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Original Article

Coexistence of Acute Ischemic Stroke and Acute Bone Fracture during Hospitalization

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SUMMARY

Background: Stroke and bone fracture may manifest as risk factors and complications for each other. Stroke and bone fracture may occur concurrently in patients presented to the emergency department.
Methods: Between January 2007 and December 2018, we retrospectively found 30 patients with coexistent acute ischemic stroke and bone fracture during hospitalization.
Results: Concurrent stroke and fracture (initial stroke), stroke followed by fracture (initial stroke), and fracture followed by stroke (initial fracture) occurred in 17, 4, and 9 patients, respectively. Femur was the most common fracture location. Stroke or fracture was initially overlooked in 4 of 17 patients (24%) with concurrent stroke and bone fracture. Both age and the admission National Institutes of Health Stroke Scale (NIHSS) score exhibited a positive linear correlation with the discharge modified Rankin Scale (mRS). Univariate logistic regressions found that significant factors influencing unfavorable outcome (mRS > 3) were an admission NIHSS score > 5, age > 70 years, urinary catheterization, nasogastric insertion, anterior circulation, and initial fracture. Stepwise regression analyses showed that an admission NIHSS score > 5 (odds ratio [OR]: 48.36, 95% confidence interval [CI]: 1.19–1963.26, $p = 0.040$), age > 70 years (OR: 30.03, 95% CI: 1.57–574.48; $p = 0.024$), and anterior circulation (OR: 27.41, 95% CI: 1.31–572.65; $p = 0.033$) were significant predictors of unfavorable outcomes with a prediction value of up to 0.938.
Conclusion: Coexistence of acute stroke and bone fracture is an uncommon but serious condition. Neurologists, orthopedics and emergency physicians need to be more vigilant toward this concomitance with careful clinical evaluation.

1. Introduction

Stroke and bone fracture are two major disorders of patients presenting to the emergency department with functional disability. Stroke has been the fourth leading cause of death in Taiwan over the past two decades and the leading cause of prolonged disability among elderly people. Bone fracture also results in a considerable period of motor dysfunction, particularly in elderly people. Bone fracture and ischemic stroke have many common risk factors, including aging, hypertension, diabetes mellitus, smoking, alcohol consumption, and low bone mineral density.[1] Stroke and bone fracture are risk factors as well as complications for each other. Although vertebral fracture comprises the majority of bone fracture, hip fracture occurs most commonly on the paretic side after a stroke.[2] The risk of stroke doubles after a hip fracture and remains elevated for up to 10 years after.[3,4] Reported data show that the incidence of previous stroke ranges from 4% to 15% in patients with hip fracture,[5] and the incidence of stroke reaches 4% in patients with hip fracture receiving surgical repair.[1]

Bone fracture and stroke can occur in different sequences. Most previous studies have addressed the latent effect of stroke on bone fracture or vice versa. However, studies have rarely discussed the acute stage of both the conditions. Poplingher et al. reported that the interval between a bone fracture and a previous stroke was longer than 6 months in most patients, and an interval of less than a week was associated with poor functional recovery.[5] Kanis et al. analyzed the time course of any increase in the bone fracture risk after stroke in 16.3 million hospitalizations.[2] However, fractures at the time of first admission to the hospital in association with stroke were excluded in their study. Patients with simultaneous acute bone fracture and acute stroke have less optimal outcomes than patients with a single injury. This study aimed to identify the clinical features and outcomes of patients with coexistent acute ischemic stroke and bone fracture during the same period of hospitalization.

2. Methods

2.1. Patient selection

Patients who were treated for ischemic stroke in the neurological ward and those who were treated for bone fracture in the orthopedic ward between January 2007 and December 2018 were retrospectively reviewed. The study was conducted in accordance

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with the Declaration of Helsinki, with the approval from the Institutional Review Board of the Taipei Tzu Chi Hospital (as no. 08-XD-053). Patients with both ischemic stroke and fracture included in the list of discharge diagnosis were selected for further chart review. Inclusion criterion for the final enrollment of patients was coexistence of acute ischemic stroke and acute bone fracture during the same period of hospitalization. Patients who had concurrent stroke and bone fracture and who had stroke followed by fracture were categorized as having initial stroke, whereas patients with initial fracture followed by stroke were categorized as having initial fracture.

2.2. Data collection

We collected the following details relating to each patient: age, sex, sequence of and interval between stroke and fracture, location of fracture and stroke, risk factors for stroke, the National Institutes of Health Stroke Scale (NIHSS) score on admission, the necessity for nasogastric tube insertion and indwelling urinary catheterization, and the hospital length of stay (LOS). Outcomes were evaluated using the NIHSS score, the Barthel index, and the modified Rankin Scale (mRS) at discharge. In total, information on seven risk factors for vascular disease was collected, including old age (> 65 years), hypertension, diabetes mellitus, hyperlipidemia, heart disease, previous stroke, and smoking.

2.3. Classification of stroke subtypes and outcome measurement

Location of stroke was grouped into anterior or posterior circulation depending on arterial perfusion from the carotid or vertebrobasilar system to the infarcted area, respectively. We classified the etiology of ischemic stroke according to the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria, namely large artery atherosclerosis, small vessel occlusion, cardioembolism (atrial fibrillation), other determined etiology, and undetermined etiology.[6] Considering that patients in the studied group had two serious injuries, an mRS score of > 3 was considered an indicator of an unfavorable outcome.

2.4. Statisticl analysis

Distribution of measured variables was skewed; therefore, means and medians alongside the 25th and 75th percentiles were used to explain the range. We used the Mann-Whitney U test to evaluate differences in continuous variables and Fisher's exact test for categorical comparisons of data. Significant predictors (age and the NIHSS score on admission) in the univariate analysis were transformed into dichotomous variables, with the optimal cut-off levels determined according to the Youden index by using receiver operating characteristic curves plotted for unfavorable outcomes. Subsequently, variables were included in a stepwise backward logistic regression model to identify the most significant factors associated with unfavorable outcomes. The predictive performance levels of variables were compared using *C*-statistics for unfavorable outcomes. $p < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS (version 24, SPSS, Inc., Chicago, IL, USA).

3. Results

3.1. Characteristics of the study cohort

A combination of ischemic stroke and bone fracture in the final diagnosis was found in 124 patients. During the same 12-year study period, there were 4558 patients admitted to the neurological ward for acute ischemic stroke. After excluding patients who had a diagnosis of stroke or fracture based on their prior history (not an active problem), a total of 30 patients with coexistent acute ischemic stroke and acute bone fracture during hospitalization were enrolled, which comprised 0.66% (30/4558) of all patients with acute ischemic stroke. All 30 patients were admitted through the emergency department. The clinical features and outcomes of these 30 patients are summarized in Table 1. The 30 patients included 9 men and 21 women with a mean age of 76.1 ± 10.3 years. Concurrent stroke and bone fracture occurred in 17 patients (initial stroke), stroke followed by fracture (initial stroke) occurred in 4 patients, and fracture followed by stroke (initial fracture) occurred in 9 patients. The mean interval between stroke and fracture was 3 ± 4 days (0–14 days). Among 21 patients with initial stroke, 16 patients (76%) were admitted to the neurological ward. Among 9 patients with initial fracture, 8 patients (89%) were admitted to the orthopedic ward. Patients might have been transferred to other departments for further treatment by the corresponding specialty (Table 1). Finally, 77% and 23% patients were discharged from neurological and orthopedic wards, respectively. Among 17 patients with concurrent stroke and fracture, stroke or fracture was initially overlooked in 4 patients (24%), including undiagnosed malleolus, lumbar spine, and radius fractures in 3 patients admitted for stroke and undiagnosed lacunar stroke in one patient admitted for radial fracture. Fracture of the femur occurred in 53% patients (16/30) and was the most common location of fracture. Except in 4 patients with a spinal fracture, fractures tended to occur more on the paretic side of stroke in 67% patients (12/18) with initial stroke and occurred in 25% patients (2/8) with initial fracture ($p = 0.089$). Surgical treatment for fracture was performed in 69% of patients with a femoral fracture and in 50% of all 30 patients. Among 9 patients with initial fracture, 4 patients developed stroke after operation; however, the remaining 5 patients could not be operated owing to the occurrence of stroke before surgery.

3.2. Clinical features and severity of stroke

All patients had at least one vascular risk factor, whereas 77% patients had three or more risk factors. Small vessel disease, large artery atherosclerosis, and cardioembolism were noted in 13, 9, and 8 patients. Stroke was located at the anterior circulation in 18 patients and at the posterior circulation in 12 patients. A total of 11 patients received urinary catheterization during hospitalization. Among these 11 patients, 10 patients also received nasogastric tube insertion. The median NIHSS score on admission was 5 (range 2–30). The NIHSS score on admission had a positive linear correlation with age. Both age and the NIHSS score on admission had a positive linear correlation with the discharge NIHSS and mRS scores and a negative linear correlation with the discharge Barthel index score (Table 2). The NIHSS score on admission also had a positive linear correlation with the hospital LOS. Ten of 14 patients (71%) with a fracture on the paretic limb had small vessel occlusion while 10 of 12 patients (83%) with a fracture on different sides of paretic limbs were large artery atherosclerosis or cardioembolism ($p = 0.0047$). Compared with patients who had fracture on the same side of paretic limbs, patients who had fracture on different sides of paretic limbs had a higher NIHSS score on admission (median 9.5, range 2–30 vs. median 4.0, range 2–21; $p = 0.0318$), higher percentage of nasogastric tube insertion (67% vs. 7%; $p = 0.0029$), and urinary catheterization (67% vs. 14%; $p = 0.0138$). Median hospital LOS was 19.5 (5–64) days. Longer hospital LOS was observed in patients who received nasogastric

Table 1
Clinical features of 30 patients with coexistence of acute ischemic stroke and bone fracture during hospitalization.

No. of patient	Age	Sex	Initial symptom	Hospitalization	Fracture location	Stroke location	Interval between fracture and stroke (days)	Fracture surgery	Total LOS (days)	TOAST	Admission NIHSS	Discharge NIHSS	Discharge Barthel Index	Discharge mRS
1	83	F	Concurrent	I-O	R Femur	Post	0	Yes	15	Small	2	2	50	3
2	58	M	Concurrent	I-O	L Malleolus	Ant	0	Yes	11	Small	2	1	90	0
3	94	F	Fracture	O-O	L Femur	Ant	14	Yes	22	Large	22	20	0	5
4	58	M	Stroke	N-O	L Femur	Post	7	Yes	18	Small	3	3	80	2
5	75	F	Concurrent	N-N	Spine	Ant	0	No	8	Small	4	3	50	3
6	85	F	Concurrent	N-N	Spine	Post	0	No	32	Large	7	6	20	5
7	70	F	Concurrent	O-N	R Radius	Post	0	Yes	23	Small	6	5	40	3
8	74	F	Concurrent	N-N	L Humerus	Post	0	No	5	Large	6	2	65	4
9	82	F	Concurrent	N-N	R Patella	Post	0	No	11	Small	4	3	85	2
10	63	F	Concurrent	N-N	L Clavicle	Post	0	No	5	Large	5	5	65	3
11	70	M	Stroke	N-O	R Femur	Ant	4	Yes	19	Small	4	4	40	4
12	87	M	Stroke	N-N	R Femur	Ant	3	Yes	26	Cardio	3	5	20	4
13	72	F	Concurrent	N-N	R Femur	Ant	0	No	44	Small	3	1	20	5
14	87	F	Fracture	O-N	R Femur	Ant	4	No	28	Cardio	21	42	0	6
15	77	M	Concurrent	N-N	L Rib	Post	0	No	6	Cardio	3	3	100	1
16	73	F	Fracture	O-N	R Humerus	Ant	0	Yes	33	Large	24	15	15	4
17	72	M	Fracture	O-N	R Femur	Post	10	No	12	Small	10	6	30	4
18	83	F	Fracture	O-N	L Femur	Ant	3	No	64	Large	30	27	5	5
19	84	F	Fracture	O-N	L Femur	Ant	14	Yes	21	Small	5	4	25	4
20	89	F	Concurrent	N-N	R Humerus	Ant	0	No	33	Cardio	16	14	2	5
21	58	F	Concurrent	O-O	L Femur	Post	0	Yes	10	Large	2	1	90	1
22	86	M	Concurrent	N-N	R Femur	Ant	0	Yes	23	Cardio	18	11	25	4
23	61	M	Concurrent	N-N	R Radius	Ant	0	No	18	Small	4	3	60	3
24	85	F	Fracture	I-N	Spine	Ant	3	No	31	Cardio	10	8	20	4
25	81	F	Concurrent	N-N	L Femur	Ant	0	No	12	Large	5	2	50	4
26	71	F	Concurrent	N-N	Spine	Post	0	Yes	20	Cardio	5	4	60	4
27	80	F	Stroke	I-O	L Femur	Post	3	Yes	12	Cardio	2	1	90	2
28	84	F	Fracture	O-N	R Femur	Ant	7	Yes	27	Small	9	7	30	4
29	80	F	Concurrent	N-N	L Femur	Ant	0	Yes	29	Small	12	10	25	4
30	60	M	Fracture	O-N	L Humerus	Ant	3	No	31	Large	5	5	20	3

F, female; M, male; I, internal medical ward; N, neurological ward; O, orthopedic ward; R, right; L, left; Ant, anterior circulation; Post, posterior circulation; LOS, length of stay; TOAST, Trial of ORG 10172 in Acute Stroke Treatment criteria; Small, small vessel disease; Large, large artery atherosclerosis; Cardio, cardioembolism; NIHSS, National Institutes of Health Stroke Scale; BI, Barthel Index; mRS, modified Rankin Scale.

Table 2
Simple linear regression analyses of age and NIHSS on admission with observed variables in 30 patients with coexistent acute stroke and bone fracture.

Dependent variables	Age			NIHSS on admission		
	Equation	R^2	*p* value	Equation	R^2	*p* value
Age	-	-	-	$0.649x + 70.612$	0.226	0.0079
NIHSS on admission	$0.348x – 18.064$	0.226	0.0079	-	-	-
Length of stay (days)	$0.357x – 5.86$	0.082	0.1252	$1.071x + 12.304$	0.395	0.0002
NIHSS at discharge	$0.393x – 22.485$	0.210	0.0109	$0.997x – 0.939$	0.722	< 0.0001
Barthel index at discharge	$-1.633x + 166.644$	0.313	0.0013	$-2.733x + 65.358$	0.469	< 0.0001
mRS at discharge	$0.081x – 2.646$	0.376	0.0003	$0.108x + 2.589$	0.363	0.0004

NIHSS, National Institute of Health Stroke Scale; mRS, modified Rankin Scale.

tube insertion and urinary catheterization, had an infarct area at anterior circulation, initial fracture, an NIHSS score of > 5 on admission, and unfavorable outcomes (Table 3). There were 18 patients who had unfavorable outcomes. Additionally, the percentage of unfavorable outcomes (67%) in this group of patients was higher than that (40%) in a total of 4558 patients with ischemic stroke (p = 0.0379). No differences of traditional risk factors for stroke, such as hypertension, diabetes mellitus, hyperlipidemia, and distribution of TOAST classifications were observed between patients with initial fracture and initial stroke (Table 4). While patient with initial fracture tended to have fracture on different side of paretic limbs (p = 0.0895). Compared with 21 patients who had initial stoke, 9 patients with initial fracture had a higher percentage of anterior circulation infarct, nasogastric tube insertion, and urinary catheterization; a higher NIHSS score on admission; longer hospital LOS; higher NIHSS and mRS; lower Barthel index scores at discharge; and a higher percentage of unfavorable outcomes (Table 4).

3.3. Factors influencing unfavorable outcomes

A univariate logistic regression found that significant factors influencing unfavorable outcomes were an NIHSS score of > 5 on admission, age > 70 years, urinary catheterization, nasogastric insertion, anterior circulation, and initial fracture (Table 5). Stepwise backward regression analyses showed an NIHSS score of > 5 on admission (odds ratio [OR]: 48.36; p = 0.040), age > 70 years (OR: 30.03; p = 0.024), and anterior circulation (OR: 27.41; p = 0.033) were significant predictors of unfavorable outcomes. *C*-statistics for

Table 3
Factors associated with longer length of stay in 30 patients with coexistent acute stroke and bone fracture during hospitalization.

Clinical features	Y		N		p value*
	Median	Mean	Median	Mean	
Age > 70 years (n = 22)	22.5 (12.0–31.3)	23.4 ± 13.8	18.0 (10.3–22.0)	16.9 ± 8.2	0.1733
Female gender (n = 21)	22.0 (11.5–31.5)	23.1 ± 14.2	18.0 (11.5–24.5)	18.2 ± 7.8	0.3893
Fracture surgery (n = 15)	21.0 (15.0–26.0)	20.6 ± 6.7	18.0 (8.0–32.0)	22.7 ± 16.9	0.9338
Nasogastric insertion (n = 10)	29.5 (19.5–33.0)	28.9 ± 14.6	18.0 (10.3–25.3)	18.0 ± 10.2	0.0164
Urinary catheterization (n = 11)	31.0 (22.0–33.0)	30.3 ± 14.6	18.0 (10.0–23.0)	16.6 ± 8.4	0.0034
Anterior circulation (n = 18)	26.5 (18.8–31.5)	26.7 ± 12.9	12.0 (7.0–19.5)	14.1 ± 8.1	0.0042
Initial fracture (n = 9)	28.0 (21.5–32.0)	29.9 ± 14.4	18.0 (10.5–24.5)	18.1 ± 10.4	0.0185
NIHSS on admission > 5 (n = 13)	28.0 (22.5–32.5)	27.8 ± 13.7	15.0 (10.5–20.5)	16.9 ± 9.9	0.0069
Unfavorable outcome (mRS > 3; n = 18)	26.5 (19.8–32.3)	26.7 ± 13.1	11.5 (8.6–18.0)	14.0 ± 7.5	0.0024

* Mann-Whitney U test; data are presented as median (25th–75th percentile) or mean ± standard deviation.
NIHSS, National Institute of Health Stroke Scale; mRS, modified Rankin Scale.

Table 4
Comparison of clinical features and outcomes between patients with initial fracture and patients with initial stroke.

Clinical features	Initial fracture (n = 9)		Initial stroke (n = 21)		p value*
	Median	Mean	Median	Mean	
Age (yrs)	72.5 (84.0–86.0)	80.2 ± 10.1	75.0 (66.5–82.5)	74.3 ± 10.1	0.1180
Length of stay (days)	28.0 (21.5–32.0)	29.9 ± 14.4	18.0 (10.5–24.5)	18.1 ± 10.4	0.0185
NIHSS on admission	10.0 (7.0–23.0)	15.1 ± 9.2	4.0 (3.0–6.0)	5.5 ± 4.4	0.0013
NIHSS at discharge	8.0 (5.5–23.5)	14.9 ± 12.8	3.0 (2.0–5.0)	4.2 ± 3.5	0.0011
Barthel index at discharge	20.0 (2.5–27.5)	16.1 ± 11.9	50.0 (25.0–82.5)	53.7 ± 28.5	0.0014
mRS at discharge	4.0 (4.0–5.0)	4.3 ± 0.9	3.0 (2.0–4.0)	3.1 ± 1.4	0.0285
Female gender	7 (78%)		14 (67%)		0.6814
Hypertension	8 (89%)		18 (86%)		> 0.9999
Diabetes mellitus	5 (56%)		8 (38%)		0.4434
Hyperlipidemia	2 (22%)		5 (24%)		> 0.9999
Heart disease	3 (33%)		7 (33%)		> 0.9999
Prior stroke	3 (33%)		8 (38%)		> 0.9999
Non-lacunar infarction	6 (66%)		11 (52%)		0.6908
Fracture on paretic limb[a]	2/8 (25%)		12/18 (67%)		0.0895
Anterior circulation	8 (89%)		10 (48%)		0.0492
NIHSS on admission > 5	7 (78%)		6 (29%)		0.0196
Nasogastric tube insertion	7 (78%)		3 (14%)		0.0017
Urinary catheterization	7 (78%)		4 (19%)		0.0042
Unfavorable outcome (mRS > 3)	8 (89%)		10 (48%)		0.0492

* Mann-Whitney U or Fisher's exact test; data are presented as median (25th–75th percentile), mean ± standard deviation, or n (%).
NIHSS, National Institute of Health Stroke Scale; mRS, modified Rankin Scale.
[a] Excluding 4 patients with spinal fracture.

Table 5
Logistic model of factors influencing outcomes in 30 patients with coexistent acute ischemic stroke and bone fracture during hospitalization.

Characteristics	Better outcome (n = 12)	Unfavorable outcome[†] (n = 18)	Chi-square	Univariate logistic regression		Stepwise logistic regression	
			p	p	Odds ratio (95% CI)	p	Odds ratio (95% CI)
NIHSS on admission > 5	1 (8)	12 (67)	0.0024	0.0076	22.00 (2.27–212.91)	0.040	48.36 (1.19–1963.26)
Age > 70 years	5 (42)	17 (94)	0.0025	0.0074	23.80 (2.34–242.35)	0.024	30.03 (1.57–574.48)
Urinary catheterization	1 (8)	10 (56)	0.0182	0.0223	13.75 (1.45–130.27)	-	
Nasogastric tube insertion	1 (8)	9 (50)	0.0235	0.0364	11.00 (1.16–103.97)	-	
Anterior circulation	4 (33)	14 (78)	0.0243	0.0197	7.00 (1.36–35.94)	0.033	27.41 (1.31–572.65)
Initial fracture	1 (8)	8 (44)	0.0492	0.0580	8.80 (0.93–83.37)	-	

Data are presented as n (%); [†] Modified Rankin Scale > 3.
NIHSS, National Institute of Health Stroke Scale; CI, confidence interval.

the detection of unfavorable outcomes was 0.792 for an NIHSS score of > 5 on admission. The addition of age > 70 years and anterior circulation infarct to the regression model resulted in significant improvement of the prediction value for unfavorable outcomes of up to 0.938.

4. Discussion

Coexistence of acute stroke and bone fracture is uncommon. However, the percentage of unfavorable outcomes was higher in this group of patients than in all patients with acute ischemic stroke. Most patients had concurrent stroke and bone fracture. Stroke or fracture was initially overlooked in 24% of patients with concurrent stroke and bone fracture. Over 75% of patients having three or more risk factors for vascular disease.

Our study showed that the femoral bone was the most common site of fracture, which is a similar finding observed in previous reports.[2,5] Femoral fracture tended to occur more on the paretic side in 21 patients with initial stroke. Falling is a major cause of femoral fracture. Muscular disturbance of the paretic side from cerebrovascular disease was associated with ipsilateral bone fracture, either caused by direct impaired muscle strength of the lower limb or due to an indirect reduced self-protection response by the paretic upper limb during a fall.[7,8] Reported factors associated with fractures were old age, female sex, moderate stroke severity, prior fractures or falls, and pre-existing osteoporosis.[9] Underlying osteoporosis, particularly in elderly people and women after menopause, is an important factor for fracture. The rate of bone loss as high as 2% per week was observed during prolonged bed rest.[2] Furthermore, bone loss in paretic limbs was greater than that in their nonparetic counterparts.[10] Hamdy et al. reported that mean bony demineralization of 9.3% and 3.7% occurs in the upper and lower limbs, respectively, on the paralyzed side by the fourth month after stroke.[11] Therefore, recent studies have recommended using bone mineral density to evaluate the condition of osteoporosis in patients with stroke.[9,10]

The severity of neurological deficits during stroke onset was correlated with aging, which directly influenced the functional outcome at discharge. The percentage of non-lacunar infarction and the NIHSS score on admission were higher in patients who had fracture on the contralateral side of paretic limbs. Besides, limitation of movement of the fractured limb, which was not a stroke paretic limb, might yield a higher score than actual neurological deficits caused by stroke, leading to overestimation of the NIHSS score. However, patients with fracture on different sides still had a higher percentage of nasogastric insertion and urinary catheterization, which indicated a status of worsened activity of daily living. Using the non-paretic arm to protect injury from a fall during an acute stroke with hemiplegia could be another possible explanation of non-paretic arm fracture. The typical symptom of pain caused by bone fracture might not be perceived initially if the fracture occurs on the paretic limb with constrained movements. Hypoesthesia of the fractured limb due to stroke may also cause delayed detection of bone fracture. Furthermore, chronic pain from the bone fracture interferes with ambulation during rehabilitation, thereby lengthening hospital LOS.

Both patients with initial fracture and patients with anterior circulation infarct presented poor clinical features, including a higher percentage of having nasogastric tube insertion, urinary catheterization, longer hospital LOS, and poor outcomes in terms of higher NIHSS and mRS and lower Barthel index scores at discharge. Notable symptoms of anterior circulation, such as hemiparesis, are easily recognized, which cause more severe motor dysfunction. Minor symptoms of posterior circulation, for instance, dizziness, vertigo, double vision, and unsteady gait, might be ignored in patients who have an initial fracture with restricted daily activities. There were no differences of traditional risk factors for stroke between patients with initial fracture and with initial stroke. Compared to patients with initial stroke, patients with initial fracture admitted to the ward usual had higher degree of fracture severity which required further treatment such as surgery. Meanwhile, fracture on the different side of paretic limbs tended to occur more in initial fracture patient group, although no statistic significance was observed owing to small sample size. The influence of initial fracture on the unfavorable outcomes became not significant after adjusted by two important factors: ages > 70 and NIHSS on admission > 5. Small sample size could also be the limitation of such results. The incidence of bone fracture after stroke is higher than that of stroke after bone fracture.[1,5] However, there is dearth of information regarding the prevalence of acute stroke after acute fracture or vice versa. A recent study conducted by An et al. including a Chinese population revealed that the overall prevalence of a post-fracture acute stroke was 0.446%.[12] They also identified that a history of fracture was an independent risk factor for post-fracture ischemic stroke. The authors did not describe whether all patients were admitted for acute fracture in their study. In the present study, the prevalence of concurrent and subsequent acute fracture for patients with initial stroke was 0.46% (21/4558), which is similar to the result reported by An et al., but with a reversed disease sequence. We identified that independent factors for unfavorable outcomes were an NIHSS score of > 5 on admission, age > 70 years, and anterior circulation, with a prediction value for unfavorable outcomes of up to 0.938.

Fat embolism could be one of the causative factors for stroke in addition to traditional risk factors. The disruption of the marrow-containing bone allows globules of marrow fat to pass into venous sinuses and subsequently into systemic circulation. Fat globules may enter arterial circulation directly from the right side of the heart through a patent foramen ovale into the left atrium or filter directly through the lung capillaries to reach the arterial system.[13] In patients with a long-bone fracture, evidence of fat emboli was found in up to 40% of patients by using echocardiography[14] and in 5 patients (100%) by using transcranial Doppler monitoring for microembolic signals.[15] All transcranial Doppler microembolic signals disappeared within four days of injury, suggesting that the risk of fat emboli is the highest within the first few days after trauma.[15] However, the incidence of symptomatic fat embolism was reported in only 0.9%–2.2% patients with long-bone fracture.[16] In our study, stroke occurred immediately in one patient after surgery for fracture and within 4 days of admission in 5 patients before fracture surgery was performed. Only two patients were classified as cardioembolism by The TOAST classification. Location of the infarct area through fat embolism could be similar to that through cardioembolism. Theoretically, it is inappropriate to attribute the etiology of stroke to fat embolism in these older patients who had concomitant multiple risk factors as well as atrial fibrillation.

Stroke injuries could be exacerbated shortly before or after ischemic stroke through animal studies.[1] Neuroinflammation is a crucial mechanism of negative impact of bone fracture on stroke severity and recovery. Inflammatory cytokines (tumor necrosis factor-alpha, interleukin-1beta, and interleukin-6) are increased in peripheral blood circulation and hippocampus after tibia fracture.[17,18] Mice with both stroke and bone fracture had larger infarct volumes and more severe neurobehavioral dysfunction than mice with stroke only.[19] Because of the small sample size in our study, we were not able to compare the infarct area and stroke severity between patients with both the conditions and patients with a single episode of stroke. In spite of this, patients with concurrent ischemic stroke and long bone fracture are not suitable for thrombolytic therapy during hyperacute infarct. These patients take more risk from additional surgical treatment of fracture during hospitalization, and require longer duration of rehabilitation for functional recovery.

The present study has some limitations. First, stroke or bone fracture might have been underestimated owing to missing appropriate diagnosis in the final diagnosis. A prior history of stroke, which is a critical risk factor for both surgery and anesthesia, might be addressed in more detail in the medical records of patients admitted for bone fracture. Whereas a history of bone fracture without sequela of motor dysfunction may not be mentioned in patients admitted for stroke. Second, we were not able to identify the actual number of patients who were admitted to the orthopedic ward due to acute bone fracture or due to nonunion/malunion from previous fractures because of an inadequate coding system to distinguish between each other. Third, the type and severity of bone fracture were not included in the analyses. We did not stratify femur fracture into shaft, distal, or hip fracture owing to the small study group. Fourth, no information of long-term outcomes after discharge was available in this retrospective study.

In conclusion, coexistence of acute ischemic stroke and acute bone fracture during hospitalization is a serious condition that requires proper and prompt treatment. The NIHSS score of > 5, age > 70 years, and anterior circulation infarct are independent risk factors for unfavorable outcomes, with a prediction value of up to 0.938. To avoid inadvertently overlooked, neurologists, orthopedists, and emergency physicians need to be more vigilant toward this concomitance with careful clinical evaluation.

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Declarations of interest

None.

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