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Sex Differences in Sleep-Disordered Breathing After Stroke: Results from the BASIC Project

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Abstract

Objective/Background—Sleep-disordered breathing (SDB), an independent risk factor for stroke, is associated with worse post-stroke outcomes. Differences in the relationship between SDB and stroke may exist for women versus men. In this population-based study, we compared the prevalence of both pre- and post-stroke SDB by sex. We also explored whether menopausal status is related to post-stroke SDB.

Patients/Methods—We performed a cross-sectional study of subjects enrolled in the Brain Attack Surveillance in Corpus Christi (BASIC) project. Each subject (n=1,815) underwent a baseline interview including the Berlin Questionnaire to assess pre-stroke SDB risk and, if relevant, questions regarding menopausal status. Subjects were offered overnight SDB screening with a validated portable respiratory device (n=832 with complete data). Log Poisson and linear regression models were used to assess the differences in SDB between men and women with adjustment for demographics, stroke risk factors, stroke severity, and other potential confounders.

Results—Women were less likely than men to be at high risk for pre-stroke SDB (56.6% versus 61.9%) (prevalence ratio [PR] 0.87 for women; 95% confidence interval [CI], 0.81–0.95). A lower proportion of women than men (50.8% versus 70.2%) had post-stroke SDB by respiratory monitoring (PR 0.71; 95% CI, 0.63–0.80). SDB severity was higher for men than for women (mean difference in respiratory event index [REI] 6.5; 95% CI, 4.3–8.7). No significant association existed between post-stroke SDB and either menopausal status or age at menopause.

Conclusions—After acute ischemic stroke, SDB was more prevalent and more severe in men than in women.

Keywords

stroke; gender; obstructive sleep apnea

Introduction

Sleep-disordered breathing (SDB) is highly prevalent in the United States, with moderate-to-severe sleep apnea affecting approximately 17% of men and 9% of women aged 50–70 years.¹ SDB is an independent risk factor for stroke. The most recent meta-analysis to address the effect of sleep apnea on incident stroke included ten prospective community-based, population-based, or clinic-based studies.² Across all studies, sleep apnea was

associated with a two-fold increased risk of incident stroke (relative risk [RR] 2.10; 95% confidence interval [CI], 1.50–2.93).

Furthermore, SDB is common after stroke³, and post-stroke SDB is associated with worse outcomes. A prospective study of 120 patients with acute stroke found that respiratory event index (REI) was positively associated with death (odds ratio [OR] 1.07; 95% CI, 1.03–1.12) and dependency (OR 1.06; 95% CI, 1.01–1.11) at six months after stroke.⁴ Another study of 132 patients in rehabilitation after acute stroke demonstrated a higher risk of death among subjects with SDB than among those without, after a mean of ten years of follow-up (adjusted hazard ratio [HR] 1.76; 95% CI, 1.05–2.95).⁵

Patients with post-stroke SDB appear to differ from people with SDB in the general population. For instance, at a given obstructive sleep apnea severity, stroke patients have a lower body mass index (BMI) than non-stroke patients⁶, and snoring and daytime somnolence poorly predict SDB in stroke patients.⁷ Furthermore, validated questionnaires that perform well in the general population perform poorly in assessing SDB risk in post-stroke patients. These differences suggest that the underlying physiology of SDB may differ in stroke patients than in non-stroke patients.

Inconsistent reports have raised the possibility that differences may exist in the relationship between SDB and stroke for women versus men. The community-based Sleep Heart Health Study (SHHS) followed 5,422 participants >40 years of age without a history of stroke for a median of 8.7 years.⁸ In adjusted analysis, the obstructive apnea-hypopnea index (OAH) was associated with incident ischemic stroke in men but not in women. On the other hand, an academic-based prospective cohort study in Spain followed 967 women referred for suspected SDB who were free of stroke and coronary heart disease for a median of 6.8 years.⁹ Subjects were divided into three groups: no SDB (AHI < 10), SDB with continuous positive airway pressure (CPAP) treatment (AHI ≥ 10 and average cumulative CPAP adherence ≥ four hours per day), and SDB without CPAP treatment (AHI ≥ 10 and average cumulative CPAP adherence < four hours per day). The risk of incident stroke in the women with SDB without CPAP treatment group was substantially higher than in the women without SDB (adjusted HR 6.44; 95% CI, 1.46–28.34), results that were divergent from the SHHS findings.

In addition, observational studies have suggested that SDB is more common in post-menopausal women than in pre-menopausal women¹⁰, and that hormone replacement therapy (HRT) may reduce the risk of SDB.^{11, 12} However, others have argued that the inverse relationship between SDB and HRT may represent a healthy user phenomenon.¹³ In short, the association between menopausal status and post-stroke SDB merits further study. If post-menopausal status were found to be a risk factor for post-stroke SDB, this may suggest a role for more intensive SDB screening in this population and would support further research into the effects of HRT on post-stroke SDB.

Here we present a population-based, cross-sectional study of acute ischemic stroke patients enrolled in the Brain Attack Surveillance in Corpus Christi (BASIC) project. We compared pre-stroke SDB risk based on a validated questionnaire for female versus male subjects. We

also compared the prevalence and severity of post-stroke SDB, as measured by overnight cardiopulmonary monitoring, in women versus men. We compared pre-stroke sleep duration for female versus male subjects given a potential positive association between increased sleep duration and stroke risk.¹⁴ Finally, we explored whether menopausal status was related to post-stroke SDB prevalence.

Materials and Methods

Subjects and Data Collection

The Brain Attack Surveillance in Corpus Christi (BASIC) project is a prospective cohort study of a bi-ethnic population of stroke patients based in Nueces County, Texas. The methods of BASIC data collection have been described in detail elsewhere.¹⁵ In brief, active and passive surveillance are used to identify acute ischemic and intracerebral hemorrhage (ICH) stroke patients >45 years of age who present to one of seven Corpus Christi community hospitals. Nueces County is geographically isolated and does not contain an academic medical center, allowing for thorough case capture of stroke patients. Case validation is performed by University of Michigan stroke fellowship-trained physicians. Subjects with ICH were excluded from the present analysis given our specific interest in the relationship between ischemic stroke and SDB.

Each subject (or proxy) underwent a baseline in-person interview during which information was collected regarding the subject's race/ethnicity, smoking status, and alcohol consumption. Information extracted from each subject's medical record included age, sex, history of stroke/transient ischemic attack (TIA), hypertension, diabetes mellitus, atrial fibrillation, coronary artery disease, high cholesterol, smoking status, height, weight, and initial National Institutes of Health stroke scale (NIHSS) score.

In July 2010 we began to administer the Berlin Questionnaire as part of the baseline interview. The Berlin Questionnaire consists of BMI determination and questions related to snoring, witnessed apneas, and daytime somnolence to stratify patients into high or low SDB risk. The determination of high-risk SDB status by the Berlin Questionnaire has a reported sensitivity of 86% and specificity of 77% for SDB in the general population.¹⁶ We also asked subjects or their proxies to report the subject's number of hours of sleep per night (sleep duration). The Berlin Questionnaire and sleep duration question were used to assess pre-stroke sleep characteristics.

In January 2012 we began to ask eligible female subjects questions related to menopausal status. These questions addressed history of hysterectomy and/or oophorectomy; timing and frequency of menstrual period; age at menopause; and use of HRT. Women who had not had a menstrual period in the prior twelve months were considered post-menopausal.¹⁷ Women who were still menstruating and having regular periods in the prior 12 months were considered pre-menopausal. Women who had had irregular periods and had gone 60 days without a period in the prior twelve months were considered peri-menopausal.¹⁸

BASIC subjects were offered SDB screening with the ApneaLink Plus device if they presented within 30 days of stroke when identified through active surveillance or within 45

days of stroke when identified through passive surveillance. Exclusion criteria for SDB screening included pregnancy, current mechanical ventilation or other positive pressure ventilation, and requirement for supplemental oxygen. ApneaLink Plus device placement was performed by trained study staff. We did not select by ischemic stroke subtype^{19, 20}, stroke severity^{21, 22}, and infarction location^{20, 23, 24} as these have largely not been shown to be associated with SDB in this and other populations. In addition, we did not exclude patients based on cognitive, speech, or language deficits. Surrogate consent was allowable.

ApneaLink Plus is a well-validated²⁵ home sleep apnea test that measures oxygen saturation, pulse, nasal pressure, and respiratory effort. Compared to manually-scored polysomnography (PSG), ApneaLink Plus shows a correlation of 0.935 for the apnea index, 0.852 for the obstructive apnea index, and 0.939 for the central apnea index.²⁶ BASIC subjects who consent to SDB screening undergo overnight screening in place, that is, in the hospital, in rehabilitation, or at home, with the same device regardless of setting.²⁷ Subjects who underwent SDB screening with the ApneaLink Plus device were considered our SDB substudy.

ApneaLink Plus data were analyzed by ApneaLink Plus software using the default setting used in successful validation studies, after raw data were edited by a registered polysomnographic technologist. The REI, defined as the sum of all apneas and hypopneas averaged over the duration of the recording in hours, was calculated for each subject in our SDB substudy. Based on the prevailing definition at the onset of the study, an apnea was defined as a 80% reduction from baseline in nasal pressure lasting at least ten seconds. A hypopnea was defined as a 30% reduction from baseline in nasal pressure lasting at least 10 seconds when followed by a reduction in oxygen saturation of at least 4%. If oximetry data were unavailable for a significant duration of the recording (a rare event, as we have previously reported²⁸), a hypopnea was defined as a 50% reduction from baseline in nasal pressure lasting at least 10 seconds. We conservatively defined SDB as an REI 10 based on data showing a specificity of 1.0 and sensitivity of 0.98 with ApneaLink at this threshold when compared to standard overnight PSG.²⁹

The University of Michigan and each Nueces County hospital's institutional review board approved this project. Written informed consent for study participation was obtained from each subject or, if the subject was unable to personally consent, from his or her designated surrogate.

Statistical Methods

We used descriptive statistics to compare the distribution of demographics and risk factors by sex. We used log Poisson models to compare the prevalence of being high-risk for pre-stroke SDB based on the Berlin Questionnaire for men versus women and to compare the prevalence of post-stroke SDB (as defined by an REI 10) for men versus women. Models were run unadjusted and adjusted for pre-specified potential confounders including age, race/ethnicity, current smoking, alcohol intake (categorical: <1, 1–14, >14 drinks per week, with does not drink as the referent), hypertension, diabetes, high cholesterol, atrial fibrillation, previous stroke/TIA, BMI category (modeled as a categorical variable with non-overweight/non-obese as the referent), and NIHSS score at presentation. To compare

continuous REI and sleep duration for women versus men we used linear regression models and performed both unadjusted and adjusted analyses, as above.

To compare post-stroke SDB prevalence by menopausal status (with pre-menopausal and peri-menopausal combined as the referent) and age at natural menopause, we used log binomial models, both unadjusted and adjusted for age, race/ethnicity, and BMI category.

All statistical analyses were performed using SAS version 9.3.

Results

Subjects

During the study period (July 2010 to May 2016), 2,624 ischemic stroke patients were approached for a baseline interview. Of these, 1,815 (69.2%) agreed to be interviewed and therefore completed the Berlin Questionnaire. Interviews were obtained by proxy in 560 (30.9%). Of 1,378 eligible subjects, 968 (70.2%) consented to overnight SDB screening. Complete SDB screening data were available for 898 participants. We excluded 66 cases with race/ethnicity other than Mexican-American (MA) or non-Hispanic White (NHW), given that the small number of cases would preclude adjustment for “other” race/ethnicity in the multivariable model. We had 832 (392 female, 440 male) cases for this analysis. Interviews were obtained by proxy in 113 (13.6%) in this subset.

The baseline characteristics of the interview participants (n=1,815) are shown in Table 1. Baseline subject data for our SDB substudy subjects (n=832) are shown in Table 2. Overall our total interview sample was 50% female and 58% MA; our SDB substudy was 47% female and 65% MA. In our total interview sample, median age was higher in women (71 years; interquartile range (IQR), 60–82) than in men (66 years; IQR, 59–77, $P<0.001$). There was no significant difference in median age in our SDB study subset. The proportion of MAs was not significantly different for men versus women in our baseline interview sample or our SDB substudy.

In our baseline interview sample, a greater proportion of men than women were current smokers (28.1% compared to 15.7%, $p<0.001$). Alcohol use was significantly different between men and women ($p<0.001$), with fewer men abstaining (18.4% compared to 26.2%), more men drinking 1 to 14 drinks per week (31.9% compared to 14.7%), and more men drinking greater than 14 drinks per week (10.4% compared to 1.3%). Coronary artery disease was higher in men than women (35.7% versus 24.6%, $p<0.001$). Atrial fibrillation was less prevalent in men than women (13.9% versus 17.2%, $p=0.049$). There was no significant difference between men and women in the prevalence of diabetes, high cholesterol, hypertension, and history of stroke/TIA. Median baseline NIHSS was 4 (IQR 1–8) for men and 4 (IQR 2–10) for women. The average BMI for men was lower than that for women (median 27.5 versus 28.5, $p=0.003$). In addition, the distribution of BMI category was different for men versus women ($p<0.001$). A greater proportion of men than women were overweight (40.7% versus 29.5%) whereas a smaller proportion of men were obese (33.2% versus 43.4%).

Pre-Stroke SDB Risk and Post-Stroke SDB

In our full baseline interview sample, women were less likely than men to be at high risk for pre-stroke SDB by the Berlin Questionnaire in both unadjusted analysis (prevalence ratio [PR] 0.91 for women; 95% CI, 0.85–0.99) and adjusted analysis (PR 0.87 for women; 95% CI, 0.81–0.95) (Table 3). Sleep duration was not significantly different between men and women in unadjusted analysis. However, in adjusted analysis, women reported an average of 0.22 (95% CI, 0.02–0.41) fewer hours of sleep than men. In our SDB substudy population, we found no significant difference between men and women in pre-stroke sleep duration in unadjusted or adjusted analysis (Table 4). We found no significant difference between men and women in being high risk for pre-stroke SDB based on the Berlin Questionnaire in unadjusted analysis. However, after adjustment the association was borderline significant and was attenuated compared to the full interview sample (PR 0.90; 95% CI, 0.80–1.00).

Prevalence of post-stroke SDB as defined by REI ≥ 10 on overnight respiratory monitoring differed significantly between men and women (Table 4). A lower proportion of women than men had post-stroke SDB in both unadjusted analysis (PR 0.72; 95% CI, 0.64–0.81) and adjusted analysis (PR 0.71; 95% CI, 0.63–0.80). In addition, mean REI was higher for men than for women in both unadjusted analysis (18 versus 11, mean difference in REI 5.6; 95% CI, 3.5–7.7) and adjusted analysis (mean difference 6.5; 95% CI, 4.3–8.7). The central apnea index was very low in both sexes but higher in men (mean 2.6) than in women (1.13) (mean difference 1.48; 95% CI, 0.88–2.07).

Menopausal Status

Of the 392 women with complete SDB screening data, 89 were enrolled in the project before we began to ask questions pertaining to menopause status in January 2012. Of the remaining 303, 42 were excluded due to proxy interview; and 8 were excluded for missing data. After excluding 61 subjects who had both ovaries removed, 192 (154 post-menopausal, 33 pre-menopausal, and five peri-menopausal) subjects had data regarding their natural menopause and were included in our analysis. We found no significant association between menopausal status and post-stroke SDB or between age at menopause and post-stroke SDB, in both unadjusted and adjusted analyses (Table 5).

Discussion

Data from this sizeable population-based sample suggest that men in comparison to women have a higher prevalence of elevated SDB risk prior to acute ischemic stroke, more frequent objective evidence of SDB after stroke, and a higher mean REI after stroke, both before and after controlling for multiple potential confounders. We found that 70% of male subjects and 51% of female subjects who underwent a SDB screening study had post-stroke SDB (REI ≥ 10). These findings are consistent with previous studies that have found a high prevalence of SDB shortly after stroke.³ While men had a higher prevalence of SDB, one out of every two women in our study had SDB. These data suggest a role for SDB screening in acute stroke patients, regardless of sex.³¹

Prior small studies comparing the prevalence of post-stroke SDB in men versus women have shown inconsistent results, although the preponderance found no difference. Three prior studies did not find significant differences in post-stroke SDB prevalence by sex, although the largest of these studies included only 128 subjects.^{3, 7, 20} On the other hand, a prospective study of 293 post-stroke subjects who underwent screening with the ApneaLink device found a higher prevalence of SDB in men compared to women.²⁴ This study extends the literature by studying a larger, population-based sample and by documenting a sex difference in pre-stroke SDB risk.

Our findings are consistent with reported sex differences in SDB prevalence in non-stroke populations, where moderate-to-severe SDB is approximately twice as prevalent in men compared to women.¹ However, SDB predominance in men appears to attenuate with increasing age, with the incidence of SDB in men versus women equalizing at 50 years in one study.³⁰ The median age of our study population was 65 years, suggesting that the relationship between SDB and age may differ for men and women with acute ischemic stroke when compared to men and women in the general population. Further supporting a unique relationship between stroke and SDB, previous research has shown that predictors of SDB in the general population are not strong predictors of SDB in post-stroke patients.^{6,7}

Prior studies in this and other communities have shown that women have worse functional outcomes after stroke than men.^{32–36} Given that women had less frequent and less severe SDB after stroke, our findings suggest that differences in post-stroke SDB prevalence are unlikely to contribute to women's worse outcomes. However, differences in SDB screening and treatment may nonetheless play a role in sex outcome disparities. In addition, the impact of SDB on outcomes may differ by sex and this warrants additional study.

Prior studies have suggested that SDB is more common in post-menopausal women than in pre-menopausal women.¹⁰ In this study we found no significant association between menopausal status and prevalence of post-stroke SDB or between age at natural menopause and prevalence of SDB. The somewhat limited number of female subjects eligible for our menopausal status analysis may have limited our ability to detect a statistical difference in SDB by menopausal status, although our results did not suggest a strong association.

The strengths of our study include our large, population-based design, use of validated measurement tools, and high proportion of MA subjects. Our study also has several limitations, however. Use of a questionnaire to define high SDB risk retrospectively prior to stroke, and objective cardiopulmonary monitoring to define SDB after stroke, does not allow valid comparisons of SDB prevalence from before to after stroke. The subjective nature of the questionnaire raises concerns about accurate assessment of SDB risk, though we note that determination of high-risk status by the Berlin Questionnaire has a reported sensitivity of 86% and specificity of 77% for SDB in the general population.¹⁶ Although we used the Berlin Questionnaire in post-stroke patients, it was with respect to the pre-stroke state, and thus should approximate performance in the general population. Despite its strengths, the Berlin Questionnaire may overestimate the prevalence of SDB in men compared to women given the higher prevalence of simple snoring in men. Furthermore, to assess SDB we used a portable respiratory monitor rather than gold standard PSG. However, we would not expect

potential measurement error to differ by sex. As a cross-sectional study, inferences regarding the causal effect of stroke on SDB and vice versa are limited, although this was not the purpose of our study. The high prevalence of MAs in our study population may make our results less generalizable to other populations.

Summary/Conclusions

In conclusion, in a population-based sample of acute ischemic stroke patients, post-stroke SDB was more prevalent and more severe in men than in women. Differences in menopausal status and age at menopause were not associated with SDB prevalence in women with acute ischemic stroke.

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Table 1

Characteristics of the baseline interview participants overall and by sex.

	Overall (n=1,815) n (%) or median (Q1, Q3)	Females (n=911) n (%) or median(Q1, Q3)	Males (n=904) n (%) or median(Q1, Q3)	P value
Age (y)	68.0 (59.0, 80.0)	71.0 (60.0, 82.0)	66.0 (59.0, 77.0)	< 0.001
Race/Ethnicity				0.2334
NHW	626 (34.5)	310 (34.0)	316 (35.0)	
MA	1054 (58.1)	537 (59.0)	517 (57.2)	
Black	95 (5.2)	50 (5.5)	45 (5.0)	
Other	40 (2.2)	14 (1.5)	26 (2.9)	
Current smoker	397 (21.9)	143 (15.7)	254 (28.1)	< 0.001
Alcohol use (drinks per week)				< 0.001
Does not drink	405 (22.3)	239 (26.2)	166 (18.4)	
< 1	881 (48.6)	526 (57.7)	355 (39.3)	
1–14	422 (23.3)	134 (14.7)	288 (31.9)	
> 14	106 (5.8)	12 (1.3)	94 (10.4)	
Diabetes Mellitus	868 (48.4)	421 (46.8)	447 (50.0)	0.179
High cholesterol	869 (48.5)	446 (49.7)	423 (47.3)	0.320
Atrial Fibrillation	279 (15.6)	155 (17.2)	124 (13.9)	0.049
Hypertension	1474 (82.2)	739 (82.2)	894 (82.1)	0.995
Coronary Artery Disease	540 (30.2)	221 (24.6)	319 (35.7)	< 0.001
History of stroke/TIA	521 (29.1)	278 (30.9)	243 (27.2)	0.081
NIHSS*	4.0 (2.0, 9.0)	4.0 (2.0, 10.0)	4.0 (1.0, 8.0)	0.015
BMI (kg/m ²)	28.1 (24.8, 32.8)	28.5 (24.7, 34.2)	27.5 (24.8, 31.7)	0.003
BMI category				< 0.001
Normal weight (<25)	483 (26.6)	248 (27.2)	235 (26.0)	
Overweight (25–29.9)	637 (35.1)	269 (29.5)	368 (40.7)	
Obesity class 1 (30–34.9)	370 (20.4)	189 (20.8)	181 (20.0)	
Obesity class 2 (35–39.9)	194 (10.7)	106 (11.6)	88 (9.7)	
Obesity class 3 (≥ 40)	131 (7.2)	99 (10.9)	32 (3.5)	

NHW=non-Hispanic white; MA = Mexican-American; TIA = transient ischemic attack; NIHSS= National Institutes of Health Stroke Scale; BMI = body mass index

Table 2

Characteristics of subjects in the SDB study subset, overall and by sex (n = 832).

	Overall n (%) or median (Q1, Q3)	Females (n=392) n (%) or median(Q1, Q3)	Males (n=440) n (%) or median(Q1, Q3)	P value
Age (y)	65.0 (57.0, 76.0)	66.0 (57.0, 78.0)	64.0 (58.0, 73.0)	0.060
Race/Ethnicity (MAs)	540 (64.9)	256 (65.3)	284 (64.6)	0.818
Current smoker*	201 (24.2)	69 (17.6)	132 (30.1)	< 0.001
Alcohol use* (drinks per week)				< 0.001
Does not drink	174 (21.0)	104 (26.5)	70 (16.0)	
< 1	370 (44.6)	218 (55.6)	152 (34.8)	
1–14	226 (27.3)	63 (16.1)	163 (37.3)	
> 14	59 (7.1)	7 (1.8)	52 (11.9)	
Diabetes Mellitus	427 (51.3)	201 (51.3)	226 (51.4)	0.980
High cholesterol	424 (51.0)	209 (53.5)	215 (48.9)	0.187
Atrial Fibrillation	98 (11.8)	52 (13.3)	46 (10.5)	0.209
Hypertension	679 (81.6)	311 (79.3)	368 (83.6)	0.110
Coronary Artery Disease	243 (29.2)	91 (23.2)	152 (34.6)	< 0.001
History of stroke/TIA	235 (28.3)	114 (29.1)	121 (27.5)	0.613
NIHSS*	3.0 (1.0, 7.0)	4.0 (1.0, 7.0)	3.0 (1.0, 6.0)	0.641
BMI (kg/m ²)	28.6 (25.1, 33.2)	29.3 (25.2, 34.4)	27.9 (25.1, 32.0)	0.002
BMI category				< 0.001
Normal weight (<25)	198 (23.8)	92 (23.5)	106 (24.1)	
Overweight (25–29.9)	289 (34.7)	115 (29.3)	174 (39.6)	
Obesity class 1 (30–34.9)	195 (23.4)	93 (23.7)	102 (23.2)	
Obesity class 2 (35–39.9)	89 (10.7)	44 (11.2)	45 (10.2)	
Obesity class 3 (≥ 40)	61 (7.3)	48 (12.2)	13 (3.0)	

Table 3

Associations between sex (female versus male) and high-risk SDB, based on the Berlin Questionnaire and sleep duration for the baseline interview participants.

	Overall (n=1,775) frequency (%) or median [Q1, Q3]	Females (n=897) frequency (%) or median [Q1, Q3]	Males (n=878) frequency (%) or median [Q1, Q3]	Unadjusted PR (95% CI) or Mean Difference [95% CI]	Adjusted* PR (95% CI) or Mean Difference [95% CI]
High risk for SDB (Berlin)	1,052 (59.3)	508 (56.6)	544 (61.9)	0.91 (0.85, 0.99)	0.87 (0.81, 0.95)
Sleep Duration (hours)	8.0 [6.0, 8.0]	8.0 [6.0, 8.0]	8.0 [6.0, 8.0]	-0.096 [-0.284, 0.092]	-0.215 [-0.414, -0.016]

SDB = sleep-disordered breathing; PR = prevalence ratio

* Adjusted for age, race/ethnicity, current smoking, alcohol intake, diabetes, high cholesterol, atrial fibrillation, hypertension, previous stroke/TIA, NIHSS, BMI

Table 4

Associations between sex (female versus male) and high-risk for SDB based on Berlin Questionnaire, pre-stroke sleep duration, post-stroke SDB, and post-stroke continuous REI for the SDB substudy.

	Overall frequency (%) or median [Q1, Q3]	Females frequency (%) or median [Q1, Q3]	Males frequency (%) or median [Q1, Q3]	Unadjusted PR (95% CI) or Mean Difference [95% CI]	Adjusted* PR (95% CI) or Mean Difference [95% CI]
High risk for pre-stroke SDB (Berlin) (n=832)	504 (60.6)	227 (57.9)	277 (63.0)	0.92 (0.82, 1.03)	0.90 (0.80, 1.00)
Pre-stroke sleep duration (n=821)	8.0 [6.0, 8.0]	7.0 [6.0, 8.0]	8.0 [6.0, 8.0]	-0.17 [-0.44, 0.10]	-0.21 [-0.50, 0.08]
Post-stroke SDB (REI 10) (n=832)	508 (61.1)	199 (50.8)	309 (70.2)	0.72 (0.64, 0.81)	0.71 (0.63, 0.80)
Post-stroke REI (n=832)	14.0 [7.0, 26.0]	11.0 [6.0, 21.0]	18.0 [8.5, 32.0]	-5.59 [-7.70, -3.48]	-6.52 [-8.70, -4.33]

SDB = sleep-disordered breathing; REI=respiratory event index; PR = prevalence ratio

* Adjusted for age, race/ethnicity, current smoking, alcohol intake, diabetes, high cholesterol, atrial fibrillation, hypertension, previous stroke/TIA, NIHSS, BMI

Table 5

Association between menopausal features and post-stroke SDB (REI ≥ 10).

	Unadjusted PR (95% CI)	Adjusted* PR (95% CI)
Post-menopause (vs pre- & peri-menopausal) (n=192)	1.132 (0.77, 1.67)	1.096 (0.75, 1.61)
Age at menopause (n=149)	1.014 (0.99, 1.03)	1.010 (0.99, 1.03)

SDB = sleep-disordered breathing; REI=respiratory event index; PR = prevalence ratio

* Adjusted for age, race/ethnicity, and BMI