



A New Nomogram Model for Predicting 1-Year All-Cause Mortality After Hip Arthroplasty in Nonagenarians With Hip Fractures: A 20-Year Period Retrospective Cohort Study

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Background: China has become an ageing society and as it continues to age, it will face an increasing number of hip fractures in nonagenarians. However, few preoperative assessment tools to determine the postoperative mortality risk in nonagenarians with hip fracture were available. The aim of this study was to identify all-cause mortality risk factors after hip arthroplasty in nonagenarians with hip fractures and to establish a new nomogram model to optimize the individualized hip arthroplasty in nonagenarians with hip fractures.

Methods: We retrospectively studied 246 consecutive nonagenarians diagnosed with hip fracture from August 2002 to February 2021 at our center. During the follow-up, 203 nonagenarians with a median age of 91.9 years treated with hip arthroplasty were included, of which 136 were females and 67 were males, and 43 nonagenarians were excluded (40 underwent internal fixation and 3 were lost to follow-up). The full cohort was randomly divided into training (50%) and validation (50%) sets. The potential predictive factors for 1-year all-cause mortality after hip arthroplasty were assessed by univariate and multivariate COX proportional hazards regression on the training set, and then, a new nomogram model was established and evaluated by concordance index (C-index) and calibration curves.

Results: After analyzing 44 perioperative variables including demographic characteristics, vital signs, surgical data, laboratory tests, we identified that age-adjusted Charlson Comorbidity Index (aCCI) ($p=0.042$), American Society of Anesthesiologists (ASA) classification ($p=0.007$), Urea ($p=0.028$), serum Ca^{2+} ($p=0.011$), postoperative hemoglobin ($p=0.024$) were significant predictors for 1-year all-cause mortality after

hip arthroplasty in the training set. The nomogram showed a robust discrimination, with a C-index of 0.71 (95% CIs, 0.68–0.78). The calibration curves for 1-year all-cause mortality showed optimal agreement between the probability as predicted by the nomogram and the actual probability in training and validation sets.

Conclusion: A novel nomogram model integrating 5 independent predictive variables were established and validated. It can effectively predict 1-year all-cause mortality after hip arthroplasty in nonagenarians with hip fracture and lead to a more optimized and rational therapeutic choice.

Keywords: nomogram, nonagenarians, hip fractures, hip arthroplasty, all-cause mortality

INTRODUCTION

The aging process of China is accelerating, 115 million will be over 80 years old and 0.6 million are expected to become centenarians by 2050 (1). Population aged more than 90 years in China accounted for 15% of the global nonagenarians at the end of 2017 (2). The incidence of hip fracture increases with age (3). Unless the patients face high risk of intraoperative death or difficulties to access to surgical care, operative treatment for most hip fractures is recommended, and arthroplasty is generally preferred for the management of displaced femoral-neck fractures and unstable intertrochanteric fractures in the elderly (4, 5), because of the obvious advantages such as early weight-bearing training, reduced bed-related and implant-related complications.

Despite advances in medical and surgical treatments for geriatrics with hip fractures, postoperative mortality has increased with increasing age, especially in nonagenarians with significant comorbidity (6, 7). Several studies have investigated the risk factors contributing to mortality in the extremely old patients (8, 9), with the goal of helping clinicians and surgeons to reduce risk and improve outcomes. Nevertheless, risk factors related to 1-year mortality were rarely investigated in previous studies and few attempts have been made to quantify the contribution of established risk factors to postoperative mortality in nonagenarians with hip fracture. The aim of the present study was to develop a new nomogram model for the management of hip fractures in nonagenarians and to investigate the potential risk factors correlating with 1-year all-cause mortality after hip arthroplasty in nonagenarians.

MATERIALS AND METHODS

Date Source

We performed a retrospective cohort study to assess mortality and the risk factors that influence it following hip arthroplasty in the nonagenarians with hip fractures from August 2002 to February 2021 in Daping Hospital of Third Military Medical University (Army Medical University). The inclusion criteria were as follows: (1) patients aged more than 90 years old; (2) low-energy or fragility-type hip fractures; (3) patients who received total hip arthroplasty or hemiarthroplasty; and (4)

availability of complete clinical and follow-up data. Nonagenarians with neoplastic-related pathological hip fractures and multiple fractures, as well as non-operatively managed hip fractures were excluded from the current analysis. The study protocol was approved by the Ethics Committee of Daping Hospital of Army Medical University (2022[89]). All authors had access to the results of the study, reviewed and edited the final manuscript, and were involved in the decision to submit the manuscript for publication.

Outcome Variables

The primary outcome for this study was mortality, which was obtained from the electronic medical record (EMR) and from telephone follow-ups using a uniformed questionnaire by two trained physicians. The date of the surgery was used as the starting point of the patient's observed survival time, and the end of follow-up or the date of death was used as the observation end point. The follow-up period ended on February 28, 2022. Patients were considered lost to follow-up if they were out of contact or refused to provide the current information. In order to analyze which variables were the potential risk factors relating to postoperative mortality, 44 preoperative, intraoperative, and postoperative variables were collected and analyzed. Age-adjusted Charlson Comorbidity Index (aCCI) and ASA classification were subsequently calculated for each patient as a global measure of health status (Table 2).

Model Construction and Evaluation

The patients were randomly assigned into training (50%) and validation (50%) sets. Univariate and multivariate COX proportional hazards regression were performed on the training set to identify the significant independent factors. A nomogram was then established to present these factors and their corresponding points for the risk of 1-year all-cause mortality. The predictive accuracy and discriminative ability were determined using the C-index. Calibration of the nomogram for 1-year all-cause mortality was performed by comparing the predicted and observed probability.

Statistical Analysis

Statistical analyses were performed using R package version 4.1.0 (Institute for Statistics and Mathematics, Vienna, Austria). Categorical variables were described as count (%)

and compared using the chi-square test or Fisher’s exact test, while continuous variables were described as $\bar{x} \pm s$ and compared using the t-test. The missing values of all potential predictors (missing rate of less than 10.0%) were imputed by expectation-maximization (EM) method. Univariate Cox regression analysis was adopted to identify the potential predictive factors which reached a *p* value of less than 0.05 in training set. Then the variables with *p* < 0.05 were entered into multivariate COX proportional hazards regression to screen the significant independent factors. Hazard ratio (HR) was estimated, and the corresponding 95% confidence interval (95% CI) and *p* value were reported at the same time. The rms package was used to formulate a prognostic nomogram based on the results of multivariate analysis. The C-index and the calibration curve were applied to assess the discrimination and calibration of the nomogram. *p* < 0.05 was considered statistically significant.

RESULTS

Baseline Characteristics

During the study period, 246 nonagenarians who suffered hip fractures underwent operations. Of these, 203 patients who met the inclusion criteria were enrolled, and the remaining 43 were excluded (40 underwent internal fixation and 3 were lost to follow-up). For the 203 nonagenarians, the observed survival time was 1–120 months, average of 31.08 months, median of 60.5 months. The cumulative deaths in postoperative 1 month, 3 months, 6 months and 12 months was 21(10.3%), 30(14.8%), 37(18.2%) and 58(29.6%), respectively. The main causes of death were presented in **Table 1**. 203 eligible patients were randomly divided into training (50%, *n* = 102) and validation (50%, *n* = 101) sets. The baseline characteristics of the patients including demographic characteristics, vital signs, surgical data and laboratory tests

TABLE 1 | The main causes of 58 deaths.

System	Disease	Number
MODS	Two or more organ systems presented dysfunctional	13
Cardiogenic Disease	Myocardial Infarction, Cardiac Failure, Malignant Arrhythmia	8
Cerebral Diseases	Cerebral Infarction, Cerebral Hemorrhage	5
Respiratory Diseases	Respiratory Failure, Pulmonary Infection	4
Digestive Diseases	Gastrointestinal Hemorrhage, Infection of Digestive canal	2
Accidents	The patients fell while walking and died after a period of time in bed	2
Malignant Tumor	liver cancer	1
Dysoemia	The patients died at home and the causes of death were not confirmed by doctors	23

MODS, Multiple Organ Dysfunction Syndrome.

TABLE 2 | Demographic and clinical characteristics of the included nonagenarians with hip fracture.

Variables	Training (n = 102)	Validation (n = 101)	<i>p</i> -value
Age cohorts (years), No. (%)			
90–94	89 (87.3)	86 (85.1)	0.663
≥95	13 (12.7)	15 (14.9)	
Gender (female), No. (%)			
	72 (70.6)	64 (63.4)	0.298
Length before admission (hours), No. (%)			
≤72	46 (45.1)	46 (45.5)	0.736
73–168	34 (33.3)	39 (38.6)	
169–504	16 (15.7)	12 (11.9)	
>504	6 (5.9)	4 (4.0)	
Preoperative length of stay (days), No. (%)			
<2	47 (46.1)	32 (31.7)	0.029
2–3	16 (15.7)	30 (29.7)	
>3	39 (38.2)	39 (38.6)	
Fracture type, No. (%)			
Femoral neck fracture	37 (36.3)	48 (47.5)	0.119
Intertrochanteric fracture	65 (63.7)	53 (52.5)	
Left/Right, No. (%)			
Left	60 (58.8)	60 (59.4)	1.000
Right	42 (41.2)	41 (40.6)	
aCCI, mean (SD)	5.09 ± 1.05	5.03 ± 1.01	0.687
Pulse (beats/min), No. (%)			
<60	4 (3.9)	3 (3.0)	0.418
60–100	89 (87.3)	83 (82.2)	
>100	9 (8.8)	15 (14.9)	
Systolic pressure (mmHg), No. (%)			
90–119	9 (8.8)	18 (17.8)	0.188
120–139	34 (33.3)	38 (37.6)	
140–159	30 (29.4)	24 (23.8)	
160–179	23 (22.5)	14 (13.9)	
≥180	6 (5.9)	7 (6.9)	
Diastolic pressure (mmHg), No. (%)			
<60	8 (7.8)	9 (8.9)	0.596
60–79	54 (52.9)	57 (56.4)	
80–89	32 (31.4)	23 (22.8)	
90–99	7 (6.9)	9 (8.9)	
100–109	1 (1.0)	3 (3.0)	
Cardiac function classification, No. (%)			
NYHA I&II	73 (71.5)	68 (67.3)	0.512
NYHA III&IV	29 (28.4)	33 (32.7)	
ASA classification, No. (%)			
ASA I&II	46 (45.1)	41 (40.6)	0.571
ASA III&IV	56 (54.9)	60 (59.4)	
Operation type, No. (%)			
Hemiarthroplasty	94 (92.2)	97 (96.0)	0.373
Total hip arthroplasty	8 (7.8)	4 (4.0)	

(continued)

TABLE 2 | Continued

Variables	Training (n = 102)	Validation (n = 101)	p-value
Anesthesia, No. (%)			
Nerve block anesthesia	88 (86.3)	88 (87.1)	1.000
Intravertebral anesthesia	10 (9.8)	9 (8.9)	
General anesthesia	4 (3.9)	4 (4.0)	
Operation time (min), No. (%)			
<60	8 (7.8)	4 (4.0)	0.399
60–120	86 (84.3)	91 (90.1)	
>120	8 (7.8)	6 (5.9)	
Blood transfusion, No. (%)			
25 (24.5)	20 (19.8)	0.500	
White-cell count (×10⁹/L), No. (%)			
<4.00	2 (2.0)	3 (3.0)	0.879
4.00–10.00	75 (73.5)	72 (71.3)	
≥10.01	25 (24.5)	26 (25.7)	
Platelet count (×10⁹/L), No. (%)			
<100	11 (10.8)	17 (16.8)	0.421
100–300	82 (80.4)	74 (73.3)	
>300	9 (8.8)	10 (9.9)	
Percentage of neutrophil >75%, No. (%)			
55 (53.9)	66 (65.3)	0.116	
Hematocrit, No. (%)			
≥40 (Male), ≥35 (Female)	21 (20.6)	20 (19.8)	0.889
<40 (Male), <35 (Female)	81 (79.4)	81 (80.2)	
Albumin <35 g/L, No. (%)			
65 (63.7)	30 (70.3)	0.371	
Albumin/Globulin, No. (%)			
<1.2	56 (54.9)	48 (47.5)	0.292
1.2–2.4	45 (44.1)	53 (52.5)	
>2.4	1 (1.0)	0 (0.0)	
Lactate dehydrogenase >250 U/L, No. (%)			
28 (27.5)	23 (22.8)	0.518	
Alkaline phosphatase >125 U/L (Male) & >135 U/L (Female), No. (%)			
10 (9.8)	8 (7.9)	0.806	
Na⁺(mmol/L), No. (%)			
<135	20 (19.6)	20 (19.8)	0.764
135–145	79 (77.5)	80 (79.2)	
>145	3 (2.9)	1 (1.0)	
K⁺(mmol/L), No. (%)			
<3.5	8 (7.8)	19 (18.8)	0.030
3.5–5.5	93 (91.2)	82 (81.2)	
>5.5	1 (1.0)	0 (0.0)	
Anion gap (mmol/L), No. (%)			
<8	18 (17.6)	23 (22.8)	0.099
8–16	80 (78.4)	78 (77.2)	
>16	4 (3.9)	0 (0.0)	
Creatinine ≥97 μmmol/L, No. (%)			
28 (27.5)	19 (18.8)	0.183	
Urea >8.0 mmol/L, No. (%)			
49 (48.0)	42 (41.6)	0.398	

(continued)

TABLE 2 | Continued

Variables	Training (n = 102)	Validation (n = 101)	p-value
FIB(g/L), No. (%)			
<2	3 (2.9)	0 (0.0)	0.204
2–4	44 (43.1)	40 (39.6)	
>4	55 (53.9)	61 (60.4)	
APTT(s), No. (%)			
<24	5 (4.9)	1 (1.0)	0.292
24–40	95 (93.1)	99 (98.0)	
>40	2 (2.0)	1 (1.0)	
TT(s), No. (%)			
<11	0 (0.0)	2 (2.0)	0.495
11–18	101 (99.0)	98 (97.0)	
>18	1 (1.0)	1 (1.0)	
PT1(s), No. (%)			
<9.4	2 (2.0)	0 (0.0)	0.317
9.4–13.8	94 (92.2)	97 (96.0)	
>13.8	6 (5.9)	4 (4.0)	
PTINR, No. (%)			
<0.76	1 (1.0)	0 (0.0)	0.609
0.76–1.16	96 (94.1)	98 (97.0)	
>1.16	5 (4.9)	3 (3.0)	
D-dimmer >500 μg/L, No. (%)			
92 (90.2)	98 (97.0)	0.082	
CRP >10 mg/L, No. (%)			
80 (78.4)	90 (89.1)	0.056	
ESR >20 mm/60 min, No. (%)			
78 (76.5)	81 (80.2)	0.610	
Blood glucose(mmol/L), No. (%)			
<3.9	3 (2.9)	1 (1.0)	0.607
3.9–6.9	81 (79.4)	84 (83.2)	
≥7.0	18 (17.6)	16 (15.8)	
Total bilirubin >23 μmmol/L, No. (%)			
18 (17.6)	20 (19.8)	0.722	
Ca²⁺ <2.11 mmol/L, No. (%)			
57 (55.9)	62 (61.4)	0.477	
Cl⁻(mmol/L), No. (%)			
<99	18 (17.6)	14 (13.9)	0.516
99–110	76 (74.5)	82 (81.2)	
>110	8 (7.8)	5 (5.0)	
Preoperative hemoglobin (g/L)			
104.92 ± 18.28	107.07 ± 19.45	0.419	
Postoperative hemoglobin (g/L)			
86.82 ± 13.28	89.83 ± 13.62	0.113	

aCCI, age-adjusted Charlson Comorbidity Index; ASA classification, American Society of Anesthesiologists classification; Na⁺, serum sodium; K⁺, serum potassium; Ca²⁺, serum calcium; Cl⁻, serum chloride; FIB, fibrinogen; APTT, activated partial thromboplastin time; TT, thrombin time; PT1, prothrombin time 1; PTINR, international normalized ratio of prothrombin time; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

are listed in **Table 2**. The baseline data were similar between the training and validation set, and deaths of 30 (29.4%) and 28 (27.7%) in the training and validation set, respectively

TABLE 3 | Univariate and multivariate COX proportional hazards regression analysis of the fatal outcome of nonagenarians undergoing arthroplasty after hip fracture in the Training cohort.

Variables	Univariate COX analysis		Multivariate COX analysis	
	HR (95% CIs)	<i>p</i>	HR (95% CIs)	<i>p</i>
Age (≥ 95 years)	1.04 (0.66–1.66)	0.859		
Gender (female), No. (%)	0.91 (0.55–1.5)	0.698		
Length before admission (hours)				
≤ 72	Ref.			
73–168	1.08 (0.63–1.83)	0.786		
169–504	1.24 (0.63–2.46)	0.533		
> 504	0.62 (0.24–1.62)	0.330		
Preoperative length of stay (days)				
< 2	Ref.			
2–3	1.07 (0.54–2.12)	0.837		
> 3	1.05 (0.64–1.74)	0.842		
Fracture type (Intertrochanteric fracture)	1.5 (0.93–2.43)	0.097		
Left/Right	1.18 (0.74–1.87)	0.484		
aCCI	1.48 (1.18–1.87)	0.001	1.3 (1.01–1.67)	0.042
Pulse (beats/min)				
< 60	Ref.			
60–100	1.29 (0.4–4.11)	0.671		
> 100	1.83 (0.47–7.13)	0.384		
Systolic pressure (mmHg)				
90–119	Ref.			
120–139	0.88 (0.39–1.96)	0.750		
140–159	0.77 (0.33–1.8)	0.549		
160–179	1.08 (0.46–2.53)	0.867		
≥ 180	1.12 (0.33–3.77)	0.856		
Diastolic pressure (mmHg)				
< 60	Ref.			
60–79	0.91 (0.36–2.32)	0.840		
80–89	0.94 (0.35–2.48)	0.895		
90–99	0.38 (0.1–1.44)	0.155		
100–109	2.37 (0.27–20.61)	0.434		
Cardiac function classification (NYHA III&IV)	1.26 (0.93–1.7)	0.131		
ASA classification (ASA III&IV)	1.97 (1.22–3.18)	0.006	2.05 (1.22–3.44)	0.007
Operation type (Hemiarthroplasty)	0.88 (0.38–2.07)	0.775		
Anesthesia				
Nerve block anesthesia	Ref.			
Intravertebral anesthesia	1.16 (0.52–2.58)	0.714		
General anesthesia	1.01 (0.36–2.78)	0.989		
Operation time (min)				
< 60	Ref.			
60–120	0.88 (0.35–2.21)	0.791		
> 120	0.98 (0.32–3.03)	0.978		
Blood transfusion	1.51 (0.86–2.64)	0.148		
White-cell count ($\times 10^9/L$)				
< 4.00	Ref.			

(continued)

TABLE 3 | Continued

Variables	Univariate COX analysis		Multivariate COX analysis	
	HR (95% CIs)	p	HR (95% CIs)	p
4.00–10.00	1.3 (0.3–5.72)	0.728		
≥10.01	1.82 (0.39–8.44)	0.442		
Platelet count ($\times 10^9/L$)				
<100	Ref.			
100–300	1.14 (0.54–2.4)	0.724		
>300	1.48 (0.53–4.12)	0.451		
Percentage of neutrophil >75%	1.94 (1.2–3.13)	0.007		
Hematocrit <40 (Male), <35 (Female)	1.72 (0.92–3.21)	0.087		
Albumin <35 g/L	0.81 (0.49–1.32)	0.392		
Albumin/Globulin				
<1.2	Ref.			
1.2–2.4	0.58 (0.36–0.95)	0.029		
>2.4	0.9 (0.12–6.56)	0.916		
Lactate dehydrogenase >250 U/L	1.12 (0.67–1.86)	0.660		
Alkaline phosphatase >125 U/L (Male) & >135 U/L (Female)	1.06 (0.51–2.21)	0.877		
Na+(mmol/L)				
<135	Ref.			
135–145	0.72 (0.4–1.3)	0.270		
>145	13.36 (3.36–53.21)	<0.001		
K+(mmol/L)				
<3.5	Ref.			
3.5–5.5	0.52 (0.25–1.1)	0.085		
>5.5	7.89 (0.92–67.77)	0.060		
Anion gap (mmol/L)				
<8	Ref.			
8–16	0.95 (0.51–1.78)	0.879		
>16	1.93 (0.62–6.07)	0.258		
Creatinine $\geq 97 \mu\text{mmol/L}$	1.86 (1.14–3.04)	0.014		
Urea >8.0 mmol/L	2.02 (1.25–3.26)	0.004	1.74 (1.06–2.85)	0.028
FIB (g/L)				
<2	Ref.			
2–4	0.94 (0.27–3.19)	0.915		
>4	1.28 (0.38–4.29)	0.686		
APTT(s)				
<24	Ref.			
24–40	0.36 (0.14–0.92)	0.032		
>40	3 (0.56–16.03)	0.199		
TT(s)	3.29 (0.45–24.21)	0.242		
PT1(s)				
<9.4	Ref.			
9.4–13.8	1.05	0.946		
>13.8	0.9	0.896		
PTINR				
<0.76	Ref.			
0.76–1.16	1.87 (0.26–13.54)	0.537		

(continued)

TABLE 3 | Continued

Variables	Univariate COX analysis		Multivariate COX analysis	
	HR (95% CIs)	p	HR (95% CIs)	p
>1.16	0.79 (0.07–8.7)	0.844		
D-dimmer >500 µg/L	1.7 (0.73–3.95)	0.218		
CRP >10 mg/L	1.44 (0.81–2.54)	0.212		
ESR >20 mm/60 min	1.04 (0.61–1.78)	0.889		
Blood glucose (mmol/L)				
<3.9	Ref.			
3.9–6.9	0.56 (0.17–1.81)	0.334		
≥7.0	0.71 (0.2–2.48)	0.590		
Total bilirubin >23 µmol/L	1.52 (0.84–2.73)	0.163		
Ca ²⁺ <2.11 mmol/L	0.6 (0.37–0.95)	0.030	0.54 (0.33–0.87)	0.011
Cl ⁻ (mmol/L)				
<99	Ref.			
99–110	1.01 (0.54–1.89)	0.977		
>110	1.49 (0.56–3.98)	0.424		
Preoperative hemoglobin (g/L)	0.99 (0.98–1)	0.044		
Postoperative hemoglobin (g/L)	0.97 (0.96–0.99)	0.003	0.98 (0.96–1.00)	0.024

aCCI, age-adjusted Charlson Comorbidity Index; ASA classification, American Society of Anesthesiologists classification; Na⁺, serum sodium; K⁺, serum potassium; Ca²⁺, serum calcium; Cl⁻, serum chloride; FIB, fibrinogen; APTT, activated partial thromboplastin time; TT, thrombin time; PT1, prothrombin time 1; PTINR, international normalized ratio of prothrombin time; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

($p = 0.790$). Preoperative length of stay and serum K⁺ differed significantly between the training and validation set ($p < 0.05$), while the remaining variables between the two sets presented no difference.

Prognostic Factors for 1-Year All-Cause Mortality After Hip Arthroplasty in Nonagenarians With Hip Fractures

Table 3 that were based on the univariate and multivariate COX proportional hazards regression analysis presents the predictors for 1-year all-cause mortality in the training set of 102 cases (30 deaths). First, univariate Cox regression analysis was applied to reveal the potential prognostic predictors, and revealed that 11 of 44 predictors were significantly associated with 1-year all-cause mortality. Furthermore, the results of multivariate analysis showed that aCCI (HR = 1.3), ASA classification (III&IV, HR = 2.05), Urea (>8.0 mmol/L, HR = 1.74), serum Ca²⁺ (<2.11 mmol/L, HR = 0.54), postoperative hemoglobin (HR = 0.98) were significant predictors for 1-year all-cause mortality after hip arthroplasty in nonagenarians suffered hip fractures.

Development and Validation of the Prognostic Nomogram

Based on the Akaike information criteria (AIC), 5 independent prognostic predictors, including aCCI (HR = 1.3, 95% CI, 1.01–1.67, $p = 0.042$), ASA classification (HR = 2.05, 95% CI, 1.22–3.44, $p = 0.007$), Urea (HR = 1.74, 95% CI, 1.06–2.85, $p = 0.028$), serum Ca²⁺ (HR = 0.54, 95% CI, 0.33–0.87, $p = 0.011$),

postoperative hemoglobin (HR = 0.98, 95% CI, 0.96–1.00, $p = 0.024$) were selected for the construction of the prognostic nomogram (Figure 1). The C-index for 1-year all-cause mortality after hip arthroplasty in nonagenarians with hip fractures was 0.71 (95% CIs, 0.68–0.78). The optimal agreement between nomogram-predicted probability and the result of observation in both the training and validation set was showed clearly by the calibration curve (Figure 2).

DISCUSSION

One-year mortality after hip fractures surgery in the elderly is more than 27% (10–13). In our study, the one-year mortality is as high as 29.6% in nonagenarians. These extremely old patients have high operative risk and difficult perioperative management and require more precise treatment. Risk prediction is one of the advantages of precision medicine, and the precision of prediction models need to develop from cohort customization to personalize management. Accompanied by the development of artificial intelligence, new risk prediction models are emerging constantly, we applied Cox regression models and predictive nomogram in the current study, aimed to develop a simple and intuitive model to interpret complex clinical indicators, to help clinicians screen out high-risk patients, and to help patients understand the high mortality associated with these factors easily. To our knowledge, this is the first study to use one new nomogram model to predict the risk factors for mortality after

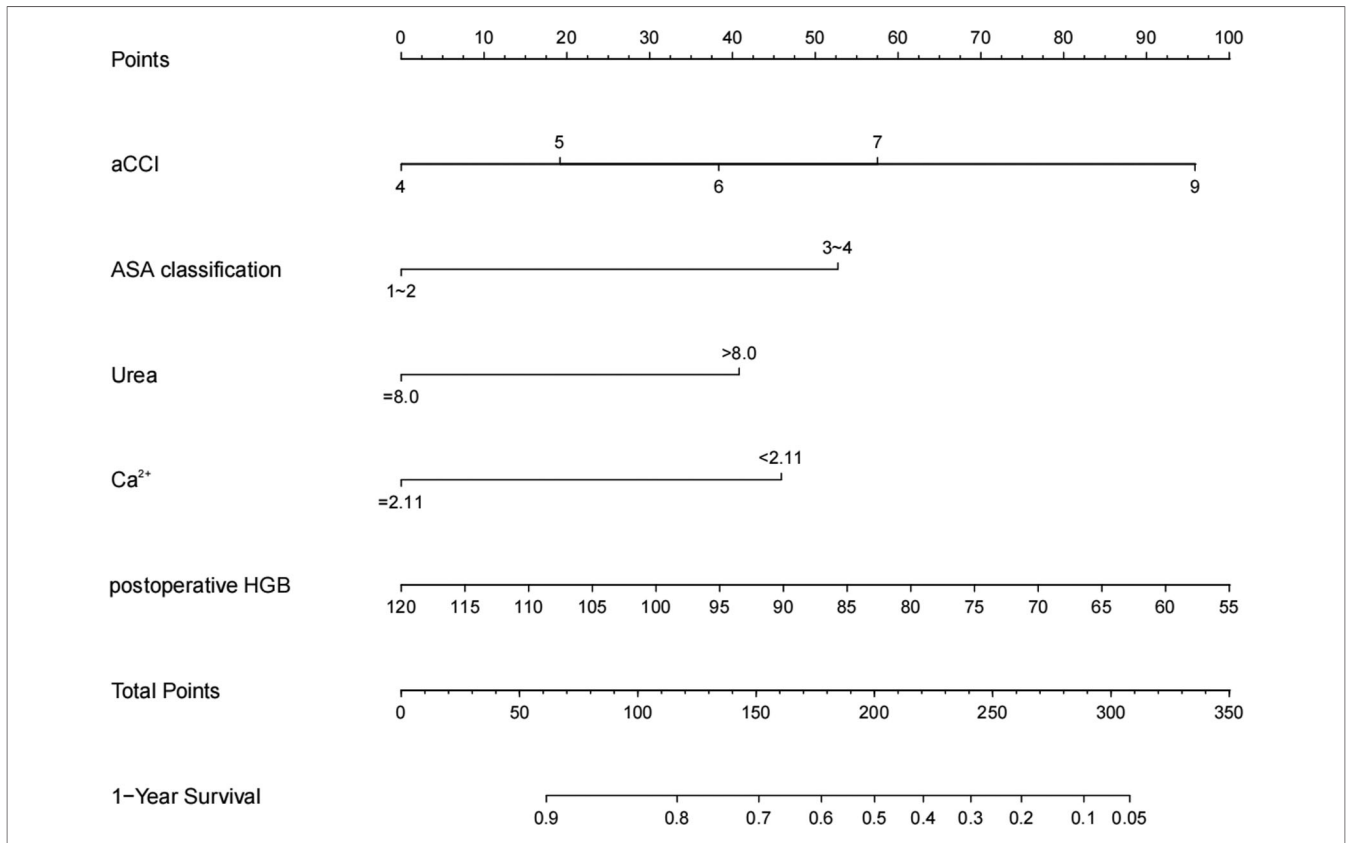


FIGURE 1 | A nomogram for prediction of 1-year mortality after arthroplasty in nonagenarians with hip fractures. aCCI, age-adjusted Charlson Comorbidity Index; ASA classification, American Society of Anesthesiologists classification; Ca²⁺, serum calcium; HGB, hemoglobin.

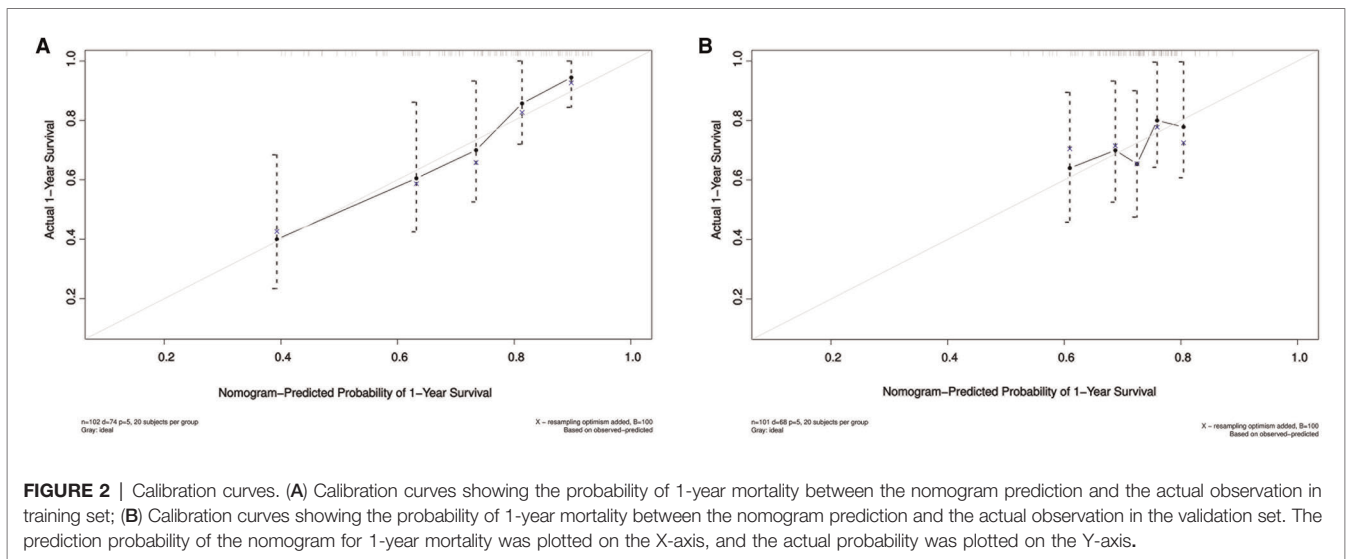


FIGURE 2 | Calibration curves. (A) Calibration curves showing the probability of 1-year mortality between the nomogram prediction and the actual observation in training set; (B) Calibration curves showing the probability of 1-year mortality between the nomogram prediction and the actual observation in the validation set. The prediction probability of the nomogram for 1-year mortality was plotted on the X-axis, and the actual probability was plotted on the Y-axis.

arthroplasty for nonagenarians with hip fractures. In the past, most relevant studies had focused on the incidence of adverse events during the postoperative hospital stay or one month

after surgery, while we followed the cohort for up to two decades, and the focus of the study was not limited to short-term survival rate but extended to medium and long-term

survival rate. We limited the subjects to over 90 years old and arthroplasty for hip fractures, so as to reduce the influence of bias and confounding factors as much as possible. A stable predictive nomogram was constructed by COX regression, and aCCI, ASA classification, Urea, serum Ca²⁺, and postoperative hemoglobin were confirmed as the potential independent risk factors for 1-year all-cause mortality after hip arthroplasty in nonagenarians with hip fractures.

Comorbidities are common in the elderly with hip fractures. Patients with three or more comorbidities or a complex medical history have significantly increased mortality compared with those with no comorbidities (14, 15). Multiple comorbidities often co-exist and interact with each other. It is difficult to summarize the overall organ or body function by analyzing a single or specific type of disease. In order to comprehensively evaluate and quantify patients' comorbidities and physiological functions, aCCI and ASA classification were introduced in our study. aCCI is an assessment tool that combines age factors and quantifies a variety of comorbidities. aCCI and Charlson comorbidity index (CCI) are both predictors of post-operative complications with aCCI being the better predictive determinant (16). The ASA classification includes five levels to assess the patient's physical condition and perioperative risk. Both aCCI and ASA classification are common tools for operative risk stratification. Previous studies have attempted to use CCI and ASA for risk stratification and suggested that CCI performed better than ASA classification in the prediction for 1-year mortality after surgery for hip fractures (17, 18). However, some studies suggested that ASA classification was an independent risk factor for it, rather than CCI (19). In our study, both aCCI and ASA classification are potential risk factors, which consists of the report of Ek et al. (20). Additionally, we realized that serum urea, as one of the indicators of renal function, is an independent risk factor for postoperative mortality. This may indicate that renal disease as a serious comorbidity has a great impact on prognosis.

Hypocalcemia occurs in more than 30% of elderly orthopedic patients (21, 22). Clinical symptoms related to it are rare, but calcium ion is an important electrolyte, neurotransmitter and coagulation factor, so perioperative hypocalcemia is closely related to blood loss (21) and delirium (23). Even more, chronic hypocalcemia can severely affect cardiac contractility and electrical activity (24), which undoubtedly increases the risk of perioperative adverse events. Xu et al. (25) found that hypocalcemia could shorten the overall survival of the elderly, and our study regarded hypocalcemia as a potential risk factor for mortality within 1 year after surgery. Chewcharat et al. (26) found that the fluctuating serum sodium trajectory and hyponatremia was associated with the high in-hospital and 1-year mortality. Hypokalemia is common in hypertensive patients with hypotensor treatment and was considered to be associated with increased all-cause and cardiovascular mortality (27). While our study did not find the potential association between hypernatremia, hypokalemia and postoperative mortality, this may be due to the limitations of sample size or the complexity of the physiology of

nonagenarians or differences in time periods. We should pay more attention to hypocalcemia and other blood indexes that may increase the mortality risk, and addressed them preoperatively for optimization of patient status for the operation.

Anemia is one of the most common complications after surgery for hip fracture in the elderly and is also an important factor leading to delirium, weakness, poor recovery of daily life, and even death (28, 29). Anemia on hospital admission is an independent predictor for long-term mortality in patients with hip fractures (30). During the perioperative period, hemoglobin is a direct indicator for the identification of anemia and the main basis for blood transfusion (31–34), meanwhile it is helpful for the classification of anemia and guiding perioperative fluid management in combination with hematocrit. Durán-Nah et al. (35) reported that intraoperative bleeding ≥ 400 mL and preoperative hemoglobin < 11 g/dL were closely related to allogeneic blood transfusion. In our study, we included not only preoperative hemoglobin but also postoperative hemoglobin to facilitate dynamic assessment of its risk. Moreover, we found that postoperative hemoglobin is more meaningful than preoperative hemoglobin, which generally reflects the body's ability to recover from the shock of surgery. Our experience in treatment of anemia is restrictive blood transfusion: when hemoglobin is lower than 80 g/L, red blood cell is given; anemia should be corrected first before operation, and hemoglobin should be tested dynamically after operation to determine the timing of blood transfusion.

There were several limitations in this study. First, be subjected to the limitations of description bias of medical records and the great time span, some information that may affect prognosis was not analyzed in detail, such as pre- and postoperative cognitive function (cognitive deficit, dementia), preoperative activity of daily living, including habitual physical activity level, preoperative residence, preoperative physical function (e.g., handgrip strength, mobility, activity of daily living index), postacute rehabilitation of the patients. Second, it is a single-center, retrospective study with relatively small sample size, which was insufficient to generate a model containing all potential confounding factors and lacked external validation. Third, the development and validation sets were affected by selection bias. Besides, due to the low mortality and small number of deaths during the period from postoperative hospitalization to six months in our study, we did not analyze the risk factors for mortality at different time points during this period.

CONCLUSION

We established and validated a novel nomogram based on aCCI, ASA classification, Urea, serum Ca²⁺ and postoperative hemoglobin, that could effectively predict 1-year all-cause mortality after hip arthroplasty in nonagenarians with hip fracture. It would be helpful for clinicians to identify high-risk

patients, conduct reasonable and individualized perioperative managements.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

Our study on human participants was reviewed and approved by the Ethics Committee of Daping Hospital of Army Medical University based in Chongqing, China (7 April 2022, ID 2022 [89]).

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AUTHOR CONTRIBUTIONS

YX proposed the conception and design of the study. XL, ZW, YW, SW, QD, WG and KP collected and assembled the data. FC, XL and ZW analyzed and interpreted the data. XL, ZW drafted the manuscript. All authors contributed to the article and approved the submitted version.

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