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Clinical Research

Self-Reported Daytime Sleepiness and Sleep-Disordered Breathing in Patients With Atrial Fibrillation: SNOozE-AF

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See editorial by Timothy and Povitz, pages 1426–1429 of this issue.

ABSTRACT

Background: Atrial fibrillation (AF) management guidelines recommend screening for symptoms of sleep-disordered breathing (SDB). We aimed to assess the role of self-reported daytime sleepiness in detection of patients with SDB and AF.

Methods: A total of 442 consecutive ambulatory patients with AF who were considered candidates for rhythm control and underwent polysomnography comprised the study population. The utility of daytime sleepiness (quantified by the Epworth Sleepiness Scale [ESS]) to predict any (apnea-hypopnea index [AHI] $\geq$ 5), moderate-to-severe (AHI $\geq$ 15), and severe (AHI $\geq$ 30) SDB on polysomnography was tested.

Results: Mean age was 60 $\pm$ 11 years and 69% patients were men. SDB was present in two-thirds of the population with 33% having moderate-to-severe SDB. Daytime sleepiness was low (median ESS = 8/24) and the ESS poorly predicted SDB, regardless of the degree of SDB tested (area under the curve: 0.48-0.56). Excessive daytime sleepiness (ESS $\geq$ 11) was present in 11.9% of the SDB population

RÉSUMÉ

Contexte : Les lignes directrices en matière de prise en charge de la fibrillation auriculaire (FA) recommandent le dépistage des symptômes d'un trouble respiratoire du sommeil (TRS). Notre objectif était d'évaluer le rôle de l'autodéclaration de la somnolence diurne dans le dépistage des patients présentant un TRS et une FA.

Méthodologie : La population étudiée comprenait 442 patients ambulatoires consécutifs présentant une FA jugés bons candidats pour une évaluation du rythme du sommeil et ayant subi une polysomnographie. Nous avons tenté de déterminer l'utilité de l'évaluation de la somnolence diurne (mesurée au moyen de l'échelle de somnolence d'Epworth [EES, *Epworth Sleepiness Scale*]) pour prédire un TRS quelconque (indice d'apnée-hypopnée [IAH $\geq$ 5), un TRS modéré ou grave (IAH $\geq$ 15) et un TRS grave (AHI $\geq$ 30) à la polysomnographie.

Résultats : Les sujets avaient en moyenne 60 $\pm$ 11 ans, et 69 % d'entre eux étaient des hommes. Les deux tiers des sujets présentaient un TRS, qui était modéré ou grave dans 33 % des cas. Le

Sleep-disordered breathing (SDB) affects up to 74% of all patients with atrial fibrillation (AF)[1] and is an independent predictor of stroke.[2] Treatment of SDB can improve arrhythmia-free survival of AF after pharmacologic treatment or catheter ablation.[3,4] This important interplay between AF and SDB has been recognized in the international AF management guidelines; current guidelines from the European Society of Cardiology and consensus from the Heart Rhythm Society both recommend screening for signs and symptoms of SDB in patients with AF, and to consider initiation of SDB therapy to improve AF treatment outcomes.[5-7]

Excessive daytime sleepiness (EDS) is an important clinical consequence of SDB that can significantly impair the quality of life of its sufferers.[8] Assessing self-reported daytime sleepiness is advocated in international sleep medicine guidelines to aid the assessment of symptom burden of patients with sleep apnea before and on therapy, and is often used to triage

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and had a negative predictive value of 43.1% and a positive predictive value of 67.5% to detect moderate-to-severe SDB. Male gender (odds ratio [OR]: 2.3, 95% confidence interval [CI]: 1.4-3.8, $P = 0.001$), obesity (OR: 3.5, 95% CI: 2.3-5.5, $P < 0.001$), diabetes (OR: 2.3, 95% CI: 1.2-4.4, $P = 0.08$), and stroke (OR: 4.6, 95% CI: 1.7-12.3, $P = 0.002$) were independently associated with an increased likelihood of moderate-to-severe SDB.

Conclusions: In an ambulatory AF population, SDB was common but most patients reported low daytime sleepiness levels. Clinical features, rather than daytime sleepiness, were predictive of patients with moderate-to-severe SDB. Lack of excessive daytime sleepiness should not preclude patients from being investigated for the potential presence of concomitant SDB.

degré de somnolence diurne était faible (score EES médian = 8/24), et le score EES s'est révélé être un mauvais prédicteur de TRS, quelle qu'en soit la gravité (aire sous la courbe : de 0,48 à 0,56). Au sein de la population ayant un TRS, 11,9 % des sujets présentaient une somnolence diurne excessive (ESS $\geq$ 11), une caractéristique ayant une valeur prédictive négative de 43,1 % et une valeur prédictive positive de 67,5 % à l'égard de la présence d'un TRS modéré ou grave. Le sexe masculin (rapport de cotes [RC] de 2,3; intervalle de confiance [IC] à 95 % : de 1,4 à 3,8; $p = 0,001$), l'obésité (RC de 3,5; IC à 95 % : de 2,3 à 5,5; $p < 0,001$), le diabète (RC de 2,3; IC à 95 % : de 1,2 à 4,4; $p = 0,08$) et l'accident vasculaire cérébral (RC de 4,6; IC à 95 % : de 1,7 à 12,3; $p = 0,002$) étaient associés de manière indépendante à une probabilité accrue de TRS modéré ou grave.

Conclusions : Dans une population de patients ambulatoires présentant une FA, les TRS étaient courants, mais la plupart des patients ont rapporté un faible degré de somnolence diurne. Ce sont les caractéristiques cliniques, plutôt que la somnolence diurne, qui permettaient de prédire la présence d'un TRS modéré ou grave. L'absence de somnolence diurne excessive ne devrait toutefois pas éliminer la nécessité d'évaluer la présence d'un TRS concomitant.

patients for SDB investigation and treatment.[9] However, in an arrhythmia clinic, the goal of SDB treatment is not just to improve EDS, but to control AF symptoms and maintain sinus rhythm. EDS is often used as a prerequisite for initiation of SDB investigations, but only a minority of patients with SDB report EDS in the cardiovascular clinics.[10-12] Therefore, patient selection for SDB investigation can pose a real clinical challenge, and potential lack of EDS in this population can further complicate this issue and warrants clarification.

We hypothesize that self-reported daytime sleepiness does not correlate with the presence or severity of SDB in patients with AF, and that self-reported daytime sleepiness lacks the sensitivity and specificity to identify SDB or guide SDB management. To test this, we conducted our study on a relatively large cohort of ambulatory patients with AF referred from our AF clinic for formal overnight sleep studies as part of their workup for AF management.

The aims of our study were to: (1) investigate the correlation between daytime sleepiness and the presence and severity of SDB, (2) characterize the population with moderate-to-severe SDB (ie, patients most likely to be treated with positive airway pressure [PAP] by sleep medicine physicians), and (3) assess the distribution of EDS and AF-related symptoms and potential implication for AF and SDB management.

Methods

Study design and population

The study included consecutive patients with symptomatic paroxysmal or persistent AF referred from the Centre for Heart Rhythm Disorders at the University of Adelaide to undergo polysomnography (PSG). All patients were considered candidates for rhythm control, and therefore screening for SDB was performed regardless of symptoms as part of a comprehensive risk factor management programme. Referrals to the Adelaide Institute for Sleep Health from January 2009 to March 2017 were screened, and patients without AF or with incomplete PSG data were excluded (Fig. 1). The study protocol was approved by the Human Research Ethics Committee of the Royal Adelaide Hospital (R20180831) and registered on Australian New Zealand Clinical Trials Registry (Trial ID: ACTRN12618001859279).

Patient characteristics

AF was confirmed by at least one 12-lead electrocardiogram. Type of AF was defined according to the 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of AF.[5] Demographic and anthropometric data were collected for all patients. Clinical risk factors were actively screened, and the **C**ongestive Heart Failure, **H**ypertension, **A**ge (≥75 years), **D**iabetes, **S**troke/Transient Ischemic Attack, **V**ascular Disease, **A**ge (65-74 years), **S**ex (Female) (CHA_2DS_2-VASc) score was calculated accordingly. Contemporaneous echocardiography measurements were obtained and pharmacologic therapy at

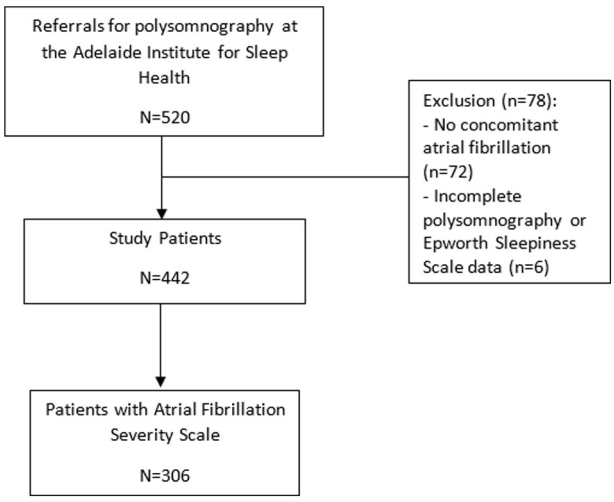

Figure 1. Study design flow diagram.

the time of PSG was recorded. Further details can be found in the Supplemental Methods.

Assessment of daytime sleepiness

To assess the degree of subjective daytime sleepiness, the Epworth Sleepiness Scale (ESS) was administered to all participants before PSG (Supplemental Fig. S1). The ESS is a validated questionnaire that requires subjects to rate their likelihood of falling asleep in several common situations. Scores range from 0 (least sleepy) to 24 (sleepiest). EDS was defined as a score of 11 or higher.

Assessment of SDB severity

All patients underwent standard overnight PSG (Somté, Compumedics, Victoria, Australia), which included continuous recordings of electroencephalography, electrooculography, and chin electromyography for sleep staging. PSG data were scored by an experienced sleep technician and reviewed and reported by a registered sleep physician according to methods described in the American Academy of Sleep Medicine manual for the scoring of sleep and associated events.[13] The apnea-hypopnea index (AHI) was calculated as the total number of apneas plus hypopneas divided by the total sleep time. SDB was considered present if the AHI was $\geq$5. SDB severity was determined according to the categories of AHI (AHI 5-14.9, mild SDB; AHI 15-29.9, moderate SDB; AHI $\geq$ 30, severe SDB; AHI $\geq$ 15, moderate-to-severe SDB)[13] (further details in Supplemental Methods).

Assessment of AF symptom burden

A subgroup of patients also underwent AF symptom burden assessment using the AF severity scale (AFSS) (Supplemental Fig. S2). The AFSS is a validated scale that ranges from 3.25 (single minimally symptomatic episode lasting minutes) to 30 (continuous highly symptomatic episode lasting > 48 hours). It encompasses 3 domains of AF: event frequency (scored 1-10), duration (scored 1.25-10), and global episode severity (scored 1-10).

Statistical analysis

Continuous variables were tested for normality in distribution using the Shapiro-Wilk test, and are presented as mean $\pm$ standard deviation or median and interquartile range as appropriate. Categorical variables are presented as count and proportion. Group differences were tested by the 2-sided Student t test or 1-way analysis of variance test for normally distributed variables, whereas the Mann-Whitney U test and Kruskal-Wallis H test were used for nonparametric variables. Differences in proportions were tested using the χ^2 or Fisher's exact test where appropriate.

Binary logistic regression analysis was used to test the univariate relationship of baseline characteristics and the presence of moderate-to-severe SDB, with the alpha value set at 0.1 to conditionally include a given variable in a multivariable forward stepwise conditional model. Hosmer and Lemeshow's goodness of fitness test was then applied to the multivariable model. Linear correlation was used to test the relationship between daytime sleepiness and degree of SDB as defined by AHI and is reported as Spearman's coefficient of correlation and coefficient of determination (R^2). To test the utility of the ESS to predict the presence of SDB, we used receiver operating characteristic analysis that allowed assessment of sensitivity and specificity of all possible cutoffs of the predictor variable. Significance was set at $P < 0.05$. All statistical analysis was performed using SPSS statistical software for Windows (Version 24; IBM Corp, CA).

Results

Study population

The study included a total of 442 patients, of whom 306 (69.2%) were men. Mean age was 60 $\pm$ 11 years and mean body mass index was 30.5 $\pm$ 5.2 kg/m^2. One hundred sixty-nine patients (38.2%) had nonparoxysmal AF. Baseline characteristics are reported in Table 1. When stratified for the presence and type of SDB, nearly one-third of the studied population had no SDB (n = 150, 33.9%), one-third had mild SDB (n = 143, 32.3%), and one-third had moderate-to-severe SDB (n = 149, 33.7%). The latter group consisted of 76 patients (17.2%) with moderate and 73 patients (16.5%) with severe SDB (Fig. 2). Seventy-seven patients (26.4%) had predominant central sleep apnea. The proportion of patients with predominant central sleep apnea was higher in mild SDB (32.2%) as opposed to the moderate (27.6%) or severe SDB (13.7%) groups, $P = 0.01$. Table 2 summarizes PSG findings in the population stratified by the presence and type of SDB.

Correlation between the ESS score and SDB

The studied population reported low levels of daytime sleepiness regardless of the presence or severity of SDB. The median ESS score for the population was 5 [3-8] and did not differ significantly when the population was stratified by SDB severity ($P = 0.18$) (Table 2). The median ESS score did not differ based on AF type (4 [3-8] vs 5 [3-8] for PAF vs non-PAF, respectively, $P = 0.417$). Figure 3 depicts the ESS score distribution using a scatterplot of all the cases, ranked by the ESS score and stratified by SDB severity.

There was a statistically significant, but very weak correlation between the ESS and AHI (Spearman's rho correlation coefficient = 0.12, 95% confidence interval [CI]: 0.02-0.21, $P = 0.01$), with only 1% of the variation in reported daytime sleepiness potentially explained by the severity of SDB (adjusted $R^2 = 0.01$, $P = 0.02$) (Fig. 4). However, there was no correlation when correcting for the presence of SDB, gender, or obesity ($R = 0.14$, 0.14, and 0.12, respectively, $P =$ not significant).

Utility of the ESS to predict SDB

The ESS performed very poorly as a predictor for SDB regardless of the degree of SDB or the cutoffs of the ESS used. Using receiver operating characteristic analysis, the area under the curve was 0.54, 0.48, 0.53, and 0.57 for any SDB, mild SDB, moderate SDB, and severe SDB, respectively ($P =$ not significant) (Supplemental Fig. S3). When combining the moderate and severe categories (AHI $\geq$ 15), the area under the curve reached statistical significance ($P = 0.04$) but remained low at 0.56 (95% CI: 0.5-0.62). Using the conventional threshold of the ESS score $\geq$ 11 to define EDS, the

Table 1. Baseline clinical characteristics per sleep-disordered breathing (SDB) category

Characteristics	No SDB	Mild SDB	Moderate SDB	Severe SDB	*P* value
Number of patients	150	143	76	73	
Male	89 (59.3)	103 (72)	57 (75)	57 (78.1)	0.01
Age, y	56.9 ± 11.8	62.1 ± 10.1	60.7 ± 9.8	61.7 ± 11	0.001
Weight, kg	87.6 ± 15.5	88.6 ± 13.9	96.5 ± 17.9	102.5 ± 20.2	<0.001
BMI, kg/m^2	29.1 ± 4.6	29.4 ± 4.3	31.3 ± 5	34.5 ± 5.7	<0.001
Obesity	47 (31.3)	54 (37.8)	39 (51.3)	54 (74)	<0.001
Hypertension	100 (66.7)	102 (71.3)	53 (69.7)	59 (80.8)	0.2
DM (or glucose intolerance)	10 (6.7)	13 (9.1)	12 (15.8)	18 (24.7)	0.001
Dyslipidaemia	59 (39.6)	69 (48.6)	34 (44.7)	42 (57.5)	0.1
Coronary artery disease	12 (8)	12 (8.4)	4 (5.3)	13 (17.8)	0.04
Cerebrovascular disease	3 (2)	5 (3.5)	5 (6.6)	8 (11)	0.02
CHA_2DS_2VASc	1.5 ± 1.2	1.8 ± 1.2	1.8 ± 1.2	2.2 ± 1.1	0.001
Nonparoxysmal AF	40 (26.7)	62 (43.4)	38 (50)	29 (39.7)	0.002
Previous AF ablation	20 (13.3)	30 (21)	11 (14.5)	11 (15.3)	0.3
Excess alcohol (> 30 g/wk)	37 (24.7)	30 (21)	17 (22.4)	9 (12.3)	0.2
Smoking					
Non-smoker	111 (74)	108 (75.5)	52 (68.4)	52 (71.2)	0.3
Ex-smoker	6 (4)	5 (3.5)	0 (0)	1 (1.4)	
Current smoker	33 (22)	30 (21)	24 (31.6)	20 (27.4)	
LVEF, %	61.3 ± 8.7	61.1 ± 8.2	61.4 ± 9.9	59.5 ± 10.8	0.6
Impaired LVF (EF < 40%)	4 (2.7)	4 (2.8)	4 (5.3)	3 (4.1)	0.7
LVIDd, cm	4.9 ± 0.9	4.8 ± 1	5.1 ± 0.9	5 ± 0.7	0.02
LA volume, cm^2	62.2 ± 31	61.8 ± 25.2	72 ± 34.5	67.8 ± 27.1	0.02
LA diameter, cm	3.7 ± 1	3.8 ± 0.9	4.1 ± 1	4.1 ± 0.9	< 0.001
NOAC	32 (21.3)	50 (35)	26 (34.2)	22 (30.1)	0.053
Warfarin	42 (28)	41 (28.7)	28 (36.8)	29 (39.7)	0.2
Aspirin	41 (27.3)	38 (26.6)	12 (15.8)	16 (21.9)	0.2
β-Blockers	78 (52)	67 (46.9)	36 (47.4)	41 (56.9)	0.5
Digoxin	8 (5.3)	5 (3.5)	5 (6.6)	8 (11)	0.2
Flecainide	59 (39.3)	40 (28)	19 (25)	17 (23.3)	0.03
Sotalol	13 (8.7)	19 (13.3)	12 (15.8)	10 (13.7)	0.4
Amiodarone	5 (3.3)	8 (5.6)	7 (9.2)	3 (4.1)	0.3
ACEi/ARB	74 (49.3)	81 (56.6)	51 (67.1)	56 (76.7)	0.001
CCB	47 (31.3)	41 (28.9)	20 (26.3)	31 (43.1)	0.1
Diuretics	15 (10)	16 (11.2)	14 (18.4)	24 (32.9)	< 0.001
MRA	6 (4.2)	11 (7.8)	7 (9.5)	7 (9.6)	0.4

Continuous variables are presented as mean ± standard deviation, whereas categorical variables are presented as number (proportions).

ACEi, angiotensin converting enzyme inhibitors; AF, atrial fibrillation; ARB, angiotensin receptor blockers; BMI, body mass index; CCB, calcium channel blockers; CHA_2DS_2VASc, **C**ongestive Heart Failure, **H**ypertension, **A**ge (≥75 years), **D**iabetes, **S**troke/Transient Ischemic Attack, **V**ascular Disease, **A**ge (65-74 years), **S**ex (Female); DM, diabetes mellitus; EF, ejection fraction; LA, left atrium; LVEF, left ventricular ejection fraction; LVF, left ventricular function; LVIDd, left ventricular internal diameter in diaostole; MRA, mineralocorticoid receptor antagonist; NOAC, non−vitamin K oral anticoagulants.

test had a sensitivity of 12% and specificity of 89.3% for detection of SDB (AHI ≥ 5) with a negative predictive value of 34.3% and a positive predictive value of 68.6%. In comparison, to detect moderate-to-severe SDB (AHI ≥ 15) with the same EDS threshold, the ESS had a slightly better sensitivity of 14.8% and specificity of 90.1% with a negative predictive value of 43.1% and a positive predictive value of 67.5%. Even when using different thresholds, the ESS continued to perform poorly as a predictor of any SDB or moderate-to-severe SDB as demonstrated in Table 3.

Characterizing AF patients with moderate-to-severe SDB: patients likely receiving PAP treatment

Of the 292 patients with any SDB (AHI ≥ 5), 149 (51%) had moderate-to-severe SDB (AHI ≥ 15) and would likely be considered for PAP treatment. The mean age for this population was 61 ± 10 years and 114 (76.5%) were men. The moderate-to-severe SDB group had higher body mass index and a higher proportion of patients with obesity (Supplemental Table S1). There was no observed difference in the left ventricular ejection fraction between these 2 groups, but the group with moderate-to-severe SDB had larger left atrial diameter (4.1 ± 1.0 vs 3.8 ± 0.9 cm, $P < 0.001$) and volume (61.8 ± 25.2 vs 69.9 ± 31 cm^3, $P < 0.02$). Baseline medications were comparable between the groups other than for angiotensin converting enzyme inhibitors/angiotensin receptor blockers (107 [71.8%] vs 81 [56.6%]) and diuretics (38 [25.5%] vs 16 [11.2%]), which were used more frequently in patients with moderate-to-severe SDB when compared with mild SDB.

The multivariable regression model constructed to assess the utility of baseline clinical characteristics to identify patients with moderate-to-severe SDB was a good fit for the data ($\chi^2 = 3.8$, degrees of freedom = 8, $P = 0.87$). We found that male gender, obesity, diabetes mellitus, and history of stroke/transient ischaemic attacks were independently associated with an increased likelihood of having moderate-to-severe SDB. Male gender (odds ratio [OR]: 2.3, 95% CI: 1.4-3.8, $P = 0.001$) and diabetes mellitus (OR: 2.3, 95% CI: 1.2-4.4, $P = 0.08$) were associated with double the likelihood to have moderate-to-severe SDB. Obesity was associated with a 3-fold increased risk of moderate-to-severe SDB (OR: 3.5, 95% CI: 2.3-5.5, $P < 0.001$), whereas the history of cerebrovascular disease increased the odds of having moderate-to-severe SDB by a factor of 4.6 (95% CI: 1.7-12.3, $P = 0.002$). In addition,

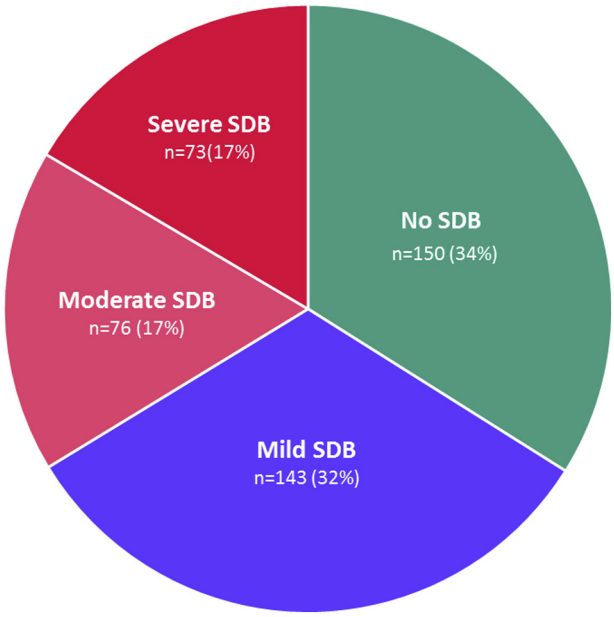

Figure 2. Distribution of patients per sleep-disordered breathing (SDB) category.

annual increments in age increased the likelihood of moderate-to-severe SDB diagnosis by approximately 2.5% (OR: 1.023, 95% CI: 1.001-1.045, $P = 0.04$). The model also adjusted for the type of AF and history of hypertension (Supplemental Table S2).

EDS and AF symptom burden: potential role in AF and SDB management

EDS. Only a small proportion of patients with diagnosed SDB reported EDS (11.9%). This did not differ if patients were stratified by AF type (11% vs 12.4% in PAF vs non-PAF, respectively, $P = 0.646$, Supplemental Table S3). Interestingly, a comparable proportion of patients with no SDB also reported EDS (10.7%). There was a nonsignificant trend towards the increased prevalence of EDS within SDB as the severity of SDB increased ($\chi^2 = 0.48$) (Fig. 3). This finding remained consistent in patients with predominant central sleep apnea (EDS prevalence of 10.9%, 23.8%, and 20% for mild, moderate, and severe SDB, respectively, $P = 0.36$). In AF patients with mild SDB where the presence of EDS might influence the decision to start PAP, most patients (90.1%) did not report EDS, and this group represents almost a third of the whole population in this study (130/442 patients [29.4%]).

AF symptom burden. AFSS questionnaire results were available for 306 patients. The mean AFSS score was 13.6 ± 5.8 (out of a maximum of 30) and did not differ when the population was stratified by the presence and degree of SDB (Fig. 5). There was no correlation between AF symptom burden and reported sleepiness ($R = -0.01$, $P = 0.7$) or AF symptom burden and SDB ($R = 0.23$, $P = 0.7$). AFSS did not differ across SDB categories when corrected for EDS or predominant central sleep apnea ($P = 0.07$ and 0.4, respectively). Patients with mild SDB were not less symptomatic with their AF than those with moderate-to-severe SDB (mean AFSS: 13.3 ± 5.9 vs 14.1 ± 5.5, $P = 0.3$).

Discussion

In this cohort of ambulatory patients with AF referred for formal overnight sleep studies, we found: (1) SDB to be prevalent, with nearly a third of the patients having moderate-to-severe SDB, a third with mild SDB, and a third with no SDB; (2) self-reported daytime sleepiness to correlate very poorly with objective measures of SDB; (3) EDS to be low, regardless of the severity of SDB; and (4) certain clinical features, such as obesity and male gender, were associated with an increased likelihood of the presence of moderate-to-severe SDB.

Albuquerque et al.[12] observed that EDS did not correlate with the severity of SDB in a selected group of 151 patients with persistent AF referred for electrical cardioversion. Our study extrapolates these findings to a larger, consecutively recruited, symptomatic AF population being considered for rhythm-control therapy, irrespective of the type of AF or the presence or absence of SDB-related symptoms. The studied population is thus more representative of the patients encountered in a typical ambulatory setting.

Given the lack of correlation between daytime sleepiness and SDB, it was not surprising to see that the ESS performed very poorly as a prediction tool for SDB, regardless of the severity of SDB being tested or the thresholds of the scale used. The ESS may have a role in establishing a baseline daytime sleepiness level, which can help monitor treatment response and potentially guide PAP therapy in selected patients if EDS is present.[9] However, in light of our findings, we stress the importance of not relying on subjective daytime sleepiness to select patients for overnight sleep studies. Had EDS been used as a prerequisite for screening for SDB in our studied population, up to 88% of the patients with any SDB

Table 2. Polysomnography characteristics per sleep-disordered breathing (SDB) category

Characteristic	No SDB	Mild SDB	Moderate SDB	Severe SDB	*P* value
Epworth Sleepiness Scale score	4 [3-7]	4 [3-7]	5 [3-9]	6 [3-9]	0.2
Apnea-hypopnea index	2.1 [1-3.6]	9.5 [6.6-11.8]	21 [18-24.3]	44 [36-65]	< 0.001
Predominant central sleep apnea	51 (34)	46 (32.2)	21 (27.6)	10 (13.7)	0.01
Total sleep time, min	326 [264-373]	329.5 [274.5-377]	318 [275.5-364.5]	277 [185-324.4]	< 0.001
Nonrapid eye movement sleep, %	82.9 ± 8.4	89.2 ± 60	93.8 ± 93.7	87.7 ± 8.8	0.001
Rapid eye movement sleep, %	16.5 ± 6.9	17.8 ± 18.5	18 ± 12.9	12.4 ± 8.9	0.001
Sleep efficacy, %	72 ± 17	72.6 ± 14.9	70.7 ± 15	64.7 ± 16.6	0.003

Continuous variables are presented as median [25th-75th percentile] or mean ± standard deviation. Categorical variables are presented as number (proportions).

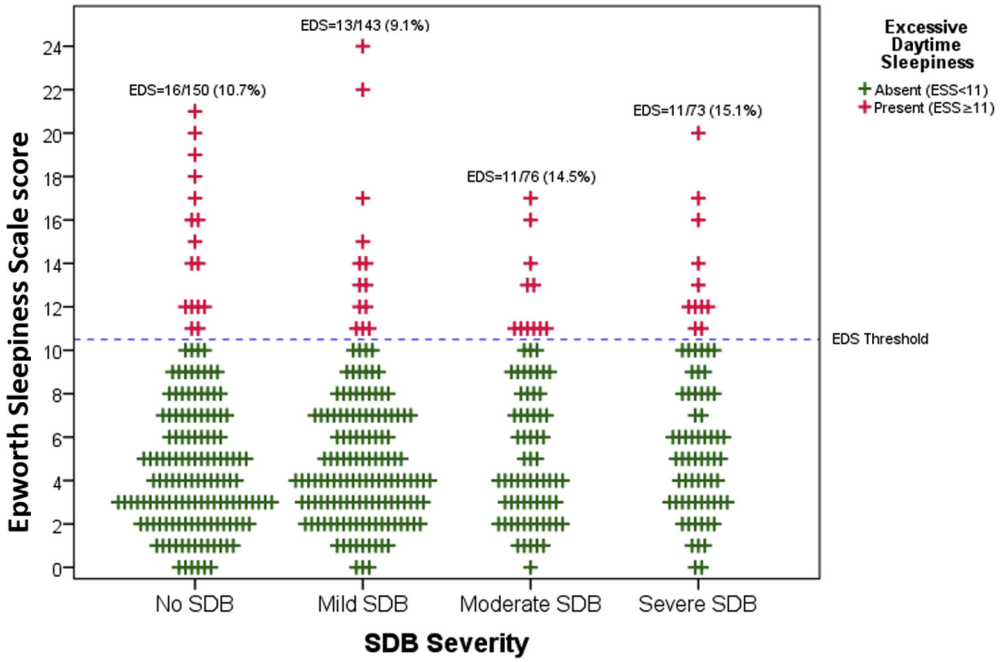

Figure 3. Scatter plot of all cases stratified by the presence and severity of sleep-disordered breathing (SDB). The *Y*-axis represents the severity of sleepiness as assessed by the Epworth Sleepiness Scale (ESS) with identical-score cases stacked horizontally. The blue dotted line represents the thresholds for excessive daytime sleepiness (EDS).

and approximately 85% of patients with moderate-to-severe SDB would have been missed. Although daytime sleepiness and SDB seem to correlate in the general population,[14] the lack of a similar correlation in patients with AF is interesting. It is possible that increased sympathetic tone in patients with AF[15,16] counteracts sleepiness due to SDB as seen in patients with stroke or heart failure.[10] It is also plausible that patients with SDB and AF have blurred perception of their symptoms and are unable to specifically attribute them to one condition or another.[17]

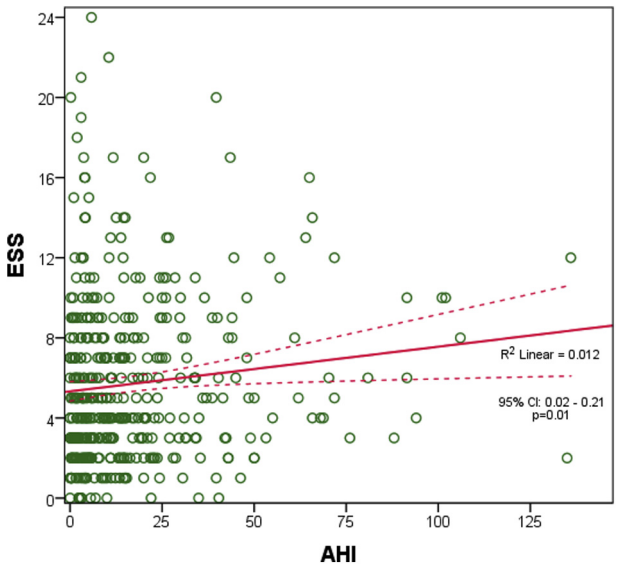

Figure 4. Correlation between the Epworth Sleepiness Scale (ESS) score and the apnea-hypopnea index (AHI). CI, confidence interval.

From a sleep-medicine perspective, PAP treatment is likely to be recommended for severe SDB regardless of EDS. However, for moderate and possibly even mild SDB, the presence of EDS can be a determinant factor in initiating PAP.[9] From an arrhythmia perspective, the current literature is scarce regarding rhythm-management outcomes in patients with AF and concomitant mild SDB, as most of the published studies are observational and use a relatively high AHI threshold for defining SDB.[3] This can pose a real management dilemma in the treatment of AF patients with mild SDB and no EDS. Our study demonstrates that this is not an uncommon scenario with nearly one-third (29.4%) of the studied population falling in this category. Contributing to this dilemma is the finding that those patients do not seem to be any less symptomatic with their AF than their counterparts with moderate-to-severe SDB.

Table 3. Sensitivity and specificity of the Epworth Sleepiness Scale (ESS) to detect any or moderate-to-severe sleep-disordered breathing (SDB) using various apnea-hypopnea-index (AHI) thresholds

	Any SDB (AHI ≥ 5)		Moderate-to-severe SDB (AHI ≥ 15)	
ESS	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
3	79.8	24.7	81.2	23.2
4	66.4	41.3	68.5	38.6
5	52.7	50.7	56.4	50.9
6	44.5	62.0	49.0	61.1
7	36.6	68.0	39.6	67.2
8	28.4	75.3	34.2	76.5
9	21.9	81.3	27.5	82.6
10	16.4	86.7	20.8	87.4
11	12.0	89.3	14.8	90.1
12	8.2	90.7	9.4	91.8

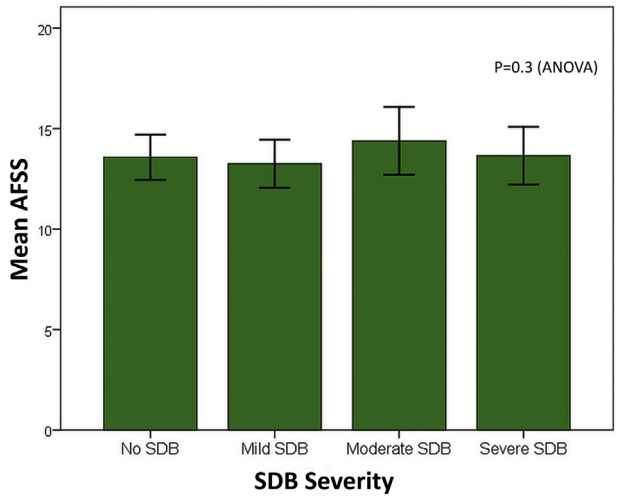

Figure 5. Mean (95% confidence interval) atrial fibrillation severity scale (AFSS) by sleep-disordered breathing (SDB) category: no SDB, 13.6 (12.4-14.7); mild SDB, 13.3 (12.1-14.4); moderate SDB, 14.4 (12.7-16.1); severe SDB, 13.7 (12.2-15.1). One-way analysis of variance (ANOVA), $P = 0.3$.

It is prudent to be able to identify AF patients with significant SDB as these are the patients most likely to benefit from SDB treatment from a rhythm-management perspective.[18] In an observational study of 62 AF patients with SDB (AHI $\geq$ 15/h) undergoing pulmonary vein isolation, PAP therapy improved arrhythmia-free survival after 1 year (71.9%) compared with non-PAP users (36.7%) and similar to a group of patients who did not have SDB (66.7%).[19] Furthermore, 2 separate meta-analyses concluded that PAP use was associated with a significant overall relative risk reduction in AF recurrence of 42%.[3,20] Our study demonstrates that the clinical features of obesity, male gender, history of cerebrovascular disease, or diabetes can help predict the presence of moderate-to-severe SDB and potentially guide patient selection for the investigation of SDB. Although PSG remains the gold standard for diagnosing SDB, simpler methods such as overnight oximetry can provide a more widely accessible option for patient screening.[21,22] Further studies are warranted to investigate whether PAP treatment of patients with AF and SDB, irrespective of EDS, can improve rhythm-management outcomes, and to determine the level of SDB severity for which PAP treatment is beneficial.

Meanwhile, for patients with AF in whom a rhythm-control strategy is followed, adopting an aggressive AF risk factor management strategy, which includes PAP initiation in patients with severe SDB or those with moderate SDB and EDS, has been shown to improve long-term arrhythmia-free survival after catheter ablation for AF.[23]

Limitations

The studied population represents patients with symptomatic AF referred for specialist management of their arrhythmia. Therefore, our results may differ had the subjects been enrolled from a sleep clinic and then tested for AF. However, the large number of patients, the consecutive data collection, and the resultant diverse population allow for the generalization of this study's findings to the cardiac outpatient clinic.

In our study, only the ESS was used to test for daytime sleepiness. There may be other questionnaires that can potentially detect SDB more accurately than the ESS such as Berlin Questionnaire or STOP-BANG. However, a recent study has demonstrated that sleep-related breathing disturbances cannot be reliably predicted using those questionnaires in patients with cardiovascular disease.[24]

Conclusions

In this ambulatory AF cohort, SDB is common (66%) but most patients with AF reported low levels of daytime sleepiness. Therefore, the lack of EDS should not preclude patients from being investigated for the potential presence of concomitant SDB. Clinical features, rather than daytime sleepiness, were predictive of patients with moderate-to-severe SDB. Whether AF management outcomes improve by treating concomitant mild or moderate SDB, particularly with no EDS, warrants further study.

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi.org/10.1016/j.cjca.2019.07.627.