



ORIGINAL RESEARCH

All-Cause Mortality Risk in Elderly Patients with Femoral Neck and Intertrochanteric Fractures: A Predictive Model Based on Machine Learning

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Introduction: The aim of this study was to identify the influencing factors for all-cause mortality in elderly patients with intertrochanteric and femoral neck fractures and to construct predictive models.

Methods: This study retrospectively collected elderly patients with intertrochanteric fractures and femoral neck fractures who underwent hip fractures surgery in the Third Hospital of Hebei Medical University from January 2020 to December 2022. Cox proportional hazards regression is used to explore the association between fractures type and mortality. Boruta algorithm was used to screen the risk factors related to death. Multivariate logistic regression was used to determine the independent risk factors, and a nomogram prediction model was established. The ROC curve, calibration curve and DCA decision curve were drawn by R language, and the prediction model was established by machine learning algorithm.

Results: Among the 1373 patients. There were 6 variables that remained in the model for intertrochanteric fractures: age (HR 1.048, 95% CI 1.014–1.083, p = 0.006), AMI (HR 4.631, 95% CI 2.190–9.795, P < 0.001), COPD (HR 3.818, 95% CI 1.516–9.614, P = 0.004), CHF (HR 2.743, 95% CI 1.510–4.981, P = 0.001), NOAF (HR 1.748, 95% CI 1.033–2.956, P = 0.037), FBG (HR 1.116, 95% CI 1.026–1.215, P = 0.011). There were 3 variables that remained in the model for femoral neck fractures: age (HR 1.145, 95% CI 1.097–1.196, P < 0.001), HbA1c (HR 1.264, 95% CI 1.088–1.468, P = 0.002), BNP (HR 1.001, 95% CI 1.000–1.002, P = 0.019). The experimental results showed that the model has good identification ability, calibration effect and clinical application value.

Conclusion: Intertrochanteric fractures is an independent risk factor for all-cause mortality in elderly patients with hip fractures. By constructing a prognostic model based on machine learning, the risk factors of mortality in patients with intertrochanteric fractures and femoral neck fractures can be effectively identified, and personalized treatment strategies can be developed.

Keywords: mortality, intertrochanteric fractures, femoral neck fractures, boruta algorithm, machine learning, prediction model

Introduction

As the global elderly population accelerates, the number of elderly patients with hip fractures is also increasing. Hip fractures are among the fractures with the highest mortality risk. 2-5

Most studies have treated hip fractures as a single, uniform condition, but it includes two major anatomic types: intertrochanteric fractures and femoral neck fractures. The former is an extracapsular fracture, and the latter is an intracapsular fracture. However, there are significant differences in postoperative morbidity and mortality between intertrochanteric fractures and femoral neck fractures. Previous studies have shown a 90-day mortality of 12.1% after intertrochanteric fractures and 9.6% after femoral neck fractures. Studies have pointed out that age, fractures type, blood transfusion and other risk factors may be related to the mortality and outcome of this fractures. By helping to identify

persons at increased risk for death or adverse outcomes, these factors could benefit patients by increasing physician vigilance in clinical decision-making.

Therefore, we aimed to answer the following research questions: What is the mortality rate, what is the prognosis, and what are the associated risk factors in the elderly population of femoral neck and intertrochanteric fractures?

Materials and Methods

Study Design and Study Population

The medical records of elderly patients who underwent surgery for intertrochanteric fractures or femoral neck fractures in the Department of Orthopedics of the Third Hospital of Hebei Medical University from January 2020 to December 2022 were retrospectively analyzed. This study met the Helsinki criteria and was approved by the Ethics Review Committee of the Third Hospital of Hebei Medical University. Due to the retrospective nature of the study, we waived informed consent from the enrollees.

Inclusion and Exclusion Criteria

Inclusion Criteria: (1) age 65 years or older. (2) The hip fracture was confirmed by MRI or X-ray. (Femoral neck fractures or intertrochanteric fractures). (3) Complete clinical data.

Exclusion criteria: (1) multiple fractures. (2) Pathological fractures. (3) Old fractures. (4) Conservative treatment. (5) Patients missing during follow-up. Ultimately, a total of 1373 patients were included in the analysis (Figure 1).

Disease Definition

An experienced orthopaedic surgeon reviews confirm a femoral neck fracture or an intertrochanteric femoral fracture and perform surgery. Use spinal anesthesia or general anesthesia. Reduction, internal fixation, or replacement were performed with the patients in the supine position on a fractures table using an image intensifier. Quality control by internal medicine specialists with recognized geriatric skills and integrated assessment and management of multi-system diseases on a holistic basis.

We define acute myocardial infarction (AMI) as perioperative blood elevated troponin I > 99% of the upper reference limit (0.04 ng/mL) and simultaneously accompanied by at least one situation: (1) new ischemic ECG changes (ST segment elevation or depression, evolutionary Q-wave, T-wave symmetric inversion); (2) ischemic symptoms; (3) the abnormal imaging evidence of new myocardial loss or new regional wall motion. Myocardial injury was defined as a baseline troponin I level above the upper limit of normal that did not meet the diagnostic criteria for myocardial infarction. In farction 11

Data Collection

We extracted the following information through the electronic medical record system: sex, age, BMI, comorbidities (hypertension, diabetes, chronic heart failure (CHF), coronary artery disease (CAD), osteoporosis, cognitive disorders, stroke and chronic obstructive pulmonary disease (COPD), chronic atrial fibrillation), fractures type, American College of Anesthesiologists (ASA) score, blood biochemical indicators at admission, preoperative waiting time, surgical method, perioperative complications (new-onset atrial fibrillation (NOAF), AMI, myocardial Injury, deep venous thrombosis (DVT), hypoproteinemia, hypokalemia, hyponatremia, anemia, pneumonia and delirium), length of stay, etc.

Outcomes and Follow-up

The primary outcome of this study was all-cause mortality at 3 years after surgery. Secondary outcomes included perioperative complications during hospitalization, preoperative wait time, and total length of stay. We divided the time of death into one, two and three years. Telephone follow-up was conducted by patients and their families. Patients who could not be reached after discharge were counted as lost to follow-up.

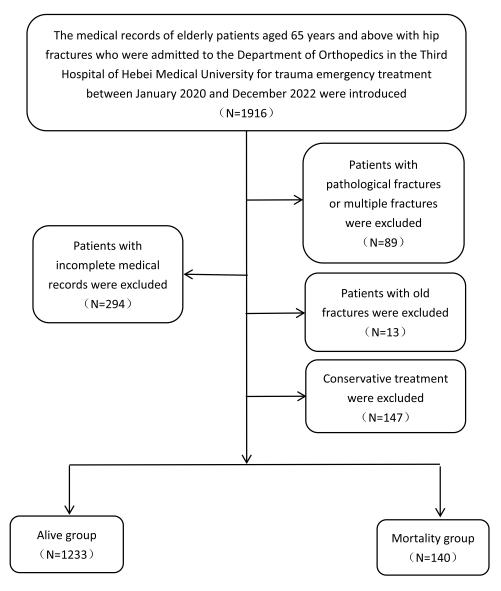


Figure I The flow diagram of this study.

Statistical Analysis

Shapiro-Wilk test was used for normality analysis of continuous parameter data, expressed as mean \pm standard deviation (SD) or median and quartile distance (IQR), and analyzed by Student 'st test or Mann Whitney *u*-test. Categorical variables are expressed as numbers (N) and percentages (%), compared using Chi-square tests or Fisher precision tests.

Kaplan-Meier (K-M) survival curve was plotted according to fractures type and Log rank test was used. Cox regression model was used to evaluate the association between fractures type and all-cause mortality. Model 1 has no adjustment covariates. Model 2 was adjusted for age and sex. Model 3 was adjusted for age, sex, injury mechanism, ASA score, CHF, COPD, CAD, acute myocardial infarction, myocardial injury, NOAF, hypoproteinemia, pneumonia, delirium, FBG, potassium, CRP, cholesterol, BNP, albumin, hemoglobin, hematocrit, creatinine, and LVEF. Boruta algorithm was used to screen out key characteristics (such as age, NOAF, FBG, BNP, etc.) that were closely related to all-cause mortality from the data of the two groups of patients. By randomly generating pseudo variables, the importance of each variable is assessed to screen out the most relevant features. The selected variables were included in multivariate COX regression analysis to determine the independent risk factors affecting prognosis for different fractures types. The Cox model is constructed and presented in the form of a nomogram. The area under the curve, correction curve and decision

curve analysis (DCA) were used to test the differentiation, correction and clinical efficacy of the prediction model. To assess the accuracy of the nomogram and the remaining seven machine learning models for predicting risk, we used the Area under the curve (AUC) of Receiver Operating Characteristics (ROC) analysis. Calibration curve analysis and decision curve analysis were used to evaluate the calibration and clinical value of this and seven other machine learning models. In addition, the RCS curve was used to clarify the relationship between the selected continuous variables and the risk of all-cause death. Double-tail P value < 0.05 was considered statistically significant. SPSS 25.0 (IBM SPSS Statistics, Armonk, NY, USA) and R (version 4.4.2) were used as statistical analysis software.

Subgroup Analysis

Subgroup analysis was performed according to fractures type, and multivariate analysis was performed. The independent risk factors for death of different types of fractures were identified, and the HR and 95% CI were shown.

Restricted Cubic Splines

In this study, we collected data on survival (the outcome variable); the age, BNP, FBG and HbA1c. The potential nonlinear relationships between the selected continuous variables and survival were examined by a Cox regression model with RCS.

Establishment and Validation of the Prediction Models

Boruta algorithm is an algorithm used for feature selection. Especially when dealing with high-dimensional data, important features closely related to target variables can be effectively identified by simulating randomness. Green areas, called acceptable variables. Are variables that are retained in the feature selection process and are considered to contribute to the performance of the model. Red areas, also called unacceptable variables. They were eventually excluded from feature selection. In this study, Boruta algorithm was used to screen predictive variables related to all-cause mortality in patients with femoral neck fractures and intertrochanteric fractures.

By incorporating these important features into various machine learning algorithms, Boosting Survival Learner (xgboost) algorithm, Random Forest Learner (RF) algorithms, Naive Bayes (NB) algorithms, Support Vector Machine (SVM) algorithm, Rpart Survival Trees Survival Learner (DT) algorithm, Multi-layer Perceptron Learner (MLP) algorithms, K-Nearest Neighbor (KNN) algorithms to predict the 3-years mortality risk in elderly hip fractures patients. Hyperparameter tuning is performed during the establishment of machine learning models. The results show that these prediction models exhibit good performance.

Result

Baseline Characteristics

Based on inclusion and exclusion criteria, 1373 femoral neck and intertrochanteric fractures were included in this study (Figure 1). Among them, 997 (72.6%) were female. The mean age of the patients was 79.58 ± 7.71 years. One hundred and forty patients died, with a mortality rate of 10.2%.

The general and surgical data of living and dead patients were compared (Table 1). There were no significant differences in gender, BMI, type of surgery, comorbidities (chronic atrial fibrillation, osteoporosis, hypertension, diabetes and stroke), biochemical indicators (HbA1c, Sodium) and perioperative complications (DVT, hypokalemia, hyponatremia and anemia) between the two groups (P < 0.05). The average age of the death group was higher than that of the survival group (P = 0.05). The average age of the death group was higher than that of the survival group (P = 0.05). The two groups also differed in terms of fractures type (P = 0.001) and preoperative waiting time (P = 0.002). To further analyze the association between fractures type and all-cause mortality, we performed a multivariate COX regression analysis.

Association Between Fractures Type and All-Cause Mortality in Elderly Patients with Hip Fractures

The incidence of all-cause mortality was higher among patients with intertrochanteric fractures (Table 1). In the Cox regression analysis, the results of Models 1 and 3 showed a significantly increased risk of death in patients with

Table I Comparison of Data Between Elderly Patients with Intertrochanteric and Femoral Neck Fractures Who Survived and Died

Characteristic	Total (n=1373)	Alive Group (n=1233)	Mortality Group (n=140)	P	
Demographics					
Age, years	79.58±7.71	79.05±7.69	84.20±6.25	<0.00	
Female gender, %	997 (72.6)	893 (72.4)	104 (74.3)	0.640	
BMI, kg/m2	23.67±4.05	23.71±4.00	23.29±4.46	0.303	
Injury Mechanism, (%)					
Low Energy	1322 (96.3)	1183 (95.9)	139 (99.3)	0.048	
High Energy	51 (3.7)	50 (4.1)	I (0.7)		
Type of fractures, (%)	656 (47.8)	607 (49.2)	49 (35.0)	0.001	
Femoral neck fractures	717 (52.2)	626 (50.8)	91 (65.0)		
Intertrochanteric fractures	, ,	, ,	, ,		
Surgery Type, (%)					
Intramedullary	832 (60.6)	741 (60.1)	91 (65.0)	0.261	
Replacement	541 (39.4)	492 (39.9)	49 (35.0)		
ASA Score, (%)	,	,	,	<0.00	
1	92 (6.7)	84 (6.8)	8 (5.7)		
II	645 (47.0)	606 (49.1)	39 (27.9)		
III	490 (35.7)	428 (34.7)	62 (44.3)		
IV	146 (10.6)	115 (9.3)	31 (22.1)		
Days from Admission to Surgery	4 (3,6)	4 (3,6)	5.00 (3,6)	0.002	
Comorbidities, %	(5,5)	(5,5)	(5,5)		
CHF	84 (6.1)	61 (4.9)	23 (16.4)	<0.00	
Chronic atrial fibrillation	75 (5.5)	67 (5.4)	8 (5.7)	0.890	
Osteoporosis	610 (44.4)	549 (44.5)	61 (43.6)	0.830	
Hypertension	744 (54.2)	672 (54.5)	72 (51.4)	0.489	
Diabetes	450 (32.8)	405 (32.8)	45 (32.1)	0.866	
Stroke	658 (47.9)	589 (47.8)	69 (49.3)	0.734	
COPD	29 (2.1)	20 (1.6)	9 (6.4)	<0.00	
CAD	369 (26.9)	318 (25.8)	51 (36.4)	0.007	
Clinical characteristics	307 (20.7)	310 (23.0)	31 (30.1)	0.007	
HbA1c, %	6.30±1.24	6.29±1.18	6.46±1.64	0.252	
FBG, mg/dL	7.80 (6.70,9.80)	7.70 (6.70,9.70)			
Sodium, mmol/L	137.50±4.91	137.53±5.02	137.30±3.75		
Potassium, mmol/L	3.86 (3.60,4.11)	3.85 (3.58,4.09)	3.96 (3.72,4.22)		
CRP, mg/L	35.85 (16.51,69.07)	34.49 (16.34,67.62)	45.05 (18.27,79.08)		
Cholesterol, mmol/L	4.10±1.77	4.07±0.99	45.05 (18.27,79.08) 4.21±4.57		
BNP, pg/mL	65 (29,138)	57 (27.50,129.50)	126 (66.75,237.50)	<0.00	
Albumin, g/L	36.58 (33.83,39.15)				
		36.77 (34.10,39.30)	34.61 (31.63,37.22)	<0.0	
Hemoglobin, g/L	112.07±17.55	112.62±17.48		0.002	
Hematocrit, %	33.32±6.31	33.49±6.36	31.81±5.65	0.003	
Creatinine, µmol/L	63.50 (54.19,78.69)	62.20 (53.68,77.27)	69.74 (57.83,87.32)	<0.00	
LVEF, %	62.12±5.84	62.25±5.73	61.01±6.71	0.035	
Perioperative complications, %	20 (2.0)	14 (13)	12 (0 ()	-0.00	
AMI	28 (2.0)	16 (1.3)	12 (8.6)	<0.00	
Myocardial Injury	142 (10.3)	119 (9.7)	23 (16.4)	0.013	
NOAF	170 (12.4)	134 (10.9)	36 (25.7)	<0.00	
DVT	378 (27.5)	342 (27.7) 36 (25.7)		0.612	
Hypoproteinemia	719 (52.4)	631 (51.2)	88 (62.9)	0.009	
Hypokalemia	400 (29.1)	351 (28.5)	49 (35.0)	0.107	
Hyponatremia	453 (33.0)	404 (32.8)	49 (35.0)	0.594	
Anemia	766 (55.8)	682 (55.3)	84 (60.0)	0.290	

(Continued)

Table I (Continued).

Characteristic	Total (n=1373)	Alive Group (n=1233)	Mortality Group (n=140)	P
Pneumonia	306 (22.3)	265 (21.5)	41 (29.3)	0.036
Delirium	45 (3.3)	33 (2.7)	12 (8.6)	<0.001

Notes: Values are presented as number of cases (%), mean ± SD or median (IQR). Values in bold indicate P < 0.05, which is considered a significant difference.

Abbreviations: BMI, Body Mass Index; ASA, American Society of Anesthesiologists; CHF, chronic heart failure; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; FBG, fasting blood glucose; CRP, C-reactive protein; BNP, B-type natriuretic peptide; LVEF, left ventricular ejection fractions; AMI, acute myocardial infarction; NOAF, new-onset atrial fibrillation; DVT, deep venous thrombosis.

Table 2 Association of Fractures Type and the Risk of All-Cause Mortality

Type of Fractures	Hazard Ratio (95% CI)					
	Model I	Р	Model 2	Р	Model 3	Р
Femoral neck fractures Intertrochanteric fractures	Reference 1.745 (1.233–2.470)	0.002	1.409 (0.992–2.002)	0.055	Reference 1.506 (1.010–2.243)	0.044

Notes: Model I: Univariate model for groups stratified by fractures type. Model 2: Adjusted for age, gender. Model 3: Adjusted for age, gender, injury mechanism. Abbreviations: ASA, score American Society of Anesthesiologists; CHF, chronic heart failure; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; AMI, acute myocardial infarction, myocardial injury; NOAF, new-onset atrial fibrillation; hypoproteinemia, pneumonia, delirium; FBG, fasting blood glucose; potassium, CRP, C-reactive protein; cholesterol, BNP, B-type natriuretic peptide, albumin; hemoglobin, hematocrit, creatinine, LVEF, left ventricular ejection fractions.

intertrochanteric fractures when compared with patients with femoral neck fractures (Table 2). The Kaplan–Meier curves in Figure 2 show that patients with intertrochanteric fractures had a high rate of all-cause mortality, and the difference was statistically significant (12.7% vs 7.5%, P = 0.001). Next, in subgroups defined by age 65–75, age 75–85, age \geq 85, male sex, female sex, intertrochanteric fractures consistently demonstrated a greater risk of mortality, regardless of whether covariates were adjusted (<u>Table S1</u>). This finding indicates that, irrespective of baseline levels, intertrochanteric fractures is associated with an increased mortality risk in elderly patients with hip fractures (HR \geq 1 in each subgroup).

Subgroup Analysis

The results presented a subgroup analysis of all-cause mortality (Table 3). Our study found that the incidence of perioperative complications in patients with intertrochanteric fractures was higher than that in patients with femoral neck fractures, especially in DVT, anemia and delirium. There were significant differences between the two groups (p < 0.05). In addition, patients with intertrochanteric fractures have a longer waiting time before surgery.

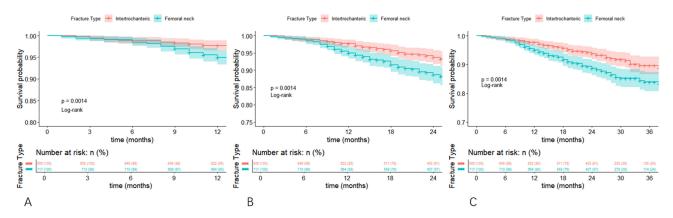


Figure 2 All-cause KM survival curve. (A) Kaplan–Meier survival analysis curves for 1-year mortality. (B) Kaplan–Meier survival analysis curves for 2-years mortality. (C) Kaplan–Meier survival analysis curves for 3-years mortality.

Table 3 Comparison of the Outcome of Intertrochanteric Fractures and Femoral Neck Fractures in Elderly Patients

Characteristic	Femoral Neck Fractures	Intertrochanteric Fractures	P
Perioperative complications, %			
AMI	11 (1.7)	17 (2.4)	0.363
Myocardial Injury	66 (10.1)	76 (10.6)	0.743
NOAF			
DVT	162 (24.7)	216 (30.1)	0.024
Hypoproteinemia	329 (50.2)	390 (54.4)	0.116
Hypokalemia	184 (28.0)	216 (30.1)	0.398
Hyponatremia	207 (31.6)	246 (34.3)	0.278
Anemia	330 (50.3)	436 (60.8)	<0.001
Pneumonia	147 (22.4)	159 (22.2)	0.918
Delirium	14 (2.1)	31 (4.3)	0.023
Outcome			
Days from Admission to Surgery	4 (3,6)	5 (3,6)	<0.001
Length of hospitalization days	11 (9,14)	12 (9,15)	0.052
Death, %	49 (7.5)	91 (12.7)	0.001

Abbreviations: AMI, acute myocardial infarction; NOAF, new-onset atrial fibrillation; DVT, deep venous thrombosis.

We next divided the patients with intertrochanteric fractures into two groups based on the preoperative waiting time: high group (Days \geq 5) and low group (Days \leq 5). Patients with longer preoperative waiting time were more likely to have perioperative AMI, NOAF and pneumonia, and also had a higher incidence of DVT (Table S2).

Selection of Variables as Predictors and Derivation of the Prediction Model

The relationships of clinical variables associated with all-cause mortality in elderly patients with intertrochanteric and femoral neck fractures are shown in <u>Table S3</u>. With Boruta algorithm, 24 variables were selected. Variables in the green area are identified as important features, and variables in the red area are unimportant features in the Boruta algorithm. All 24 variables identified as significant were then analyzed with the multivariate Cox regression model (shown in Figure 3). There were 6 variables that remained in the model for intertrochanteric fractures: age (HR 1.048, 95% CI 1.014–1.083, p = 0.006), AMI (HR 4.631, 95% CI 2.190–9.795, P < 0.001), COPD (HR 3.818, 95% CI 1.516–9.614, P = 0.004), CHF (HR 2.743, 95% CI 1.510–4.981, P = 0.001), NOAF (HR 1.748, 95% CI 1.033–2.956, P = 0.037), FBG (HR 1.116, 95% CI 1.026–1.215, P = 0.011). There were 3 variables that remained in the model for femoral neck fractures:

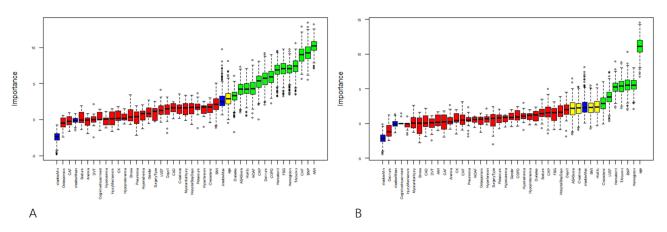


Figure 3 Feature selection based on the Boruta algorithm. Intertrochanteric fracture (A) and Femoral neck fracture (B). The horizontal axis is the name of each variable, and the vertical axis is the Z value of each variable. The green boxes represent important variables, and the red boxes represent unimportant variables.

Table 4 Prediction Factors of All-Cause Mortality

Variable	Femoral Neck Fractures HR (95% CI)	P	Variable	Intertrochanteric Fractures HR (95% CI)	P
Age	1.048 (1.014–1.083)	0.006	Age	1.145 (1.097–1.196)	<0.001
AMI	4.631 (2.190–9.795)	<0.001	HbAlc	1.264 (1.088–1.468)	0.002
COPD	3.818 (1.516–9.614)	0.004	BNP	1.001 (1.000-1.002)	0.019
CHF	2.743 (1.510–4.981)	0.001			
NOAF	1.748 (1.033–2.956)	0.037			
FBG	1.116 (1.026–1.215)	0.011			

Abbreviations: AMI, acute myocardial infarction; NOAF, new-onset atrial fibrillation; CHF, chronic heart failure; COPD, chronic obstructive pulmonary disease; FBG, fasting blood glucose; BNP, B-type natriuretic peptide.

age (HR 1.145, 95% CI 1.097–1.196, P < 0.001), HbA1c (HR 1.264, 95% CI 1.088–1.468, P = 0.002), BNP (HR 1.001, 95% CI 1.000–1.002, P = 0.019) (Table 4).

Creation and Assessment of Nomogram

Using these independent variables, we developed a nomogram model to estimate 1-year, 2-years, and 3-years mortality in patients with intertrochanteric and femoral neck fractures (Figure 4). In this study, to evaluate the predictive performance of the nomogram, we evaluated it using the receiver operating characteristic (ROC) curve and calculated the area under the curve (AUC) of 1-year mortality, 2-year mortality and 3-year mortality. In patients with intertrochanteric fractures: 0.71, 0.71 and 0.75, in patients with femoral neck fractures: 0.88, 0.81 and 0.79. This indicates the high precision of the model in terms of all-cause mortality in both groups of patients. The calibration curves revealed that the model's predicted probabilities were nearly identical to the actual probabilities, thus demonstrating its remarkable precision. This further validated the effectiveness of the COX regression model. The DCA curve shows that within the corresponding threshold range, the model has a significant value in assisting clinical decision-making, and it can provide a reliable basis for clinicians to select appropriate treatment strategies based on the survival prediction results (Figure 5).

Establishment and Validation of the Prediction Model

Figure 6 displays the ROC curves of various models, and model performance is represented by AUC values. In the group of intertrochanteric fractures: the AUC of NB was 0.833, the AUC of RF was 0.821, the AUC of xgboost was 0.806, the AUC of DT was 0.735, the AUC of SVM was 0.734, the AUC of KNN was 0.725 and the AUC of MLP was 0.626. In the group of femoral neck fractures: the AUC of xgboost was 0.807, the AUC of RF was 0.804, the AUC of NB was 0.759, the AUC of KNN was 0.698, the AUC of SVM was 0.696, the AUC of DT was 0.657 and the AUC of MLP was 0.536. According to the DCA curve (Figure S1), DT, RF, SVM, and xgboost models showed a large net benefit, indicating that the established model has robust clinical validity.

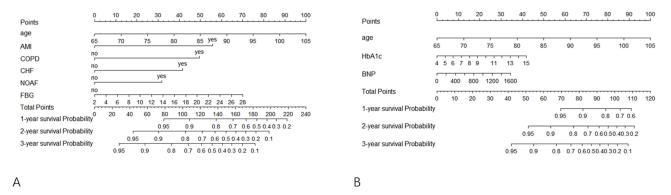


Figure 4 A model of risk prediction for all-cause mortality. (A) Risk prediction model for all-cause mortality in patients with intertrochanteric fracture. (B) Risk prediction model for all-cause mortality in patients with femoral neck fracture.

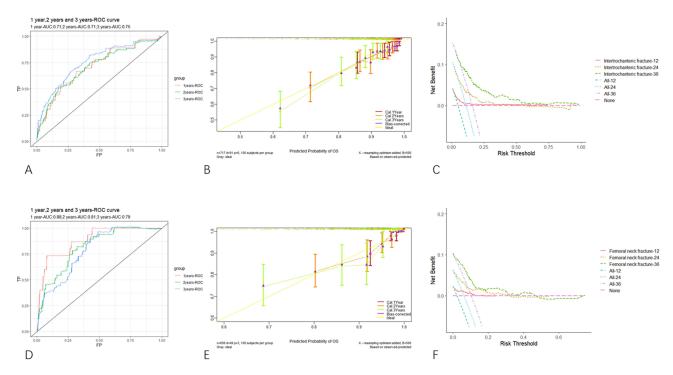


Figure 5 (A) ROC Curve of the nomogram in patients with intertrochanteric fracture. (B) The Calibration curve of the model in patients with intertrochanteric fracture. (C) DCA Curve of the model in patients with intertrochanteric fracture. (D) ROC Curve of the nomogram in patients with femoral neck fracture. (E) The Calibration curve of the model in patients with femoral neck fracture. (F) DCA Curve of the model in patients with femoral neck fracture.

Restricted Cubic Spline

Cox proportional hazards regression models with RCS were used to evaluate the linear correlation between the continuous variables (age, FBG, BNP, HbA1c) and all-cause mortality in elderly patients with intertrochanteric fractures and femoral neck fractures, and to calculate cut-off values (<u>Figure S2</u>). RCS analysis showed that there was still a linear association between these variables and all-cause mortality, with no differences between sexes. Age of 81 years, FBG of 8.06 mg/dL, BNP of 57.19 pg/mL, and HbA1c of 6.01% were determined to be the best cut-off values.

Discussion

Our study found that the all-cause mortality of elderly patients with femoral neck fractures and intertrochanteric fractures was 10.2%. Intertrochanteric fracture was an independent risk factor for all-cause mortality, and the association between the two was still significant even after adjusting for covariates. The prognosis of patients with intertrochanteric fractures is worse than that of patients with femoral neck fractures. The incidence of perioperative DVT, anemia and delirium are higher, the waiting time before surgery is longer, and the mortality is higher. Among patients with intertrochanteric fractures, those with longer waiting time before surgery have higher incidences of perioperative AMI, NOAF and pneumonia. Age, CHF, COPD, FBG, AMI and NOAF are independent risk factors for all-cause mortality in patients with intertrochanteric fractures. Age, BNP and HbA1c are independent risk factors for all-cause mortality in patients with femoral neck fractures.

An increase in mortality in intertrochanteric fractures patients has been observed in previous studies.¹² A systematic review and meta-analysis showed that the 1-year mortality rate of hip fractures in the mainland of China was 13.96%, with 17.47% for intertrochanteric fractures and 9.83% for femoral neck fractures.¹³ In our study, mortality was higher in patients with intertrochanteric fractures than in those with femoral neck fractures (12.7% vs 7.5%). Intertrochanteric fractures are associated with increased mortality in a one-year prospective cohort study.¹² Eu-Leong Yong et al found that trochanteric fractures were independently associated with increased risk of death, identifying population groups that could be targeted for intervention strategies.¹⁴ In a prospective study, intertrochanteric fractures were associated with increased mortality compared with femoral neck fractures in older women with hip fractures. The mechanism by which intertrochanteric fractures lead to excess mortality should be investigated in the future and cannot be explained by

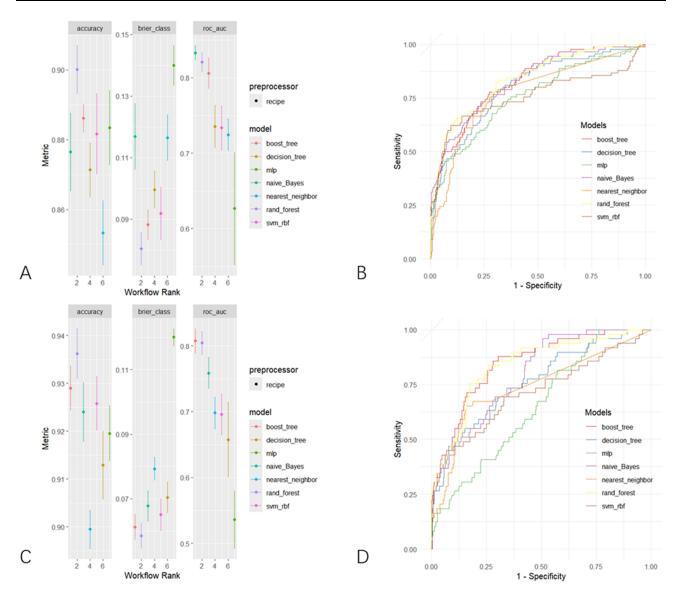


Figure 6 Receiver operating characteristic curves of machine-learning methods for prediction. A greater area under the receiver operating characteristic curve represents higher discriminative ability of the model. Area under the receiver operative characteristics curves, as well as specificity and sensitivity of each machine learning model for prediction of all-cause mortality at "best" threshold are presented with 95% Cls. "best" threshold refers to the threshold at which specificity and sensitivity are both maximized. Intertrochanteric fracture (A) and (B); Femoral neck fracture (C) and (D).

differences in age or comorbidities.¹² In our study, patients with intertrochanteric fractures were older and had more existing comorbidities than patients with femoral neck fractures, reflecting poorer underlying health status. However, even using multivariate analysis to account for age and comorbidities, several reports have found significantly higher mortality in patients with femoral intertrochanteric fractures.¹⁵ The results of our current analysis provide further evidence that after adjusting for covariates, even without these differences, we observed increased mortality in elderly patients with intertrochanteric fractures, suggesting that fractures type is an independent predictor of all-cause mortality in patients with hip fractures. This may be related to several mechanisms: (1) Blood transfusion: Anemia is prevalent among patients with hip fractures.¹⁶ Moreover, it is a modifiable factor, and the indication for blood transfusion in patients with asymptomatic postoperative hip fractures is a hemoglobin level of less than 8 g/dL. Morris et al¹⁷ reported transfusion rates of 39.4% for intertrochanteric fractures, and it is an independent risk factor for blood transfusion, ^{18,19} which is associated with increased short-term mortality to the first degree.²⁰ Kehlet²¹ believed that the occurrence of anemia in intertrochanteric fractures was related to the continuous hidden blood loss during the perioperative period. In addition, intramedullary fixation and plate fixation also increase the risk of postoperative anemia.²² At present, it is still

controversial whether red blood cell transfusion will increase the incidence of death in postoperative fragile intertrochanteric fractures.²³ Further studies are needed to confirm whether massive blood transfusions adversely affect patients' postoperative survival. (2) Fractures stability: The biomechanical properties of intertrochanteric fractures make them more unstable and the healing process may be more complicated, resulting in poor postoperative functional recovery and affecting the quality of life and survival rate of patients. (3) Age and underlying diseases: Intertrochanteric fractures usually occur in elderly patients, who usually have multiple underlying diseases (such as cardiovascular diseases, diabetes, etc)., which make them wait longer before surgery and face higher risks during surgery and recovery. Moreover, long preoperative waiting time is often associated with poor prognosis, ^{24,25} increasing the incidence of pneumonia and cardiovascular events (AMI and NOAF). A systematic review and meta-analysis of patients with hip fractures has shown that early surgical treatment after admission is an effective measure to reduce postoperative mortality and complications.²⁶ In this study, although preoperative waiting time was not an independent risk factor for death, subgroup analysis showed that patients with preoperative waiting time <5 days had a significantly better prognosis than those with preoperative waiting time ≥ 5 days. A longer waiting time often indicates a worse foundation. For such patients, we should strengthen their perioperative management to reduce the occurrence of adverse events. (4). Recovery process: After intertrochanteric fractures, patients may have a longer recovery process, and older patients are more likely to have functional loss and frailty during the recovery process, which may further increase the risk of death. ^{27,28} Comprehensive evaluation and perioperative management of these patients are helpful to reduce their mortality and improve their quality of life.

In our study, advanced age was found to be a significant risk factor for mortality, both in patients with intertrochanteric fractures and in those with femoral neck fractures. Karademir et al found age is the primary risk factor on first year mortality in patients older than 75 years old with hip fractures.²⁹ Keene et al³⁰ proposed that 1-year mortality would increase by 1% with a 1-year increase in age. With the increase in age, the elderly have a higher postoperative mortality rate due to the aging of systemic organs, deterioration of cardiopulmonary reserve, low immunity, and poor stress capacity following trauma, anesthesia, and surgery. Studies have shown that COPD, congestive heart failure, and ischemic heart disease were identified as risk factors for increased mortality in patients with proximal femoral fractures. 31,32 de Luise et al³³ analyzed persons with COPD have a 60–70% higher risk of death following hip fractures than those without COPD. In addition, hip fractures and COPD increased 1-year mortality 3-5 times that of persons without hip fractures. Thus, elderly patients with combined pulmonary disease may be more sensitive to fractures and more prone to the occurrence of multiple organ failure after surgery. Some previous studies indicate that patients with heart disease may be more likely to fall and thus sustain a hip fractures as a consequence of impaired circulation, but impaired circulation may also increase the likelihood of dying after having sustained a fractures.³⁴ In our study, chronic heart failure, AMI and NOAF were independently associated with all-cause mortality in patients with intertrochanteric fractures. This not only highlights the importance of monitoring all aspects of the respiratory and cardiovascular systems, especially in patients with concomitant chronic diseases of major organs, but also the need for multidisciplinary care. Studies have shown that admission hyperglycemia is an independent risk factor for 30-day readmission after hip fractures surgery in the elderly.³⁵ We found that FBG was an independent risk factor for mortality in patients with intertrochanteric fractures and HbA1c was independently associated with mortality in patients with femoral neck fractures, suggesting that routine blood glucose testing at admission and perioperative blood glucose control may help reduce adverse events in this vulnerable population.

This study has several limitations. First, it is a single-center, retrospective cohort study, which has an inherent limitation, and some patients were lost to follow-up. Although nomogram had been extensively tested in self-initiated inhouse validation testing, but further studies on multiple patients and external data from multiple locations are required to further confirm the results. We could not obtain the accurate causes of death from their family members, so the cause of death was not analyzed in this study.

Conclusion

Intertrochanteric fracture is an independent risk factor for all-cause mortality in elderly patients with hip fractures. By constructing a prognostic model based on machine learning, the risk factors of mortality in patients with intertrochanteric

fractures and femoral neck fractures can be effectively identified, and the perioperative management can be strengthened to develop personalized treatment strategies.

Data Sharing Statement

The data used to support the fundings of this study are available from Zhiqian Wang upon request.

Ethics Approval and Consent to Participate

The research conducted at the third Hospital of Hebei Medical University was authorized by the institutional review board in accordance with Helsinki guidelines, and approval for waiving informed consent was granted. All data were anonymized before the analysis to safeguard patient privacy.

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References

- 1. Liu Y, Peng M, Lin L, et al. Relationship between American Society of Anesthesiologists (ASA) grade and 1-year mortality in nonagenarians undergoing hip fracture surgery. Osteoporosis Int. 2015;26(3):1029–1033. doi:10.1007/s00198-014-2931-y
- 2. Smith T, Pelpola K, Ball M, et al. Pre-operative indicators for mortality following Hip fracture surgery: a systematic review and meta-analysis. *Age Ageing*. 2014;43(4):464–471. doi:10.1093/ageing/afu065
- 3. Li S, Sun T, Liu Z. Excess mortality of 1 year in elderly hip fracture patients compared with the general population in Beijing, China. *Arch Osteoporos*. 2016;11(1):35. doi:10.1007/s11657-016-0289-9
- 4. Haentjens P, Magaziner J, Colon-Emeric CS, et al. Meta-analysis: excess mortality after hip fracture among older women and men. *Ann Intern Med.* 2010;152(6):380–390. doi:10.7326/0003-4819-152-6-201003160-00008
- 5. Obada B, Georgeanu V, Iliescu M, et al. Clinical outcomes of total hip arthroplasty after femoral neck fractures vs. osteoarthritis at one year follow up-A comparative, retrospective study. *Int Orthop.* 2024;48(9):2301–2310. doi:10.1007/s00264-024-06242-0
- 6. Frisch NB, Wessell N, Charters M, et al. Hip fracture mortality: differences between intertrochanteric and femoral neck fractures. *J Surg Orthop Adv.* 2018;27(1):64–71.
- 7. Seyedi HR, Mahdian M, Khosravi G, et al. Prediction of mortality in hip fracture patients: role of routine blood tests. *Arch Bone Jt Surg-Ab*. 2015;3 (1):51–55.
- 8. Ray RI, Aitken SA, McQueen MM, et al. Predictors of poor clinical outcome following Hip fracture in middle aged-patients. *Injury.* 2015;46 (4):709–712. doi:10.1016/j.injury.2014.11.005
- 9. Lee D, Jo JY, Jung JS, et al. Prognostic factors predicting early recovery of pre-fracture functional mobility in elderly patients with hip fracture. *Ann Rehabil Med-Arm.* 2014;38(6):827–835. doi:10.5535/arm.2014.38.6.827
- 10. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction (2018). J Am Coll Cardiol. 2018;72(18):2231–2264. doi:10.1016/j.jacc.2018.08.1038
- 11. Devereaux PJ, Biccard BM, Sigamani A, et al. Association of postoperative high-sensitivity troponin levels with myocardial injury and 30-day mortality among patients undergoing noncardiac surgery. *JAMA-J Am Med Assoc.* 2017;317(16):1642–1651. doi:10.1001/jama.2017.4360
- 12. Haentjens P, Autier P, Barette M, et al. Survival and functional outcome according to hip fracture type: a one-year prospective cohort study in elderly women with an intertrochanteric or femoral neck fracture. *Bone.* 2007;41(6):958–964. doi:10.1016/j.bone.2007.08.026
- 13. Cui Z, Feng H, Meng X, et al. Age-specific 1-year mortality rates after hip fracture based on the populations in mainland China between the years 2000 and 2018: a systematic analysis. *Arch Osteoporos*. 2019;14(1):55. doi:10.1007/s11657-019-0604-3
- 14. Yong E, Ganesan G, Kramer MS, et al. Risk factors and trends associated with mortality among adults with hip fracture in Singapore. *JAMA Netw Open.* 2020;3(2):e1919706. doi:10.1001/jamanetworkopen.2019.19706
- 15. Karagiannis A, Papakitsou E, Dretakis K, et al. Mortality rates of patients with a Hip fracture in a southwestern district of Greece: ten-year follow-up with reference to the type of fracture. Calcified Tissue Int. 2006;78(2):72–77. doi:10.1007/s00223-005-0169-6
- 16. Jang SY, Cha YH, Yoo JI, et al. Blood transfusion for elderly patients with hip fracture: a nationwide cohort study. *J Korean Med Sci.* 2020;35(37): e313. doi:10.3346/jkms.2020.35.e313
- 17. Morris R, Rethnam U, Russ B, et al. Assessing the impact of fracture pattern on transfusion requirements in Hip fractures. *Eur J Trauma Emerg S*. 2017;43(3):337–342. doi:10.1007/s00068-016-0655-8

- Farrow L, Brasnic L, Martin C, et al. A nationwide study of blood transfusion in hip fracture patients: linked analysis from the Scottish Hip Fracture Audit and the Scottish National Blood Transfusion Service. Bone Joint J. 2022;104-B(11):1266–1272. doi:10.1302/0301-620X.104B11. BJJ-2022-0450.R1
- 19. Guo J, He Q, Li Y. Development and validation of machine learning models to predict perioperative transfusion risk for hip fractures in the elderly. *Ann Med.* 2024;56(1):2357225. doi:10.1080/07853890.2024.2357225
- Guo J, Geng Q, Xu K, et al. Development and validation of models for predicting mortality in intertrochanteric fracture surgery patients with perioperative blood transfusion: a prospective multicenter cohort study. Int J Surg. 2024;110(8):4754–4766. doi:10.1097/JS9.000000000001472
- 21. Foss NB, Kehlet H. Hidden blood loss after surgery for Hip fracture. J Bone Joint Surg Br. 2006;88(8):1053–1059. doi:10.1302/0301-620X.88B8.17534
- 22. Kumar D, Mbako AN, Riddick A, et al. On admission haemoglobin in patients with Hip fracture. *Injury*. 2011;42(2):167–170. doi:10.1016/j. injury.2010.07.239
- 23. Smeets SJM, Verbruggen JPAM, Poeze M. Effect of blood transfusion on survival after hip fracture surgery. Eur J Orthop Surg Tr. 2018;28 (7):1297–1303. doi:10.1007/s00590-018-2205-z
- 24. He M, Liu J, Deng X, et al. The postoperative prognosis of older intertrochanteric fracture patients as evaluated by the Chang reduction quality criteria. *Bmc Geriatr.* 2022;22(1):928. doi:10.1186/s12877-022-03641-z
- 25. Greve K, Ek S, Bartha E, et al. Waiting more than 24 hours for hip fracture surgery is associated with increased risk of adverse outcomes for sicker patients: a nationwide cohort study of 63,998 patients using the Swedish hip fracture register. *Acta Orthop.* 2023;94:87. doi:10.2340/17453674.2023.9595
- 26. Simunovic N, Devereaux PJ, Sprague S, et al. Effect of early surgery after hip fracture on mortality and complications: systematic review and meta-analysis. Can Med Assoc J. 2010;182(15):1609–1616. doi:10.1503/cmaj.092220
- 27. Xu P, Xu Y. Risk factors and nomogram predictive model of severe postoperative complications in elderly patients with intertrochanteric fractures. *Pak J Med Sci.* 2024;40(7):1566–1571. doi:10.12669/pjms.40.7.9242
- 28. Pulkkinen P, Gluer CC, Jamsa T. Investigation of differences between hip fracture types: a worthy strategy for improved risk assessment and fracture prevention. *Bone*. 2011;49(4):600–604. doi:10.1016/j.bone.2011.07.022
- 29. Karademir G, Bilgin Y, Ersen A, et al. Hip fractures in patients older than 75 years old: retrospective analysis for prognostic factors. *Int J Surg*. 2015;24(Pt A):101–104. doi:10.1016/j.ijsu.2015.11.009
- 30. Keene GS, Parker MJ, Pryor GA. Mortality and morbidity after hip fractures. *BMJ-Brit Med J.* 1993;307(6914):1248–1250. doi:10.1136/bmi.307.6914.1248
- 31. Walter N, Szymski D, Kurtz S, et al. Factors associated with mortality after proximal femoral fracture. *J Orthop Traumatol*. 2023;24(1):31. doi:10.1186/s10195-023-00715-5
- 32. Li SG, Sun TS, Liu Z, et al. Factors influencing postoperative mortality one year after surgery for hip fracture in Chinese elderly population. *Chinese Med J-Peking*. 2013;126(14):2715–2719.
- 33. de Luise C, Brimacombe M, Pedersen L, et al. Chronic obstructive pulmonary disease and mortality following hip fracture: a population-based cohort study. Eur J Epidemiol. 2008;23(2):115–122. doi:10.1007/s10654-007-9211-5
- 34. Vestergaard P, Rejnmark L, Mosekilde L. Increased mortality in patients with a hip fracture-effect of pre-morbid conditions and post-fracture complications. *Osteoporosis Int.* 2007;18(12):1583–1593. doi:10.1007/s00198-007-0403-3
- 35. Tang W, Ni X, Yao W, et al. The correlation between admission hyperglycemia and 30-day readmission after Hip fracture surgery in geriatric patients: a propensity score-matched study. *Front Endocrinol*. 2024;15(1340435). doi:10.3389/fendo.2024.1340435

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