Heliyon 9 (2023) e20342

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Development of a prediction model for postoperative complications and economic burden analysis in older patients with hip fractures

Haoning Shi [a,1], Ying Gao [a,b,1], Wanying Zhao [c], Hongyu Wang [c], Xueqian Wu [c], Fei Wang [c], Xiao Yang [a,*], Jing Li [c,**]

[a] School of Nursing, Weifang Medical University, Weifang 261053, Shandong Province, PR China
[b] Linyi People's Hospital, Linyi 276034, Shandong Province, PR China
[c] School of Public Health, Weifang Medical University, Weifang 261053, Shandong Province, PR China

A R T I C L E I N F O

Keywords:
Elderly
Hip fracture
Postoperative complications
Risk factors
Nomogram
Economic burden

A B S T R A C T

Purpose: The high rates of disability and mortality due to postoperative complications of hip fractures in the elderly, especially the oldest-old individuals, have become an increasingly serious global public health concern. This study aimed to establish a nomogram prediction model and analyze the economic burden to guide clinical decision-making and improve patient prognosis.
Methods: Data of 514 patients aged over 80 years with hip fractures who received surgical treatment were retrospectively collected, and the patients were divided into training and validation cohorts. Independent risk factors for postoperative complications were identified based on logistic regression analysis, and a nomogram was constructed. The model was evaluated for its discrimination and consistency using receiver operating characteristic (ROC) curves and calibration curves, and for its clinical benefit using decision curve analysis (DCA). The economic burden was analyzed using propensity score matching (PSM).
Results: The American Society of Anesthesiologists (ASA) classification ≥III, anemia, male sex, diabetes mellitus, and the number of comorbidities were found to be independent risk factors for postoperative complications in oldest-old patients with hip fracture (all $P < 0.05$). The areas under the curve (AUC) of the nomogram prediction model for the training and validation cohorts were 0.743 and 0.767, respectively, indicating reliable discrimination. The calibration curves and DCA showed that the model has good consistency and high benefits. The direct economic burden of postoperative complications for the patients was US$1045.10.
Conclusions: The nomogram model can accurately quantify the risk of postoperative complications among oldest-old patients with hip fractures and guide clinical professionals to implement early and targeted preventive treatment for high-risk patients.

* Corresponding author. School of Nursing, Weifang Medical University, Weifang, Shandong Province 261053, China.
** Corresponding author. School of Public Health, Weifang Medical University, Weifang, Shandong Province 261053, China.
E-mail addresses: yx0204@163.com (X. Yang), lijing@wfmc.edu.cn (J. Li).
[1] The authors contributed equally: Haoning Shi and Ying Gao.

https://doi.org/10.1016/j.heliyon.2023.e20342
Received 14 June 2023; Received in revised form 16 September 2023; Accepted 19 September 2023
Available online 20 September 2023

1. Introduction

Hip fracture has become a global public health concern due to its considerable morbidity, mortality, and risk of disability [1,2]. The risk of fractures has been reported to increase exponentially with age, with the global population aged over 80 years expected to double by 2050 and the number of patients with hip fractures expected to rise to 4.5 million [3,4]. A previous study showed that patients who underwent nonoperative treatment had a four-fold higher risk of death one year after hip fracture than those who underwent surgical treatment [5]. Early surgical treatment for hip fractures has been recommended by multiple guidelines unless patients are in poor health conditions or at a high risk of intraoperative death [2,6].

Although early surgeries can help to reduce complications and mortality due to prolonged bed rest, frailty is common among the oldest-old patients [7], and the presence of fracture trauma and surgical stress may lead to considerable postoperative complications, such as pulmonary infection, delirium, deep vein thrombosis (DVT), and myocardial infarction [8,9]. A national cohort study in Denmark found that patients with postoperative lung infection after hip fracture had a 30-day mortality risk that was more than four times that of patients without infection [8]. Early identification of patients at high risk for postoperative complications is therefore critical to facilitate clinical decision-making and improve their prognoses.

To the best of our knowledge, most of the prior studies have been conducted on elderly people aged over 65 years, but the oldest-old patients may differ from young elderlies in terms of functional ability, lifestyle, and comorbidities [10]; therefore, some of the risk factors for postoperative complications of hip fractures that have been identified in prior studies may not be applicable among the oldest-old patients, and there is also a lack of analysis regarding the economic burden incurred by their postoperative complications. Therefore, the present study aimed to establish an individualized nomogram prediction model of postoperative complications in the oldest-old patients with hip fractures through retrospective analysis as well as to analyze the economic burden associated with complications, in order to improve patient prognosis and save healthcare resources.

2. Methods

2.1. Study subjects

This was a retrospective cohort study of oldest-old patients with hip fractures who were hospitalized and underwent surgical treatment in the Department of Trauma and Orthopedics of Weifang People's Hospital, a tertiary care referral center in China, from January 2017 to November 2022. The study was approved by the Ethics Review Committee of Weifang Medical University (2023YX106). The inclusion criteria were: (1) patients aged ≥80 years; (2) patients diagnosed with unilateral femoral neck fracture or intertrochanteric fracture; (3) patients who underwent total hip arthroplasty, hemiarthroplasty, open reduction internal fixation, or closed reduction internal fixation; and (4) patients with low-energy injury. Exclusion criteria were: (1) patients with malignant tumors or pathological fractures; (2) patients with multiple fractures; (3) patients with incomplete medical records; and (4) patients with acute complications (e.g., DVT, pulmonary infection, and delirium) before surgery.

2.2. Treatment for subjects

All the patients underwent routine physical examination, imaging examination, laboratory tests, and electrocardiography after admission and were anticoagulated with low-molecular-weight heparin sodium until it was discontinued 12 h before surgery. For patients not contraindicated for surgical treatment, their type of anesthesia was determined according to the consultation recommendations of the department of anesthesiology, and prophylactic intravenous infusion of cefazolin sodium 1 g was administered within 30–60 min before surgery. All the patients received surgical treatment performed by the same professional team; complete hemostasis was achieved by electrocoagulation, local tranexamic acid injection, and selective placement of negative pressure drainage vessels. The patients were given intravenous infusion of cefazolin sodium 1 g every 8 h within 24 h after surgery to prevent infection. Meanwhile, low-molecular-weight heparin sodium (4000AXaIU, ih, qd) was administered early after surgery, and oral rivaroxaban tablets (10 mg, qd) or apixaban tablets (2.5 mg, bid) were given as of 35 days after surgery to prevent postoperative DVT.

2.3. Data collection and outcome evaluation

Two well-trained professional investigators from the hospital information system (HIS) collected perioperative data of all the subjects. The demographic, clinical, and laboratory data that might influence the subjects' postoperative complications were reviewed retrospectively in strict accordance with the study protocol. The demographic characteristics included age, sex, the modified 5-item frailty index (mFI-5), comorbidities (e.g., hypertension, diabetes mellitus, coronary heart disease, stroke, chronic lung disease, cardiac arrhythmia), and the number of medical comorbidities. The clinical data mainly included type of fracture, type of surgery, time from fracture to surgery, time from admission to surgery, American Society of Anesthesiologists (ASA) classification, blood loss, and other intraoperative information. The preoperative laboratory test data mainly included routine complete blood count, electrolytes, and liver and kidney function. If a subject had repeated laboratory tests before surgery, only the latest one was recorded for the present study. All the above information was entered into structured spreadsheets and double-checked by researchers.

The primary outcome of the present study was whether the subjects developed postoperative complications, and the date of discharge of the subjects was used as the endpoint of observation. In this study, postoperative complications included postoperative delirium, postoperative pulmonary complications (PPCs), surgical site infection (SSI), urinary tract infection, sepsis or septic shock, acute renal failure, DVT, stroke, myocardial infarction, heart failure, stress ulcer bleeding, and death. The diagnostic criteria for postoperative delirium are based on the Diagnostic and Statistical Manual of Mental Disorders: 5th Ed (DSM-5, developed by the American Psychiatric Association) [11]. According to European Perioperative Clinical Outcome (EPCO), PPCs mainly include atelectasis, pulmonary infection, pleural effusion, and respiratory failure [12].

2.4. Statistical analysis

Continuous variables were presented as mean ± standard deviation (SD) or median and interquartile ranges (IQRs) and were analyzed using student's t-test or Mann-Whitney *U* test based on whether the variables were normally distributed. Categorical variables were presented as counts (percentages) and were analyzed using Chi-square test or Fisher's exact test based on their frequencies.

Table 1
Baseline characteristics of the subjects.

Characteristics	Complications (n = 73)	Non-complications (n = 288)	*P* value	Characteristics	Complications (n = 73)	Non-complications (n = 288)	*P* value
Age, years			**0.026***	Number of comorbidities	3 (2–0)	2 (1–3)	**<0.001***
≤87	47 (64.4%)	222 (77.1%)		**During the surgery**			
>87	26 (35.6%)	66 (22.9%)		Blood transfusion	31 (42.5%)	111 (38.5%)	0.540
Sex			**0.003***	SpO_2, %			**0.011***
Male	28 (38.4%)	62 (21.5%)		<90	15 (20.5%)	28 (9.7%)	
Female	45 (61.6%)	226 (78.5%)		≥90	58 (79.5%)	260 (90.3%)	
Type of fracture			0.790	Hypotension	40 (54.8%)	136 (47.2%)	0.248
Femoral neck	36 (49.3%)	137 (47.6%)		Duration of operation, minutes	70.0 (53.0–99.5)	70.0 (57.0–92.0)	0.993
Intertrochanteric	37 (50.7%)	151 (52.4%)		Blood loss, mL	150 (100–200)	100 (100–200)	0.586
Hypertension	40 (54.8%)	153 (53.1%)	0.798	Infusion volume, mL	1000 (1000–1500)	1000 (500–1000)	**0.044***
Diabetes mellitus	21 (28.8%)	43 (14.9%)	**0.006***	Hemoglobin, g/L	94.87 ± 21.67	100.40 ± 19.16	0.194
Coronary heart disease	25 (34.3%)	60 (20.8%)	**0.016***	**Before the surgery**			
Stroke	16 (21.9%)	61 (21.2%)	0.891	WBC count, 10^9/L	7.7 (6.3–9.4)	8.0 (6.5–9.6)	0.755
Chronic lung disease	6 (8.2%)	8 (2.8%)	0.070	NLR	5.1 (3.5–7.8)	5.2 (3.5–7.4)	0.621
Cardiac arrhythmia	10 (13.7%)	28 (9.7%)	0.323	MLR	0.5 (0.3–0.7)	0.4 (0.3–0.6)	0.096
PNI			**0.009***	RBC count, 10^{12}/L	3.6 (3.2–4.1)	3.7 (3.3–4.0)	0.373
<41	31 (42.5%)	77 (26.7%)		HCT, %	32.41 ± 5.92	33.47 ± 4.93	0.166
≥41	42 (57.5%)	211 (73.3%)		PLT, 10^9/L	189 (156–238)	201 (164–242)	0.319
Anemia			**0.023***	PLR	181 (121–223)	180 (132–222)	0.688
No	27 (37.0%)	144 (50.0%)		Serum sodium, mmol/L	138 (135–141)	138 (135–140)	0.548
Mild	29 (39.7%)	110 (38.2%)		Serum potassium, mmol/L	4.1 (3.7–4.3)	3.9 (3.6–4.2)	0.318
Moderate or above	17 (23.3%)	34 (11.8%)		Serum calcium, mmol/L	2.1 (2.1–2.3)	2.2 (2.1–2.3)	0.443
Medication	9 (12.3%)	26 (9.0%)	0.725	TBIL, μmol/L	15.7 (10.8–23.0)	16.3 (12.2–22.7)	0.595
Type of surgery			0.835	Total protein, g/L	61.95 ± 5.92	62.91 ± 5.89	0.212
Hip arthroplasty	35 (47.9%)	142 (49.3%)		Albumin, g/L	35.98 ± 3.89	37.08 ± 3.67	**0.024***
Internal fixation	38 (52.1%)	146 (50.7%)		Blood glucose, mmol/L	6.1 (5.3–8.3)	5.9 (5.3–6.9)	0.126
Type of anesthesia			0.418	Urea, mmol/L	7.0 (5.6–10.6)	6.6 (5.1–8.2)	**0.016***
General	8 (11.0%)	23 (8.0%)		Creatinine, μmol/L	66.0 (51.5–84.0)	58.0 (50.3–72.0)	0.058
Intraspinal	65 (89.0%)	265 (92.0%)		ALT, U/L	16.11 ± 20.60	12.65 ± 5.87	0.160
ASA classification			**<0.001***	AST, U/L	23.95 ± 20.10	18.95 ± 6.67	**0.040***
II	7 (9.6%)	89 (30.9%)		ALP, U/L	84.59 ± 29.91	79.22 ± 23.96	0.106
III	54 (74.0%)	187 (64.9%)		25 (OH) D_3, ng/mL	13.72 ± 8.15	14.36 ± 8.14	0.670
IV	12 (16.4%)	12 (4.2%)		TC, mmol/L	3.73 ± 1.07	4.21 ± 0.92	0.195
mFI-5	1 (0–2)	1 (0–1)	**<0.001***	HDL-C, mmol/L	1.10 ± 0.19	1.23 ± 0.27	0.181
Time from fracture to surgery, days	5.0 (3.0–8.0)	3.4 (2.3–6.2)	**0.043***	LDL-C, mmol/L	2.20 ± 0.89	2.57 ± 0.89	0.272
Time from admission to surgery, days	3.0 (2.0–4.0)	2.0 (2.0–3.0)	**0.003***	CRP, mg/L	53.05 ± 43.58	33.22 ± 36.62	0.127

Notes: Data are presented as counts (percentages), means ± standard deviations, or median (1st quartile-3rd quartile) as appropriate. Medication: medications that may cause delirium prior to admission, such as sedative-hypnotics, etc. *$P < 0.05$.
AbbreviationsPNI, Prognostic Nutritional Index; ASA, American Society of Anesthesiologists; mFI-5, Modified 5-Item Frailty Index; SpO2, Saturation of peripheral oxygen; WBC, white blood cell; NLR, neutrophil-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; RBC, red; blood cell; HCT, hematocrit; PLT, platelet; PLR, platelet-to-lymphocyte ratio; TBIL, total bilirubin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; CRP, c-reactive protein.

The subjects of this study were randomly assigned to a training cohort (70% of the data), which was used to establish the prediction model, and a validation cohort (30% of the data), which was used to estimate the performance of the model. In this study, $P < 0.05$ (two-tailed) was considered to be statistically significant.

All the statistical analyses of this study were performed using SPSS 26.0 (SPSS Software, Chicago, USA) and R 4.2.0 (R Software, Vienna, Austria). Potential risk factors with non-zero coefficients were screened out based on the least absolute shrinkage and selection operator (LASSO) logistic regression [13], and multivariate logistic regression analysis was further performed to establish a prediction model for postoperative complications in the oldest-old patients with hip fractures. An online interactive dynamic nomogram system was constructed using the "Shiny" package in R, and receiver operating characteristic (ROC) curves and calibration curves were used to evaluate the discrimination and consistency of the model, respectively. To evaluate the clinical benefit of the model, we used decision curve analysis (DCA) to determine the net benefit at different threshold probabilities. For the analysis of economic burden, we conducted 1:1 propensity score matching (PSM) to match subjects to the complication and non-complication groups by controlling the

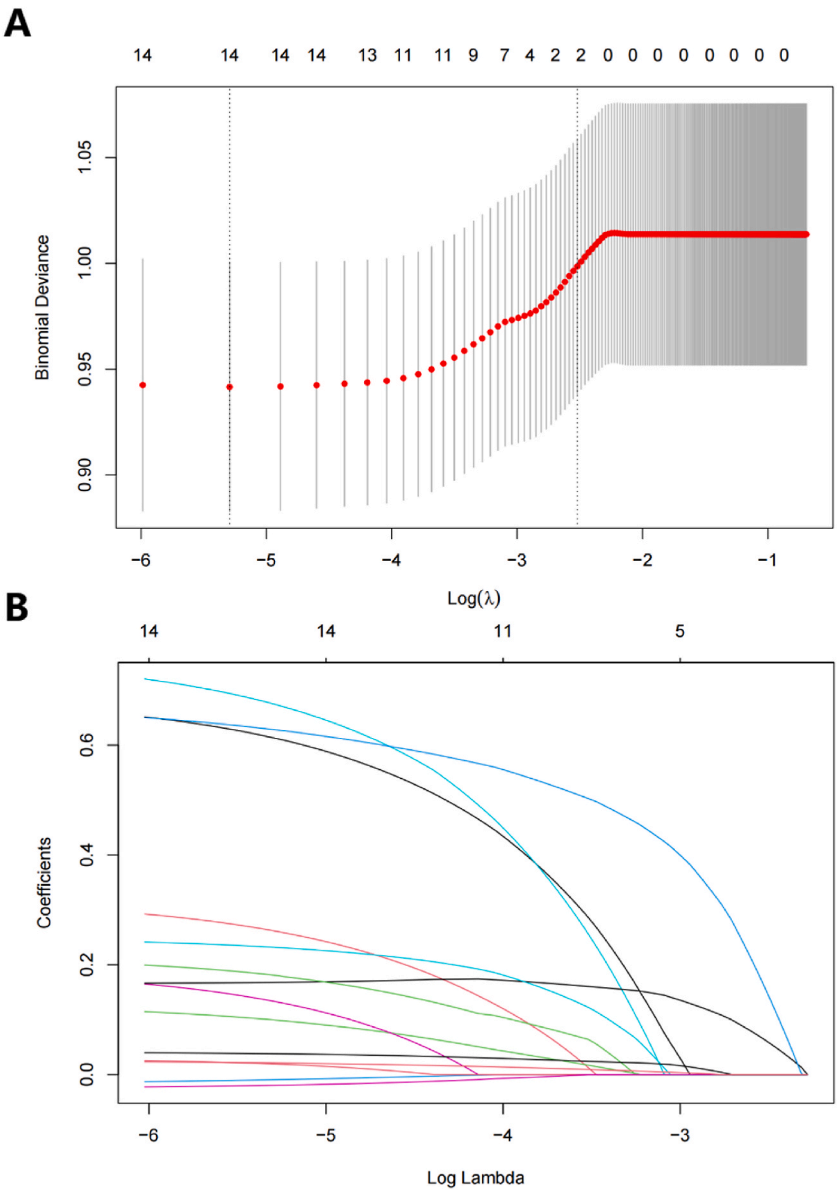

Fig. 1. LASSO regression 10-fold cross-validation and screening of clinical variables. (**A**) The dashed line on the left represents the mean-squared error, indicating that the model has the best prediction performance ($\lambda = 0.00503$); The dashed line on the right represents the cross-validated mean-squared error within the range of 1 standard error from the minimum value, which further reduces the number of variables due to its stricter penalization ($\lambda = 0.08040$). (B) With the increase of the penalization coefficient (λ), the regression coefficient of the prediction variable gradually decreases to 0.

covariates of age, sex, type of fracture, and type of surgery.

3. Results

3.1. Baseline characteristics of subjects

A total of 716 subjects met the eligibility criteria for this study. Some subjects were excluded due to multiple fractures (45), malignant tumors (35), incomplete medical records (9), or acute preoperative complications (113). Finally, 514 subjects were included in this study. Among them, 104 (20.2%) developed postoperative complications, including postoperative delirium (29.8%), PPCs (41.3%), SSI (12.5%), urinary tract infections (5.8%), DVT (12.5%), stroke (7.7%), myocardial infarction or heart failure (9.6%), and stress ulcer bleeding (7.7%). It should be noted that some subjects had multiple postoperative complications.

In this study, 361 subjects (70%) and 153 subjects (30%) were randomly assigned to the training cohort and validation cohort, respectively. There was no significant difference in general data between the two groups ($P > 0.05$). The baseline characteristics of the subjects in the training cohort are shown in Table 1. In the total training cohort, 75.1% were female and 24.9% were male. There were 92 subjects aged over 87 years (25.5%). The most common preoperative complication was hypertension (193, 53.5%), followed by anemia (190, 52.6%). Calculated by summing and dividing the number of historical variables by 5 (n/5; range 0.0–1.0), mFI-5 has been demonstrated to effectively reflect frailty [14]. There were 67 subjects (18.6%) with moderate or higher frailty with mFI-5 > 0.2, and 95 subjects (26.3%) had more than 3 comorbidities.

3.2. Selection of factors for the prediction model

LASSO regression analysis was performed on the 16 variables showing statistical significance in the univariate analysis (Table 1). At the optimal lambda.min, 14 variables with non-zero coefficients were selected as potential risk factors, excluding SpO_2 and infusion volume (Fig. 1A and B). In this study, 14 potential predictors were further included in the multivariate logistic regression analysis, and 5 independent risk factors were screened out, including male sex (OR 2.24, 95%CI 1.21–4.15; P = 0.010), diabetes mellitus (OR 2.01, 95%CI 1.02–3.94; P = 0.042), number of comorbidities (OR 1.29, 95%CI 1.08–1.54; P = 0.005), ASA classification [III (OR 2.35, 95% CI 0.98–5.63; P = 0.055) and IV (OR 5.42, 95%CI 1.63–18.05; P = 0.006)] and anemia [mild (OR 1.27, 95%CI 0.68–2.38; P = 0.453); moderate or above (OR 2.83, 95%CI 1.30–6.17; P = 0.009)] (Table 2).

3.3. Development and validation of the prediction model

With the use of the five independent predictors determined by the multivariate logistic regression analysis and their corresponding regression coefficients, the individualized nomogram prediction model of postoperative complications in oldest-old patients with hip fracture was developed (Fig. 2A) and made available online (https://shi-haoning.shinyapps.io/Complications_DynNomapp/, Fig. 2B). As shown in Fig. 3A, the area under the ROC curve (AUC) of the prediction model was 0.743 (95%CI 6682–0.803) and 0.767 (95%CI 6666–0.868) in the training and validation cohorts, respectively, suggesting a good predictive ability of the model. The Hosmer-Lemeshow test of the training and validation cohorts showed 0.806 and 0.391, respectively, and the calibration curves of the model were reasonably close to the ideal curve, indicating that the anticipated results produced by the model were in line with the observed results (Fig. 3B and C).

Table 2
Multivariate logistic regression analysis of risk factors for postoperative complications after hip fracture.

Variable	β-Coefficient	OR (95%CI)	*P* value
Sex			
Female	Ref.		
Male	0.808	2.244 (1.213, 4.149)	0.010
Diabetes mellitus			
No	Ref.		
Yes	0.698	2.010 (1.024, 3.944)	0.042
Number of comorbidities	0.252	1.286 (1.078, 1.535)	0.005
ASA classification			0.022
II	Ref.		
III	0.855	2.351 (0.982, 5.628)	0.055
IV	1.689	5.416 (1.625, 18.050)	0.006
Anemia			0.030
No	Ref.		
Mild	0.240	1.272 (0.679, 2.381)	0.453
Moderate or severe	1.042	2.834 (1.302, 6.168)	0.009

Abbreviations: ASA, American Society of Anesthesiologists; OR, odds ratio; CI, confidence interval; Ref, reference.

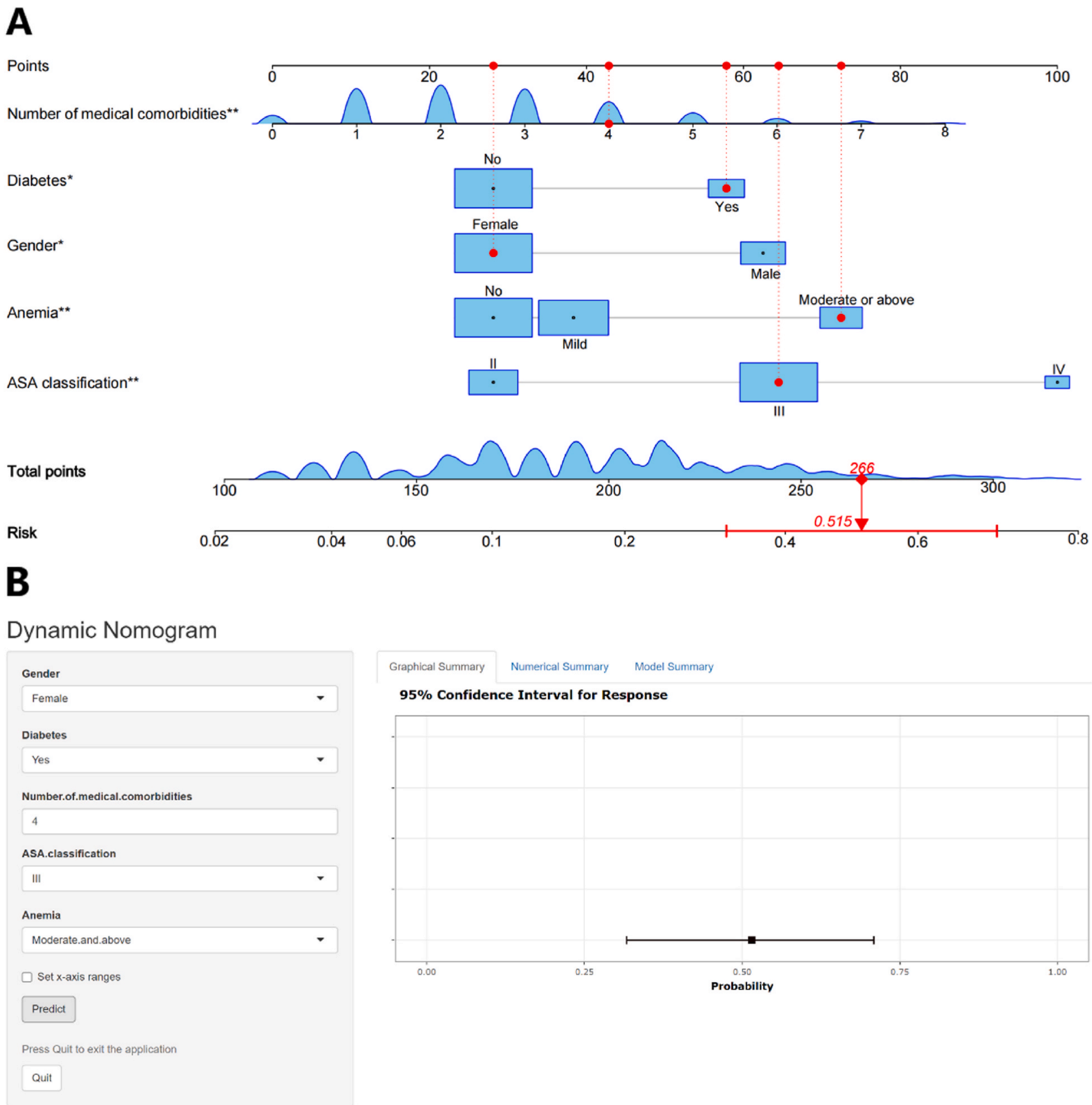

Fig. 2. The clinical nomogram predicting the probability of postoperative complications. (**A**) The nomogram was established using the training cohort by incorporating five parameters (ASA classification, anemia, male sex, diabetes, and the number of medical comorbidities), and the probability of postoperative complications was finally determined by reading the score above each risk factor. (**B**) The dynamic online nomogram is accessible at https://shi-haoning.shinyapps.io/Complications_DynNomapp/.

3.4. Clinical utility of the nomogram

The DCA of the nomogram of the training and validation cohorts is presented in Fig. 4. The probability of high-risk threshold is the probability of postoperative complications predicted by the model. This study suggested that this prediction model could facilitate the identification of patients at high risk of postoperative complications and inform clinical decision-making. The results showed that the threshold probabilities of the training and validation cohorts were 0%–73% and 3%–58%, respectively, indicating that the model could bring great net benefit for oldest-old patients with hip fractures.

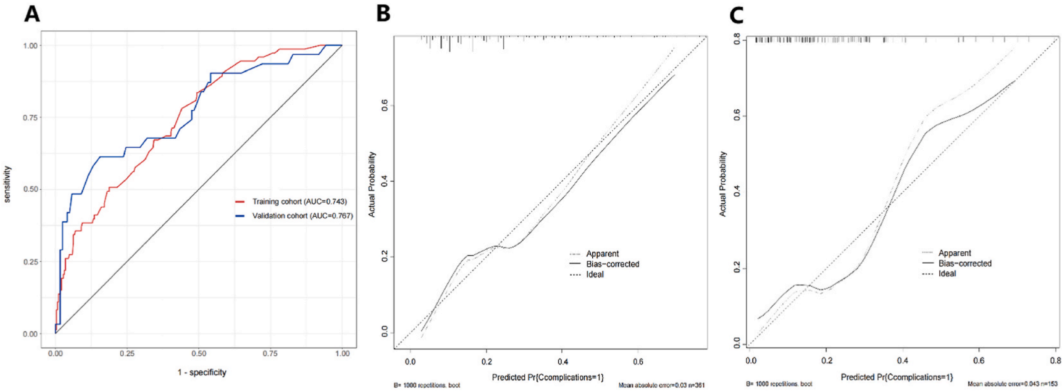

Fig. 3. Evaluation of discrimination and consistency of the prediction model for postoperative complications after hip fracture. (**A**) ROC curves of the prediction model; (**B**) calibration curves of the prediction model for the training cohort; (**C**) calibration curves of the prediction model for the validation cohort.

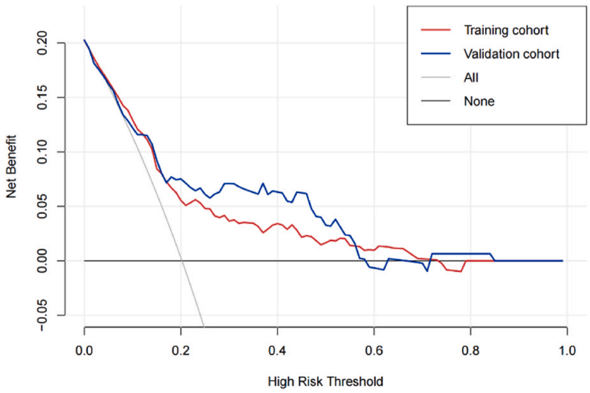

Fig. 4. Decision curve analysis of the nomogram using the training and validation cohorts. The threshold probability and net benefit are represented on the X and Y axes, respectively. The black line and the grey line represent the two extreme conditions, with the black line indicating that no patients developed postoperative complications and none of them had received any intervention and the grey line indicating that all the patients developed postoperative complications and had received interventions.

3.5. Economic burden incurred by postoperative complications

A total of 99 pairs of subjects were successfully matched using PSM (Tables 3 and 4). Patients with postoperative complications paid significantly more for medications, treatments, laboratory tests, examinations, and hospitalization, and had significantly longer hospital stay compared to patients without complications ($P < 0.05$); the direct economic burden of patients with postoperative complications reach US$1045.10. The total cost for subjects with multiple complications was US$8380.58, significantly higher than US$3871.75 among patients without complications. Furthermore, the subjects with cardiac complications and PPCs had an increased

Table 3
Costs and length of hospital stay of patients with and without complications (2022 US$).

Measurements	Complications (n = 99)	Non-complications (n = 99)	Differences	*Z* value	*P* value
Total cost	5553.93 (4304.41–7796.46)	4508.83 (3484.11–5623.78)	1045.10	−4.855	**<0.001***
Medication	804.54 (579.12–1511.29)	553.78 (370.44–783.87)	250.76	−5.389	**<0.001***
Treatment	550.97 (380.78–1062.97)	374.89 (282.82–519.22)	176.08	−5.240	**<0.001***
Blood transfusion	66.88 (0.00–200.65)	66.88 (0.00–133.77)	0	−1.610	0.107
Laboratory tests	419.77 (302.72–691.81)	309.56 (240.06–394.47)	110.21	−4.802	**<0.001***
Examinations	373.10 (244.56–535.80)	293.56 (197.74–376.30)	79.54	−3.254	**0.001***
Surgery	2756.81 (1958.69–3368.53)	2507.60 (1846.62–3176.71)	249.21	−1.559	0.119
Supplies	60.05 (0.91–137.12)	74.94 (8.05–109.85)	−14.89	−0.822	0.411
Hospitalization	77.35 (44.20–138.13)	50.89 (38.68–87.53)	26.46	−3.597	**<0.001***
Length of hospital stay	13.00 (8.00–18.00)	8.00 (6.60–12.00)	5.00	−4.591	**<0.001***

Notes: Data are presented as median (1st quartile-3rd quartile). *$P < 0.05$.

Table 4
Total cost for subjects with different complications (2022 US$).

Complications	Expenditure in the complications	Expenditure in the non-complications	Differences	*Z* value	*P* value
Multiple complications	8380.58 (5694.09–14168.93)	4508.83 (3484.11–5623.78)	3871.75	−4.867	**<0.001***
Postoperative delirium	5258.39 (4470.86–6236.67)	4508.83 (3484.11–5623.78)	749.56	−2.259	**0.024***
PPCs	6240.89 (4409.78–8616.57)	4508.83 (3484.11–5623.78)	1732.06	−3.663	**<0.001***
SSI	4651.58 (3759.74–6240.35)	4508.83 (3484.11–5623.78)	142.75	−1.168	0.243
Urinary tract infections	5694.43 (4825.87–34307.48)	4508.83 (3484.11–5623.78)	1185.60	−2.378	**0.017***
DVT	4888.36 (3836.82–8325.39)	4508.83 (3484.11–5623.78)	379.53	−1.350	0.177
Cardiac complications	6356.60 (4538.11–15938.68)	4508.83 (3484.11–5623.78)	1847.77	−2.618	**0.009***

Notes: Data are presented as median (1st quartile-3rd quartile). $^*P < 0.05$.
Abbreviations: PPCs, postoperative pulmonary complications; SSI, surgical site infections; DVT.
deep vein thrombosis.

economic burden of US$1847.77 and US$1732.06, respectively.

4. Discussion

As postoperative complications of hip fracture can result in poor health outcomes and a significant financial burden in the oldest-old patients, identifying patients at high risk of postoperative complications in advance can greatly improve the quality of care as well as the public health care system. In the present study, we found that ASA classification, anemia, male sex, diabetes mellitus, and the number of comorbidities were significant predictors of postoperative complications during hospitalization among oldest-old patients with hip fractures; we also, for the first time, established an individualized dynamic nomogram prediction model to quantify the risk of postoperative complications. The nomogram showed good discrimination and consistency, and it may help to provide a reference for targeted treatments to achieve greater net benefits.

It is well known that elderlies with multiple comorbidities are prone to physical dysfunction, which may affect their prognosis; the general condition and comorbidities are also factors taken account by anesthesiologists to determine the ASA classification [15]. Prior studies have shown that the ASA classification is predictive of the postoperative status of elderly patients with hip fractures [15,16]. Comorbidities are reported to increase the risk of complications and in-hospital death among patients with hip fractures, and the risk tends to increase as the number of comorbidities increase [17]. A national cohort study in Sweden showed that, regardless of gender, a higher ASA classification was consistently associated with higher risks of postoperative complications, particularly cardiovascular complications, in patients with hip fractures [18]. Similarly, the present study found that for every additional number of comorbidities, the risk of postoperative complications increased by 1.3 times. The risk of postoperative complications was also positively correlated with ASA classification; in particular, patients who had an ASA classification of IV were 5.4 times more likely to experience postoperative complications than those with an ASA classification of II. Therefore, clinicians should pay attention to the underlying diseases and the ASA classification of elderly patients, and a multidisciplinary team may be needed to adjust the treatment to further reduce the risk of postoperative complications.

The degree of anemia can reflect changes in physiological reserves and physical status, and a prospective cohort study found that anemia was a risk factor for postoperative pneumonia in patients with hip fracture [19]. Bhaskar et al. reported that patients with hip fracture whose hemoglobin was 80–100 g/L on admission had a one-year mortality of 49.2% ($P < 0.001$), indicating that hemoglobin could be used as a surrogate marker for mortality after hip fracture [20]. The present study showed that anemia was a risk factor for postoperative complications among the oldest-old patients with hip fractures, with a 2.8-fold increased risk of complications in patients with moderate or severe anemia compared with patients without anemia. Moreover, a study using data from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) found that preoperative anemia was an effective predictor of postoperative blood transfusion in patients with hip fractures [21], and that blood transfusion per se has been shown to have an immunosuppressive effect and was found associated with the occurrence of postoperative complications [22,23]. Taken together, anemia is a significant modifiable risk factor in oldest-old patients with hip fractures, and it is necessary to improve perioperative management and early correction of anemia for high-risk patients.

The present study showed that male sex was an independent risk factor for postoperative complications in the oldest-old patients with hip fractures (OR = 2.2), which is consistent with the findings of Lefaivre et al. [17] In a prospective multicenter cohort study, Ekström et al. [24] found that males with hip fractures were at significantly higher risk of postoperative pneumonia, cardiac complications, and short-term death than females ($P < 0.05$), which was interpreted as the impact of a higher number of comorbidities and poorer general condition in males. Some studies have also identified the male sex as a risk factor for postoperative pneumonia in patients with hip fracture (OR = 2.1–3.4) [25,26]. In addition to being an independent variable, biological sex may also affect the development of postoperative complications through the patients' habits, health concerns and other factors. Therefore, further studies on the impact of sex/gender may be necessary to improve preoperative care and promote health education.

As a common chronic metabolic disease, diabetes mellitus is prone to causing microangiopathy and immunosuppression in patients with long-term hyperglycemia, which may reduce the regeneration and repair of tissues, thereby affecting recovery [27]. The present study suggested that the oldest-old patients with diabetes have twice the risk of postoperative complications after hip fractures compared to their counterparts without diabetes, which was in line with prior findings [19,28]. Several studies have found that fasting blood glucose of more than 110 mg/dL or 200 mg/dL is a risk factor for postoperative infection among patients with hip fractures, suggesting that fasting blood glucose may better reflect the status of glycemic control than the history of diabetes mellitus [29,30]. Therefore, further studies are necessary to determine the scope of perioperative glycemic regulation and the impact of glycemic control on elderly patients with hip fractures, and medical professionals should strengthen blood glucose monitoring in patients with hip fractures to reduce their risk of postoperative complications.

Previous studies have shown that hospital-acquired conditions (HACs) following surgery not only increase patient suffering, affect patient prognosis, and prolong the length of hospital stay, but also increase the economic burden on patients and hospitals [31]. Similar results were found in the present study, with a direct economic burden of US$1045.10 for the oldest-old patients with hip fractures who developed postoperative complications; the complications also incurred the most significant rise in medication costs, with a direct economic burden of US$250.76. This may be related to increased use of antibiotics due to postoperative complications, especially postoperative infections. In addition, among all the complications, cardiac and pulmonary complications incurred the highest costs, suggesting that preventive control of postoperative complications and preventive care for modifiable risk factors are essential to reduce the economic burden of patients.

The strengths of the present study are the development of a prediction model targeting elderly people aged over 80 years, who have the highest incidence of hip fractures; the model is based on preoperative and intraoperative clinical and laboratory tests, and the interactive and dynamic online model can facilitate clinicians to predict the risk of postoperative complications for each patient. This study also evaluated the economic burden incurred by postoperative complications among the oldest-old patients with hip fractures, which is helpful for raising clinical attention to postoperative complications and improving patient care and management.

The present study has some limitations. First, the subjects in this study were from a single institution, and the lack of external validation from multicenter studies might have affected the generalization and application of the prediction model in other regions. Second, the subjects were observed during their hospitalization only, and 30-day mortality and 1-year survival rate were not evaluated. Third, this is a retrospective cohort study, which might be susceptible to selection bias and information bias, and further prospective multicenter studies are needed to confirm the findings and optimize this prediction model.

5. Conclusions

The present study found that the ASA classification, anemia, male sex, diabetes mellitus, and the number of comorbidities were independent risk factors for postoperative complications during hospitalization among the oldest-old patients with hip fractures and established a dynamic online nomogram prediction model to identify high-risk patients. This model can facilitate accurate quantification of the risk of postoperative complications in patients with hip fractures and guide early targeted preventive treatment for high-risk patients. This study may also provide a reference for controlling the associated economic burden and promoting the patients' postoperative recovery.

Author contribution statement

Haoning Shi; Ying Gao; Xiao Yang; Jing Li: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.
Haoning Shi; Ying Gao; Wanying Zhao; Hongyu Wang: Contributed reagents, materials, analysis tools or data, Performed the experiments.
Xueqian Wu; Fei Wang: Analyzed and interpreted the data.

Funding statement

This study was funded by Shandong Traditional Chinese Medicine Science and Technology Project (No. M-2022235); Weifang Medical Science and Technology Development Plan Project (No. 2021YX047); High Quality Professional Degree Teaching Case Base Project of Shandong Province (No. SDYAL2022149); Public Domestic Visiting Program of Weifang Medical University (No. 20237-10).

Data availability statement

The authors do not have permission to share data.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] C. Zhang, J. Feng, S. Wang, P. Gao, L. Xu, J. Zhu, et al., Incidence of and trends in hip fracture among adults in urban China: a nationwide retrospective cohort study, PLoS Med. 17 (8) (2020), e1003180, https://doi.org/10.1371/journal.pmed.1003180.
[2] M. Bhandari, M. Swiontkowski, Management of acute hip fracture, N. Engl. J. Med. 377 (21) (2017) 2053–2062, https://doi.org/10.1056/NEJMcp1611090.
[3] P. Sambrook, C. Cooper, Osteoporosis, Lancet. 367 (9527) (2006) 2010–2018, https://doi.org/10.1016/S0140-6736(06)68891-0.

[4] J.A. Cauley, D. Chalhoub, A.M. Kassem, G. Fuleihan, Geographic and ethnic disparities in osteoporotic fractures, Nat. Rev. Endocrinol. 10 (6) (2014) 338–351, https://doi.org/10.1038/nrendo.2014.51.
[5] E. Tay, Hip fractures in the elderly: operative versus nonoperative management, Singap. Med. J. 57 (4) (2016) 178–181, https://doi.org/10.11622/smedj.2016071.
[6] National Institute for Health and Care Excellence (NICE), Hip fracture: management, Clinical guideline, Available from: https://www.nice.org.uk/guidance/cg124. (Accessed 18 January 2023).
[7] A. Clegg, J. Young, S. Iliffe, M.O. Rikkert, K. Rockwood, Frailty in elderly people, Lancet 381 (9868) (2013) 752–762, https://doi.org/10.1016/S0140-6736(12)62167-9.
[8] K.E. Kjørholt, N.R. Kristensen, D. Prieto-Alhambra, S.P. Johnsen, A.B. Pedersen, Increased risk of mortality after postoperative infection in hip fracture patients, Bone 127 (2019) 563–570, https://doi.org/10.1016/j.bone.2019.07.023.
[9] E.M. Kim, G. Li, M. Kim, Development of a risk score to predict postoperative delirium in patients with hip fracture, Anesth. Analg. 130 (1) (2020) 79–86, https://doi.org/10.1213/ANE.0000000000004386.
[10] M.T. Lam, C.W. Sing, G. Li, A. Kung, K. Tan, C.L. Cheung, Development and validation of a risk score to predict the first hip fracture in the oldest old: a retrospective cohort study, J Gerontol A Biol Sci Med Sci 75 (5) (2020) 980–986, https://doi.org/10.1093/gerona/glz178.
[11] American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, fifth ed., American Psychiatric Association, Arlington, VA, 2013, pp. 286–298.
[12] I. Jammer, N. Wickboldt, M. Sander, A. Smith, M.J. Schultz, P. Pelosi, et al., Standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine: European Perioperative Clinical Outcome (EPCO) definitions: a statement from the ESA-ESICM joint taskforce on perioperative outcome measures, Eur. J. Anaesthesiol. 32 (2) (2015) 88–105, https://doi.org/10.1097/EJA.0000000000000118.
[13] J. Friedman, T. Hastie, R. Tibshirani, Regularization paths for generalized linear models via coordinate descent, J Stat Softw 33 (1) (2010) 1–22.
[14] S. Subramaniam, J.J. Aalberg, R.P. Soriano, C.M. Divino, New 5-factor modified frailty index using American College of Surgeons NSQIP data, J. Am. Coll. Surg. 226 (2) (2018) 173–181.e8, https://doi.org/10.1016/j.jamcollsurg.2017.11.005.
[15] G. Kastanis, A. Topalidou, K. Alpantaki, M. Rosiadis, K. Balalis, Is the ASA score in geriatric hip fractures a predictive factor for complications and readmission? Scientifica (Cairo) (2016) (2016), 7096245 https://doi.org/10.1155/2016/7096245.
[16] S.M. Mitchell, A.S. Chung, J.B. Walker, J.W. Hustedt, G.V. Russell, C.B. Jones, Delay in hip fracture surgery prolongs postoperative hospital length of stay but does not adversely affect outcomes at 30 days, J. Orthop. Trauma 32 (12) (2018) 629–633, https://doi.org/10.1097/BOT.0000000000001306.
[17] K.A. Lefaivre, S.A. Macadam, D.J. Davidson, R. Gandhi, H. Chan, H.M. Broekhuyse, Length of stay, mortality, morbidity and delay to surgery in hip fractures, J Bone Joint Surg Br 91 (7) (2009) 922–927, https://doi.org/10.1302/0301-620X.91B7.22446.
[18] A.C. Meyer, H. Eklund, M. Hedström, K. Modig, The ASA score predicts infections, cardiovascular complications, and hospital readmissions after hip fracture - a nationwide cohort study, Osteoporos. Int. 32 (11) (2021) 2185–2192, https://doi.org/10.1007/s00198-021-05956-w.
[19] H. Lv, P. Yin, A. Long, Y. Gao, Z. Zhao, J. Li, et al., Clinical characteristics and risk factors of postoperative pneumonia after hip fracture surgery: a prospective cohort study, Osteoporos. Int. 27 (10) (2016) 3001–3009, https://doi.org/10.1007/s00198-016-3624-5.
[20] D. Bhaskar, M.J. Parker, Haematological indices as surrogate markers of factors affecting mortality after hip fracture, Injury 42 (2) (2011) 178–182, https://doi.org/10.1016/j.injury.2010.07.501.
[21] A. Arshi, W.C. Lai, B.C. Iglesias, E.J. McPherson, E.N. Zeegen, A.I. Stavrakis, et al., Blood transfusion rates and predictors following geriatric hip fracture surgery, Hip Int. 31 (2) (2021) 272–279, https://doi.org/10.1177/1120700019897878.
[22] K.J. Koval, A.D. Rosenberg, J.D. Zuckerman, G.B. Aharonoff, M.L. Skovron, R.L. Bernstein, et al., Does blood transfusion increase the risk of infection after hip fracture? J. Orthop. Trauma 11 (4) (1997) 260–265, https://doi.org/10.1097/00005131-199705000-00004. ; discussion 265-6,.
[23] F. García-Alvarez, R. Al-Ghanem, I. García-Alvarez, A. López-Baisson, M. Bernal, Risk factors for postoperative infections in patients with hip fracture treated by means of Thompson arthroplasty, Arch. Gerontol. Geriatr. 50 (1) (2010) 51–55, https://doi.org/10.1016/j.archger.2009.01.009.
[24] W. Ekström, B. Samuelsson, S. Ponzer, T. Cederholm, K.G. Thorngren, M. Hedström, Sex effects on short-term complications after hip fracture: a prospective cohort study, Clin. Interv. Aging 10 (2015) 1259–1266, https://doi.org/10.2147/CIA.S80100.
[25] X. Wang, L. Dai, Y. Zhang, Y. Lv, Gender and low albumin and oxygen levels are risk factors for perioperative pneumonia in geriatric hip fracture patients, Clin. Interv. Aging 15 (2020) 419–424, https://doi.org/10.2147/CIA.S241592.
[26] D.D. Bohl, R.A. Sershon, B.M. Saltzman, B. Darrith, C.J. Della Valle, Incidence, risk factors, and clinical implications of pneumonia after surgery for geriatric hip fracture, J. Arthroplasty 33 (5) (2018) 1552–1556.e1, https://doi.org/10.1016/j.arth.2017.11.068.
[27] N. Jafar, H. Edriss, K. Nugent, The effect of short-term hyperglycemia on the innate immune system, Am. J. Med. Sci. 351 (2) (2016) 201–211, https://doi.org/10.1016/j.amjms.2015.11.011.
[28] M. Hälleberg Nyman, J.E. Johansson, K. Persson, M. Gustafsson, A prospective study of nosocomial urinary tract infection in hip fracture patients, J. Clin. Nurs. 20 (17–18) (2011) 2531–2539, https://doi.org/10.1111/j.1365-2702.2011.03769.x.
[29] T. Ma, K. Lu, L. Song, D. Wang, S. Ning, Z. Chen, et al., Modifiable factors as current smoking, hypoalbumin, and elevated fasting blood glucose level increased the SSI risk following elderly hip fracture surgery, J. Invest. Surg. 33 (8) (2020) 750–758, https://doi.org/10.1080/08941939.2018.1556364.
[30] S.C. Chang, J.I. Lai, M.C. Lu, K.H. Lin, W.S. Wang, S.S. Lo, et al., Reduction in the incidence of pneumonia in elderly patients after hip fracture surgery: an inpatient pulmonary rehabilitation program, Medicine (Baltim.) 97 (33) (2018), e11845, https://doi.org/10.1097/MD.0000000000011845.
[31] S.R. Horn, T.C. Liu, J.A. Horowitz, C. Oh, C.A. Bortz, F.A. Segreto, et al., Clinical impact and economic burden of hospital-acquired conditions following common surgical procedures, Spine 43 (22) (2018) E1358–E1363, https://doi.org/10.1097/BRS.0000000000002713.