Lack of Association between Family History of Stroke and 1-year Outcomes after Acute Ischemic Stroke in Chinese

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Familial aggregation of stroke suggested that genetic factors may play an important role in the occurrence of ischemic stroke. A meta-analysis of 53 independent studies of family history of stroke (FHstroke) showed that FHstroke was a potential risk factor for a stroke's onset, with an odds ratio (OR) values of 1.8 and 1.3 estimated from case-control and cohort studies, respectively [1]. Similar results were observed from the Framingham Study as well, and the risk of stroke is nearly three times as high for people if their parents had a stroke before 65 years [2].

However, data on the relationship between FHstroke and outcomes of ischemic stroke are limited and inconsistent. Research by BASIC showed that FHstroke was positively correlated with poor functional outcome at discharge (defined as mRS = 2–6) and with mortality at 90 days of onset but not statistically significant [3], while Meschia et al. [4] identified that FHstroke was not associated with a 90-day outcome of stroke. Data from Korea also suggested that FHstroke did not affect a short-term outcome after stroke [5]. More surprisingly, Hertzberg et al. found that the percentage of patients back to family after discharge was higher in those with FHstroke [6], seemingly suggesting that outcome of patients with FHstroke was not poor. Additionally, Katarina et al. noted that FHstroke was associated with a good outcome at 3 months of onset, regardless of stroke subtypes or vascular risk factors [7].

Little is known about the association of FHstroke with outcomes in Chinese populations. Given the genetic diversity among different ethnic populations, the present study was undertaken to assess whether FHstroke is associated with 1-year outcomes after acute ischemic stroke. FHstroke was defined as a history of stroke in at least one patient's first-degree relatives (including their parents, siblings, children).

A retrospective analysis on 1-year outcomes among patients with acute ischemic stroke from the China National Stroke Registry (CNSR) cohort was performed. Detailed study design and methods about CNSR were published earlier [8]. 7,702 validated first-ever acute ischemic stroke events were consecutively collected. Approximately 92.9 percentage patients ($n = 7,153$) were interviewed and have a 1-year follow-up outcome. Of these patients, mean ages were 64 years, and 38.7% were female. There were 874 cases (12.2%) with a positive FHstroke. These patients were 5 years younger than those without FHstroke (60 ± 12 versus [vs.] 65 ± 13 years, $P < 0.01$), and most patients were middle aged (58.1% vs. 40.8%). There were more male (66.2% vs. 60.7%, $P < 0.01$), more overweight, and obese patients (45.9% vs. 37.9%, $P < 0.01$), a more moderate to heavy drinkers and smokers (15.4% vs. 10.1%, $P < 0.01$; and 50.6% vs. 37.8%, $P < 0.01$, respectively) in the patients with FHstroke. Vascular risk factors such as hypertension, diabetes, and hyperlipidemia were significantly more frequent in patients with FHstroke (64.1% vs. 56.2%, $P < 0.01$; and 21.9% vs. 18.0%, $P < 0.01$; and 18.6% vs. 7.4%, $P < 0.01$, respectively), while the histories of atrial fibrillation and coronary heart disease were not significantly different between two groups. The severity of neurological deficit was also similar between two groups (Table 1).

One-year outcomes after stroke onset were analyzed by multi-variable logistic regression models, and the result is displayed in Table 2. Among 874 FHstroke cases, 11.4% (100/874) with recurrent new stroke vs. 14.9% (937/6279) stroke recurrence among those without FHstroke, the percent of poor outcomes (defined by mRS = 3–6) were 24.8% (217/874, including 68 dead and 149 depended) in patients with FHstroke, which was 29.4% (1844/6279, including 784 dead and 1060 depended) in patients

Table 1 Demographics and clinical characteristics of participants with family history of stroke (FHstroke) (n = 7153)

	FHstroke		P-value
	Yes (n = 874)	No (n = 6279)	
Age, year	60 ± 12	65 ± 13	<0.01
≤45, year	99 (11.3)	473 (7.5)	
46–64, year	508 (58.1)	2561 (40.8)	
≥ 65, year	267 (30.5)	3245 (51.7)	
Female, n (%)	295 (33.8)	2470 (39.3)	<0.01
Ethnicity (Han), n (%)	847 (96.9)	6090 (97.0)	0.90
BMI categories, kg/m ²			
Normal	454 (54.1)	3499 (62.2)	<0.01
Overweight	322 (38.4)	1837 (32.7)	
Obesity	63 (7.5)	290 (5.2)	
Hypertension, n (%)	560 (64.1)	3525 (56.2)	<0.01
Diabetes mellitus, n (%)	191 (21.9)	1129 (18.0)	<0.01
Atrial fibrillation or flutter, n (%)	50 (5.7)	419 (6.7)	0.29
Coronary heart disease, n (%)	111 (12.7)	769 (12.2)	0.70
Hyperlipidemia, n (%)	161 (18.6)	462 (7.4)	<0.01
Smoking, n (%)	442 (50.6)	2375 (37.8)	<0.01
Moderate or heavy alcohol consumption, n (%)	135 (15.4)	635 (10.1)	<0.01
NIHSS score at admission, n (%)			
≤3	319 (38.3)	2447 (40.6)	0.36
4–14	423 (50.8)	2909 (48.2)	
≥15	90 (10.8)	676 (11.2)	

SD, standard deviation; BMI (body mass index): normal weight = 18.5–24.9, overweight = 25–29.9, obesity = BMI of 30 or greater; NIHSS, National Institutes of Health Stroke Scale.

without FHstroke. FHstroke did not show any correlation on 1-year stroke outcomes (OR 1.07, 95% CI: 0.85–1.34 for stroke recurrence and OR 0.87, 95% CI: 0.65–1.15 for death or dependency, respectively) after controlling potential confounding factors including age, gender, body mass index, hypertension, diabetes mellitus, hyperlipidemia, smoking, and moderate or heavy alcohol consumption (Table 2).

The data of patient's medication compliance were collected at 6 months and 1 year after stroke onset. Patients who were compliant with secondary prevention medications significantly decreased with the extension of follow-up time, especially antico-

Table 2 Adjusted association of family history of stroke (FHstroke) with 1-year outcomes (n = 7153)

Endpoint	FHstroke		OR*	95% CI
	Yes (n = 874)	No (n = 6279)		
Death or dependency, n (%)	217 (24.8)	1844 (29.4)	1.07	(0.85, 1.34)
Stroke recurrence, n (%)	100 (11.4)	937 (14.9)	0.87	(0.65, 1.15)

OR, odds ratio; patients with FHstroke versus those without FHstroke; CI, confidence interval. *Adjusted for age, gender, BMI, hypertension, diabetes mellitus, hyperlipidemia, smoking, and moderate or heavy alcohol consumption.

agulants and lipid-lowering agents (7.5% at 6 months vs. 3.2% at 1 year, $P < 0.01$; 49.6% at 6 months vs. 18.9% at 1 year, $P < 0.01$, respectively). However, the percentage of patient compliance to antiplatelet agents or antihypertensive agents at 1 year after stroke onset was significantly higher in patients with FHstroke than that in those without FHstroke (57.2% vs. 47.4%, $P < 0.01$; 51.4% vs. 42.1%, $P < 0.01$, respectively).

The present data showed that acute ischemic stroke patients with FHstroke had more vascular risk factors, but their 1-year outcomes were not poor. This was probably correlated with good long-term compliance to secondary stroke prevention medications in patients with FHstroke. After adjusted for other confounding factors, there was no association between FHstroke and 1-year outcomes after acute ischemic stroke in Chinese. The results indicated that FHstroke was not independent factor affecting the prognosis of ischemic stroke.

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Conflict of Interest

The authors declare no conflict of interest.

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