

SCIENTIFIC INVESTIGATIONS

Association between risk of obstructive sleep apnea and cognitive performance, frailty, and quality of life among older adults with atrial fibrillation

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Study Objectives: Geriatric impairments and obstructive sleep apnea (OSA) are prevalent among older patients with atrial fibrillation (AF). Little is known about the association between OSA and geriatric impairments, including frailty, cognitive performance, and AF-related quality of life. The objective of this study was to examine the associations of OSA with frailty, cognitive performance, and AF-related quality of life among older adults with AF.

Methods: Data from the Systemic Assessment of Geriatrics Elements-AF study were used, which included AF participants 65 years and older and with a CHA₂DS₂-VASc ≥ 2 . The STOP-BANG questionnaire was used to assess the risk of OSA. Multivariable logistic regression models were used to examine the association between risk of OSA and geriatric impairments, adjusting for sociodemographic, geriatric, and clinical characteristics.

Results: A total of 970 participants (mean age 75 years; 51% male) were studied. Of the 680 participants without a medical history of OSA, 26% (n = 179) of participants had a low risk of OSA, 53% (n = 360) had an intermediate risk, and 21% (n = 141) had a high risk for OSA. Compared to those with low risk of OSA, participants with an intermediate or high risk of OSA were more likely to be frail (adjusted odds ratio = 1.67, 95% confidence interval: 1.08–2.56; adjusted odds ratio = 3.00, 95% confidence interval: 1.69–5.32, respectively) in the fully adjusted models.

Conclusions: Our findings identify a group of patients at high risk who would benefit from early screening for OSA. Future longitudinal studies are needed to assess the effect of OSA treatment on frailty, physical functioning, and quality of life among patients with AF.

Keywords: atrial fibrillation, obstructive sleep apnea, frailty, cognitive performance, AF-related quality of life

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Geriatric impairments and obstructive sleep apnea (OSA) are common and adversely affect the outcomes of patients with atrial fibrillation. However, there are extremely limited data on the association between geriatric elements and OSA among older adults with atrial fibrillation.

Study Impact: Despite guideline recommendations of early screening for symptoms of OSA and treatment of OSA among patients with atrial fibrillation, screening remains lagging. In this study, we found that patients at intermediate or high risk for OSA were more likely to be frail and, therefore, identified a group of patients who would benefit from early screening for OSA.

INTRODUCTION

Atrial fibrillation (AF) is the most prevalent cardiac arrhythmia worldwide, affecting approximately 5 million individuals in the United States alone.¹ Patients with AF often have multiple comorbidities. Geriatric impairments, including frailty, cognitive impairment, and poor health-related quality of life, commonly occur and adversely affect various outcomes including treatment outcomes and mortality.^{2,3} Obstructive sleep apnea (OSA) is also highly prevalent among patients with AF,⁴ affecting nearly 1 in 5 of these individuals. Older patients with both AF and OSA have higher risks of major bleeding, hospitalizations, and worse functional status compared to those patients with AF but free from OSA.⁵

Geriatric impairments may be additional risk factors for OSA. However, whether OSA is associated with geriatric impairments such as frailty and quality of life among patients with AF has not been examined. Lower cognitive performance has been reported among AF patients with OSA compared to those without.⁶ Among patients with AF, guidelines suggest clinicians use common signs and symptoms of AF to determine if OSA screening is appropriate.⁷ Therefore, identifying risk factors of OSA would help identify groups of patients with AF who are at high risk and who could benefit from screening, emphasizing the guideline recommendations of early screening for symptoms of OSA and treatment of OSA among patients with AF.⁸

Using data from the Systematic Assessment of Geriatric Elements (SAGE)-AF study,⁹ we examined the associations between OSA and frailty, cognitive performance, and AF-related quality of life among older men and women with AF. We hypothesize that patients at a high risk for OSA would be frail, cognitively impaired, and have lower AF-related quality of life.

METHODS

Study population

The present study used data from the prospective multicenter cohort study, SAGE-AF.⁹ Details of the study protocol and recruitment of participants have been previously described.^{9,10} In brief, between 2016 and 2018, participants were recruited from several clinics in Massachusetts and Georgia. Eligible participants included patients aged 65 years and older who were diagnosed with nonvalvular AF and had a CHA₂DS₂-VASc ≥ 2 (congestive heart failure/left ventricular ejection fraction $\leq 40\%$, hypertension, age ≥ 75 years, diabetes mellitus, stroke/transient ischemic attack/thromboembolism history, vascular disease, age:65–74 years, female sex).¹¹ Patients with documentation of an absolute contraindication to oral anticoagulation, those who were unable to provide informed consent,¹² and those who did not speak English were deemed ineligible. The Institutional Review Boards at the University of Massachusetts Medical School, Mercer University, and Boston University approved this study. Prior to formal study enrollment, each eligible participant provided written informed consent.

Participants' baseline medical records were reviewed by trained research staff who underwent routine quality control checks. Trained study staff abstracted participants' demographic, clinical, and laboratory characteristics. The sociodemographic characteristics included age, sex, race, marital status, and level of education. Clinical factors included type of AF, time since AF diagnosis, body mass index (BMI), lifestyle and medical history (ie, alcohol use, anemia, asthma/chronic obstructive pulmonary disease, diabetes, heart failure, hypertension, major bleeding, myocardial infarction, peripheral vascular disease (PVD), obstructive sleep apnea, renal disease, and stroke/transient ischemic attack), calculated stroke and bleeding risk scores, and relevant laboratory findings. Participants also completed a structured interview and comprehensive geriatric assessments for frailty, cognitive performance, and AF-related quality of life. Participants self-reported whether or not they had a fall in the past 6 months and had any sensory deficits (ie, visual or hearing).

Risk for obstructive sleep apnea

The STOP-BANG questionnaire (do you Snore loudly, do you often feel Tired, has anyone Observed you stop breathing, do you have high blood Pressure, BMI, Age, Neck circumference, Gender), an 8-item questionnaire, was used to assess the risk of OSA among SAGE-AF participants at the year 2 follow-up examination. All items of the STOP-BANG questionnaire were self-reported by study participants, with the exception of the assessment of their neck circumference. This was measured by study research personnel, as is recommended.¹³ For each of the

8 STOP-BANG questions, answering "Yes" equates to 1 point on the scale. STOP-BANG uses a validated 8-point scale to categorize OSA risk into low, intermediate or high: 1) a score of 0–2 indicates a low risk of OSA, 2) a score of 3–5 indicates an intermediate risk, and 3) a score of 6–8 indicates a high risk.^{13–15}

Assessment of frailty, cognitive performance, and AF-related quality of life

The Cardiovascular Health Survey frailty scale,¹⁶ a 5-component model of frailty that includes weight loss/shrinking, slow gait speed (15-foot times walk), exhaustion, poor physical activity measured by the Minnesota Leisure Time Activity questionnaire,¹⁷ and weakness (grip strength), was used to assess frailty in study participants at baseline. Each component received a single point with total score ranging from 0 to 5. A participant was considered to be robust if none of the criteria were met, prefrail if 1 or 2 criteria were met, and frail if ≥ 3 criteria were met.¹⁶

The Montreal Cognitive Assessment Battery, a 30-item screening tool, was used to assess cognitive performance among SAGE-AF participants at baseline. Scores range between 0 and 30 with lower scores indicating poorer cognitive performance. Participants with a score ≤ 23 were classified as being cognitively impaired.^{18,19}

The Atrial Fibrillation Effect on Quality of Life (AFEQT) questionnaire, a 20-item questionnaire, was used to assess participants' AF-related quality of life at baseline.²⁰ Participants self-reported the degree to which AF has affected their quality of life in the past 4 weeks. An overall AFEQT score, ranging from 0 to 100, was derived by adding the responses to 3 subscales: 1) daily activities, 2) symptoms, and 3) treatment concerns. Participants with an AFEQT score ≥ 80 indicate a higher reported quality of life.²¹

Statistical analysis

We compared the levels of risk for OSA according to SAGE-AF participants' sociodemographic, clinical, geriatric, and psychosocial characteristics. The chi-square test was used to examine differences in categorical variables, and unpaired *t*-tests were used to examine between group differences for continuous variables.

Separate multivariable binary logistic regression models were used to examine the association between the risk for OSA with each of the following: 1) frailty, 2) cognitive performance, and 3) AF-related quality of life. A model building approach was used to examine the impact of potential confounding variables. We adjusted for variables based on their clinical relevance as well as their level of significance ($P < .05$) in their independent association with the risk of OSA. In model 1, sociodemographic variables including age, sex, race, and marital status were included. Subsequently, we added clinical variables (ie, BMI, symptoms of AF, type of AF, AF duration, and medical history of diabetes mellitus type 2 and renal disease) and smoking status in model 2. A secondary analysis was performed to examine the association between medical history of OSA (collected at baseline) and frailty, cognitive performance, and

AF-related quality of life. All statistical analysis were performed using SAS c9.4 (SAS Institute Inc., Cary, NC).

RESULTS

A total of 970 SAGE-AF participants were included in the present study. The mean age of our study sample was 75 years old. Approximately half were men; 87% were non-Hispanic White and 57% were married; 60% had paroxysmal AF. The mean BMI of participants and the average time since AF diagnosis were 29 kg/m² and 5 years, respectively. Approximately one-third of participants were cognitively impaired, and two-thirds were frail or prefrail. The average AFEQT score was 81, suggesting a relatively high AF-related quality of life among participants.

One-third (n=290) of participants had a medical history of OSA. Of the 680 participants without a medical history of OSA, 26% (n = 179) of participants had a low risk of OSA, 53% (n=360) had an intermediate risk of OSA, and 21% (n=141) had a high risk for OSA.

Risk of OSA and frailty, cognitive performance, and AF-related quality of life

A higher proportion of women (85%) and non-Hispanic White participants (91%) were in the low OSA risk group (Table 1; P < .001 and P < .04, respectively). A higher proportion (43%) of participants with cognitive impairment were in the intermediate OSA risk group (Table 1; P < .01). A higher proportion of participants with a medical history of diabetes, hypertension, and PVD were in the high risk of OSA risk group (Table 1; P < .01).

Participants with an intermediate or high, compared to those with a low risk of OSA, were more likely to be frail than not frail after adjusting for other sociodemographic and clinical variables (Table 2; adjusted odds ratio [OR]= 1.67, 95% confidence interval [CI]: 1.08–2.56; adjusted OR = 3.00, 95% CI: 1.69–5.32, respectively).

Participants with an intermediate risk of OSA, compared to those with a low risk of OSA, were more likely to be cognitively impaired than not impaired in the unadjusted model (Table 3; unadjusted OR = 1.54, 95% CI: 1.06–2.23). This association, however, was no longer statistically significant

Table 1—Participants’ characteristics according to their risk of OSA.

Characteristics	Low Risk (n = 179)	Intermediate Risk (n = 360)	High Risk (n = 141)	P
Sociodemographic				
Age, y, mean (SD)	76 (7.3)	77 (7.1)	75 (5.9)	.07
Women, n (%)	152 (84.9)	174 (48.3)	25 (17.7)	<.001
Non-Hispanic White, n (%)	163 (91.1)	303 (84.2)	127 (90.1)	.04
Married, n (%)	87 (49.2)	199 (55.9)	102 (72.3)	<.001
College graduate or more, n (%)	86 (48.9)	146 (41.1)	76 (53.9)	.02
Clinical				
BMI, kg/m ² , mean (SD)	26 (4.3)	29 (5.3)	32 (6.4)	<.001
Type of AF, n (%)				
Paroxysmal	113 (63.1)	203 (56.4)	74 (52.5)	.23
Persistent	37 (20.7)	92 (25.6)	47 (33.4)	
Permanent	11 (6.2)	21 (6.9)	8 (5.7)	
Left ventricular ejection fraction, mean (SD)	55 (11.3)	56 (11.4)	54 (11.4)	.10
Electrocardiogram				
Atrial fibrillation, n (%)	45 (27.4)	104 (31.7)	40 (30.5)	.92
Normal sinus, n (%)	66 (40.2)	118 (36.0)	44 (33.6)	
Heart rate, beats/min, mean (SD)	71 (13.5)	70 (12.2)	72 (15.5)	.22
Time since AF diagnosis, y, mean (SD)	5 (4.3)	5 (4.2)	5 (4.5)	.58
Treatment approach, n (%)				
Rate control	96 (53.6)	200 (55.6)	82 (58.2)	.72
Rhythm control	83 (46.4)	160 (44.4)	59 (41.8)	
On anticoagulation	158 (88.3)	302 (83.9)	127 (90.1)	.13
Medical history, n (%)				
Alcohol use	50 (27.9)	108 (30.0)	53 (37.6)	.15
Anemia	52 (29.1)	96 (26.7)	33 (23.4)	.53
Asthma/COPD	29 (16.2)	71 (19.7)	35 (24.8)	.16
Diabetes	24 (13.4)	84 (23.3)	39 (27.7)	<.01
Hypertension	149 (83.2)	322 (89.4)	133 (94.3)	<.01

(continued on following page)

Table 1—Participants' characteristics according to their risk of OSA. (Continued)

Characteristics	Low Risk (n = 179)	Intermediate Risk (n = 360)	High Risk (n = 141)	P
Major bleeding	24 (13.4)	59 (16.4)	27 (19.2)	.38
Myocardial infarction	23 (12.9)	75 (20.8)	29 (20.6)	.06
Peripheral vascular disease	15 (8.4)	51 (14.2)	24 (17.0)	.06
Renal disease	32 (17.9)	92 (25.6)	47 (33.3)	<.01
Stroke/TIA	16 (8.9)	35 (9.7)	13 (9.2)	.95
Hemoglobin g/dl, mean (SD)	13 (2)	13 (2)	14 (2)	<.01
Charlson Comorbidity Index, mean (SD)	5 (1.7)	6 (1.9)	6 (2.6)	.04
Risk scores, mean (SD)				
CHA ₂ DS ₂ -VASc	4 (1.5)	4 (1.6)	4 (1.6)	.08
HAS-BLED	3 (1.0)	3 (1.1)	3 (1.1)	<.01
Psychosocial, geriatric and patient-reported				
Frailty, n (%)				
Not frail	83 (46.4)	137 (38.1)	48 (34.0)	.08
Prefrail	76 (42.5)	192 (53.3)	81 (57.5)	
Frail	20 (11.2)	31 (8.6)	12 (8.5)	
Social isolation, n (%)	19 (10.6)	45 (12.5)	18 (12.8)	.78
Fall in past 6 months, n (%)	32 (17.9)	80 (22.2)	28 (19.9)	.49
Cognitive impairment (MOCA ≤ 23), n (%)	63 (35.2)	164 (45.6)	46 (32.6)	<.01
AFEQT score, mean (SD)	84 (15.6)	83 (15.7)	81 (16.7)	.15
Current smoker, n (%)	6 (3.4)	12 (3.3)	4 (2.8)	<.001

AF = atrial fibrillation, BMI = body mass index, AFEQT = AF-related quality of life, CHA₂DS₂-VASc = stroke risk score, COPD = chronic obstructive pulmonary disease, HAS-BLED = bleeding risk score, MOCA = Montreal Cognitive Assessment, SD = standard deviation, TIA = transient ischemic attack.

after adjusting for sociodemographic, clinical, and health behavioral variables in regression models 1 and 2.

Participants at high risk for OSA, compared to those with a low risk of OSA, were more likely to have a low AF-related quality of life after adjusting for sociodemographic variables (**Table 4**; adjusted OR = 2.20, 95% CI: 1.29–3.76). This association, however, was no longer statistically significant after adjusting for clinical and health behavioral variables in regression model 2.

Medical history of OSA and frailty, cognitive performance, and AF-related quality of life

Participants with a paroxysmal type of AF, a higher average BMI, a medical history of anemia, asthma, diabetes, heart

failure, hypertension, and major bleeding were significantly more likely to have a medical history of OSA. Similarly, a higher proportion of frail participants (18%) and those with a lower AF-related quality of life were significantly more likely to have a medical history of OSA (**Table S1** in the supplemental material).

Participants with a medical history of OSA, compared to those without, were more likely to be frail and have a low AF-related quality of life after adjusting for other sociodemographic and clinical variables (**Table S2** and **Table S4** in the supplemental material; adjusted OR = 1.59, 95% CI: 1.12–2.24; adjusted OR = 1.80, 95% CI: 1.27–2.55, respectively).

Participants with a medical history of OSA, compared to those without, were less likely to be cognitively impaired than not impaired in the unadjusted model (**Table S3** in the

Table 2—ORs (95% CIs) for being “frail” vs “not frail” with risk of OSA (STOP-BANG score).

Risk of OSA	OR (95% CI)		
	Unadjusted	Model 1	Model 2
Low	Ref	Ref	Ref
Intermediate	1.41 (0.98, 2.02)	1.83 (1.20–2.79)	1.67 (1.08–2.56)
High	1.68 (1.06, 2.64)	3.58 (2.05–6.26)	3.00 (1.69–5.32)

Model 1: Adjusted for sociodemographic variables: age, sex, race, marital status. Model 2: Adjusted for variables in model 1, clinical variables (BMI, symptoms of AF; type of AF; AF duration; medical history of DM2, renal disease) and smoking status. AF = atrial fibrillation, BMI = body mass index, CI = confidence interval, DM2 = diabetes mellitus type 2, OR = odds ratio, OSA = obstructive sleep apnea, Ref = reference.

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Table 3—ORs (95% CIs) for cognitive impairment vs not cognitively impaired with risk of OSA (STOP-BANG score).

Risk of OSA	OR (95% CI)		
	Unadjusted	Model 1	Model 2
Low	Ref	Ref	Ref
Intermediate	1.54 (1.06, 2.23)	1.21 (0.78–1.87)	1.16 (0.75–1.81)
High	0.89 (0.56, 1.42)	0.80 (0.45–1.41)	0.71 (0.39–1.28)

Model 1: Adjusted for sociodemographic variables: age, sex, race, marital status. Model 2: Adjusted for variables in model 1, clinical variables (BMI, symptoms of AF; type of AF; AF duration; medical history of DM2, renal disease) and smoking status. AF = atrial fibrillation, BMI = body mass index, CI = confidence interval, DM2 = diabetes mellitus type 2, OR = odds ratio, OSA = obstructive sleep apnea, Ref = reference.

supplemental material; unadjusted OR = 0.79, 95% CI: 0.59–1.05). The statistical significance of the associations between medical history of OSA and cognitive impairment were attenuated after multivariable adjustment for key covariates, including age and BMI.

DISCUSSION

In this contemporary study of older adults with AF in whom risk for OSA was characterized systematically, we observed a high prevalence of participants with an intermediate risk for OSA (53%). We also found that participants with an intermediate or high risk for OSA had higher odds of being frail but did not observe an association with cognitive performance after adjustment for potential confounders.

Geriatric impairments, including frailty and impaired cognition, commonly occur in patients with AF and have been shown to be associated with poor anticoagulation adherence and treatment-related outcomes, including increased risk of stroke and all-cause mortality.^{22,23} On the other hand, OSA is also highly prevalent among patients with AF and is associated with higher risks of major bleeding and hospitalizations, poorer treatment outcomes, and often contributes to the maintenance and recurrence of AF.²⁴ To the best of our knowledge, no prior study has examined the association between OSA and geriatric elements including frailty and AF-related quality of life among patients with AF. Examining the associations between STOP-BANG assessed at year 2 and our study outcomes will help us identify patients at high risk who would benefit from screening for OSA.

Our study showed that participants at an intermediate or high risk for OSA were more likely to be frail, after adjusting for other potential confounders. In a cross-sectional study of 1,042 healthy adults, severe sleep-disordered breathing was associated with a greater likelihood of components of the frailty measure, including slow walking speed and low grip strength.²⁵ Health care providers need to be increasingly aware that OSA may be associated with frailty in older adults with AF and, therefore, consider early screening for OSA in these patients, which may provide an avenue for early treatment of OSA.

In the present study, participants with an intermediate risk of OSA, compared to those with low risk of OSA, were more likely to be cognitively impaired. These associations were, however, no longer statistically significant after adjusting for other potentially confounding variables. In a study that included 122 participants with AF, participants with sleep apnea had lower cognitive performance and had greater difficulties concentrating compared to those without OSA.⁶ In contrast, our study features a larger sample of patients diverse in geographic location and comorbid conditions. Differences between our findings and previous studies could be related to the questionnaires used to determine OSA and cognitive performance and to differences in the sociodemographic and clinical characteristics of the respective study samples.

Our study also showed that participants at high risk for OSA reported a lower AF-related quality of life. This association was no longer significant after adjusting for clinical confounding variables. However, our secondary analysis showed that a medical history of OSA was significantly associated with a lower AF-related quality of life. Prior studies have shown lower health-related quality of life among patients with OSA,²⁶ and poor sleep

Table 4—ORs (95% CIs) for reporting low AF-related quality of life “AFEQT < 80” (vs. high) with risk of OSA (STOP-BANG score).

Risk of OSA	OR (95% CI)		
	Unadjusted	Model 1	Model 2
Low	Ref	Ref	Ref
Intermediate	1.17 (0.80, 1.71)	1.48 (0.98–2.24)	1.41 (0.90–2.20)
High	1.36 (0.86, 2.17)	2.20 (1.29–3.76)	1.83 (1.01–3.30)

Model 1: Adjusted for sociodemographic variables: age, sex, race, marital status. Model 2: Adjusted for variables in model 1, clinical variables (BMI, symptoms of AF; type of AF; AF duration; medical history of DM2, renal disease) and smoking status. AF = atrial fibrillation, AFEQT = AF-related quality of life, BMI = body mass index, CI = confidence interval, DM2 = diabetes mellitus type 2, OR = odds ratio, OSA = obstructive sleep apnea, Ref = reference.

quality has also been shown to negatively impact quality of life among patients with hypertrophic obstructive cardiomyopathy.²⁷

In the present large observational study, we sought to understand the links between OSA and key geriatric domains that impact AF outcomes and care. Our findings identify high-risk groups that may benefit from current guideline recommendations of screening for OSA among patients with AF. We hypothesize that OSA might be associated with frailty among patients with AF due to changes in physical function. This may be attributed to the symptoms of OSA, including fatigue, excessive daytime sleepiness, and poor sleep quality. Health care providers should identify and screen patients at high risk as well as recommend early lifestyle and medical interventions aimed at treating OSA and its associated symptoms.

Study strengths and limitations

This study has several strengths. First, we used data from a multicenter prospective cohort of older adults with AF with detailed sociodemographic, clinical, geriatric, and psychosocial characteristics. Second, study participants had multiple comorbidities that were accounted for in our analysis, enhancing the generalizability of our findings to older patient populations with AF. Third, we utilized standardized, validated instruments to assess the risk of OSA, AF-related quality of life, frailty, and cognitive performance, increasing the validity and reproducibility of our study findings. However, several limitations should be noted. Our study cohort consists mainly of White participants, which limits the generalizability of our findings to ethnic minority groups. In addition, the present study examined the association between the risk of OSA collected at year 2 and the principal outcomes of interest collected at baseline. Literature showed no change in participants' STOP-BANG scores over time, which addresses the limitation of temporality.²⁸ Furthermore, our study cohort was recruited from mostly academic medical centers, which may limit the generalizability of our findings to community-based practices. Lastly, data on polysomnography were not collected, therefore, we did not examine the association between apnea-hypopnea index and our study outcomes.

CONCLUSIONS

Our study showed that an intermediate or high risk of OSA among older adults with AF is associated with a greater likelihood of being frail. These findings highlight groups of patients at high risk who may benefit from early screening. Future longitudinal studies are needed to examine the impact of OSA on geriatric elements and whether OSA treatment increases quality of life and improves physical functioning in older adults with AF.

ABBREVIATIONS

AF, atrial fibrillation
 AFEQT, atrial fibrillation related quality of life
 BMI, body mass index
 CI, confidence interval
 OR, odds ratio

OSA, obstructive sleep apnea

SAGE, Systematic Assessment of Geriatric Elements

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