



# Reduction quality in lateral view of X-ray and hypoalbuminemia are associated with postoperative mortality in elderly pertrochanteric fracture patients

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**Background:** Pertrochanteric fracture is one of the most prevalent public health issues across the world for the elderly population. The purpose of this study was to investigate the association between surgical factors and postoperative mortality in patients with intramedullary nail-treated pertrochanteric fractures.

**Methods:** A retrospective cohort study was designed to evaluate the pertrochanteric fracture patients treated with intramedullary nail between January 2016 to February 2021. The surgical factors included the Dorr morphology, Arbeitsgemeinschaft für Osteosynthesefragen/Orthopedic Trauma Association (AO/OTA) classification of fractures, the tip-apex distance (TAD), location of the cephalic screw, reduction quality in anterior-posterior (AP) and lateral views, the integrity of the lateral wall, and the design of cephalic screws. Using univariate and multivariate Cox proportional hazard models, the association between these risk factors and postoperative mortality in patients with this type of fractures was evaluated.

**Results:** A total of 169 pertrochanteric fracture patients treated with intramedullary nails were included in our study, with the average age of  $82.68 \pm 5.93$  years. The mortality rates at 3 months, 1 year, and the end of follow-up were 4.14%, 11.24%, and 26.04%, respectively. According to the univariate Cox analysis, age, gender, preoperative levels of hemoglobin (Hb) and albumin (Alb) were associated with a poor overall survival (OS) ( $P < 0.05$ ). After multivariate adjustment, the pre-operative level of Alb ( $P < 0.001$ ) and the reduction in lateral view ( $P < 0.001$ ) were shown to be independent risk factors for poor OS.

**Conclusions:** The preoperative hypoalbuminemia and reduction quality in lateral view were associated with postoperative mortality in our study. Therefore, optimizing both parameters could improve the prognosis in elderly pertrochanteric fracture patients.

**Keywords:** Pertrochanteric fracture; intramedullary nail; surgical factors; reduction quality in lateral view; mortality

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## Introduction

Hip fragility fractures are one of the most common public health issues across the world as the population ages (1,2). According to recent studies, it is predicted that the number of hip fracture cases in China will grow six-fold from 0.7 million instances in 2013 to 4.5 million cases in 2050 (2,3).

Between 1/3 and 1/2 of all hip fractures are pertrochanteric fractures, which are a frequent injury. The mortality rate of this type of fracture at 1 year varies from 14% to 36% (4). For quick rehabilitation and healing after fractures, surgical fixation is advised. The most popular method for fixing the fractures is intramedullary nailing, particularly for unstable fractures (5). However, even after surgery, 25% of patients with these fractures need to be cared for at home, and more than 50% lose the ability to walk independently (6,7).

In prior studies, the mortality rate of pertrochanteric fracture has been linked to a variety of clinical parameters, including age, gender, American Society of Anesthesiologists (ASA) score, time to surgery, and surgeon grade (8-12). Multiple studies have also examined surgical factors, such as fracture classification, tip-apex distance (TAD), position of the lag screw, augmentation, and reduction quality, in relation to implant failure in pertrochanteric fractures (13-17). In the initial postoperative phase, surgical factors are crucial determinants of a patient's capacity for unrestricted weight-bearing, in addition with patient-dependent factors (e.g., previous mobility and dementia). Long-term immobility compromises the dignity of elderly and weak individuals and raises the risk of post-operative complications, such as delirium, thrombosis, hospital-acquired infection, pressure-mediated skin injury, loss of muscular strength, and diminished rehabilitation potential (18). To our knowledge, despite the fact that surgical factors have been shown to be independent risk factors for implant failure, few studies have examined the association between surgical factors and post-operative mortality rate (19-21).

In this study, we aimed to examine the association between the postoperative mortality of patients with intramedullary nail-treated pertrochanteric fractures and surgical factors, including the Dorr morphology, Arbeitsgemeinschaft für Osteosynthesefragen/Orthopedic Trauma Association (AO/OTA) classification of fractures (22), TAD, location of the cephalic screw, reduction quality in anterior-posterior (AP) and lateral views, the integrity of the lateral wall, and the design of cephalic screws. We present this article in accordance with the STROBE reporting checklist (available at <https://qims.amegroups.com/article/>

[view/10.21037/qims-23-424/rc](https://doi.org/10.21037/qims-23-424/rc)).

## Methods

### *Patients and study design*

The retrospective study was approved by the Institutional Review Board (IRB) of Peking University First Hospital (No. 2021-432) and the requirement for individual consent for this retrospective analysis was waived. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Between January 2016 and February 2021, this retrospective analysis examined the pertrochanteric fracture patients who received internal fixation with intramedullary nails at Peking University First Hospital. The inclusion criteria were as follows: (I) age  $\geq 70$  years; (II) diagnosed with pertrochanteric fracture; (III) fracture fixed using intramedullary nail. The exclusion criteria were as follows: (I) pathological fracture; (II) fracture treated with plate or hip arthroplasty; (III) fracture treated conservatively; (IV) incomplete data or lost follow-up.

### *Surgical and postoperative management*

Prior to surgery, all patients were assessed with routine AP and lateral radiographs in bilateral hips. Upon completion of preoperative preparations, all patients had surgery as quickly as possible while under regional or general anesthesia. In a supine posture on a traction table, intramedullary nailing was performed on patients with pertrochanteric fractures. All operations were carried out under fluoroscopic supervision. Utilizing a traction table and closed manipulation procedures, patients underwent closed reduction. When the operating surgeon felt that reduction was insufficient, supplementary percutaneous or open reduction procedures were used to maximize reduction. After surgery, standard AP and lateral radiographs of the bilateral hips were acquired. Depending on the patient, fracture morphology, reduction, and implant site, the patient was able to bear no, partial, or full weight. After discharge, patients were contacted and followed up by telephone. The minimal follow-up duration was 12 months after surgery. If the patient had died before the follow-up time, the date of death was recorded.

### *Data collection*

The basic information of patients, including age and gender, ASA score, preoperative waiting time, anesthetic type, blood



**Figure 1** The intramedullary canal width (B) was measured at the position of 10 cm below the mid-lesser trochanter. The intramedullary canal diameter was measured at the level of the mid-lesser trochanter (A).  $CCR = B/A$ . CCR, canal-to-calcar ratio.

transfusion information, pre-operative levels of hemoglobin (Hb) and albumin (Alb), were retrieved with care from their electronic medical records. Additionally, the preoperative and postoperative radiographs were measured to establish the surgical factors. The surgical factors included the Dorr morphology, AO/OTA classification of fractures, TAD, location of the cephalic screw, reduction quality in AP and lateral views, the integrity of the lateral wall, and the design of cephalic screws. As for the measurement of surgical indicators in postoperative radiographs, 2 trained orthopedic surgeons with junior titles measured or evaluated the indicators without knowing other information of patients. If the results diverged, a senior orthopedic surgeon re-measured or re-evaluated.

The Dorr morphology was evaluated as described by Dorr *et al.* (23). The intramedullary canal width (B) was measured at the position of 10 cm below the mid-lesser trochanter. Also measured was the intramedullary canal diameter at the level of the mid-lesser trochanter (A). Canal-to-calcar ratio (CCR) was calculated as the ratio of B to A and was used to assess the proximal femoral morphology. The Dorr morphology was defined as follows: Type A  $<0.5$  CCR, Type B as  $0.5\text{--}0.75$  CCR, and Type C  $>0.75$  CCR (Figure 1). There was no case of Dorr Type C in our study.

The TAD was firstly described by Baumgaertner *et al.* in 1995 (17) and is defined as the sum of the distance from

the tip of the lag screw to the apex of the femoral head measured on the AP and lateral radiograph.

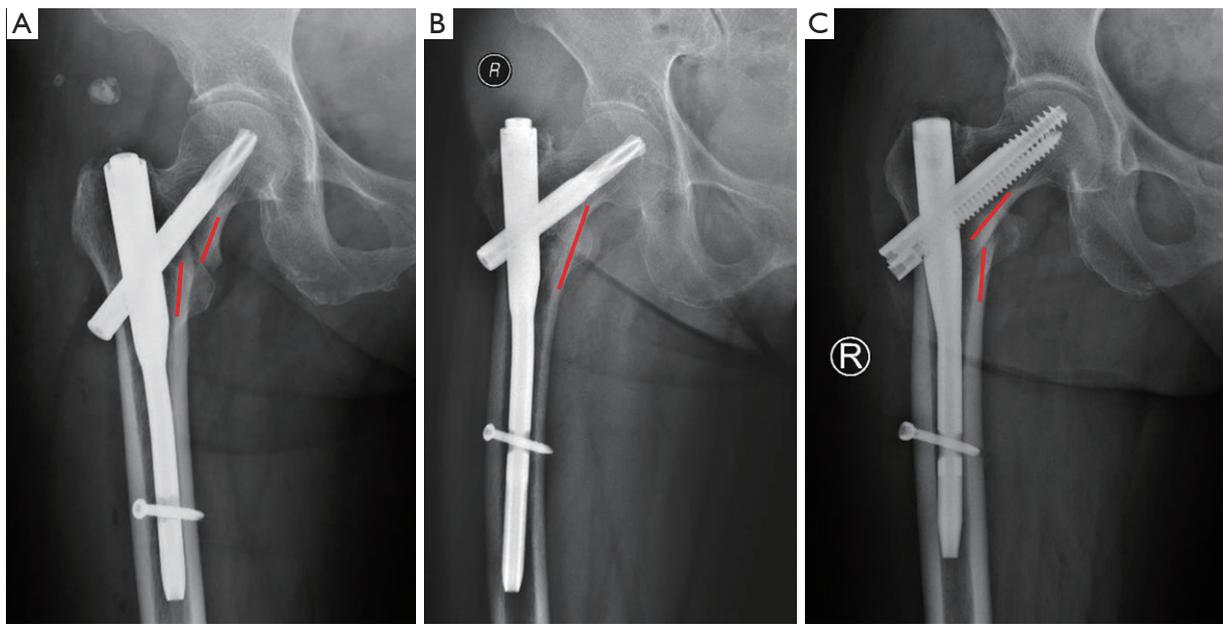
On the postoperative radiographs, the location of the cephalic screw was assessed as reported by Cleveland *et al.* (24). On the AP and lateral radiographs, the placement of the cephalic screw in the femoral head was classified as superior, middle, or inferior. The cephalic screw in the center or inferior of the femoral head on the AP view and in center on the lateral view were defined as proper position, whereas all other positions were considered as improper.

According to the studies by Baumgaertner *et al.* (25) and Chang *et al.* (26), the quality of reduction of AP and lateral fractures was assessed using AP and lateral X-rays, respectively. In the AP view, it was defined as good that the femoral neck-shaft angle was slight valgus or normal for alignment, and that the medial cortical support was positive and neutral, and no more than 4 mm of displacement of any fragment. In the lateral view, an angulation of  $20^\circ$  for alignment and a positive or neutral anteromedial cortical contact were considered good reduction. If the reduction did not meet the criteria in AP or lateral view, the reduction was rated poor (Figures 2,3).

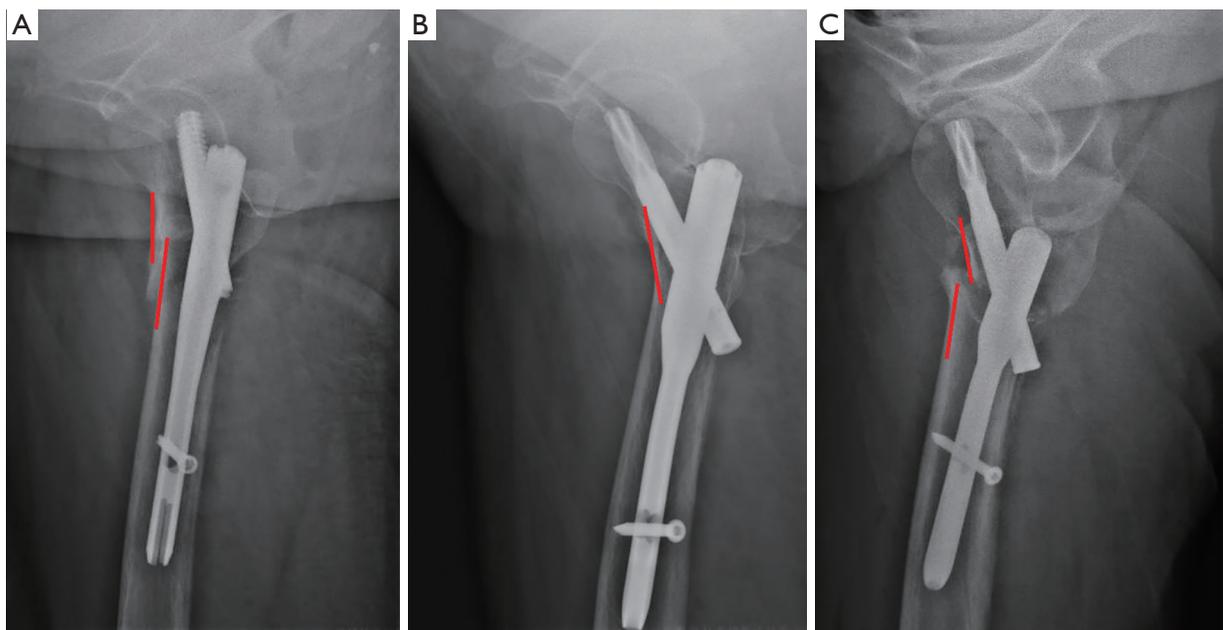
On preoperative radiographs or computed tomography (CT) scans, the lateral femoral wall fracture was characterized as a fracture line that crosses the lateral wall (27). According to the difference in cephalic screws, the intramedullary nails in our research were categorized as either single blade devices (PFNa; AO Synthes, Raynham, MA, USA) or double screw devices (InterTAN; Smith & Nephew, London, UK).

### Statistical analysis

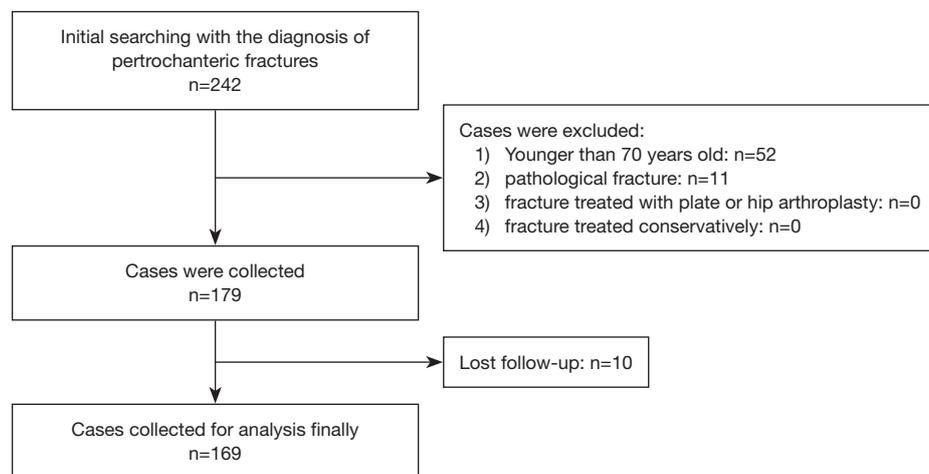
The categorical variables were quantified and evaluated using the chi-square test. Continuous variables were recorded as the mean  $\pm$  standard deviation and evaluated using either the Student's *t*-test or the Wilcoxon rank-sum test. The Kaplan-Meier technique was used to plot survival curves. Initially, the risk factors for postoperative mortality were evaluated using a univariate Cox proportional hazards regression model with a significance level of  $P < 0.05$ . The selected covariates were subsequently examined using backward stepwise multivariate Cox proportional hazards regression, and variables with  $P$  values  $< 0.05$  were determined to be the final predictors. All statistical analyses were performed using SPSS 26.0 (IBM Corp., Armonk, NY, USA).



**Figure 2** The AP image reveals three types of medial cortical support. (A) Positive medial cortex support: the proximal femoral head-neck fragment is displaced medially to the upper medial edge of the distal femoral shaft fragment; (B) neutral position: the medial cortex of head-neck and the shaft fragments are smoothly contacted; (C) negative medial cortex support: the head-neck fragment is displaced laterally to the upper medial edge of the shaft fragment, which lost the medial cortex support from the femoral shaft. AP, anterior-posterior.



**Figure 3** The postoperative reduction subtype in the lateral view of radiographs. (A) Positive anteromedial support: the proximal femoral head-neck fragment is displaced anteriorly to the anterior cortex of the distal bone fragment; (B) neutral position: the anterior cortex of head-neck and the shaft fragments are smoothly contacted; (C) negative anteromedial support: the anterior cortex of the proximal bone fragment is displaced to the medullary cavity of the distal bone fragment.



**Figure 4** The flowchart of screening patients.

## Results

From January 2016 to February 2021, a total of 242 pertrochanteric fracture patients were treated at our institution. We excluded patients under the age of 70 ( $n=52$ ), those treated with plates or arthroplasty ( $n=11$ ), and those who were lost to follow-up ( $n=10$ ). Finally, a total of 169 pertrochanteric fracture patients treated with intramedullary nails were included in our study, with the average age of  $82.68 \pm 5.93$  years (as shown in *Figure 4*). There were 48 males and 121 females among the participants. The Spinal anesthesia group included 120 patients (71%); the number of patients in the General anesthesia group was 49 (29%). There were 21 (12.4%) patients with open reduction and 148 (87.6%) patients with closed reduction. The basic characteristics are all shown in *Table 1*. The mean survival time of enrolled patients was  $34.11 \pm 19.89$  months, and the death rates at 3 months, 1 year, and the end of follow-up were 4.14%, 11.24%, and 26.04%, respectively (*Figure 5*). The specifics of assessing surgical factors, such as AO/OTA classification of fractures, Dorr morphology, TAD, location of the cephalic screw, reduction quality in the AP and lateral views, the integrity of the lateral wall, and the design of cephalic screws, are displayed in *Table 1*.

According to the univariate Cox analysis, among the basic characteristics, age [hazard ratio (HR) 1.054, 95% confidence interval (CI): 1.005–1.106,  $P=0.031$ ], gender (HR 2.063, 95% CI: 1.137–3.745,  $P=0.017$ ), pre-operative levels of Hb (HR 0.975, 95% CI: 0.957–0.993,  $P=0.006$ ) and Alb (HR 0.825, 95% CI: 0.768–0.885,  $P<0.001$ ) were associated with a poor overall survival (OS). However, there

**Table 1** Basic characteristics and surgical factors of included patients

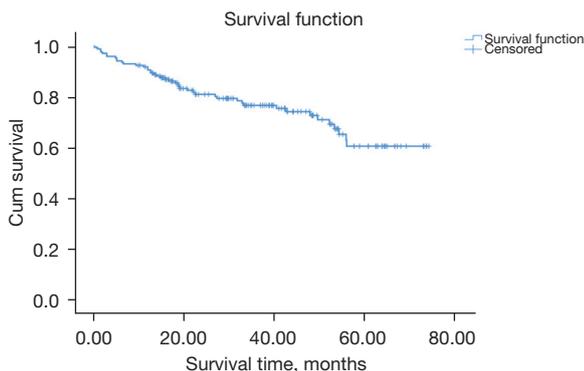
Characteristics	Data, n (%) or mean $\pm$ SD
Age (years)	82.68 $\pm$ 5.93
Gender	
Male	48 (28.4)
Female	121 (71.6)
Anesthesia	
Spinal	120 (71.0)
General	49 (29.0)
ASA score	
2	74 (43.8)
3	88 (52.1)
4	7 (4.1)
Preoperative waiting time (days)	4.47 $\pm$ 2.78
Blood transfusion	
Yes	93 (55.0)
No	76 (45.0)
Hemoglobin (g/L)	111.41 $\pm$ 16.95
Albumin (g/L)	36.15 $\pm$ 3.73
AO/OTA classification	
31A1	31 (18.3)
31A2	133 (78.7)
31A3	5 (3.0)

**Table 1** (continued)

**Table 1** (continued)

Characteristics	Data, n (%) or mean $\pm$ SD
Dorr morphology	
Type A	68 (40.2)
Type B	101 (59.8)
TAD (mm)	19.93 $\pm$ 4.29
Cephalic screw position	
Good	120 (71.0)
Poor	49 (29.0)
Reduction in AP view	
Good	131 (77.5)
Poor	38 (22.5)
Reduction in lateral view	
Good	156 (92.3)
Poor	13 (7.7)
Lateral wall fracture	
No	135 (79.9)
Yes	34 (20.1)
Design of cephalic screws	
Single blade	129 (76.3)
Double screws	40 (23.7)

SD, standard deviation; ASA score, American Society of Anesthesiologists score; AO/OTA, Arbeitsgemeinschaft für Osteosynthesefragen/Orthopedic Trauma Association; TAD, tip-apex distance; AP, anterior-posterior.



**Figure 5** The Kaplan-Meier curve showing the overall survival of the included patients.

**Table 2** Univariate Cox regression analyses of basic characteristics with total follow-up all-cause mortality

Factors	HR (95% CI)	P
Age (per 1-year increase)	1.054 (1.005–1.106)	0.031*
Gender	2.063 (1.137–3.745)	0.017*
Male		
Female		
Anesthesia	1.444 (0.713–2.924)	0.308
Spinal		
General		
ASA score		
2	1.000 (Reference)	
3	1.668 (0.225–12.380)	0.617
4	1.533 (0.206–11.427)	0.677
Preoperative waiting time (days)	1.027 (0.938–1.123)	0.565
Blood transfusion	0.616 (0.333–1.140)	0.123
No		
Yes		
Hemoglobin (g/L)	0.975 (0.957–0.993)	0.006*
Albumin (g/L)	0.825 (0.768–0.885)	<0.001*

\*,  $P < 0.05$  with significant difference. HR, hazard ratio; CI, confidence interval; ASA score, American Society of Anesthesiologists score.

were no statistically significant differences in anesthesia type, ASA score, pre-operative waiting time, and blood transfusion ( $P > 0.05$ ; as shown in *Table 2*). For the measuring surgical factors, poor reduction in lateral view (HR 2.626, 95% CI: 1.170–5.896,  $P = 0.019$ ) was significantly associated with the higher overall mortality at the end of follow-up. In terms of Dorr morphology, TAD, position of cephalic screw, reduction in AP view, the integrity of lateral wall, and the design of cephalic screws, the difference had no statistical significance ( $P > 0.05$ ; as shown in *Table 3*).

The pertinent variables discovered by univariate Cox regression analysis were included into a multivariable Cox proportional risk model. The multivariate analysis revealed that the lower pre-operative level of Alb (HR 0.851, 95% CI: 0.780–0.929,  $P < 0.001$ ) and the poor reduction in lateral view (HR 0.298, 95% CI: 0.129–0.689,  $P < 0.001$ ) were

**Table 3** Univariate Cox regression analyses of measuring surgical factors with total follow-up all-cause mortality

Factors	HR (95% CI)	P
AO/OTA classification		
31A1	1.000 (Reference)	
31A2	0.374 (0.039–3.616)	0.396
31A3	1.419 (0.194–10.364)	0.730
Dorr morphology (Type A/Type B)	0.578 (0.306–1.094)	0.092
TAD, mm	1.026 (0.961–1.095)	0.450
Cephalic screw position (Good/Poor)	1.665 (0.800–3.465)	0.173
Reduction in AP view (Good/Poor)	1.679 (0.890–3.167)	0.110
Reduction in lateral view (Good/Poor)	2.626 (1.170–5.896)	0.019*
Lateral wall fracture (No/Yes)	0.695 (0.351–1.375)	0.296
Design of cephalic screws (Single blade/Double screws)	1.526 (0.694–3.261)	0.338

\*, P<0.05 with significant difference. HR, hazard ratio; CI, confidence interval; TAD, tip-apex distance; AO/OTA, Arbeitsgemeinschaft für Osteosynthesefragen/Orthopedic Trauma Association; AP, anterior-posterior.

**Table 4** Multivariate Cox regression analyses of selected factors with total follow-up all-cause mortality

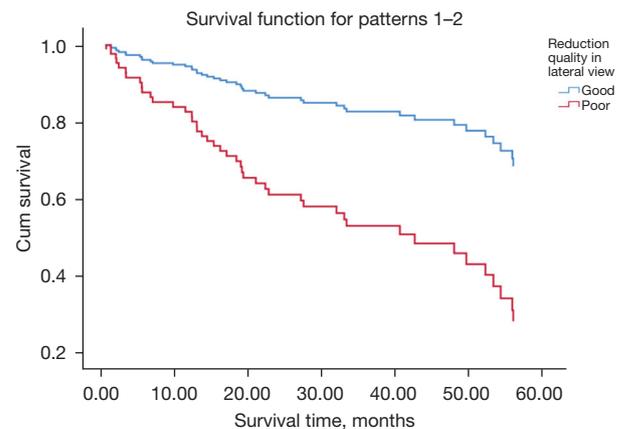
Factors	HR (95% CI)	P
Age (per 1-year increase)	1.027 (0.975–1.082)	0.315
Gender	1.553 (0.791–3.051)	0.201
Hemoglobin, g/L	0.986 (0.967–1.006)	0.164
Albumin, g/L	0.851 (0.780–0.929)	<0.001*
Reduction in lateral view (good/poor)	0.298 (0.129–0.689)	<0.001*

\*, P<0.05 with significant difference. HR, hazard ratio; CI, confidence interval.

independent risk factors for poor OS (Table 4 and Figure 6).

## Discussion

According to our study, the preoperative level of Alb and the reduction quality in lateral view are associated with postoperative mortality in elderly pertrochanteric fracture patients. Surgical operation is the first choice for the treatment of this type of fracture. In unstable fracture



**Figure 6** The adjusted survival curves for the included patients according to the reduction quality in lateral view (multivariable Cox regression analyses adjusted with age, gender, preoperative levels of Hb and Alb). Hb, hemoglobin; Alb, albumin.

patterns, it is widely acknowledged that intramedullary fixation is superior to extramedullary implants (5). Many previous studies have investigated the prognostic factors for the postoperative mortality of pertrochanteric fracture patients, such as age, gender, ASA score, and preoperative waiting time (8-12). The relationship between mortality rate and surgical factors, which have been shown to be associated with implant failure, has not been widely investigated in prior research.

In our study, we investigated the relationship between survival of pertrochanteric fracture patients treated with intramedullary nails and surgical factors, including Dorr morphology, TAD, position of cephalic screw, reduction in AP and lateral views, the integrity of lateral wall, and the design of cephalic screws. Among the variables, fracture reduction quality in the lateral view appeared to be an important predictor of postoperative mortality in this type of fractures patients.

Some previous studies have indicated the correlation between fracture reduction quality and the postoperative survival of elderly patients with pertrochanteric fractures. He *et al.* (28) found that compared with patients with an excellent reduction, those with an acceptable reduction had a 1.1-fold increase in mortality at the 1-year follow-up, whereas those with a poor reduction had a 13.8-fold increase in mortality. A study including 329 patients revealed that there appeared to be a correlation between fracture reduction and postoperative survival of geriatric hip fracture patients at 1 year (20). Unlike previous investigations, we assessed the reduction quality of fracture

in the AP and lateral views separately, as opposed to combining them. To our knowledge, few people have found that reduction quality in the lateral view was probably the key factor influencing the postoperative mortality of pertrochanteric fracture patients, even more than reduction quality in the AP view, which seemed to have no impact on the survival of patients. In previous studies, AP radiographs were used more often for assessing reduction quality, and there was lack of consensus regarding the quality of fracture reduction in lateral radiographs. Tsukada *et al.* (29) revealed that excessive sliding occurred following the surgical treatment for pertrochanteric fractures with posterior displacement of the head and neck fragment. Momii *et al.* (30) found that inadequate reduction on either the AP or lateral views was correlated with significant postoperative sliding. The research by Kristan *et al.* (14) demonstrated that reduction of pertrochanteric fractures in lateral view influenced the healing rate of fracture and walking ability after half a year. These prior studies and our own study highlight that surgeons must make every effort to improve the reduction quality of pertrochanteric fractures specially in the lateral view in clinical practice.

Pain and biomechanics are 2 potential causes for the correlation between reduction quality of fractures and patient survival. The primary aim of pertrochanteric fracture surgery is early mobilization to prevent problems associated with bed rest and death (31). Poorly reduced fractures may be more painful than anatomically reduced fractures, resulting in delayed mobility and extended bed rest (32). Furthermore, instability caused by mal-reduction can result in limb shortening, loss of abductor function, and implant-related complications (major ones such as cut-out, or minor ones such as lateral hip pain by shortening of the column, etc.), all of which can lead to negative outcomes (33).

In addition, when patients are at a greater risk of death and it is considered more important to proceed with fixation and strive for a shorter surgical time than to continue striving to improve the reduction, surgeons may tolerate a poorer reduction. Similarly, the increased operative time, soft tissue dissection, and blood loss associated with open reduction compared to closed reduction may not be in the best interest of the patient, or their functional demands may be reduced, allowing them to accept a poor reduction. In addition, unskilled surgeons are more likely to perform a poor fracture reduction, and the surgeon's experience, not the fracture reduction itself, may have more important impact on the patient's outcome (20). The findings encourage us to a better fracture comprehension and especially to

concentrate on the quality of the reduction (14,20).

Several previous studies have also examined the association between femoral bone quality and postoperative mortality. In the study by Nyholm *et al.* (34), it was found that patients with displaced femoral neck fractures with a thinner cortex had an increased risk of mortality. Nevertheless, similar to our findings, another study found that indicators of femoral bone quality, such as CCR and Dorr type, were not substantially related with the postoperative survival of patients with pertrochanteric fracture (21). This might be due to the differences in bone quality between pertrochanteric and femoral neck fracture of the femur (35). Other surgical factors involving fracture type (AO/OTA classification), implant position (TAD, position of cephalic nails), the integrity of lateral wall, and the design of cephalic screws were found to have no correlation with patient survival in our study, despite having a strong correlation with the final success of operations (36).

Numerous prior studies have demonstrated that preoperative factors such as age, gender, ASA score, and preoperative waiting time are linked with mortality risk (8-12). However, after multivariate adjustment, the preoperative level of Alb was the only factor associated with the mortality of patients in our study. Serum Alb is a routine clinical test, considered a biomarker of inflammation and nutritional status, and a reliable indicator of malnutrition. Hypoalbuminemia is considered an indicator of inflammation, hypercoagulability, and liver disease (37,38). The effect of inflammation on lower Alb levels is a major cause of morbidity and associated mortality (39-41). Therefore, serum Alb levels have been associated with a variety of diseases, and although some studies have not provided direct evidence (42), others have reported that lower serum Alb concentrations are associated with cardiovascular mortality, acute respiratory distress syndrome, acute stroke, chronic kidney disease, and other complications (43-47). In fact, a meta-analysis showed that hypoalbuminemia was an independent predictor of poor prognosis (48), which appeared to be independent of nutritional status and inflammation. Miyanishi *et al.* (49) demonstrated that low serum Alb level, which was considered a marker of health status, was a significant factor influencing the 4-year mortality after hip fracture. Therefore, for patients with hip fractures, preoperative hypoproteinemia is closely associated with postoperative mortality. Chang *et al.* (50) conducted a meta-analysis and found that delaying the operation time significantly increased mortality. We hypothesized that the small sample

size and short duration of follow-up may have contributed to some of the disparities across the trials.

The study has several limitations. First, it is retrospective research and has inherent biases. Second, although Baumgaertner *et al.* (25) and Chang *et al.* (26) demonstrated their reduction quality criteria, there is no universally approved consensus for either anterior-posterior view or lateral view reduction criteria. Third, some other factors, such as following up by phone, lost cases, and so on, may have caused deviations in the results. Fourth, we included 169 patients from a single institution; this small sample size reduced the generalizability of our findings. Consequently, well-designed, multicenter investigations with larger samples are required.

## Conclusions

A sufficient preoperative level of Alb and a good reduction quality in lateral view are associated with lower postoperative mortality in elderly pertrochanteric fracture patients. Geriatrics and orthopedic surgeons should notice these parameters to improve their results. Therefore, to improve the prognosis of patients, every effort should be made to optimize reduction quality of pertrochanteric fractures, particularly in lateral view.

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## Footnote

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <https://qims.amegroups.com/article/view/10.21037/qims-23-424/coif>). The authors have no conflicts of interest to declare.

*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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Institutional Review Board (IRB) of Peking University First Hospital (No. 2021-432) and the requirement for individual consent for this retrospective analysis was waived.

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