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Background and Purpose—The association between body mass index and mortality caused by subtypes of stroke among postmenopausal women in terms of smoking status and age at menopause remains controversial.

Methods—The data were derived from a cohort study of 3321 with 17.8 years of follow-up (1985 to 2002). Hazard ratios (HRs) and 95% CIs for strokes as related to body mass index were estimated by Cox proportional hazard models adjusted for age, hypertension, smoking, drinking, occupation, education, self-reported health, and age at menopause. A stratified analysis was conducted by age at menopause and smoking status.

Results—The obese group (body mass index $\geq$27.5 kg/m^2) had higher risks of total stroke mortality (HR, 1.59; 95% CI, 1.05 to 2.42) and hemorrhagic stroke mortality (HR, 2.91; 95% CI, 1.37 to 6.19) than the normal weight group (18.5$\leq$ body mass index $<$23.0). Among ever smokers, the obese group showed significantly increased risks of total stroke mortality (HR, 2.33; 95% CI, 1.00 to 5.43) and ischemic stroke mortality (HR, 7.21; 95% CI, 1.18 to 44.3). Obesity had more effect on stroke mortality among women who experienced menopause at age $<$50 than women with age $\geq$50. For the obese group of the former, the HR of total stroke was 2.04 (95% CI, 1.25 to 3.34) and that of hemorrhagic stroke 6.46 (95% CI, 2.42 to 17.25).

Conclusions—In this prospective study, obesity raised the risks of total stroke mortality and hemorrhagic stroke mortality among Korean menopausal women. It was more evident with women who experienced menopause at age $<$50. The obese group of ever smokers was at an increased risk of ischemic stroke mortality. **(*Stroke*. 2009;40:3428-3435.)**

Key Words: Asian ■ cohort study ■ body mass index ■ Korean ■ menopause ■ mortality ■ smoking ■ stroke

Being overweight is a well-documented risk factor for chronic diseases, including stroke.[1–4] However, the association between body mass index (BMI) and hemorrhagic stroke is less clear.[5–7] Stroke is a leading cause of disability and death among elderly women in developed countries.[8] In 2005, the mortality rate from stroke in South Korean women was 67.3 deaths/100 000 person-years.[9]

Most women experience strokes relatively late in life. Incidence climbs precipitously after menopause and incidence rates are particularly high in Asians and blacks.[8,10] Menopause is a pathophysiological change that begins at an average age of 50 years, but the mechanism through which menopause exerts its effect on vascular incidents remains unknown.[11] Smoking as a risk factor for stroke is well documented. A few studies assessed women who had menopause at younger than normal ages and reported the increased risks of coronary heart disease and stroke. However, how differently obesity affects stroke between ever smokers and never smokers or between women going through early menopause and late menopause is not yet clearly established.[4,11,12] Moreover, the relationship between stroke and BMI might be different in relatively lean Korean women.[4]

With the increased longevity of women and the growing socioeconomic burden from stroke, we need to identify risk factors pertaining to strokes of postmenopausal women to help prevent stroke.[13] In this study, we examined the relationship between BMI and stroke mortality by smoking status and age at menopause in postmenopausal Korean women.

Methods

Study Population

This study used the data from the Kangwha Cohort and included 3648 South Korean women at least 55 years old. The Kangwha Cohort was first established to examine risk factors influencing the development of various cancers, cerebrovascular disease, and other causes of death in the elderly. The population recruited for Kangwha Cohort study included residents $\geq$55 years who were born before 1930 in 10 administrative districts *eup*s and *myeon*s in Korea of Kangwha County on February 28, 1985, based on their resident

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registration records (total, 9378; male, 3938; female, 5440). A total of 6372 persons (2724 males, 3648 females) agreed to participate in the interview and medical examination in the 1985 survey. The proportion of participation was 67.9%.[12] To avoid the confounding of pre-existing diseases, data for 95 women who died or followed up only before January 1, 1986, were excluded from analysis as were data for 73 women with missing BMI information. We also excluded data for women with strokes at entry (n=47), not having menopause (n=12), without known menopausal status (n=71), and who had taken oral contraceptives (n=29). We then analyzed the remaining data set for 3321 postmenopausal subjects.

Data Collection

Baseline data included self-reported information from study participants. Trained staff reviewed completed questionnaires and entered the data. Questions on reproductive factors included menopause and first childbirth, marital status, and number of children. Age at menopause was recorded with the age at which each participant reported her last menstruation. Lifestyle-related factors, including smoking habits and alcohol consumption, were described. Weight and height were determined with participants wearing light clothing. BMI was calculated as the weight (kg) divided by the square of height (m^2). Blood pressure measurements were taken in a seated position by a trained investigator using a standard mercury sphygmomanometer. The blood pressure measurement training was provided with an educational audiotape that the London School of Hygiene & Tropical Medicine produced; and the interobserver error in blood pressure measurement was within 2 mm Hg. Systolic blood pressure and diastolic blood pressure were measured as the first and fifth Korotkoff sounds, respectively.[14] Blood pressure was measured once per person. The study subjects were followed up from March 1985 until December 31, 2002, and the follow-up period for each subject was calculated in months. The total observed person-times was 45 362 person-years, median person-times was 17.5 person-years (interquartile range, 9.5 to 17.8), and mean person-times was 13.6 person-years (SD, 5.3). The study was approved by the Institutional Review Boards of Yonsei University (Institutional Review Board approval number 4-2007-0182).

Outcome Ascertainment

Deaths among subjects from January 1, 1992, to December 31, 2002, were confirmed by matching the information to death records from the National Statistical Office. Data for those who died from March 15, 1985, to December 31, 1991, were collected either through calls and visits of trained surveyors twice a year or from records of burial and death certificates of *eup* and *myeon* offices that are administrative branch offices of the local government in Korea. Causes of death from 1992 to 2002, which were provided by the National Statistical Office of Korea, were presented in accordance with the International Classification of Disease, Tenth Revision, whereas causes of death before 1992 were coded under International Classification of Disease, Tenth Revision by 2 medical doctors.

The main outcome variables for this study were death due to total, hemorrhagic, and ischemic stroke as defined by International Classification of Disease, Tenth Revision (I60 to I69, I60 to I62, and I63, respectively).

Statistical Analysis

Cox proportional hazards models were used to evaluate the relation between baseline BMI and stroke mortality. Subjects were divided into 5 groups by BMI (kg/m^2)[15]: <18.5, 18.5 to 22.9, 23.0 to 24.9, 25.0 to 27.4, and ≥27.5. Analyses were adjusted for the following covariates: age at entry, hypertension (on hypertension medication, systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg versus systolic blood pressure <140 mm Hg and diastolic blood pressure <90 mm Hg), smoking status (never, ever), drinking status (current drinker, nondrinker), occupation (agriculture, other), education (never, elementary school, middle school or over), age at menopause (<50, ≥50), and self-reported health compared with the same age group (better, similar, worse). Additionally, we performed a stratified analysis according to smoking status and age at menopause (<50 [early menopause] and ≥50 [late menopause]). Hazard ratios (HRs) and 95% CIs were expressed for the results and probability values were calculated by the 2-tailed test. All statistical analyses were done using SAS software, Version 9.1 (SAS Institute, Cary, NC).

Results

During the 17.8 years of follow-up, we identified 248 strokes: 54 hemorrhagic and 26 ischemic causes among the study participants. The average BMI was 22.7 kg/m^2; a majority of subjects had BMI <25.0 kg/m^2. Just 7.9% had BMI >27.5 kg/m^2. More than half (59.0%) had hypertension; approximately 10% used alcohol. Past smokers were just 2.0%. Most of subjects engaged in agriculture. Almost all subjects (98.8%) had received no formal education or had been educated only at an elementary school level (Table 1).

Unadjusted HR shows that age at entry, hypertension, and women with BMI ≥27.5 kg/m^2 significantly increased the risk of total stroke mortality. However, women who received an elementary education only had a significantly reduced risk of total stroke mortality compared with those with no education. BMI used as a continuous variable, hypertension, and BMI ≥27.5 kg/m^2 significantly increased the risk of hemorrhagic stroke mortality, whereas women who experienced menopause at age ≥50 and were current smokers had a significantly elevated risk of ischemic stroke mortality (Table 1).

Women with BMI ≥27.5 kg/m^2 were younger, more likely to have hypertension, more never smokers, and with a higher education level than those with a BMI of 18.5 to 22.9 kg/m^2 (Table 2). Age at menopause had no significant relationship with BMI category. In multivariate-adjusted analyses for all women, the HR (95% CI) for mortality of total stroke and hemorrhagic stroke were significantly higher for women with BMI ≥27.5 kg/m^2 than for women with a BMI of 18.5 to 22.9 kg/m^2 (Table 2).

Among current and past smokers, unadjusted HR showed that BMI ≥27.5 kg/m^2 was significantly associated with total stroke mortality (HR, 2.35) and hemorrhagic stroke mortality (HR, 5.30). After adjustment for age at entry, hypertension and other variables, women with BMI ≥27.5 kg/m^2 had a significantly increased risk of total stroke mortality ($P=0.050$), which was raised 1.09 times every BMI increase of 1 kg/m^2 ($P=0.038$). After adjustment for confounders, high BMI (BMI ≥27.5 kg/m^2) was borderline significantly associated with hemorrhagic stroke mortality ($P=0.082$). Among ever smokers, obese women (BMI ≥27.5 kg/m^2) had a significantly high unadjusted HR for ischemic stroke mortality and, after adjustment for confounders, were still at significantly high risk for the mortality (HR, 7.21; Table 3; Figure). Among women who did not smoke, the unadjusted and multivariate-adjusted HR showed that BMI was not associated with total stroke mortality and ischemic stroke mortality. However, the high BMI group (≥27.5 kg/m^2) had a higher risk of hemorrhagic stroke mortality than the normal BMI group (18.5≤ BMI <23.0 kg/m^2; Table 3; Figure).

Among women who experienced menopause at age <50, the obese group (BMI ≥27.5 kg/m^2) showed higher risks of total stroke mortality and hemorrhagic stroke mortality than the normal weight group (18.5≤ BMI <23.0 kg/m^2) in both

Table 1. Baseline Characteristics of Subjects and Unadjusted HR for Stroke Mortality

Characteristics	No. Mean	(%) (SD)	Unadjusted HR (95% CI) Total Strokes (I60 to I69)	Hemorrhagic Strokes (I60 to I62)	Ischemic Strokes (I63)
Age at entry, years*	66.7	(8.2)	1.07 (1.05–1.09)	1.00 (0.96–1.04)	1.02 (0.96–1.08)
Age at menopause, years*	46.8	(5.2)	1.00 (0.98–1.03)	1.02 (0.97–1.08)	1.07 (0.98–1.16)
BMI, kg/m^2*	22.7	(3.2)	1.04 (1.00–1.08)	1.12 (1.03–1.21)	1.01 (0.89–1.14)
	No.	(%)			
Hypertension†					
No	1361	(41.0)	1.00	1.00	1.00
Yes	1955	(59.0)	2.78 (2.08–3.73)	2.49 (1.35–4.57)	1.77 (0.79–3.97)
Age at menopause					
<50	2169	(65.3)	1.00	1.00	1.00
≥50	1152	(34.7)	1.02 (0.78–1.32)	1.29 (0.75–2.22)	2.51 (1.15–5.47)
BMI, kg/m^2					
<18.5	286	(8.6)	1.12 (0.67–1.87)	0.71 (0.16–3.02)	1.37 (0.30–6.19)
18.5–22.9	1623	(48.9)	1.00	1.00	1.00
23.0–24.9	679	(20.4)	1.25 (0.91–1.72)	1.36 (0.67–2.78)	1.01 (0.35–2.91)
25.0–27.4	471	(14.2)	1.04 (0.71–1.51)	1.39 (0.63–3.05)	1.63 (0.60–4.42)
≥27.5	262	(7.9)	1.63 (1.08–2.45)	3.32 (1.59–6.92)	1.10 (0.24–4.96)
Smoking					
Never smoker	2508	(75.5)	1.00	1.00	1.00
Current smoker	747	(22.5)	1.32 (0.98–1.77)	1.08 (0.56–2.10)	2.48 (1.09–5.60)
Past smoker	66	(2.0)	1.46 (0.60–3.56)	1.29 (0.18–9.38)	4.07 (0.54–30.74)
Drinking					
Nondrinker	2983	(89.8)	1.00	1.00	1.00
Current drinker	338	(10.2)	0.99 (0.66–1.49)	0.68 (0.24–1.87)	0.33 (0.04–2.43)
Education					
No education	2672	(80.5)	1.00	1.00	1.00
Elementary school	607	(18.3)	0.67 (0.48–0.95)	0.93 (0.48–1.82)	1.23 (0.52–2.92)
Middle school or over	41	(1.2)	0.58 (0.14–2.33)	1.44 (0.20–10.47)	0.0

*Mean (SD).
†Hypertension defined as on hypertension medication or systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg.

unadjusted analysis and multivariate-adjusted analysis (Table 4). For hemorrhagic stroke, unadjusted and multivariate-adjusted HRs (95% CI) for women of BMI ≥27.5 kg/m^2 were 7.08 (95% CI, 2.73 to 18.3) and 6.46 (2.42 to 17.3), respectively. However, there was no significant relationship between BMI and ischemic stroke mortality in those women going through menopause early. Among women who experienced late menopause (age ≥50), BMI was not significantly associated with mortality from total stroke, hemorrhagic stroke. or ischemic stroke (Table 4; Figure).

Discussion

In this prospective cohort study of Korean postmenopausal women, it is of interest to note that BMI was an independent predictor of mortality for total stroke, particularly for hemorrhagic stroke. The association for death due to the total and hemorrhagic stroke mortality was stronger among women who experienced early menopause but not among those who experienced late menopause. Meanwhile, among total postmenopausal women, BMI was not associated with ischemic stroke mortality, whereas among smoking postmenopausal women, the obese women (BMI ≥27.5 kg/m^2) had a significantly high risk of ischemic stroke mortality (adjusted HR, 7.21) in our data.

Although being overweight, particularly obesity, is known to be a risk factor for the incidence or death of cardiovascular disease,[16] study results on the relationship between obesity and stroke mortality in Asian populations are not always consistent.[3,4,17] Some studies have also noted a substantially increased risk of total and ischemic strokes among both men and women with a high BMI.[5,18,19] However, the association between hemorrhagic stroke and BMI was inconsistent,[5,20–22] although another large prospective cohort study among middle-aged women in Korea[4] found a positive association. Asian populations have higher incidences of hemorrhagic stroke and also higher percentages of body fat and less muscle mass compared with Western populations.[23] Our study findings imply that being overweight or obese may contribute to total and hemorrhagic stroke mortality in Asian populations.

Table 2. Baseline Characteristics of Subjects and HR for Stroke Mortality by BMI

Variables	BMI, kg/m^2					*P* Value*
	<18.5	18.5–22.9	23.0–24.9	25.0–27.5	≥27.5	
No. of women	286	1623	679	471	262	
Person-years of follow up	3 319	21 951	9 535	6 926	3 632	
	Mean (SD)					
Age at entry, years	70 (8.6)	67.2 (8.4)	66.1 (7.8)	64.9 (7.3)	64.8 (7.4)	<0.0001
Age at menopause, years	46 (4.8)	46.7 (4.9)	46.7 (4.9)	47 (5.3)	46.9 (5.0)	0.100
	Numbers (%)					
Hypertension†						
No	138 (48.3)	714 (44.1)	264 (38.9)	174 (36.9)	71 (27.1)	<0.0001
Yes	148 (51.7)	904 (55.9)	415 (61.1)	297 (63.1)	191 (72.9)	
Age at menopause, years						
<50	198 (69.2)	1049 (64.6)	465 (68.5)	291 (61.8)	166 (63.4)	0.081
≥50	88 (30.8)	574 (35.4)	214 (31.5)	180 (38.2)	96 (36.6)	
Smoking						
Never smoker	152 (53.1)	1189 (73.3)	566 (83.4)	384 (81.5)	217 (82.8)	<0.0001
Current smoker	129 (45.1)	399 (24.6)	101 (14.9)	76 (16.1)	42 (16)	
Past smoker	5 (1.7)	35 (2.2)	12 (1.8)	11 (2.3)	3 (1.1)	
Drinking						
Nondrinker	253 (88.5)	1456 (89.7)	612 (90.1)	423 (89.8)	239 (91.2)	0.872
Current drinker	33 (11.5)	167 (10.3)	67 (9.9)	48 (10.2)	23 (8.8)	
Self-reported health compared with the same age						
Better	42 (14.7)	374 (23.1)	157 (23.1)	105 (22.3)	51 (19.5)	0.001
Similar	150 (52.4)	847 (52.3)	382 (56.3)	269 (57.1)	147 (56.1)	
Worse	94 (32.9)	400 (24.7)	140 (20.6)	97 (20.6)	64 (24.4)	
Occupation						
Agriculture	226 (79)	1341 (82.7)	552 (81.3)	365 (77.5)	192 (73.3)	0.002
Other	60 (21)	281 (17.3)	127 (18.7)	106 (22.5)	70 (26.7)	
Education						
No education	248 (86.7)	1311 (80.8)	559 (82.3)	353 (74.9)	201 (76.7)	0.002
Elementary school	37 (12.9)	290 (17.9)	114 (16.8)	107 (22.7)	59 (22.5)	
Middle school or over	1 (0.3)	21 (1.3)	6 (0.9)	11 (2.3)	2 (0.8)	
	Multivariate adjusted HR (95% CI)‡					
Total strokes (I60–I69)	1.00 (0.60–1.68)	1.00	1.28 (0.93–1.76)	1.12 (0.76–1.64)	1.59 (1.05–2.42)	1.05 (1.01–1.09)§
Hemorrhagic strokes (I60–I62)	0.70 (0.16–3.00)	1.00	1.36 (0.66–2.81)	1.32 (0.60–2.93)	2.91 (1.37–6.19)	1.10 (1.02–1.19)§
Ischemic strokes (I63)	1.26 (0.27–5.82)	1.00	1.13 (0.39–3.27)	1.68 (0.61–4.58)	1.13 (0.24–5.21)	1.01 (0.89–1.15)§

*P value for analysis of variance or χ^2 tests.

†Hypertension defined as on hypertension medication or systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg.

‡Adjusted for age at entry (years), hypertension (on hypertension medication, systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 versus systolic blood pressure <140 mm Hg and diastolic blood pressure <90 mm Hg), education (never, elementary school, middle school or over), occupation (agriculture, other), drinking (current drinker, nondrinker), smoking (ever smoker, never smoker), age at menopause (<50, ≥50), and self-reported health compared with the same age group (better, similar, worse).

§BMI was used as a continuous variable per 1 kg/m^2.

In this study, women who experienced early menopause showed an increased association between BMI and mortality from total strokes, particularly hemorrhagic stroke, whereas no significant association between BMI and stroke mortality was found among women who experienced late menopause. Although Asian women are relatively thin and scarcely show high obesity rate (BMI ≥30 kg/m^2), the association between BMI and stroke mortality differs with studies for Asian women. Of many possible reasons, menopause may be a factor causing the difference. Menopause is known to increase the risk of cardiovascular disease and subsequently the risk of mortality from cardiovascular disease.[4,10,12] However, only a few studies have examined the relationship between age at menopause and the incidence and death of stroke,[10,13,24–26]

Table 3. HR for Stroke Mortality by Smoking and BMI

	Ever Smoker (N=813)				Never Smoker (N=2508)			
BMI, kg/m^2	No. of Deaths	Unadjusted HR (95% CI)	Age and Hypertension Adjusted HR (95% CI)*	Multivariate Adjusted HR (95% CI)†	No. of Deaths	Unadjusted HR (95% CI)	Age and Hypertension Adjusted HR (95% CI)*	Multivariate Adjusted HR (95% CI)†
Total strokes								
<18.5	7	0.89 (0.39–2.01)	0.98 (0.43–2.24)	0.96 (0.42–2.19)	10	1.23 (0.64–2.38)	1.16 (0.60–2.24)	1.09 (0.56–2.12)
18.5–22.9	32	1.00	1.00	1.00	75	1.00	1.00	1.00
23.0–24.9	11	1.30 (0.66–2.58)	1.35 (0.68–2.68)	1.34 (0.67–2.67)	48	1.29 (0.90–1.86)	1.24 (0.87–1.79)	1.25 (0.87–1.80)
25.0–27.4	7	0.99 (0.44–2.25)	1.05 (0.46–2.37)	1.02 (0.45–2.32)	29	1.09 (0.71–1.67)	1.11 (0.72–1.71)	1.15 (0.74–1.77)
≥27.5	7	2.35 (1.04–5.32)	2.27 (0.99–5.19)	2.33 (1.00–5.43)	22	1.55 (0.97–2.50)	1.46 (0.90–2.35)	1.45 (0.90–2.34)
Continuous‡	64	1.08 (1.01–1.16)	1.08 (1.00–1.17)	1.09 (1.00–1.17)	184	1.03 (0.98–1.08)	1.03 (0.98–1.08)	1.03 (0.98–1.08)
Hemorrhagic strokes								
<18.5	0	0.0	0.0	0.0	2	1.32 (0.30–5.79)	1.32 (0.30–5.80)	1.28 (0.29–5.66)
18.5–22.9	6	1.00	1.00	1.00	14	1.00	1.00	1.00
23.0–24.9	1	0.64 (0.08–5.29)	0.55 (0.07–4.62)	0.66 (0.08–5.78)	11	1.58 (0.72–3.49)	1.50 (0.68–3.31)	1.57 (0.71–3.48)
25.0–27.4	2	1.52 (0.31–7.54)	1.38 (0.28–6.85)	1.32 (0.25–6.85)	7	1.40 (0.57–3.48)	1.31 (0.53–3.27)	1.41 (0.56–3.51)
≥27.5	3	5.30 (1.32–21.21)	3.78 (0.90–15.83)	3.73 (0.84–16.49)	8	3.04 (1.28–7.25)	2.67 (1.11–6.41)	2.75 (1.14–6.63)
Continuous‡	12	1.21 (1.04–1.41)	1.17 (1.00–1.37)	1.16 (0.98–1.36)	42	1.09 (1.00–1.20)	1.08 (0.98–1.18)	1.08 (0.99–1.19)
Ischemic strokes								
<18.5	1	1.12 (0.13–10.03)	1.11 (0.12–10.04)	1.19 (0.13–11.10)	1	1.36 (0.17–11.04)	1.37 (0.17–11.21)	1.45 (0.18–11.99)
18.5–22.9	4	1.00	1.00	1.00	7	1.00	1.00	1.00
23.0–24.9	1	0.94 (0.11–8.41)	0.95 (0.11–8.53)	0.88 (0.10–8.02)	4	1.14 (0.33–3.89)	1.07 (0.31–3.67)	1.14 (0.33–3.93)
25.0–27.4	2	2.20 (0.40–12.00)	2.22 (0.40–12.20)	1.98 (0.35–11.23)	4	1.57 (0.46–5.36)	1.45 (0.42–4.98)	1.54 (0.44–5.34)
≥27.5	2	6.05 (1.11–33.09)	6.25 (1.06–36.76)	7.21 (1.18–44.27)	0	0.0	0.0	0.0
Continuous‡	10	1.18 (0.99–1.40)	1.18 (0.98–1.42)	1.17 (0.97–1.42)	16	0.93 (0.79–1.10)	0.92 (0.77–1.09)	0.92 (0.78–1.09)

*HR (95% CI) adjusted for age at entry (years) and hypertension (on hypertension medication, systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 versus systolic blood pressure <140 mm Hg and diastolic blood pressure <90 mm Hg).

†HR (95% CI) adjusted for age at entry (years), hypertension (on hypertension medication, systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg versus systolic blood pressure <140 mm Hg and diastolic blood pressure <90 mm Hg), education (never, elementary school, middle school or over), occupation (agriculture, other), drinking (current drinker, nondrinker), age at menopause (<50 years old, ≥50), and self-reported health compared to the same age group (better, similar, worse).

‡BMI was used as a continuous variable per 1 kg/m^2.

and whether BMI affects stroke mortality differently between women who experienced early menopause and late menopause is very rarely studied. The findings that BMI may increase cardiovascular disease in elder women remain controversial.[16] The results of this study imply that the time of menopause has an effect on the relation between BMI and stroke mortality, but the mechanism through which menopause exerts its effect remains unknown.

Among ever smokers, the obese group showed significantly increased risks of mortality from total and ischemic stroke. However, no association between BMI and stroke mortality was observed among never smokers. For hemorrhagic stroke, there was no big difference between BMI and mortality of ever smokers and those of never smokers. The inconsistent results of association between BMI and subtypes of stroke have been reported, and one of the reasons may depend on whether smoking status was stratified.[4] The smoking adversely affects mortality risk and smokers are known to be leaner than nonsmokers. Also, smoking has been reported to lower the age at menopause.[27] This study stratified subjects into ever smokers and never smokers and examined the relationship between BMI and stroke mortality. Meanwhile, in a Korean study conducted for middle-aged women, among never smokers, BMI was related with ischemic and hemorrhagic stroke, but among smokers, ischemic stroke was related with high BMI and hemorrhagic stroke was increased at the lowest BMI group (BMI <18.5 kg/m^2). Such differences among studies are supposed to result from study design, age and socioeconomic status of subjects, stroke diagnosis method, and analysis method. Whether stroke risk or mortality differs with smoking status is inconclusive and requires further study.

The prospective design of this study coupled with long-term follow-up data minimized bias caused by differences in reporting of BMI as a result of stroke mortality. In addition, the self-administered questionnaires and anthropometric measurements were collected by trained surveyors. Thus, the probable information bias due to self-reporting was minimized.[12]

This study has several limitations to be discussed. First, women were asked of the age when they experienced their last menstruation but not questioned to specify whether it was natural or surgical. In this study, chronic diseases, hospitalization history, and, if they had ever been hospitalized, kind of disease were questioned. No one in the study population had cancers of the genitourinary system. There was no report for operations such as hysterectomy. Women who experienced their last menstruation <1 year ago were just 6.

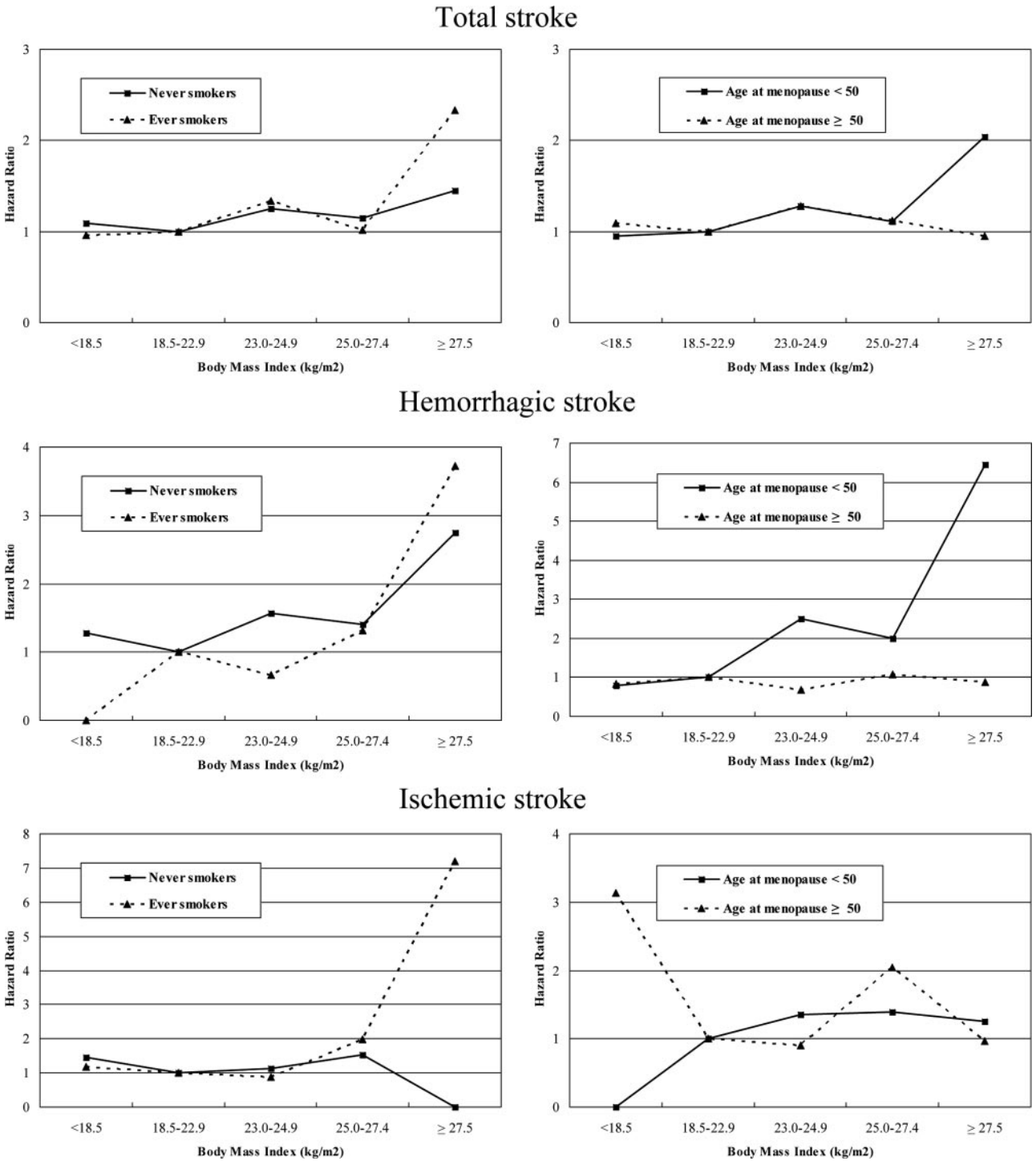

Figure. Association between BMI and subtypes of stroke mortality by smoking (ever smoker versus never smoker) and age at menopause (age at menopause <50, age at menopause ≥50) among Korean postmenopausal women in the Kangwha Cohort study. Multivariate adjusted for age at entry, hypertension (on hypertension medication, systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥ 90 mm Hg versus systolic blood pressure <140 mm Hg and diastolic blood pressure <90 mm Hg), drinking status (current drinker, nondrinker), occupation (agriculture, other), education (never, elementary school, middle school or over), self-reported health compared with the same age group (better, similar, worse), smoking status (ever smoker, never smoker), and/or age at menopause (<50, ≥50).

Therefore, our subjects are reasonably supposed to have experienced natural menopause that has no menstruation for >12 months. Second, covariates and etiologic mediators such as the use of hormone replacement therapy, antiplatelet/anticoagulant therapy, diabetes, and atrial fibrillation, which may affect stroke mortality, was not surveyed in details. However, hormone replacement therapy and antiplatelet/anticoagulant therapy were rarely introduced in Korea before 1985. Hospitalization experiences for diabetes were 4 cases. Atrial fibrillation was not reported and their prevalence rate

Table 4. HR for Stroke Mortality by Age at Menopause and BMI

	Age at Menopause <50 (N=2169)				Age at Menopause ≥50 (N=1152)			
BMI, kg/m^2	No. of Deaths	Unadjusted HR (95% CI)	Age and Hypertension Adjusted HR (95% CI)*	Multivariate Adjusted HR (95% CI)†	No. of Deaths	Unadjusted HR (95% CI)	Age and Hypertension Adjusted HR (95% CI)*	Multivariate Adjusted HR (95% CI)†
Total strokes								
<18.5	11	1.13 (0.59–2.13)	1.02 (0.54–1.93)	0.95 (0.50–1.80)	6	1.11 (0.47–2.62)	1.22 (0.51–2.88)	0.83 (0.10–6.55)
18.5–22.9	66	1.00	1.00	1.00	41	1.00	1.00	1.00
23.0–24.9	40	1.30 (0.88–1.93)	1.27 (0.85–1.88)	1.28 (0.86–1.91)	19	1.17 (0.68–2.02)	1.23 (0.71–2.12)	0.67 (0.19–2.40)
25.0–27.4	22	1.06 (0.66–1.72)	1.08 (0.66–1.75)	1.11 (0.68–1.81)	14	0.99 (0.54–1.82)	1.10 (0.60–2.03)	1.07 (0.34–3.38)
≥27.5	22	2.07 (1.28–3.35)	2.02 (1.24–3.28)	2.04 (1.25–3.34)	7	0.97 (0.43–2.15)	0.92 (0.41–2.05)	0.87 (0.19–3.98)
Continuous‡	161	1.06 (1.01–1.11)	1.06 (1.01–1.12)	1.07 (1.02–1.12)	87	0.99 (0.93–1.06)	1.00 (0.93–1.06)	1.00 (0.87–1.15)
Hemorrhagic strokes								
<18.5	1	0.85 (0.11–6.83)	0.92 (0.11–7.37)	0.79 (0.10–6.39)	1	0.63 (0.08–4.87)	0.75 (0.10–5.77)	0.78 (0.10–6.19)
18.5–22.9	8	1.00	1.00	1.00	12	1.00	1.00	1.00
23.0–24.9	9	2.41 (0.93–6.26)	2.30 (0.89–5.98)	2.50 (0.96–6.55)	3	0.64 (0.18–2.27)	0.63 (0.18–2.25)	0.65 (0.18–2.33)
25.0–27.4	5	1.99 (0.65–6.07)	1.84 (0.60–5.64)	2.00 (0.65–6.20)	4	0.98 (0.32–3.03)	0.98 (0.31–3.06)	1.06 (0.34–3.36)
≥27.5	9	7.08 (2.73–18.34)	6.23 (2.37–16.42)	6.46 (2.42–17.25)	2	0.95 (0.21–4.23)	0.80 (0.18–3.58)	0.87 (0.19–3.97)
Continuous‡	32	1.19 (1.08–1.31)	1.17 (1.06–1.29)	1.18 (1.07–1.30)	22	1.01 (0.88–1.15)	0.99 (0.87–1.13)	1.00 (0.88–1.15)
Ischemic strokes								
<18.5	0	0.0	0.0	0.0	2	2.61 (0.53–12.95)	2.76 (0.55–13.80)	3.14 (0.57–17.46)
18.5–22.9	5	1.00	1.00	1.00	6	1.00	1.00	1.00
23.0–24.9	3	1.28 (0.31–5.35)	1.21 (0.29–5.10)	1.35 (0.31–5.79)	2	0.81 (0.16–4.03)	0.82 (0.17–4.07)	0.90 (0.18–4.51)
25.0–27.4	2	1.23 (0.24–6.35)	1.13 (0.22–5.90)	1.39 (0.27–7.32)	4	1.90 (0.54–6.74)	2.00 (0.56–7.15)	2.05 (0.57–7.44)
≥27.5	1	1.28 (0.15–10.91)	1.11 (0.13–9.71)	1.26 (0.14–11.12)	1	0.93 (0.11–7.70)	0.86 (0.10–7.22)	0.96 (0.11–8.16)
Continuous‡	11	1.08 (0.90–1.29)	1.06 (0.88–1.28)	1.08 (0.90–1.29)	15	0.95 (0.80–1.12)	0.95 (0.80–1.12)	0.95 (0.80–1.13)

*HR (95% CI) adjusted for age at entry (years) and hypertension (on hypertension medication, systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg versus systolic blood pressure SBP <140 mm Hg and diastolic blood pressure <90 mm Hg).

†HR (95% CI) adjusted for age at entry (years), hypertension (on hypertension medication, systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg versus systolic blood pressure <140 mm Hg and diastolic blood pressure <90 mm Hg), education (never, elementary school, middle school or over), occupation (agriculture, other), drinking (current drinker, nondrinker), smoking (ever smoker, never smoker), and self-reported health compared with the same age group (better, similar, worse).

‡BMI was used as a continuous variable per 1 kg/m^2.

was very low. However, not to research such factors to adjust must be a limitation. Third, death record follow-up is different between 1985 to 1991 and 1992 to 2002. However, stroke deaths from 1985 to 1991 were relatively small at 54 cases (22%), and even when the analysis was made with cases from 1992 to 2002 only, the result was similar. Fourth, the validity of diagnosis of stroke in the death certificates was not examined separately. A study reported that the accuracy of diagnosis of cerebrovascular disease in Korean health insurance claims from 1993 to 1997 was 83%.[28] CT and MRI started to be widely used in the diagnosis of stroke in Korea from the mid-1990s.[4] Therefore, there might be a limitation in the validity of diagnosis of stroke made in late 1980s and early 1990s. Fifth, among all stroke diagnoses, a minority was identified as a subtype of stroke. Accordingly, decreased statistical power and possible selection bias in the analysis of stroke subtypes cannot be ruled out. Sixth, subjects were Korean populations of age ≥55, less obese than Western populations, and having scarce hormone replacement therapy experiences. Thus, there must be a limitation to generalizing the results of this study and applying them to other populations who are more obese and receive hormone replacement therapy more often. Seventh, this study relied on the memory of responders regarding age at menopause, which may be subject to recall bias.[13] Eighth, sample sizes and numbers of cases were small, which limited our examination of the association between stroke and all BMI categories of the World Health Organization Asian population classification and may have decreased the statistical power of some analyses.

In this study of Korean postmenopausal women, the obesity group (BMI ≥27.5 kg/m^2) had higher risks of mortality from total and hemorrhagic stroke than the normal weight group (18.5≤ BMI <23.0 kg/m^2). Obesity had a particularly increased effect on women who experienced early menopause than women who experienced late menopause for the risk of mortality from total and hemorrhagic stroke. Among ever smokers, the obese group showed significantly increased risks of mortality from total and ischemic stroke. However, no significant association between BMI and stroke mortality was observed among never smokers, except for hemorrhagic stroke. Further study is required to clarify whether obesity is an independent risk factor for mortality from hemorrhagic stroke and whether BMI, especially obesity, affects the incidence/death of subtypes of stroke differently according to smoking status or age at menopause.

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Disclosures

None.

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