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ORIGINAL RESEARCH

A Nomogram for Prediction of Postoperative Pneumonia Risk in Elderly Hip Fracture Patients

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Purpose: Pneumonia is one of the common complications of hip fracture. This study aimed to evaluate the risk factors and apply a nomogram to predict postoperative pneumonia in elderly hip fracture patients.

Materials and Methods: From August 2014 to October 2019, 1113 hip fracture patients who were older than 65 years and underwent surgical treatment in our hospital were subjects of this study. Univariate and multivariate Cox analyses were used to identify independent risk factors. A predictive nomogram model was built, and the discrimination and calibration were determined by receiver operating characteristic and calibration plot.

Results: A total of 166 patients developed pneumonia after operation (14.91%, pneumonia group) while the remaining 947 patients did not (85.09%, non-pneumonia group). According to the results, body mass index (OR, 0.76, 95% CI, 0.70 to 0.84, P<0.001), serum albumin (OR, 0.86, 95% CI, 0.79 to 0.93, P<0.001), c-reactive protein (OR, 1.01, 95% CI, 1.00 to 1.92, P=0.011), functional status (OR, 2.94, 95% CI, 1.69 to 5.10, P<0.001) and time to surgery (OR, 4.56, 95% CI, 2.64 to 7.88, P<0.001) were identified as independent risk factors of pneumonia. The area under the curve value for postoperative pneumonia risk was 0.905, and the P-value of the Hosmer-Lemeshow calibration test was 0.529.

Conclusion: Our nomogram model can be used to predict the risk of pneumonia in elderly hip fractures after surgery and provide clinicians with guidance for better perioperative intervention to improve prognosis and reduce mortality.

Keywords: pneumonia, elderly, hip fracture, risk factors, nomogram

Introduction

At present, osteoporotic hip fractures have become a major health problem, and its devastating consequences included functional decline, institutionalization, and even mortality.[1] The incidence of osteoporotic hip fractures increases as the population ages, and is predicted to increase by 1.4 times by 2025.[2] Most elderly patients with hip fractures are treated by surgery because of worsened outcomes without surgical operation.

As many as 30% of patients die within one year after hip fractures, and one-third of them die in hospital.[3] The cause of mortality in elderly people with hip fractures is mainly due to postoperative complications such as wound infection, pneumonia, deep vein thrombosis, urinary tract infections, and cardiovascular and cerebrovascular events.[4–8] Therefore, perioperative management and prevention of postoperative complications have recently become the focus of treatment for geriatric hip fractures.

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Pneumonia is one of the common complications of hip fracture and the incidence is between 5% and 10%.[9–15] Most postoperative pneumonia cases are caused by gram-negative aerobic bacteria including Pseudomonas, Klebsiella and Enterobacteriaceae. Given the high incidence of pneumonia in elderly hip fracture patients, it has become increasingly important to identify risk factors of pneumonia. Therefore, early detection of hip fracture patients with a tendency towards developing into pneumonia and implementing the effective intervention therapy can significantly reduce the complications and improve patient prognosis.

The purpose of this study is to determine the risk factors associated with pneumonia after hip fracture surgery and to establish a nomogram model to predict the incidence.

Materials and Methods

Inclusion and Exclusion Criteria

This study followed the guidelines of the "Declaration of Helsinki" and was approved by the hospital's ethics committee (Research Ethics Committee of the Second Affiliated Hospital of Wenzhou Medical University, L-2020-22). The data were analyzed anonymously and personal identifiers were completely removed; therefore, the requirement for informed consent was waived.

We retrospectively collected data from our hospital on geriatric hip fracture patients between August 2014 and October 2019. The eligibility criteria were: 1) femoral intertrochanteric fractures (International Classification of Diseases, 10th Revision [ICD-10] S72.1); 2) caused by a low-energy injury (eg, falls from standing height and osteoporosis); 3) ages ≥65 years; 4) recipients of surgeries including open or closed reduction internal fixation. Exclusion criteria included: 1) pathological fractures; 2) multiple fractures or multiple trauma; 3) conservative treatment; 4) loss of data; 5) history of hip fracture; 6) pneumonia occurred before surgery. In the end, there were 1113 patients included in the final analysis (Supplementary Figure).

Diagnosis of Pneumonia

In brief, the diagnostic criteria for pneumonia referred to "radiologic criteria" (chest radiographs and computed tomography) and "signs/symptoms/laboratory criteria". Postoperative Pneumonia was defined as those who did not have pneumonia before surgery but had new or increased lung infiltration on the chest X-ray and/or computed tomography images after surgery.

Analysis of Risk Factors

Blood tests were taken on the first day after admission. In our study, patients were characterized at baseline in terms of age, gender, body mass index (BMI), hemoglobin, serum albumin, c-reactive protein (CRP), creatinine, functional status, current smoking status, current drinking status, length of hospital stay, intensive care unit (ICU) admission and in-hospital mortality. The patient's previous medical history was evaluated, including diabetes, hypertension, myocardial infarction, heart failure, arrhythmia, chronic obstructive pulmonary disease (COPD), asthma and malignancy. Factors related to surgery were also assessed, including time to surgery, operative time, blood transfusion, anesthesia type, American Society of Anesthesiologists (ASA) classification.

Statistical Analysis

Continuous variables were expressed as the means ± standard deviations, and categorical variables were expressed as percentages. Comparisons between groups were performed using the χ^2-test, Fisher's exact test, and Student's *t*-test. Univariate analyses were used to evaluate the associations between different factors and the postoperative pneumonia. In order to determine the independent risk factors, variables achieving a significance of $P < 0.1$ were selected for multivariable analyses. Then, based on the regression coefficients of independent variables, we established the nomogram prediction model of postoperative pneumonia. The distinction of dichotomous results was usually evaluated by calculating the area under the curve (AUC) of the receiver operating characteristic (ROC) curve. Generally, a prediction model with an AUC of 0.5–0.75 was considered acceptable, and AUC> 0.75 means that the model shows excellent discriminative. In addition, the decision curve analysis was carried out to assess the net benefit of the nomogram to the decision. Statistical analyses were carried out using R version 3.6.1 for Windows (R Foundation for Statistical Computing, Vienna, Austria) and EmpowerStats (http://www.empowerstats.com, X&Y Solutions, Inc., Boston, MA). P values less than 0.05 (two-sided) were considered statistically significant.

Table 1 Baseline Characteristics

Variable	Total (n= 1113)	Without Pneumonia (n=947)	With Pneumonia (n=166)	P-value*
Age, years	79.9 ± 7.5	78.8 ± 7.2	86.4 ± 5.8	<0.001
BMI, Kg/m^2	23.6 ± 3.0	24.1 ± 2.8	20.6 ± 2.4	<0.001
Hemoglobin, g/L	105.8 ± 13.8	105.9 ± 14.0	104.8 ± 12.8	0.335
Serum albumin, g/dL	36.7 ± 3.1	37.3 ± 2.6	33.3 ± 3.4	<0.001
C-reactive protein, mg/L	58.8 ± 32.3	54.0 ± 29.2	85.8 ± 35.5	<0.001
Creatinine, μmol/L	83.6 ± 67.9	83.6 ± 64.6	83.9 ± 84.3	0.950
Operative time, min	52.1 ± 11.4	51.9 ± 10.8	53.0 ± 14.1	0.225
Length of hospital stay, days	9.1 ± 3.6	8.4 ± 1.4	13.3 ± 7.4	<0.001
Gender				0.450
Male	384 (34.5%)	331 (35.0%)	53 (31.9%)	
Female	729 (65.5%)	616 (65.0%)	113 (68.1%)	
Anesthesia type				0.240
Regional	819 (73.6%)	703 (74.2%)	116 (69.9%)	
General	294 (26.4%)	244 (25.8%)	50 (30.1%)	
ASA classification				<0.001
1	120 (10.8%)	117 (12.4%)	3 (1.8%)	
2	549 (49.3%)	523 (55.2%)	26 (15.7%)	
3	390 (35.0%)	280 (29.6%)	110 (66.3%)	
4	54 (4.9%)	27 (2.9%)	27 (16.3%)	
Functional status				<0.001
Independent	905 (81.3%)	828 (87.4%)	77 (46.4%)	
Dependent	208 (18.7%)	119 (12.6%)	89 (53.6%)	
Time to surgery				<0.001
Less than 48 h	635 (57.1%)	611 (64.5%)	24 (14.5%)	
More than 48 h	478 (42.9%)	336 (35.5%)	142 (85.5%)	
Smoking				0.287
No	911 (81.9%)	780 (82.4%)	131 (78.9%)	
Yes	202 (18.1%)	167 (17.6%)	35 (21.1%)	
Drinking				0.977
No	958 (86.1%)	815 (86.1%)	143 (86.1%)	
Yes	155 (13.9%)	132 (13.9%)	23 (13.9%)	
Blood transfusion				0.970
No	826 (74.2%)	703 (74.2%)	123 (74.1%)	
Yes	287 (25.8%)	244 (25.8%)	43 (25.9%)	
Diabetes				0.512
No	886 (79.6%)	757 (79.9%)	129 (77.7%)	
Yes	227 (20.4%)	190 (20.1%)	37 (22.3%)	
Hypertension				0.607
No	536 (48.2%)	453 (47.8%)	83 (50.0%)	
Yes	577 (51.8%)	494 (52.2%)	83 (50.0%)	

(*Continued*)

Table 1 (Continued).

Variable	Total (n= 1113)	Without Pneumonia (n=947)	With Pneumonia (n=166)	P-value*
Myocardial infarction				0.518
No	1062 (95.4%)	902 (95.2%)	160 (96.4%)	
Yes	51 (4.6%)	45 (4.8%)	6 (3.6%)	
Heart failure				0.721
No	1060 (95.2%)	901 (95.1%)	159 (95.8%)	
Yes	53 (4.8%)	46 (4.9%)	7 (4.2%)	
Arrhythmia				0.913
No	1048 (94.2%)	892 (94.2%)	156 (94.0%)	
Yes	65 (5.8%)	55 (5.8%)	10 (6.0%)	
COPD				0.002
No	999 (89.8%)	861 (90.9%)	138 (83.1%)	
Yes	114 (10.2%)	86 (9.1%)	28 (16.9%)	
Asthma				0.520
No	1101 (98.9%)	936 (98.8%)	165 (99.4%)	
Yes	12 (1.1%)	936 (98.8%)	165 (99.4%)	
Malignancy				0.488
No	1070 (96.1%)	912 (96.3%)	158 (95.2%)	
Yes	43 (3.9%)	35 (3.7%)	8 (4.8%)	
ICU admission				<0.001
No	1025 (92.1%)	897 (94.7%)	128 (77.1%)	
Yes	88 (7.9%)	50 (5.3%)	38 (22.9%)	
In-hospital mortality				<0.001
No	1080 (97.0%)	931 (98.3%)	149 (89.8%)	
Yes	33 (3.0%)	16 (1.7%)	17 (10.2%)	

Notes: Data are presented as the mean and the standard deviation with the range in parenthesis or expressed as the number with the percentage in parenthesis. *P-value, differences between patients with pneumonia and control.

Abbreviations: ASA score, American Society of Anesthesiologists score; BMI, body mass index; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit.

Results

From August 2014 to October 2019, 1113 hip fracture patients who were older than 65 years and underwent surgical treatment in our hospital were subjects of this study. Among them, 166 patients developed pneumonia after operation (14.91%, pneumonia group) while the remaining 947 patients did not (85.09%, non-pneumonia group) (Table 1). The average age of patients with pneumonia was 86.4 ± 5.8 years, which was significantly higher than the age of the control group ($P < 0.001$). The ratio of males among patients with pneumonia was 31.9% (53/166), which was similar to non-pneumonia group ($P = 0.450$). There was a statistically significant difference in BMI between the pneumonia group and the control group, 20.6 ± 2.4 Kg/m^2 and 24.1 ± 2.8 Kg/m^2, respectively ($P < 0.001$). Among patients with pneumonia, the serum albumin and CRP were 33.3 ± 3.4 g/dL and 85.8 ± 35.5 mg/L, whereas among the control participants, the serum albumin and CRP were 37.3 ± 2.6 g/dL and 54.0 ± 29.2 mg/L ($P < 0.001$ and $P < 0.001$, respectively). The ASA classification 1, 2, 3, and 4 were 1.8%, 15.7%, 66.3% and 16.3% in pneumonia patients, and 12.4%, 55.2%, 29.6% and 2.9% in non-pneumonia patients ($P < 0.001$). Compared to pneumonia group, the percentage of patients with the time interval between injury and surgery was ≥48 h was significantly lower in the non-pneumonia group (84.2% VS 46.2%, $P < 0.001$). The proportion of patients with dependent functional status was significantly higher in the pneumonia patients than in the control group (53.6% vs 12.6%, $P < 0.001$). In terms of prognostic implications, the elderly patients who developed pneumonia had a longer hospital stay, a higher frequency of ICU admission and a higher mortality rate during hospitalization than patients without pneumonia ($P < 0.001$, Table 1). Other baseline

Table 2 Multivariable Logistic Regression of Predictors for Postoperative Pneumonia

Variable	OR	95% CI	P value
Age, years	1.03	0.99, 1.07	0.126
BMI, Kg/m^2	0.76	0.70, 0.84	<0.001
Serum albumin, g/dL	0.86	0.79, 0.93	<0.001
C-reactive protein, mg/L	1.01	1.00, 1.02	0.011
ASA classification			
1	Ref.		
2	0.59	0.16, 2.16	0.423
3	1.46	0.39, 5.44	0.575
4	0.94	0.20, 4.53	0.941
Functional status			
Independent	Ref.		
Dependent	2.94	1.69, 5.10	<0.001
Time to surgery			
Less than 48 h	Ref.		
More than 48 h	4.56	2.64, 7.88	<0.001
COPD			
No	Ref.		
Yes	0.76	0.37, 1.58	0.469

Note: Data are presented as the odds ratio with the confidence interval in parenthesis.
Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; OR, odds ratio; CI, confidence interval.

data between the pneumonia group and non-pneumonia group showed no significant differences.

The results of univariate analysis showed that the significant risk factors were age, BMI, serum albumin, CRP, ASA classification, functional status, time to surgery and COPD ($P < 0.01$). After multivariate logistic regression analysis, BMI, serum albumin, CRP, functional status and time to surgery were identified as independent risk factors of pneumonia associated with elderly patients after a hip fracture (Table 2).

Then, we established a nomogram for predicting postoperative pneumonia including the five independent risk factors based on the multivariate logistic regression analysis (Figure 1). To use the nomogram, the points corresponding to each prediction variable were obtained, and then the sum of the points was calculated as the total score, and the predicted risk corresponding to the total score was the probability of postoperative pneumonia. We drew the ROC curve of predicted probability and calculated the AUC value. The AUC value for postoperative pneumonia risk was 0.905, suggesting that the nomogram prediction model has an excellent discrimination (Figure 2). The Hosmer-Lemeshow test also showed that the nomogram prediction model had good calibration ability ($P = 0.529$, Figure 3A). We assumed that the predicted probability above the defined threshold would determine the treatment decision for the patients, while the predicted probability below the threshold would generate other decisions. Therefore, we established a decision analysis curve to assess the net benefit of the nomogram to the decision. The result indicated that the nomogram was applicable when the threshold was in the range of 0.03 to 0.76 due to the net benefit (Figure 3B).

Discussion

Hip fracture is one of the common causes of hospitalization in the elderly patients. Postoperative pneumonia is the main complication of hip fracture surgery in the elderly,

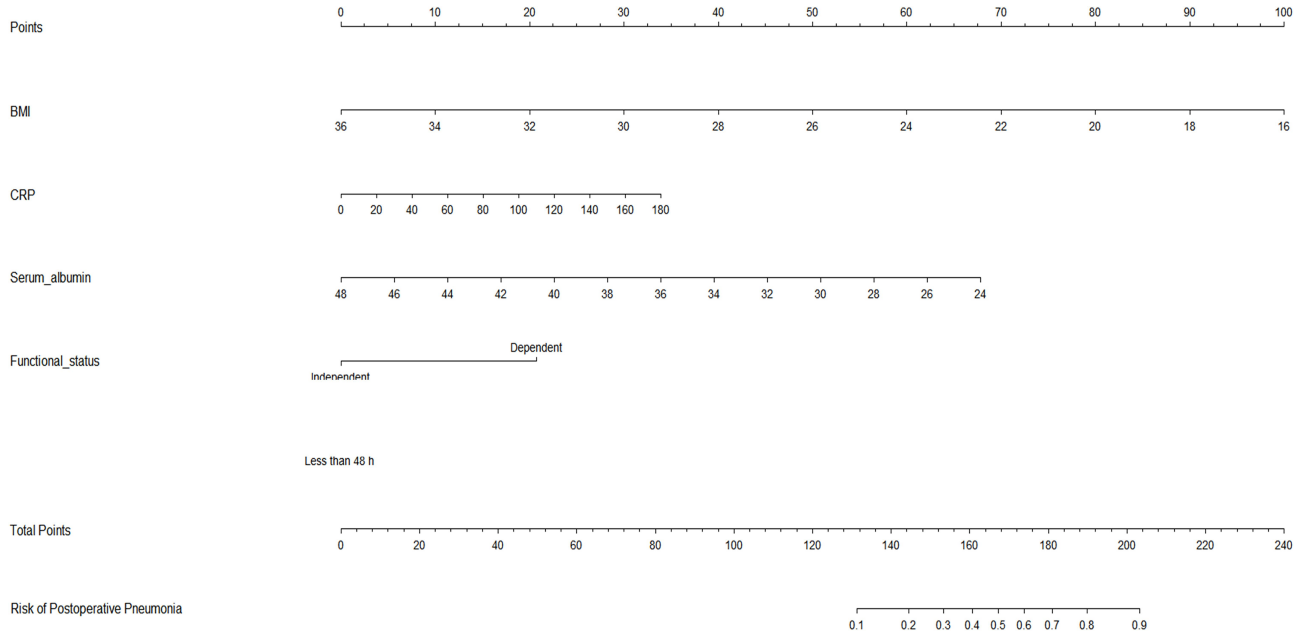

Figure 1 Predictive nomogram for postoperative pneumonia. To use the nomogram, the points corresponding to each prediction variable were obtained, then the sum of the points was calculated as the total score, and the predicted risk corresponding to the total score was the probability of postoperative pneumonia.

with a mortality rate as high as 30% to 44%.[16] Roche et al showed that postoperative pneumonia was diagnosed in 8.8% of elderly hip fracture patients, which was the most common complications and resulted in increased mortality.[17] In a study about geriatric hip fracture complications in 153,613 Canadian patients, the incidence of postoperative pneumonia was also 4.9%.[18] Lv et al also reviewed 1429 patients who underwent hip fracture surgery in China, and 4.9% of them developed postoperative pneumonia.[13] Recently, Jang et al retrospectively analyzed 14,736 Korean hip fracture patients ≥65 years old, 11.05% of patients suffered from pneumonia during hospitalization.[19] However, 14.9% of elderly hip fracture patients were identified as pneumonia after surgery in this study, which was slightly higher than the previous articles. This might be related to the increasing social aging in recent years.

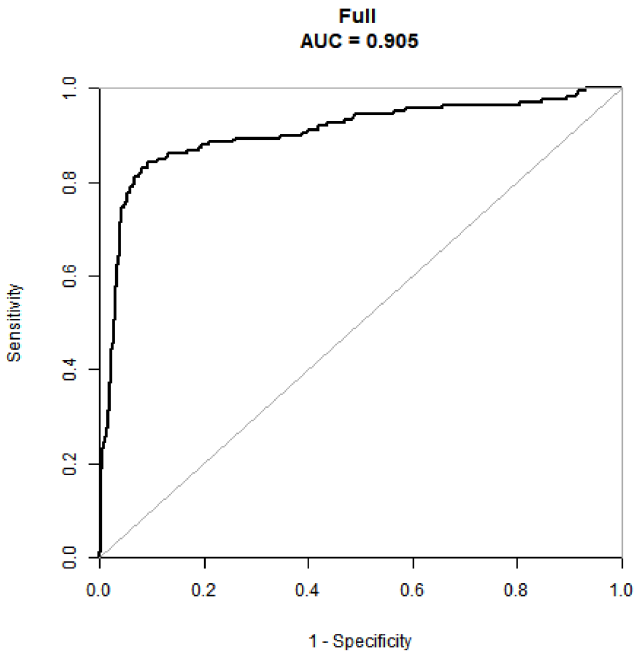

Figure 2 ROC curves for validating the discrimination of the nomogram prediction model.

Among elderly hip fracture patients, the risk factors for postoperative pneumonia development remained controversial. Potential risk factors for postoperative pneumonia might include age, gender, BMI, hemoglobin, serum albumin, CRP, functional status, current smoking status, heart failure, COPD, time to surgery, operative time, blood transfusion and ASA classification.[12,13,20–23] In the present study, BMI, CRP, serum albumin, functional status and time to surgery were identified as independent risk factors for postoperative pneumonia (Table 2). On the other hand, no significant differences were observed in the hemoglobin, creatinine, gender, anesthesia type, blood transfusion, current smoking status, current drinking status, operative time, history of hypertension, history of diabetes, history of circulatory disease and history of malignancy.

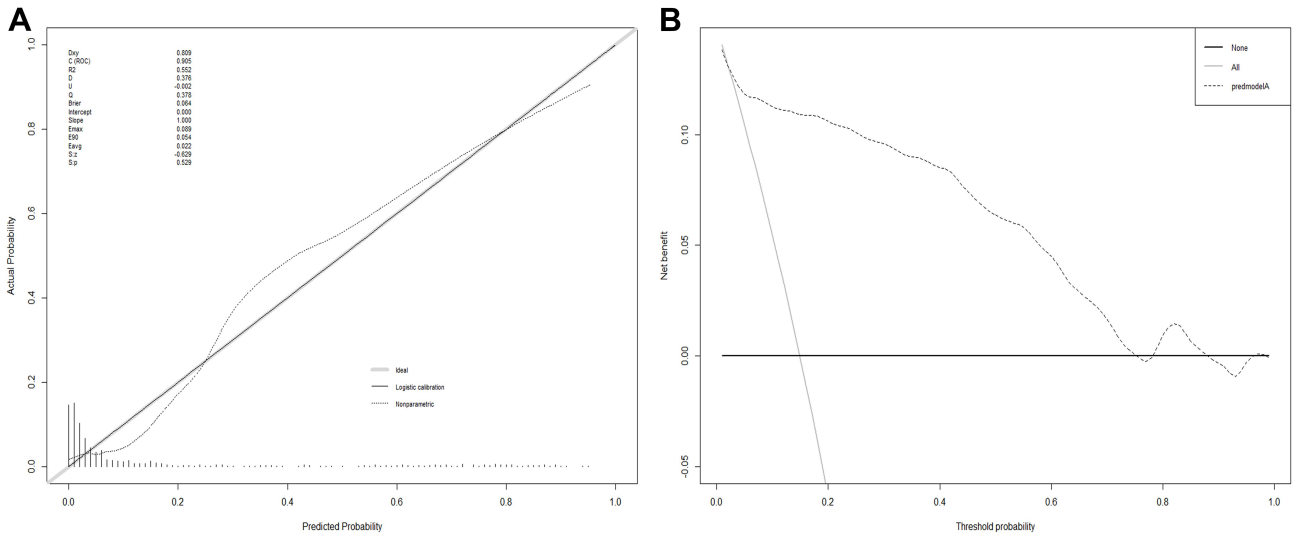

Figure 3 Calibration and decision plot of the nomogram for the probability of postoperative pneumonia. (**A**) Calibration plot. (**B**) Decision plot.

Some previous studies had shown that complications after orthopedic surgery were usually associated with higher BMI.[24,25] However, malnutrition, low BMI and serum albumin had been maintained as risk factors for postoperative pneumonia.[20,26,27] The reason might be that elderly patients often had difficulty swallowing, which could lead to low body mass index, malnutrition and aspiration pneumonia. And malnourished patients had weak immune defenses and were susceptible to infections. We found that patients with high CRP levels before surgery were prone to postoperative pneumonia. Similarly, Takao et al reported that preoperative high C-reactive protein levels were a risk factor for acute exacerbation of interstitial lung disease after non-pulmonary surgery.[28] The reason for this phenomenon perhaps was that high CRP induced macrophages to secreted various inflammatory cytokines, such as tumor necrosis factor alpha and interleukin (IL) −1.

Many studies and guidelines recommended that older patients with hip fractures underwent surgery as soon as possible because early surgery could reduce postoperative complications and mortality.[29–32] This was consistent with our results. Patients who were delayed in receiving surgical treatment had an increased risk of postoperative pneumonia. Advocating early surgery was beneficial for early restoration of motor function and reduction of complications associated with bed rest. In addition, we found that patients with dependent functional status had an increased probability of developing postoperative pneumonia. Such patients were often elderly and long-term bedridden, which was probably the main reason.

In this study, elderly patients who developed pneumonia after hip fracture had a longer hospital stay, a higher frequency of ICU admission and a higher mortality rate during hospitalization than patients without pneumonia. Taking preventive measures for patients with a high risk of postoperative pneumonia could improve the prognosis process and reduce hospitalization costs. Interventions included maintaining an upright posture while eating, encouraging coughing and deep breathing exercises, raising the head of the bed to at least 30 degrees, encouraging out of bed walking through good pain control, and performing oral hygiene with chlorhexidine twice each day.[33]

There were several limitations in our study. First, this was a retrospective study, and selection bias was unavoidable. Second, we did not collect information on preoperative and intraoperative drug use, perioperative antibiotic use and care programs. Third, the data in this article came from a single center and the amount of data was limited.

Conclusion

In this study, we found that BMI, CRP, serum albumin, functional status and time to surgery were the independent risk factors for postoperative pneumonia. Our nomogram model can be used to predict the risk of pneumonia in elderly hip fractures after surgery, and provide clinicians with guidance for better perioperative intervention to improve prognosis and reduce mortality.

Data Sharing Statement

Patient data comes from our hospital's medical record follow-up database, transparent and available.

Ethical Statement

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study followed the guidelines of the "Declaration of Helsinki" and was approved by the hospital's ethics committee (Research Ethics Committee of the Second Affiliated Hospital of Wenzhou Medical University, L-2020-22). The data were analyzed anonymously and personal identifiers were completely removed; therefore, the requirement for informed consent was waived.

Code Availability

Statistical analyses were carried out using R version 3.6.1 for Windows (R Foundation for Statistical Computing, Vienna, Austria) and EmpowerStats (http://www.empowerstats.com, X&Y Solutions, Inc., Boston, MA).

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Author Contributions

Guangheng Xiang and Yi-Min Weng contributed to the conception and design. Yi-Min Weng, Yongzeng Feng and Jian Xiao contributed to the administrative support. Guangheng Xiang, Tao Xu, Zili He, Chen-Rong Ke and Xiaoyu Dong contributed to the provision of study materials or patients. Guang-Heng Xiang, Yongzeng Feng and Jian Xiao contributed to the collection and assembly of data. Guangheng Xiang, Chen-Rong Ke and Xiaoyu Dong contributed to the data analysis and interpretation. All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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Disclosure

Guangheng Xiang, Xiaoyu Dong, Tao Xu, Yongzeng Feng, Zili He, Chenrong Ke, Jian Xiao and Yi-Min Weng have no conflicts of interest to disclose in relation to this article. The authors declare no competing financial interests.

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