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ORIGINAL RESEARCH

Gender and Low Albumin and Oxygen Levels are Risk Factors for Perioperative Pneumonia in Geriatric Hip Fracture Patients

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Introduction: Pneumonia is a serious complication following hip fracture and is the primary risk factor for 30-day mortality after surgery. Modifying several laboratory factors may improve the outcomes of fragile hip fracture patients who are 80 years or older.

Purpose: To investigate several adjustable factors for perioperative pneumonia in order to improve patient prognosis and reduce mortality.

Patients and Methods: We retrospectively reviewed in-hospital hip fracture data from patients who were 80 years or over between January 1, 2014, and November 31, 2014, from Beijing Jishuitan Hospital. Patients were divided into two groups: perioperative pneumonia (POP) group and non-perioperative pneumonia (non-POP) group. Logistic regression models were used to identify independent risk factors. Statistical significance was set at 5% ($p<0.05$).

Results: The incidence of perioperative pneumonia (POP) in patients 80 years and older was 11.3% (33/293). Male patients had a higher incidence of POP (20/96 cases, 20.83%) compared to females (13/197, 6.6%)($P<0.001$). Higher neutrophilic granulocyte percentages (78.148%±9.162% in POP vs 81.959%±6.142% in Non-POP, P=0.033) and lower albumin levels ($\chi^2=2.25$, P=0.039) were observed in the POP group at baseline. After multivariate logistic regression, we observed that males (OR=3.402, P=0.048), lower albumin levels (OR=10.16, P=0.001) and PaO2 levels (OR=2.916, P=0.007) were independent risk factors for POP.

Conclusion: Low albumin and oxygen levels and the male gender were risk factors for perioperative pneumonia in geriatric hip fracture patients.

Keywords: hip fracture, pneumonia, elderly, perioperative, male, hypoalbuminemia, arterial blood gas analysis

Introduction

Osteoporosis-related hip fractures in the geriatric population are fairly common.[1–3] Nearly 1.5 million individuals experience hip fractures per year worldwide, and this number is expected to grow with the aging population.[1] Approximately 6.3 million people will suffer hip fractures by 2050.[4,5] Pneumonia is a serious complication following hip fracture and is a primary risk factor for 30-day mortality after surgery.[6,7] Lv et al[8] demonstrated that the all-cause mortality of patients with postoperative pneumonia was markedly higher compared to patients without postoperative pneumonia at 30 days after surgery (hazard ratio 3.05). This effect was still observable at 1 year (hazard ratio 1.87) and 2 years (hazard ratio 1.57) after surgery. Age was identified as a significant factor for poor prognosis. A study of 240 elderly hip fracture patients (≥65 years) demonstrated that patients over 80 years old had

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a higher risk of developing pneumonia.[9] A population-based surveillance for community-acquired pneumonia found that the highest annual incidence of pneumonia was among patients ≥80 years.[10] Age, the number of comorbidities and chronic obstructive pulmonary disease were correlated with the occurrence of perioperative pneumonia after hip fracture in elderly patients.[8,11] However, all of these conditions are unalterable factors. Whether these factors lead to the occurrence of perioperative pneumonia in patients 80 years and over is unknown. Certain laboratory indexes may be associated with the prognosis of hip fractures. Modifying these laboratory factors may improve the outcome of fragile hip fracture patients 80 years and older.

The main aim of our study was to investigate several adjustable factors for perioperative pneumonia in order to improve patient prognosis and reduce mortality.

Materials and Methods

Patients

We retrospectively reviewed in-hospital hip fracture patient data between January 1, 2014, and November 31, 2014, obtained from Beijing Jishuitan Hospital. The database was constructed meticulously by trained personnel. Consecutive hip fracture patients who were 80 years and older were identified using this electronic patient record database. The inclusion criteria for retrospective analysis included: (1) patients who had a femoral neck or intertrochanteric fracture within a month of admission; (2) patients 80 years and older; (3) in-patients who had the intention to undergo hip fracture surgery. Hip fractures were confirmed by X-ray or computed tomography. Perioperative pneumonia was defined as: (1) presence of new respiratory symptoms such as coughing and expectoration after hip fracture and during the perioperative period; (2) progressive chronic respiratory symptoms including coughing, expectoration, and shortness of breath; (3) fever or hypothermia; (4) new infiltrations observed in chest X-rays or computed tomography. Patients with pathologic fractures were excluded from this analysis.

Patient Characteristics

Demographic data including age, gender, major comorbidities, and smoking were recorded. Major comorbidities included chronic obstructive pulmonary disease, hypertension, coronary heart disease, arrhythmia, type 2 diabetes, prior incidence of stroke, chronic renal failure, dementia, Parkinson's disease, and cancer.

Laboratory indicators included complete blood counts, arterial blood gas analysis and biochemical analyses (serum albumin, creatinine, urea nitrogen, alanine transaminase, aspartate transaminase, gamma-glutamyl transpeptidase, alkaline phosphatase, electrolytes). Laboratory measurements and chest examinations (X-ray or computed tomography) were performed at the time of admission.

Fracture and treatment details were recorded, including fracture type, treatment, the American Society of Anesthesiologists (ASA) score and anesthesia method.

For regression analyses, several continuous factors were transformed into grading variables. White blood cell levels were stratified as leukopenia, normal or leukocytosis. Hemoglobin levels were stratified into dichotomous variables as anemia or normal. Albumin levels were classified into low albumin and normal levels. PaO2 was classified as normal, hypoxemia or respiratory failure.

The study protocol was approved by the institutional review board at Peking University Health Science Center. A written informed consent was obtained from all the patients at the time of admission, with which the tissue, blood and other samples might be used for scientific research but did not relate to patient's privacy.

Statistical Analysis

Patients were divided into two groups, ie, the perioperative pneumonia (POP) group, and the non-perioperative pneumonia (non-POP) group. Normally distributed variables were presented as mean±standard deviation, and non-normally distributed variables were presented as median with quartiles. Student's *t*-test or Mann–Whitney *U*-test was used for continuous variables to compare differences between groups, while the chi-square test or Fisher exact test was used for categorical variables. Logistic regression models were used to identify independent risk factors. All variables that showed statistical differences were included for univariate logistic regression analyses and then for multivariate logistic regression analyses if statistical significance was observed in univariate analyses. All statistical analyses were performed using the Statistical Product and Service Solutions (SPSS) software version 23.0 (IBM Corporation, Chicago, USA). Statistical significance was set at 5% ($p<0.05$).

Results

Baseline Characteristics

Of the 293 patients included in this retrospective analysis, there were 96 males and 197 females. The average age was

85.1 years (85.1±3.3). The incidence of perioperative pneumonia (POP) in patients 80 years and older was 11.3% (33/293). Demographic characteristics and major comorbidities are summarized in Table 1. Fracture and treatment details are summarized in Table 2. Baseline laboratory variables are shown in Table 3. Male patients had a higher incidence of POP (20/96, 20.8%) compared to females (13/197, 6.6%) (P<0.001). Patients in the POP group were more likely smokers (8/33,24.2% vs.24/260,9.2%), (P=0.009). There were no significant differences between intertrochanteric and femoral neck fracture patients (χ^2=0.042, P=0.84). Surgical procedures and types of anesthesia were not associated with the development of perioperative pneumonia. Higher neutrophilic granulocyte percentages (χ^2=−2.24, P=0.033) and low albumin levels (χ^2=2.25, P=0.039) were observed in the POP group at baseline.

Risk Factors for Post-Hip Fracture Pneumonia

Logistic regression analysis was performed to identify factors that may be associated with POP in patients 80 years and older. We observed that the male gender, smoking, hypoalbumin and PaO2 levels (hypoxemia or respiratory failure) were risk factors for perioperative pneumonia after hip fracture in elderly patients (≥80 years old) (Table 4, univariate analysis). After multivariate logistic regression, we observed that the male gender (OR=3.402, P=0.048), low albumin levels (OR=10.16, P=0.001) and PaO2 levels (OR=2.916, P=0.007) were independent risk factors for POP (Table 5).

Table 2 Fractures and Treatment Details

Items	Non-POP (n=260)	POP (n=33)	χ^2	P-value
Fracture type			0.042	0.837
Intertrochanteric	131	16		
Femoral neck	129	17		
Surgical procedures			1.394	0.498
Intramedullary fixation	36	2		
Hip replacement	184	18		
Other procedures	4	1		
ASA scores			0.390	0.532
I/II	209	25		
III/IV	51	8		
Anesthesia method			0.029	0.866
General	24	2		
Regional	200	19		

Notes: Other procedures included extramedullary fixation, external fixation, and simple fixation.
Abbreviations: Non-POP, non- perioperative pneumonia; POP, perioperative pneumonia; ASA, American society of anesthesiologists.

Discussion

Pneumonia is a serious complication after hip fracture during the perioperational period. Patients with postoperative pneumonia have a significantly higher 30-day all-cause death rate (27.1%) compared to patients without postoperative pneumonia (1.1%).[8] Advanced age is an important risk factor for postoperative pneumonia. Patients who are 80 years and older have a higher risk of post-hip fracture pneumonia. However, only a few studies had focused on the higher risk of postoperative pneumonia in patients 80 years and older. In this study, we observed

Table 1 Demographic Characteristics and Major Comorbidities

Item	Non-POP (n=260)	POP(n=33)	χ^2 or t value	P-value
Age (years)	85.1±3.4	84.5±3.2	0.692	0.490
Gender(male/female)	76/184	20/13	13.086	0.000*
Smoking(%)	24(9.2%)	8(24.2%)	6.783	0.009*
COPD(%)	8(3.1%)	2(6.1%)	0.791	0.374
Hypertension	130(50%)	18(54.6%)	0.242	0.623
Coronary heart disease	48(18.5%)	10(30.3%)	2.586	0.108
Arrhythmia	14(5.4%)	2(6.1%)	0.026	0.872
Type 2 diabetes	44(16.9%)	6(18.2%)	0.033	0.856
Prior stroke	45(17.3%)	6(18.2%)	0.016	0.901
Chronic renal failure	10(3.9%)	3(9.1%)	1.900	0.168
Dementia	4(1.5%)	1(3.0%)	0.389	0.533
Parkinson's disease	10(3.9%)	1(3.0%)	0.054	0.816
Tumors	34(13.1%)	4(12.1%)	0.024	0.878

Note: *P<0.05.
Abbreviations: Non-POP, non- perioperative pneumonia; POP, perioperative pneumonia; COPD, chronic obstructive pulmonary disease.

Table 3 Baseline Laboratory Examinations

Items	Non-POP (n=260)	POP(n=33)	t value	P value
Arterial Blood Gas Analysis				
Oxygen pressure	73.00±13.45	67.57±17.78	1.492	0.138
Carbon dioxide pressure	34.40±6.24	33.71±5.19	0.439	0.661
Oxygen saturation	94.47±2.56	92.39±4.61	1.824	0.085
Blood Routine Test				
Leukocyte	9.28±3.56	10.70±2.19	−1.605	0.111
Hemoglobin	124.02±15.33	123.71±16.36	0.080	0.937
Platelet	204.42±68.06	221.00±88.53	−0.908	0.365
Neutrophilic granulocyte percentage	78.15±9.162	81.96±6.14	−2.243	0.033*
Serum Biochemical Analyses				
Alanine transaminase	14.97±25.87	30.41±68.69	−0.918	0.372
Aspartate transaminase	21.48±36.71	31.06±41.55	−0.994	0.322
Serum albumin	39.90±5.20	34.99±8.55	2.246	0.039*
Alkaline phosphatase	76.05±46.76	55.94±18.11	1.788	0.076
Gamma-glutamyl transpeptidase	31.13±29.49	38.75±28.16	−0.976	0.331
Creatinine	72.38±27.70	80.65±19.71	−1.189	0.237
Urea nitrogen	7.38±3.10	8.88±3.08	−1.867	0.064
Electrolytes				
Potassium	4.19±0.47	4.07±0.43	1.002	0.318
Sodium	139.83±10.01	138.75±5.66	0.435	0.664
Chlorine	105.07±3.59	104.41±4.64	0.685	0.494

Note: *P<0.05.
Abbreviations: Non-POP, non- perioperative pneumonia; POP, perioperative pneumonia.

Table 4 Univariate Logistic Regression Analyses for Risk Factors of POP

Variables	χ^2 value	p value
Gender, male	13.086	0.000*
Smoking history	6.783	0.009*
Oxygen level	6.707	0.035*
Hypoalbuminemia	14.350	0.000*
Neutrophilic granulocyte level, elevated	2.299	0.129

Note: *P<0.05.
Abbreviation: POP, perioperative pneumonia.

Table 5 Multivariate Logistic Regression Analyses for Risk Factors of POP

Variables	OR	95% CI		p value
		Lower	Upper	
Gender, male	3.402	1.012	11.439	0.048*
Smoking	2.580	0.440	15.113	0.293
Hypoalbuminemia	10.159	2.698	38.251	0.001*
Oxygen level	2.916	1.346	6.316	0.007*

Note: *P<0.05.
Abbreviations: POP, perioperative pneumonia; OR, odds ratio; CI, confidence interval.

that hypoalbuminemia, hypoxemia and the male gender were independent risk factors for post-hip fracture pneumonia in patients 80 years and older. Of these factors, hypoalbuminemia and hypoxemia were adjustable factors. Sufficient nutrition and oxygen therapy may reduce the chances of perioperative pneumonia in these fragile patients and hence improve prognosis.

Several studies have demonstrated that the incidence of postoperative pneumonia in hip fracture patients were 4.1–4.9%.[8,11] In our study, we found that the incidence of perioperative pneumonia in hip fracture patients 80 years and older was 11.3%, and was significantly higher compared to the general population of patients with hip fractures. One reason could be that the patients in our study were much older. In addition, several studies only included post-operative patients. We found that 12 of the 33 patients were not suitable to undergo surgery due to poor health. We could have excluded 36.4% of the patients if we only included post-surgical patients. However, we believe that it is better to include all patients with hip fractures who were 80 years and above to determine all risk factors for the development of post-hip fracture pneumonia. We need to pay special attention to this patient cohort to improve prognosis.

Malnutrition is prevalent among the elderly. Corti et al[12] investigated 4116 individuals (≥71 years of age) who resided in communal settings and demonstrated that serum albumin levels were an independent risk factor for 1-year mortality. In a cohort study involving 2513 Caucasian females (≥45 years of age), Huang et al[13] demonstrated that hypoalbuminemia was associated with hip fractures. In addition, a retrospective cohort study[14] of 29,377 geriatric patients (≥65 years of age) found that hypoalbuminemia was a strong independent risk factor for mortality following hip fracture surgery. Our study demonstrated that low albumin levels were also a risk factor for perioperative pneumonia in elder hip fracture patients (≥80 years of age). Patients with hypoalbuminemia have lower nutritional reserves and weaker immune systems. However, it is a modifiable factor. Nutritional supplements and reversing hypoalbuminemia may be potentially helpful to reduce perioperative pneumonia rates in elderly hip fracture patients. From a public health perspective, improving nutritional status in elderly patients would be beneficial. Additional studies are needed the determine the effect of nutritional supplements in elderly hip fracture patients.

The role of arterial blood gases during hip fracture surgery is unclear. The guidelines of risk assessment for non-cardiothoracic surgeries do not mention arterial blood gases.[15] We found that oxygen levels in arterial blood was a risk factor for perioperative pneumonia in elderly hip fracture patients. Lower oxygen levels are often related to pulmonary and cardiovascular diseases. A large number of patients do not visit their doctors on a regular basis and neglect their symptoms. Hence, self-reported comorbidities may be underestimated. Our study demonstrated that arterial blood gases may be useful for predicting perioperative pneumonia. Whether arterial blood gas analysis should be recommended for preoperative risk assessment of hip fracture surgery requires further study. Additional studies should be performed to determine the role of arterial blood gases, especially in developing countries.

Cigarette smoking is a risk factor for postoperative pneumonia.[16,17] Current smokers and higher smoking frequency further increase the risk of postoperative pneumonia.[18] In our study, smoking was a risk factor identified by univariate logistic regression analyses, but not in multivariate logistic regression analyses. Additional studies using larger patient cohorts are necessary to determine whether smoking increases the incidence of postoperative pneumonia in hip fracture patients aged 80 years and above.

There were several limitations to our study. First, retrospective observational studies, in general, have an inherent bias. However, the dataset that was used was from a prospective database that was accurately constructed by trained staff. Second, the analysis was performed using a dataset obtained from a single center with a relatively small patient cohort size. Patient admission bias could have been present. Additional multi-center studies using larger patient cohorts are necessary to validate our findings. Third, comorbidities were obtained using patient self-reports and hence could have been underestimated due to some patients not visiting the doctor and their symptoms not being diagnosed. The focus of this study was to identify factors that could be improved, hence not properly reporting comorbidities that may be risk factors for pneumonia could have affected the final conclusions of our study.

Conclusion

The male gender, low albumin, and oxygen levels are risk factors for perioperative pneumonia in hip fracture patients 80 years and older.

Disclosure

The authors report no conflicts of interest in this work.

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