Article

Journal of Orthopaedic Surgery

Journal of Orthopaedic Surgery
27(3) 1–8
© The Author(s) 2019
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/2309499019866965
journals.sagepub.com/home/osj
SAGE

Predictive factors of mortality of patients with fragility hip fractures at 1 year after discharge: A multicenter, retrospective study in the northern Kyushu district of Japan

Atsushi Kimura[1], Yoshihiro Matsumoto[1], Yoshifumi Wakata[2], Akiko Oyamada[3], Masanobu Ohishi[4], Toshifumi Fujiwara[1], Ko Ikuta[5], Kuniyoshi Tsuchiya[6], Naohisa Tayama[7], Shinji Tomari[8], Hisaaki Miyahara[9], Takao Mae[10], Toshihiko Hara[11], Taichi Saito[12], Takeshi Arizono[13], Kozo Kaji[14], Taro Mawatari[15], Masami Fujiwara[16], Riku Sakimura[17], Kunichika Shin[18], Kenichi Ninomiya[19], Kazutoshi Nakaie[20], Yasuaki Antoku[21], Shoji Tokunaga[22], Naoki Nakashima[23], Yukihide Iwamoto[14] and Yasuharu Nakashima[1]

[1] Department of Orthopaedic Surgery, Graduate School of Medical Science, Kyushu University, Fukuoka, Japan
[2] Department of Medical Informatics, Institute of Biomedical Sciences, Tokushima University Graduate School, Tokushima, Japan
[3] Department of Orthopaedic Surgery, Saga Handicapped Children's Hospital, Saga, Japan
[4] Department of Orthopaedic Surgery, Chihaya Hospital, Fukuoka, Japan
[5] Department of Orthopaedic Surgery, Karatsu Red Cross Hospital, Saga, Japan
[6] Department of Orthopaedic Surgery, JCHO Kyushu Hospital, Fukuoka, Japan
[7] Department of Orthopaedic Surgery, Steel Memorial Yawata Hospital, Fukuoka, Japan
[8] Department of Orthopaedic Surgery, Fukuoka Red Cross Hospital, Fukuoka, Japan
[9] Department of Orthopaedic Surgery, National Kyushu Medical Center, Fukuoka, Japan
[10] Department of Orthopaedic Surgery, Saga-ken Medical Center Koseikan, Saga, Japan
[11] Department of Orthopaedic Surgery, Aso Iizuka Hospital, Fukuoka, Japan
[12] Department of Orthopaedic Surgery, Fukuoka City Hospital, Fukuoka, Japan
[13] Department of Orthopaedic Surgery, Kyushu Central Hospital, Fukuoka, Japan
[14] Department of Orthopaedic Surgery, Kyushu Rosai Hospital, Fukuoka, Japan
[15] Department of Orthopaedic Surgery, Hamanomachi Hospital, Fukuoka, Japan
[16] Department of Orthopaedic Surgery, Sada Hospital, Fukuoka, Japan
[17] Department of Orthopaedic Surgery, Harasanshin Hospital, Fukuoka, Japan
[18] Department of Orthopaedic Surgery, Saiseikai Yahata General Hospital, Fukuoka, Japan
[19] Department of Orthopaedic Surgery, Koga Hospital 21, Fukuoka, Japan
[20] Department of Orthopaedic Surgery, Fukuoka-Higashi Medical Center, Fukuoka, Japan
[21] Faculty of Medicine, Hospital Informatic Center, Oita University, Oita, Japan
[22] Clinical Research Support Center Kyushu, Fukuoka, Japan
[23] Medical Information Center, Kyushu University Hospital, Fukuoka, Japan

Corresponding author:
Yoshihiro Matsumoto, Department of Orthopaedic Surgery, Graduate School of Medical Science, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan.
Email: ymatsu@ortho.med.kyushu-u.ac.jp

Abstract

Purpose: Fragility hip fractures (FHFs) are associated with a high risk of mortality, but the relative contribution of various factors remains controversial. This study aimed to evaluate predictive factors of mortality at 1 year after discharge in Japan. **Methods:** A total of 497 patients aged 60 years or older who sustained FHFs during follow-up were included in this study. Expected variables were finally assessed using multivariable Cox proportional hazards models. **Results:** The 1-year mortality rate was 9.1% (95% confidence interval: 6.8–12.0%, $n = 45$). Log-rank test revealed that previous fractures ($p = 0.003$), Barthel index (BI) at discharge ($p = 0.011$), and place-to-discharge ($p = 0.004$) were significantly associated with mortality for male patients. Meanwhile, body mass index (BMI; $p = 0.023$), total Charlson comorbidity index (TCCI; $p = 0.005$), smoking ($p = 0.007$), length of hospital stay (LOS; $p = 0.009$), and BI ($p = 0.004$) were the counterparts for females. By multivariate analyses, previous vertebral fractures (hazard ratio (HR) 3.33; $p = 0.044$), and BI <30 (HR 5.42, $p = 0.013$) were the predictive variables of mortality for male patients. BMI <18.5 kg/m^2 (HR 2.70, $p = 0.023$), TCCI $\geq$5 (HR 2.61, $p = 0.032$), smoking history (HR 3.59, $p = 0.018$), LOS <14 days (HR 13.9; $p = 0.007$), and BI <30 (HR 2.76; $p = 0.049$) were the counterparts for females. **Conclusions:** Previous vertebral fractures and BI <30 were the predictive variables of mortality for male patients, and BMI <18.5 kg/m^2, TCCI $\geq$5, smoking history, LOS <14 days, and BI <30 were those for females. Decreased BI is one of the independent and preventable risk factors. A comprehensive therapeutic approach should be considered to prevent deterioration of activities of daily living and a higher risk of mortality.

Keywords

activities of daily living, Barthel index, body mass index, frail elderly, hip fractures, mortality rate, osteoporosis

Date received: 30 March 2019; Received revised 24 June 2019; accepted: 30 June 2019

Introduction

In a rapidly aging population, the prevalence of osteoporosis-related fragility hip fractures (FHFs) is increasing. According to the worldwide projections for FHF, the total number of FHFs in 1990 was estimated to be 1.25 million; this figure is expected to reach approximately 2.6 million by 2025 and 4.5 million by 2050.[1] The incidence is assumed to be the highest in Asia, and the number of patients with FHFs is increasing drastically in Japan.[1,2]

Numerous studies have reported that hip fractures lead to not only decreased ability for daily living and quality of life but also an increased risk of death.[3–10] Haleem et al. reviewed 36 studies and reported the 1-year mortality rate for FHFs to be as high as 22–29%.[11] Considering that most patients could die due to comorbidities or postoperative complications and not always the fracture itself, it is necessary to identify patients who should receive interventions to reduce their risk of mortality. Various predictive factors have been reported to be associated with an increased risk of mortality, but the relative risk contributions of these factors remain unclear. Hu et al. reviewed 75 studies and identified 12 predictors of mortality with strong evidence.[12] However, the associations between short-term mortality and body mass index (BMI), surgical delay, bone mineral density (BMD) and osteoporosis treatment, length of hospitalization, and patients' acquired activity of daily living (ADL) at discharge remain unclear. In addition, the risk of mortality 1 year after FHF that is associated with reduced BMD at the time of injury remains unclear.[6] Therefore, in this retrospective study, the factors that could predict mortality at 1 year after discharge were identified and evaluated using Kaplan–Meier methods and multivariable Cox proportional hazards models.

Patients and methods

Study design and participants

Five-hundred and seventeen patients aged 60 years or older who were consecutively treated for hip fracture at our 17 affiliated hospitals between March 2013 and March 2016 in the northern Kyushu district of Japan and were followed up to 1 year after discharge were included in this study. The exclusion criteria included patients who suffered from high-energy trauma and pathologic fracture. Patients or their family members were interviewed biannually about the patient's vital status after discharge by a questionnaire or a telephone interview. We defined death after discharge as an endpoint and time from discharge to death was calculated. This study was reviewed and approved by the institutional review board of authors' affiliated institutions. Written informed consent was obtained from all patients before their participation.

Data collection

The following data were collected on admission: sex, age, BMI, total Charlson comorbidity index (TCCI),[13] alcohol consumption (over three units of alcohol per day), smoking, BMD, osteoporosis treatment, and previous fractures. We also reviewed the following variables related to hospitalization for FHF: surgical delay, type of fracture and operation, Barthel index (BI) at discharge, length of hospital stay (LOS), and place to discharge.

Each variable was categorized as follows. Age was categorized as <75 years, 75≤ and <85 years, and ≥85 years. BMI was categorized as BMI <18.5 kg/m^2, 18.5≤ BMI <25 kg/m^2, and BMI ≥25 kg/m^2, according to the previous report.[3,14] For each patient, the number of comorbidities was ascertained from the database and then TCCI was calculated by adding the number of relevant comorbidities with the score derived from the patient's age.[13] We used the median as the cutoff value (TCCI = 4). Lumbar BMD was measured at L2–L4 vertebrae and femoral BMD was measured at the femoral neck of the non-fractured hip. Each BMD data was evaluated based on the young adult mean (YAM) value and categorized as follows: normal, YAM ≥80%; osteopenia, 70%≤ YAM <80%; and osteoporosis, YAM <70%. When BMD data from the both locations were available and those categories were different, we adopted the worse one as a result of BMD measurement. Osteoporosis treatment was defined as "yes" if a patient had undergone treatment prior to admission. Otherwise, treatment was categorized as "no." Previous fracture was defined as a history of fragility fractures in locations other than the hip. Vertebral fracture, a possible risk factor for mortality by itself,[15] was identified and categorized separately from other two minor variables (none and others). Surgical delay was defined as the interval between the date of injury and the date of surgery. We stratified it every 2 days: delay <2 days, 2≤ delay <4 days, 4≤ delay <6 days, and delay ≥6 days. Type of surgery was categorized as either arthroplasty or internal fixation. BI at discharge was used to assess a patient's basic functional status, in other words, patient's ADL,[16] stratified as BI ≥70, 30≤ BI <70, and BI <30, according to the previous report.[5] LOS was defined as the time between admission and discharge from the hospital of initial treatment, stratified as LOS ≥35 days, 28≤ LOS <35 days, 14≤ LOS <28 days, and LOS <14 days, because a patient with hip fracture would be usually treated along a clinical pathway with a standard hospital stay of 2–4 or 5 weeks in Japan. "Place to discharge" refers to residence after discharge and was categorized as home, other medical institution, or others. Especially, "other medical institution" included general hospitals, recovery hospitals, sanatoriums, and clinics.

Statistical analyses

For categorical variables, absolute numbers and relative frequencies were calculated. For continuous variables, means and standard deviations were calculated. For non-normally distributed data, medians and interquartile range were used. Comparison of basic characteristics between male and female patients was conducted, and the difference between two groups was statistically analyzed using Mann–Whitney *U* test for non-parametric variables or Fisher's exact test for more than two variables, as appropriate (Table 1).

The 1-year mortality after discharge was calculated by Kaplan–Meier method. We also plotted the curves for each categorized variable and conducted log-rank test to seek significant association with 1-year mortality. Subsequently, significant variables in the test were introduced into Cox proportional hazards models to evaluate each factor's independent effect on mortality, and the hazard ratios (HRs) with their 95% confidence interval (CI) was estimated. The whole analyses were conducted by sex, because gender bias was considered not to be ignored.

Data were censored at the middle of the follow-up period when a secondary fragility fracture occurred or there was a loss to follow-up. Patients who were alive 1 year after discharge completed the 1-year follow-up period. All analyses were performed using JMP version 13.0. A two-sided $p < 0.05$ was considered as statistically significant.

Results

We retrospectively identified 517 patients who sustained FHFs in the 3-year period from 2013 to 2016 and they could be followed up until death or 1 year following discharge. Among these patients, 1 patient was excluded from this study due to the refusal to cooperate, and 19 patients were also excluded due to the lack of principal data (date of death: $n = 2$, BI at discharge: $n = 16$, BMI on admission: $n = 1$). As a result, 497 patients who were consecutively treated for FHFs are included in this study.

Patients' data are summarized in Table 1. The mean age on admission was 82 years, and approximately three times as many patients were women than men. Average BMI was significantly lower in female patients than in male patients (19.8 kg/m^2 vs. 20.5 kg/m^2, $p = 0.042$). One or more principal comorbidities were found in 437 patients (87.9%). Among these comorbidities, morbidity of hypertension was significantly higher in female patients than in male patients (50.0% vs. 35.5%, $p = 0.009$). On the other hand, that of chronic kidney disease was significantly higher in male patients (13.1% vs. 6.9%, $p = 0.048$), but the value of TCCI was almost same between these two groups. BMD has been measured during hospitalization at lumbar spine in 379 patients and at femoral neck in 451 ones, and both measurements were significantly lower in female patients than in male patients (L-spine: 69.0% vs. 81.5% and femoral neck: 58.0% vs. 62.0%, $p < 0.001$ and $p = 0.037$, respectively). As for age, surgical delay, and morbidity of previous fractures, there was no significant difference between two groups.

Except for one patient, all patients were treated surgically. Type of fracture and operation showed the approximately same tendency. Total hip arthroplasty was performed for six intracapsular hip fractures. LOS and BI at discharge were not significantly different.

Table 1. Comparison of basic characteristics between male and female patients.[a]

	Total ($n = 497$)	Male ($n = 107$)	Female ($n = 390$)	p Value[b]
Age (years)	82.1 (7.9)	81.5 (8.2)	82.2 (7.8)	0.31
BMI (kg/m^2)	20.4 (3.3)	19.8 (3.2)	20.5 (3.4)	0.042[c]
Surgical delay (days)	4.27 (2.3–6.9)	4.79 (2.6–8.0)	4.17 (2.3–6.7)	0.25
Principal comorbidities, n (%)				
Hypertension	233 (46.9)	38 (35.5)	195 (50.0)	0.009[c]
Diabetes mellitus	94 (18.9)	22 (20.6)	72 (18.5)	0.68
Stroke	64 (12.9)	13 (12.1)	51 (13.1)	0.87
CKD	41 (8.2)	14 (13.1)	27 (6.9)	0.048[c]
LC	22 (4.4)	7 (6.5)	15 (3.8)	0.29
Cardiac arrhythmia	22 (4.4)	4 (3.7)	18 (4.6)	1.00
Malignancy	21 (4.2)	5 (4.7)	16 (4.1)	0.79
CTD	19 (3.8)	1 (0.9)	18 (4.6)	0.09
Cardiac insufficiency	16 (3.2)	5 (4.7)	11 (2.8)	0.32
TCCI	4.00 (4.0–5.0)	5.00 (4.0–5.0)	4.00 (4.0–5.0)	0.23
BMD (YAM, %)				
L-spine ($n = 379$)	71.0 (62.0–84.0)	81.5 (66.0–94.5)	69.0 (62.0–81.0)	<0.001[c]
Femoral neck ($n = 451$)	58.0 (50.0–68.5)	62.0 (52.5–71.0)	58.0 (49.0–68.0)	0.037[c]
Previous fracture, n (%)				
Vertebra	59 (11.9)	11 (10.3)	48 (12.3)	0.62
Distal radius	19 (3.8)	1 (0.9)	18 (4.6)	0.09
Proximal humerus	10 (2.0)	1 (0.9)	9 (2.3)	0.70
Others	44 (8.9)	12 (11.2)	32 (8.2)	0.34
Type of fracture, n (%)				0.89
Femoral neck	282 (56.7)	60 (56.1)	222 (56.9)	
Trochanteric	202 (40.6)	45 (42.1)	157 (40.3)	
Sub-trochanteric	13 (2.6)	2 (1.9)	11 (2.8)	
Type of operation, n (%)	(Total = 495)[d]	(Total = 107)	(Total = 388)	0.058
Arthroplasty	204 (41.2)	53 (49.5)	157 (40.5)	
Nail/CHS	209 (42.2)	46 (43.0)	163 (42.0)	
Hansson-pin/CCS	49 (9.9)	6 (5.6)	43 (11.1)	
Others	33 (6.7)	2 (1.9)	25 (6.4)	
LOS (days)	22.0 (18.0–29.0)	23.0 (19.0–29.0)	22.0 (17.3–29.0)	0.32
BI at discharge	60.0 (35.0–85.0)	55.0 (25.0–77.5)	60.0 (40.0–85.0)	0.067
1-year mortality, n (%)	45 (9.1)	20 (19.0)	25 (6.3)	<0.001[c]

BMI: body mass index; CKD: chronic kidney disease; LC: liver cirrhosis; CTD: connective tissue disease; TCCI: total Charlson comorbidity index; YAM: young adult mean; BMD: bone mineral density; CHS: compression hip screw; CCS: cannulated cancellous screw; LOS: length of hospital stay; BI: Barthel index; SD: standard deviation.
[a]Unless specified otherwise, the results are presented as mean (SD) or median with interquartile range.
[b]The difference between two groups was statistically analyzed using Mann–Whitney U test or Fisher's exact test, as appropriate.
[c]Statistically significant variables at $p < 0.05$.
[d]One patient was treated conservatively, and the other patient's data were missing.

In total, 45 patients (20 males and 25 females) died within 1 year of discharge, and the total mortality, calculated with the Kaplan–Meier method, was 9.1% (95% CI: 6.8–12.0%, Figure 1). The mortality rate was significantly higher in males than in females (19.0% vs. 6.3%, $p < 0.001$). The results of categorization of each patient's variable with the number of deaths and proportion within each category were described in Table 2.

The relationships between 1-year mortality and each variable were also elucidated by the methods. Log-rank test revealed that previous fracture ($p = 0.003$), BI at discharge ($p = 0.011$), and place to discharge ($p = 0.004$) were significantly associated with 1-year mortality for male patients. On the other hand, BMI ($p = 0.023$), TCCI ($p = 0.005$), smoking ($p = 0.007$), LOS ($p = 0.009$), and

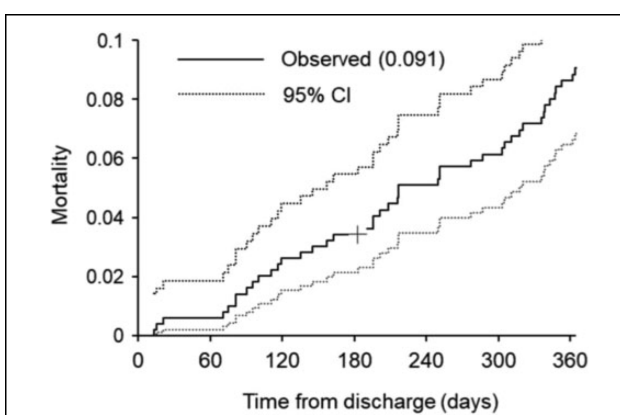

Figure 1. A curve for death in 497 consecutive patients with FHFs. FHF: fragility hip fracture.

Table 2. Categorization of patients' variables that may affect 1-year mortality after FHFs and number of death.[a]

Variables	Number of patients (%)	Number of death (%)	Variables	Number of patients (%)	Number of death (%)
Sex		Total = 45	Osteoporosis treatment		Total = 45
Female	390 (78.5)	25 (55.6)	Yes	112 (22.5)	8 (17.8)
Male	107 (21.5)	20 (44.4)	No	385 (77.5)	37 (82.2)
Age (years)			Previous fracture		
Age <75	82 (16.5)	2 (4.4)	None	377 (75.9)	32 (71.1)
75≤ age <85	202 (40.6)	17 (37.8)	Vertebra	59 (11.9)	9 (20.0)
Age ≥85	213 (42.9)	26 (57.8)	Others	61 (12.2)	4 (8.9)
BMI (kg/m^2)			Type of fracture		
18.5≤ BMI <25	295 (59.4)	17 (37.8)	Intracapsular	282 (56.7)	19 (42.2)
BMI <18.5	158 (31.8)	26 (57.8)	Trochanteric	215 (43.3)	26 (57.8)
BMI ≥25	44 (8.9)	2 (4.4)	Type of operation		
Surgical delay (days)			Arthroplasty	203 (41.0)	17 (37.8)
Delay <2	95 (19.2)	4 (8.9)	Internal fixation	292 (59.0)	28 (62.2)
2≤ delay <4	125 (25.2)	11 (24.4)	LOS (days)		
4≤ delay <6	117 (23.6)	10 (22.2)	LOS ≥35	79 (15.9)	3 (6.7)
Delay ≥6	159 (32.1)	20 (44.4)	28≤ LOS <35	63 (12.7)	5 (11.1)
TCCI			14≤ LOS <28	333 (67.0)	32 (71.1)
TCCI <5	272 (54.7)	16 (35.6)	LOS <14	22 (4.4)	5 (11.1)
TCCI ≥5	225 (45.3)	29 (64.4)	BI at discharge		
Alcohol consumption[b]			BI ≥70	208 (41.9)	11 (24.4)
No	465 (93.6)	42 (93.3)	30≤ BI <70	190 (38.2)	13 (28.9)
Yes	32 (6.4)	3 (6.7)	BI <30	99 (19.9)	21 (46.7)
Smoking			Place to discharge		
Never	400 (80.5)	30 (66.7)	Home	45 (9.1)	3 (6.7)
Current or past smoker	97 (19.5)	15 (33.3)	Other medical institution	427 (85.9)	36 (80.0)
BMD			Others	25 (5.0)	6 (13.3)
Normal	37 (7.4)	1 (2.2)			
Osteopenia	84 (16.9)	9 (20.0)			
Osteoporosis	376 (75.7)	35 (77.8)			

BMI: body mass index; TCCI: total Charlson comorbidity index; BMD: bone mineral density; LOS: length of hospital stay; BI: Barthel index; FHF: fragility hip fracture.
aAll the results are presented as absolute number (frequency).
[b]"Yes" means drinking alcohol more than three units per day.

BI at discharge ($p = 0.004$) were significant risk of mortality for female patients (Table 3).

The final Cox models included the following variables: previous fracture, BI at discharge, and place to discharge for male patients, and BMI, TCCI, smoking, LOS, and BI at discharge for female patients (Table 4). In male patients, previous vertebral fractures and BI <30 were significantly higher risk of short-term mortality (HR 3.33 and 5.42, $p = 0.044$ and 0.013, respectively) compared with the reference group. However, place to discharge was not associated with the mortality. In female patients, BMI <18.5 kg/m^2, TCCI ≥5, and smoking history were found to be the predictive preexisting variables for 1-year mortality (HR 2.70, 2.61, and 3.59, $p = 0.023$, 0.032, and 0.018, respectively). Astonishingly, the shortest LOS patients' group (LOS <14 days) had as much as 14-focal risk of mortality than the reference one (LOS ≥35 days, $p = 0.007$). Also, just like the male patients, BI <30 were the significantly high risk of mortality for female patients (HR 2.76, $p = 0.049$).

Kaplan–Meier curves of TCCI and LOS for female patients are shown in Figure 2. Mortality of the female patients whose TCCI was more than 4 at injury was significantly higher than that of the others over an entire study period (Figure 2(a)). As evidenced in Figure 2(b), 1-year mortality of LOS <14 days group was the highest than that of any other LOS group in female patients. However, none of the patients of LOS <14 days group died within 2 months from discharge.

Kaplan–Meier curves of BI at discharge for all patients are shown in Figure 3. Irrespective of gender, the lowest BI group (BI <30) showed a tendency toward increased risk of mortality throughout the study period (Figure 3(a) and (b)). It was also revealed that BI at discharge significantly increased as the LOS extended only in female patients (Online Supplemental Figure 1(a) and (b)).

Discussion

In this retrospective study, aiming to identify predictors of 1-year mortality in FHF patients, previous vertebral fracture and BI <30 were found to be the increased risk of death for male patients. Meanwhile, BMI <18.5 kg/m^2, TCCI ≥5,

Table 3. Log-rank test toward each variable of 497 consecutive patients.

Male patients ($n = 107$)		Female patients ($n = 390$)	
Variables	p Value	Variables	p Value
Age	0.12	Age	0.11
BMI	0.12	BMI	0.023[a]
Surgical delay	0.73	Surgical delay	0.23
TCCI	0.72	TCCI	0.005[a]
Alcohol consumption	0.62	Alcohol consumption	0.39
Smoking	0.29	Smoking	0.007[a]
BMD	0.32	BMD	0.51
Osteoporosis treatment	1.00	Osteoporosis treatment	0.58
Previous fracture	0.003[a]	Previous fracture	0.77
Type of fracture	0.29	Type of fracture	0.13
Type of operation	0.62	Type of operation	0.85
LOS	0.54	LOS	0.009[a]
BI at discharge	0.011[a]	BI at discharge	0.004[a]
Place to discharge	0.004[a]	Place to discharge	0.70

BMI: body mass index; TCCI: total Charlson comorbidity index; BMD: bone mineral density; LOS: length of hospital stay; BI: Barthel index.
aStatistically significant variables at $p < 0.05$.

Table 4. Multivariate analysis among selected categories based on the results of log-rank test using Cox proportional hazard models.

Male patients ($n = 107$)			
Variables	Hazard ratio[a]	95% CI[a]	p Value
Previous fractures			
None	Reference		
Vertebra	3.33	1.04–9.45	0.044[b]
Others	1.92	0.28–8.19	0.46
BI at discharge			
BI ≥70	Reference		
30≤ BI <70	2.37	0.57–12.6	0.24
BI <30	5.42	1.39–29.9	0.013[b]
Place to discharge			
Home	Reference		
Other medical institution	0.64	0.09–13.5	0.72
Others	2.11	0.22–48.3	0.54

Female patients ($n = 390$)			
Variables	Hazard ratio	95% CI	p Value
BMI			
18.5≤ BMI <25	Reference		
BMI <18.5	2.70	1.15–6.61	0.023[b]
BMI ≥25	1.49	0.21–6.30	0.64
TCCI			
TCCI <5	Reference		
TCCI ≥5	2.61	1.08–6.94	0.032[b]
Smoking			
Never	Reference		
Current or past smoker	3.59	1.28–8.82	0.018[b]
LOS			
LOS ≥35	Reference		
28≤ LOS <35	4.29	0.86–77.7	0.08
14≤ LOS <28	5.05	0.63–103.7	0.13
LOS <14	13.9	1.99–276.2	0.007[b]
BI at discharge			
BI ≥70	Reference		
30≤ BI <70	0.70	0.23–2.09	0.51
BI <30	2.76	1.01–8.03	0.049[b]

BI: Barthel index; BMI: body mass index; TCCI: total Charlson comorbidity index; LOS: length of hospital stay; CI: confidence interval.
[a]Hazard ratio, corresponding 95% CI, and p values were obtained using Cox proportional hazard models.
[b]Statistically significant variables at $p < 0.05$.

smoking history, LOS <14 days, and BI <30 were the counterparts for female patients. However, other predictors were found not to be associated with death after 1-year follow-up. We found only BI at discharge to be associated with 1-year mortality for both sexes. LOS and BI at discharge were closely related to each other only in females (Online Supplemental Figure 1).

Previous studies have shown mixed results on postoperative mortality at 1 year after FHF, ranging from 10.3%[5] to as high as 40%.[10] One-year mortality rate was only 9.1% in the present study, and the mortality in a Japanese population is lower than the ones generally reported in Europe, North America, and South America.[4,5,12,17] It is not clear what these regional differences of the mortality come from, but a recent systematic review reported several mortality predictors including advanced age, male gender, poor activities of daily living, and multiple comorbidities, which were true of our study except for age.[12] Many patients could have died because of their worsened general conditions despite the success of primary treatment.[18] Therefore, preoperative assessment and stabilization should be undertaken rigorously before surgery.[5]

TCCI was not so different between males and females, although raised TCCI was an independent risk of mortality for female patients. Preexisting neurological, kidney, respiratory, and gastrointestinal disorders were reported to associate with increased short-term mortality with geriatric hip fractures.[19] TCCI is a sum of all comorbidities combined with the score derived from the patient's age and is reported to be a good preoperative indicator of mortality in elderly patients with hip fractures.[13] If the TCCI was more than 5, 1-year mortality rate was reported to increase linearly with the TCCI.[13] Elderly patients are supposed to have various comorbidities and poor general conditions, so in treating elderly patients with FHFs, not only the fracture but also other comorbidities must be considered.[4]

In this study, performance of activities of daily living was assessed using BI[5,16] and patients with the lowest BI showed a significant high mortality (males: $p = 0.013$, females: $p = 0.049$). Considering that the decreased BI reflects deterioration of patient's activities of daily living, its impairment could lead to an increased risk of mortality. Similarly, BI at discharge has been reported to be a significant determinant of mortality risk in a multicenter prospective cohort study involving 33 medical facilities in Japan.[5]

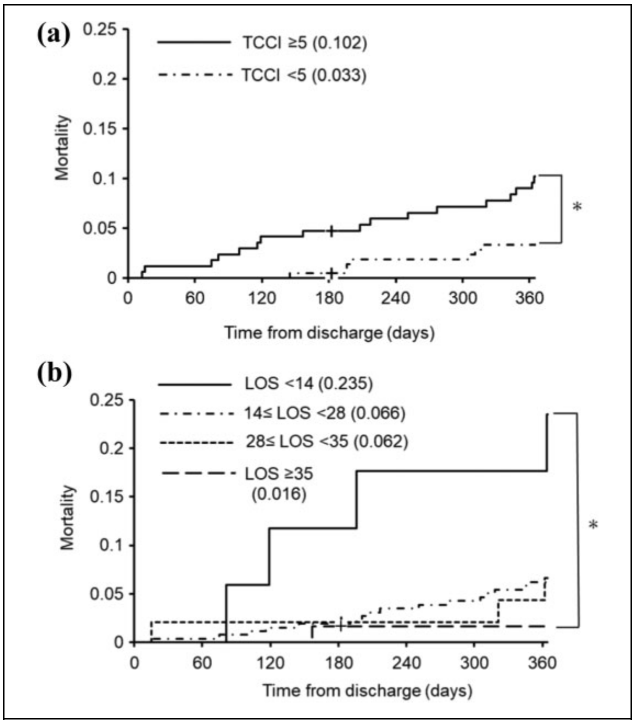

Figure 2. Curves for death stratified by (a) TCCI (*$p < 0.01$) and (b) LOS (*$p < 0.001$) for females. One-year mortality was statistically evaluated via log-rank analyses. TCCI: total Charlson comorbidity index; LOS: length of hospital stay.

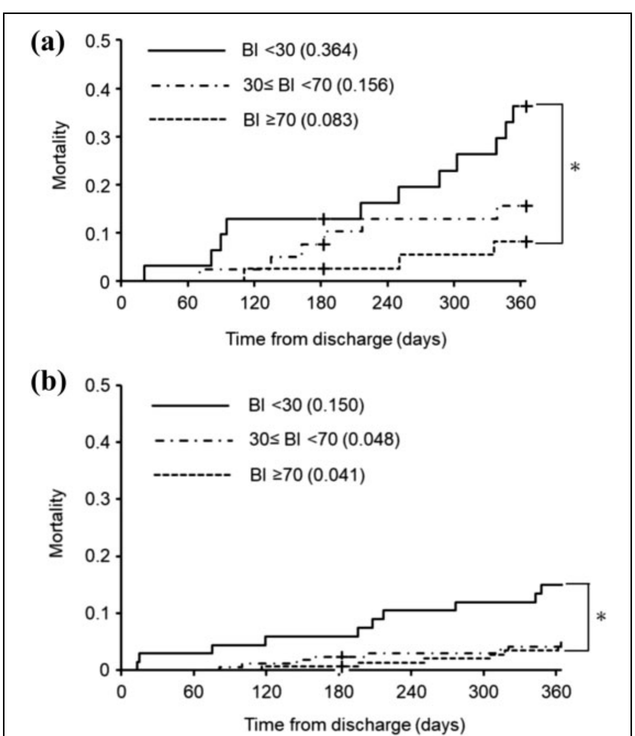

Figure 3. Curves for death stratified by BI at discharge for (a) male and (b) female patients. One-year mortality was statistically evaluated via log-rank analyses. *$p < 0.01$. BI: Barthel index.

In this study, more than half of our deceased patients had a low BMI of 18.5 kg/m^2 or less (Table 2) and that was also an independent and significant risk of death in female patients ($p = 0.023$). In aforementioned systematic review, decreased BMI, and low serum albumin or malnutrition were found not strong-, but moderate-evidenced predictors of death.[12] Another previous cohort study reported that elderly patients with FHF have a higher rate of malnutrition or are at risk of malnutrition.[20] In this study, average BMI was significantly low in female patients, and deterioration of BMI was one of the independent risks of mortality. Malnutrition and sarcopenia often occur in rehabilitation settings and are associated with poorer rehabilitation outcome and physical function.[21] Sarcopenia is related to worse metabolic and functional health, thus increasing the risk of all-cause mortality.[22] This theory was supported by a study in Japan which reported a high prevalence of sarcopenia and reduced leg muscle mass in patients with sustained FHF.[23] Treatment of nutrition-related sarcopenia requires appropriate nutrition management to improve muscle mass.[21] Taken together, preventing deterioration of ADLs with early interventions such as rehabilitation and appropriate nutritional support might be important for reducing the mortality rate after FHFs.

Surprisingly, a shorter duration of hospitalization increased the risk of short-term mortality in female patients. In particular, LOS <14 days was associated with a 14-fold higher risk compared with LOS ≥35 days. Similarly, a recent observational cohort study of 6143 patients who sustained hip fractures[3] reported that LOS <10 days is an independent risk factor for mortality. The increased risk of death with "LOS <14 days" could suggest the poorly conditioned patients were discharged quickly to other medical institutions, although none of the patient with the shortest LOS group died within 2 months from discharge. Remarkably, BI at discharge significantly increased as the LOS extended in female patients (Online Supplemental Figure 1). The median BI of the longest LOS group was almost twice as many as that of the shortest LOS groups (data not shown). We speculate that shorter hospitalization may be associated with fewer adjuvant interventions, such as nutrition and physical training, resulting in unsatisfactory ADL recovery. Short LOS might not be a guarantee of quality and cost-effectiveness if the patients are discharged without acquiring optimized conditions.[3]

This study has several limitations. First, although we have analyzed several risk factors, additional information such as original gait pattern, severity of comorbidities, presence of cognitive impairment, and rehabilitation programs after discharge were not available for adjustment. Preoperative patient's disability and physical conditions or postoperative treatment might have affected LOS, place to discharge, and 1-year mortality after sustaining hip fractures. Second, this study did not ascertain the primary and exact cause of death of patients during 1-year follow-up period, since it was hard to access personal information, especially cause of death, via the manual intervention. Third, lack of BMD data could affect the result of univariate analysis (23.8% of BMD at the lumbar spine and 9.3% of BMD at hip could not be measured). However, it is unlikely that only low BMD could directly influence the short-term mortality since fracture itself would have only a marginal effect on total mortality. Finally, potential residual confounding factors related to the observational study design might limit the ability to draw definitive conclusions.

In summary, we performed a multicenter, retrospective study to identify factors that could predict mortality at 1 year after FHFs. Previous vertebral fractures and BI <30 were the predictive variables of mortality for male patients, and BMI <18.5 kg/m^2, TCCI ≥ 5, smoking history, LOS <14 days, and BI <30 were those for females. Decreased BI is one of the independent and preventable risk factors of mortality in both patients group. A comprehensive therapeutic approach should be considered to prevent deterioration of activities of daily living and a higher risk of mortality.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Atsushi Kimura https://orcid.org/0000-0003-2552-1200

Supplemental material

Supplemental material for this article is available online.

References

1. Gullberg B, Johnell O, and Kanis JA. World-wide projections for hip fracture. *Osteoporos Int* 1997; 7: 407–413.
2. Hagino H, Endo N, Harada A, et al. Survey of hip fractures in Japan: recent trends in prevalence and treatment. *J Orthop Sci* 2017; 22: 909–914.
3. Lund CA, Moller AM, Wetterslev J, et al. Organizational factors and long-term mortality after hip fracture surgery. A cohort study of 6143 consecutive patients undergoing hip fracture surgery. *PLoS One* 2014; 9: e99308.
4. Muraki S, Yamamoto S, Ishibashi H, et al. Factors associated with mortality following hip fracture in Japan. *J Bone Miner Metab* 2006; 24: 100–104.
5. Ishidou Y, Koriyama C, Kakoi H, et al. Predictive factors of mortality and deterioration in performance of activities of daily living after hip fracture surgery in Kagoshima, Japan. *Geriatr Gerontol Int* 2017; 17: 391–401.
6. Diamantopoulos AP, Hoff M, Hochberg M, et al. Predictors of short- and long-term mortality in males and females with hip fracture—a prospective observational cohort study. *PLoS One* 2013; 8: e78169.
7. Meessen JM, Pisani S, Gambino ML, et al. Assessment of mortality risk in elderly patients after proximal femoral fracture. *Orthopedics* 2014; 37: e194–200.
8. Lystad RP, Cameron CM, and Mitchell RJ. Mortality risk among older Australians hospitalised with hip fracture: a population-based matched cohort study. *Arch Osteoporos* 2017; 12: 67.
9. Heyes GJ, Tucker A, Marley D, et al. Predictors for 1-year mortality following hip fracture: a retrospective review of 465 consecutive patients. *Eur J Trauma Emerg Surg* 2017; 43: 113–119.
10. Karademir G, Bilgin Y, Ersen A, et al. Hip fractures in patients older than 75 years old: retrospective analysis for prognostic factors. *Int J Surg* 2015; 24: 101–104.
11. Haleem S, Lutchman L, Mayahi R, et al. Mortality following hip fracture: trends and geographical variations over the last 40 years. *Injury* 2008; 39: 1157–1163.
12. Hu F, Jiang C, Shen J, et al. Preoperative predictors for mortality following hip fracture surgery: a systematic review and meta-analysis. *Injury* 2012; 43: 676–685.
13. Lau TW, Fang C, and Leung F. Assessment of postoperative short-term and long-term mortality risk in Chinese geriatric patients for hip fracture using the Charlson comorbidity score. *Hong Kong Med J* 2016; 22: 16–22.
14. Solbakken SM, Meyer HE, Stigum H, et al. Excess mortality following hip fracture: impact of self-perceived health, smoking, and body mass index. A NOREPOS study. *Osteoporos Int* 2017; 28: 881–887.
15. Center JR, Nguyen TV, Schneider D, et al. Mortality after all major types of osteoporotic fracture in men and women: an observational study. *Lancet* 1999; 353: 878–882.
16. Collin C, Wade DT, Davies S, et al. The Barthel ADL index: a reliability study. *Int Dis Stud* 1988; 10: 61–63.
17. Pereira SR, Puts MT, Portela MC, et al. The impact of prefracture and hip fracture characteristics on mortality in older persons in Brazil. *Clin Orthop Relat Res* 2010; 468: 1869–1883.
18. Hasegawa Y, Suzuki S, and Wingstrand H. Risk of mortality following hip fracture in Japan. *J Orthop Sci* 2007; 12: 113–117.
19. Bliemel C, Buecking B, Oberkircher L, et al. The impact of pre-existing conditions on functional outcome and mortality in geriatric hip fracture patients. *Int Orthop* 2017; 41: 1995–2000.
20. Koren-Hakim T, Weiss A, Hershkovitz A, et al. The relationship between nutritional status of hip fracture operated elderly patients and their functioning, comorbidity and outcome. *Clin Nutr* 2012; 31: 917–921.
21. Wakabayashi H and Sakuma K. Rehabilitation nutrition for sarcopenia with disability: a combination of both rehabilitation and nutrition care management. *J Cache Sarcop Muscle* 2014; 5: 269–277.
22. Wall BT, Dirks ML, and van Loon LJ. Skeletal muscle atrophy during short-term disuse: implications for age-related sarcopenia. *Ageing Res Rev* 2013; 12: 898–906.
23. Hida T, Ishiguro N, Shimokata H, et al. High prevalence of sarcopenia and reduced leg muscle mass in Japanese patients immediately after a hip fracture. *Geriatr Gerontol Int* 2013; 13: 413–420.