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ORIGINAL RESEARCH

Development of an Online Nomogram for Predicting Postoperative Hypoalbuminemia in Older Adults Following Femoral Neck Fractures

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Objective: Postoperative hypoalbuminemia after total hip arthroplasty (THA) in older adults with femoral neck fractures can increase the risk of postoperative infection and lengthen hospital stays. The purpose of this study was to construct an online nomogram that can be used for the clinical preoperative assessment of older adults to reduce the incidence of postoperative complications.

Methods: This study included older adults who underwent THA for femoral neck fracture at Northern Jiangsu People's Hospital between December 2018 and April 2022. Univariate and multivariate logistic regression analyses were performed for the training cohort to identify independent risk factors. The area under the ROC curve (AUC), calibration curve, and decision curve analysis (DCA) of the training group (n=306) and the validation group (n=131) were plotted to assess the model performance.

Results: Multivariate logistic regression analysis revealed 5 independent risk factors, including Age, body mass index (BMI), surgery time, preoperative blood calcium level, and preoperative erythrocyte sedimentation rate (ESR). We constructed a nomogram, and the area under the curve (AUC) of the nomogram was 0.763 (95% CI 0.705–0.820) for the training group and 0.750 (95% CI 0.665–0.835) for the validation group. The calibration curve showed good consistency between the predicted and actual probabilities. Decision curve analysis (DCA) showed that using the nomogram had a high net benefit.

Conclusion: Old age, lower BMI, longer surgery time, preoperative blood calcium level and preoperative ESR are independent risk factors for postoperative hypoalbuminemia after THA in older adults with femoral neck fractures. The online nomogram had high predictive values for to predict clinical postoperative hypoalbuminemia older adults with femoral neck fracture.

Keywords: total hip arthroplasty, hypoalbuminemia, dynamic nomogram, older adults, femoral neck fractures

Introduction

Femoral neck fractures commonly occur in older adults due to direct or indirect force below the femoral head and above the root of the femoral neck. Total hip arthroplasty (THA) is a principal surgical treatment approach for displaced femoral neck fractures.[1,2] Currently, THA has a high success rate of 90%.[3,4] However, research has demonstrated that the estimated mortality rate of patients with femoral neck fractures may be 20% or higher one year after injury.[5]

Hypoalbuminemia is one factor which may explain this within the early post-operative period. Hypoalbuminemia after THA often results in delayed wound healing, infection, nonunion, and prolonged hospital stays, which increase the personal and economic burden on patients and their families. In addition, Kyun-Ho Shin et al reported that early postoperative hypoalbuminemia was an independent risk factor for acute kidney injury following hip fracture surgery in older adults.[6] Furthermore, Yibing Yu et al identified hypoalbuminemia as an important risk factor for pulmonary infection after hip surgery in older adults, which seriously impedes postoperative recovery and may even result in patient death.[7] Clinical observations have revealed that older adults often experience short-term hypoalbuminemia after THA surgery. Hypoalbuminemia is defined as a serum albumin concentration less than 35 g/L,[8] and when the serum albumin

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concentration falls below 30 g/L, clinical intervention such as human serum albumin infusion is necessary. While human serum albumin has notable clinical applications for shock resulting from blood loss, trauma, burns, cerebral edema and increased intracranial pressure from brain injury, among others, its use in older adults may be counterproductive due to the presence of various chronic diseases such as chronic renal failure.[9,10] Therefore, exploring the causes and early warning factors of hypoalbuminemia in older adults is essential for implementing early interventions and preventing negative outcomes associated with these complications.

At present, while there have been some studies on the risk factors for human albumin infusion after surgery, there is still no agreement on the risk factors for postoperative hypoalbuminemia after THA in older adults, particularly in those with femoral neck fractures. Thus, the primary objective of this retrospective analysis was to identify the risk factors for hypoalbuminemia in older adults who underwent THA for femoral neck fractures. And we also established a nomogram prediction model for postoperative hypoalbuminemia after THA in older adults with femoral neck fracture using R software and constructed a ROC curve to evaluate the ability of the nomogram model to predict postoperative hypoalbuminemia. Furthermore, we created an online dynamic nomogram for clinical evaluation. These predictors of postoperative hypoalbuminemia can guide clinicians in the prevention and treatment of this condition in older adults treated for femoral neck fracture.

Patients and Methods

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Northern Jiangsu People's Hospital (Acceptance No. 2022KY212). Patients who underwent THA due to femoral neck fracture at Northern Jiangsu People's Hospital from December 2018 to April 2022 were included. A total of 481 patients were included; 39 patients (aged < 60 years) and 5 patients with incomplete clinical data were excluded. The relevant inclusion and exclusion criteria are described in the flow chart. (Figure 1) Since this was a retrospective study, the requirement for informed consent from each participant was waived by the ethics committee.

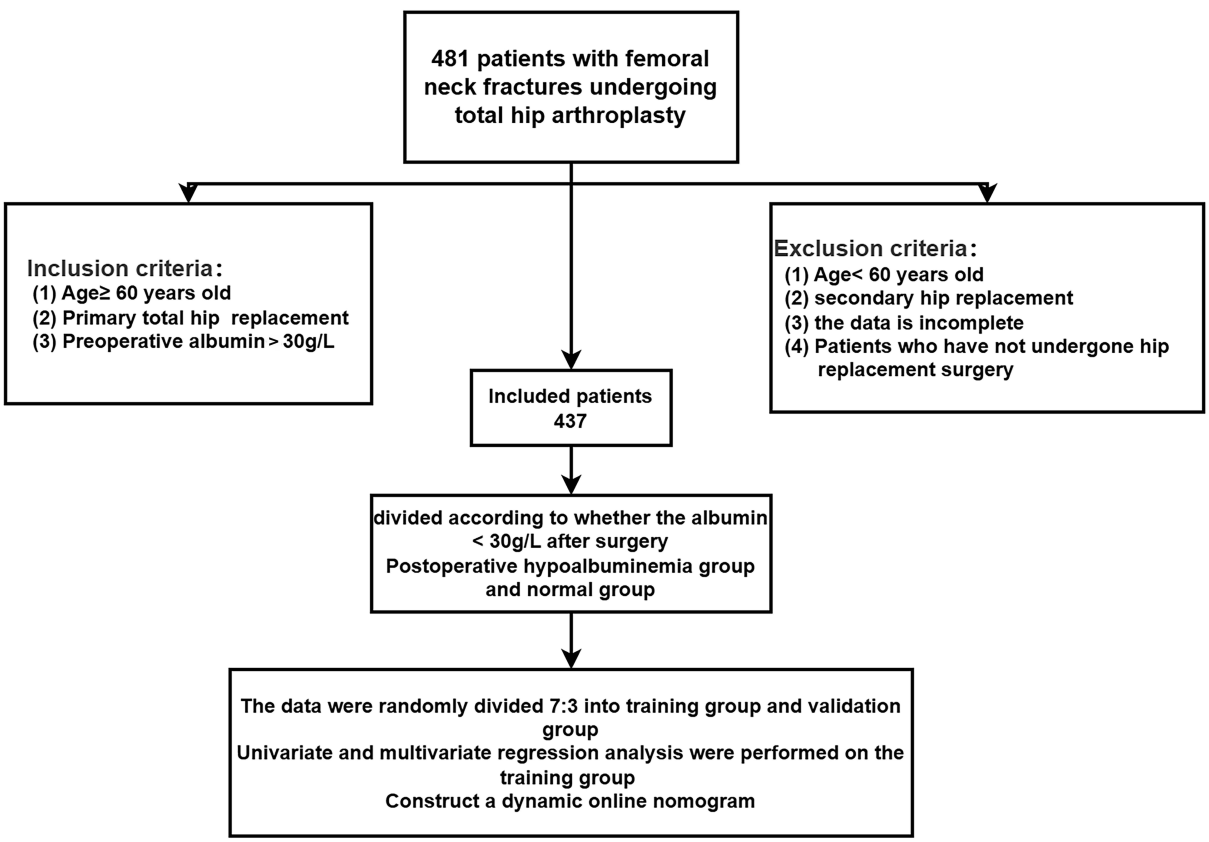

Figure 1 The flow chart of inclusion and exclusion criteria.

Data Collection

This study referred to clinical and literature materials and used liver function re-examination and biochemical testing to identify a serum albumin level <30 g/L as an indication for the infusion of human albumin in patients with hypoalbuminemia. Therefore, in this study, subjects with a postoperative minimum albumin level <30 g/L were classified as the hypoalbuminemia group, while the remaining subjects were included in the control group.[11]

The data collected included age, height, weight, body mass index (BMI), hypertension, diabetes, cardiovascular disease, previous fracture history, American society of anesthesiologists score (ASA), extent, surgery time, preoperative hematocrit (HCT), preoperative hemoglobin (HGB), preoperative red blood cells (RBC), preoperative platelets (PLT), preoperative prothrombin time (PT), preoperative activated partial thrombin time (APTT), preoperative international normalized ratio (INR), preoperative thrombin time (TT), preoperative fibrinogen (FIB), preoperative blood calcium, preoperative c-reactive protein (CRP), preoperative erythrocyte sedimentation rate (ESR), preoperative DD polymer, preoperative blood pressure, mode of anesthesia, liver function, gastrointestinal disease, and length of stay (LOS).

Statistical Analysis

All the statistical analyses were performed with SPSS (version 26) and R software (version 4.2.1). Continuous variables are expressed as the mean ± standard deviation (M ± SD), and categorical variables are expressed as counts and percentages [N (%)]. Continuous variables were tested by independent samples t tests, and categorical variables were tested by chi-square tests. In this study, a *P* value < 0.05 was considered to indicate statistical significance.

All patient data were randomly divided into training and validation groups a ratio of 7:3 using R software (version 4.2.1). [Table S1] and the data in the training group (n=306) and validation group (n=131) were no difference. The data in the training group is used for model building, and the data in the validation group is used to validate the model. First, we performed univariate regression analysis in the training group using SPSS (version 26.0) to find factors associated with postoperative hypoalbuminemia in older adults with femoral neck fractures. Then, R software (version 4.2.1) was used to conduct multivariate logistic regression analysis, and the function included in the rms package was used to screen variables with the backward method. The screening criteria were (P <0.05) to determine the independent risk factors for hypoalbuminemia. Finally, nomograms were created using the results of the multiple logistic regression analysis. ROC curves, calibration curves and DCA clinical decision curves were plotted for the training and validation groups by R software (version 4.2.1).

Results

Basic Information in Patient Information

A total of 437 patients were divided into two groups according to the serum albumin level after surgery: the nonhypoalbuminemia group (N=288, 65.9%) and the hypoalbuminemia group (N=149, 34.1%). Among them, there were 137 (31.4%) male patients and 300 (68.6%) female patients. The average age was 71.58± 5.64 years, the surgery time was 72.95 ± 26.29 minutes, and the preoperative blood calcium level was 2.24 ± 0.12, with an average BMI of 23.19 ± 3.44. In addition, the preoperative ESR was 24.23 ± 17.82. [Table 1].

Analysis of Correlated and Independent Risk Factors in the Training Group

A total of 306 patients participated in the training group. Univariate analysis revealed that 13 variables were significantly different (p< 0.05). The parameters included age, weight, BMI, surgery time, preoperative HGB, preoperative RBC, preoperative HCT, preoperative FIB, preoperative blood calcium, preoperative CRP, preoperative ESR, preoperative DD polymer, and preoperative systolic blood pressure (SBP). [Table 2] Multivariate logistic regression analysis revealed 5 independent risk factors, including age, BMI, surgery time, preoperative blood calcium, and preoperative ESR. [Table 3].

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Table 1 Basic Information in Patient

Hypoalbuminaemia			
	No (N=288)	**Yes (N = 149)**	**P**
Age	71.03±5.51	72.63 ± 5.76	0.005
Height	163.00±7.26	162.61±7.71	0.603
Weight	62.79±10.43	59.35±9.77	0.001
BMI	23.59±3.42	22.43±3.38	0.001
Surgery Time	70.14±25.74	78.40±26.58	0.002
HGB	126.3±15.84	117.73±14.43	<0.001
RBC	4.11±0.53	3.84±0.49	<0.001
HCT	37.83±4.38	35.52±4.24	<0.001
PTL	176.8±64.93	178.35±71.99	0.821
PT	13.32±1.52	13.69±1.29	0.012
APTT	38.26±5.78	39.09±6.16	0.161
INR	1.45±3.83	1.36±3.92	0.824
TT	17.76±2.20	17.82±1.42	0.749
FIB	3.72±0.86	3.89±1.11	0.109
DD polymer	5.24±5.18	6.59±5.91	0.019
Blood calcium	2.26±0.11	2.20±0.11	<0.001
CRP	25.86±25.35	30.05±31.36	0.160
ESR	21.58±16.72	29.36±18.80	<0.001
SBP	150.9±21.82	147.42±21.58	0.105
DBP	80.10±12.94	77.41±12.14	0.036
LOS	11.13±4.15	12.47±4.85	0.004
Gender			
Male	92 (31.9%)	45 (30.2%)	0.710
Female	196 (68.1%)	104 (69.8%)	
Hypertension			
Without	146 (50.7%)	75 (50.3%)	0.943
With	142 (49.3%)	74 (49.7%)	
Type 2 Diabetes			
Without	220 (76.4%)	121 (81.2%)	0.249
With	68 (23.6%)	28 (18.8%)	
Cardiovascular disease			
Without	225 (78.1%)	107 (71.8%)	0.143
With	63 (21.9%)	42 (28.2%)	
Fracture			
Without	242 (84.0%)	132 (88.6%)	0.198
With	46 (16.0%)	17 (11.4%)	
ASA			
<3	164 (56.9%)	75 (50.3%)	0.188
≥3	124 (43.1%)	74 (49.7%)	
Extent			
Left	169 (58.7%)	76 (51.0%)	0.125
Right	119 (41.3%)	73 (49.0%)	
Anesthesia			
SA	242 (84.0%)	127 (85.2%)	0.741
GA	46 (16.0%)	22 (14.8%)	
Gastrointestinal diseases			
Without	226 (78.5%)	121 (81.2%)	0.503
With	62 (21.5%)	28 (18.8%)	

(*Continued*)

Table 1 (Continued).

	Hypoalbuminaemia		
	No (N=288)	**Yes (N = 149)**	**P**
Liver function			
Without	238 (82.6%)	124 (83.2%)	0.878
With	50 (17.4%)	25 (16.8%)	

Abbreviations: BMI, Body Mass Index; HGB, preoperative hemoglobin; RBC, preoperative red blood cells; HCT, preoperative Hematocrit; PTL, preoperative platelets; PT, preoperative prothrombin time; APTT, preoperative activated partial thrombin time; INR, preoperative international normalized ratio; TT, preoperative thrombin time; FIB, preoperative fibrinogen; CRP, preoperative C-reactive protein; ESR, preoperative erythrocyte sedimentation rate; SBP, preoperative systolic blood pressure; DBP, preoperative diastolic blood pressure; LOS, Length Of Stay; ASA, American Society of Anesthesiologists score; SA, subarachnoid anaesthesia; GA, general anaesthesia.

Development and Validation of a Nomogram to Predict the Risk of Hypoalbuminemia in Older Adults After THA for Femoral Neck Fracture

Five independent predictors of age, BMI, surgery time, preoperative blood calcium, and preoperative ESR, were used to construct a nomogram (Figure 2a). An online dynamic nomogram was constructed. (Figure 2b).

Table 2 Univariate Regression Analysis

	β	OR	95% CI	P
Age	0.054	1.056	1.012~1.102	**0.013**
Height	0.012	1.013	0.980~1.046	0.458
Weight	−0.031	0.969	0.946~0.993	**0.011**
BMI	−0.122	0.885	0.821~0.954	**0.002**
Surgery Time	0.013	1.013	1.003~1.022	**0.008**
HGB	−0.031	0.969	0.954~0.985	**<0.001**
RBC	−0.844	0.430	0.268~0.690	**<0.001**
HCT	−0.103	0.902	0.853~0.954	**<0.001**
PTL	0.000	1.000	0.997~1.003	0.989
PT	0.138	1.148	0.930~1.417	0.198
APTT	0.013	1.013	0.972~1.055	0.538
INR	0.004	1.004	0.949~1.062	0.892
TT	0.011	1.012	0.881~1.161	0.870
FIB	0.307	1.360	1.054~1.755	**0.018**
DD polymer	0.045	1.046	1.002~1.091	**0.038**
Blood calcium	−6.201	0.002	0.000~0.024	**<0.001**
CRP	0.010	1.010	1.001~1.019	**0.027**
ESR	0.020	1.020	1.006~1.033	**0.004**
SBP	−0.011	0.989	0.978~1.000	**0.043**
DBP	−0.015	0.985	0.967~1.004	0.127
LOS	0.067	1.069	1.012~1.130	0.016
Gender	−0.298	0.743	0.444~1.242	0.257
Hypertension	0.019	1.020	0.632~1.644	0.937
Type 2 Diabetes	−0.128	0.880	0.497~1.557	0.660
Cardiovascular disease	0.399	1.491	0.870~2.555	0.147
Fracture	−0.371	0.690	0.340~1.398	0.303
ASA	−0.142	0.867	0.537~1.401	0.560

(*Continued*)

Table 2 (Continued).

	β	OR	95% CI	P
Extent	0.414	1.512	0.935~2.447	0.092
Anesthesia	−0.006	0.994	0.499~1.977	0.985
Gastrointestinal diseases	−0.022	0.979	0.545~1.757	0.943
Liver function	−0.204	0.816	0.431~1.544	0.531

Note: The bold variables indicate those with P < 0.05 in the univariate analysis.
Abbreviations: BMI, Body Mass Index; HGB, preoperative hemoglobin; RBC, preoperative red blood cells; HCT, preoperative Hematocrit; PTL, preoperative platelets; PT, preoperative prothrombin time; APTT, preoperative activated partial thrombin time; INR, preoperative international normalized ratio; TT, preoperative thrombin time; FIB, preoperative fibrinogen; CRP, preoperative C-reactive protein; ESR, preoperative erythrocyte sedimentation rate; SBP, preoperative systolic blood pressure; DBP, preoperative diastolic blood pressure; LOS, Length Of Stay; ASA, American Society of Anesthesiologists score.

Table 3 Multivariate Regression Analysis

	β	OR	95% CI	P
Age	0.051	1.053	1.005 ~1.103	**0.031**
BMI	−0.096	0.909	0.839 ~0.984	**0.019**
Surgery Time	0.018	1.018	1.008 ~1.029	**0.001**
Blood calcium	−6.068	0.002	0.000 ~0.032	**<0.001**
ESR	0.020	1.020	1.005 ~1.035	**0.007**

Note: The bold variables indicate those with P < 0.05 in the multivariate analysis.
Abbreviations: BMI, Body Mass Index; ESR, preoperative erythrocyte sedimentation rate.

In the training group, the AUC of the nomogram was 0.763 (95% CI 0.705–0.820). High accuracy was observed in predicting the risk of hypoalbuminemia in older adults after THA for femoral neck fracture (Figure 3a). Furthermore, the calibration curves showed good agreement between the predicted and observed results (Figure 3b). DCA in risk threshold (0.10–0.72) showed a greater net benefit in predicting the risk of hypoalbuminemia in older adults after THA for femoral neck fracture according to the nomogram (Figure 3c).

In the validation group, the AUC of the nomogram was 0.750 (95% CI 0.665–0.835). Higher accuracy was observed in predicting the risk of hypoalbuminemia in older adults after THA for femoral neck fracture (Figure 3d). Furthermore, the calibration curves showed good agreement between the predicted and observed results (Figure 3e). DCA in risk threshold (0.05–0.66) showed a greater net benefit in predicting the risk of hypoalbuminemia in older adults after THA for femoral neck fracture according to the nomogram (Figure 3f).

The total population included in the study showed that the area under the ROC curve (AUC) was 0.761 for the multiple factors included in the model, which was far greater than that of only one of the factors included, indicating that the model had good predictive ability in the overall sample population (Figure 4).

Discussion

Albumin, a protein synthesized solely in the liver and the most abundant in plasma, plays a crucial role in maintaining homeostasis. Human serum albumin (HSA), the most prevalent protein in plasma, plays a vital role in maintaining plasma colloid osmotic pressure and transporting substances throughout the body. Research indicates that short-term hypoalbuminemia after fracture or trauma is often linked to reduced HSA synthesis, hastened decomposition, direct loss, and degradation of vascular endothelial polysaccharide protein.[12] Hypoalbuminemia, a condition characterized by low levels of albumin in the blood, is not solely attributed to reduced protein synthesis but can also be a result of multiple factors, such as decomposition, exudation, and protein intake.[13] Hypoalbuminemia is also closely linked to several

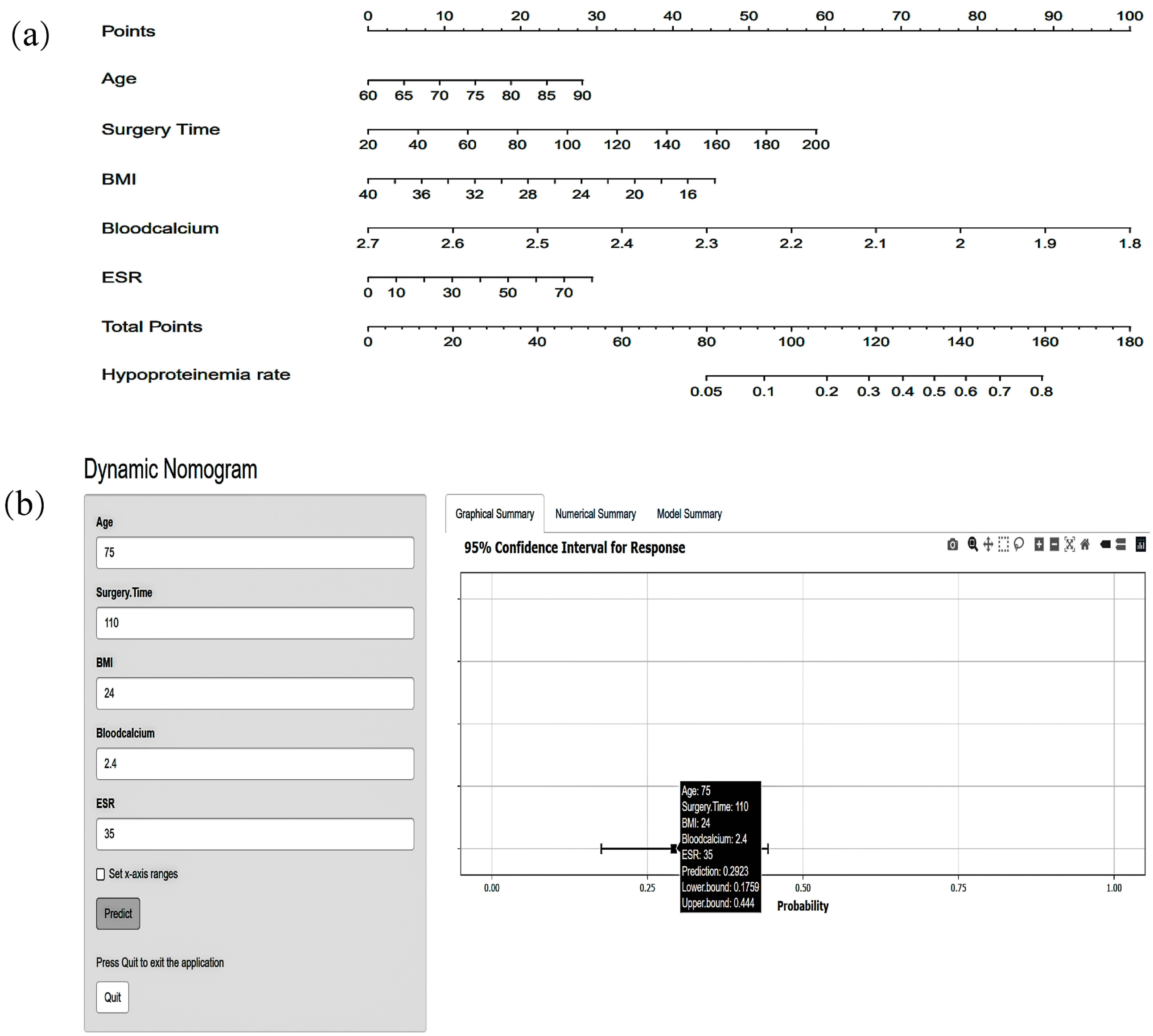

Figure 2 (**a**) A nomogram for predicting postoperative hypoalbuminemia in older adults following femoral neck fractures; (**b**) An online dynamic nomogram for predicting postoperative hypoalbuminemia in older adults following femoral neck fractures.

systemic diseases, such as malignancy, liver disease, kidney disease, and inflammation.[14] Therefore, during retrospective analysis, common demographic data, clinical or laboratory indicators pertaining to such diseases were also included in the baseline data. Our study revealed that age, weight, BMI, surgery time, preoperative HGB, RBC, HCT, FIB, blood calcium, CRP, ESR and DD polymer levels were related to postoperative hypoalbuminemia.[15] Among these indicators, age, BMI, surgery time, preoperative blood calcium, and preoperative ESR were identified as the five independent risk factors and were incorporated into the prediction model. Moreover, an attempt was made to apply the prediction model to preoperative clinical interventions by constructing a simple online dynamic nomogram.

In our study, older adults were found to have a higher prevalence of hypoalbuminemia, and compared with the proportion of patients aged 60 years, the proportion of patients aged 90 years increased by approximately 28 points in the nomogram. The reason may be related to the nutritional status of the patient.[16] Because albumin is a transport protein, it can also be regarded as a nutritional marker indicating the nutritional status of patients after surgery.[17] Moreover, we found that preoperative HGB, RBC, and preoperative HCT were associated with the occurrence of postoperative hypoalbuminemia in older adults according to the univariate regression analysis ($p < 0.001$); although these parameters

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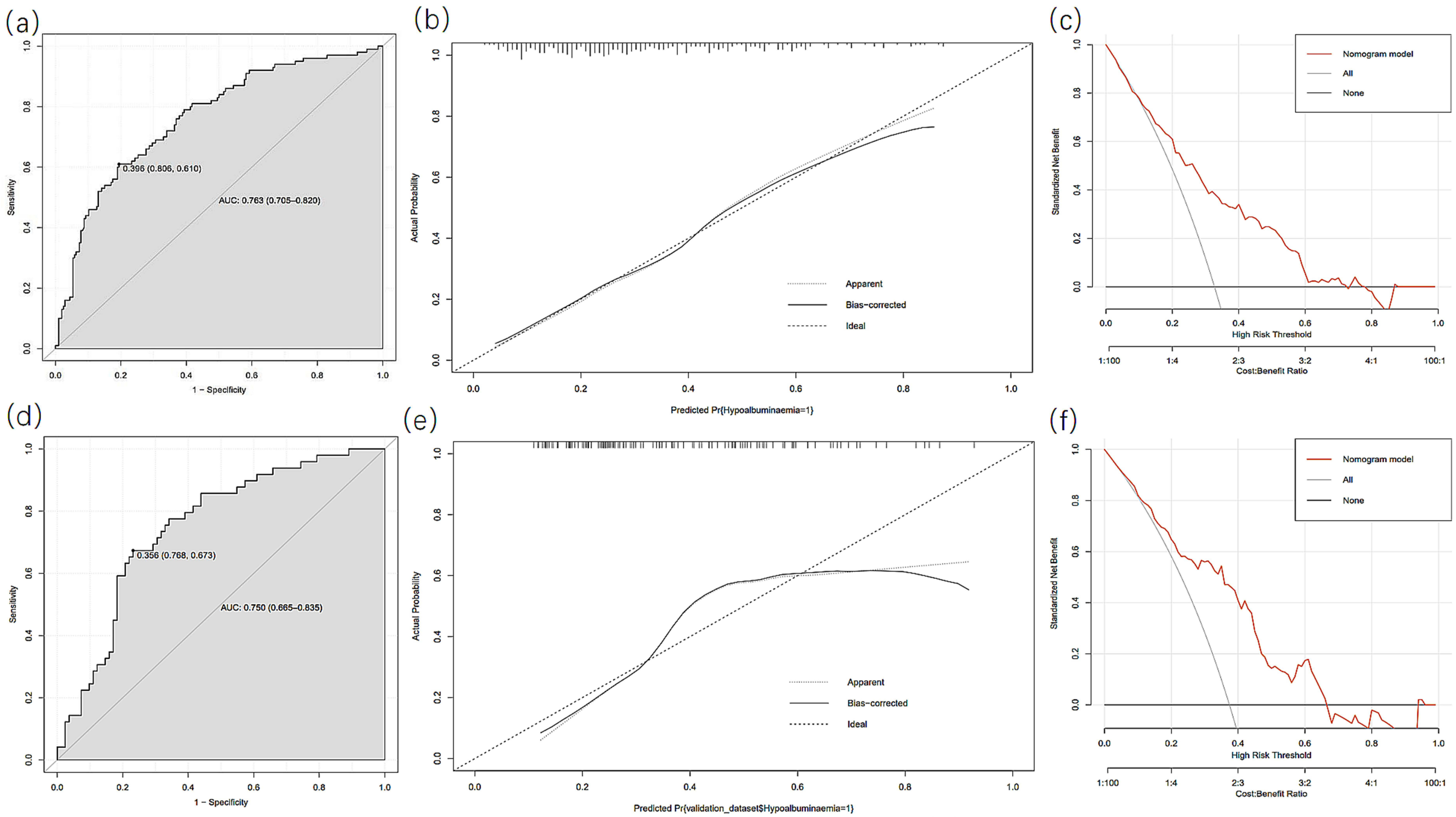

Figure 3 (**a**) ROC curve in training group to evaluate prediction accuracy; (**b**) calibration curve in training group; (**c**) decision curve analysis in training group (**d**) ROC curve in validation group to evaluate prediction accuracy;(**e**) calibration curve in validation group; (**f**) decision curve analysis in validation group.

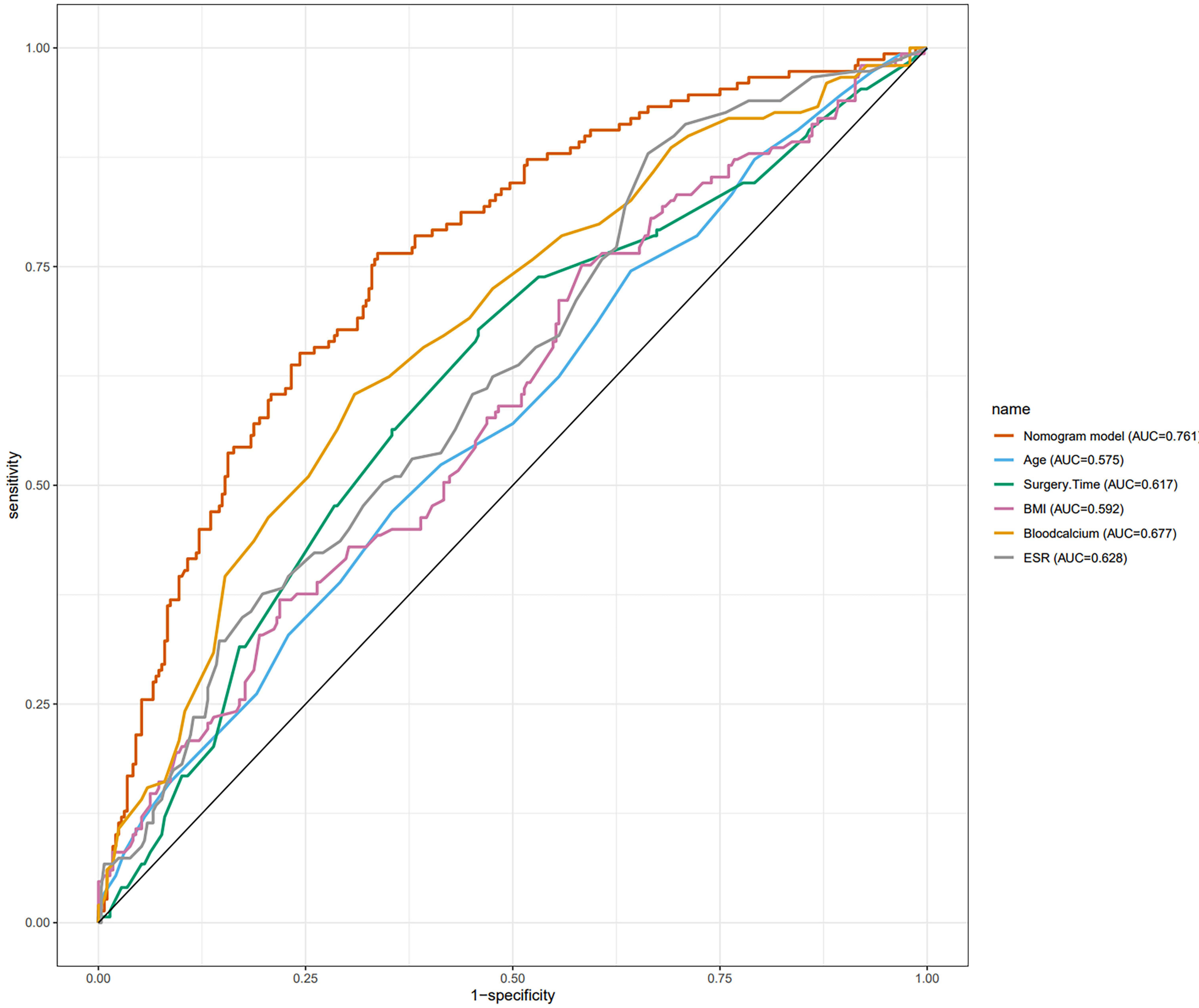

Figure 4 The ROC curve in the total population.

were not included in the multivariate regression model, based on these three clinical indicators, we further speculated that patients with hypoproteinemia after surgery had a certain degree of anemia before surgery. As an effective indicator of nutritional outcome, anemia also reflects the nutritional status of patients to some extent.[18]

In addition, our study revealed that patients with a lower BMI were more prone to postoperative hypoalbuminemia. On the one hand, since older adults with a low BMI often have other systemic diseases and decreased organ function, the digestion and absorption capacity of the gastrointestinal tract decreases, especially the metabolism and production of albumin by the liver.[19] On the other hand, low-weight older adults have more serious reactions to surgical anesthesia and stress than high-weight young patients, and patients with a higher BMI are more tolerant to surgery.[20,21] In addition to reflecting the nutritional status of older adults, BMI and hypoalbuminemia are also important markers of death in older adults. In this study, for every 4-point decrease in BMI, the nomogram gained 8 points of weight. Therefore, clinically, we should be more vigilant, especially for older adults with lower BMIs. Reasonably increasing the intake of high protein foods before surgery and timely nutritional supplementation after surgery will help reduce the occurrence of post-operative hypoalbuminemia.

At the same time, previous reports have shown that longer surgery time also increase the risk of hypoalbuminemia, which is consistent with our findings.[22] This is mainly due to the increased consumption caused by the prolongation of surgery time. Prolonged surgeries are often associated with a higher incidence of damage and therefore an increase in

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intraoperative blood loss. This process is accompanied by the consumption and loss of albumin. Although fluids are administered during the surgery, it is not sufficient to compensate for the loss of albumin. According to the nomogram, the score increased by 27 points for every 100 minutes of surgery time. This suggests that when performing surgery on older adults, surgeons need to formulate individualized treatment plans for patients before surgery and shorten the surgery time as much as possible to avoid adverse outcomes caused by postoperative hypoalbuminemia.

Previous studies have shown that another important cause of hypoalbuminemia is inflammation.[23] In older adults who sustain a femoral neck fracture, the increased permeability of blood vessels due to inflammation leads to albumin loss. Additionally, in elective surgeries requiring fluid replacement, increased total water content in the serum, interstitium, and cells due to fluid replacement can cause vasodilation and result in albumin loss. A decrease in the serum albumin concentration often correlates with an increase in the ESR, which aligns with our research findings. Another prospective study demonstrated an independent association between elevated inflammatory markers and hypoalbuminemia.[24]

At the same time, our study revealed that patients with lower preoperative blood calcium levels were more likely to develop postoperative hypoalbuminemia. For every 0.1 decrease in blood calcium, the weight of the nomogram increased by approximately 11 points. Calcium exists in three forms in the blood, of which approximately 40% is combined with albumin.[25,26] Therefore, changes in blood calcium levels directly impact the proportion of calcium bound to serum albumin. When preoperative testing indicates a decrease in blood calcium, it often suggests a potential decrease in serum albumin as well.

Clinically, postoperative hypoalbuminemia often leads to a variety of complications. This is especially true for older adults with underlying disease. Examples include acute kidney injury, postoperative pneumonia, and osteoporosis.[27–29] These adverse outcomes often lead to prolonged hospitalization of older adults and greatly increase the economic burden of patients. In addition, univariate regression analysis revealed that patients with postoperative hypoalbuminemia had a longer hospital stay ($P = 0.016$), and in previous reports, hypoalbuminemia also led to hospitalization after brain tumor surgery.[30] Therefore, it is particularly important to prevent postoperative hypoalbuminemia in older adults with femoral neck fractures. Clinically, patients with postoperative hypoalbuminemia often receive an infusion of human serum albumin. On the one hand, the infusion of human serum albumin indeed accelerated the recovery of some patients, but at the same time, we also found that for some older adults with liver and heart failure, the infusion of albumin may have increased the physical burden of the patients.[31,32] Based on previous studies,[33] people have constructed clinical prediction models to study the risk factors of a certain disease, but the risk factors for hypoalbuminemia after THA in older adults with femoral neck fracture have yet to be studied, and the previous prediction models are static nomograms, and it is difficult to verify and improve clinically. Therefore, for the occurrence of postoperative hypoalbuminemia in older adults with femoral neck fractures, we hope to apply the prediction model to a part of clinical preoperative evaluation by constructing a simple online dynamic nomogram to help clinicians[34].

Due to the limitations of the clinical prediction model, we aimed to build this prediction model through reasonable statistical methods to achieve better prediction results. In addition, as a retrospective clinical study, there may be some bias in the data collected because the included data were obtained from the same hospital; therefore, different populations in different regions may have different final results. Finally, we did not include postoperative indicators because this study used preoperative clinical indicators to predict the risk of hypoalbuminemia, which may have led to the loss of some important variables considering only preoperative indicators. We hypothesized that larger sample multicenter studies would lead to more accurate predictive models.

Conclusions

In conclusion, old age, lower BMI, longer surgery time, preoperative blood calcium level and preoperative ESR are independent risk factors for postoperative hypoalbuminemia in older adults after THA for femoral neck fractures. The nomogram prediction model constructed by R language and simple online tools has good accuracy. This model can be used to predict and screen patients with postoperative low serum albumin in advance to reasonably control the surgery duration and inflammation through active food protein supplementation. Moreover, through validation, we confirmed that the model has high value in predicting hypoalbuminemia in older adults after THA for femoral neck fracture.

Data Sharing Statement

Data are available under reasonable request to the corresponding author.

Ethical Approval

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Northern Jiangsu People's Hospital (Acceptance No. 2022KY212).

Consent to Participate

The need for informed consent from patients was waived by the board, since it was a retrospective cross sectional study, and all the data were collected and analyzed anonymously without any potential harm to the patients.

Consent to Publish

The need for informed consent from patients was waived by the board, since it was a retrospective cross sectional study, and all the data were collected and analyzed anonymously without any potential harm to the patients.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no conflicts of interest for this work.

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