



Predisposing factors for contralateral hip fractures in elderly patients over 80 years old

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The prevalence of hip fractures has gradually become a major public health issue, particularly among elderly individuals, usually due to the aging population and related ill health. These types of fractures have often been known to be caused by low-energy falls and are related to significant health complications, increased mortality rates, and high health costs.^[1] The consequences of hip fractures go beyond the immediate physical injuries to encompass extended hospital stays, rehabilitation, and poor quality of life for the affected individuals. Researchers indicate that hip fracture rates are on the rise and point to the pressing need for effective prevention and therapeutic strategies directed at this particular demographic group.^[2,3] Contralateral hip fracture following an initial fracture is particularly common among elderly patients, where previous studies showed between 11 and 15% may fracture on the opposite side within a decade following the initial fracture.^[4-6] A contralateral hip fracture

ABSTRACT

Objectives: This study aims to identify risk factors associated with contralateral hip fractures in elderly patients over 80 years old following an initial hip fracture.

Patients and methods: Between May 2015 and April 2018, a total of 1,138 elderly patients (303 males, 805 females; median age: 85 years; interquartile range [IQR], 82 to 88 years) who were hospitalized for hip fractures were retrospectively analyzed. Data on demographics, comorbidities, and biochemical markers were collected during the initial hospitalization. Patients were followed for up to two years to identify cases of contralateral hip fractures. Risk factors were analyzed using univariate analyses and a Cox proportional hazards model using odds ratios (ORs) and confidence intervals (CIs).

Results: Of the patients, 98 (8.61%) experienced a contralateral hip fracture within two years. The incidence rates at 12 months and 24 months were 4.3% and 8.61%, respectively. Multivariable analysis identified chronic obstructive pulmonary disease (OR=0.393, 95% CI: 0.183-0.841), increasing Charlson Comorbidity Index (OR=1.308, 95% CI: 1.029-1.662), lower extremity deep vein thrombosis (OR=0.168, 95% CI: 0.079-0.354), pneumonia (OR=0.133, 95% CI: 0.075-0.236), and urinary tract infection (OR=0.113, 95% CI: 0.058-0.220) as significant risk factors for contralateral hip fractures.

Conclusion: Several key risk factors were found to be associated with contralateral hip fractures in elderly patients over 80 years old. Specifically, chronic obstructive pulmonary disease, increased Charlson Comorbidity Index, lower extremity deep vein thrombosis, pneumonia, and urinary tract infections significantly increased the risk of contralateral hip fractures. These findings highlight the importance of comprehensive assessment and targeted interventions in high-risk patients to mitigate the risk of subsequent fractures. Our results underscore the need for early identification of at-risk individuals and the implementation of preventive strategies to improve patient outcomes.

Keywords: Contralateral hip fracture. elderly patients, epidemiology. hip fracture. risk factors.

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occurs in elderly patients after a primary fracture with an incidence ranging from 6.8 to 16%.^[7,8] It is associated with higher mortality rates, increased health problems, and higher loss of self-sufficiency

compared to subjects with a single hip fracture.^[9,10] The majority of risk factors set up in the literature refer to the long-term incidence of subsequent fractures within a decade. However, it should be underlined that the risk of the second hip fracture is maximum during the first year after the first fracture, whereas more than half of them happen in a period of two years and more than 70% happen within a period of four years.^[11-14]

Given the significant morbidity and mortality associated with contralateral hip fractures in elderly patients, it is crucial to identify the specific combinations of risk factors which constitute the risky group to inform targeted prevention strategies and improve patient outcomes. While previous studies have identified several risk factors associated with contralateral hip fractures, including advanced age, comorbidities such as chronic obstructive pulmonary disease (COPD), deep vein thrombosis (DVT), pneumonia, and urinary tract infections, and frailty,^[5,15,16] there are still critical gaps in our understanding. Most prior research has focused on long-term outcomes over a decade, whereas the risk of a second hip fracture is highest in the first few years after the initial fracture.^[11-14] In the present study, we aimed to evaluate the short- to mid-term risk of contralateral hip fractures in elderly patients aged 80 and older.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at Capital Medical University, Department of Emergency between May 31st, 2015 and April 30th, 2018. This study included elderly patients with hip fractures who were admitted for the first time and underwent surgery at our hospital. The patients were over 80 years old at the time of their fracture, and follow-up data was available for at least 24 months.^[14] Inclusion criteria were as follows: age ≥ 80 years; first occurrence of hip fracture (femoral neck fracture, intertrochanteric fracture, and subtrochanteric fracture) and surgical treatment at our hospital; low-energy injury in fracture patients; and the patients in whom contralateral hip fracture were diagnosed within three weeks after the bone fracture. Exclusion criteria were as follows: age under 80 years; incomplete patient data records; recurrence of ipsilateral hip fracture (periprosthetic fracture), case-based fracture, and bilateral hip fracture within two years after the first hip fracture surgery; death within two years of follow-up; and patients who undergo artificial hip replacement or hip replacement surgery undergo

internal fixation surgery on the other side of the previous fracture. Finally, a total of 1,138 patients (303 males, 805 females; median age: 85 years; interquartile range [IQR], 82 to 88 years) who met the inclusion criteria were recruited. Based on the follow-up results, the patients were divided into two groups: Group 1 (n=1,040) who did not experience a second contralateral hip fracture and Group 2 (n=98) who did experience a second contralateral hip fracture. The study flowchart is shown in Figure 1. Written informed consent was obtained from each patient. The study protocol was approved by the Beijing Jishuitan Hospital Ethics Committee (Date: 04.12.2024, No: [K2004] [502]-00). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Outcome measures and variables

We recorded demographic characteristics and risk factors. We collected the patient's sex, age, height, weight, and living conditions (independent, partially dependent, totally Dependent), as well as fracture types, through inquiry from the medical records. The major comorbidities included coronary heart disease, hypertension, arrhythmia, cardiac insufficiency, diabetes, cerebrovascular disease, peripheral vascular disease, COPD, malignant tumor, chronic renal insufficiency, liver disease, thyroid disease, Parkinson's disease, autoimmune disease, and calculated the Charlson Comorbidity Index (CCI) and modified Frailty Index of Five Deficits (mFI-5). Preoperative blood counts and biochemical analyses were performed, including white blood cell (WBC) count, hemoglobin (HGB), platelet (PLT) count, alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin (ALB), glucose (GLU), urea (UREA), creatinine (CREA), calcium (Ca), inorganic phosphorus (IP), potassium (K), sodium (Na), creatine kinase-MB (CK-MB), cardiac troponin I (CTNI), prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (APTT), D-dimer (D-D), pH, partial pressure of carbon dioxide (PCO₂), partial pressure of oxygen (PO₂), lactic acid (Lac), oxygen saturation (SO₂), total procollagen type 1 N-terminal propeptide (tP1NP), β -C-terminal telopeptide of type I collagen (β -CTX), osteocalcin (OC), 25-hydroxyvitamin D (25-(OH) VD3), and parathyroid hormone (PTH). Additionally, bone mineral density (BMD) measurements were recorded for patients who underwent dual-energy X-ray absorptiometry (DEXA) scans as part of their routine care. Data regarding osteoporosis treatment, including the use of bisphosphonates, selective

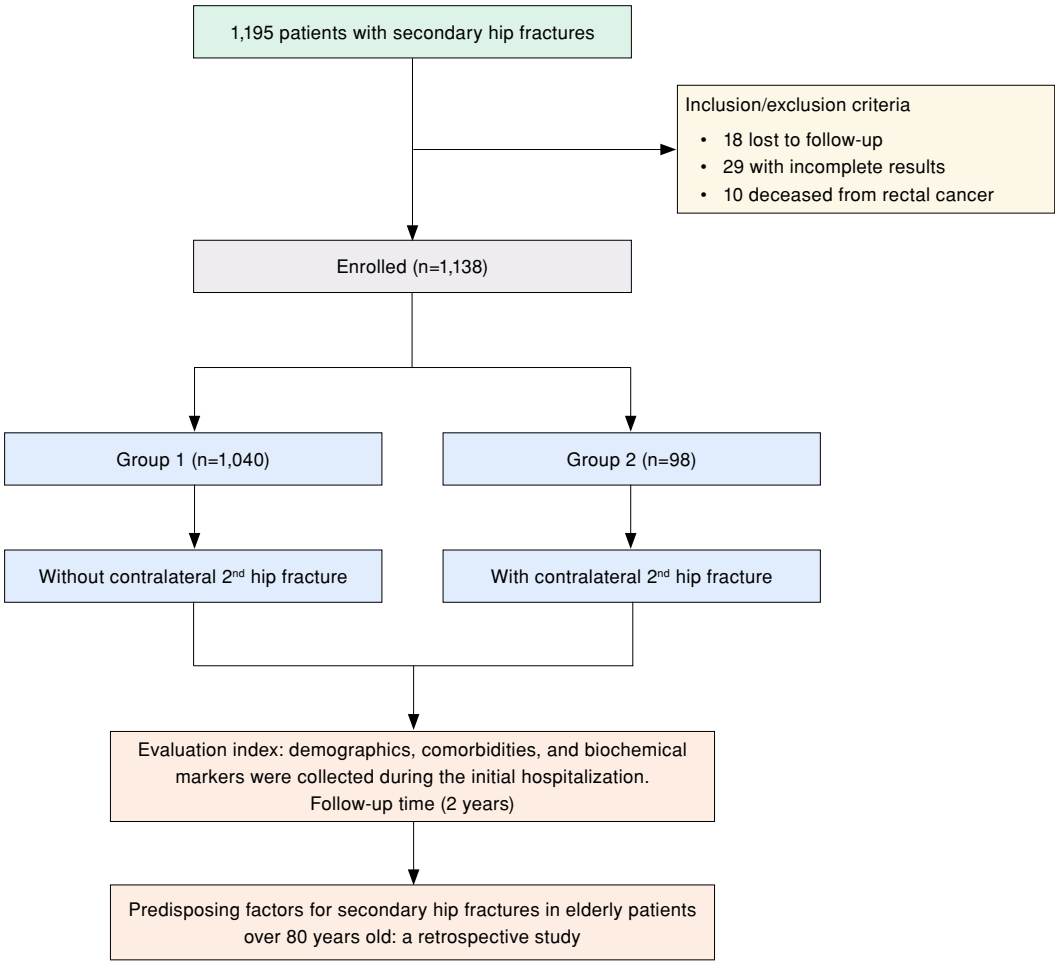


FIGURE 1. Study flowchart.

estrogen receptor modulators, and other relevant therapies, were also collected from the medical records. The treatment measures were executed by experienced orthopedic surgeons and rehabilitation specialists, while the outcome assessments were conducted by a team comprising attending physicians, research nurses, and a biostatistician. This multidisciplinary approach ensured the quality and reliability of both the treatment and the assessment processes.

Follow-up

In our study, from the time of the first hip fracture as the starting point, the patients were followed for 90 days, 180 days, 360 days, 540 days, and 720 days, with contralateral hip fracture and loss of follow-up as the endpoint.^[14] The choice of a two-year follow-up period was based on previous research indicating that the risk of a second hip fracture is highest within the first two years after

the initial fracture.^[11-14] This period is critical for identifying and managing risk factors to prevent subsequent fractures.

Statistical analysis

Statistical analysis was performed using the SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). The normality of quantitative data was assessed using the Shapiro-Wilk test. Continuous data were presented in mean ± standard deviation (SD) or median and IQR, 25th-75th), while categorical data were presented in number and frequency. Comparisons between the groups were conducted using the independent samples t-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data. Categorical data were compared using the chi-square test or Fisher exact test. Univariate analyses were performed to identify potential risk factors associated with contralateral hip fractures. Factors with a

p value of <0.05 were included in the multivariate analysis. Cox proportional hazards regression models were used to assess the independent risk factors for contralateral hip fractures, with hazard ratios (HRs) and 95% confidence intervals (CIs) calculated. The proportional hazards assumption of the Cox model was tested using Schoenfeld residuals. The Kaplan-Meier survival analysis was performed to illustrate the survival differences between groups. Missing data were handled using multiple imputation to minimize bias. A p value of <0.05 was considered statistically significant.

RESULTS

The characteristics of the two patient groups are presented in Table I. Among the fracture types, femoral neck fractures accounted for 532 (46.8%), intertrochanteric fractures accounted for 592 (52%), and subtrochanteric fractures 14 (1.2%). Among the 1,138 patients, 64.6% were independently mobile. Over the course of the two-year follow-up period, 98 patients developed contralateral fractures. The overall median age at the time of the first hip fracture without a second contralateral hip fracture (Group 1) was 85 (range, 82 to 88) years, while the mean age for those with a second contralateral hip fracture (Group 2) was 85.5 (range, 83 to 88) years. In terms of age distribution, the cohort was comprised of 56.6% patients aged 80-85, 29.4% aged 86-90, and 14% aged over 90 years old. Bone mineral density measurements were available for 762 (67.0%) patients, with a mean BMD of 0.72 ± 0.15 g/cm² in Group 1 and 0.68 ± 0.27 g/cm² in Group 2 ($p=0.034$). Osteoporosis treatment was documented in 402 (40.1%) patients, with a higher proportion in Group 2 (55.1%) compared to Group 1 (38.7%, $p=0.048$).

Incidence of contralateral hip fractures

The univariate analysis showed that higher sodium serum levels, pH, PO₂, and SO₂ and lower lactate levels were associated with a higher tendency to suffer a contralateral hip fracture. Contralateral hip fractures also presented acute chest infections more frequently, and also urinary and tract infections and DVT during the follow-up. These patients also had significant increases in the following conditions: arrhythmia, chronic heart failure, cerebrovascular disease, peripheral vascular disease, COPD, chronic kidney disease, and Alzheimer's disease. They also had a higher CCI score and 5-mFI, indicating a greater overall burden of comorbidities and frailty.

According to Cox's proportional hazards regression, some of the risk factors had a significant relationship with a high incidence of contralateral hip fractures, COPD, DVT, pneumonia, and urinary tract infection during the follow-up (Table II).

In follow-up studies, 98 patients, which were 8.61% of the studied group, developed a contralateral fracture within two years of their initial hip fracture. Rates of occurrence accordingly for contralateral fractures within 90, 180, 270, 360, 450, 540, and 630 days were 1.14%, 2.20%, 2.81%, 4.3%, 5.1%, 5.71%, and 6.77%, respectively (Figure 2). The incidence rates of contralateral fractures at 90 days, 180 days, 270 days, 360 days, 450 days, 540 days, 630 days, and 720 days were 0.0%, 0.9%, 1.8%, 3.6%, 4.5%, 4.8%, 5.7%, and 6.6%, respectively. Contralateral fracture rates were recorded at 1.1%, 2.2%, 2.7%, 4.1%, 4.8%, 5.7%, 6.8%, and 9.1% for 90 days, 180 days, 270 days, 360 days, 450 days, 540 days, 630 days, and 720 days, respectively (Figure 3). In the 80-85-year age group, there were 49 cases, while the incidences of contralateral fracture were 1.2%, 1.7%, 2.0%, 3.4%, 4.0%, 4.3%, 5.6%, and 7.6%, respectively, at 90, 180, 270, 360, 450, 540, 630, and 720 days. For the age group 86-90 years, which consisted of 35 cases, the contralateral fracture rates were as follows: at 90 days, 1.2%; 180 days, 3.6%; 270 days, 5.1%; 360 days, 7.2%; 450 days, 8.1%; 540 days, 9.0%; 630 days, 9.6%; and 720 days, 10.5%. Of the 14 cases in the age group above 90, the incidence rates at 90, 180, 270, 360, 450, 540, 630, and 720 days were 0.6%, 1.3%, 1.3%, 1.9%, 3.1%, 4.3%, 5.7%, and 8.8%, respectively (Figure 4). Over time, the incidence of contralateral hip fracture increases continuously (Table III).

Combinations of risk factors

In addition to identifying individual risk factors, we explored the combined effects of these factors on the risk of contralateral hip fractures. Our analysis revealed that patients with a combination of COPD and a high CCI (≥ 3) had a particularly elevated risk of experiencing a contralateral hip fracture within the two-year follow-up period. Specifically, patients with both COPD and a CCI ≥ 3 had an HR of 2.45 (95% CI: 1.52-3.96) compared to those without these conditions.

Similarly, patients with both lower extremity DVT and a history of pneumonia or urinary tract infections were also at a significantly higher risk. The combined presence of DVT and either pneumonia or urinary tract infection was associated with an HR of 2.10 (95% CI: 1.34-3.28) for contralateral hip

TABLE I
Comparison of possible factors associated with second fracture in two-year follow-up between two groups

| | Total number (n=1,138) | | Group 1 (n=1,040) | | Group 2 (n=98) | | <i>p</i> |
|--|---------------------------|-------|----------------------|-------|-------------------|-------|----------|
| | n | % | n | % | n | % | |
| Age (year) | 85 | 82.88 | 85 | 82.88 | 85.5 | 83.88 | 0.149 |
| Age group | | | | | | | 0.312 |
| 80-85 | 645 | 56.6 | 596 | 57.3 | 49 | 50 | |
| 86-90 | 334 | 29.4 | 299 | 28.7 | 35 | 35.7 | |
| >90 | 159 | 14.0 | 145 | 1.39 | 14 | 14.3 | |
| Sex | | | | | | | 0.121 |
| Male | 333 | 29.3 | 311 | 29.9 | 22 | 22.4 | |
| Female | 805 | 70.7 | 729 | 70.1 | 76 | 77.6 | |
| Fracture type | | | | | | | 0.021 |
| Femoral neck fracture | 532 | 46.8 | 474 | 45.6 | 58 | 59.2 | |
| Intertrochanteric fracture | 592 | 52.0 | 554 | 53.3 | 38 | 38.8 | |
| Subtrochanteric fracture | 14 | 1.2 | 12 | 1.2 | 2 | 2.0 | |
| Ambulatory capacity | | | | | | | 0.627 |
| Independent | 735 | 64.6 | 676 | 65 | 59 | 60.2 | |
| Partially dependent | 369 | 32.4 | 333 | 32 | 36 | 36.7 | |
| Totally dependent | 34 | 3.0 | 31 | 3.0 | 3 | 3.1 | |
| Comorbid disease | | | | | | | |
| Hypertension | 619 | 54.4 | 565 | 54.3 | 54 | 55.1 | 0.883 |
| Coronary heart disease | 268 | 23.6 | 238 | 22.9 | 30 | 30.6 | 0.085 |
| Arrhythmia | 90 | 7.9 | 77 | 7.4 | 13 | 13.3 | 0.040 |
| Cardiac insufficiency | 58 | 5.1 | 44 | 4.2 | 14 | 14.3 | <0.001 |
| Diabetes mellitus | 176 | 15.5 | 195 | 18.8 | 19 | 19.4 | 0.877 |
| Cerebrovascular disease | 217 | 19.1 | 184 | 17.7 | 33 | 33.7 | <0.001 |
| Peripheral vascular diseases | 16 | 1.4 | 12 | 1.2 | 4 | 4.1 | 0.019 |
| COPD | 47 | 4.1 | 38 | 3.8 | 9 | 9.2 | 0.009 |
| Malignant tumor | 54 | 4.7 | 46 | 4.4 | 8 | 8.2 | 0.096 |
| Chronic kidney disease | 38 | 3.3 | 29 | 2.8 | 9 | 9.2 | 0.001 |
| Liver disease | 11 | 1 | 9 | 0.9 | 2 | 2.0 | 0.256 |
| Thyroid gland diseases | 16 | 1.4 | 14 | 1.3 | 2 | 2.0 | 0.577 |
| Alzheimer's disease | 64 | 5.6 | 46 | 4.4 | 18 | 18.4 | <0.001 |
| Parkinson | 19 | 1.7 | 15 | 1.4 | 4 | 4.1 | 0.051 |
| Autoimmune disease | 11 | 1 | 10 | 1.0 | 1 | 1.0 | 0.955 |
| Complications during follow-up period | | | | | | | |
| Pneumonia | 37 | 3.2 | 17 | 1.6 | 20 | 20.4 | <0.001 |
| Urinary tract infection | 19 | 1.7 | 5 | 0.5 | 14 | 14.3 | <0.001 |
| Lower extremity deep vein thrombosis | 17 | 1.5 | 7 | 0.7 | 10 | 10.2 | <0.001 |
| Bone mineral density (g/cm ²), (mean±SD) | 762 | 67.0 | 0.72±0.15 | | 0.68±0.27 | | 0.034 |
| Osteoporosis treatment | 456 | 40.1 | 402 | 38.7 | 54 | 55.1 | 0.048 |
| Charlson Comorbidity Index | 4 | 3.5 | 4 | 3.5 | 5 | 4.6 | <0.001 |
| 5-mFI | 1 | 0.2 | 1 | 0.2 | 1 | 1.2 | 0.011 |

COPD: Chronic obstructive pulmonary disease; 5-mFI: 5-factor modified frailty index.

fractures within two years (Table IV). The presence of multiple comorbidities, particularly respiratory conditions and infections, could synergistically increase the risk of subsequent fractures.

DISCUSSION

In the present study, we evaluated the short- to mid-term risk of contralateral hip fractures in elderly patients aged 80 and older. Our findings

TABLE II
Comparison of blood test results associated with second fracture in two-year follow-up between two groups

| | Group 1 (n=1,040) | | Group 2 (n=98) | | p |
|----------------------------|-------------------|-----------|----------------|-----------|-------|
| | Median | Min-Max | Median | Min-Max | |
| WBC ($\times 10^9/L$) | 9.9 | 7.8-12.1 | 9.6 | 7.4-12.1 | 0.531 |
| HGB (g/L) | 115 | 103-125.5 | 115 | 104-128 | 0.584 |
| PLT ($\times 10^9/L$) | 190 | 153-237 | 199 | 165-235 | 0.394 |
| ALT (U/L) | 13 | 10-17 | 12 | 9-15 | 0.052 |
| AST (U/L) | 19 | 16-23 | 19 | 15-22 | 0.285 |
| TP (g/L) | 63.9 | 59.6-67.7 | 65.25 | 60.1-68.7 | 0.143 |
| ALB (g/L) | 39.7 | 37.3-41.7 | 39.2 | 37-42 | 0.944 |
| GLU (mmol/L) | 7.7 | 6.7-9.6 | 7.5 | 6.6-9.6 | 0.283 |
| UREA (mmol/L) | 7.4 | 5.9-9.4 | 7.4 | 6.0-9.5 | 0.913 |
| CREA ($\mu\text{mol/L}$) | 63 | 51-80 | 64.5 | 49-83 | 0.644 |
| Ca (mmol/L) | 2.3 | 2.2-2.3 | 2.3 | - | 0.556 |
| IP (mmol/L) | 1.0 | 0.8-1.1 | 1.0 | 0.8-1.1 | 0.507 |
| K (mmol/L) | 3.9 | 3.6-4.2 | 4.0 | 3.7-4.2 | 0.223 |
| Na (mmol/L) | 138 | 136-140 | 139 | 137-141 | 0.002 |
| CK-MB (ng/mL) | 1.7 | 1.1-2.7 | 1.6 | 1.2-2.6 | 0.517 |
| CTNI (ng/mx) | 0.1 | 0.0-0.3 | 0.1 | 0.0-0.3 | 0.465 |
| PT (s) | 13 | 12.4-13.5 | 12.7 | 12.0-12.7 | 0.069 |
| INR | 1.0 | 1.0-1.1 | 1 | 1.0-1.1 | 0.233 |
| APTT (s) | 28.1 | 25.6-31 | 27.5 | 24.7-30.6 | 0.078 |
| D-D (mg/L) | 9.0 | 4.1-19.2 | 13.1 | 4.1-26.6 | 0.051 |
| PH | 7.4 | 4.1-19.2 | 7.4 | 7.4-7.5 | 0.022 |
| PCO ₂ (mmHg) | 31.7 | 29.1-34.6 | 30.1 | 28.9-34.1 | 0.193 |
| PO ₂ (mmHg) | 72.9 | 65.7-83 | 78.6 | 70.5-86.6 | 0.001 |
| Lac (mmol/L) | 1.0 | 0.8-1.5 | 1.25 | 0.7-1.6 | 0.036 |
| SO ₂ (%) | 95.3 | 93.5-96.8 | 96.0 | 94.7-97.2 | 0.010 |
| tP1NP (ng/mL) | 48.4 | 32.4-84.6 | 48.4 | 29.9-83.4 | 0.867 |
| β -CTX (ng/mL) | 0.6 | 0.4-0.8 | 0.5 | 0.4-0.8 | 0.816 |
| OC (ng/mL) | 13.6 | 9.8-18.8 | 13.7 | 9.7-19.6 | 0.977 |
| 25-(OH)VD3 (ng/mL) | 10.2 | 7.6-16.2 | 10.5 | 7.2-16.2 | 0.905 |
| PTH (pg/mL) | 53.8 | 7.6-16.2 | 53.9 | 40.7-75.7 | 0.493 |

WBC: White blood cell; HGB: Hemoglobin; PLT: Platelet; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; TP: Total protein; ALB: Albumin; GLU: Glucose; CREA: Creatinine; Ca: Calcium; IP: Inorganic phosphorus; K: Potassium; Na: Sodium; CK-MB: Creatine kinase-MB; CTNI: Cardiac troponin I; PT: Prothrombin time; INR: International normalized ratio; APTT: Activated partial thromboplastin time; D-D: D-dimer; PCO₂: Partial pressure of carbon dioxide; PO₂: Partial pressure of oxygen; Lac: Lactic acid; SO₂: Oxygen saturation; tP1NP: Total procollagen type 1 N-terminal propeptide; β -CTX: β -C-terminal telopeptide of type 1 collagen; OC: Osteocalcin; 25-(OH)VD3: 25-hydroxyvitamin D; PTH: Parathyroid hormone.

highlight the importance of proactive management of comorbid conditions and complications in elderly patients with hip fractures. Early identification and treatment of infections, DVT, and other complications may help reduce the risk of subsequent fractures. Aggressive management of COPD to improve respiratory function and mobility, prompt treatment of infections to prevent hospitalization and deconditioning, and prophylactic measures

against DVT can all contribute to better outcomes. Additionally, our study underscores the need for comprehensive geriatric assessments to identify high-risk patients and implement targeted interventions, such as fall prevention programs and optimized medical management of comorbidities.

The current study focuses on hip fractures among elderly aged 80 and above, and a retrospective analysis of a considerable sample

was performed, thereby attempting to present the real situation in terms of hip fractures among the elderly population. A contralateral hip fracture following an initial hip fracture is a frequent finding in older adults; incidence rates vary between 2.3 and 13.8%.^[18-21] In all, 1,138 patients

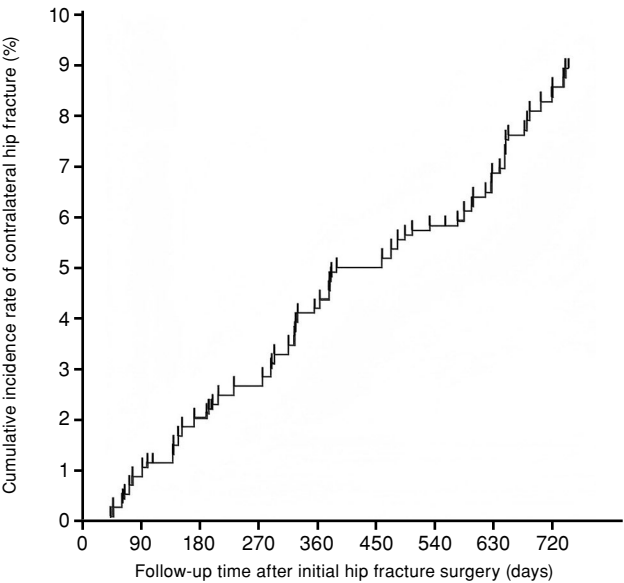


FIGURE 2. Cumulative incidence rate of contralateral fractures within two years after hip fracture surgery in the elderly.

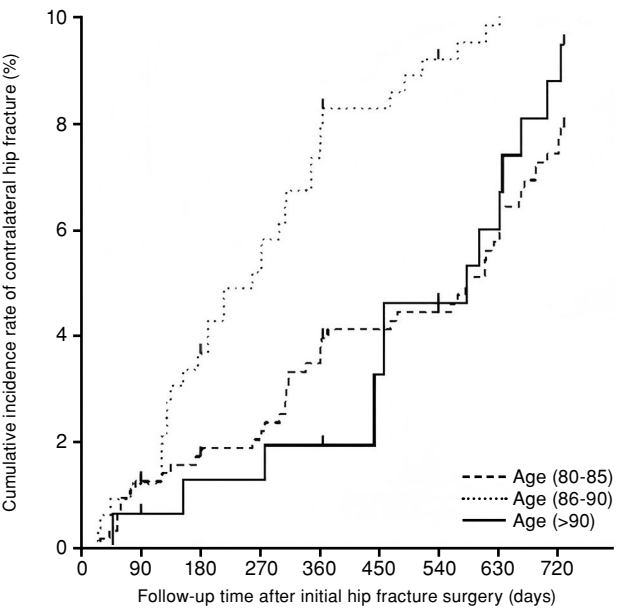


FIGURE 3. Cumulative incidence rate of contralateral fractures within two years after hip fracture surgery in elderly patients of different age groups.

developed an index hip fracture within the study period, of which 98 suffered a contralateral hip fracture within a period of 24 months. Thus, the incidence rate of a second hip fracture in one year is 4.3%, and 8.61% after two years is comparable with studies previously reported.^[21] Our study also suggests the incidence rate of secondary fractures in the elderly population is on the rise in most age groups and both sexes. This is particularly important, as our findings suggest that the prevalence of contralateral fractures tends to increase significantly over time, thereby supporting the need for the continued monitoring and active management of at-risk patients.^[2]

Our study represents the first report on risk factors for a second fracture in elderly patients over the age of 80 years. In the current study, we hypothesized that some patients with underlying medical conditions might be at a higher risk for sustaining a second contralateral hip fracture after an initial hip fracture. Of these, from our previous meta-analysis study, the risk factors significantly associated with a second contralateral hip fracture included female sex, institutional living, poor vision, osteoporosis, dementia, dizziness, cardiac disease, and respiratory diseases.^[10] In contrast, other reports indicate that neither age nor sex should be considered risk factors for secondary fractures.^[22] In our series, patients who suffered a contralateral hip fracture were found to be significantly older at the time of the index hip fracture compared to those

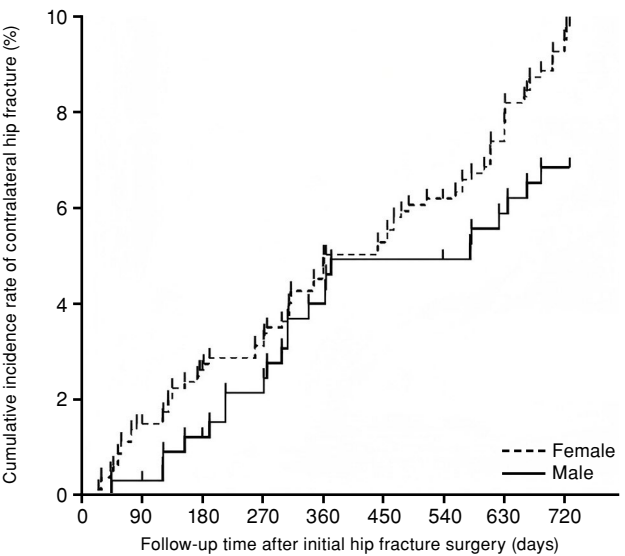


FIGURE 4. Cumulative incidence rate of contralateral fractures within two years after hip fracture surgery in the elderly of different sexes.

TABLE III
Multivariable COX regression analysis of factors affecting two-year second fracture after hip fracture surgery

| | <i>p</i> | OR | 95% CI | |
|---------------------------------------|----------|-------|--------|-------|
| | | | Lower | Upper |
| Chronic obstructive pulmonary disease | 0.016 | 0.393 | 0.183 | 0.841 |
| Increasing Charlson score | 0.028 | 1.308 | 1.029 | 1.662 |
| Lower extremity deep vein thrombosis | 0.000 | 0.168 | 0.079 | 0.354 |
| Pneumonia | 0.000 | 0.133 | 0.075 | 0.236 |
| Urinary tract infection | 0.000 | 0.113 | 0.058 | 0.220 |
| CI: Confidence interval. | | | | |

TABLE IV
Impact of combinations of risk factors on the risk of contralateral hip fractures

| Risk factor combination | HR | CI |
|---|------|-----------|
| COPD + Charlson comorbidity index ≥ 3 | 2.45 | 1.52-3.96 |
| Lower extremity deep vein thrombosis + pneumonia or urinary tract infection | 2.10 | 1.34-3.28 |
| HR: Hazard ratio; CI: Confidence interval; COPD: Chronic obstructive pulmonary disease. | | |

patients who did not suffer a subsequent fracture. However, no significant relation between age and sex was noted with secondary fractures in the present study.

It has also been seen that respiratory diseases are one of the major risk factors for second hip fractures.^[23,24] The type of respiratory disease that characterized our study group was essentially asthma and COPD. Besides having markedly impaired respiratory function, patients with severe-to-moderate COPD are often systemically ill and may have received systemic corticosteroids for the condition over the long term, either or both of which further increase their risk for reduced BMD. Patients with respiratory disease are often less active than other patients. This is frequently associated with disuse syndrome, as this patient with respiratory illness might be more vulnerable to a succession of falls and a successive fracture. Chapman et al.^[25] found that the prevalence of COPD increased appreciably with increasing age. The ratio of patients with respiratory disease was low, but in the second-fracture group it was about double of that in unilateral fracture group, perhaps owing to the mean age being higher, which may account for the high proportion of patients having respiratory disease. In addition, hip fracture patients enjoy extremely poor mobility, and long-term bed rest after surgery can easily result in respiratory infections, acute COPD exacerbation, reduction in

bone cell activity, and even further decline in bone density. The vicious circle of the two eventually leads to repeated contralateral bone fracture, which seriously influences the prognosis and quality of life for the patient while increasing medical burden.^[26-28] Elderly patients with respiratory diseases should be closely monitored and treated. As the most significant underlying strategy for the prevention of secondary injuries would involve hip protectors that fit properly, changes in their living environment will also be required.^[29]

The implications of our results extend beyond mere identification of risk factors; they also have substantial relevance for clinical practice and policy formulation. Our findings align with several international studies that have identified COPD and high comorbidity indices as significant risk factors for secondary hip fractures. A study by Ryg et al.^[8] reported that patients with COPD had a higher risk of secondary hip fractures, similar to our results. Additionally, the CCI has been widely recognized as a predictor of fracture risk in elderly populations, as demonstrated by Reyes et al.,^[30] who found that a CCI score of ≥ 3 was associated with a 50% greater risk of hip fracture. Our study further validates these findings, emphasizing the importance of comprehensive geriatric assessment in identifying high-risk patients. Comparatively, secondary fractures on the opposite side following an initial fracture are linked to elevated CCI

scores.^[31,32] Since the CCI score was established as a significant predictor of fracture risk, appropriate comprehensive geriatric assessment may be important in risk stratification and treatment individualization. Therefore, we would recommend the following: a patient with severe disease or with a high number of comorbidities is medically optimized for falls risk assessment before being discharged.

In this study, we investigated the incidence and related risk factors of contralateral hip fractures in elderly patients over the age of 80 following their first hip fracture, which has significant implications for clinical practice. Our study fills a knowledge gap by providing valuable insights into this specific population. Compared to previous studies, we identified complications that occurred during the follow-up period, such as DVT and infectious diseases including pneumonia and urinary tract infections, which have not been previously reported. These complications were found to be risk factors for second contralateral fractures, and their specific mechanisms require further study.

In the current study, we explored various patient-related factors such as age, sex, comorbidities, and serum biochemical markers, in relation to the incidence of contralateral hip fractures. Previous research has identified the significant impact of these factors on fracture risk; however, the underlying mechanisms still remain inadequately understood. Through rigorous statistical analyses, including univariate and multivariate models, this research seeks to delineate the critical risk factors associated with contralateral hip fractures in older adults. The findings would contribute to the development of targeted clinical interventions and preventive measures to mitigate fracture risk in this vulnerable population.^[33]

Furthermore, our study highlights the importance of postoperative management and the need for continued monitoring of patients with high comorbidity indices and respiratory diseases. These findings may inform the development of targeted interventions, such as fall prevention programs and optimized medical management of comorbidities, to reduce the incidence of secondary fractures. Future research should focus on validating these findings in diverse populations and exploring the role of biochemical markers and genetic factors in fracture risk, which could lead to the development of personalized prevention strategies.

Nonetheless, our study has several limitations. First, the retrospective design of the study led to a considerable amount of missing data. Second, the patient population was exclusively Asian. Third, BMD was not assessed, given that there was no discrepancy in the history of osteoporosis treatment between the two groups. Future multi-center, large-scale, prospective studies are needed to validate our findings in diverse populations and address the limitations of retrospective designs in order to develop and test targeted interventions, such as fall prevention programs, optimized medical management of comorbidities, and the use of hip protectors, to mitigate the risk of secondary fractures.

In conclusion, several key risk factors were found to be associated with contralateral hip fractures in elderly patients over 80 years old. Specifically, COPD, increased CCI scores, lower extremity DVT, pneumonia, and urinary tract infections were found to significantly increase the risk of contralateral hip fractures. Furthermore, our analysis revealed that certain combinations of these risk factors, such as COPD combined with a high CCI and DVT combined with a history of pneumonia or urinary tract infections, pose an even greater risk. These findings highlight the importance of comprehensive assessment and targeted interventions in high-risk patients to mitigate the risk of subsequent fractures. Our results underscore the need for early identification of at-risk individuals and the implementation of preventive strategies to improve patient outcomes.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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