Sex Differences in Outcomes and Associated Risk Factors After Acute Ischemic Stroke in Elderly Patients: A Prospective Follow-up Study

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Stroke has a greater effect on women. However, sex differences in outcome and factors associated with outcome among elderly patients are unknown. From January 2009 to December 2011, 810 patients with acute ischemic stroke aged 75 years or older were recruited in China. Clinical profile and risk factors were recorded. Outcomes and associated risk factors at 12 and 36 months after stroke were assessed by sex. Hypertension, diabetes mellitus, dyslipidemias, and obesity prevalence rates were higher in women than in men; opposite trends were found for smoking and alcohol consumption. The mortality rate at 12 months after stroke was significantly greater in men than in women (23.3% versus 16.6%, $P = .015$). Large-artery atherothrombotic and cardioembolic stroke subtypes were risk factors for mortality, recurrence, and dependency in both sexes. In men, atrial fibrillation was a risk factor of mortality at 12 months after stroke (relative ratio [RR], 2.12; 95% confidence interval [CI], 1.38-3.27), but obesity was a protective factor of mortality at 36 months after stroke (RR, .30; 95% CI, .10-.94). However, in women, atrial fibrillation was a risk factor of recurrence at 12 months (RR, 2.32; 95% CI, 1.31-4.12) and dependency at 36 months after stroke (RR, 7.68; 95% CI, 1.60-36.82). We assessed sex differences in stroke outcomes and associated risk factors at 12 and 36 months after stroke in a large hospital-based stroke registry of elderly patients from Northern China. Thus, it is crucial to emphasize risk management to elderly patients to reduce mortality, recurrence, and dependency after stroke. **Key Words:** Ischemic stroke—outcome—long-term—elderly—China.

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A recent report has demonstrated that stroke was the second most common cause of death and the third most common cause of reduced disability-adjusted life years worldwide in 2010.[1] It has been recognized that stroke has a greater impact on women than on men.[2,3] Previous studies have reported significant sex differences for both stroke incidence and outcome. Although age-specific stroke incidence and mortality rates are higher among men, the absolute number of stroke cases is higher among women and poststroke outcomes are also worse in women compared with men; this is likely because women live longer than men, and the risk of stroke increases with age.[4,5] As projected, these differences will become increasingly significant in the coming decades.

China has experienced growth of an increasingly aged population during recent decades; those aged 75 years or older accounted for 3.5% of the population in 2013, and there were 200 million elderly residents aged 65 years and older in 2014.[6,7] Thus, the burden of disease, especially diseases with a higher incidence among the elderly, including stroke and cardiovascular disease, is predicted to increase in the future unless disease prevention among the elderly is specifically addressed. Regarding sex differences in the incidence of stroke in China, it was recently reported that there was a significant increase in the incidence of first-ever stroke in women annually and a declining trend in the male/female incidence ratio in rural China over the past 21 years.[8] Nevertheless, sex differences in outcome after acute ischemic stroke (AIS) among elderly stroke patients is currently unknown.

In this study, we assessed the sex differences in stroke outcome and associated risk factors among elderly patients from a hospital-based stroke registry in China.

Materials and Methods

From January 2009 to December 2011, we recruited consecutive patients with AIS who were hospitalized in the Stroke Unit of Tianjin Medical University General Hospital and Tianjin Haibin People's Hospital, China, within 72 hours after stroke onset. Stroke was defined according to the World Health Organization's criteria, and a diagnosis of AIS was confirmed in all patients based on the evidence of neuroimaging (including computed tomography and magnetic resonance imaging).[9] Patients with transient ischemic attack were excluded from this study. Patients aged 75 years or older were included in this study.

According to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria, stroke subtypes were classified as large-artery atherothrombotic (LAA), cardioembolic (CE), small-artery occlusion (SAO), other causes, and undetermined.[10] Stroke severity was categorized into 3 groups using the TOAST National Institutes of Health Stroke Scale (NIHSS): mild (NIHSS score $\leq$7), moderate (NIHSS score 8-16), and severe (NIHSS score $\geq$17).[11]

Stroke risk factors included a medical history of hypertension (defined as self-reported history of hypertension or using antihypertension drugs), diabetes mellitus (DM, defined as history of DM or using hypoglycemic medications at discharge), dyslipidemias (defined as self-reported history of all types of dyslipidemia or oral antidyslipidemia drugs or using antidyslipidemia drugs at discharge), atrial fibrillation (AF, defined as history of AF, confirmed by at least 1 electrocardiogram or the presence of the arrhythmia during hospitalization), and modifiable lifestyle factors, including current smoking status, alcohol consumption, and obesity (body mass index $\geq$30 kg/m^2).

Assessed outcomes included cumulative mortality, recurrence, and dependency rates at 12 and 36 months after stroke. Death was defined as all-cause mortality at the corresponding time points after hospital admission, which is the end point event in this study. Recurrence was defined as all new-onset vascular events, including stroke, myocardial infarction, and venous thrombosis 30 days after stroke; those dead patients resulted from recurrence of stroke, myocardial infarction, and deep venous thrombosis were included but those dead patients resulted from other diseases were excluded. Dependency was defined as a modified Rankin scale score of 3 or more; those dead patients were excluded.[12] All patients those were interviewed in the outpatient department were assessed dependency status.

Follow-up was conducted according to a predetermined procedure; the trained neurologists re-examined patients in the outpatient department at 3, 12, 24, and 36 months after stroke. All patients were followed up by face-to-face interview or by telephone visiting for those patients re-examined nearby.

The ethics committee of the Tianjin Medical University General Hospital approved the study, and the patients or their next-of-kin provided informed consent for participation.

Sex differences in continuous variables, which were presented as means (standard deviations), were compared using the Student t test, and the dependency rate was assessed using logistic regression models; sex differences in outcomes were assessed using logistic regression models and were presented using unadjusted and adjusted relative ratios (RRs) and 95% confidence intervals (CIs). Sex differences in cumulative survival and recurrence-free rates were presented by the Kaplan–Meier's survival curve. The multivariate analysis was adjusted by stroke subtypes and risk factors as the covariates, including stroke subtypes, severity, and risk factors. The stroke subtypes were analyzed by LAA, CE, and SAO because there were less cases of another 2 subtypes (7 cases for other determined stroke and 9 cases for undetermined stroke). All statistical analyses were performed using SPSS, version 15.0 (SPSS Inc., Chicago, IL), and P values less than .05 for 2-tailed tests were considered statistically significant.

Results

During the study period, 871 consecutive AIS patients were hospitalized in the stroke unit of the Tianjin Medical University General Hospital, China. Of these, 750 patients (86.1%) were interviewed in the outpatient department, 60 patients (6.9%) by telephone visiting, and 61 patients (7%) were excluded because they were lost to follow-up at 12 months; 810 patients (93%) were analyzed for outcomes at 12 months. Similarly, 317 patients (71.4%) were interviewed in the outpatient department, 88 patients