgaard K, *et al*. Epidemiology of massive transfusion: A binational study from Sweden and Denmark. Crit Care Med 2016;44:468-77.
4. Behera SK, Senapati SB, Mishra SS, Das S. Management of superior sagittal sinus injury encountered in traumatic head injury patients: Analysis of 15 cases. Asian J Neurosurg 2015;10:17-20.
5. O'Keeffe SD, Davenport DL, Minion DJ, Sorial EE, Endean ED, Xenos ES. Blood transfusion is associated with increased morbidity and mortality after lower extremity revascularization. J Vasc Surg 2010;51:616-21.e6213.
6. Rangarajan K, Subramanian A, Pandey RM. Determinants of mortality in trauma patients following massive blood transfusion. J Emerg Trauma Shock 2011;4:58-63.
7. Reppucci ML, Pickett K, Stevens J, Phillips R, Recicar J, Annen K, *et al.* Massive transfusion in pediatric trauma-does more blood predict mortality? J Pediatr Surg 2022;57:308-13.
8. Kim JS, Han DI, Choi KS, Sim BS. Problems of massive transfusion in neurosurgical. Field J Korean Neurosurg Soc 1976;5:185-94.
9. Saringcarinkul A, Chuasuwan S. Maximum surgical blood order schedule for elective neurosurgery in a university teaching hospital in Northern Thailand. Asian J Neurosurg 2018;13:329-35.
10. Tunthanathip T, Ratanalert S, Sae-Heng S, Oearsakul T, Sakarunchai I, Kaewborisutsakul A, *et al*. Prognostic factors and clinical nomogram predicting survival in high-grade glioma. J Cancer Res Ther 2021;17:1052-8.
11. Kaewborisutsakul A, Tunthanathip T. Development and internal validation of a nomogram for predicting outcomes in children with traumatic subdural hematoma. Acute Crit Care 2022;37:429-37.
12. Jia M, Sheng Y, Chen G, Zhang W, Lin J, Lu S, *et al*. Development and validation of a nomogram predicting the risk of recurrent lumbar disk herniation within 6 months after percutaneous endoscopic lumbar discectomy. J Orthop Surg Res 2021;16:274.
13. Tunthanathip T, Duangsuwan J, Wattanakitrungroj N, Tongman S, Phuenpathom N. Comparison of intracranial injury predictability between machine learning algorithms and the nomogram in pediatric traumatic brain injury. Neurosurg Focus 2021;51:E7.
14. Patil V, Shetmahajan M. Massive transfusion and massive transfusion protocol. Indian J Anaesth 2014;58:590-5.
15. Chidester SJ, Williams N, Wang W, Groner JI. A pediatric massive transfusion protocol. J Trauma Acute Care Surg 2012;73:1273-7.
16. Taweesomboonyat C, Kaewborisutsakul A, Tunthanathip T, Saeheng S, Oearsakul T. necessity of in-hospital neurological observation for mild traumatic brain injury patients with negative computed tomography brain scans. JHSMR 2020;28:267-74.
17. Huang H, Cao M. Development and validation of a nomogram to predict intraoperative blood transfusion for gastric cancer surgery. Transfus Med 2021;31:250-61.
18. Hosmer DW, Lemeshow S. A goodness-of-fit test for the multiple logistic regression model. Commun Stat 1980;10:1043-69.
19. Han K, Song K, Choi BW. How to develop, validate, and compare clinical prediction models involving radiological parameters: Study design and statistical methods. Korean J Radiol 2016;17:339-50.
20. Austin PC, Steyerberg EW. Interpreting the concordance statistic of a logistic regression model: Relation to the variance and odds ratio of a continuous explanatory variable. BMC Med Res Methodol 2012;12:82.
21. Tunthanathip T. Development of Nomograms for Neurosurgery. Translational Medicine in Neurosurgery. Bangkok: Sahamit Pattana Printing; 2022. p. 111-34.
22. Mitra B, Olaussen A, Cameron PA, O'Donohoe T, Fitzgerald M. Massive blood transfusions post trauma in the elderly compared to younger patients. Injury 2014;45:1296-300.
23. Akaraborworn O, Siribumrungwong B, Sangthong B, Thongkhao K. Massive blood transfusion for trauma score to predict massive blood transfusion in trauma. Crit Care Res Pract 2021:2021;3165390.
24. Zhang J, Zhang F, Dong JF. Coagulopathy induced by traumatic brain injury: Systemic manifestation of a localized injury. Blood 2018;131:2001-6.
25. Tunthanathip T. Traumatic cerebrovascular injury. In: Oearsakul T, editor. Traumatic Brain Injury and Cervical Spine Injury. Bangkok: Sahamit Pattana Printing; 2022. p. 373-84.
26. Hardy JF, De Moerloose P, Samama M. Massive transfusion and coagulopathy: Pathophysiology and implications for clinical management. Can J Anaesth 2004;51:293-310.
27. Mandrekar JN. Receiver operating characteristic curve in diagnostic test assessment. J Thorac Oncol 2010;5:1315-6.
28. Kang J, Kim HS, Lee EB, Uh Y, Han KH, Park EY, *et al*. Prediction model for massive transfusion in placenta previa during cesarean section. Yonsei Med J 2020;61:154-60.
29. Chico-Fernández M, García-Fuentes C, Alonso-Fernández MA, Toral-Vázquez D, Bermejo-Aznarez S, Alted-López E. Massive transfusion predictive scores in trauma. Experience of a transfusion registry. Med Intensiva 2011;35:546-51.
30. Chang CM, Hung JH, Hu YH, Lee PJ, Shen CC. Prediction of preoperative blood preparation for orthopedic surgery patients: A supervised learning approach. Appl Sci 2018;8:1559.
31. Mitterecker A, Hofmann A, Trentino KM, Lloyd A, Leahy MF, Schwarzbauer K, *et al*. Machine learning-based prediction of transfusion. Transfusion 2020;60:1977-86.
32. Roelen CA, Bültmann U, Van Rhenen W, Van der Klink JL, Twisk JW, Heymans MW. External validation of two prediction models identifying employees at risk of high sickness absence: Cohort study with 1-year follow-up. BMC Public Health 2013;13:105.
33. Pourhoseingholi MA, Baghestani AR, Vahedi M. How to control confounding effects by statistical analysis. Gastroenterol Hepatol Bed Bench 2012;5:79-83.
34. Tunthanathip T, Sae-Heng S, Oearsakul T, Kaewborisutsakul A, Taweesomboonyat C. Economic impact of a machine learning-based strategy for preparation of blood products in brain tumor surgery. PLoS One. 2022;17:e0270916.

35. Tunthanathip T, Ratanalert S, Sae-Heng S, Oearsakul T, Sakaruncchai I, Kaewborisutsakul A, *et al*. Prognostic factors and nomogram predicting survival in diffuse astrocytoma. J Neurosci Rural Pract 2020;11:135-43.

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