Injury, Int. J. Care Injured 50 (2019) 1529–1533

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Relationship of chronic obstructive pulmonary disease severity with early and late mortality in elderly patients with hip fracture

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ARTICLE INFO

Keywords:
Hip fracture
Mortality
Risk factor
COPD

ABSTRACT

Introduction: We conducted a comparative study to compare patients with and without chronic obstructive pulmonary disease (COPD) and to analyze the effect of COPD severity on mortality in elderly patients with hip fractures who were diagnosed by pulmonologists. The purposes of this study were to compare early and late mortality after hip fracture between COPD and non-COPD patients and to assess risk factors of mortality after hip fractures in elderly patients with COPD.

Methods: This study included 1294 patients (1294 hips) who were diagnosed as having unilateral femoral neck or intertrochanteric fractures and who underwent surgery at two hospitals between 2004 and 2017. The patients were categorized into a non-COPD group (853 patients) and a COPD group (441 patients; mild-to-moderate [354 patients] and severe-to-very severe COPD subgroups [87 patients]). The cumulative crude mortality rate was calculated, and 30-day, 60-day, 3-month, 6-month, and 1-year mortality rates were compared between the non-COPD and COPD groups. Logistic regression analysis was conducted to identify independent factors associated with mortality.

Results: The 30-day, 60-day, 3-month, 6-month, and 1-year postoperative cumulative mortality rates were 1.3%, 2.5%, 3.5%, 6.6%, and 10.7%, respectively, in the non-COPD group, and 2.9%, 5.7%, 7.7%, 11.8%, and 16.6%, respectively, in the COPD group ($p = 0.049$, $p = 0.004$, $p = 0.002$, $p = 0.002$, and $p = 0.004$, respectively). The 30-day, 60-day, 3-month, 6-month, and 1-year postoperative cumulative mortality rates in the severe-to-very severe COPD group were 4.6%, 6.9%, 11.5%, 20.7%, and 26.4%, respectively. In elderly patients with hip fracture, COPD increased the risk of mortality for 1.6 times and 1.7 times at 3 months and 1 year postoperative, respectively. In subgroup analysis, severe-to-very severe COPD was associated with 1.55-fold and 1.65-fold increased postoperative mortality risk at 6 months and 1 year respectively, as compared with mild-moderate COPD.

Conclusions: In elderly patients with hip fracture, the comparison between the COPD and non-COPD patients revealed that COPD was an independent factor of mortality at a minimum of 1-year follow-up, and COPD severity in patients with hip fracture was also a risk factor of 6-month and 1-year mortality.

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by progressive airflow limitation [1,2]. The pathophysiology of COPD is complex, and the disease is related to genetic and environmental factors such as smoking and occupational risk factors [1]. COPD is currently the fourth leading cause of death worldwide but has been predicted by the World Health Organization to become the third most common cause of death by the year 2020 [2].

COPD is commonly related with osteoporosis and osteoporotic fractures, and the possible mechanism is reduced bone mineral density due to low body weight, smoking, low physical activity, and uses of steroids [3–6]. Of osteoporosis fractures, hip fracture is considered one of the most serious and important events due to high morbidity, mortality, and socioeconomic burdens [7,8]. In fact,

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https://doi.org/10.1016/j.injury.2019.05.021
0020-1383/

COPD among perioperative risk factors in elderly patients with hip fracture is considered to be closely related with high mortality, and few studies reported on the relationship between COPD and mortality after hip fracture [9–11]. However, most of these studies reported COPD as a risk factor of mortality after hip fracture on the basis of data from claims database, the operational definition of COPD, and data from a sex-specific database [12,13].

Therefore, we designed a comparative study to compare patients with and without COPD and to analyze the effect of COPD severity on mortality in elderly patients with hip fractures who were diagnosed by pulmonologists. The purpose of this study was to compare early and late mortality after hip fracture between COPD and non-COPD patients and to assess risk factors of mortality after hip fractures in elderly patients with COPD. In addition, we also investigated whether there is a difference in mortality according to the severity of COPD through subgroup analysis.

Materials and methods

The design and protocol of this retrospective study were approved by the institutional review board of our hospital (IRB No. 2018-11-024-001).

This study included 1899 elderly patients (2069 hips) who were diagnosed as having unilateral femoral neck or intertrochanteric fractures and who underwent surgery at two hospitals between 2004 and 2017. The exclusion criteria were as follows: had not undergone a pulmonary function test (PFT; 321 patients), had a previous surgery of the affected or unaffected lower extremity (155 patients), age of < 65 years (90 patients), multiple fractures (30 patients), and pathological fracture (9 patients; Fig. 1). The remaining 1294 patients (1294 hips) were categorized into a non-COPD group (853 patients) and a COPD group (441 patients). The COPD group consisted of patients who had been diagnosed with COPD or those who had an obstructive pattern in the PFT that was confirmed by a pulmonologist to be indicative of COPD at the preoperative evaluation.

A diagnosis of COPD was established based on pulmonary function test using the criteria of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guideline. Subjects with a ratio of forced expiratory volume in one second (FEV1) to functional vital capacity (FVC)<0.7 were considered to have COPD. Severity of airflow limitation was classified according to the GOLD criteria (stage I, mild FEV1 ≥ 80%, stage II, moderate 50%≤FEV1 < 80%, stage III, severe 30%≤FEV1 < 50%, stage IV, very severe FEV1 < 30%) [14,15]. Pulmonary function test with spirometer was performed in accordance with the GOLD guideline by certificated technicians. For each patient, spirometer was performed repeatedly for three times and the best data was taken as the patient's result. For subgroup analysis, 441 patients in the COPD group were categorized into mild-to-moderate (354 patients) and severe-to-very severe COPD subgroups (87 patients).

Demographic data, including age, sex, presence of COPD, COPD severity, operation date, diagnosis (femoral neck or intertrochanteric fracture), type of surgery (internal fixation or arthroplasty), type of anesthesia (general or spinal), presence of intensive care unit admission, medical comorbidities on the basis of the modified Charlson's comorbidity index (CCI) [16], and 30-day, 60-day, 3-month, 6-month, and 1-year mortality rates, were obtained by reviewing medical records and radiological findings.

Routine follow-up visits were scheduled at 6 weeks; 3, 6, 9, and 12 months; and every year thereafter. Patients who were unable to attend follow-up evaluations were interviewed by telephone. Clinical information was collected by 1 orthopedic surgeon and 2 nurses. Mortality status was determined using hospital records and/or by interviewing the patient's family. A systematic search for death certificates at the National Statistical Office was conducted for patients who were lost to follow-up.

Statistical analysis

The 30-day, 60-day, 3-month, 6-month, and 1-year cumulative crude mortality rates were calculated and compared between the non-COPD and COPD groups.

Age, sex, diagnosis, type of surgery, medical comorbidities based on the CCI, presence of COPD, and COPD severity were assessed to determine the relationship with mortality. We used the chi-square or Fisher exact tests for categorical variables, and the *T* test for numerical variables. All two-sided p values of <0.05 were

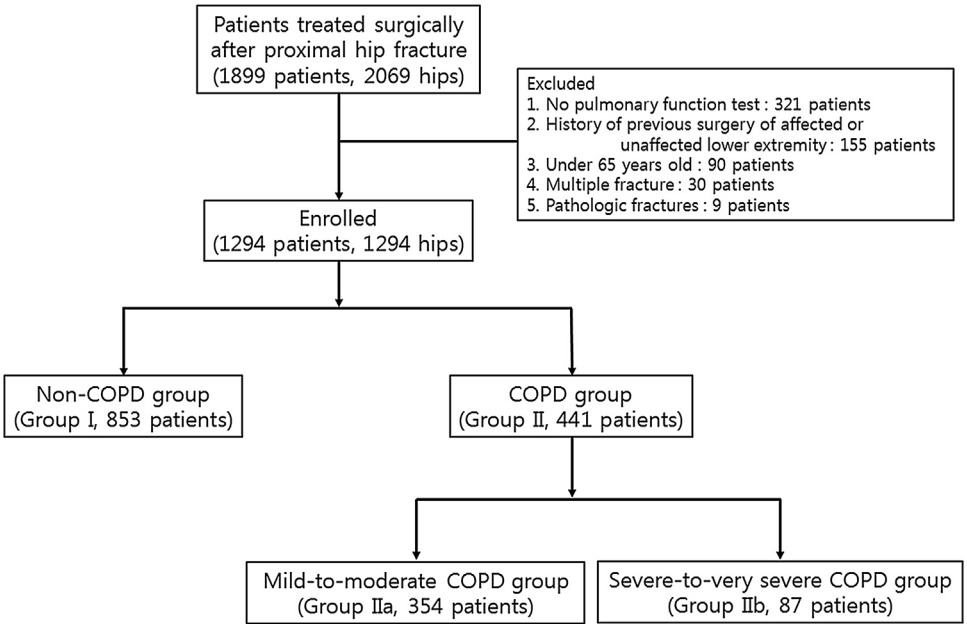

Fig. 1. Flowchart of the study subjects.

considered significant. Multivariate analysis was performed using age, sex, diagnosis, type of surgery, and CCI, as these variables had p values of <0.10. Logistic regression analysis was conducted to identify independent factors associated with mortality. Statistical analysis was performed using IBM SPSS Statistics version 20.0 (IBM, Chicago, IL, USA).

Results

Of 1294 patients, 441 (34%) had COPD. The 30-day, 60-day, 3-month, 6-month, and 1-year postoperative cumulative mortality rates were respectively 1.3%, 2.5%, 3.5%, 6.6%, and 10.7% in the non-COPD group, and 2.9%, 5.7%, 7.7%, 11.8%, and 16.6% in the COPD group ($p = 0.049$, $p = 0.004$, $p = 0.002$, $p = 0.002$, and $p = 0.004$, respectively; Table 1) (Fig. 2). The COPD group was older, had a higher percentage of males, and had higher CCIs ($p < 0.05$).

To evaluate the risk factors of 30-day, 60-day, 3-month, 6-month, and 1-year mortality in the elderly patients with hip fractures, adjusted multivariate analysis was performed. As a result, age (hazard ratio [HR], 1.07; 95% confidence interval [CI], 1.01–1.12; $p = 0.019$) was identified as the factor that affected 30-day mortality, and age (HR, 1.08; 95% CI, 1.03–1.12; $p < 0.001$) and sex (HR, 2.26; 95% CI, 1.21–4.24; $p = 0.011$) were identified as the factors that affected 60-day mortality. The factors that affected 3-month mortality were sex (HR, 2.19; 95% CI, 1.28–3.77; $p = 0.004$), age (HR, 1.08; 95% CI, 1.04–1.11; $p < 0.001$), and presence of COPD (HR, 1.55; 95% CI, 1.32–1.93; $p = 0.025$). The factors that affected 6-month mortality were sex (HR, 2.31; 95% CI, 1.5–3.54; $p < 0.001$), age (HR, 1.07; 95% CI, 1.04–1.1; $p < 0.001$), and presence of COPD (HR, 1.65; 95% CI, 1.43–1.99; $p = 0.045$). The factors that affected 1-year mortality were sex (HR, 3.45; 95% CI, 2.4–4.96; $p < 0.001$) and age (HR, 1.07; 95% CI, 1.05–1.1; $p < 0.001$).

In the 441 patients with COPD, the 30-day, 60-day, 3-month, 6-month, and 1-year postoperative cumulative mortality rates were respectively 2.5%, 5.4%, 6.8%, 9.6%, and 14.1% in the mild-to-moderate COPD group (354 patients), and 4.6%, 6.9%, 11.5%, 20.7%, and 26.4% in the severe-to-very severe COPD group (87 patients; $p = 0.297$, $p = 0.605$, $p = 0.175$, $p = 0.008$, and $p = 0.009$, respectively; Table 2) (Fig. 2). Between the two groups, the severe-to-very severe COPD group had a higher percentage of males ($p < 0.05$).

To evaluate the risk factors of 6-month and 1-year mortality in the COPD patients with hip fracture, adjusted multivariate analysis was performed. The factors that affected 6-month mortality were age (HR, 1.07; 95% CI, 1.03–1.11; $p = 0.001$) and COPD severity (HR, 1.65; 95% CI, 0.88–3.09; $p = 0.012$). The factors that affected 1-year mortality were age (HR, 1.07; 95% CI, 1.03–1.11; $p < 0.001$), sex (HR: 2.86; 95% CI, 1.64–4.99; $p < 0.001$), and COPD severity (HR, 1.54; 95% CI, 1.3–1.98; $p = 0.042$).

Discussion

Elderly patients with COPD are known to have a high risk of fragility fractures [5,17,18]. The purpose of this study was to compare mortality and assess the risk factors of hip fractures in patients with and without COPD. The principal findings are that the 30-day, 60-day, 3-month, 6-month, and 1-year postoperative cumulative mortality rates were higher in the COPD group (2.9%, 5.7%, 7.7%, 11.8%, and 16.6%, respectively) than in the non-COPD group (1.3%, 2.5%, 3.5%, 6.6%, and 10.7%, respectively; $p = 0.049$, $p = 0.004$, $p = 0.002$, $p = 0.002$, and $p = 0.004$, respectively). The 30-day, 60-day, 3-month, 6-month, and 1-year postoperative cumulative mortality rates in the severe-to-very severe COPD group were 4.6%, 6.9%, 11.5%, 20.7%, and 26.4%, respectively. In elderly patients with hip fracture, COPD was an independent risk factor of one-year-mortality after surgery as it increased the risk of mortality for 1.6 times and 1.7 times at 3 months and 1 year postoperative, respectively. In subgroup analysis, severe-to-very severe COPD was associated with 1.55-fold and 1.65-fold increased postoperative mortality risk at 6 months and 1 year respectively, as compared with mild-moderate COPD.

Higher mortality rates after hip fractures in patients with COPD were reported in several studies. [12,13,19] Luise et al. performed a comparative study of mortality after hip fractures between COPD and non-COPD patients using data from 11,985 patients in a claims database. Among 707 COPD patients with hip fractures, the 30-day, 90-day, and 1-year mortality rates were 16.9%, 25.8%, and 41.8%, respectively. In addition, compared with the patients without COPD, the relative risk (RR) of mortality after hip fracture in those with COPD was 1.58 (95% CI, 1.30–1.90) at 30 days, 1.52 (95% CI, 1.30–1.77) at 90 days, 1.58 (95% CI, 1.40–1.78) at 1 year, and 1.71 (95% CI, 1.55–1.88) overall [12]. However, their studies had some limitations, including the indirect data used that were based on the diagnostic code and operational definition of COPD. Another large-scale study on mortality after hip fracture in 12,646 men with COPD reported that the 1-year mortality rates in patients with severe-to-very severe and mild-to-moderate COPD were 40.2% and 31.0%, respectively, and that in non-COPD subjects was 28.8% [13]. However, their study included only men with COPD with hip fractures and did not include control groups for comparison. To overcome those limitations of previous studies, the patients in this study had COPD diagnosis during a previous clinic visit or hospitalization by a pulmonologist and underwent a PFT at the time of injury were included, and compared with a non-COPD control group. Among the patients with hip fractures, those with COPD had a significant higher postoperative mortality rate than those without COPD. The 30-day, 60-day, 3-month, 6-month, and 1-year postoperative overall mortality rates in the COPD group

Table 1
Comparison between Non-COPD group and COPD group.

	Non-COPD (N = 853)	COPD (N = 441)	p-value
Age (years)±SD	80.83 ± 7.54	82.25 ± 8.02	0.002
Gender (male:female)	176(20.6%)/677(79.4%)	177(40.1%)/264(59.9%)	<0.001
Diagnosis (neck/intertrochanter)	360(42.2%)/493(57.8%)	170(38.5%)271(61.5%)	0.211
CCI ± SD	2.05 ± 3.56	2.73 ± 2.16	<0.001
Operation (IF/arthroplasty)	287(33.6%)/566(66.4%)	192(43.5%)/249(56.5%)	0.001
Anesthesia (general/spinal)	375(44%)/478(56%)	185(42%)/256(58%)	0.515
Presence of ICU admission	92(10.8%)	50(11.3%)	0.779
30-days mortality	11(1.3%)	13(2.9%)	0.049
60-days mortality	21(2.5%)	25(5.7%)	0.004
90-days mortality	30(3.5%)	34(7.7%)	0.002
180-days mortality	56(6.6%)	52(11.8%)	0.002
1-year mortality	91(10.7%)	73(16.6%)	0.004

COPD: chronic obstructive pulmonary disease, SD: standard deviation, N: number, CCI: Charlson comorbidity index, IF: internal fixation, ICU: intensive care unit.

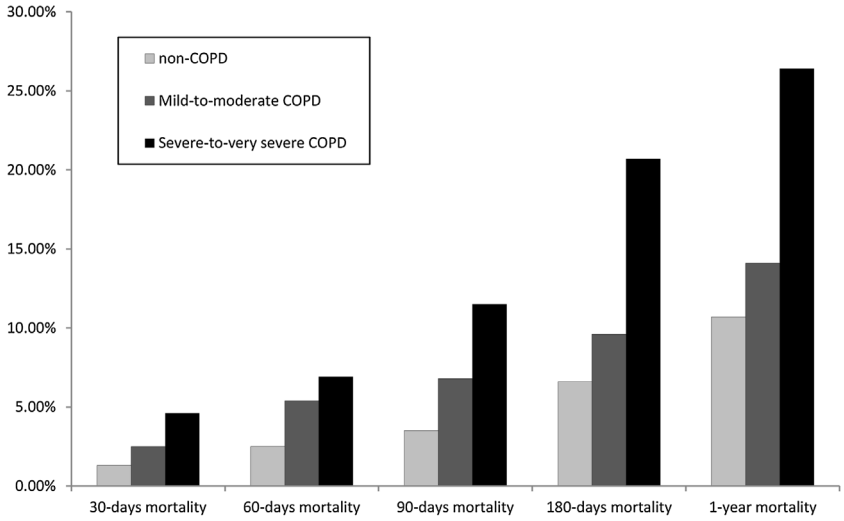

Fig. 2. A graph of mortality according to presence and severity of chronic obstructive pulmonary disease (COPD) during follow-up periods.

Table 2
Comparison between COPD groups according to severity of PFT.

	Mild-to-moderate COPD(N = 354)	Severe-to-very severe COPD(N = 87)	p-value
Age (years)±SD	82.32 ± 8.02	81.97 ± 8.07	0.717
Gender (male:female)	126(35.6)/228(64.4%)	51(58.6%)/36(41.4%)	<0.001
Diagnosis (neck/intertrochanter)	136(38.4%)/218(61.6%)	34(39.1%)/53(60.9%)	0.903
CCI ± SD	2.77 ± 2.18	2.57 ± 2.10	0.445
Operation (IF/arthroplasty)	160(45.2%)/194(54.8%)	32(36.8%)/55(63.2%)	0.184
Anesthesia (general/spinal)	150(42.4%)/204(57.6%)	35(40.2%)/52(59.8%)	0.809
Presence of ICU admission	36(10.2%)	14(16.1%)	0.131
30-days mortality	9(2.5%)	4(4.6%)	0.297
60-days mortality	19(5.4%)	6(6.9%)	0.605
90-days mortality	24(6.8%)	10(11.5%)	0.175
180-days mortality	34(9.6%)	18(20.7%)	0.008
1-year mortality	50(14.1%)	23(26.4%)	0.009

were 2.9%, 5.7%, 7.7%, 11.8%, and 16.6%, respectively. However, although the 30-day, 60-day, 3-month, 6-month, and 1-year postoperative mortality rates in the severe-to-very severe COPD group were significantly higher than those in the mild-to-moderate COPD group in this study, these were lower than those in previous studies. The reasons for this discrepancy might be related with the differences in demographic characteristics such as age, sex, COPD severity, and diagnostic criteria [19]. In addition, the COPD group in this study consisted only of enrolled patients with the possibility of undergoing operation, which means that these patients had relatively better physical conditions.

In this study, the proportion of severe-to-very severe group in males was significantly higher than those of the mild-to-moderate group, and the mortality in male with COPD was also higher than female. The severity of COPD in male might be related with higher mortality than female. This finding is similar with previous studies [20–22]. Previous studies have reported that male gender with hip fracture has poor clinical outcomes compared with female.

COPD in elderly patients with hip fractures is a well-known risk factor of mortality. Luise et al. reported that COPD emerged as a risk factor of mortality after fracture in the 30-day follow-up evaluation and that patients with COPD had a 60–70% higher risk of mortality after hip fracture than those without COPD [12]. Regan et al. reported that male patients with severe COPD were associated with a significant risk of 30-day and 1-year mortality after surgical intervention in those with hip fractures [13]. Dodd et al. assessed risk factors associated with 30-day mortality in 24,805 patients who sustained a hip/pelvis fracture using data from a claims database and found that a history of COPD was a risk factor of 30-day mortality [23]. According to previous reports, COPD and COPD severity are important risk factors of early and later mortality. In this study, COPD became a significant risk factor of mortality after surgical intervention at the 3-months follow-up. In the subgroup analysis of mortality in COPD patients, COPD severity became a significant risk factor of mortality at the 6-months follow-up. However, we could not find a relationship between COPD and 30-day and 60-day mortality. This might be related to the limited sample size and different patient cohorts because the COPD group in this study included only patients enrolled after surgical intervention for hip fracture.

Our study has several limitations. First, this was a retrospective study, and selection bias might have been introduced. However, we minimized the selection bias in patient enrollment by using data from an electronic medical record database and calculating the mortality rate based on a systematic search for death certificates at the National Statistical Office. Second, in the mortality rate analysis, medical comorbidities, which can substantially impact mortality in elderly populations, were not adequately considered. However, we used the CCI to minimize the bias due to different medical conditions. Third, the definition of COPD used in this study might be much stricter for the diagnosis of COPD, possibly excluding patients with COPD, and COPD severity was defined using only one-time PFT data on admission after injury. Finally, we tried to draw the best result from 3 repeated trial of spirometer as was recommended by the GOLD guideline for PFT. However, severe pain accompanying the hip fracture might have resulted in under-

estimation of PFT even with the best performed result. Under such circumstances, COPD stood out as an important risk factor for mortality in patients with hip fracture. Considering the situation, COPD might be more important factor for survival in patients with hip fracture.

In conclusion, in elderly patients with hip fracture, the comparison between the COPD and non-COPD patients revealed that COPD was an independent factor of mortality at a minimum of 1-year follow-up, and COPD severity in patients with hip fracture was also a risk factor of 6-month and 1-year mortality.

Conflict of interest

The authors declare that they have no conflict of interest.

Funding

No funding was received for the completion of this work.

Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors.

Ethics statement

The study design and protocol were approved by the institutional review board of the Eulji University Hospital (EMC-IRB No. 2018-11-024-001). Written informed consent was waived for all patients involved in this study.

COPD: chronic obstructive pulmonary disease, PFT: pulmonary function test, SD: standard deviation, N: number, CCI: Charlson comorbidity index, IF: internal fixation, ICU: intensive care unit.

Acknowledgments

No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this study by any of the authors.

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