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Original Contribution

Sleep-disordered Breathing and Frailty in the Cardiovascular Health Study Cohort

Yohannes W. Endeshaw, Mark L. Unruh, Michael Kutner, Anne B. Newman, and Donald L. Bliwise

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Sleep-disordered breathing (SDB) is associated with pathophysiology that may influence the development and progression of frailty. Using data collected in 1995–1996, the authors explored the relation between SDB and components of frailty among 1,042 participants of the Cardiovascular Health Study. Diagnosis of SDB was based on the results of overnight polysomnography, and severe SDB was defined as an apnea-hypopnea index of >30 per hour of sleep. Slow walking speed, low grip strength, exhaustion, low physical activity, and unexplained weight loss were referred to as frailty indicator variables. There were 584 (56%) female and 458 (44%) male participants, and the mean age was 77 (standard deviation, 4) years. There was independent association between severe SDB and 1 or more frailty indicator variables (adjusted odds ratio = 4.85, 95% confidence interval: 1.40, 16.78), slow walking speed (adjusted odds ratio = 2.67, 95% confidence interval: 1.04, 6.84), and low grip strength (adjusted odds ratio = 3.29, 95% confidence interval: 1.36, 7.96) among female study participants. The finding of an independent association between SDB and frailty indicator variables among older women could have important implications in interventions aimed at preventing or delaying the progression of frailty.

frailty; hand strength; mobility limitation; muscle strength; sleep apnea syndromes; weight loss

Abbreviation: SDB, sleep-disordered breathing.

Sleep-disordered breathing (SDB) is a common disorder among community-dwelling older adults, with the prevalence of a moderate-to-severe form of the disease estimated to be 20% among those ≥60 years of age (1). This disorder is characterized by periods of apnea and hypopnea that often result in intermittent arousals from sleep and oxygen desaturations. These episodes of arousals and oxygen desaturations have multiple consequences, such as increased sympathetic activity (2), activation of certain inflammatory pathways (3), and endothelial dysfunction (4), which are reported to mediate the adverse effects of SDB on the different organ systems. Among young and middle-aged adults, SDB has been described to be associated with cardiovascular diseases such as hypertension (5) and coronary artery disease (6), stroke (7), and metabolic abnormalities such as impaired glucose tolerance (8). However, the contribution of SDB to morbidity and mortality in older adults (aged >65 years) is not well characterized, with only a few studies reporting significant associations between SDB and increased disease burden (9–11).

Because SDB causes hormonal, inflammatory, and metabolic abnormalities that favor catabolic activities (12, 13), it could contribute to the development and progression of frailty. Frailty, a condition characterized by a decrease in physiologic reserve and increased risk for adverse health-related outcomes, is a common condition among older adults (14). It is a construct based on impairment of 5 physiologic domains, which include mobility, balance, muscle strength, physical activity, and endurance, and on nutrition, and it is considered to have multifactorial etiology (15). Frailty is also regarded to be the final common pathway in the development of disability, institutionalization, and death among older adults (16). In order to further understand the relevance of the high prevalence of SDB in older adults, this report examines the relation between SDB and impairment in physiologic domains comprising frailty. In this study, we explored the association between SDB and the frailty-related characteristics in community-dwelling older adults. We hypothesized that older adults with SDB would have impaired mobility, reduced muscle strength, decreased

Correspondence to Dr. Yohannes W. Endeshaw, Division of Geriatrics and Gerontology, Department of Medicine, Emory University School of Medicine, 1841 Clifton Road NE, No. 535, Atlanta, GA 30329 (e-mail: yendesh@emory.edu).

Table 1. Characteristics of Excluded and Included Study Participants ($N = 1,248$), Cardiovascular Health Study, 1995–1996

Characteristic	Not Included in Current Analysis ($n = 206$)		Included in Current Analysis ($n = 1,042$)		Total ($N = 1,248$)	
	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%
Age, years	77 (5)		77 (4)		77 (5)	
Gender						
Female		62		56		57
Male		38		44		43
Race**						
African American		27		17		18
Caucasian		73		83		82
Marital status						
Currently married		65		71		70
Currently not married		35		29		30
Education, years						
0–11		25		20		22
12–15		52		55		54
≥16		23		25		24
No. of prescription medications*	4 (3)		3 (2)		3 (3)	
Body mass index, kg/m^2 [a]	27 (5)		27 (4)		27 (5)	
≥2 cardiovascular morbidities		16		13		13
≥1 ADL disabilities***		34		15		18
Apnea-hypopnea index >30[a]		12		12		12
Slow walking speed***[a]		35		20		22
Low grip strength[a]		25		25		25

Abbreviations: ADL, activities of daily living; SD, standard deviation.

* $P < 0.01$; ** $P < 0.001$; *** $P < 0.0001$.

[a] Not included in the current analysis were body mass index ($n = 128$), apnea-hypopnea index >30 ($n = 140$), slow walking speed ($n = 113$), and lost grip strength ($n = 80$).

endurance and physical activity, and unexplained weight loss.

MATERIALS AND METHODS

Study populations

Data were derived from 2 partially overlapping epidemiologic studies, the Cardiovascular Health Study and the Sleep Heart Health Study. The design and protocol of these studies are previously described in detail elsewhere (17, 18) but are briefly outlined below. The Cardiovascular Health Study is a community-based, prospective study of older adults aged ≥65 years established in 1988. The main objective of the study is to identify the risk factors associated with the onset and progression of cardiovascular disease. A total of 5,888 (3,393 women, 2,495 men) community-dwelling older adults from 4 communities (Forsyth County, North Carolina; Sacramento County, California; Washington County, Maryland; and Pittsburgh, Pennsylvania) were recruited. Demographic and clinical data, including information related to frailty, were collected at intervals of 1–2 years. The Sleep Heart Health Study is also a community-based, prospective study that started in 1994, and its primary objective is to determine if SDB defined by polysomnography is associated with increased risk of coronary heart disease, stroke, and mortality. Study participants for the Sleep Heart Health Study were recruited from previously established epidemiologic cohorts that included 3 of the 4 Cardiovascular Health Study communities (Sacramento County, California; Washington County, Maryland; and Pittsburgh, Pennsylvania). These 3 sites contributed 1,248 (716 female and 532 male) subjects. Because baseline polysomnography in the Sleep Heart Health Study was performed in 1995–1996, we relied upon clinical data collected by the Cardiovascular Health Study during the same period of time (1995–1996, year 8).

Frailty-related measures

Components of frailty that were included in this study are slow walking speed, low grip strength, exhaustion, low physical activity, and unexplained weight loss (14, 19). For the purpose of this study, these individual components of frailty are referred to as ''frailty indicator variables.'' Walking speed was measured by the time it took to walk

Table 2. Distribution of Demographic and Frailty Indicator Variables in Female and Male Study Participants, Cardiovascular Health Study, 1995–1996[a]

Variable	Females (n = 588)		Males (n = 454)		Total (N = 1,042)		Comparison[b]	
	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	*P* Value	χ^2 Value
Age, years	76.4 (4.3)		76.7 (4.5)				0.208	
Race[c]								
White		82		84		83	0.412	
Black		17		15		16		
Slow walking speed[d]		23		17		20	0.030	4.69
Low grip strength[e]		27		23		25	0.091	2.86
Low physical activity[f]		20		20		20	0.799	0.07
Exhaustion		21		17		19	0.117	2.47
Unexplained weight loss		9		8		8	0.49	0.48
No. of frailty indicator variables							0.033	6.83
0		39		47		43		
1–2		52		35		49		
≥3		9		8		8		

Abbreviation: SD, standard deviation.

[a] Study participants with values higher than the cutoff values for walking speed and lower than the cutoff points for grip strength and physical activity were considered to have slow walking speed, low grip strength, and low physical activity, respectively (13).

[b] Mann-Whitney test for continuous variables and chi-square test for categorical variables.

[c] Race = other in 6 participants.

[d] Cutoff values (14)—men with height ≤173 cm = 7 seconds and >173 cm = 6 seconds; women with height ≤159 cm = 7 seconds and >159 cm = 6 seconds.

[e] Cutoff values—men with body mass index ≤24 kg/m^2 = 29 kg, 24.1–26 kg/m^2 = 30 kg, 26.1–28 kg/m^2 = 30 kg, and >28 kg/m^2 = 32 kg; women with body mass index ≤23 kg/m^2 = 17 kg, 23.1–26 kg/m^2 = 17.3 kg, 26.1–29 kg/m^2 = 18 kg, and >29 kg/m^2 = 21 kg.

[f] Cutoff values—men: 382 kcal/week; women: 270 kcal/week.

15 feet (4.572 m) at a usual pace (20), and grip strength was measured in the dominant hand by a hand-held JAMAR dynamometer set at level 2 (Patterson Medical Products, Inc., Bolingbrook, Illinois) (20). For grip strength, a total of 3 attempts in maximal effort were performed, and the average value in kilograms was recorded. Physical activity was derived from the Modified Minnesota Leisure Time Activities questionnaire, which was based on whether a person performed any of the 18 activities and the frequency and duration of these activities in the prior week (21). Cutoff values for walking speed (adjusted for gender and height), grip strength (adjusted for gender and body mass index), and physical activity (adjusted for gender) were used as described by Fried et al. (14). Walking speed cutoff values for men with a height of ≤173 cm and >173 cm were 7 seconds and 6 seconds, respectively, and for women with a height of ≤159 cm and >159 cm, they were 7 seconds and 6 seconds, respectively. Grip strength cutoff values for men with a body mass index of ≤24, 24.1–26, 26.1–28, and >28 kg/m^2 were 29 kg, 30 kg, 30 kg, and 32 kg, respectively; for women with a body mass index of ≤23, 23.1–26, 26.1–29, and >29 kg/m^2, the values were 17, 17.3, 18, and 21 kg, respectively. Cutoff points for physical activity were 382 kcal/week and 270 kcal/week for men and women, respectively. Study participants with values higher than the cutoff values for walking speed and lower than the cutoff points for grip strength and physical activity were considered to have a slow walking speed, low grip strength, and low physical activity, respectively. Because Cardiovascular Health Study data on physical activity were not collected during the 1995–1996 cycle (year 8), we utilized the data obtained in 1992–1993 (year 5). The presence of exhaustion was determined by positive responses to 2 questions from the Center for Epidemiologic Studies Depression Scale questionnaire (''I felt that everything I did was an effort'' and ''I could not get going'') (22). Study participants who reported either of these symptoms 3 or more days of the week (choices were less than 1 day, 1–2 days, 3–4 days, and 5–7 days per week) were considered as having exhaustion. Unintentional weight loss was defined as self-reported weight loss of >10 pounds in the preceding year, with no dietary changes, exercise, illness, surgery, or medications as the indicated reasons for losing weight.

Sleep-related data

Self-reported sleep complaints were obtained from sleep-related questionnaires, and objective sleep data were derived from the result of a single night's polysomnography performed in the homes of study participants (Compumedics

Table 3. Selected Clinical and Sleep-related Characteristics by Gender, Cardiovascular Health Study, 1995–1996

Variable	Females (n = 588)		Males (n = 454)		Total (N = 1,042)		Comparison[a]	
	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	*P* Value	χ^2 Value
Obese (body mass index[b] ≥30)		27		19		23	0.001	8.79
≥2 cardiovascular/cerebrovascular morbidities		12		14		13	0.406	
Low 3MSE score		11		12		12	0.587	
Use of antidepressant medications		6		5		5	0.502	
Use of ≥5 prescription medications		23		20		22	0.289	
Epworth Sleepiness Scale score	6.6 (4.1)		8.0 (4.4)		7.0 (4.0)		<0.001	
Sleep-related complaints		21		13		18	<0.001	10.94
Sleep time, %								
Stage 1	4.5 (3.4)		7.4 (5.6)		5.8 (4.7)		<0.001	
Stage 2	53.6 (12.6)		63.1 (11.3)		57.7 (12.9)		<0.001	
Stages 3 and 4	23.1 (12.9)		11.4 (10.5)		17.9 (13.3)		<0.001	
Rapid eye movement stage	18.8 (6.6)		18.1 (6.7)		18.5 (6.6)		0.092	
Sleep efficiency[c]	80.8 (11.3)		77.7 (11.2)				<0.001	
Total apnea-hypopnea index	12.5 (11.2)		18.9 (15.2)		15.3 (13.4)		<0.001	
Central apnea index	0.3 (1.6)		1.6 (4.9)		0.9 (3.6)		<0.001	
Time in oxygen saturation <90%, %	3.8 (10.1)		5.5 (13.5)		4.5 (11.8)		0.022	
Apnea-hypopnea index >30		7		18		12	<0.001	26.15

Abbreviations: 3MSE, Modified Mini-Mental State Examination; SD, standard deviation.
[a] Mann-Whitney test for continuous variables and chi-square test for categorical variables.
[b] Weight (kg)/height $(m)^2$.
[c] Sleep efficiency = total sleep time divided by total time in bed (recording time).

P Series System; Abbotsford, Victoria, Australia). Difficulty initiating sleep was defined as self-reported sleep latency of >30 minutes or trouble falling asleep more than 15 days per month, whereas difficulty maintaining sleep was defined as waking up from sleep and difficulty going back to sleep or waking up too early in the morning more than 15 days per month (choices were never or rarely, 2–4 days, 5–15 days, and ≥16 days per month). Participants with either difficulty initiating or maintaining sleep were considered to have sleep-related complaints. Procedures for the performance and scoring of polysomnography in the Sleep Heart Health Study are described in greater detail elsewhere (18), but in brief, recordings included an electroencephalogram, electrooculogram, chin electromyogram, thoracic and abdominal movement, nasal-oral airflow, and finger pulse oximetry. Scoring of sleep stages and apnea and hypopnea events was performed by standard procedures (23). The apnea-hypopnea index, indicating the number of apneas and hypopneas per hour of sleep, was utilized to determine the severity of SDB. Apnea was defined as a decrease in the amplitude of air flow to ≤25% of the amplitude of the baseline breathing for ≥10 seconds associated with at least a 4% decrease in oxygen saturation or arousal from sleep, and hypopnea was defined as a decrease in the amplitude of airflow to less than 70% of the amplitude of baseline breathing for ≥10 seconds associated with at least a 4% decrease in oxygen saturation or arousal from sleep. Severe SDB was defined as an apnea-hypopnea index of >30 per hour of sleep. In addition, the percentage of sleep time spent in oxygen saturation of less than 90% was used to quantify the severity of oxygen desaturation.

Other variables

Demographic and clinical variables previously reported to show an independent association and included in this analysis are described below (24, 25). Body mass index was calculated as weight (kilograms) divided by height (m^2), and daytime sleepiness was assessed with the Epworth Sleepiness Scale. Subjects were asked to transcribe the names of medications that were prescribed to them by their doctor on a data-collection form, and this information was used to determine the number of prescription medications used by each participant (26). A history of hypertension, diabetes mellitus, congestive heart failure, myocardial infarction, atrial fibrillation, stroke, and transient ischemic attack was used to determine cardiovascular and cerebrovascular disease status, and participants with 2 or more of these conditions were considered to have significant cardiovascular or cerebrovascular disease. Cognition status was determined on the basis of the Modified Mini-Mental State Examination score and adjusted for age and educational status. Study participants whose adjusted score was below the 25th percentile were considered to have a low Modified Mini-Mental State Examination score. Use of tricyclic

Table 4. Logistic Regression Model Predicting 1 or More Frailty Indicator Variables, Cardiovascular Health Study, 1995–1996

Sex and Variable	Logistic Regression Model			
	Univariate		Multivariate	
	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval
Women				
Severe sleep-disordered breathing (apnea-hypopnea index: $\leq 30 = 0$, $>30 = 1$)	2.58	1.21, 5.48	4.85	1.40, 16.78
Age, years			1.08	1.03, 1.13
Race (Caucasians = 0, African Americans = 1)			1.29	0.78, 2.16
Obesity (body mass index $<30 = 0$, $\geq 30 = 1$)			2.90	1.82, 4.61
Cardiovascular/cerebrovascular disease			1.23	0.69, 2.19
Low 3MSE score			1.53	0.82, 2.83
Use of antidepressants			1.59	0.70, 3.59
Obesity × severe sleep-disordered breathing[a]			0.13	0.03, 0.68
Men				
Severe sleep-disordered breathing (apnea-hypopnea index: $\leq 30 = 0$, $>30 = 1$)	1.18	0.73, 1.92	1.08	0.58, 2.00
Age, years			1.08	1.03, 1.13
Race (Caucasians = 0, African Americans = 1)			4.78	2.48, 9.22
Obesity (body mass index $<30 = 0$, $\geq 30 = 1$)			1.98	1.08, 3.63
Cardiovascular/cerebrovascular disease			1.90	1.06, 3.41
Low 3MSE score			1.79	0.91, 3.52
Use of antidepressants			1.52	0.59, 3.95
Obesity × severe sleep-disordered breathing[a]			0.78	0.23, 2.65

Abbreviation: 3MSE, Modified Mini-Mental State Examination.

[a] Other interaction terms (age × sleep-disordered breathing, race × sleep-disordered breathing) not statistically significant. Adjusted odds ratio for sleep-disordered breathing stratified by obesity status—nonobese: odds ratio = 4.77 (95% confidence interval: 1.34, 16.54); obese: odds ratio = 0.61 (95% confidence interval: 0.21, 1.82).

antidepressants or serotonin reuptake inhibitors was used to indicate depression. A score for the activities of daily living was determined by using a modified version of the Health Interview Survey Supplement on Aging questionnaire (27), and individuals who required assistance to get out of bed, eat, dress, use the toilet, bathe, and walk around their home were considered to have activities of daily living disability.

Statistical analysis

Of a total of 5,888 individuals that participated in the Cardiovascular Health Study, 1,248 (21%) were recruited for the Sleep Heart Health Study and underwent overnight polysomnography; 1,042 of the 1,248 participants (83%) for whom information on all 5 of the frailty indicator variables and on the apnea-hypopnea index was available were included in the analysis. The characteristics of those who were included and not included in the current analysis are shown in Table 1.

To determine the relation between SDB and frailty indicator variables, we categorized participants into 2 groups based on their apnea-hypopnea index of >30 (severe SDB) and ≤ 30 (without severe SDB). The chi-square for categorical variables and Mann-Whitney tests for continuous variables were used to determine the statistical significance of differences in the distribution of demographic and clinical characteristics between those with and without severe SDB. A series of logistic regression analyses were performed with 1 or more frailty indicator variables, slow walking speed, or low grip strength as dependent variables and severe SDB as the independent variable. Demographic and clinical variables that have been reported to have significant associations with frailty, such as age in years, gender, racial group, obesity (body mass index, ≥ 30 kg/m^2), cardiovascular or cerebrovascular disease, Modified Mini-Mental State Examination score, and use of antidepressant medication, were included in the model as covariates. Clinical variables, such as daytime sleepiness and sleep-related complaints, were not included as covariates, as they were considered to be in the putative ''causal pathway'' in the relation between SDB and the frailty indicator variables. Relevant interaction terms, which included age × SDB, race × SDB, and obesity × SDB, were created and added to the model one at a time, and interaction terms that significantly contributed to the model were retained. Because differences in severity of SDB have been described in females and

Table 5. Logistic Regression Model Predicting Slow Walking Speed, Cardiovascular Health Study, 1995–1996

Sex and Variable	Logistic Regression Model			
	Univariate		Multivariate	
	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval
Women				
Severe sleep-disordered breathing (apnea-hypopnea index $\leq 30 = 0$, $>30 = 1$)	2.99	1.58, 5.66	2.67	1.04, 6.84
Age, years			1.12	1.07, 1.18
Race (Caucasians = 0, African Americans = 1)			3.11	1.84, 5.25
Obesity (body mass index $<30 = 0$, $\geq 30 = 1$)			2.32	1.42, 3.80
Cardiovascular/cerebrovascular disease			1.17	0.64, 2.14
Low 3MSE score			2.89	1.59, 5.22
Use of antidepressants			0.61	0.23, 1.62
Obesity × severe sleep-disordered breathing[a]			0.73	0.18, 2.95
Men				
Severe sleep-disordered breathing (apnea-hypopnea index $\leq 30 = 0$, $>30 = 1$)	1.26	0.68, 2.32	1.16	0.51, 2.65
Age, years			1.09	1.03, 1.15
Race (Caucasians = 0, African Americans = 1)			5.31	2.74, 10.29
Obesity (body mass index $<30 = 0$, $\geq 30 = 1$)			1.82	0.86, 3.85
Cardiovascular/cerebrovascular disease			1.76	0.87, 3.54
Low 3MSE score			2.03	1.02, 4.05
Use of antidepressants			1.59	0.54, 4.66
Obesity × severe sleep-disordered breathing[a]			0.85	0.19, 3.83

Abbreviation: 3MSE, Modified Mini-Mental State Examination.

[a] Other interaction terms (age × sleep-disordered breathing, race × sleep-disordered breathing) not statistically significant.

males (28), analyses were performed after stratification by gender. In order to validate the model, logistic regression analysis was performed with activities of daily living disability as the dependent variable and severe SDB and covariates mentioned above as independent variables. Data analyses were performed by using SPSS for Windows, version 15, software (SPSS, Inc., Chicago, Illinois).

RESULTS

Frailty indicator variables

Slow walking speed, low grip strength, exhaustion, low physical activity, and unexplained weight loss were exhibited by 20%, 25%, 19%, 20%, and 8% of the study participants, respectively. Overall, no frailty indicator variables were found in 444 (42%) participants, while 343 (33%), 166 (16%), and 89 (9%) participants had 1, 2, and 3 or more frailty indicator variables, respectively. The distribution of frailty indicator variables in female and male study participants is shown in Table 2. Compared with participants with no frailty indicator variables, those with 1 or more frailty indicator variables were older (mean age = 77 (standard deviation, 5) years vs. 76 (standard deviation, 4) years, $P < 0.01$); more likely to be women (61% vs. 53% for women and men, respectively ($\chi^2 = 6.74$, $P = 0.009$), obese (body mass index, ≥ 30) (29% vs. 16%, $\chi^2 = 23.59$, $P < 0.001$), to take 5 or more medications (27% vs. 15%, $\chi^2 = 19.13$, $P < 0.001$, respectively), and to endorse excessive daytime sleepiness (Epworth Sleepiness Scale $\geq$ 10) (30% vs. 22%, $\chi^2 = 8.01$, $P = 0.005$).

Sleep characteristics

A sleep-related complaint was reported by 18% of the study participants, and women were more likely to report this as compared with men, despite having a significantly higher polysomnography-defined total sleep time (mean = 354 (standard deviation, 70) vs. mean = 337 (standard deviation, 61) minutes ($P < 0.001$)), increased sleep efficiency, and favorable sleep stage distribution (Table 3).

A sleep-related complaint was more likely to be reported by those who had a slow walking speed compared with those with normal walking speed (26% vs. 16%, respectively; $\chi^2 = 9.66$, $P = 0.001$), low physical activity compared with those with normal physical activity (23% vs. 17%, respectively; $\chi^2 = 4.20$, $P = 0.040$), and those with 1 or more frailty indicator variables compared with those with no frailty indicator variables (20% vs. 16%, $\chi^2 = 3.69$, $P = 0.055$).

Table 6. Logistic Regression Model Predicting Low Grip Strength, Cardiovascular Health Study, 1995–1996

Sex and Variable	Logistic Regression Model			
	Univariate		Multivariate	
	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval
Women				
Severe sleep-disordered breathing (apnea-hypopnea index $\leq 30 = 0$, $>30 = 1$)	2.54	1.35, 4.78	3.29	1.36, 7.96
Age, years			1.08	1.03, 1.13
Race (Caucasians = 0, African Americans = 1)			0.38	0.21, 0.70
Obesity (body mass index $<30 = 0$, $\geq 30 = 1$)			3.21	2.04, 5.05
Cardiovascular/cerebrovascular disease			1.20	0.62, 1.95
Low 3MSE score			1.85	1.00, 3.43
Use of antidepressants			0.83	0.36, 1.91
Obesity × severe sleep-disordered breathing[a]			0.31	0.08, 1.20
Men				
Severe sleep-disordered breathing (apnea-hypopnea index $\leq 30 = 0$, $>30 = 1$)	0.84	0.46, 1.52	0.51	0.22, 1.19
Age, years			1.11	1.06, 1.17
Race (Caucasians = 0, African Americans = 1)			1.46	0.73, 2.95
Obesity (body mass index $<30 = 0$, $\geq 30 = 1$)			0.82	0.39, 1.74
Cardiovascular/cerebrovascular disease			0.83	0.40, 1.69
Low 3MSE score			0.90	0.42, 1.94
Use of antidepressants			1.30	0.47, 3.59
Obesity × severe sleep-disordered breathing[a]			2.06	0.43, 9.86

Abbreviation: 3MSE, Modified Mini-Mental State Examination.

[a] Other interaction terms (age × sleep-disordered breathing, race × sleep-disordered breathing) not statistically significant.

Both the apnea-hypopnea index and hypoxic burden (percent of sleep time spent in oxygen saturation below 90%) were higher in men as compared with women (Table 3). The proportions of female and male participants with no SDB (apnea-hypopnea index, <5/hour), mild SDB (apnea-hypopnea index, 5–15/hour), moderate SDB (apnea-hypopnea index, >15–30/hour), and severe SDB (apnea-hypopnea index, >30/hour) were 25%, 47%, 20%, and 7%, as well as 13%, 38%, 31%, and 18%, respectively ($\chi^2 = 61.15$, $P < 0.001$), indicating a higher burden of the SDB among men.

Relation between SDB and frailty indicator variables

The relation between severe SDB and slow walking speed and between severe SDB and low grip strength was statistically significant among women ($\chi^2 = 12.33$, $P < 0.001$; $\chi^2 = 8.92$, $P < 0.003$ for slow speed and low grip strength, respectively), but not among men. Among female study participants with and without severe SDB, there were 9 (21%), 29 (67%), and 5 (12%) and 221 (41%), 277 (51%), and 47 (7%) participants with 0, 1–2, and 3 or more frailty indicator variables, respectively ($\chi^2 = 6.44$, $P < 0.040$); while among male study participants with and without severe SDB, there were 35 (44%), 40 (50%), and 5 (6%) and 179 (47%), 163 (44%), and 32 (9%) participants with 0, 1–2, and 3 or more frailty indicator variables, respectively ($P = 0.529$).

Tables 4–7 show unadjusted and adjusted odds ratios for frailty indicator variables and activities of daily living impairment for female and male study participants. The likelihood of a slow walking speed, low grip strength, and activities of daily living disability was significantly increased among participants with severe SDB as compared with those without severe SDB among female study participants and not among male study participants.

DISCUSSION

There was a significant relation between severe SDB and slow walking speed, low grip strength, and activities of daily living disability demonstrated among study participants in this study, raising the possibility that SDB may contribute to the development or progression of frailty among older adults. However, this relation was observed only among females and not among males, suggesting a gender-specific effect of SDB. This is an unexpected finding because, given the increased prevalence and severity of SDB among male study participants, we would have expected a stronger association between SDB and these frailty indicator variables among men than among women. Among study participants

Table 7. Logistic Regression Model Predicting Activities of Daily Living Disability, Cardiovascular Health Study, 1995–1996[a]

Sex and Variable	Logistic Regression Model			
	Univariate		Multivariate	
	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval
Women				
Severe sleep-disordered breathing (apnea-hypopnea index $\leq 30 = 0$, $>30 = 1$)	2.78	1.43, 5.42	2.08	1.02, 4.24
Age, years			1.09	1.04, 1.15
Race (Caucasians = 0, African Americans = 1)			1.16	0.64, 2.10
Obesity (body mass index $<30 = 0$, $\geq 30 = 1$)			2.61	1.61, 4.24
Cardiovascular/cerebrovascular disease			0.67	0.33, 1.36
Low 3MSE score			2.34	1.25, 4.40
Use of antidepressants			1.43	0.60, 3.39
Men				
Severe sleep-disordered breathing (apnea-hypopnea index $\leq 30 = 0$, $>30 = 1$)	1.93	0.99, 3.77	1.58	0.76, 3.29
Age, years			1.01	0.94, 1.09
Race (Caucasians = 0, African Americans = 1)			1.15	0.48, 2.76
Obesity (body mass index $<30 = 0$, $\geq 30 = 1$)			2.52	1.27, 5.05
Cardiovascular/cerebrovascular disease			2.27	1.07, 4.85
Low 3MSE score			1.47	0.63, 3.44
Use of antidepressants			1.87	0.58, 6.04

Abbreviation: 3MSE, Modified Mini-Mental Status Examination.
[a] Interaction terms did not show statistically significant association.

with an apnea-hypopnea index of $\leq$30/hour, there were no statistically significant differences in specific frailty indicator variables, including slow walking speed and low grip strength, between men and women (data not shown), implying that the differences that were observed are not due to gender characteristics per se. There is some precedent for gender-specific associations of SDB among older adults. For example, a significant relation between SDB and hypertension, history of diabetes, and low high-density lipoprotein cholesterol has been reported in older women (age, $\geq$65 years), whereas these relations were not statistically significant in older men (29).

Several mechanisms can explain the findings in this study. One hypothesis is that, by the time an individual reaches old age, he/she may have developed protective mechanisms to the adverse effect of SDB (30). Although this may partially explain the relation between SDB and the frailty indicator variables among men, it is not immediately obvious how such an effect would account for the positive findings among women. Among women, female hormones have been reported to confer some protection against airway collapse during sleep and, thus, prevent apnea and hypopnea events (31). However, this protection may be lost after menopause, and this is thought to explain the increase in the prevalence and severity of SDB reported among postmenopausal women (32). We would, thus, propose that SDB among older women might have progressed more rapidly later in life when compared with men and, as a result, we are observing an association between SDB and morbidity that was masked at earlier ages. In support of this, at least in 1 longitudinal study, the downward trajectories of grip strength (i.e., a specific frailty indicator variable) among an older population were greater among women (19% decline over 4 years) than among men (12% decline over 4 years) (33). These findings suggest that postmenopausal status could be a predisposing factor to declines in muscle strength, and it is possible that this relation could be mediated, at least in part, by the increased incidence of SDB among this subgroup of women.

Pathophysiologic changes that occur in SDB include hormonal and inflammatory pathways that enhance catabolic activities and impede anabolic actions (12, 13), and it is plausible that these activities may accelerate the age-dependent decline in muscle mass and strength, as well as walking speed. Because low grip strength and slow walking speed have been reported to predict disability and mortality among community-dwelling older adults (34, 35), our finding may have important implications for interventions aimed at prevention of these adverse outcomes. Of note, 1 previous study has reported a significant association between the oxygen desaturations index (a proxy for SDB) and activities of daily living disability among hospitalized older adults (36), and our finding confirms and extends this previous report.

A body mass index of $\geq$30 kg/m^2 was a significant predictor of slow walking speed and low grip strength in both men and women, and this finding is in line with previous

studies that have shown a significant association between obesity and decreased functional status and frailty among older women, a condition referred to as ''sarcopenic obesity'' (37). We would stress that such obesity effects appear to be independent of SDB (Tables 4–7). This finding is in contrast to the commonly held idea that portrays frailty to be synonymous with underweight. In addition, the relation between severe SDB and 1 or more frailty indicator variables was stronger among nonobese study participants (Table 4), and this may indicate the complex relation between SDB and obesity that has been described before (38).

These findings should be interpreted in light of a number of limitations. First, the cross-sectional design of this study does not allow inference of causality in the relation between SDB and slow walking speed and low grip strength. Although SDB could contribute to the development of these frailty indicator variables, a ''reverse causal pathway,'' with low muscle strength contributing to the development of SDB in the elderly, could also be hypothesized. For example, it is plausible that the age-associated decrease in muscle mass (sarcopenia) could impact the upper airway muscles responsible for airway patency during sleep and, consequently, increase the risk of apnea and hypopnea events. A decrease in the activities of the upper airway dilator muscles in older adults has been previously reported, suggesting that older adults would be at increased risk for upper airway collapse during sleep (39). Further studies would be required to determine the direction of the relation between SDB and slow walking speed and low grip strength. In addition, despite previous reports (40), we did not find statistically significant associations between SDB and low activity. However, the physical activity data utilized in this study were collected during year 5 of the Cardiovascular Health Study (1992–1993), and the data may not accurately reflect the activity status of participants in year 8 (1995–1996), the year the sleep study was performed. This factor may partly explain the absence of significant association between SDB and low physical activity observed in this study.

In summary, the results of this cross-sectional study indicate an independent association between severe SDB and slow walking speed, low grip strength, one or more frailty indicator variables, and activities of daily living disability among community-dwelling older women. Because slow walking speed and low grip strength have been reported to predict disability, the results of this study would have important implications for interventions aimed at preventing or delaying the development of frailty and disability among older adults. To our knowledge, this is the first study that reported a significant association between severe SDB and slow walking speed and low grip strength among community-dwelling older women, and future studies would be required to determine the temporal profile of this association.

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Author affiliations: Division of Geriatrics and Gerontology, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia (Yohannes Endeshaw); Renal Electrolyte Division, Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania (Mark Unruh); Department of Biostatistics, Emory University School of Medicine, Atlanta, Georgia (Michael Kutner); Division of Geriatrics, Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania (Anne Newman); and Department of Neurology, Emory University School of Medicine, Atlanta, Georgia (Donald Bliwise).

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