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Post-stroke Fractures in a Bi-ethnic Community

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Abstract

Background—Mexican Americans have increased stroke risk and lower fracture risk compared with non-Hispanic whites, but little is known about post-stroke fracture risk in Mexican Americans. The objective was to describe post-stroke fracture risk in a bi-ethnic population and to compare risk by ethnicity.

Methods—In the Brain Attack Surveillance in Corpus Christi Project, strokes were identified through hospital surveillance (2000–2004) and validated by neurologists (n=2,389). Inpatient claims for fractures were ascertained (2000–2004) and cross-referenced with strokes. Survival free from fracture (any and hip) post-stroke was estimated and compared by ethnicity. Cox regression was used to test the association of ethnicity and fracture risk adjusted for confounders. Interaction terms for ethnicity and age were considered.

Results—Mean age was 71 years (sd=13); 54% were Mexican American; 52% were women. Mean follow-up was 4 years. There were 105 fractures (hip 33%). Survival free of any fracture and of hip fracture did not differ by ethnicity in unadjusted analyses. Increasing age, female gender, intracerebral hemorrhage and greater stroke severity were associated with risk of any fracture, but ethnicity was not. Ethnicity was associated with risk of hip fracture but this association was modified by age (p=0.02), where Mexican Americans were protected from hip fractures at younger but not older ages.

Conclusion—Stroke patients were at high fracture risk, with a 10% risk at 5 years. Mexican Americans were protected from hip fractures at younger but not older ages. Both elderly Mexican Americans and non-Hispanic whites should be targeted for fracture prevention post-stroke.

Introduction

Fractures are a critical component of poor long-term stroke outcome. Roughly 6–15% of stroke patients experience a fracture within five years of their stroke.(1, 2) Fractures, in turn, may increase the risk of mortality and poor functional outcome, particularly among those with prior stroke.(3–5) US studies of the risk of post-stroke fractures have focused on predominantly non-Hispanic white (NHW) populations.(6, 7) Mexican Americans (MAs) have an increased risk of stroke compared with NHWs, particularly at younger ages.(8) In the general population, MA women have a lower risk of fractures compared with NHW women, particularly for hip fractures.(9, 10) However, little is known regarding the risk of

post-stroke fractures in MAs. The primary objective of this study was to describe the risk of fracture post-stroke in a bi-ethnic population and to compare the risk by ethnicity. A secondary objective was to compare fracture risk by stroke type (ischemic versus hemorrhagic).

Materials and Methods

Data for this project are from the Brain Attack Surveillance in Corpus Christi (BASIC) Project. Detailed methods for this project have been published.(8, 11) Briefly, active and passive surveillance were used to capture strokes among residents of Nueces County, Texas aged 45 years for the time period January 1, 2000 through December 31, 2004. Cases were screened by trained abstractors from the seven hospitals in the county by searching emergency room and admission logs for validated screening terms. Abstractors also routinely canvassed intensive care units and hospital floors for in-house strokes or cases not ascertained through screening logs. Passive review of hospital ICD-9 discharge codes for stroke (430–438; excluding 433.x0, 434.x0 (x=1–9); 437.0, 437.2, 437.3, 437.4, 437.5, 437.7, 437.8 and 438) and of neurology offices located in the county was also conducted. Eligible cases were validated by neurologists using source documentation, blinded to subjects' age and ethnicity, based on published criteria.(12) Standard definitions for ischemic stroke, intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH) were used.(8) Validation of cases occurred prior to cross-referencing with fracture claims data. If an individual experienced multiple strokes during the study time period, the first event was considered the index event for the analysis. A history of stroke prior to the study time period was not exclusionary. This study was approved by the Institutional Review Board at the University of Michigan and by the local hospital systems.

Fractures

Claims for fractures as a principal or secondary diagnosis in an inpatient setting were ascertained from all hospitals in the county for the time period January 1, 2000 through December 31, 2004. ICD-9-CM codes for fractures included: 805.xx, 807.xx excluding 807.5 and 807.6, 813.xx, 812.xx, 814.xx, 808.0–808.9, 820.xx, 821.xx, 823.xx, 824.xx, and 733.1x. Fracture claims were cross-referenced with stroke cases using five identifiers: first name, last name, medical record number, date of birth, and permanent address zip code. At least three of the five identifiers must have been identical to be considered a match with a stroke case. For a small fraction of cases, manual review of the data was necessary due to errors in name spelling, transposed numbers, and patients with non-matching medical record due to presentation to a different hospital. Only fractures occurring after the index stroke were considered.

Demographics and Other Covariates

Demographic characteristics were abstracted from the medical record. We have previously demonstrated high agreement between race-ethnicity documented in the medical record and self-reported race-ethnicity.(11) Cases with a race-ethnicity other than NHW or MA were excluded due to small numbers. A history of previous stroke/TIA and diabetes and stroke severity were abstracted from the medical record. Stroke severity was measured by the National Institutes of Health Stroke Scale (NIHSS) using previously validated methods.(13)

Statistical Analysis

Demographics and other characteristics were summarized as frequencies and percents for categorical variables and means and standard deviations for continuous variables. The distribution of fracture location was summarized overall and by ethnicity. For each

individual, time in days from the stroke (based on date of presentation to the hospital or neurology office) to fracture (based on date of admission for fracture hospitalization), end of follow-up (12/31/2004) or death was calculated. Survival free from any fracture and from hip fracture post-stroke was estimated using Kaplan Meier survival analysis. Survival estimates were calculated overall, by ethnicity (MA versus NHW), and by stroke type (ICH versus ischemic stroke). Log rank tests were used to compare survival distributions by ethnicity and stroke type. Cases of SAH were not included in the comparison by stroke type due to small numbers. Cumulative risk of any fracture and of hip fracture was summarized at 30 days, 1 year and 5 years post-stroke. Cumulative risk of any fracture and of hip fracture as of the end of follow-up was also summarized by ethnicity and age group (45–59, 60–74, 75). Cox proportional hazards models were used to investigate the association between ethnicity (MA versus NHW) and risk of any fracture and of hip fracture. Models were run unadjusted and adjusted for age (modeled continuously), gender (female versus male), history of diabetes (yes/no), history of stroke/TIA, stroke type (ICH versus ischemic stroke) and stroke severity (modeled categorically as two indicator variables representing scores of 3–6 and 7 with 2 as the referent). Categories for NIHSS were based on tertiles of the distribution. In addition, interaction terms for age (modeled continuously) and ethnicity were added to the multivariable models to determine if the association of ethnicity with risk of any fracture or of hip fracture was modified by age. Cases of SAH were excluded from the models due to small numbers. For all survival analyses, cases were censored at death or end of the follow-up (12/31/2004). Statistical analyses were conducted in SAS version 9.13.

Results

Table 1 presents demographics and baseline characteristics for the study population (n = 2,389). Mean age of the cases was 71 years (sd = 13). Fifty-four percent of the cases were MA, and 52% were women. Eighty-three percent of the cases were ischemic stroke, 14% ICH and 3% SAH. Mean NIHSS score was 7.1 (sd = 9.0).

Mean follow-up post-stroke was 1,506 days (sd = 8). There were 105 fractures during the follow-up period (Table 2). Mean time to any fracture was 405 days (sd = 359). Hip fractures were the most common fracture location comprising 33% of all fractures. Cumulative risk of any fracture post-stroke was 0.4% at 30 days, 3.3% at 1 year and 9.7% at 5 years (Table 3). Cumulative risk of hip fracture was 0.2% at 30 days, 1.2% at 1 year and 2.6% at 5 years. Figure 1 displays the survival free of any fracture and of hip fracture by ethnicity and by stroke type. Survival free of any fracture (p = 0.93) and of hip fracture (p = 0.20) did not differ by ethnicity. Risk of any fracture was significantly greater for ICH compared with ischemic strokes (p = 0.04) but risk of hip fracture did not differ by stroke type (p = 0.70).

Ethnicity was not associated with risk of any fracture in unadjusted (hazard ratio (HR) = 0.98; 95% confidence interval (CI): 0.67–1.45) or adjusted analyses (HR = 1.06; 95% CI: 0.70–1.60), and the ethnicity association was not modified by age (p = 0.50) (Table 4). In the multivariable model, age, gender, stroke type and stroke severity were significantly associated with risk of any fracture, while diabetes and history of stroke/TIA were not. Older cases were more likely to have any fracture post-stroke (HR = 1.03; 95% CI: 1.01–1.05). Women were two and a half times more likely to have any fracture post-stroke compared with men (HR = 2.45; 95% CI: 1.59–3.78), and cases of ICH were roughly two times more likely to have any fracture compared with ischemic stroke cases (HR = 1.93; 95% CI: 1.11–3.34). Cases with higher NIHSS had greater risk of any fracture (NIHSS 3–6: HR = 2.21; 95% CI: 1.40–3.49; NIHSS 7: HR = 1.27; 95% CI: 0.72–2.22) compared with

those with lower scores (0–2), although the comparison between those with the highest (7) and lowest NIHSS scores (0–2) did not reach significance.

Ethnicity was not associated with risk of hip fracture in unadjusted analysis (HR = 0.65; 95% CI: 0.67–1.45). However, in the multivariable model, the ethnicity-hip fracture association was modified by age ($p = 0.03$) such that MAs were protected from hip fractures at younger ages but not at older ages (Table 4). At 65 years, risk of hip fracture was roughly 70% less in MAs compared with NHWs (HR = 0.33; 95% CI: 0.10–1.09). At 85 years, MAs were no longer protected from hip fracture (HR = 1.59; 95% CI: 0.72–3.55). The protection from hip fracture at younger ages in MAs was due to a very low risk in this population before age 75. Cumulative risk of hip fracture at the end of follow-up was 0.8% in MAs ages 60–74 compared with 2.9% in NHWs in the same age range. There were no hip fractures in either ethnic group before age 60. In the multivariable model, older age was associated with increased risk of hip fracture but this association varied by ethnicity ($p = 0.03$). In MAs, there was an 11% increase in risk of hip fracture for each one-year increase in age (HR = 1.11; 95% CI: 1.05–1.18). In NHWs, the age association was less strong and of borderline significance (HR = 1.03; 95% CI: 0.99–1.07). Female gender (HR = 1.85; 95% CI: 0.89–3.81) was also associated with increased risk of hip fracture but this association did not reach significance (Table 4).

Discussion

In this bi-ethnic population, stroke patients were at high risk for fractures, with a roughly 10% risk at 5 years. Our finding of a 3% fracture risk at 1 year post-stroke is consistent with estimates from stroke populations in Sweden and New Zealand, as well as estimates from administrative data in the US.(2, 6, 7, 14) Also in keeping with other studies was the predominance of hip fractures, consistent with a fall mechanism that is common after stroke. (1, 2) However, the current study identified more rib and lower leg fractures than previous work. Interestingly, fractures other than hip were more prevalent among MAs than NHWs (73% versus 58%) suggesting that causes of post-stroke fractures should be further investigated in the MA population.

Ethnicity was associated with risk of hip but not any fracture. The association with hip fracture varied with age such that at younger ages, MAs were protected from hip fracture; although risk of hip fracture was low across both ethnic groups before age 75. This protection is not surprising as MAs, particularly women, have been shown to have somewhat greater bone mineral density than NHWs in the general population,(15, 16) and osteoporotic fractures, especially hip fractures, have been reported as occurring less frequently in MA women than NHW women.(9, 10) The influence of age on risk of hip fracture was greater in MAs such that at older ages the ethnic difference in risk of hip fractures was no longer apparent. Reasons for this greater age effect in MAs, such as ethnic differences in bone loss with age overall or specifically post-stroke, should be further investigated. Other explanations, such as age-related ethnic differences in stroke rehabilitation or osteoporosis prophylaxis, are also possible. A recent study found that Hispanic stroke patients admitted to inpatient rehabilitation facilities had lower admission and discharge functional status ratings compared with NHW patients, and ethnic differences in functional status were most pronounced at oldest ages.(17) However, there are little data available on ethnic differences in use of and responsiveness to post-stroke rehabilitation services. Studies of the general US population have reported a low prevalence (4%) of antiosteoporosis medication use in older Mexican Americans, as well as a lower prevalence of antiosteoporosis medication use in middle-aged Hispanic women compared with white women, but information in stroke populations is lacking.(18, 19)

Irrespective of the reasons for the observed age-ethnicity effect, the current findings suggest that both elderly MAs and NHWs should be targeted for bone fracture prevention post-stroke. To date, randomized clinical trials of bisphosphonates given in the acute post-stroke period (three days to 90 days) have been conducted in Japan and England, with promising results regarding bone loss and hip fractures; however, these trials were limited by relatively small numbers.(20–22) US clinical trials of bone sparing therapies early after stroke are needed, particularly of intravenous agents that may be preferential to oral agents, given the probability of dysphagia and inability to stay seated for the recommended time frame in post-stroke patients.(23)

Greater risk of any fracture was seen in patients with ICH compared with ischemic stroke. Prior studies have not reported increased fracture risk in hemorrhagic stroke patients, although these studies had somewhat fewer ICH cases and thus may have had limited power to detect an association.(1, 7) ICH is associated with greater stroke severity than ischemic stroke.(24) The multivariable analysis adjusted for stroke severity using an NIHSS collected from the medical record, though it is possible that this adjustment did not fully account for differences in severity or immobility which could explain the observed association between stroke type and fracture risk. Further study in other populations with a more detailed assessment of functional status and potential confounders is needed to replicate and explain this association. If the association between ICH and fracture risk is found in additional populations, more intensive efforts at post-ICH fracture prevention may be warranted. In contrast to the results for any fracture, stroke type was not associated with risk of hip fracture, though power to assess this association may have been limited.

In this study, post-stroke fractures occurred more frequently in women. The magnitude of our observed gender association was consistent with a previous study of post-stroke fractures.(1) This finding is not surprising given the higher prevalence of osteoporosis in women than men.(15) Studies have also shown that low bone mineral density in women is associated with an increased risk of stroke.(25–27) Therefore, increased risk of post-stroke fractures in women may be related to decreased bone density prior to stroke but could also be due to more accelerated osteoporosis on the affected side post-stroke in women. Studies have shown that women have increased bone loss following stroke compared to men, especially if further from menopause.(28–30)

Little information exists about the association between stroke severity and risk of fractures. In the current analysis, individuals with intermediate stroke severity defined by an NIHSS of 3–6 had a higher risk of any fracture than the lowest NIHSS group (0–2), but individuals with the highest NIHSS (≥ 7) did not have a higher fracture risk and even trended toward being protected from hip fracture. This parallels the U-shaped relationship that has been suggested between physical impairment and falls in community-dwelling stroke patients.(31) Authors have proposed that those who are less mobile will have less opportunity to fall, but results are conflicting.(14, 31–33) An association between ambulatory status and fractures has not been established.(1, 2) More research is needed to confirm our findings, especially given that the NIHSS categories were selected post-hoc.

Some limitations of this study warrant discussion. Fractures were identified from claims data only and therefore it is possible that we underestimated fracture risk. If care-seeking patterns for fractures differ by ethnicity, our measures of the association of ethnicity and post-stroke fracture may be biased. In addition, exclusion of fractures that were not admitted to the hospital may have altered the distribution of fracture locations. Information on the side of the fracture and the side of the neurological deficit was not available. Some important covariates, such as cognitive status, pre-stroke function and history of fracture,(1) were not included in the multivariable models. We were also unable to investigate the possible

contribution of body mass index to the ethnicity-fracture association as these data were unavailable. We did not have data on cause of fractures, which may have informed the mechanisms underlying the observed ethnic association. We also did not have information on whether the patients used any protection for hip fractures. Finally, this study was conducted in one bi-ethnic community and therefore results may not be generalizable to other populations with different sociodemographic characteristics.

Conclusion

Post-stroke fractures result in significant morbidity and mortality. In this bi-ethnic population-based study, stroke patients were at high risk for fractures, with a roughly 10% risk at 5 years. MAs were protected from hip fractures at younger but not older ages, and the impact of age on hip fracture risk was greater in MAs than NHWs. Reasons for these ethnic differences require replication and further study. The current findings suggest that, despite the lower risk of bone fracture in MAs in general, both elderly MAs and NHWs should be targeted for bone fracture prevention post-stroke, such as fall prevention strategies, weight-bearing exercise, smoking cessation, adequate intake of calcium and vitamin D, and consideration of pharmacological therapies.

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Figure 1.

Kaplan Meier survival curves depicting risk of any fracture and of hip fracture post-stroke ($n = 2,389$) by ethnicity (a–b) and stroke type (c–d), Brain Attack Surveillance in Corpus Christi (BASIC) Project (2000–2004). MA = Mexican American, NHW = non-Hispanic white, ICH = intracerebral hemorrhage.

Table 1

Baseline characteristics of stroke cases (n = 2,389), Brain Attack Surveillance in Corpus Christi (BASIC) Project, Nueces County, Texas (2000–2004).

	Overall (n=2,389)	Any fracture (n=105)*	No fracture (n=2,285)
Ethnicity			
MA	54.3%	56.7%	54.2%
NHW	45.7%	43.3%	45.8%
Age (mean (SD))	71.2 (12.5)	74.0 (12.4)	71.1 (12.5)
Gender			
Male	47.6%	27.9%	48.5%
Female	52.4%	72.1%	51.5%
Stroke type			
Ischemic	83.0%	83.7%	83.0%
ICH	13.8%	15.3%	13.7%
SAH	3.2%	1.0%	3.3%
NIHSS (mean (SD))	7.1 (9.0)	5.2 (4.5)	7.2 (9.1)
History of stroke	30.3%	33.7%	30.1%

* One MA patient had two lower leg fractures on the same day.

MA = Mexican American, NHW = non-Hispanic white, SD = standard deviation, ICH = intracerebral hemorrhage, SAH = subarachnoid hemorrhage, NIHSS = NIH Stroke Scale

Table 2

Distribution of fracture location among stroke cases with a fracture (n = 105), Brain Attack Surveillance in Corpus Christi (BASIC) Project, Nueces County, Texas (2000–2004).

	Overall		NHW		MA	
Fracture location	n	%	n	%	n	%
Hip	35	33.3	19	42.2	16	26.7
Upper arm	14	13.3	7	15.6	7	11.7
Rib	12	11.4	6	13.3	6	10.0
Lower leg *	11	10.5	4	8.9	7	11.7
Lower arm	10	9.5	2	4.4	8	13.3
Vertebrae	9	8.6	2	4.4	7	11.7
Thigh	8	7.6	3	6.7	5	8.3
Pelvis	5	4.8	2	4.4	3	5.0
Wrist	1	1.0	0	0.0	1	1.7
Total	105	100	45	100	60	100

* One MA patient had two lower leg fractures on the same day.

MA = Mexican American, NHW = non-Hispanic white

Table 3

Cumulative risk of any fracture and of hip fracture post-stroke (n = 2,389), Brain Attack Surveillance in Corpus Christi (BASIC) Project, Nueces County, Texas (2000–2004).

	30 day	1 year	5 year
Any fracture			
Overall	0.4%	3.3%	9.7%
Ischemic	0.4%	3.0%	9.0%
ICH	0.5%	7.9%	19.3%
SAH	0.0%	0.0%	4.7%
ICH/SAH combined	0.4%	6.2%	15.2%
Hip fracture			
Overall	0.2%	1.2%	2.6%
Ischemic	0.2%	1.1%	2.6%
ICH	0.0%	2.6%	2.6%
SAH *	-	-	-
ICH/SAH combined	0.0%	2.0%	2.0%

* There were no hip fractures among SAH cases.

MA = Mexican American, NHW = non-Hispanic white, ICH = intracerebral hemorrhage, SAH = subarachnoid hemorrhage, NIHSS = NIH Stroke Scale

Table 4

Multivariable models of predictors of any fracture and of hip fracture post-stroke (n = 2,389), Brain Attack Surveillance in Corpus Christi (BASIC) Project (2000–2004).

	Hazard Ratio	95% CI
Any fracture		
MA vs NHW	1.06	0.70–1.60
Age (years)	1.03	1.01–1.05
Female vs Male	2.45	1.59–3.78
Diabetes	1.14	0.74–1.74
ICH vs IS	1.93	1.11–3.34
Stroke/TIA history	1.08	0.72–1.63
Mid NIHSS (3–6) *	2.21	1.40–3.49
High NIHSS (7) *	1.27	0.72–2.22
Hip fracture		
MA vs NHW †		
Age 65	0.33	0.10–1.09
Age 85	1.59	0.72–3.55
Age (years) †		
MA	1.11	1.05–1.18
NHW	1.03	0.99–1.07
Female vs Male	1.85	0.89–3.75
Diabetes	0.60	0.25–1.42
ICH vs IS	1.46	0.51–4.21
Stroke/TIA history	1.55	0.79–3.05
Mid NIHSS (3–6) *	1.74	0.85–3.56
High NIHSS (7) *	0.47	0.15–1.46

* NIHSS: referent group (0–2).

† A significant interaction between ethnicity and age for hip fracture was found (p = 0.03). Therefore, hazard ratios are shown stratified for these terms.

MA = Mexican American, NHW = non-Hispanic white, ICH = intracerebral hemorrhage, IS = ischemic stroke, NIHSS = NIH Stroke Scale