

BMJ Open Partial pressure of oxygen level at admission as a predictor of postoperative pneumonia after hip fracture surgery in a geriatric population: a retrospective cohort study

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To cite: Ji Y, Li X, Wang Y, *et al*. Partial pressure of oxygen level at admission as a predictor of postoperative pneumonia after hip fracture surgery in a geriatric population: a retrospective cohort study. *BMJ Open* 2021;**11**:e048272. doi:10.1136/bmjopen-2020-048272

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2020-048272>).

Received 24 December 2020
Accepted 12 October 2021



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ABSTRACT

Objective To identify whether the partial pressure of oxygen in arterial blood (PaO₂) level at admission is an independent risk factor as a prognostic biomarker to predict postoperative pneumonia (POP) in the geriatric population who have undergone hip fracture surgical repair at our hospital.

Design A retrospective cohort study.

Setting This is a retrospective chart review of POP after hip fracture surgery in China.

Participants In training cohort, patients aged ≥65 years who had hip fracture surgery between 1 January 2018 and 30 November 2019. In the validation cohort, a series of patients who underwent hip fracture surgery between 1 January 2020 and 28 February 2020.

Interventions Receiver operating characteristic (ROC) analysis was used to obtain the area under the ROC curve (AUC) and cut-off values of PaO₂ to predict POP. A binomial logistic regression model was used to identify potential risk factors for POP by analysing demographic distribution factors, laboratory results, preoperative comorbidities and surgical factors. Then the regression model was validated using an independent cohort.

Results In the training cohort, ROC curves were generated to compare the predictive performance of PaO₂ for the occurrence of POP, and the area under the receiver operating characteristic curve (AUC) was 0.653 (95% CI 0.577 to 0.729, p<0.0001), with sensitivity and specificity values of 60.0% and 63.8%, respectively. The cut-off value of the PaO₂ for POP was 72.5 mm Hg. Binary logistic regression analysis revealed that hypoxaemia (PaO₂ <72.5 mm Hg) at hospital admission (OR=3.000, 95% CI 1.629 to 5.528; p<0.0001) was independent risk factors associated with POP after hip fracture surgery. In the validation cohort, PaO₂ had a predictive effect for POP (AUC 0.71, 95% CI 0.541 to 0.891).

Conclusions The current study revealed that the PaO₂ level at hospital admission is a simple and widely available biomarker predictor of POP after hip fracture surgery in elderly patients.

INTRODUCTION

Hip fractures represent a major public health concern in the geriatric population

Strengths and limitations of this study

- A retrospective real-world observational study.
- To ensure that our choice patients is representative, our sample in training cohort includes all patients aged ≥65 years who had hip fracture surgery were eligible retrospectively reviewed between 1 2018 and 30 November 2019 at our hospital.
- This study used a multivariate logistic regression analysis to control all potential confounders.
- The partial pressure of oxygen in arterial blood level at admission might be influenced by several factors that may cause a deviation in the conclusion.
- The problem of reverse causality is an important limitation of this study.

because the population continues to age and the absolute number of hip fractures is set to increase. The number of hip fractures occurring worldwide is expected to increase significantly from 1.66 million in 1990 to surpass 6 million by the year 2050.¹ Hip fractures are classified according to the anatomical location of fracture into fractures of the intertrochanteric regions and femoral neck.^{2 3} Several treatment options exist for hip fractures, including total hip arthroplasty (THA), hemiarthroplasty, internal fixation and non-operative treatment. Surgery to treat hip fracture has been known as the gold-standard treatment in the geriatric population.⁴ Mortality following hip fractures is high despite the advances in regional anaesthesia and surgical techniques. Several studies have reported that the mortality rates after hip fracture surgical repair in the elderly range from 6.2% to 7.0% within the 1-month follow-up.^{5 6} Moreover, up to 14.1%–30.0% of the patients with a hip fracture die within the first year after surgical repair.^{7 8} Current studies have

found that pre-existing comorbidities and postoperative complications are associated with the high morbidity and mortality of hip fracture.⁹ Among all the postoperative complications in the hip fracture population, postoperative pneumonia (POP) is one of the most frequent and devastating complications.^{6 10} Previous studies have shown that POP affects 4.6%–13.9% of all patients with hip fracture.^{9 11 12} In clinical practice, even after providing perioperative care and standard therapy, patients with POP still have higher unsatisfactory outcomes and mortality. Additionally, 11.4%–14.0% of patients with hip fracture with POP die within 30 days compared with only 1.7%–5.7% of those without POP.^{13–15} Previously, reported risk factors for developing POP include male sex, older age, diabetes, chronic obstructive pulmonary disease (COPD), hypoalbuminaemia, prior stroke and multiple-organ failure.^{12 15 16}

Arterial blood gas (ABG) is an effective method to estimate partial pressure of oxygen in arterial blood (PaO_2), partial pressure of carbon dioxide in arterial blood (PCO_2) and acid–base and pH (potential of hydrogen (PH)) values, usually to assess the oxygen status and/or acid–base status.¹⁷ ABG is frequently used to test inpatients admitted for hip fracture in the geriatric population. PaO_2 is a simple and easy parameter to obtain in the hospital, and the PaO_2 level is associated with increased short-term or long-term adverse events after surgery in elderly patients with hip fracture.¹⁸ PaO_2 appears to be useful for preoperative evaluation. However, to our knowledge, few studies have investigated the admission room air partial pressure of oxygen level as a risk factor to predict POP in the elderly population undergoing surgical repair of hip fractures. Therefore, we performed a retrospective review of patients aged 65 years or older hospitalised for hip fractures at our hospital. This study was aimed to evaluate the relationship between the PaO_2 level at admission and POP and to identify whether the PaO_2 level at admission is an independent risk factor as a prognostic biomarker to predict POP in the geriatric population who have undergone hip fracture surgical repair at our hospital. Furthermore, the results could contribute to stratify risk for geriatric population and provide moderate evidence for clinicians to determine appropriate therapeutic strategies.

MATERIALS AND METHODS

Study population

This was a single-centre retrospective cohort study of the electronic medical records of all elderly patients 65 years of age or older who underwent surgery for an acute closed hip fracture at the Honghui Hospital, Xi'an Jiaotong University, a 1500-bed, large-scale, university-affiliated hospital located in Shannxi, China, between 1 January 2018 and 30 November 2019. We reviewed the medical records of 1123 patients who fulfilled the following criteria and were eligible for inclusion or exclusion. Ultimately, a total of 901 patients with hip fracture

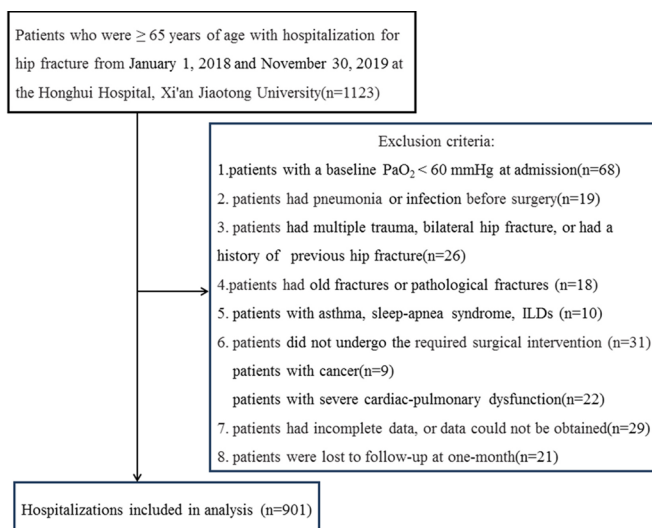


Figure 1 Flowchart of the patient selection process. **ILD, interstitial lung disease; PaO_2 , partial pressure of oxygen in arterial blood.**

were considered suitable to enter the training cohort. In the validation cohort, a series of 160 new patients who underwent surgery for an acute closed hip fracture in the same hospital between 1 January 2020 and 28 February 2020 was used to validate the model, which was constructed in the training phase. The inclusion criterion was a new confirmation of a femoral neck or intertrochanteric fracture using X-ray and/or CT in patients aged 65 years or older. The exclusion criteria were as follows: (1) patients with a baseline room air PaO_2 of <60 mm Hg at admission; (2) patients with X-ray-confirmed and/or CT-confirmed preoperative infection or preoperative pneumonia; (3) patients with multiple traumas, bilateral hip fracture or a history of hip fracture; (4) patients with old fractures or pathological fractures; (5) patients with asthma, sleep-apnea syndrome and interstitial lung diseases; (6) patients with incomplete or unavailable data; (7) patients who did not undergo the required surgical intervention; and (8) patients lost to follow-up within the 30-day postoperative period. The flowchart representing the selection of study participants is shown in figure 1.

Patient and public involvement

No patient was involved.

Data collection

All patients in the two independent cohorts had basic demographic distribution, laboratory test results and comorbid conditions, and preoperative and operative characteristics were collected for each patient. The patients' demographic characteristics included age, gender, height and weight. Comorbid conditions were identified from either the admission notes or charts. The list of major comorbidities included circulatory abnormalities (hypertension and coronary heart disease), COPD, type 2 diabetes and prior stroke (stroke was previously diagnosed by cranial CT). Blood samples were collected

for routine laboratory parameters. In addition to the ABG analysis results (PaO_2 , pH and PaCO_2), we recorded the haemoglobin (Hb) level, white blood cell (WBC) count, platelet (PLT) count, creatinine (Cr) level, blood urea nitrogen (BUN) level, total bilirubin (TBIL) level, glutamic pyruvic transaminase (ALT) level and glutamic oxaloacetic transaminase (AST) level for each patient within the first 24 hours of admission to our hospital. All the patients underwent chest radiography before surgery. The fracture and treatment details, including the fracture type, surgical type, duration of the surgery, intraoperative blood loss, time interval from injury to operation (defined as the difference between the injury date and operation date) and the length of hospital stay, were also collected. Two well-trained members of the study team performed the clinical reviews. Regardless of whether POP was a complication after surgery, the data were extracted from the medical records of each patient and recorded in a standardised form, and then the patients were followed up 30 days postoperatively to track the occurrence of POP.

Diagnosis of POP

The primary end point for this study was the diagnosis of POP in the first 30 days postoperatively. The diagnosis of POP was established when a patient developed a new and persistent pulmonary infiltrate on chest X-ray and/or CT images, and then those who were considered to present POP also had to meet one or more of the following criteria: (1) presence of new and/or progressive and steady clinical symptoms, including cough, dyspnoea or expectoration; (2) moist rale and/or lung consolidation by clinical examination; (3) body temperature abnormalities (body temperature $>38^\circ\text{C}$ or body temperature $<36.0^\circ\text{C}$); (4) WBC abnormalities (white cell count $>10\times 10^9/\text{L}$ or $<4\times 10^9/\text{L}$); and (5) positive bacterial culture of blood samples or sputum samples.^{12 15 16}

Statistical analysis

The patients were divided into two groups according to whether they developed pneumonia: a POP group and a non-POP group. Continuous, normally distributed variables were expressed as means \pm SD. Additionally, non-normally distributed parameters were expressed as medians with IQRs (25% and 75%). The clinical characteristics were compared between the two groups. Normally distributed and equal variance continuous variables were analysed using Student's t-test, and the non-normal data were tested using the Mann-Whitney U test. To study such categorical variables, the number of patients in each category (sex, fracture type, surgical approaches and comorbidities) was counted and recorded as absolute values and percentage, and univariate analysis by Pearson's χ^2 test was performed to examine potential risk factors among categorical variables. Receiver operating characteristic (ROC) curve and area under the curve analyses were performed to evaluate the predictive performance of PaO_2 for the occurrence of POP within 30 days after the operation. POP groups and non-POP

groups as dichotomous dependent variables, the admission PaO_2 levels as independent variables. Use ROC curve to identify the optimal cut-off values for predicting POP. Binomial multivariable logistic regression analysis using the forward stepwise selection method was conducted to determine potential risk factors that significantly predict 30-day POP in patients following hip fracture surgery and to determine the associations between PaO_2 level and POP in the elderly patients with hip fracture. First, univariate analysis was performed to evaluate the relationship between POP and all the covariates (including patient demographics, preoperative comorbidities, laboratory test results and operative characteristics). Variables with p values of <0.1 were considered for inclusion in the adjusted multivariable logistic regression analysis. The outcomes of the regression analysis were expressed as ORs with 95% CIs. Subgroup analysis was performed by repeating the binomial univariate and multivariate analyses, excluding patients with a diagnosis of COPD. The parameters of the logistic model from the training phase were applied to an independent cohort of 160 patients for validating the diagnostic performance of the selected risk factors. The level of significance was set at $p<0.05$, and all tests were two sided. All the statistical analyses were performed using SPSS software standard V.19.0.

RESULTS

Baseline demographic and clinical characteristics of the POP groups and non-POP groups

During the study period, for the training cohort, the demographic distribution, laboratory test results, comorbid conditions, and preoperative and operative characteristics of the 901 patients who had undergone operative fixation for hip fracture are summarised in table 1. Fifty-five patients were diagnosed with POP (6.1%, 55 of 901 patients). At admission evaluation, the PaO_2 level of the POP group was significantly lower than that of the non-POP group (71.70 ± 9.20 vs 77.19 ± 10.04 , $p<0.0001$). However, no difference was found between the patients in the POP and non-POP groups in the PaCO_2 , PH, Cr, BUN, ALT, AST, TBIL, white blood cell (WBC), PLT and Hb levels. Compared with patients in the non-POP group, those in the POP group were significantly older (78.5 ± 7.0 vs 81.6 ± 7.7 years, $p=0.001$). However, sex and BMI were not related to occurrence rate of POP. Compared with patients in the non-POP group, those in the POP group had more preexisting comorbid conditions, such as COPD (14 (25.5%) vs 52 (6.1%), $p<0.0001$) and prior stroke (20 (36.3%) vs 180 (21.2%), $p=0.009$). However, no statistically significant difference was found among the groups on diabetes history and circulatory comorbidities (hypertension and coronary heart disease). Additionally, patients in the POP group had a longer time interval from injury to operation than patients in the non-POP group (11.6 ± 7.1 vs 6.3 ± 4.7 , $p<0.0001$), and the length of hospital stay in the POP group was longer than that in the non-POP group (13.1 ± 9.8 vs 9.2 ± 3.3 , $p<0.0001$). However,

Table 1 Comparison of the clinical characteristics of the POP groups and non-POP groups

Items	POP (N=55)	Non-POP (N=846)	χ^2 or t value	P value
Age (years)	81.6±7.7	78.5±7.0	3.22	0.001
Sex, male/female	23/32	280/566	1.76	0.185
BMI (kg/m ²)	22.2±2.1	22.3±1.8	1.56	0.211
COPD, n (%)	14 (25.5)	52 (6.1)	28.36	<0.0001
Type 2 diabetes, n (%)	11 (25)	186 (21.9)	0.12	0.73
Circulatory diseases, n (%)				
Coronary artery disease	28 (50.9)	424 (50.1%)	0.022	0.883
Hypertension	24 (43.6)	392 (46.3%)	0.151	0.697
Prior stroke, n (%)	20 (36.3)	180 (21.2)	6.806	0.009
PaO ₂ (mm Hg)	71.70±9.20	77.19±10.04	3.916	<0.0001
PaCO ₂ (mm Hg)	39.16±5.19	38.43±5.61	0.930	0.353
PH	7.42±0.4	7.4±0.36	0.488	0.625
WBC (10×10 ⁹ /L)	8.4±3.1	7.8±2.6	1.469	0.142
PLT (10×10 ⁹ /L)	179±7	183±66	0.381	0.703
Hb (g/L)	109.9±16.8	114.5±18.7	1.711	0.087
Cr (μmol/L)	74±33	68±23	1.77	0.076
BUN (mmol/L)	7.1±2.9	6.7±3.3	0.69	0.488
ALT (U/L)	21.3±22.5	16.9±16	1.895	0.058
AST (U/L)	19.1±9.8	19.3±9.4	0.206	0.837
TBIL (μmol/L)	17.2±11.1	17.0±9.7	0.105	0.917
Surgical duration (min)	85.0±32.1	85.6±27.4	0.16	0.873
Blood loss (mL)	230±139	232±142	0.127	0.899
Time from injury to surgery (days)	11.6±7.1	6.3±4.7	7.882	<0.0001
Length of hospital stay (days)	13.1±9.8	9.2±3.3	7.137	<0.0001
Fracture type, n (%)			0.238	0.626
Femoral neck fracture	27 (49.1)	444 (52.5)		
Intertrochanteric fracture	28 (50.1)	402 (47.5)		
Surgical approaches, n (%)			1.326	0.515
Total hip arthroplasty	4 (11.1)	102 (21.4)		
Intramedullary fixation	26 (14.8)	402 (14.1)		
Half hip replacement	25 (74.1)	342 (64.5)		

ALT, glutamic pyruvic transaminase; AST, glutamic oxaloacetic transaminase; BMI, body mass index; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; Cr, creatinine; Hb, haemoglobin; PaO₂, partial pressure of oxygen in arterial blood; PCO₂, partial pressure of carbon dioxide in arterial blood; PH, potential of hydrogen; PLT, platelet; POP, postoperative pneumonia; TBIL, total bilirubin; WBC, white blood cell.

no statistically significant difference was found among the groups concerning surgical duration, fracture type (femoral neck fracture or intertrochanteric fracture), selection of surgical approach (half hip replacement, THA or internal fixation) and intraoperative blood loss.

ROC curve analysis for PaO₂ at admission to predict the occurrence of POP

As mentioned previously, a significant difference was found in the admission PaO₂ levels between the non-POP and POP groups. Therefore, ROC curves were generated

to compare the predictive performance of PaO₂ levels for the occurrence of POP. Patients who with POP and non-POP as dichotomous dependent variables, the admission PaO₂ levels as independent variables. The area under the receiver operating characteristic curve (AUC) for predicting POP was 0.653 (95% CI 0.577 to 0.729, $p<0.0001$), with sensitivity and specificity values of 60.0% and 63.8%, respectively (figure 2). The optimal cut-off value of the PaO₂ for POP was 72.5 mm Hg. In this study, we classified an arterial oxygen partial pressure less than

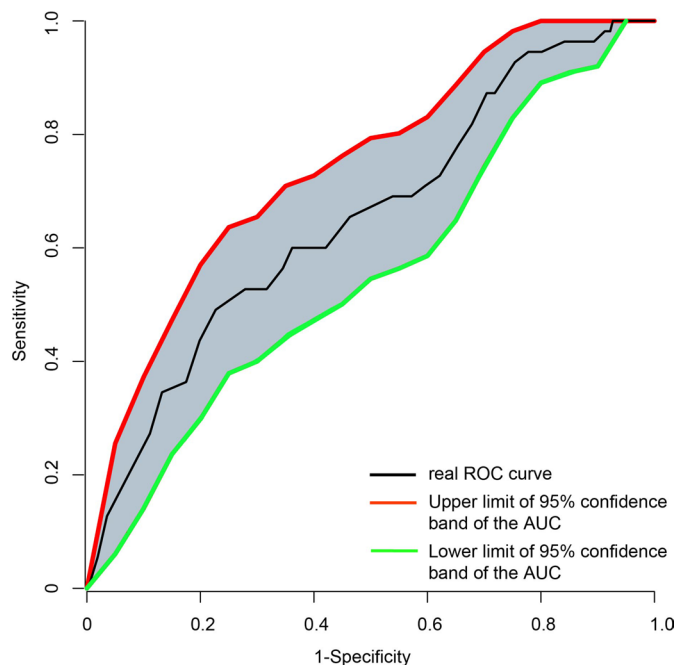


Figure 2 ROC curve analysis for POP after hip fracture surgery in training cohort
 Revealed an AUC of 0.653 (95% CI 0.577 to 0.729, $p < 0.0001$), with sensitivity and specificity values of 60.0% and 63.8%, respectively. The cut-off value of the PaO_2 for the POP was 72.5 mm Hg. AUC, area under the receiver operating characteristic curve; POP, postoperative pneumonia; ROC, receiver operating characteristic.

72.5 mm Hg as hypoxaemia ($\text{PaO}_2 < 72.5$ mm Hg), and all values not defined as hypoxaemia were defined as normal arterial PaO_2 ($\text{PaO}_2 \geq 72.5$ mm Hg).

Comparison incidence of POP and length of hospital stay in the hypoxaemia group ($\text{PaO}_2 < 72.5$ mm Hg) and normal PaO_2 group ($\text{PaO}_2 \geq 72.5$ mm Hg)

For the outcome analyses, the PaO_2 levels were stratified as follows: hypoxaemia group ($\text{PaO}_2 < 72.5$ mm Hg) and normal PaO_2 group ($\text{PaO}_2 \geq 72.5$ mm Hg). The previous data showed that 339 patients were diagnosed with hypoxaemia ($\text{PaO}_2 < 72.5$ mm Hg) (37.6%, 339 of 901 patients), and 562 patients were normal PaO_2 group ($\text{PaO}_2 \geq 72.5$ mm Hg) (62.4%, 562 of 901 patients), respectively. Patients in the hypoxaemia group ($\text{PaO}_2 < 72.5$ mm Hg) tended to have higher rates of POP (33 (9.7%) vs 22

(3.9%), $p < 0.0001$) than patients in the reference group with normal PaO_2 ($\text{PaO}_2 \geq 72.5$ mm Hg). Furthermore, the length of hospital stay in the hypoxaemia group ($\text{PaO}_2 < 72.5$ mm Hg) was longer than that in the normal PaO_2 group ($\text{PaO}_2 \geq 72.5$ mm Hg) (9.8 ± 3.8 vs 9.1 ± 3.1 , $p = 0.009$) (table 2). However, no statistically significant difference was found between the two groups regarding age and sex.

Predictive factors for POP using univariate and multivariable analyses

The consequences of univariate and multivariate analyses of preoperative or intraoperative potential clinical risk factors according to POP are summarised in table 3. From the univariate analysis, admission hypoxaemia ($\text{PaO}_2 < 72.5$ mm Hg) (OR=2.647, 95% CI 1.515 to 4.622; $p = 0.001$), age (OR=1.068, 95% CI 1.025 to 1.113; $p = 0.002$), COPD (OR=5.214, 95% CI: .672 to 10.73; $p < 0.0001$), prior stroke (OR=2.253, 95% CI 1.277 to 3.977; $p = 0.005$) and time interval from injury to operation (OR=1.118, 95% CI 1.076 to 1.161; $p < 0.0001$) were confirmed to be remarkably related to POP. Thereafter, a multivariate analysis model was implemented to identify the independent clinical factors for POP. Admission hypoxaemia ($\text{PaO}_2 < 72.5$ mm Hg) (OR=3.000, 95% CI 1.629 to 5.528; $p < 0.0001$), COPD (OR=3.653, 95% CI 1.744 to 7.653; $p = 0.001$), prior stroke (OR=2.406, 95% CI 1.292 to 4.479; $p = 0.006$) and time interval from injury to operation (OR=1.116, 95% CI 1.075 to 1.159; $p < 0.0001$) were still in the model after adjustment. Patients with admission hypoxaemia ($\text{PaO}_2 < 72.5$ mm Hg) were at three times greater risk of POP than patients with normal PaO_2 levels ($\text{PaO}_2 \geq 72.5$ mm Hg) (table 3).

Comparison of the incidence of POP and the length of hospital stay between the hypoxaemia group ($\text{PaO}_2 < 72.5$ mm Hg) and normal arterial PaO_2 group ($\text{PaO}_2 \geq 72.5$ mm Hg) in patients without COPD

To assess the influence of COPD on outcomes, we performed an additional analysis excluding patients with a history of COPD ($n = 66$ (7.3%)). Subgroup analysis of patients ($n = 835$) revealed that 305 patients were diagnosed with hypoxaemia ($\text{PaO}_2 < 72.5$ mm Hg) (36.5%, 305 of 835 patients), and 530 patients in the normal arterial PaO_2 group ($\text{PaO}_2 \geq 72.5$ mm Hg). Patients in the

Table 2 Comparison of the incidence of POP and length of hospital stay between the hypoxaemia group ($\text{PaO}_2 < 72.5$ mm Hg) and normal arterial PaO_2 group ($\text{PaO}_2 \geq 72.5$ mm Hg)

Variable	$\text{PaO}_2 \geq 72.5$ mm Hg (N=562)	$\text{PaO}_2 < 72.5$ mm Hg (N=339)	χ^2 or t value	P value
Age (years)	78.3 \pm 7.2	79.1 \pm 6.8	1.359	0.175
Sex, male/female	182/380	123/216	1.435	0.231
POP, n (%)	22 (3.9)	33 (9.7)	12.49	0.000
Length of hospital stay (days)	9.1 \pm 3.1	9.8 \pm 3.8	2.6	0.009

PaO_2 , partial pressure of oxygen in arterial blood; POP, postoperative pneumonia.

**Table 3** Predictive factors for POP using univariate and multivariable analyses

Variables	Univariate		Multivariable	
	OR (95% CI)	P value	OR (95% CI)	P value
Age (years)	1.068 (1.025 to 1.113)	0.002	1.044 (0.998 to 1.092)	0.062
Sex (female)	1.453 (0.834 to 2.530)	0.187		
BMI (kg/m ²)	0.949 (0.829 to 1.086)	0.446		
COPD	5.214 (2.672 to 10.73)	<0.0001	3.653 (1.744 to 7.653)	0.001
Type 2 diabetes	0.887 (0.449 to 1.752)	0.730		
Coronary artery disease	1.042 (0.604 to 1.798)	0.883		
Hypertension	0.897 (0.517 to 1.554)	0.697		
Prior stroke	2.253 (1.277 to 3.977)	0.005	2.406 (1.292 to 4.479)	0.006
Hypoxaemia	2.647 (1.515 to 4.622)	0.001	3.000 (1.629 to 5.528)	<0.0001
Hb	0.986 (0.972 to 1.003)	0.055	0.989 (0.973 to 1.005)	0.180
PaCO ₂	1.021 (0.977 to 1.067)	0.352		
PH	1.999 (0.700 to 5.675)	0.299		
Cr	1.009 (0.999 to 1.019)	0.077	1.005 (0.995 to 1.016)	0.311
BUN	1.024 (0.957 to 1.097)	0.489		
ALT	1.008 (0.997 to 1.019)	0.168		
AST	0.997 (0.967 to 1.028)	0.837		
TBIL	1.001 (0.974 to 1.029)	0.917		
WBC	1.076 (0.967 to 1.187)	0.143		
PLT	0.999 (0.995 to 1.003)	0.703		
Surgical duration time	0.998 (0.988 to 1.008)	0.744		
Blood loss	1.000 (0.996 to 1.003)	0.899		
Time from injury to surgery	1.118 (1.076 to 1.161)	<0.0001	1.116 (1.075 to 1.159)	<0.0001
Fracture type	0.873 (0.506 to 1.507)	0.626		
Surgical approaches	0.942 (0.704 to 1.259)	0.666		

ALT, glutamic pyruvic transaminase; AST, glutamic oxaloacetic transaminase; BMI, body mass index; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; Cr, creatinine; Hb, haemoglobin; PCO₂, partial pressure of carbon dioxide in arterial blood; PH, potential of hydrogen; PLT, platelet count; POP, postoperative pneumonia; TBIL, total bilirubin; WBC, white blood cell.

hypoxaemia group (PaO₂ <72.5 mm Hg) tended to have higher rates of POP (25 (8.1%) vs 16 (3.0%), p=0.001) than patients in the normal arterial PaO₂ group (PaO₂ ≥72.5 mm Hg). Furthermore, the length of hospital stay in the hypoxaemia (PaO₂ <72.5 mm Hg) group was longer than that of patients in the normal PaO₂ group (PaO₂ ≥72.5 mm Hg) (9.6±3.8 vs 9.1±3.2, p=0.044) (table 4). However, no statistically significant differences were found between the two groups regarding age and sex.

Predictive factors for POP using univariate and multivariable analyses after excluding patients with COPD

The consequences of univariate and multivariate analyses of potential clinical risk factors after excluding patients with COPD are summarised in table 5. From the univariate analysis, admission hypoxaemia (PaO₂ <72.5 mm Hg) (OR=2.868, 95% CI 1.506 to 5.462; p=0.001), age (OR=1.046, 95% CI 1.000 to 1.094; p=0.049), prior

Table 4 Comparison of the incidence of POP and length of hospital stay between the hypoxaemia group (PaO₂ <72.5 mm Hg) and the normal PaO₂ group (PaO₂ ≥72.5 mm Hg) in patients without COPD

Variable	PaO ₂ ≥72.5 mm Hg (N=530)	PaO ₂ <72.5 mm Hg (N=305)	χ ² or t value	P value
Age (years)	78.1±7.3	78.8±6.8	1.337	0.182
Sex, male/female	168/362	105/200	0.655	0.418
POP, n (%)	16 (3.0)	25 (8.1)	11.12	0.001
Length of hospital stay (days)	9.1±3.2	9.6±3.8	2.017	0.044

COPD, chronic obstructive pulmonary disease; PaO₂, partial pressure of oxygen in arterial blood; POP, postoperative pneumonia.

Table 5 Predictive factors for POP using univariate and multivariable analyses after excluding patients with COPD

Variables	Univariate		Multivariable	
	OR (95% CI)	P value	OR (95% CI)	P value
Age (years)	1.046 (1.000 to 1.094)	0.049	1.033 (0.985 to 1.083)	0.186
Sex (female)	1.472 (0.777 to 2.788)	0.236		
BMI (kg/m ²)	0.972 (0.830 to 1.140)	0.730		
Type 2 diabetes	0.864 (0.392 to 1.904)	0.717		
Coronary artery disease	0.977 (0.521 to 1.830)	0.941		
Hypertension	0.795 (0.421 to 1.504)	0.697		
Prior stroke	2.562 (1.345 to 4.877)	0.004	2.685 (1.350 to 5.5337)	0.005
Hypoxaemic	2.868 (1.506 to 5.462)	0.001	3.112 (1.564 to 6.195)	0.001
Hb	0.985 (0.969 to 1.001)	0.064	0.983 (0.966 to 1.003)	0.052
PaCO ₂	0.981 (0.923 to 1.043)	0.536		
PH	1.177 (0.840 to 1.6558)	0.197		
Cr	1.004 (0.992 to 1.017)	0.492		
BUN	0.997 (0.907 to 1.096)	0.951		
ALT	1.008 (0.995 to 1.020)	0.227		
AST	0.996 (0.962 to 1.032)	0.838		
TBIL	1.002 (0.971 to 1.034)	0.918		
WBC	1.153 (1.031 to 1.289)	0.013	1.230 (1.089 to 1.389)	0.001
PLT	1.001 (0.996 to 1.005)	0.793		
Surgical duration time	1.003 (0.993 to 1.014)	0.537		
Blood loss	1.001 (0.999 to 1.003)	0.611		
Time from injury to surgery	1.100 (1.057 to 1.145)	<0.0001	1.134 (1.084 to 1.187)	<0.0001
Fracture type	1.191 (0.636 to 2.232)	0.585		
Surgical approaches	0.931 (0.665 to 1.301)	0.674		

ALT, glutamic pyruvic transaminase; AST, glutamic oxaloacetic transaminase; BMI, body mass index; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; Cr, creatinine; Hb, hemoglobin; PCO₂, partial pressure of carbon dioxide in arterial blood; PH, potential of hydrogen; PLT, platelet count; POP, postoperative pneumonia; TBIL, total bilirubin; WBC, white blood cell count.

stroke (OR=2.562, 95% CI 1.345 to 4.877; p=0.004), WBC (OR=1.153, 95% CI 1.031 to 1.289; p=0.013) and time interval from injury to operation (OR=1.100, 95% CI 1.057 to 1.145; p<0.0001) were found to be remarkably associated with POP. Thereafter, the multivariate analysis model was implemented to identify predictive clinical factors for POP. Admission hypoxaemia (PaO₂ <72.5 mm Hg) (OR=3.112, 95% CI 1.564 to 6.195; p=0.001), prior stroke, (OR=2.685, 95% CI 1.350 to 5.5337; p=0.005), WBC (OR=1.230, 95% CI 1.089 to 1.389; p=0.001) and time interval from injury to operation (OR=1.134, 95% CI 1.084 to 1.187; p<0.0001) were still in the model after adjustment. Patients with admission hypoxaemia (PaO₂ <72.5 mm Hg) were at 3.327 times greater risk of POP than patients with normal PaO₂ (PaO₂ ≥72.5 mm Hg) levels after excluding patients with COPD (table 5).

Validation of predictive accuracy of the logistic regression model

There was no significant difference in the distribution of baseline characteristic, preoperative or intraoperative potential clinical factors between the training and validation data sets. The detail information could be found in

online supplemental table 1. The parameters estimated from the training data set were used to predict the probability of being diagnosed with POP for the independent validation cohort (n=160). Similarly, the predicted probability was used to construct the ROC curve. The analysis demonstrated that the PaO₂ level at admission had high accuracy in discriminating patients with higher risk of having POP from non-POP patients after hip fracture surgery in a geriatric population (AUC: 0.71, 95% CI 0.541 to 0.891; sensitivity 70%, specificity 66%) (figure 3).

DISCUSSION

The main findings of this retrospective study were that the incidence rates of POP after operative fixation for hip fracture was 6.1% in the geriatric population 30 days after surgery. ROC curve analysis for admission PaO₂ to predict the occurrence of POP with the cut-off value was 72.5 mm Hg. The rates of POP were significantly higher in patients with hypoxaemia (PaO₂ <72.5 mm Hg) at hospital admission than in patients with normal PaO₂ (PaO₂ ≥72.5 mm Hg). Additionally, patients with POP had a prolonged

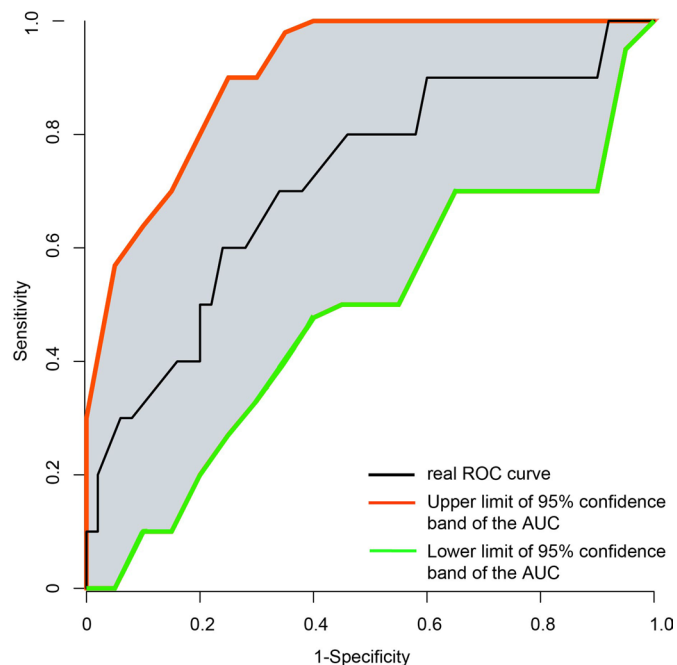


Figure 3 ROC curve analysis for POP after hip fracture surgery in validation cohort

Revealed an AUC of 0.71 (95% CI 0.541 to 0.891, $p=0.022$), with sensitivity and specificity values of 70% and 66%, respectively. AUC, area under the receiver operating characteristic curve; POP, postoperative pneumonia; ROC, receiver operating characteristic.

hospital stay than those without POP. Binary logistic regression analysis illustrated that hospital admission with hypoxaemia ($\text{PaO}_2 < 72.5 \text{ mm Hg}$) was associated with a threefold increase in the rate of POP after operative fixation for hip fracture in the elderly patients. The current research also revealed that COPD, prior stroke and time interval from injury to operation were independent and predominant risk factors for POP after operative fixation for hip fracture in the geriatric population. These findings persisted after excluding patients with COPD from the cohort. Furthermore, it was validated in an independent series of patients after hip fracture surgery.

POP is a frequent complication in the geriatric population after hip fracture surgery. In our study, the frequency of POP was 6.1%, which compared favourably with the values previously reported in the literature.^{12 15} Not only is POP a serious medical problem but also it can significantly increase morbidity and mortality, representing a high healthcare burden and increased hospital stay.^{15 19} We used ROC curve analysis for POP after hip fracture surgery. The admission PaO_2 levels were found to be a fair prognostic marker with an ROC curve showing an AUC of 65.3%, and the cut-off value of the PaO_2 for the POP was 72.5 mm Hg, a value that agrees with that in previous studies.^{20 21} Furthermore, it was validated in an independent series of patients after hip fracture surgery. In the validation set, the AUC was 0.71, and the sensitivity and specificity were 0.70 and 0.66, respectively.

In the current paper, 37.6% (339 of 901 patients) of our patients had hypoxaemia ($\text{PaO}_2 < 72.5 \text{ mm Hg}$), and a multiple logistic regression model was used to study 901 patients who had undergone surgery for hip fracture. We identified by statistical analysis that hypoxaemia ($\text{PaO}_2 < 72.5 \text{ mm Hg}$) at hospital admission was an independent predictor of POP, a finding that is in line with operative fixation for hip fracture in the geriatric population.²² Compared with normal arterial PaO_2 ($\text{PaO}_2 \geq 72.5 \text{ mm Hg}$), hypoxaemia ($\text{PaO}_2 < 72.5 \text{ mm Hg}$) was associated with an increase in POP by more than 3.0-fold and 3.112-fold in an analysis that excluded patients with COPD. These results were consistent with data previously published by Zhang *et al*,¹⁸ which showed that hospitalised patients who had undergone operative fixation for hip fracture had higher POP when they had hypoxaemia at admission. Moreover, Wang *et al*²³ observed that hypoxaemia (OR=2.916) was independent risk factor for posthip fracture pneumonia in patients 80 years and older when they retrospectively reviewed 293 in-hospital patient data. The PaO_2 levels were more applicable to patients with hip fracture in predicting POP. Furthermore, Vold *et al*²⁴ revealed that low oxygen saturation was independently correlated with all-cause mortality and lung disease-related mortality in a cohort study. Similar to previous research results, our results showed an association between hypoxaemia ($\text{PaO}_2 < 72.5 \text{ mm Hg}$) and POP. Moreover, multiple logistic analyses showed that the development of POP in patients with hypoxaemia ($\text{PaO}_2 < 72.5 \text{ mm Hg}$) was not associated with age, gender, other laboratory parameters or surgical duration, fracture type and surgical approach. Only hypoxaemia ($\text{PaO}_2 < 72.5 \text{ mm Hg}$), COPD, prior stroke and time from injury to surgery were independent variables associated with a higher risk of developing POP. One strength of our study is that we focused on identifying risk factors for POP after hip fracture in the elderly patients. The clinician should perform more cautious monitoring and appropriate management to prevent POP in the geriatric population. One avoidance strategy comprises a comprehensive perioperative evaluation of older individuals: patients with one or more of the aforementioned risk factors identified for POP and those needing careful monitoring and respiratory care. Previous research results have recommended that postoperative or preoperative respiratory care, including the selective use of a nasogastric tube, percussion, postural drainage, vibration, suctioning, deep breathing exercises, chest physiotherapy and early mobilisation, should be routinely performed as effective methods to reduce POP.^{11 19 25 26}

ABG analysis is an important laboratory test that provides valuable information about the acid-base status, oxygenation, gas exchange and lung ventilation.²⁷ On patient arrival at the hospital, three key parameters were selected to assess the pulmonary function of patients with hip fracture who have undergone operative fixation and to determine the roles of ABG in predicting the risk of POP complications. PaO_2 is an important factor for ABG. It is

the partial pressure of oxygen that indicates the dissolved oxygen in the plasma and not the oxygen bound to Hb in the human body,^{28 29} and it quickly and easily provides data on the oxygenation status, reflecting the ability of the lungs to acquire oxygen during respiration. PaO₂ also represents the balance in the body's oxygen supply and demand. In our study, hypoxaemia (PaO₂ <72.5 mm Hg) was independently associated with the 30-day POP, but the PCO₂ or pH level showed no relationship with POP, suggesting that hypoxaemia (PaO₂ <72.5 mm Hg) is likely to be intrinsically involved in the adverse events of these patients. Additionally, the incidence of POP increased as PaO₂ decreased. The OR of patients with hypoxaemia (PaO₂ <72.5 mm Hg) compared with those with normal PaO₂ (PaO₂ ≥72.5 mm Hg) was 3.0, indicating that the incidence of POP in patients with abnormal PaO₂ (PaO₂ ≥72.5 mm Hg) was three times that in patients with hypoxaemia (PaO₂ <72.5 mm Hg). This information should be considered in the surgical treatment of patients with hip fracture. Therefore, it is suggested that the admission PaO₂ level is important to assess the risk of POP in patients who have undergone operative fixation for hip fracture. Chang *et al*¹¹ reported that the incidence of pneumonia was lower in elderly patients with hip fractures who received the postoperative pulmonary rehabilitation programme after surgery.

Which mechanisms underpin the association between PaO₂ and POP? The two main organ systems responsible for oxygen delivery in the body and maintaining homeostasis are the respiratory and cardiovascular systems. The abnormal function of any of these two would lead to the development of hypoxaemia and its detrimental consequences.³⁰ Underlying chronic lung diseases with low exercise capacity and pulmonary functions, as well as surgery under general anaesthesia, can be responsible for POP.³¹ The basic characteristic of COPD is airflow limitation, in all patients with COPD, often manifested as the decrease in pH and PaO₂ and an increase in PaCO₂.³² To rule out the effect of COPD on hypoxaemia, we conducted subgroup analysis. When patients with COPD were excluded from the analysis, the differences persisted between the groups, and hypoxaemia (PaO₂ <72.5 mm Hg) was also a risk factor for POP after surgery. Thus, COPD is not the main factor affecting the PaO₂ level. Sorbini *et al*²⁰ pointed out that both age and the cardiac and respiratory physical status of patients may directly influence the PaO₂ levels. Additionally, when studying patients awaiting elective major intrathoracic or peripheral vascular surgery, they found a mean PaO₂ value of 80 mm Hg in patients of 45 years or younger, and 74 mm Hg in those older than 45 years. Additionally, Marshall and Wyche³³ reported that normal ageing causes PaO₂ and functional residual capacity to decrease. Their research results showed that the regression equation that correlated the ages of the patients with their PaO₂ level was PaO₂=102-0.33×(age). Age induced a decrease in the PaO₂ level likely because of the rise in the ventilation/perfusion mismatch, along with individuals becoming older.³⁴ The reduction in PaO₂ after

70 years of age is approximately 0.43 mm Hg/year.³⁰ Our study subjects were aged 65 years or older, and the study showed that the admission PaO₂ level of 71.70±9.20 mm Hg in the POP group was significantly lower than that of 77.19±10.04 mm Hg in the non-POP group, a finding that is consistent with previous research.

In the present study, patients with hypoxemia (PaO₂ <72.5 mm Hg) had a prolonged hospital stay after hip fracture surgery. Importantly, the incidence of POP leads to prolonged hospital stays, which are of significant clinical and economic importance. Geriatric populations often have more comorbidities and have a worse prognosis. Consistent with previous research reports,^{22 35} our research also demonstrated that patients with POP had more comorbidities. COPD and prior stroke were significantly associated with POP in geriatric populations with hip fractures. Therefore, it is important to detect those who are at risk of postoperative complications and/or death, especially considering the increase in ageing and comorbidities in previous years.³⁶ Some authors have argued that the advantage of surgical repair in 48 hours of injury.³⁷ Simunovic *et al*³⁸ suggested that early surgical treatment of hip fracture (<24, <48 or <72 hours) was associated with a significant reduction in mortality. Earlier surgery was also associated with reduced risk of POP. Importantly, our results are consistent with those reporting a significant influence of surgical delay on POP. Prolonged time interval from injury to operation was identified as a risk factor for POP in regression analysis after adjustment (OR=1.116). However, it is unknown whether improvement in the PaO₂ levels by preoperative prehabilitation reduces the risk of POP after hip fracture surgery. Future studies are warranted. Our study possessed some limitations. First, it was a single-center study with a retrospective and non-randomised design. All the analysed data were drawn from an archived hospital database. The optimal diagnostic cut-off value in our results were analysed from a single centre, and the result was generalised and required large-scale clinical validation, and future studies are warranted. Thus, the causality between the partial pressure of oxygen level at admission and POP risk factors cannot be determined. Despite this, our study identified the PaO₂ level at admission as a risk factor for POP. Second, in our study, the main end point was the occurrence of POP in the 30-day postoperative period. Additionally, other factors may affect the development of POP that were not considered during retrospective analysis. This study lacked an assessment of the patient's nutritional status (marked by serum albumin value), activities of daily living (ADL) and dysphagia ability, which have also affected the occurrence of POP in previous studies.^{16 39 40} Furthermore, information about patients was collected only from 30 days after the operation, an activity that could lead to missed cases of POP that occurred after this period. The third point is that we did not examine other markers of respiratory function, such as the preoperative 6 min walk distance and pulmonary function tests. The PaO₂ levels may not always reflect tissue oxygen delivery



and use. There may be various clinical factors affecting the arterial PaO₂ level. Therefore, respiratory function was only based on hypoxaemia, indicating that we underestimated the real prevalence of poor respiratory function. Moreover, we focused only on the partial pressure of oxygen level at admission and did not study perioperative, or dynamic changes in the PaO₂ levels during this period and their relationship with POP. These situations should be considered as research objects in a future study. The last point is ROC curve analysis for admission PaO₂ to predict the occurrence of POP with the AUC around 0.7 in our research. The AUC is not high enough, which leads to its limited accuracy of prediction. The predictors of disease are generally multifaceted, and a single index has limited predictive power for disease. Therefore, the inference of our results needs further validation in large, randomised controlled trials and prospective, multi-centre, parallel controlled trials.

CONCLUSION

The current study revealed that the PaO₂ level at hospital admission is a simple and widely available biomarker predictor of POP after hip fracture surgery in elderly patients. Thus, patients who undergo surgery for hip fracture should have their PaO₂ levels measured routinely at admission, and patients admitted to the hospital with hypoxaemia (PaO₂ <72.5 mm Hg) should be subjected to more cautious monitoring and appropriate management to prevent POP. Further prospective studies are needed to confirm this important finding.

Acknowledgements We thank AJE (www.aje.com) for English language editing a draft of this article. All the authors of this article are immensely grateful to their respective universities and institutes for their technical assistance and valuable support in the completion of this research project.

Contributors YJ and JW conceived and designed the study, and helped to draft and revise the manuscript. XL and YW were responsible for data collection and data analysis. LC and HT were statisticians and were responsible for data analysis. NL was responsible for data validation and wrote the manuscript. JW responsible for the overall content as the guarantor. All authors read, revised and approved the final manuscript.

Funding This work was supported by Shaanxi Natural Science Foundation of China (number 2019JQ-536).

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval The Human Research Ethics Committee of Honghui Hospital, Xi'an Jiaotong University, approved the present study protocol (No. 202001004) before the study onset and complied with the principle plan in the 1964 Helsinki Declaration. The requirement for written informed consent was exempted because the study was a retrospective analysis. The information from the patients we studied was anonymised.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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