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A History of Falls is Associated with a Significant Increase in Acute Mortality in Women after Stroke

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Background and Purpose The risks of falls and fractures increase after stroke. Little is known about the prognostic significance of previous falls and fractures after stroke. This study examined whether having a history of either event is associated with poststroke mortality.

Methods We analyzed stroke register data collected prospectively between 2003 and 2015. Eight sex-specific models were analyzed, to which the following variables were incrementally added to examine their potential confounding effects: age, type of stroke, Oxfordshire Community Stroke Project classification, previous comorbidities, frailty as indicated by the prestroke modified Rankin Scale score, and acute illness parameters. Logistic regression was applied to investigate in-hospital and 30-day mortality, and Cox proportional-hazards models were applied to investigate longer-term outcomes of mortality.

Results In total, 10,477 patients with stroke (86.1% ischemic) were included in the analysis. They were aged 77.7±11.9 years (mean±SD), and 52.2% were women. A history of falls was present in 8.6% of the men (n=430) and 20.2% of the women (n=1,105), while 3.8% (n=189) of the men and 12.9% of the women (n=706) had a history of both falls and fractures. Of the outcomes examined, a history of falls alone was associated with increased in-hospital mortality [odds ratio (OR)=1.33, 95% confidence interval (CI)=1.03−1.71] and 30-day mortality (OR=1.34, 95% CI=1.03−1.73) in women in the fully adjusted models. The Cox proportional-hazards models for longer-term outcomes and the history of falls and fractures combined showed no significant results.

Conclusions The history of falls is an important factor for acute stroke mortality in women. A previous history of falls may therefore be an important factor to consider in the short-term stroke prognosis, particularly in women.

Key Words stroke, falls, fractures, mortality, prognosis.

INTRODUCTION

Stroke and falls have a large impact on society. Stroke is the second largest cause of death and the leading source of disability,[1] and the lasting neurological symptoms of stroke could increase the risk of falls.[2,3] It is well established that falls are associated with increased morbidity and mortality. People who experience falls are also more likely to have other chronic conditions such as diabetes, arthritis, osteoporosis, and indeed stroke,[4,5] all of which contribute to a pre-existing increased risk of falls,[3] with some of these morbidities also being risk factors for stroke.

While it is recognized that falling after stroke increases mortality, little is known about the effects of previous falls or low-trauma fractures on mortality after stroke. While low bone mineral density has been linked to stroke incidence[6] and is a strong factor associated with fracture risk,[4,5,7] the links between previous falls and low-impact fractures on mortali-

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ty outcomes after stroke remain unclear. Identifying such links may have important prognostic implications, including for identifying those patients with stroke who require targeted intervention.

The aim of the current study was therefore to determine whether a history of falls or a history of falls and fractures is associated with immediate mortality and predicts longer-term mortality after stroke.

METHODS

Study population

The study population was drawn from the Norfolk and Norwich University Hospital Stroke and Transient Ischaemic Attack Register (NNSTR) in East Anglia, UK, which has a catchment population of approximately 750,000 people. The NNSTR was set up in late 1996, with regular annual record linkage of comorbid conditions and mortality status after stroke, thereby providing a unique opportunity to examine the outcomes of these patients over a long-term follow-up. The register received research database ethical approval from the Newcastle and Tyneside National Health Service and the Research Ethics Committee (approval no. 12/NE/0170). The study protocol was approved by the Steering Committee of the Register.

Data collection

The data collection methods have been described previously.[8-10] In brief, the data entry team entered paper and electronic records into the stroke register database prospectively, under supervision by clinicians. Patients were included if they had a confirmed ischemic or hemorrhagic stroke based on clinical examinations, the medical history, and neuroimaging results. Only the first recorded stroke in the database was used in the analysis of each patient. The prestroke modified Rankin Scale (mRS) score is commonly used to measure the level of disability (with 0 indicating no disability, 5 indicating severe disability and requiring constant nursing care, and 6 indicating being dead), and it was confirmed from medical records or from the history as reported by patients and relatives.

The predicting variables used in the study were a history of falls and a history of falls and fractures. A history of falls or fractures was defined as either event occurring before the date of the stroke event. This indicated that falls occurred in women at a median of 1.44 years before their stroke [interquartile range (IQR)=3.72 years] while fractures occurred at a median of 2.24 years (IQR=4.54 years); the corresponding values for men were 1.16 years (IQR=3.21 years) and 1.50 years (IQR=4.24 years), respectively. The International Classification of Diseases tenth revision (ICD-10) codes for the occurrence of falls were W00 to W19, while those for fractures were ICD-10 codes S82, S72, S62, S52, S42, S32, S22, S12, S02, T14.2, and T10. Patients who had a history of fractures were only included if they also had a history of falls, since the fractures were then more likely to be associated with low-trauma (i.e., fractures associated with falls and therefore frailty, not high energy trauma).

Statistical analysis

The statistical analysis was performed using SPSS Statistics (version 24, IBM Corp., Armonk, NY, USA). In the analysis we used sex-specific data to fully examine the effects of a history of falls and fractures stratified according to sex, since women are more likely to fall than men and are also more prone to osteoporosis.[3,4] Descriptive statistics were calculated separately for men and women, with and without a history of falls or a history of falls and fractures. Continuous variables are presented as mean±SD values, while categorical variables are presented as number and percentage values. Characteristic data were compared between patient groups using independent-samples *t*-tests for continuous variables and chi-squared tests for categorical variables.

We investigated the effects of a history of either falls alone or of both falls and fractures on the stroke prognosis in terms of mortality at six different time periods for men and women separately. The outcomes were defined by mortality at these time points: in-hospital, 0−30, 31−90, 91−365, 366−1,095 (1−3 years), and 1,096−3,650 days (3−10 years). These time points were selected to allow the in-hospital and short-, medium-, and long-term effects of a history of either falls alone or falls and fractures on poststroke mortality to be examined accurately, without deaths during the previous time points distorting the results. Binary logistic regression was used to obtain odds ratios (ORs) for the short-term analysis of in-hospital mortality and mortality up to 30 days, while Cox proportional-hazards model regression was used to obtain hazard ratios for the longer-term analysis of mortality from day 31 onward.

The variables included in regression models examining mortality outcomes were chosen based on our own work and that of others that have shown impacts on stroke mortality. We incorporated the identified variables in eight models that were analyzed separately for men and women: Models A−F, where Model F was the fully adjusted model, and Models C2 and G were used for two sensitivity analyses. These models were constructed to fully analyze, in a step-by-step approach, the complex relationships between falls, fractures, and stroke mortality in order to examine the potential confounding effects of variables incrementally added to the following adjusted models:

A) Not adjusted.

B) Adjusted for age, stroke type (ischemic or hemorrhagic), and Oxfordshire Community Stroke Project (OCSP) classification (lacunar stroke, partial anterior circulation stroke, posterior circulation stroke, and total anterior circulation stroke).

C) Further adjusted for the presence of pre-existing comorbidities before stroke (previous strokes, transient ischemic attacks, congestive heart failure, coronary heart disease, atrial fibrillation, myocardial infarction, diabetes, hypertension, peripheral vascular disease, chronic kidney disease, chronic obstructive pulmonary disease, dementia, hyperlipidemia, and cancer).

C2) Used in a sensitivity analysis to examine the effects of a previous history of stroke on the results, adjusting for the same variables as in Model C but excluding patients who had a previous history of stroke.

D) Further adjusted for prestroke disability (mRS score=0−5).[11,12]

E) Further adjusted for the acute illness parameters of the admission white blood cell count and C-reactive protein.[13,14]

F) Further adjusted for the acute illness parameters of the admission serum sodium, albumin, and glucose.[15-17]

G) Used in a sensitivity analysis to examine the impact of the prestroke mRS score (a measure of frailty) on outcomes by removing this variable from the final adjusted model (Model F).

Missing data were excluded from each successive model.

RESULTS

In total, 11,729 stroke cases were recorded between January 2003 and April 2015. Applying the exclusion criteria of the study as detailed in Supplementary Fig. 1 (in the online-only Data Supplement) resulted in 10,477 cases for inclusion in the analysis. Although set up in 1996, cases before 2003 were excluded since electronic record linkage for some variables (e.g., blood tests and extensive comorbidity linkage through electronic records) was not available before this time. Six stroke events were excluded due to the patients being younger than 18 years, and 990 were excluded due to them being related to the second or third admission of the same patient during the study period (to avoid duplicate data, we only included stroke cases that were the first recorded in the register for each patient). A further 102 were excluded because they were lost to follow-up, and lastly 154 were excluded because they had a history of fractures but not a history of falls. Therefore, 10,477 people with stroke recorded for the first time in the register during the study period were included in the analysis.

The cohort was aged 77.7±11.9 years (mean±SD); 47.8% were men (*n*=5,003) and 52.2% women (*n*=5,474). A history of falls was observed in 14.7% of cases (*n*=1,535), 72.0% of which involved women. A history of falls and fractures combined was observed in 8.5% of cases (*n*=895), most of which (78.9%) involved women. Ischemic stroke occurred in 86.1% of the cases, with the most common OCSP stroke classification (31.0%) being partial anterior circulation stroke. Most (59.0%) of the patients had a prestroke mRS score of 0. The prevalence of a history of both falls and falls and fractures increased with age and was significantly higher in women: 20.2% of the women had a history of falls compared with only 8.6% of the men, and 12.9% of the women had a history of both falls and fractures compared with 3.8% of the men. The distribution of stroke types was similar between those with and without a history of falls.

Tables 1 and 2 list the basic data characteristics for those with and without a history of falls or a history of falls and fractures in men and women, respectively. The prestroke mRS score was higher in the presence of a history of falls in both men and women. The prevalence rates of dementia, hypertension, previous stroke, congestive heart failure, coronary heart disease, atrial fibrillation, diabetes, chronic kidney disease, and chronic obstructive pulmonary disease were higher in patients with a history of falls or a history of falls and fractures than in nonfallers ($p<0.05$). A history of transient ischemic attacks was more common in women with a history of falls or a history of falls and fractures ($p<0.001$), while there was no such association in men. Peripheral vascular disease was associated with a history of falls alone in both men ($p<0.001$) and women ($p=0.018$) and with a history of falls and fractures in men only ($p<0.001$). In women, hyperlipidemia was only associated with a history of falls ($p=0.011$), as was myocardial infarction ($p=0.007$). In men, hyperlipidemia was also associated with a history of falls ($p=0.036$), and a history of myocardial infarction was associated with both a history of falls and a history of falls and fractures ($p=0.005$ and <0.001 respectively). Cancer was not significantly associated with a history of falls or a history of falls and fractures in women ($p\geq0.377$), while it was significantly associated with a history of falls ($p<0.001$) but not with history of both falls and fractures ($p=0.226$) in men.

Table 3 presents the effects of a history of falls on mortality in both men and women. The patients were divided into two categories for the analysis: those with and without a history of falls. The analyzed event was the number of deaths occurring during the specified time period, and this was divided by the total number of patients in that period. The total number of cases examined in the models decreased as the number of adjusted variables increased, which was due to any cases with missing data being excluded from the analysis. The in-hospital mortality rate was significantly higher in

Table 1. Characteristics of men with stroke and a history of falls alone or of both falls and fractures compared with no history

Characteristic	Falls		$p^{\S}$	Falls and fractures		$p^{\|\|}$
	No	Yes		No	Yes	
Age group, years						
<65	900 (19.7)	36 (8.4)	<0.001	919 (19.1)	17 (9.0)	<0.001
65–70	603 (13.2)	17 (4.0)		612 (12.7)	8 (4.2)	
71–80	1,474 (32.2)	107 (24.9)		1,526 (31.7)	55 (29.1)	
81–89	1,337 (29.2)	189 (44.0)		1,449 (30.1)	77 (40.7)	
90<	259 (5.7)	81 (18.8)		308 (6.4)	32 (16.9)	
Type of stroke*						
Infarct	3,907 (85.9)	376 (88.1)	0.223	4,115 (86.0)	168 (88.9)	0.260
Hemorrhage	640 (14.1)	51 (11.9)		670 (14.0)	21 (11.1)	
OCSP classification						
Lacunar stroke	979 (21.4)	85 (19.8)	0.021	1,026 (21.3)	38 (20.1)	0.817
Partial anterior circulation stroke	1,404 (30.7)	136 (31.6)		1,484 (30.8)	56 (29.6)	
Posterior circulation stroke	829 (18.1)	60 (14.0)		858 (17.8)	31 (16.4)	
Total anterior circulation stroke	781 (17.1)	75 (17.4)		818 (17.0)	38 (20.1)	
Undetermined	263 (5.8)	40 (9.3)		293 (6.1)	10 (5.3)	
Missing	317 (6.9)	34 (7.9)		335 (7.0)	16 (8.5)	
Prestroke mRS score						
0	3,138 (68.6)	155 (36.0)	<0.001	3,231 (67.1)	62 (32.8)	<0.001
1	489 (10.7)	50 (11.6)		518 (10.8)	21 (11.1)	
2	250 (5.5)	53 (12.3)		274 (5.8)	25 (13.2)	
3	244 (5.3)	83 (19.3)		288 (6.0)	39 (20.6)	
4	117 (2.6)	36 (8.4)		135 (2.8)	18 (9.5)	
5	46 (1.0)	12 (2.8)		51 (1.1)	7 (3.7)	
Missing	289 (6.3)	41 (9.5)		313 (6.5)	17 (9.0)	
In-hospital mortality	821 (18.0)	133 (30.9)	<0.001	895 (18.6)	59 (31.2)	<0.001
Comorbidities						
Previous stroke	406 (8.9)	83 (19.3)	<0.001	455 (9.5)	34 (18.0)	<0.001
Transient ischemic attack	128 (2.8)	18 (4.2)	0.102	139 (2.9)	7 (3.7)	0.513
Congestive heart failure	318 (7.0)	71 (16.5)	<0.001	357 (7.4)	32 (16.9)	<0.001
Coronary heart disease	841 (18.4)	131 (30.5)	<0.001	916 (19.0)	56 (29.6)	<0.001
Atrial fibrillation	573 (12.5)	131 (30.5)	<0.001	653 (13.6)	51 (27.0)	<0.001
Myocardial infarction	220 (4.8)	34 (7.9)	0.005	234 (4.9)	20 (10.6)	<0.001
Diabetes	473 (10.3)	76 (17.7)	<0.001	515 (10.7)	34 (18.0)	0.002
Hypertension	1,193 (26.1)	211 (49.1)	<0.001	1,305 (27.1)	99 (52.4)	<0.001
Peripheral vascular disease	124 (2.7)	26 (6.0)	<0.001	136 (2.8)	14 (7.4)	<0.001
Chronic kidney disease	143 (3.1)	48 (11.2)	<0.001	168 (3.5)	23 (12.2)	<0.001
Chronic obstructive pulmonary disease	213 (4.7)	66 (15.3)	<0.001	247 (5.1)	32 (16.9)	<0.001
Dementia	74 (1.6)	54 (12.6)	<0.001	102 (2.1)	26 (13.8)	<0.001
Hyperlipidemia	206 (4.5)	29 (6.7)	0.036	221 (4.6)	14 (7.4)	0.073
Cancer	591 (12.9)	82 (19.1)	<0.001	642 (13.3)	31 (16.4)	0.226
Biochemistry						
Admission C-reactive protein within the normal range	1,576 (34.5)	152 (35.3)	0.032	1,666 (34.6)	62 (32.8)	0.007
Admission C-reactive protein above the normal range	2,152 (47.1)	179 (41.6)		2,256 (46.9)	75 (39.7)	
Admission C-reactive protein, missing data	845 (18.5)	99 (23.0)		892 (18.5)	52 (27.5)	
Admission sodium†	138.74±3.85	137.84±4.94	<0.001	138.71±3.91	137.45±5.02	<0.001
Admission glucose††	1.93±0.33	1.92±0.39	0.197	1.92±0.33	1.95±0.43	0.012
Admission albumin†	37.70±5.23	34.87±6.00	<0.001	37.56±5.31	34.91±5.92	0.015
Admission white blood cell count††	2.21±0.38	2.24±0.39	0.246	2.21±0.38	2.26±0.39	0.614

Normal C-reactive protein range=0–10 mg/L. Data are *n* (%) or mean±SD values.
*Missing data were removed from this analysis since there were no missing cases, †Independent *t*-test, ††Natural logarithm of values used so as to produce a normal distribution, §*p* values for differences between patients with and without a history of falls (overall *p* for categorical data), ||*p* values for differences between patients with and without a history of falls and fractures (overall *p* for categorical data).
mRS: modified Rankin Scale, OCSP: Oxfordshire Community Stroke Project.

Table 2. Characteristics of women with stroke and a history of falls alone or of both falls and fractures compared with no history

Characteristic	Falls		$p^{\dagger}$	Falls and fractures		$p^{\S}$
	No	Yes		No	Yes	
Age group, years						
<65	452 (10.3)	28 (2.5)	<0.001	463 (9.7)	17 (2.4)	<0.001
65–70	363 (8.3)	33 (3.0)		376 (7.9)	20 (2.8)	
71–80	1,221 (27.9)	175 (15.8)		1,291 (27.1)	105 (14.9)	
81–89	1,667 (38.2)	517 (46.8)		1,848 (38.8)	336 (47.6)	
90<	666 (15.2)	352 (31.9)		790 (16.6)	228 (32.3)	
Type of stroke						
Infarct	3,768 (86.2)	974 (88.1)	0.136	4,128 (86.6)	614 (87.0)	0.886
Hemorrhage	585 (13.4)	125 (11.3)		621 (13.0)	89 (12.6)	
Missing	16 (0.4)	6 (0.5)		19 (0.4)	3 (0.4)	
OCSP classification						
Lacunar stroke	928 (21.2)	211 (19.1)	0.001	1,004 (21.1)	135 (19.1)	0.108
Partial anterior circulation stroke	1,362 (31.2)	342 (31.0)		1,488 (31.2)	216 (30.6)	
Posterior circulation stroke	647 (14.8)	129 (11.7)		691 (14.5)	85 (12.0)	
Total anterior circulation stroke	927 (21.2)	258 (23.3)		1,016 (21.3)	169 (23.9)	
Undetermined	264 (6.0)	75 (6.8)		285 (6.0)	54 (7.6)	
Missing	241 (5.5)	90 (8.1)		284 (6.0)	47 (6.7)	
Prestroke mRS score						
0	2,582 (59.1)	305 (27.6)	<0.001	2,688 (56.4)	199 (28.2)	<0.001
1	491 (11.2)	156 (14.1)		548 (11.5)	99 (14.0)	
2	352 (8.1)	142 (12.9)		397 (8.3)	97 (13.7)	
3	389 (8.9)	213 (19.3)		479 (10.0)	123 (17.4)	
4	181 (4.1)	126 (11.4)		232 (4.9)	75 (10.6)	
5	77 (1.8)	61 (5.5)		97 (2.0)	41 (5.8)	
Missing	297 (6.8)	102 (9.2)		327 (6.9)	72 (10.2)	
In-hospital mortality	1,009 (23.1)	386 (34.9)	<0.001	1,149 (24.1)	246 (34.8)	<0.001
Comorbidities						
Previous stroke	431 (9.9)	189 (17.1)	<0.001	507 (10.6)	113 (16.0)	<0.001
Transient ischemic attack	104 (2.4)	57 (5.2)	<0.001	125 (2.6)	36 (5.1)	<0.001
Congestive heart failure	322 (7.4)	179 (16.2)	<0.001	409 (8.6)	92 (13.0)	<0.001
Coronary heart disease	602 (13.8)	283 (25.6)	<0.001	724 (15.2)	161 (22.8)	<0.001
Atrial fibrillation	600 (13.7)	316 (28.6)	<0.001	740 (15.5)	176 (24.9)	<0.001
Myocardial infarction	192 (4.4)	70 (6.3)	0.007	229 (4.8)	33 (4.7)	0.881
Diabetes	351 (8.0)	143 (12.9)	<0.001	413 (8.7)	81 (11.5)	0.015
Hypertension	1,259 (28.8)	581 (52.6)	<0.001	1,492 (31.3)	348 (49.3)	<0.001
Peripheral vascular disease	87 (2.0)	35 (3.2)	0.018	104 (2.2)	18 (2.5)	0.536
Chronic kidney disease	101 (2.3)	53 (4.8)	<0.001	123 (2.6)	31 (4.4)	0.007
Chronic obstructive pulmonary disease	142 (3.3)	75 (6.8)	<0.001	174 (3.6)	43 (6.1)	0.002
Dementia	93 (2.1)	160 (14.5)	<0.001	150 (3.1)	103 (14.6)	<0.001
Hyperlipidemia	157 (3.6)	58 (5.2)	0.011	180 (3.8)	35 (5.0)	0.131
Cancer	420 (9.6)	116 (10.5)	0.377	462 (9.7)	74 (10.5)	0.509
Biochemistry						
Admission C-reactive protein within the normal range	1,460 (33.4)	385 (34.8)	0.365	1,598 (33.5)	247 (35.0)	0.467
Admission C-reactive protein above the normal range	2,077 (47.5)	499 (45.2)		2,259 (47.4)	317 (44.9)	
Admission C-reactive protein, missing data	832 (19.0)	221 (20.0)		911 (19.1)	142 (20.1)	
Admission sodium*	138.08±4.33	137.95±5.06	<0.001	138.10±4.43	137.73±4.84	0.003
Admission glucose*†	1.94±0.32	1.90±0.32	0.688	1.94±0.32	1.90±0.32	0.723
Admission albumin*	37.12±5.47	35.08±5.95	<0.001	36.98±5.50	34.88±6.16	<0.001
Admission white blood cell count*†	2.24±0.39	2.20±0.39	0.890	2.24±0.39	2.21±0.39	0.712

Normal C-reactive protein range=0–10 mg/L, Data are *n* (%) or mean±SD values.
*Independent *t*-test, †Natural logarithm of values used so as to produce a normal distribution, ‡*p* values for differences between patients with and without a history of falls (overall *p* for categorical data), §*p* values for differences between patients with and without a history of falls and fractures (overall *p* for categorical data).
mRS: modified Rankin Scale, OCSP: Oxfordshire Community Stroke Project.

Table 3. Effects of a history of falls on mortality after stroke in men and women

Mortality time period and model	Men				Women			
	Deaths/ patients with falls	Deaths/ patients without falls	OR*/HR† (95% CI)	*p*	Deaths/ patients with falls	Deaths/ patients without falls	OR*/HR† (95% CI)	*p*
In-hospital*								
Model A	133/430	821/4,573	2.05 (1.65–2.55)	<0.001	386/1,105	1,009/4,369	1.79 (1.55–2.06)	<0.001
Model B	122/394	784/4,241	1.47 (1.12–1.93)	0.005	363/1,012	962/4,121	1.55 (1.30–1.84)	<0.001
Model C	122/394	784/4,241	1.17 (0.88–1.56)	0.285	363/1,012	962/4,121	1.35 (1.12–1.62)	0.002
Model C2	86/317	650/3,845	1.24 (0.90–1.71)	0.189	282/836	800/3,707	1.42 (1.16–1.74)	0.001
Model D	99/357	689/3,984	0.99 (0.72–1.35)	0.926	315/921	842/3,846	1.19 (0.97–1.45)	0.092
Model E	75/274	574/3,243	0.94 (0.67–1.31)	0.700	244/724	692/3,117	1.29 (1.04–1.60)	0.019
Model F	49/200	452/2,510	0.99 (0.67–1.48)	0.978	189/557	536/2,434	1.33 (1.03–1.71)	0.028
Model G	62/220	510/2,664	1.10 (0.76–1.58)	0.616	221/613	613/2,611	1.47 (1.16–1.86)	0.001
0–30 days*								
Model A	125/430	798/4,573	1.94 (1.55–2.42)	<0.001	358/1,105	954/4,369	1.72 (1.48–1.98)	<0.001
Model B	116/394	761/4,241	1.45 (1.11–1.90)	0.006	339/1,012	916/4,121	1.46 (1.23–1.75)	<0.001
Model C	116/394	761/4,241	1.14 (0.86–1.51)	0.365	339/1,012	916/4,121	1.31 (1.09–1.58)	0.004
Model C2	83/317	641/3,845	1.16 (0.84–1.60)	0.360	262/836	768/3,707	1.35 (1.10–1.65)	0.004
Model D	97/357	664/3,984	1.06 (0.78–1.45)	0.704	295/921	792/3,846	1.20 (0.98–1.47)	0.076
Model E	73/274	550/3,243	1.07 (0.77–1.48)	0.699	229/724	650/3,117	1.30 (1.05–1.61)	0.018
Model F	53/200	437/2,510	1.26 (0.86–1.85)	0.234	177/557	514/2,434	1.34 (1.03–1.73)	0.027
Model G	64/220	495/2,664	1.17 (0.82–1.67)	0.400	206/613	594/2,611	1.42 (1.12–1.81)	0.004
31–90 days†								
Model A	49/305	243/3,775	2.61 (1.92–3.55)	<0.001	105/747	302/3,415	1.63 (1.31–2.04)	<0.001
Model B	45/278	234/3,480	1.62 (1.16–2.25)	0.004	95/673	285/3,205	1.16 (0.91–1.48)	0.221
Model C	45/278	234/3,480	1.29 (0.92–1.82)	0.145	95/673	285/3,205	0.95 (0.73–1.22)	0.664
Model C2	35/234	192/3,204	1.59 (1.09–2.34)	0.017	77/574	244/2,939	1.01 (0.77–1.34)	0.924
Model D	37/260	209/3,320	1.05 (0.72–1.54)	0.795	87/626	262/3,054	0.80 (0.61–1.05)	0.111
Model E	28/201	173/2,693	0.96 (0.65–1.43)	0.837	63/495	213/2,467	0.83 (0.63–1.08)	0.163
Model F	18/147	127/2,073	0.84 (0.51–1.39)	0.503	50/380	158/1,920	0.79 (0.58–1.08)	0.143
Model G	21/156	143/2,169	1.16 (0.76–1.78)	0.491	56/407	173/2,017	0.94 (0.70–1.27)	0.701
91–365 days†								
Model A	47/256	355/3,532	1.91 (1.41–2.58)	<0.001	118/642	332/3,113	1.81 (1.47–2.23)	<0.001
Model B	45/233	333/3,246	1.32 (0.96–1.81)	0.087	111/578	319/2,920	1.34 (1.07–1.67)	0.010
Model C	45/233	333/3,246	1.20 (0.86–1.67)	0.281	111/578	319/2,920	1.17 (0.92–1.48)	0.191
Model C2	35/199	294/3,012	1.22 (0.85–1.76)	0.279	86/497	290/2,695	1.10 (0.85–1.43)	0.464
Model D	43/223	303/3,111	1.00 (0.71–1.41)	0.984	102/539	294/2,792	1.08 (0.84–1.38)	0.570
Model E	28/173	246/2,520	0.90 (0.63–1.29)	0.568	81/432	236/2,254	1.11 (0.86–1.44)	0.438
Model F	24/129	195/1,946	0.64 (0.41–1.00)	0.051	64/330	187/1,762	1.08 (0.80–1.45)	0.616
Model G	25/135	212/2,026	0.82 (0.53–1.24)	0.343	71/351	201/1,844	1.12 (0.84–1.47)	0.444
366–1,095 days†								
Model A	47/209	347/3,177	2.24 (1.65–3.04)	<0.001	97/524	329/2,781	1.63 (1.30–2.05)	<0.001
Model B	44/188	343/2,913	1.51 (1.10–2.08)	0.011	96/467	327/2,601	1.12 (0.89–1.41)	0.349
Model C	44/188	343/2,913	1.34 (0.96–1.88)	0.089	96/467	327/2,601	1.16 (0.91–1.49)	0.224
Model C2	38/164	301/2,718	1.60 (1.12–2.28)	0.009	82/411	297/2,405	1.16 (0.89–1.51)	0.268
Model D	43/180	326/2,808	1.19 (0.84–1.68)	0.335	90/437	307/2,498	1.03 (0.79–1.33)	0.836
Model E	38/145	251/2,274	1.12 (0.78–1.63)	0.532	71/351	250/2,018	1.01 (0.77–1.32)	0.973
Model F	28/105	193/1,751	1.14 (0.73–1.78)	0.563	60/266	191/1,575	0.97 (0.70–1.33)	0.830
Model G	29/110	206/1,814	1.26 (0.82–1.93)	0.303	63/280	207/1,643	1.10 (0.82–1.49)	0.526

Table 3. Effects of a history of falls on mortality after stroke in men and women (continued)

Mortality time period and model	Men				Women			
	Deaths/ patients with falls	Deaths/ patients without falls	OR*/HR† (95% CI)	*p*	Deaths/ patients with falls	Deaths/ patients without falls	OR*/HR† (95% CI)	*p*
1,096–3,650 days‡								
Model A	26/162	349/2,830	1.37 (0.92–2.04)	0.121	57/427	378/2,452	0.87 (0.66–1.15)	0.340
Model B	26/144	349/2,570	1.12 (0.75–1.67)	0.581	57/371	377/2,274	0.71 (0.54–0.95)	0.019
Model C	26/144	349/2,570	1.19 (0.79–1.79)	0.412	57/371	377/2,274	0.85 (0.63–1.14)	0.266
Model C2	21/126	315/2,417	1.30 (0.83–2.04)	0.246	51/329	334/2,108	0.94 (0.69–1.28)	0.708
Model D	24/137	328/2,482	1.10 (0.71–1.71)	0.655	52/347	361/2,191	0.85 (0.62–1.17)	0.319
Model E	21/107	275/2,023	1.12 (0.71–1.78)	0.619	39/280	277/1,768	0.83 (0.58–1.19)	0.306
Model F	16/77	214/1,558	1.19 (0.70–2.03)	0.521	29/206	216/1,384	0.88 (0.59–1.31)	0.530
Model G	18/81	229/1,608	1.39 (0.85–2.27)	0.194	32/217	227/1,436	0.90 (0.62–1.29)	0.563

Model A: unadjusted. Model B: Model A+age, stroke type (ischemic or hemorrhagic), and OCSP classification (lacunar stroke, partial anterior circulation stroke, posterior circulation stroke, and total anterior circulation stroke). Model C: Model B+prestroke comorbidities (previous strokes, transient ischemic attacks, congestive heart failure, coronary heart disease, atrial fibrillation, myocardial infarction, diabetes, hypertension, peripheral vascular disease, chronic kidney disease, chronic obstructive pulmonary disease, dementia, hyperlipidemia, and cancer). Model C2: Model C–patients with a history of stroke. Model D: Model C+prestroke disability mRS score=0–5. Model E: Model D+acute illness parameters of admission white blood cell count and C-reactive protein. Model F: Model E+acute illness parameters of admission sodium, albumin, and glucose. Model G: Model F–prestroke disability mRS score.

*Analysis up to and including 30 days, †Analysis from 31 days onward.

CI: confidence interval, HR: hazard ratio, mRS: modified Rankin Scale, OCSP: Oxfordshire Community Stroke Project, OR: odds ratio.

women with a history of falls than in those with no such history [OR=1.33, 95% confidence interval (CI)=1.03–1.71] in the fully adjusted model (Model F). Model C2 was used in a sensitivity analysis of the effects of a previous history of stroke on the results, and it yielded *p* values closely matching those of Model C, implying that our results remained significant. Model D (adjusting for the prestroke mRS score) resulted in a loss of significance in the results of our detailed analysis (OR=1.19, 95% CI=0.97–1.45), but the significance remained in the fully adjusted model. The results for Model G, which examined the potential effects of frailty on the outcomes by removing the prestroke mRS score from Model F, remained essentially unchanged, except for a higher significance level (i.e., lower *p* value) for in-hospital mortality in women with a history of falls alone (Table 3). This suggests that prestroke frailty may serve as a mediator for these outcomes. A significant association was also present for the in-hospital mortality among men in the unadjusted model, although the association was no longer significant after adjusting for comorbidities in Model C (OR=1.17, 95% CI= 0.88–1.56).

A history of falls was significantly associated with increased short-term mortality (0–30 days) in women (OR=1.34, 95% CI=1.03–1.73) in the fully adjusted model. This showed a very similar pattern to the in-hospital mortality in women, with the significance being lost in Model D (OR=1.20, 95% CI=0.98–1.47) but returning in the subsequent increasingly adjusted models. Model G also produced a lower *p* value than Model F, again indicating that prestroke frailty may contribute to these outcome associations. When adjusting for comorbidities, the significance was lost for the 0- to 30-day mortality in men in Model C (OR=1.14, 95% CI=0.86–1.51).

There were no consistent significant associations between a history of falls and longer-term mortality outcomes.

Table 4 presents the effects of a history of both falls and fractures on mortality in men and women. No association was found between a history of falls and fractures on mortality after stroke in the fully adjusted models for both men and women.

We have also included graphs for the Cox proportional-hazards models that display the mortality rate over the entire follow-up period for men (Fig. 1) and women (Fig. 2) with and without a history of falls (Figs. 1A and 2A, respectively), and with and without a history of fractures (Figs. 1B and 2B, respectively).

DISCUSSION

This is the first report in the literature of the rates of acute mortality in-hospital and at 0–30 days being significantly higher in poststroke women with a history of falls than in those without such a history. However, no similar association was found in men, and there was no association between the predictor of the history of falls and fractures combined and mortality. Our findings suggest that a history of falls may be of prognostic use especially for women who are admitted with a stroke. While it is unclear whether this is mere reflec-

Table 4. Effects of a history of falls and fractures on mortality after stroke in men and women

Mortality time period and model	Men				Women			
	Deaths/ patients with falls and fractures	Deaths/ patients without falls and fractures	OR*/HR† (95% CI)	*p*	Deaths/ patients with falls and fractures	Deaths/ patients without falls and fractures	OR*/HR† (95% CI)	*p*
In-hospital*								
Model A	59/189	895/4,814	1.99 (1.45–2.73)	<0.001	246/706	1,149/4,768	1.68 (1.42–1.99)	<0.001
Model B	54/173	852/4,462	1.54 (1.04–2.26)	0.031	235/657	1,090/4,476	1.39 (1.14–1.71)	0.001
Model C	54/173	852/4,462	1.17 (0.77–1.77)	0.469	235/657	1,090/4,476	1.29 (1.05–1.59)	0.018
Model C2	38/141	698/4,021	1.33 (0.84–2.12)	0.227	186/549	896/3,994	1.34 (1.07–1.69)	0.012
Model D	42/157	746/4,184	0.90 (0.57–1.42)	0.652	198/589	959/4,178	1.11 (0.89–1.40)	0.360
Model E	31/113	618/3,404	0.82 (0.50–1.34)	0.426	159/466	777/3,375	1.23 (0.96–1.57)	0.096
Model F	19/85	482/2,625	0.94 (0.53–1.66)	0.819	124/353	601/2,638	1.25 (0.93–1.66)	0.135
Model G	26/94	546/2,790	1.09 (0.65–1.83)	0.759	148/391	686/2,833	1.39 (1.06–1.82)	0.017
0–30 days*								
Model A	53/189	870/4,814	1.77 (1.28–2.45)	0.001	226/706	1,086/4,768	1.60 (1.34–1.90)	<0.001
Model B	49/173	828/4,462	1.38 (0.94–2.04)	0.104	217/657	1,038/4,476	1.29 (1.05–1.59)	0.014
Model C	49/173	828/4,462	1.03 (0.68–1.57)	0.880	217/657	1,038/4,476	1.22 (0.99–1.50)	0.068
Model C2	32/141	692/4,021	0.95 (0.58–1.53)	0.823	173/549	857/3,994	1.28 (1.01–1.61)	0.039
Model D	40/157	721/4,184	0.91 (0.58–1.43)	0.677	185/589	902/4,178	1.11 (0.88–1.40)	0.369
Model E	29/113	594/3,404	0.85 (0.52–1.37)	0.494	149/466	730/3,375	1.22 (0.96–1.56)	0.106
Model F	20/85	470/2,625	0.94 (0.54–1.66)	0.840	114/353	577/2,638	1.22 (0.91–1.64)	0.185
Model G	25/94	534/2,790	0.90 (0.53–1.52)	0.688	134/391	666/2,833	1.28 (0.98–1.69)	0.074
31–90 days†								
Model A	15/136	277/3,944	1.59 (0.95–2.68)	0.080	68/480	339/3,682	1.58 (1.22–2.05)	0.001
Model B	14/124	265/3,634	1.07 (0.62–1.83)	0.817	64/440	316/3,438	1.18 (0.89–1.55)	0.247
Model C	14/124	265/3,634	0.80 (0.45–1.40)	0.429	64/440	316/3,438	1.06 (0.80–1.40)	0.709
Model C2	12/109	215/3,329	1.00 (0.54–1.84)	0.989	52/376	269/3,137	1.11 (0.81–1.52)	0.514
Model D	11/117	235/3,463	0.58 (0.31–1.10)	0.097	56/404	293/3,276	0.91 (0.67–1.22)	0.522
Model E	7/84	194/2,810	0.56 (0.30–1.07)	0.079	42/317	234/2,645	0.90 (0.66–1.21)	0.478
Model F	5/65	140/2,155	0.57 (0.26–1.24)	0.154	33/239	175/2,061	0.92 (0.65–1.31)	0.650
Model G	7/69	157/2,256	0.87 (0.45–1.69)	0.677	39/257	190/2,167	1.07 (0.77–1.49)	0.683
91–365 days†								
Model A	30/121	372/3,667	2.65 (1.83–3.84)	<0.001	79/412	371/3,343	1.83 (1.44–2.33)	<0.001
Model B	28/110	350/3,369	1.81 (1.23–2.67)	0.003	76/376	354/3,122	1.40 (1.08–1.80)	0.010
Model C	28/110	350/3,369	1.62 (1.08–2.43)	0.020	76/376	354/3,122	1.28 (0.99–1.66)	0.062
Model C2	26/97	303/3,114	1.93 (1.26–2.95)	0.002	59/324	317/2,868	1.23 (0.92–1.64)	0.165
Model D	26/106	320/3,228	1.29 (0.84–1.98)	0.243	69/348	327/2,983	1.21 (0.92–1.59)	0.180
Model E	13/77	261/2,616	1.21 (0.77–1.90)	0.400	55/275	262/2,411	1.27 (0.95–1.68)	0.103
Model F	12/60	207/2,015	0.93 (0.53–1.62)	0.785	43/206	208/1,886	1.30 (0.94–1.79)	0.108
Model G	13/62	224/2,099	1.33 (0.80–2.22)	0.279	48/218	224/1,977	1.26 (0.92–1.71)	0.147
366–1,095 days†								
Model A	21/91	373/3,295	2.22 (1.43–3.45)	<0.001	61/333	365/2,972	1.56 (1.19–2.05)	0.001
Model B	19/82	368/3,019	1.51 (0.95–2.39)	0.084	60/300	363/2,768	1.10 (0.84–1.45)	0.495
Model C	19/82	368/3,019	1.22 (0.75–2.01)	0.424	60/300	363/2,768	1.15 (0.87–1.53)	0.332
Model C2	16/71	323/2,811	1.39 (0.82–2.36)	0.222	50/265	329/2,551	1.10 (0.81–1.49)	0.563
Model D	18/80	351/2,908	0.97 (0.58–1.63)	0.915	56/279	341/2,656	1.05 (0.78–1.41)	0.731
Model E	16/64	273/2,355	0.97 (0.56–1.67)	0.910	44/220	277/2,149	1.02 (0.75–1.39)	0.904
Model F	14/48	207/1,808	1.06 (0.55–2.02)	0.869	37/163	214/1,678	1.04 (0.73–1.50)	0.821
Model G	15/49	220/1,875	1.41 (0.77–2.59)	0.265	39/170	231/1,753	1.14 (0.80–1.61)	0.476

Table 4. Effects of a history of falls and fractures on mortality after stroke in men and women (continued)

Mortality time period and model	Men				Women			
	Deaths/ patients with falls and fractures	Deaths/ patients without falls and fractures	OR*/HR† (95% CI)	*p*	Deaths/ patients with falls and fractures	Deaths/ patients without falls and fractures	OR*/HR† (95% CI)	*p*
1,096–3,650 days†								
Model A	9/70	366/2,922	1.03 (0.53–1.99)	0.934	31/272	404/2,607	0.74 (0.51–1.06)	0.101
Model B	9/63	366/2,651	0.83 (0.43–1.61)	0.575	31/240	403/2,405	0.61 (0.42–1.88)	0.008
Model C	9/63	366/2,651	0.89 (0.46–1.74)	0.734	31/240	403/2,405	0.68 (0.47–0.98)	0.039
Model C2	8/55	328/2,488	1.06 (0.52–2.15)	0.869	27/215	358/2,222	0.70 (0.47–1.05)	0.083
Model D	9/62	343/2,557	0.81 (0.41–1.60)	0.537	29/223	384/2,315	0.72 (0.49–1.06)	0.100
Model E	9/48	287/2,082	0.67 (0.31–1.46)	0.311	19/176	297/1,872	0.67 (0.43–1.06)	0.085
Model F	8/34	222/1,601	0.68 (0.27–1.74)	0.423	13/126	232/1,464	0.75 (0.46–1.23)	0.253
Model G	8/34	239/1,655	0.80 (0.32–1.98)	0.623	13/131	246/1,522	0.73 (0.46–1.16)	0.180

*Analysis up to and including 30 days, †Analysis from 31 days onward.
CI: confidence interval, HR: hazard ratio, OR: odds ratio.

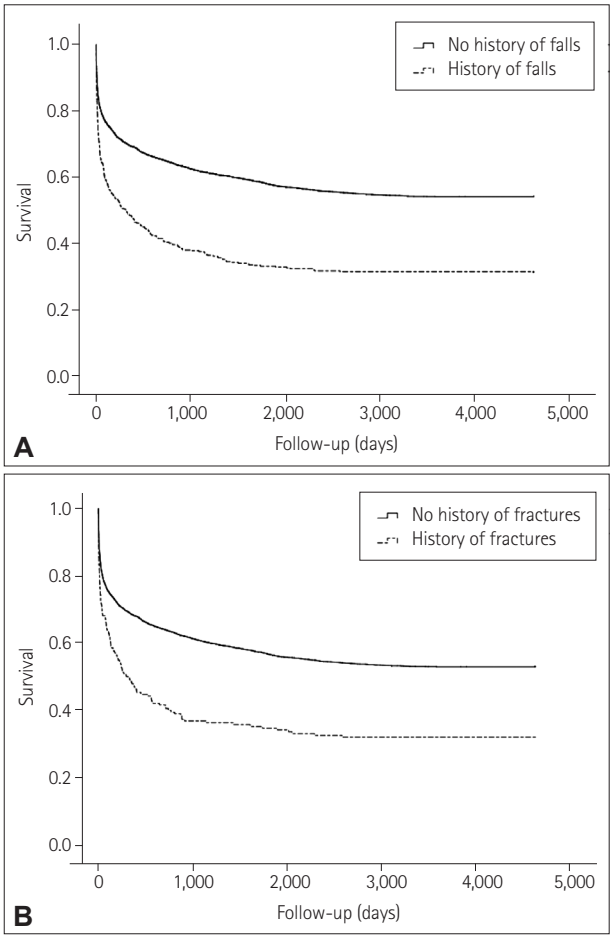

Fig. 1. A: Kaplan-Meier curve showing the probability of survival across the whole follow-up period in men with a history of falls compared to those with no history of falls. B: Kaplan-Meier curve showing the probability of survival across the whole follow-up period in men with a history of fractures compared to those with no history of fractures.

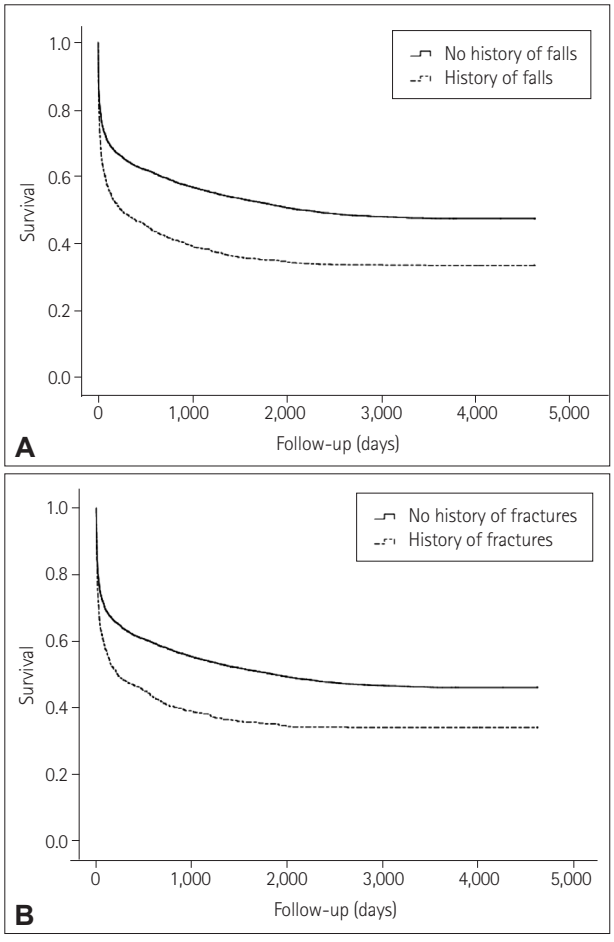

Fig. 2. A: Kaplan-Meier curve showing the probability of survival across the whole follow-up period in women with a history of falls compared to those with no history of falls. B: Kaplan-Meier curve showing the probability of survival across the whole follow-up period in women with a history of fractures compared to those with no history of fractures.

tion of frailty, sensitivity analysis that involved removing prestroke frailty, as indicated by the prestroke mRS score, did not significantly alter the results.

These findings raise the possibility of implementing targeted approaches to improve the poststroke outcomes for the at-risk population, for example by providing fall-prevention measures such as targeted balance training and ensuring a safe environment or reviewing current medications.[18,19] This may be particularly beneficial for women with a history of falls who also have risk factors for stroke.

Previous studies have shown not only that the bone mineral density (an indicator of osteoporosis) decreases after stroke but also that a previous low bone mineral density increases the risk of having a stroke,[6,20,21] poststroke mortality,[22] and fracture risk,[23] with previous fractures having also been shown to be a risk factor for future fractures.[7] A study reported on in 1991 found that the risk of death from stroke was increased in women with osteopenia and aged at least 65 years, but showed that most of this risk was unrelated to the occurrence of fractures.[24] A prospective study of osteoporotic fractures reported on in 1993 showed an association with low bone mineral density and stroke occurrence in women older than 65 years.[25] It was also recently demonstrated that hip fractures increase the risk of stroke.[26]

In contrast, the present study found no significant association between the predictor of falls and fractures combined and poststroke mortality. This finding is similar to Browner et al.[24] reporting in 1991 that fractures were unrelated to death from stroke. Similar results were also reported by Mussolino et al.[27] in 2003, who found no association between bone mineral density and mortality after stroke in their population of 3,402 white and black men and women aged 45−74 years who were followed up from 1971 to 1992.

There are a few plausible reasons for explaining our apparently unexpected result that a history of falls associated with a history of fractures did not increase the mortality risk. Firstly, the group sample was relatively small, which could have introduced a type 2 statistical error. Secondly, we might not have adequately controlled for confounders, resulting in the presence of residual confounding or other known and unknown confounders.

A previous study followed up 3,257 Chinese patients older than 55 years for 8 years, and found frailty to be associated with a significantly increased risk of recurrent falls but not fractures, which is also known to be associated with higher mortality.[28] Moreover, in our study we also did not distinguish between histories of single and multiple falls, and so those without fractures may have also experienced multiple falls, which is known to be associated with worse mortality outcomes.[29]

While this study may have unveiled a potential area of risk management to improve clinical outcomes poststroke, future investigations need to determine the mechanisms underlying the association between previous falls and mortality, even though we have shown that frailty may act as a mediator in this association. This should lead to targeted preventative therapies that are effective at reducing mortality.

Tables 1 and 2 indicate that the prestroke mRS score was higher when there was a history of falls, indicating greater disability prior to the stroke. This may partly explain the mortality increase in this group shown using Model G and the loss of significance in Model D. It could be argued that it is therefore unsurprising that the mortality rate is higher among those with a history of falls than in those without such a history. However, we still found a significant association even when the comorbidities and previous disability (an indicator of frailty) were accounted for in women in our fully adjusted models. Examining the links between comorbidity burden, history of falls, and acute mortality outcomes may yield a better understanding of this finding, and also whether specific comorbidities affect the poststroke prognosis relating to a history of falls. Further research directions could include exploring if having a history of falls increases the risk of future comorbidities after stroke.

While the analyzed data provided a unique opportunity to examine the links between a history of falls or a history of falls and fractures and stroke mortality over a long-term follow-up, this study was subject to some limitations. We did not have information on the bone mineral density status of patients, and the history of falls and fractures were based on ICD-10 codes, which may have underestimated their true prevalence in this patient population. Nevertheless, these limitations are likely to only have attenuated the relationships. We attempted to minimize the possible effect of the lack of bone mineral density data by combining falls and fractures into one predicting variable, meaning that the fractures were more likely to be low-trauma fragility fractures related to osteoporosis. There was a considerable amount of missing data in the final models, but the sample size remained adequate and our careful approach to constructing the models reduced the potential effects of any missing data. It is also important to note that we were able to control for important acute illness markers−which are known to influence mortality outcome in stroke−in the final models.

In summary, a previous history of falls was associated with increased acute mortality in women but not in men after stroke. In both sexes, the history of previous falls and fractures combined was not associated with any effect on mortality. The results obtained in this study imply that a history of falls may be an important factor to consider in the prognosis of stroke, particularly in women. Most instances of

stroke mortality are acute, with inpatient mortality being the largest burden and of great concern to patients, relatives, and clinicians. This study has therefore made an important contribution by identifying a new marker for an increased risk of mortality after stroke. Further research should attempt to identify the factors underlying this increase in mortality, with the aim of developing targeted interventions that can improve stroke mortality outcomes.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.3988/jcn.2017.13.4.411.

Conflicts of Interest

The authors have no financial conflicts of interest.

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REFERENCES

1. Hopewell JC, Clarke R. Emerging risk factors for stroke: what have we learned from mendelian randomization studies? *Stroke* 2016;47:1673-1678.
2. Schmid AA, Yaggi HK, Burrus N, McClain V, Austin C, Ferguson J, et al. Circumstances and consequences of falls among people with chronic stroke. *J Rehabil Res Dev* 2013;50:1277-1286.
3. Chang VC, Do MT. Risk factors for falls among seniors: implications of gender. *Am J Epidemiol* 2015;181:521-531.
4. Myint PK, Poole KE, Warburton EA. Hip fractures after stroke and their prevention. *QJM* 2007;100:539-545.
5. Moayyeri A, Alrawi YA, Myint PK. The complex mutual connection between stroke and bone health. *Arch Biochem Biophys* 2010;503:153-159.
6. Myint PK, Clark AB, Kwok CS, Loke YK, Yeong JK, Luben RN, et al. Bone mineral density and incidence of stroke: European prospective investigation into cancer-norfolk population-based study, systematic review, and meta-analysis. *Stroke* 2014;45:373-382.
7. Woolf AD, Akesson K. Preventing fractures in elderly people. *BMJ* 2003;327:89-95.
8. Kwok CS, Skinner J, Metcalf AK, Potter JF, Myint PK. Prior antiplatelet or anticoagulant therapy and mortality in stroke. *Heart* 2012;98:712-717.
9. White JR, Bettencourt-Silva JH, Potter JF, Loke YK, Myint PK. Changes in antiplatelet use prior to incident ischaemic stroke over 7 years in a UK centre and the association with stroke subtype. *Age Ageing* 2013;42:594-598.
10. Bettencourt-Silva J, De La Iglesia B, Donell S, Rayward-Smith V. On creating a patient-centric database from multiple hospital information systems. *Methods Inf Med* 2012;51:210-220.
11. Kwok CS, Potter JF, Dalton G, George A, Metcalf AK, Ngeh J, et al. The SOAR stroke score predicts inpatient and 7-day mortality in acute stroke. *Stroke* 2013;44:2010-2012.
12. Myint PK, Clark AB, Kwok CS, Davis J, Durairaj R, Dixit AK, et al. The SOAR (Stroke subtype, Oxford Community Stroke Project classification, Age, prestroke modified Rankin) score strongly predicts early outcomes in acute stroke. *Int J Stroke* 2014;9:278-283.
13. Di Napoli M, Schwaninger M, Cappelli R, Ceccarelli E, Di Gianfilippo G, Donati C, et al. Evaluation of C-reactive protein measurement for assessing the risk and prognosis in ischemic stroke: a statement for health care professionals from the CRP Pooling Project members. *Stroke* 2005;36:1316-1329.
14. Grau AJ, Boddy AW, Dukovic DA, Buggle F, Lichy C, Brandt T, et al. Leukocyte count as an independent predictor of recurrent ischemic events. *Stroke* 2004;35:1147-1152.
15. Carter AM, Catto AJ, Mansfield MW, Bamford JM, Grant PJ. Predictive variables for mortality after acute ischemic stroke. *Stroke* 2007;38:1873-1880.
16. Mukarram F, Gottesman RF, Marsh E. Glucose on admission associated with post-stroke outcome. *Stroke* 2016;47:ATP353.
17. Adekunle-Olarinde IR, McCall SJ, Barlas RS, Wood AD, Clark AB, Bettencourt-Silva JH, et al. Addition of sodium criterion to SOAR stroke score. *Acta Neurol Scand* 2017;135:553-559.
18. Luk JK, Chan TY, Chan DK. Falls prevention in the elderly: translating evidence into practice. *Hong Kong Med J* 2015;21:165-171.
19. Gill TM, Pahor M, Guralnik JM, McDermott MM, King AC, Buford TW, et al. Effect of structured physical activity on prevention of serious fall injuries in adults aged 70-89: randomized clinical trial (LIFE Study). *BMJ* 2016;352:i245.
20. Jørgensen L, Engstad T, Jacobsen BK. Bone mineral density in acute stroke patients: low bone mineral density may predict first stroke in women. *Stroke* 2001;32:47-51.
21. Chen YC, Wu JC, Liu L, Huang WC, Cheng H, Chen TJ, et al. Hospitalized osteoporotic vertebral fracture increases the risk of stroke: a population-based cohort study. *J Bone Miner Res* 2013;28:516-523.
22. Nordström A, Eriksson M, Stegmayr B, Gustafson Y, Nordström P. Low bone mineral density is an independent risk factor for stroke and death. *Cerebrovasc Dis* 2010;29:130-136.
23. Dennis MS, Lo KM, McDowall M, West T. Fractures after stroke: frequency, types, and associations. *Stroke* 2002;33:728-734.
24. Browner WS, Seeley DG, Vogt TM, Cummings SR. Non-trauma mortality in elderly women with low bone mineral density. Study of Osteoporotic Fractures Research Group. *Lancet* 1991;338:355-358.
25. Browner WS, Pressman AR, Nevitt MC, Cauley JA, Cummings SR. Association between low bone density and stroke in elderly women. The study of osteoporotic fractures. *Stroke* 1993;24:940-946.
26. Tsai CH, Lin CL, Hsu HC, Chung WS. Increased risk of stroke among hip fracture patients: a nationwide cohort study. *Osteoporos Int* 2015;26:645-652.
27. Mussolino ME, Madans JH, Gillum RF. Bone mineral density and stroke. *Stroke* 2003;34:e20-e22.
28. Fang X, Shi J, Song X, Mitnitski A, Tang Z, Wang C, et al. Frailty in relation to the risk of falls, fractures, and mortality in older Chinese adults: results from the Beijing Longitudinal Study of Aging. *J Nutr Health Aging* 2012;16:903-907.
29. Sylliaas H, Idland G, Sandvik L, Forsen L, Bergland A. Does mortality of the aged increase with the number of falls? Results from a nine-year follow-up study. *Eur J Epidemiol* 2009;24:351-355.