A Nomogram Based on Clinical Characteristics for Predicting Multiple Organ Dysfunction Syndrome(MODS) Following Multiple Trauma Patients

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Abstract

Background

Multiple organ dysfunction syndrome (MODS) is the one of common complications,and the leading cause of late mortality in multiple trauma patients.The present study aims to develop and validate a nomogram based on clinical characteristics in order to identify the patients with multiple trauma who were at risk of developing MODS.

Methods

An retrospective cohort study was performed with data from January 2011 to December 2019,totally 770 patients with multiple trauma were enrolled in our study.They were randomly categorized into training set (n=514) and validation set (n=256).The univariate and multivariate logistic regression analyses were used to screen the predictors for multiple trauma patients who were at risk of developing MODS from training set data.Then we established a nomogram based on these above predictors.The discriminative capacity was assessed by receiver operating characteristic (ROC) curve area under the curve (AUC), and the predictive precision was depicted by calibration plot.The Hosmer-Lemeshow test was used to evaluate the the model's goodness of fit.

Results

Our study showed that age,ISS,hemorrhagic shock,heart rate,blood glucose,D-dimer and APTT were independent risk factors for MODS in patients with multiple trauma by multivariate logistic regression analysis.A nomogram was established on basis of these above risk factors.The area under the curve (AUC) was 0.868 (95% confidence interval [CI]:0.829-0.908) in the training set and 0.884 (95% confidence interval [CI]:0.833-0.935) in the validation set.The Hosmer-Lemeshow test has a *p* value of 0.227 in training set and 0.554 in validation set respectively,which confirm the model's goodness of fit.Calibration plot showed that the predicted and actual incidence of MODS probability were fitted well on both internal and external validations.

Conclusions

The present nomogram had a well predictive precision and discrimination capacity,which can facilitate improved screening and early identification of multiple trauma patients who were at high risk of developing MODS.

Background

Multiple Organ Dysfunction Syndrome (MODS) is one of the common complications of multiple trauma patients,as well as the leading cause of late mortality[1].During the last decades,the survival rate of multiple trauma patients improved with modern damage control concept,but the incidence of MODS continued to be high,as much as 30% in some seriously multiple trauma patients[2].A prospective study

by Matthias et al.[3]showed an overall incidence of MODS of 32.7% in multiple trauma patients,and the mortality of patients developing multiple organ dysfunction syndrome（MODS）following multiple trauma was approach to 50%.

To date,despite enhanced understanding of MODS pathogenesis,there have been no effective therapy,and prevention is still crucial for MODS[4].Therefore,early identification of multiple trauma patients who were at risk of developing MODS can help to timely prevention and intervention,and may improve these patient's prognosis.Recently studies showed several specific biomarkers could be useful in predicting high risk patients to develop posttraumatic MODS.A study by Haasper[5] showed procalcitonin(PCT) had a high sensitivity for predicting the development of MODS(sensitivity was 0.88).Kleinveld[6] found that the combination of anti-inflammatory proteins interleukin 1receptor antagonist(IL-1RA) and Clara cell protein 16(CC-16) was most strongly associated with the development MODS by multivariate analysis.A retrospective cohort study[7] showed plasma levels of Neutrophil gelatinase-associated lipocalin(NGAL), paracrine osteoprtegerin(OPG) and IL-6 were significantly elevated in MODS+ group,and these biomarkers positively correlated with MODS score and diagnosis of MODS.Kong et al.[8]found that delta neutrophil index (DNI)values of >3.25% and >5.3% at 12h post-admission were significant predictors of the development of MODS and 30-days mortality,respectively,in trauma patients.In addition,the AUC of combined detection of NF-κB（1.20,IL-6（25.1 ug/L and TNF-α（2.20 ng/ml in peripheral blood in predicting MODS was 0.853,95%CI(0.659,0.977)[9].

These above specific biomarkers had a certain guiding significance for predicting developing of MODS in patients with multiple trauma.However,these biomarkers were not routinely performed in clinical particularly in emergency room,because of cumbersome laboratory techniques or high cost associated with these approaches currently inhibited their clinical implementation.Therefore,it is quite necessary to explore a easy-to-use and reliable predictive model for MODS following multiple trauma patients.

The purpose of this study was to screen the independent risk factors for the development of MODS in patients with multiple trauma by using easily available clinical indicators in the early stage(within 24 hours after trauma),and then establish and validate a nomogram in order to detect high-risk patients who are likely to develop MODS.

Methods

Study Design and setting

This is a retrospective observational study.Medical records of multiple trauma patients admitted to the Affiliated Hospital of Jiangsu University from January 2011 to December 2019 were investigated.Patients who met the diagnostic criteria of multiple trauma and admitted within 24 hours after trauma were included.Exclusion criteria was patients admitted exceed 24 hours after trauma,patients with incomplete clinical data,and patients who quit therapy or transfered to other hospital halfway.

The patients were randomly divided into training set and validation set at a 2:1 ratio.The univariate and multivariate logistic regression analyses were used to screen the predictors for multiple trauma patients who were at risk of developing MODS from training set data.Then the predictors were used to establish a nomogram.Internal and external validation were performed in training set and validation set respectively.The discriminative capacity was assessed by receiver operating characteristic (ROC) curve area under the curve (AUC) and the predictive precision using calibration plot (Figure 1).

Data Collection

Each patient's clinical and laboratory information within 24h after trauma was collected through electronic medical records.Elementary clinical information included gender,age,injury mechanism,hemorrhagic shock upon admission,damage control surgery,pre-existing disease,injury severity score(ISS),number of injury sites,mean arterial pressure (MAP),length of stay (LOS) and heart rate.

Laboratory variables included neutrophil,lymphocyte,platelet (PLT),hemoglobin(Hb),blood glucose,activated partial thromboplastin time (APTT),fibrinogen (FBG) and D-dimer.

The presence and evolution of MODS was determined based on Sequential Organ Failure Assessment (SOFA) scoring.MODS was defined by the occurrence of a total SOFA score greater than 5,affecting two or more organs[10].

Data Analysis

Statistical results were presented as the mean ± standard deviation for normal data,and interquartile (IQR) and median were used for non-normal data.The categorical variables were presented as percentages and numbers.The non-normally distributed continuous variables were compared using Wilcoxon Mann-Whitney tests and the normally distributed continuous variables were compared using unpaired Student t-tests.Fisher's exact/Chi-squared tests were utilized to evaluate categorical variables.Multivariate logistic stepwise regression were used to determine predictive factors that were significant with a p value of less than 0.05 on univariate analysis.

The nomogram was established in terms of results of logistic regression analyses using R 3.6.2 with the rms package.The discrimination of the model's were assessed in terms of the receiver operating characteristic (ROC) curve area under the curve (AUC).The closer the AUC value is to 1,the better discrimination capacity the prediction model has.Generally,a prediction model that performs with an AUC of 0.5-0.75 is considered acceptable,and AUC>0.75 indicates the model shows excellent discrimination.

In addition, calibration curves were performed to assess the consistency of nomogram predicted chance and the actual incidence of MODS.Goodness of fit was assessed by using Hosmer-Lemeshow test.

Statistical analysis were conducted using SPSS version 26.0 (IBM,Armonk,NY,USA).Difference were considered significant when *p* value was less than 0.05.

This study was approved by the Institutional Review Board of the Affiliated Hospital of Jiangsu University.The need to obtain informed consent was waived because of the retrospective nature of the study.

Results

Demographic characteristics

This study included totally 770 patients with multiple trauma.They were randomly divided into training set (n=514) and validation set (n=256) at a 2:1 ratio.220 patients with multiple trauma developed multiple organ dysfunction syndrome (MODS)eventually.Of those,142 patients in training set,and 78 patients in validation set respectively.The basic clinical characteristics for the training set and validation set are listed in Table 1.All of the variables were not statistical significant difference between training set and validation set(P□0.05).

Univariate and multivariate logistic regression of the training set

In training set,Patients were classified into two groups according to patients meet the criteria of MODS or not,including MODS group and non-MODS group.Of which 142 individuals with multiple trauma in MODS group,372 patients in non-MODS group.Univariate analysis showed age,injury mechanism,hemorrhagic shock,mortality,ISS,heart rate,MAP,neutrophil,hemoglobin,blood glucose,FBG,APTT,D-dimer and LOS were statistical significant difference between MODS group and non-MODS group(P□0.05) (Table 2).The above variables except mortality and LOS were subjected to the multivariate logistic stepwise regression analysis for screening the predictors of MODS.The results showed that only age(HR=2.603,95% confidence interval [CI]:1.522-4.453,P□0.001),ISS(HR=1.124,95% confidence interval [CI]:1.084-1.167,P□0.001),hemorrhagic shock(HR=2.067,95% confidence interval [CI]:1.075-3.974,P□0.05),heart rate(HR=1.022,95% confidence interval [CI]:1.008-1.036,P□0.01),D-dimer(HR=1.008,95% confidence interval [CI]:1.002-1.015,P□0.01),blood glucose(HR=1.091,95% confidence interval [CI]:1.016-1.171,P□0.05) and APTT(HR=1.047,95% confidence interval [CI]:1.017-1.079,P□0.01)were independent risk factors for developing MODS with multiple trauma (Figure 2).

Development of MODS predictive nomogram for patients with multiple trauma

The predictive nomogram showed in Figure 3.The nomogram was established on basis of the coefficients gained from multivariate logistic regression analysis,which included age,hemorrhagic shock,heart rate,blood glucose,D-dimer,ISS and APTT.Each value of the factors was allocated the score in the point scale axis.By summing up each single score and using that value in the total points scale axis,the total score could be easily calculated to predict the probability of MODS in patients with multiple trauma.A higher score of total points indicated a greater chance of MODS developing from multiple trauma patients.

Internal validation of the predictive nomogram

Internal validation of training set,the predictive nomogram validated a excellent discriminative capacity of AUC 0.868(95% CI:0.829-0.908)(Figure 4A).The calibration curve disclosed that predicted nomogram possibilities of MODS following multiple trauma estimated actual probabilities(Figure 4B).

External validation of the predictive nomogram

External authentication was achieved by comparing the predictive nomogram and individual actual possibility in the validation group.For validation group,the predictive nomogram AUC was 0.884(95% CI:0.833-0.935)(Figure 5A).The calibration cureve revealed that there was well consistence among predicted and actual possibilities(Figure 5B).

Hosmer-Lemeshow test

In order to evaluate model's goodness of fit,the Hosmer-Lemeshow test was performed(Table 3).in training set,X-squared=10.561,P value=0.227(P>0.05);in validation set,X-squared=6.839,P value=0.554(P>0.05).This indicates the present model's goodness of fit was well on both internal validation and external validation.

Discussion

The poor outcome of MODS developing from multiple trauma has been attracted scientific extensive attention.The researches regarding predicting MODS following multiple trauma has been increasing.However,most studies focused on the specific biomarkers,lacking a predicting model which can easy available in clinical.Thus,our study was conducted by using clinical characteristics within 24 hours onset to screen the risk factors of MODS.The result revealed that age,ISS,hemorrhagic shock,heart rate,blood glucose,D-dimer and APTT were independent risk factors of MODS developing from multiple trauma patients.Our study demonstrated the present nomogram was constructed depending on these above independent risk factors,which had a well performance in discriminative capacity and predictive precision.

Most studies defined geriatric trauma patients as patients over the age of 65 years[11].Due to geriatric patients generally decreased physiological reserves and suffered from underlying diseases,they were more susceptible for high mortality rate and fatal complications, particularly MODS[12].Alteration in the cardiovascular and respiratory systems exacerbated the potential to hypoxia and shock,pre-existing conditions of the respiratory system increased the risk for pneumonia,as well as acute respiratory distress syndrome(ARDS)[11].Despite the severity of the injury is equivalent,geriatric patients have worse outcome than younger patients[13].A study reported by Aldrian showed that elderly patients with multiple trauma had a significantly higher incidence of MODS compared to younger group(17.8% vs 7.1%,p=0.02)[14].Similarly,in our study the ratio of geriatric patients (age over 65 years) in MODS group had a significance higher than non-MODS group(31.7% vs 20.7%,p=0.009).

Injury severity score (ISS) is based on the abbreviated injury scale (AIS),and is the most prevalence trauma score in clinical[15].ISS is initially as a tool of comparison injury severity for multiple trauma patients.Over time,much of research demonstrated that the ISS is not only a tool for comparison of injury severity,but also a strongly correlation with mortality in multiple trauma patients[16].Generally,patients with multiple trauma that defined ISS ≥ 16 points associated with a mortality risk of 10%,which called as severe multiple trauma[17].Additionally,A retrospective study showed injury severity score (ISS) was not only the one of independent risk factors of mortality,but also was the only one independent risk factor of complications and ICU length of stay[18].ISS has been associated with mortality but the association between ISS and MODS is yet known.In our study,MODS group had a significantly higher ISS compared to non-MODS group(31.16±6.57 vs 23.72±7.20,P□0.001),and multivariate logistic regress analysis showed ISS could be as a predictor for MODS following multiple trauma.

Patients with multiple trauma were often accompanying with coagulation disorder when shock,severe injury or tissue damage.Trauma-induced coagulopathy is caused by multiple factors,such as anemia, hemodilution,hypothermia,acidosis,shock,and serious trauma itself[19].D-dimer has been extensively investigated for diagnosis of venous thromboembolism(VTE)[20].Recently study showed that D-dimer may reflect the imbalance between proinflammatory and anti-inflammatory cytokines.Moreover,D-dimer levels were associated not only with mortality but also with the development of severe sepsis or septic shock,multiple organ dysfunction syndrome(MODS)[21].Activated partial thromboplastin time (APTT) is a frequently used screening coagulation test to evaluate deficiency in intrinsic and common pathways,which also used for heparin therapy monitoring and detecting circulating inhibitors of blood coagulation[22].A study showed in patients with septic shock caused by intra-abdominal infection,APTT,PT and D-dimer levels on admission to the ICU were significantly associated with AKI,furthermore,APTT was an independent predictor of 30-day mortality[23]. Hemostasis-related parameters have a significant impact on severity and outcome prediction of patients with sepsis,of which included APTT and D-dimer[24].In line with previous studies,our results showed that APTT and D-dimer upon admission can be used to predict MODS developing from multiple trauma.The pathogenesis of MODS induced by coagulopathy is possibly owing to dysregulation of hemostatic system may lead to microvascular thrombosis and hypoperfusion,and that the altered fibrinolytic mechanisms might then induce tissue ischemia and tissue necrosis,and eventually MODS.

It is well known that hemorrhagic shock is a frequently complication in severe multiple trauma patients,which may lead to MODS even death.Hemorrhagic shock has been proposed as an main driver of systemic inflammation,gut barrier disruption,endothelial damage and coagulation dysfunction,all these factors may contributed to the development of MODS[25].A animal model experiment demonstrated that hemorrhagic shock add to the systemic inflammatory reaction early after multiple trauma,aggravate pulmonary damage and worsen renal and endothelial function,which might lead to the development of early multiple organ dysfunction syndrome[26].Furthermore,it is by now generally accepted that hemorrhagic shock induced a vicious cycle of outcomes,consisting of hypothermia,acidosis,and

coagulopathy-otherwise known as the lethal triad[27].Besides,hemorrhagic shock can lead to a imbalance between oxygen supply and consumption,and this anoxia result in a change from aerobic to anaerobic metabolism.Lactic acidosis ensues,and if uncorrected,MODS and death follow[28].Consequently,we regarded hemorrhagic shock as a crucial predictor for developing MODS.

Blood glucose on admission is known to be as a predictor for in-hospital mortality in multiple trauma patients[29-30].Hyperglycemia admission is not only due to diabetic hyperglycemia,but also stress-induced hyperglycemia[31].The metabolic manifestation of the stress response is characterised by hyperglycemia mediated by a number of neural and humoral mechanism,of which included catecholamines release,hepatic gluconeogenesis activated,increased levels of cortisol,glucagon,and epinephrine[32].Generally,the magnitude of the stress response is proportional to the magnitude of tissue damage[33].Previous study showed early hyperglycemia was associated with multiple organ failure (MOF)after trauma[34].Our results was consistent with previous study,which blood glucose was a predictos for MODS in patients with multiple trauma.And a study speculated low β-cell function was strong correlations with the presence of MODS[35].

HR is considered not only a physiological indicator but also a prognostic marker.Numerous studies have shown that increased heart rate (HR) was associated with higher mortality in several cardiac disorders[36].Recently study demonstrated HR is also associated with mortality in trauma patients,which showed mortality after trauma increase outside the heart rate range of 70 to 89 beats per minute[37].In addition,a heart rate≥90 bpm at the time of MODS diagnosis is an independent risk factor for increased 28-day mortality[38].Heart rate is elevated beyond physiologically useful compensatory mechanism thus increasing myocardial oxygen demand,and contributing itself to a poor outcome[39].MODS was a severe complication of multiple trauma,our study demonstrated increased HR may be predicting for MODS following multiple trauma patients.

Limitations

There are several potential limitations in present study.First,it is a single center study,the training set and validation set came from the same institution.It may be less comparable than studies using multicentric sampled population.Second,it was well known that inflammatory cytokines play a important role in developing MODS.but the present nomogram model was not included inflammatory indicators such as C reactive protein or PCT.Lastly,our sample size was relatively small,so that could not included more variables.

Conclusion

In summary,we conducted a nomogram for predicting MODS in patients with multiple trauma based on clinical characteristics within onset 24 hours,which had a well predictive accuracy and discrimination capacity,and could be application in early identification of MODS in patients with multiple trauma.According to the present nomogram,clinicians could estimate intuitionally the probabilities of

occurrence of MODS following multiple trauma patients.Nonetheless,further study with larger sample size or prospective cohort study are needed to evaluate and validate the present nomogram.

Declarations

Ethics approval and consent to participate

This study was approved by the institutional review board of the Affiliated Hospital of Jiangsu University.Informed consent from the patients was waived because this study is retrospective,which does not influence the outcome of treatment and diagnosis.

Consent of publication

Not applicable.

Availability of data and material

Due to the nature of this study,participants of this study did not agree for their data to be shared publicly.If needed,please contact autor for data requests.

Competing interests

All authors declare that they have no competing interests.

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Author’s contributions

Zhenjun miao designed and conceived this study and wrote the manuscript,Faxing Wei and Feng Zhou collected the data,provided proffessional discussions and suggestions.All authors read and approved the final manuscript.

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References

1. Sauaia A,Moore F A,Moore E E,Postinjury Inflammation and Organ Dysfunction.Crit Care Clin.2017;33(1):167-191.
2. Shepherd,J.M.Cole,E.Brohi,K.Contemporary Patterns of Multiple Organ Dysfunction in Trauma.Shock.2017 Apr;47(4):429-435.

3. Frohlich M,Lefering R,Probst C,Paffrath T,Schneider M M,Maegele M,et al.Epidemiology and risk factors of multiple-organ failure after multiple trauma: an analysis of 31,154 patients from the TraumaRegister DGU. J Trauma Acute Care Surg.2014;76(4):921-928.
4. Philip S. Barie, Lynn J. Hydo, Fredric M. Pieracci, Jian Shou, and Soumitra R. Eachempati.Multiple Organ Dysfunction Syndrome in Critical Surgical Illness.Surg Infect (Larchmt) . 2009 Oct;10(5):369-377.
5. Haasper C,Kalmbach M,Dikos G D,Meller R,Muller C,Krettek C,et al.Prognostic value of procalcitonin (PCT) and/or interleukin-6 (IL-6) plasma levels after multiple trauma for the development of multi organ dysfunction syndrome (MODS) or sepsis.Technol Health Care . 2010;18(2):89-100.
6. Kleinveld D J,Tuip-de Boer A M,Hollmann M W,Juffermans N P.Early increase in anti-inflammatory biomarkers is associated with the development of multiple organ dysfunction syndrome in severely injured trauma patients.Trauma Surg Acute Care Open.2019;4(1):e000343.
7. Peters H,Macke C,Mommsen P,Zeckey C,Clausen J D,Krettek C,et al.Predictive Value of Osteoprotegerin and Neutrophil Gelatinase-associated Lipocalin on Multiple Organ Failure in Multiple Trauma.In Vivo.Sep-Oct 2019;33(5):1573-1580.
8. Kong T,Park Y S,Lee H S,Kim S,Lee J W,You J S,et al.The delta neutrophil index predicts development of multiple organ dysfunction syndrome and 30-day mortality in trauma patients admitted to an intensive care unit: a retrospective analysis.Sci Rep.2018 Nov 30;8(1):17515.
9. Zeng,J.Values of detection of NF-kappaB activation level combined with IL-6 and TNF-alpha levels in peripheral neutrophils in the prediction of multiple organ dysfunction syndrome in patients with severe multiple trauma.Exp Ther Med.2018 Sep;16(3):2478-2482.
10. Cole,S.Gillespie,P.Vulliamy and K. Brohi, Multiple organ dysfunction after trauma.Br J Surg.2020 Mar;107(4):402-412.
11. Dimitriou,R.Calori,G.M.Giannoudis,P.V.Polytrauma in the elderly:specific considerations and current concepts of management.Eur J Trauma Emerg Surg.2011 Dec;37(6):539-548.
12. De Vries,R.Reininga,I.H.F.de Graaf,M.W.Heineman,E.El.Moumni, M.Wendt,K.W.Older polytrauma: Mortality and complications.Injury.2019 Aug;50(8):1440-1447.
13. Rupprecht,H.Heppner,H.J.Wohlfart,K.Turkoglu,A.The geriatric polytrauma: Risk profile and prognostic factors.Ulus Travma Acil Cerrahi Derg.2017 Mar;23(2):156-162.
14. Aldrian,S.Nau,T.Koenig,F.Vecsei,V.Geriatric polytrauma.Wien Klin Wochenschr.2005 Feb;117(4):145-149.
15. Elgin,L.B.Appel,S.J.Grisham,D.Dunlap,S.Comparisons of Trauma Outcomes and Injury Severity Score J Trauma Nurs.Jul/Aug 2019;26(4):199-207.
16. Schroter,C.Urbanek,F.Fromke,C.Winkelmann,M.Mommsen,P.Krettek,C.et al.Injury severity in polytrauma patients is underestimated using the injury severity score: a single-center correlation study in air rescue.Eur J Trauma Emerg Surg . 2019 Feb;45(1):83-89.
17. Paffrath,T.Lefering,R.Flohe,S.TraumaRegister,D.G.U.How to define severely injured patients? – an Injury Severity Score (ISS) based approach alone is not sufficient.Injury.2014 Oct;45 Suppl 3:S64-69.

18. Pettit, N.R.Wood,T.Lieber,M.O'Mara,M.S.Intensive care unit design and mortality in trauma patients.J Surg Res.2014 Aug;190(2):640-647.
19. Satoshi Gando,Mineji Hayakawa.Pathophysiology of Trauma-Induced Coagulopathy and Management of Critical Bleeding Requiring Massive Transfusion.Semin Thromb Hemost.2016 Mar;42(2):155-165.
20. Weitz,J.I.Fredenburgh,J.C.Eikelboom,J.W.A Test in Context: D-Dimer.J Am Coll Cardiol.2017 Nov 7;70(19):2411-2420.
21. Shorr,A.F.Thomas,S.J.Alkins,S.A.Fitzpatrick,T.M.Ling,G.S.D-dimer Correlates With Proinflammatory Cytokine Levels and Outcomes in Critically Ill Patients.Chest.2002 Apr;121(4):1262-1268.
22. Esmedere Eren,S.Karakukcu,C.Ciraci,M. Z.Ustundag,Y.Karakukcu,M.Activated partial thromboplastin time derivative curves:helpful diagnostic tool in mixing test interpretation.Blood Coagul Fibrinolysis.2018 Jun;29(4):410-414.
23. Xu,Z.Cheng,B.Fu,S.Liu,X.Xie,G.Li,Z.et al.X.Coagulative biomarkers on admission to the ICU predict acute kidney injury and mortality in patients with septic shock caused by intra-abdominal infection.Infect Drug Resist.2019 Sep 4;12:2755-2764.
24. Mihajlovic,D.Lendak,D.Mitic,G.Cebovic,T.Draskovic,B.Novakov,A.Brkic, S.Prognostic value of hemostasis-related parameters for prediction of organ dysfunction and mortality in sepsis.Turk J Med Sci.2015;45(1):93-98.
25. Halbgebauer,R.Braun,C.K.Denk,S.Mayer,B.Cinelli,P.Radermacher,P.et al.Hemorrhagic shock drives glycocalyx, barrier and organ dysfunction early after polytrauma.J Crit Care.2018 Apr;44:229-237.
26. Denk,S.Weckbach,S.Eisele,P.Braun,C.K.Wiegner,R.Ohmann,J. J.et al.Role of Hemorrhagic Shock in Experimental Polytrauma.Shock.2018 Feb;49(2):154-163.
27. Owattanapanich,N.Chittawatanarat,K.Benyakorn,T.Sirikun,J.Risks and benefits of hypotensive resuscitation in patients with traumatic hemorrhagic shock: a meta-analysis.Scand J Trauma Resusc Emerg Med.2018 Dec 17;26(1):107.
28. Suresh,M.R.Chung,K.K.Schiller,A.M.Holley,A.B.Howard,J.T.Convertino,V.A.Unmasking the Hypovolemic Shock Continuum:The Compensatory Reserve.J Intensive Care Med.2019 Sep;34(9):696-706.
29. Saad, S.Mohamed,M.Ellabban,G.Moghazy,A.El-kamash,S.Venous glucose, serum lactate and base deficit as biochemical predictors of mortality in patients with polytrauma.Ulus Travma Acil Cerrahi Derg.2016 Jan;22(1):29-33.
30. Torabi,M.Mazidi,S.F.Baneshi,M.R.Blood sugar changes and hospital mortality in multiple trauma.Am J Emerg Med.2018 May;36(5):816-819.
31. Su,W.T.Wu,S.C.Chou,S.E.Huang,C.Y.Hsu,S.Y.Liu,H.T.et al.Higher Mortality Rate in Moderate-to-Severe Thoracoabdominal Injury Patients with Admission Hyperglycemia Than Nondiabetic Normoglycemic Patients.Int J Environ Res Public Health.2019 Sep 25;16(19):3562.
32. Walia,S.Sutcliffe,A.J.The relationship between blood glucose, mean arterial pressure and outcome after severe head injury:an observational study.Injury.2002 May;33(4):339-344.

33. Bochicchio,G.V.Bochicchio,K.M.Joshi,M.Ilahi,O.Scalea,T.M.Acute Glucose Elevation Is Highly Predictive of Infection and Outcome in Critically Injured Trauma Patients.Ann Surg.2010 Oct;252(4):597-602.
34. Richards,J.E.Scalea,T.M.Mazzeffi,M.A.Rock,P.Galvagno,S.M.Jr.Does Lactate Affect the Association of Early Hyperglycemia and Multiple Organ Failure in Severely Injured Blunt Trauma Patients?Anesth Analg.2018 Mar;126(3):904-910.
35. El-Sherbini, SA.Marzouk,H.El-Sayed,R.Hosam-ElDin,S.Etiology of hyperglycemia in critically ill children and the impact of organ dysfunction.Rev Bras Ter Intensiva.Jul-Sept 2018;30(3):286-293.
36. Oliva F,Sormani P,Contri R,Campana C,Carubelli V,Cirò A,et al.Heart rate as a prognostic marker and therapeutic target in acute and chronic heart failure.Int J Cardiol.2018 Feb 15;253:97-104.
37. Ley,E.J.Singer,M.B.Clond,M.A.Ley,H.C.Mirocha,J.Bukur,M.et al.Admission heart rate is a predictor of mortality.J Trauma Acute Care Surg.2012 Apr;72(4):943-947.
38. Hoke,R.S.Muller-Werdan,U.Lautenschlager,C.Werdan,K.Ebelt,H.Heart rate as an independent risk factor in patients with multiple organ dysfunction: a prospective, observational study.Clin Res Cardiol.2012 Feb;101(2):139-147.
39. Liu,N.T.Kramer,G.C.Khan,M.N.Kinsky,M.P.Salinas,J.Is heart-rate complexity a surrogate measure of cardiac output before,during,and after hemorrhage in a conscious sheep model of multiple hemorrhages and resuscitation?J Trauma Acute Care Surg.2015 Oct;79(4 Suppl 2):S93-100.

Tables

Table 1 Baseline characteristics of the patients in training set and validation set

Characteristics	Training set(n=514)	Validation set(n=256)	*P* value
Gender			0.335
Male	377(73.3%)	196(76.6%)	
Female	137(26.7%)	60(23.4%)	
Age			0.739
≥65 years	392(76.3%)	198(77.3%)	
<65 years	122(23.7%)	58(22.7%)	
Injury Mechanism			0.115
Motor vehicle accident	302(58.8%)	161(62.9%)	
Fall	106(20.6%)	58(22.7%)	
other	106(20.6%)	37(14.5%)	
Hemorrhagic Shock			0.122
Yes	96(18.7%)	60(23.4%)	
No	418(81.3%)	196(76.6%)	
Pre-existing disease			0.792
Yes	131(25.5%)	63(24.6%)	
No	383(74.5%)	193(75.4%)	
Mortality			0.059
Survivor	453(88.1%)	213(83.2%)	
Non-survivor	61(11.9%)	43(16.8%)	
MODS			0.411
Yes	142(27.6%)	78(30.5%)	
No	372(72.4%)	178(69.5%)	
Damage control surgery			0.146
Yes	191(37.2%)	109(42.6%)	
No	323(62.8%)	147(57.4%)	
ISS	25.78±7.78	26.91±8.15	0.062
Number of injury sites	2.32±0.75	2.30±0.77	0.701
Heart rate(bpm)	88.50±19.27	89.09±19.81	0.691

MAP(mmHg)	93.00±19.13	90.26±22.07	0.090
Neutrophil(×109/L)	11.19±5.51	11.29±5.39	0.824
Platelet(×109/L)	184.93±77.79	179.02±66.69	0.299
Hemoglobin(g/L)	124.00±24.05	121.19±24.86	0.132
Blood glucose(mmol/L)	8.28±3.33	8.12±3.13	0.529
FBG(g/L)	2.36±1.14	2.28±1.12	0.343
APTT(s)	26.44±11.42	27.83±14.93	0.190
LOS(days)	23.00(13.00,42.00)	23.50(14.00,41.00)	0.898
D-dimer(mg/L)	13.76(4.98,35.72)	14.86(5.29,40.09)	0.271
Lymphocyte ($\times 10^9$/L)	1.20(0.80,2.70)	1.30(0.80, 2.50)	0.904

ISS,injury severity score;MAP,mean arterial pressure;FBG,fibrinogen;APTT,activated partial thromboplastin time;MODS,multiple organ dysfunction syndrome;LOS,length of stay.

Table 2 Univariate analyses of factors associated with MODS in the training set

Characteristics	MODS group(n=142)	Non-MODS (n=372)	*P* value
Gender			0.391
Male	108(76.1%)	269(72.3%)	
Female	34(23.9%)	103(27.7%)	
Age			0.009
≥65 years	97(68.3%)	295(79.3%)	
65 years	45(31.7%)	77(20.7%)	
Injury Mechanism			0.020
Motor vehicle accident	96(67.6%)	206(55.4%)	
Fall	27(19.0%)	79(21.2%)	
other	19(13.4%)	87(23.4%)	
Hemorrhagic Shock			0.000
Yes	56(39.4%)	40(10.8%)	
No	86(60.6%)	332(89.2%)	
Pre-existing disease			0.123
Yes	43(30.3%)	88(23.7%)	
No	99(69.7%)	284(76.3%)	
Mortality			0.000
Survivor	100(70.4%)	353(94.9%)	
Non-survivor	42(29.6%)	19(5.1%)	
Damage control surgery			0.718
Yes	51(35.9%)	140(37.6%)	
No	91(64.1%)	232(62.4%)	
ISS	31.16±6.57	23.72±7.20	0.000
Number of injury sites	2.27±0.86	2.34±0.69	0.343
Heart rate(bpm)	98.50±22.61	84.69±16.32	0.000
MAP(mmHg)	86.22±22.79	95.59±16.86	0.000
Neutrophil(×109/L)	12.31±5.83	10.77±5.33	0.005
Platelet(×109/L)	177.20±88.68	187.88±73.14	0.202

Hemoglobin(g/L)	117.29±27.52	126.56±22.09	0.000
Blood glucose(mmol/L)	9.56±3.99	7.79±2.89	0.000
FBG(g/L)	2.13±1.34	2.45±1.04	0.005
APTT(s)	31.28±18.70	24.29±5.91	0.000
LOS(days)	36.00(12.00,57.00)	21.00(13.00,35.00)	0.003
D-dimer(mg/L)	29.84(10.98,56.46)	9.92(3.19,25.46)	0.000
Lymphocyte(×10^9/L)	1.30(0.80□3.40)	1.20(0.80□2.30)	0.517

ISS,injury severity score;MAP,mean arterial pressure;FBG,fibrinogen;APTT,activated partial thromboplastin time;LOS,length of stay.

Table 3 Hosmer-Lemeshow test

Group	X-squared	Degree of freedom	*P* value
Training set	10.561	8	0.227
Validation set	6.839	8	0.554

Figures

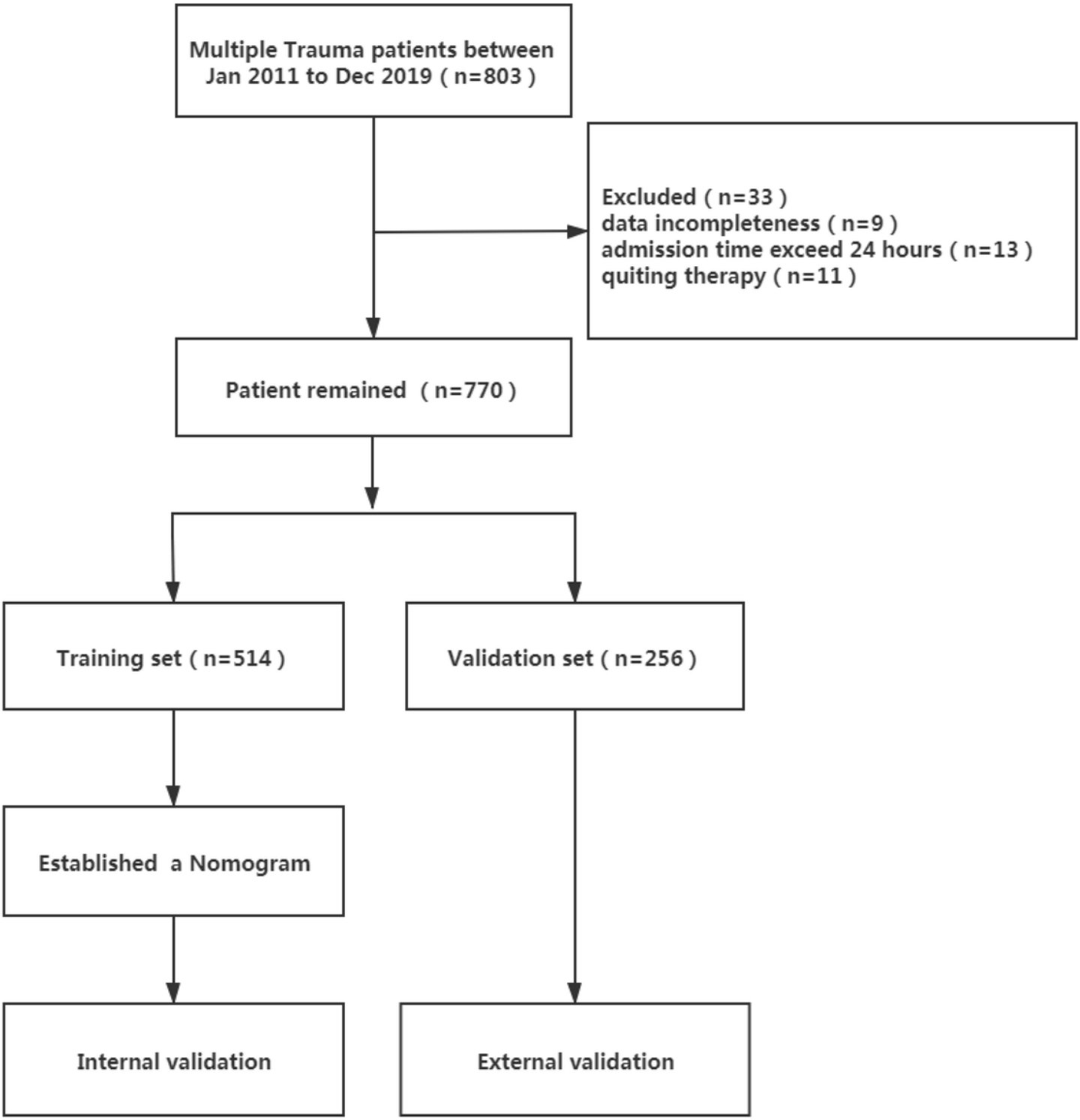

Figure 1

Study flow chart

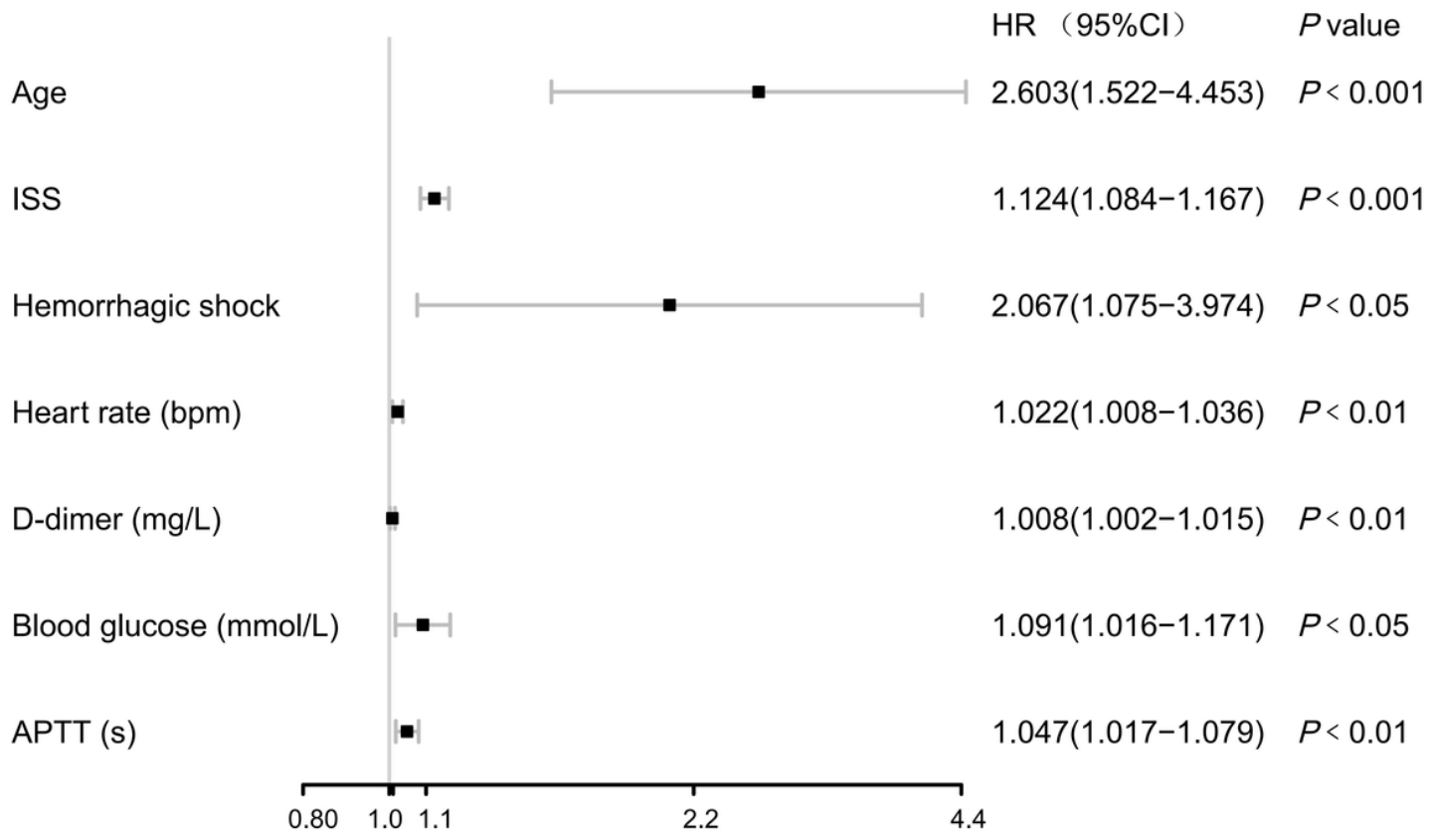

Figure 2

Forestplot of independent risk factors for MODS in patients with multiple trauma.ISS,injury severity score;APTT,activated partial thromboplastin time.

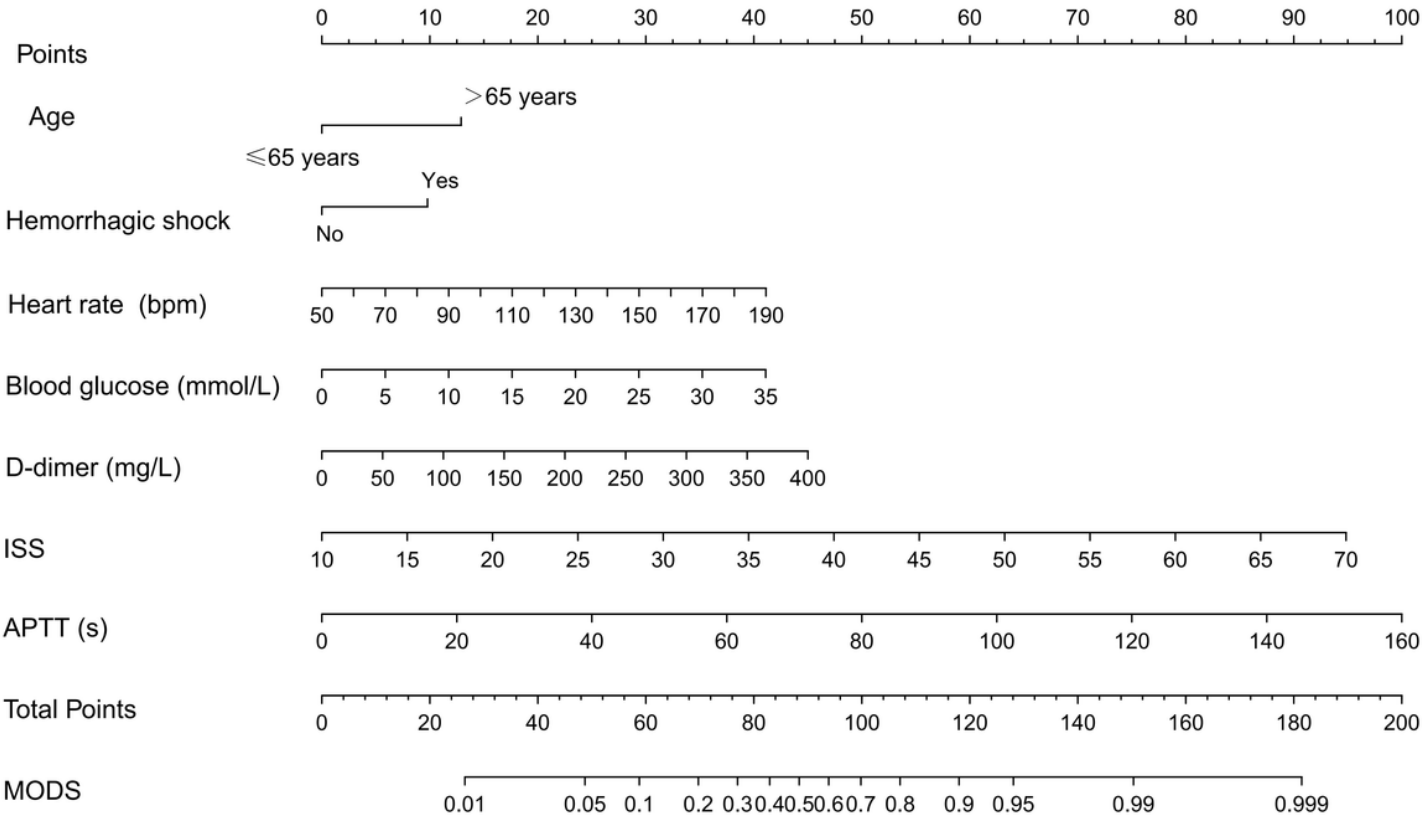

Figure 3

Nomogram model for predicting the risk of MODS in patients with multiple trauma. ISS,injury severity score;APTT,activated partial thromboplastin time.

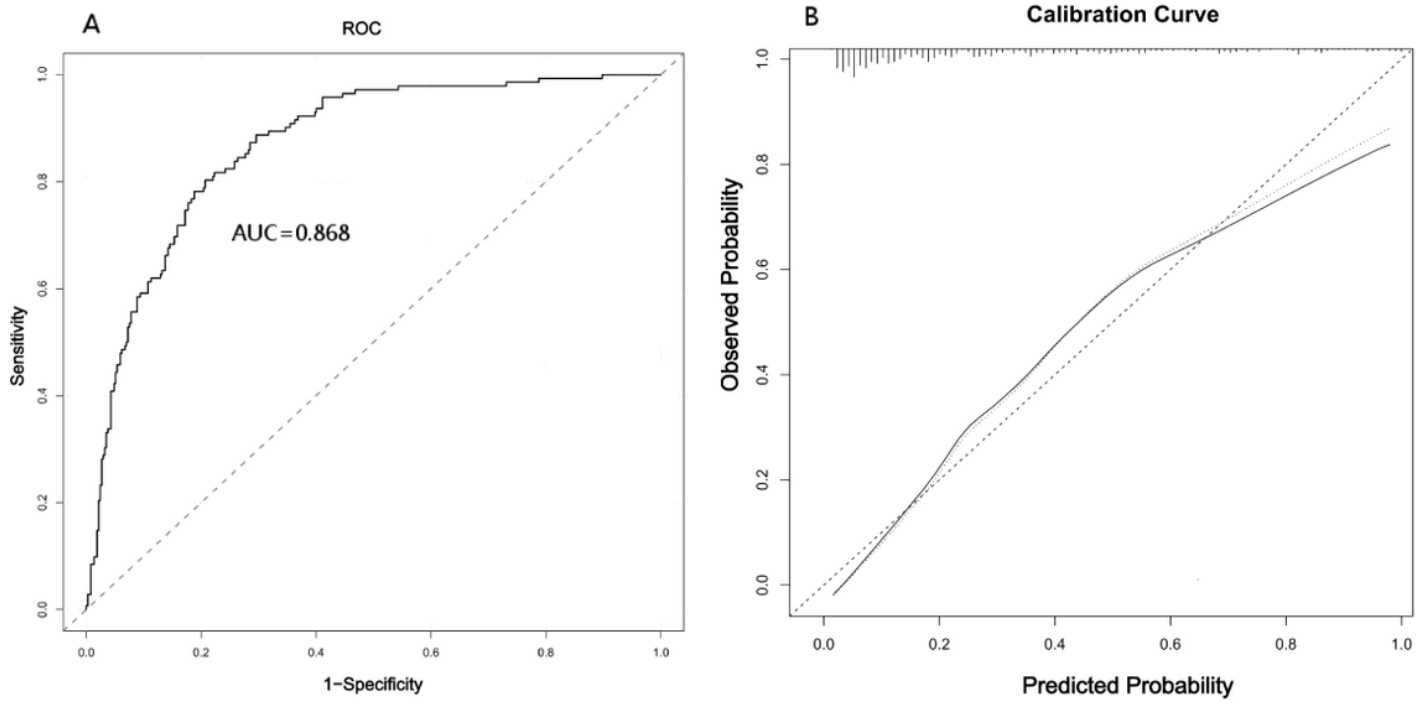

Figure 4

Internal validation of nomogram in the training set.A Discriminative capacity:AUC of the ROC curve was 0.868(95% CI:0.829-0.908).B Calibration curve:The dotted line indicates perfect prediction by an ideal model.The solid line depicts the model’s performance.ROC,receiver operating characteristic;AUC,area under the curve.

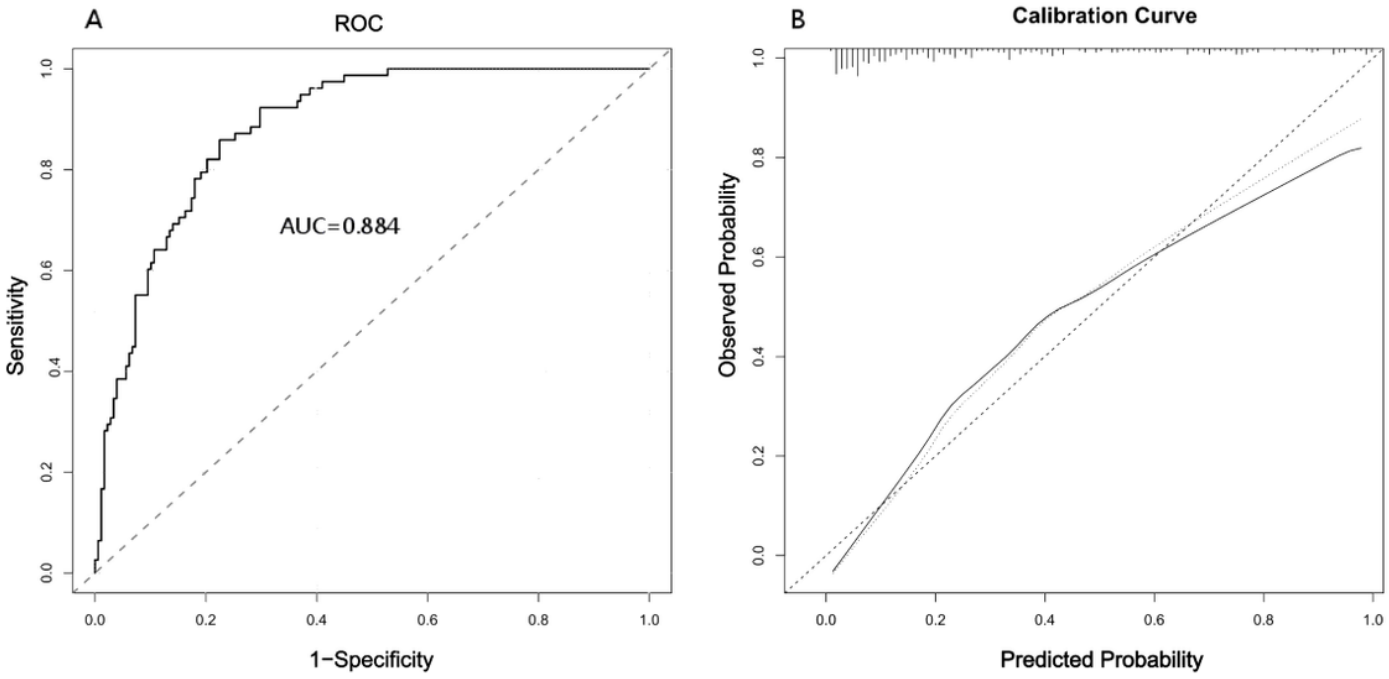

Figure 5

External validation of nomogram in the validation set.A Discriminative capacity:AUC of the ROC curve was 0.884(95% CI:0.833-0.935).B Calibration curve:The dotted line indicates perfect prediction by an ideal model.The solid line depicts the model’s performance.ROC,receiver operating characteristic;AUC,area under the curve.