Gender Differences in the Functional Recovery after Acute Stroke

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Background and Purpose   Interest in gender differences in the effects of acute stroke is growing worldwide. However, gender differences in functional recovery after acute stroke in the Korean population have yet to be evaluated. The aim of this investigation was to compare long-term functional outcomes between male and female after acute stroke.

Methods   Patients with acute stroke were enrolled prospectively between January 2005 and January 2009. Baseline characteristics, risk factors, stroke subtypes, time delay from onset to arrival at a hospital, active treatment, and stroke severity were compared between male and female. Differences in mortality and disability at discharge, and at 3 months and 1 year after stroke onset were also investigated. Functional disabilities were categorized into two groups: good outcome (score on modified Rankin scale ≤2) and poor outcome (score on modified Rankin scale >2).

Results   Among 1,055 patients with acute stroke, 575 were male (aged 64.83±11.98 years, mean ±SD) and 480 were female (aged 70.09±13.02 years). There were no gender differences in mortality at 3 months and 1 year after stroke. The frequency of poor outcomes was higher in female patients than in male patients at discharge (39.8% versus 30.9%, respectively; p=0.003), the 3 months follow-up (32.3% versus 20.8%, respectively; p<0.001), and the 1 year follow-up (31.1% versus 18.7%, respectively; p=0.001). After adjusting for multiple confounding factors including age and stroke severity, the female gender persisted as a predictor of poor functional outcome at 3 months and 1 year after stroke.

Conclusions   Female patients have greater difficulty than male patients in recovering from a disabled state after acute stroke. Future studies should investigate the causes of this gender difference.
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Key Words   gender differences, stroke, disability, outcome.

Introduction

Stroke is the major cause of adult disability worldwide.[1,2] Although it is known that there are gender differences in various factors of stroke, such as risk factors, clinical manifestations, mortalities, and functional outcomes, they have received attention only recently.[3-5] Gender differences in stroke are worthy of investigation because female stroke patients-who have a higher prevalence of stroke due to a longer life expectancy-will be a greater burden to our society than male stroke patients.[6]

The few studies that have analyzed gender differences in stroke[4,7-9] have produced diverse results, but there are several common findings: compared with males, females tend to be older at stroke onset, have a higher prevalence of atrial fibrillation but a lower prevalence of cardiovascular disease,[8,10-13] and are less likely to receive acute treatment.[6,14,15] However, the existence of gender differences in other stroke factors, such as mortality and functional outcome, remains controversial.[7-9,16,17] In one European Multicenter Study,[16] female patients exhibited significant disabilities and handicaps at the 3 months poststroke follow-up, whereas 3 months survival was the same in males and females. In the Framingham Heart Study,[17] 34% of the women were disabled at 6 months poststroke, compared with only 16% of the men. According to the results of the Registry of the Canadian Stroke Network,[8] women were more likely than men to be discharged to long-term care and had greater disabilities at 6 months poststroke. However, mortality and quality of life at 6 months poststroke were similar in males and females.

There are currently no long-term follow-up studies of func-

tional outcomes after stroke in Korea. The aim of the present study was thus to compare the long-term functional outcomes between male and female patients with acute stroke in a single hospital-based stroke registry.

Methods

Between January 2005 and January 2009, 1,055 consecutive patients with acute stroke (i.e., within 7 days after symptom onset) were identified at Soonchunhyang University Hospital. We separated patients according to gender and prospectively analyzed their baseline characteristics, mortality, and functional outcomes at discharge and at 3 months and 1 year after stroke onset. We compared the mean age, time delay from symptom onset to hospital arrival, and risk factors between the genders. The risk factors included past history of hypertension (previous diagnosis, current treatment, or blood pressures of $\geq$160/95 mmHg in at least two subsequent measurements), diabetes mellitus (previous diagnosis or current treatment with insulin or oral hypoglycemic medications, or a fasting plasma glucose level of $\geq$126 mg/dL in at least two subsequent measurements), hyperlipidemia (diagnosis or current treatment with lipid-lowering agents, or serum low-density lipoprotein concentration of $\geq$160 mg/dL), smoking (currently or previously), and potential cardioembolic source.

The existences of previous transient ischemic attack (acute neurological deficit of vascular origin, lasting <24 hours) and stroke (including ischemic or hemorrhagic stroke) were also analyzed. We also investigated compliance with medication for risk factors in those patients with at least one more risk factors. Stroke subtype was classified according to the Trial of Org 10,172 in Acute Stroke Treatment criteria.[18]

We analyzed various variables at admission and discharge. At admission, gender differences were assessed in stroke severity according to the National Institutes of Health Stroke Scale (NIHSS), and in the use of intravenous recombinant tissue plasminogen activator (rt-PA). At discharge, the duration of hospital stay, achievement of anticoagulation for high-risk patients of cardioembolic source, stroke severity, functional outcome on the modified Rankin scale (mRS), and mortality during hospitalization were analyzed. The initial neurologic deficits were categorized using the NIHSS into mild (score $\leq$7), moderate (score >7 and $\leq$16), and severe (score >16).

Functional outcome as determined by mRS score and mortality were followed up at 3 months and 1 year after stroke onset in the available survivors. The mRS scores were dichotomized into $\leq$2 (good functional outcome) and >2 (poor outcome). These assessments were made via telephone or face-to-face interview at outpatient clinic.

Univariate and multivariate analyses were performed with SPSS version 15.0 for Windows (SPSS Inc, Chicago, IL, USA). Univariate analysis was performed using the χ^2 test for dichotomous variables and the t-test for continuous variables. The level of statistical significance was set at $p<0.05$. Multivariate analysis was carried out with a logistic regression model. Variables with a probability of $p<0.1$ in univariate analysis were included in the multivariate analysis. The results of the logistic regressions are presented using 95% confidence intervals (CIs). Other data are presented as mean$\pm$SD values except where stated otherwise.

Results

Among 1,055 patients, 480 (45.4%) were female. Baseline variables stratified according to gender are summarized in Table 1. The females (aged 70.09$\pm$13.02 years) were significantly older than the males (aged 64.83$\pm$11.98 years). Females exhibited a significantly higher prevalence of hyperlipidemia than males (22.5% versus 16.1%, respectively; p=0.008) and a lower prevalence of smoking (6.8% versus 46.9%, respectively; $p<$ 0.001). No differences were found for prevalence of previous transient ischemic attack, stroke, hypertension, diabetes, and cardioembolic source. Female patients appeared to comply better with medication for risk factors than did male patients, but the difference was statistically insignificant (87.6% versus 82.3%, respectively; p=0.052). Among the subtypes of stroke, the prevalence of small-vessel occlusion was significantly lower in females than in males (14% versus 19.8%, respectively; p=0.013). There were no significant differences in the time from symptom onset to arrival at the hospital, use of intravenous rt-PA, and anticoagulation for high-risk patients of cardioembolic source. Stroke severities according to NIHSS score at admission (5.72$\pm$ 6.34 versus 5.12$\pm$5.82, respectively; p=0.024) and discharge (5.43$\pm$9.06 versus 4.49$\pm$7.88, respectively; p= 0.005) were significantly higher in females than males. The duration of hospitalization was significantly longer for females than for males (20.69 $\pm$39.78 versus 16.91$\pm$25.89 days, respectively; p=0.04). The in-hospital mortality rate (5.6% versus 3.1%; p=0.046) was significantly higher in females than in males, but there was no difference in mortality at 3 months (2% versus 1.4%, respectively; p=0.507) and 1 year (4.4% versus 2.5%, respectively; p=0.227) after stroke onset.

Gender differences in functional outcome for survivors during hospitalization, at discharge, and at 3 months and 1 year after stroke onset are presented in Table 2. The 20 patients who died while hospitalized and the 58 patients within 3 months from stroke onset were excluded at 3 months analysis. The 13 patients who died during the 3 months follow-up period and the 189 patients within 1 year from stroke onset were excluded at 1 year analysis. The mRS score was thus checked in 775 patients

Table 1. Differences in baseline characteristics between females and males. Data are mean±SD or *n* (%) values

Variable	Female (*n*=480)	Male (*n*=575)	*p*
Age (years)	70.09±13.02	64.83±11.98	0.041*
Risk factors			
Previous TIA	14 (2.9%)	17 (3.0%)	0.978
Previous stroke	64 (13.4%)	102 (17.7%)	0.054
Hypertension	300 (62.6%)	346 (60.1%)	0.395
Diabetes mellitus	140 (29.2%)	192 (33.3%)	0.153
Hyperlipidemia	108 (22.5%)	93 (16.1%)	0.008*
Smoking	30 (6.8%)	270 (46.9%)	0.000*
Cardioembolic source	83 (17.3%)	79 (13.7%)	0.105
Medication for risk factor	289 (87.6%)	317 (82.3%)	0.052
Stroke subtype			
Large-artery atherosclerosis	178 (37.2%)	218 (37.8%)	0.819
Small-vessel occlusion	67 (14%)	114 (19.8%)	0.013*
Cardioembolic infarction	61 (12.7%)	56 (9.7%)	0.126
Stroke of undetermined etiology			
Two episodes or more	32 (6.7%)	28 (4.9%)	0.204
Incomplete	50 (10.4%)	48 (8.3%)	0.241
Negative	11 (2.3%)	13 (2.3%)	0.966
Stroke of other determined etiology	10 (2.1%)	16 (2.8%)	0.472
TIA	23 (4.8%)	33 (5.7%)	0.503
Hemorrhagic stroke	40 (8.3%)	41 (7.1%)	0.465
Time delay from onset to admission (hours)	34.79±44.45	35.01±44.55	0.794
Use of intravenous rt-PA	32 (29.9%)	29 (21.0%)	0.110
Severity at admission			0.103
Mild (NIHSS ≤7)	394 (82%)	501 (87.1%)	
Moderate (7<NIHSS≤16)	49 (10.2%)	44 (7.7%)	
Severe (NIHSS>16)	35 (7.3%)	30 (5.2%)	
Duration of hospitalization (days)	20.69±39.78	16.91±25.89	0.040*
Anticoagulation for high-risk patients of cardioembolic source	32 (55.2%)	26 (51%)	0.662
Mortality			
At discharge	27 (5.6%)	18 (3.1%)	0.046*
From discharge to 3 months	7 (2.0%)	6 (1.4%)	0.507
From 3 months to 1 year	11 (4.4%)	8 (2.5%)	0.227

*p<0.05.
TIA: transient ischemic attack, NIHSS: National Institutes of Health Stroke Scale, rt-PA: recombinant tissue plasminogen activator.

(77.73%) at 3 months and in 566 patients (71.19%) at 1 year poststroke. Data on the premorbid functional status were only available for 468 patients (44.36%) after commencement of the new Web-based stroke registry (Clinical Research Center for Stroke). Premorbid functional status as assessed by mRS was worse in females than in males (0.75±1.28 versus 0.67±1.08, respectively; *p*=0.015). The mRS score at discharge was 2.23±1.81 in females and 1.95±1.66 in males. Female patients exhibited a higher frequency of poor outcomes than male patients at discharge (39.8% versus 30.9%, respectively; *p*=0.003), and at 3 months (32.3% versus 20.8%, respectively; *p*<0.001) and 1 year (31.1% versus 18.7%, respectively; *p*=0.001) after stroke onset.

In patients with mild neurologic deficits, a poor outcome (mRS score >2) was experienced by 28.1%/21.3% (females/males) at discharge, and by 25.7%/14.5% at 3 months and 25.2%/13% at 1 year after stroke onset. In the moderate group these percentages were 97.8%/95.3%, 87.5%/95.5%, and 87.5%/87.5%, respectively, and in the severe group they were 97.1%/100%, 92.3%/78.6%, and 100%/87.5%, respectively.

The results of multiple logistic regression analysis for predicting poor functional outcome at 3 months and 1 year after acute stroke are presented in Table 3. Among the baseline characters, old age and stroke severity at admission were strongly positive predictors of 3 months and 1 year poor functional outcome. Older age was associated with a greater risk of poor

Table 2. Gender differences in functional outcome after acute stroke. Data are mean±SD or *n* (%) values

Variable	Females	Males	*p*
Premorbid mRS score	0.75±1.28	0.67±1.08	0.015*
mRS score at discharge	2.23±1.81	1.95±1.66	0.001*
Good outcome (≤2)	284 (60.2%)	391 (69.1%)	0.003*
Poor outcome (>2)	188 (39.8%)	175 (30.9%)	
mRS score at 3 months	1.87±1.52	1.57±1.36	0.001*
Good outcome (≤2)	235 (67.7%)	339 (79.2%)	0.000*
Poor outcome (>2)	112 (32.3%)	89 (20.8%)	
mRS score at 1 year	1.81±1.56	1.31±1.32	0.000*
Good outcome (≤2)	173 (68.9%)	256 (81.3%)	0.001*
Poor outcome (>2)	78 (31.1%)	59 (18.7%)	

*$p<0.05$.
mRS: modified Rankin scale.

Table 3. Multiple logistic regression analysis evaluating predictors of poor functional outcome at 3 months and 1 year after stroke onset

Variable	3 months mRS score		*p*	1 year mRS score		*p*
	OR	95% CI		OR	95% CI	
Female	1.59	1.02-2.49	0.040*	1.74	1.01-2.99	0.042*
Age (years)						
66-75	1.65	1.03-2.65	0.035*	1.36	0.77-2.39	0.280
76-85	3.04	1.80-5.14	0.000*	3.30	1.78-6.10	0.000*
>85	20.65	7.31-58.35	0.000*	51.36	10.33-255.31	0.000*
Severity						
Moderate	7.72	4.64-12.85	0.000*	8.54	4.57-15.93	0.000*
Severe	13.35	5.67-31.43	0.000*	17.08	5.65-51.60	0.000*
Small-vessel occlusion	0.55	0.31-0.99	0.047*	0.49	0.24-1.02	0.057
Previous history of stroke	2.42	1.46-4.01	0.001*	2.56	1.38-4.75	0.003*
Risk factors						
Hypertension	0.81	0.53-1.22	0.317	0.85	0.52-1.39	0.518
Diabetes mellitus	1.60	1.05-2.45	0.028*	2.07	1.26-3.42	0.004*
Hyperlipidemia	1.30	0.81-2.09	0.271	1.06	0.58-1.92	0.845
Cardioembolic source	0.89	0.52-1.53	0.685	0.89	0.47-1.71	0.745

*$p<0.05$.
OR: odds ratio, CI: confidence interval, mRS: modified Rankin scale.

functional outcome at 3 months [66-75 years, odds ratio (OR)= 1.65, 95% CI=1.03-2.65, *p*=0.035; 76-85 years, OR=3.04, 95% CI=1.80-5.14, *p*<0.001; >85 years, OR=20.65; 95% CI=7.31-58.35, *p*<0.001], and at 1 year after stroke onset (66-75 years, OR=1.36; 95% CI=0.77-2.39, *p*=0.280; 76-85 years, OR=3.30, 95% CI=1.78-6.10, *p*<0.001; >85 years, OR=51.36; 95% CI= 10.33-255.31, *p*<0.001). More-severe stroke also carried a greater risk of poor functional outcome at 3 months (moderate, OR= 7.72, 95% CI=4.64-12.85, *p*<0.001; severe, OR=13.35, 95% CI= 5.67-31.43, *p*<0.001) and at 1 year (moderate, OR=8.54, 95% CI=4.57-15.93, *p*<0.001; severe, OR=17.08, 95% CI=5.65-51.60, *p*<0.001) after stroke onset. Diabetes (3 months poststroke, OR= 1.60, 95% CI=1.05-2.45, *p*=0.028; 1 year poststroke, OR=2.07, 95% CI=1.26-3.42, *p*=0.004) and previous history of stroke (3 months poststroke, OR=2.42, 95% CI= 1.46-4.01, *p*=0.001; 1 year poststroke, OR=2.56, 95% CI= 1.38-4.75, *p*=0.003) were signifi-

cant predictors of poor functional outcomes at 3 months and 1 year. In contrast, small-vessel occlusion had a protective effect against a 3-month poor functional outcome (OR=0.55, 95% CI= 0.31-0.99, *p*=0.047). After adjusting for multiple confounding factors, the female gender consistently remained a predictor of poor functional outcome at 3 months (OR=1.59, 95% CI=1.02-2.49, *p*=0.04) and 1 year (OR=1.74, 95% CI=1.01-2.99, *p*=0.042) after stroke onset.

Discussion

We have demonstrated herein that females are older at stroke onset and have a worse functional outcome at 3 months and 1 year after stroke onset than males, but the mortality rate did not differ between the genders. After adjusting for various confounding factors including age, stroke severity, and risk factors,

the female gender persisted as a predictor of poor functional outcome at 3 months and 1 year after stroke onset. Our results mean that females tend to live longer but with greater disability than males following acute stroke.

Previous studies have suggested the occurrence of worse functional outcomes among females following stroke, and have offered reasons for this finding. One study explained the worse functional outcomes in females by a worse preadmission functional status among females, and weaker social support, with more women than men being widowed and living alone.[8] In another study,[16] that female gender was a significant predictor of disability and handicap was attributed to the balance of medical and social factors, and women being more frail, making them more vulnerable. Our study also revealed a worse functional outcome for females than males for up to 1 year following stroke. Considering that no differences between males and females were found with regard to prior control of risk factors or acute management during hospitalization, the worse functional outcome of females revealed in the present study suggests that Korean women find it more difficult to recover from the disabled state after discharge.

A census in 2004 conducted by the Korean Ministry of Health, Welfare, and Family Affairs[19] found that 66.1% of elderly females but only 11.6% of elderly males were unmarried. In addition, 29.3% of elderly females but only 6.6% of elderly males lived alone. The social status of females in Korea differs markedly from their counterparts in Western countries. In East Asian societies, including Korea, Confucianism has served as the foundation for ethical conduct in socioeconomic and political areas of life during the past 500 years.[20] The social activities of women have been very restricted and their health relatively ignored because of the Confucian understanding of woman, which follows a patriarchal-feudalistic male chauvinism. At senescence, women would be unmarried and have no caregivers, and thus little will to recover. Another possible cause of worse functional outcomes in females is their higher prevalence of poststroke depression.[9,21-23] In one study,[21] females were diagnosed with major depression after stroke twice as frequently as males. Poststroke depression may delay recovery from the disabled state.

Several studies have found that women receive less active treatment.[7,8,24,25] Other studies[9,24] have found that women have little chance of arriving at a treatment center within a 3-hour time window to receive thrombolytic therapy, and the use of premorbid and at-discharge medication of aspirin and warfarin is lower among women. Although the patients included in our study were limited to those admitted to a single hospital and involved a relatively small number, there was no difference in the treatment modalities applied to the genders.

Furthermore, there were no differences in time delay from stroke onset to arrival at the hospital, use of rt-PA, and the rate of anticoagulation for high-risk patients of cardioembolic source.

Gender differences in risk factors and stroke subtypes have been reported previously. Some studies found that the prevalence of atrial fibrillation and cardioembolic infarction of stroke subtypes were higher in female patients than in male patients.[10-13] In one large-scale Korean study,[26] hyperlipidemia, hypertension, and cardioembolic source were found more frequently in females than in males. However, in our study there were no gender differences in cardioembolic source, including atrial fibrillation. Instead, female patients exhibited a higher prevalence of hyperlipidemia. With regard to stroke subtype, small-vessel occlusion was found less frequently in the female patients. The differences in distribution of stroke risk factors and subtypes might be due to the small sample, regional characteristics, or the restriction of the use of a single hospital-based registry.

Various results of stroke mortality rate have been reported. Between 1999 and 2004 mortality rate in the USA was higher in women than in men at <35 years and >85 years of age; the rate was lower in the remaining age group (i.e., 35-84 years).[27] One Korean study[26] found that the rate of mortality from any cause was higher for women than for men, but after adjusting for confounding factors men had the higher death rate because of the higher prevalence of cardiovascular disease and due to ethnic or racial differences. In our study the rate of death from any cause at discharge was higher for females than for males, and no differences were found at the 3 months and 1 year follow-ups. This higher rate of mortality at discharge among females might be due to their older age and higher severity of stroke symptoms on admission.

Our study was subject to some limitations. First, it was a hospital-center-based study rather than a population or multicenter-based one, and thus the findings cannot be considered representative of all Korean stroke patients. Second, prestroke mRS data were not available for all of the patients, and so we did not include premorbid functional status in the multivariate analysis. Finally, there was no information about caregivers, economic status, educational level, or familial support after discharge, all of which can influence functional outcomes.

While the functional outcome at discharge has been investigated previously, there has been no study of long-term functional outcome after stroke for females in Korea. The findings of our study suggest that females find it difficult to recover from the poststroke disabled state, which could result in them becoming a greater socioeconomic burden than males. More attention should be paid to establishing the causes of this problem, and to developing gender-specific management guidelines for female Korean stroke patients.

Conflicts of Interest

The authors have no financial conflicts of interest.

REFERENCES

1. Adamson J, Beswick A, Ebrahim S. Is stroke the most common cause of disability? *J Stroke Cerebrovasc Dis* 2004;13:171-177.
2. Kavanagh S, Knapp M, Patel A. Cost and disability among stroke patients. *J Public Health Med* 1999;21:385-394.
3. Smith DB, Murphy P, Santos P, Phillips M, Wilde M. Gender differences in the Colorado Stroke Registry. *Stroke* 2009;40:1078-1081.
4. Petrea RE, Beiser AS, Seshadri S, Kelly-Hayes M, Kase CS, Wolf PA. Gender differences in stroke incidence and poststroke disability in the Framingham Heart Study. *Stroke* 2009;40:1032-1037.
5. Knoflach M, Kiechl S, Penz D, Zangerle A, Schmidauer C, Rossmann A, et al. Cardiovascular risk factors and atherosclerosis in young women; atherosclerosis risk factors in female youngsters (ARFY Study). *Stroke* 2009; 40:1063-1069.
6. Niewada M, Kobayashi A, Sandercock PA, Kamiński B, Członkowska A; International Stroke Trial Collaborative Group. Influence of gender on baseline features and clinical outcomes among 17,370 patients with confirmed ischaemic stroke in the international stroke trial. *Neuroepidemiology* 2005;24:123-128.
7. Gargano JW, Reeves MJ; Paul Coverdell National Acute Stroke Registry Michigan Prototype Investigators. Sex differences in stroke recovery and stroke-specific quality of life: results from a statewide stroke registry. *Stroke* 2007;38:2541-2548.
8. Kapral MK, Fang J, Hill MD, Silver F, Richards J, Jaigobin C, et al. Sex differences in stroke care and outcomes: results from the Registry of the Canadian Stroke Network. *Stroke* 2005;36:809-814.
9. Glader EL, Stegmayr B, Norrving B, Terént A, Hulter-Asberg K, Wester PO, et al. Sex differences in management and outcome after stroke: a Swedish national perspective. *Stroke* 2003;34:1970-1975.
10. Roquer J, Campello AR, Gomis M. Sex differences in first-ever acute stroke. *Stroke* 2003;34:1581-1585.
11. Kolominsky-Rabas PL, Weber M, Gefeller O, Neundoerfer B, Heuschmann PU. Epidemiology of ischemic stroke subtypes according to TOAST criteria: incidence, recurrence, and long-term survival in ischemic stroke subtypes: a population-based study. *Stroke* 2001;32:2735-2740.
12. Gray LJ, Sprigg N, Bath PM, Boysen G, De Deyn PP, Leys D, et al. Sex differences in quality of life in stroke survivors: data from the Tinzaparin in Acute Ischaemic Stroke Trial (TAIST). *Stroke* 2007;38:2960-2964.
13. Arboix A, Oliveres M, García-Eroles L, Maragall C, Massons J, Targa C. Acute cerebrovascular disease in women. *Eur Neurol* 2001;45:199-205.
14. Reid JM, Dai D, Gubitz GJ, Kapral MK, Christian C, Phillips SJ. Gender differences in stroke examined in a 10-year cohort of patients admitted to a Canadian teaching hospital. *Stroke* 2008;39:1090-1095.
15. Schumacher HC, Bateman BT, Boden-Albala B, Berman MF, Mohr JP, Sacco RL, et al. Use of thrombolysis in acute ischemic stroke: analysis of the Nationwide Inpatient Sample 1999 to 2004. *Ann Emerg Med* 2007;50:99-107.
16. Di Carlo A, Lamassa M, Baldereschi M, Pracucci G, Basile AM, Wolfe CD, et al. Sex differences in the clinical presentation, resource use, and 3-month outcome of acute stroke in Europe: data from a multicenter multinational hospital-based registry. *Stroke* 2003;34:1114-1119.
17. Kelly-Hayes M, Beiser A, Kase CS, Scaramucci A, D'Agostino RB, Wolf PA. The influence of gender and age on disability following ischemic stroke: the Framingham study. *J Stroke Cerebrovasc Dis* 2003;12:119-126.
18. Adams HP Jr, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke* 1993;24:35-41.
19. Korean Ministry health, welfare and family affairs. http://www.mw.go.kr/.
20. Son HC. The Confucian understanding of women. *Cathol Philos* 2005; 7:109-147.
21. Aström M, Adolfsson R, Asplund K. Major depression in stroke patients. A 3-year longitudinal study. *Stroke* 1993;24:976-982.
22. Paradiso S, Robinson RG. Gender differences in poststroke depression. *J Neuropsychiatry Clin Neurosci* 1998;10:41-47.
23. Shimoda K, Robinson RG. Effects of anxiety disorder on impairment and recovery from stroke. *J Neuropsychiatry Clin Neurosci* 1998;10:34-40.
24. Foerch C, Misselwitz B, Humpich M, Steinmetz H, Neumann-Haefelin T, Sitzer M; Arbeitsgruppe Schlaganfall Hessen. Sex disparity in the access of elderly patients to acute stroke care. *Stroke* 2007;38:2123-2126.
25. Deng YZ, Reeves MJ, Jacobs BS, Birbeck GL, Kothari RU, Hickenbottom SL, et al. IV tissue plasminogen activator use in acute stroke: experience from a statewide registry. *Neurology* 2006;66:306-312.
26. Oh MS, Yu KH, Rho JK, Lee BC; Korean Stroke Registry Study Group. Gender differences in the motality and outcome of stroke patients in Korea. *Cerebrovas Dis* 2009;28:427-434.
27. Reeves MJ, Bushnell CD, Howard G, Gargano JW, Duncan PW, Lynch G, et al. Sex differences in stroke: epidemiology, clinical presentation, medical care, and outcomes. *Lancet Neurol* 2008;7:915-926.