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Obstructive Sleep Apnea During Rapid Eye Movement Sleep, Daytime Sleepiness, and Quality of Life in Older Men in Osteoporotic Fractures in Men (MrOS) Sleep Study

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Study Objectives: Assess the association between REM predominant obstructive sleep apnea (OSA), sleepiness, and quality of life in a community-based cohort of men ≥ 65 years-old.

Design, Intervention and Measurements: A cross-sectional analysis of 2,765 subjects from the Outcomes of Sleep Disorders in Older Men (MrOS Sleep) Study was performed to identify subjects with an apnea hypopnea index (AHI) < 15 (n = 2,044). Subjects were divided into groups based on the AHI in REM sleep (< 5 [referent group], 5 to < 15, 15 to < 30, and ≥ 30). Daytime somnolence, sleep-related quality of life, sleep disturbance, general quality of life, depressive symptoms, and health status were quantified using Epworth Sleepiness Scale (ESS), Functional Outcomes of Sleep Questionnaire (FOSQ), Pittsburgh Sleep Quality Index (PSQI), Short Form-12 (SF-12), Geriatric Depression Scale-15 (GDS), and self-perceived health status, respectively.

Results: Prevalence of REM-predominant OSA (AHI-REM ≥ 5) was 42.8% if OSA was defined as AHI ≥ 15 and 14.4% if OSA was defined as AHI ≥ 5. Higher AHI-REM was associated with polysomnographic indices of poorer sleep architecture (reduced total sleep time, sleep efficiency, REM sleep duration and proportion). Adjusting for age, BMI, and study site, higher AHI-REM was not associated with subjective sleep measures (ESS, FOSQ, PSQI), lower quality of life (SF-12), or greater depressive symptoms (GDS).

Conclusions: In a community-based sample of older adult men ≥ 65 years-old, REM-predominant OSA was highly prevalent and was associated with objective indices of poorer sleep quality on polysomnography but not with subjective measures of daytime sleepiness or quality of life.

Keywords: Sleep apnea syndromes, sleep apnea, obstructive; sleep, rapid eye movement, disorders of excessive somnolence, epidemiology, older adults, quality of life

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Obstructive sleep apnea (OSA), as defined by an apnea hypopnea index (AHI) ≥ 5, is present in 24% to 62% of community dwelling elderly (age ≥ 65 years), and moderate to severe OSA with an AHI ≥ 15 has been noted in 19% to 44%.[1-3] OSA has been associated with excessive daytime sleepiness, decreased quality of life, impaired cognition, hypertension, stroke, diastolic dysfunction, left atrial enlargement, and insulin resistance.[4-13] Little is known about OSA confined only to REM sleep (REM-predominant OSA).[14-17] This is of particular interest, given that disordered breathing events in REM sleep are often of longer duration and associated with a greater degree of oxygen desaturation than NREM sleep.[18,19]

REM-predominant OSA also poses a difficult dilemma for the practicing clinician. There is lack of data regarding the association between REM-predominant OSA and quality of life as well as cardiovascular and metabolic outcomes. It is not clear if isolated REM-only OSA needs to be treated or if during continuous positive airway pressure (CPAP) titration, pressure should be increased for REM events if the overall AHI is in the normal range. The prevalence and impact of REM-predominant OSA is not clear due to differences in sample size and patient populations of various studies and the adjustments used in various studies to compensate for the effect of AHI in NREM (AHI-NREM) on AHI in REM (AHI-REM) sleep.[14-17,20] This is further confounded by REM-predominant OSA being more prominent in women and relatively younger population and less common in individuals with severe OSA.[14-17,20,21]

BRIEF SUMMARY

Current Knowledge/Study Rationale: It is not known if REM-predominant obstructive sleep apnea (OSA) affects quality of life and sleepiness and if isolated REM-only OSA needs to be treated.

Study Impact: In a community-based sample of older adult men ≥ 65 years-old, REM-predominant OSA was highly prevalent and was associated with objective indices of poorer sleep quality on polysomnography but not with subjective measures of daytime sleepiness or quality of life.

The prevalence and impact of REM-predominant OSA in individuals older than 65 years is not known. The average age of the subjects in most studies of OSA has been between 49-65 years, and individuals older than 65 have been excluded in most studies.[17,22-24] In some studies REM related OSA was more common in the younger population,[15,16] while in other studies such as the Sleep Heart Health Study, subjects with more severe REM-predominant OSA were older.[22] Our primary objective was to define the prevalence of REM-predominant OSA in the Osteoporotic Fractures in Men Sleep study (MrOS Sleep Study) cohort and determine whether REM-predominant OSA was associated with sleepiness and quality of life in older male adults. Our secondary objective was to describe the demographic and polysomnography (PSG) characteristics of older men with REM-predominant OSA.

METHODS

Population

From March 2000 through April 2002, 5,994 men aged 65 years and older were recruited for participation in the prospective Osteoporotic Fractures in Men (MrOS) Study from population-based listings in 6 areas of the United States: Birmingham, Alabama; Minneapolis, Minnesota; Palo Alto, California; Pittsburgh, Philadelphia; Portland, Oregon and San Diego, California.[25,26] To be eligible for the study, men had to be able to walk without assistance, not have had bilateral hip replacement or a medical condition that (in the judgment of the investigator) would result in imminent death at the time of enrollment, and were willing to give informed consent and undergo the study procedures. There were no other exclusion criteria.[25]

In an ancillary study, from December 2003 through March 2005, subjects were invited to have in-home polysomnography (PSG) and actigraphy as part of Outcomes of Sleep Disorders in Older Men (MrOS Sleep) Study.[2] Of the 5,994 men enrolled in the MrOS Study, 3,135 (52.3%) were enrolled in the MrOS Sleep Study. All participants provided written informed consent, and the study protocols were approved by the institutional review boards at each respective study site and at the data coordinating center in San Francisco, California. The MrOS sleep visit was completed between December 2003 and March 2005. A total of 3,135 participants attended the sleep visit. Men were screened for use of mechanical devices during sleep including continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BPAP), mouthpiece for snoring or sleep apnea, or oxygen therapy. In general, those who reported nightly use of any of these devices were excluded from the MrOS Sleep Study; however, the study sample does include 11 men who reported use of one of these devices < 2 times per week. In the present analysis, data were analyzed from 2,765 subjects who took part in the MrOS Sleep Study and had adequate PSG signal quality available for ≥ 4 h, as well as adequate REM staging data (**Figure 1**).[2]

Polysomnography

In-home sleep studies were performed using unattended PSG (Safiro, Compumedics, Inc., Melbourne, Australia). The recording montage consisted of 2 central (C_3/A_2 and C_4/A_1) electroencephalographic leads, bilateral electroculograms, a bipolar submental electromyogram, thoracic and abdominal respiratory inductance plethysmography, airflow (using nasal-oral thermocouple and nasal pressure cannula), finger pulse oximetry, electrocardiogram, body position (mercury switch sensor), and bilateral leg movements (piezoelectric sensors). Trained certified staff members performed home visits for setup of the sleep study units. After sensors were placed and calibrated, signal quality and impedance were checked, and sensors were repositioned as needed to improve signal quality, replacing electrodes if impedances were greater than 5 kΩ, using approaches similar to those used in the Sleep Heart Health Study.[27-29] Staff returned the next morning to collect the equipment and download the data to the Central Sleep Reading Center (Cleveland, OH) for centralized scoring by trained technicians using standard criteria.[27,29]

Subjects included in the present analysis included MrOS Sleep Study participants who had PSG with adequate scoring of REM sleep based on availability of reliable staging data. Less than 1% of the subjects had ≤ 10 min of REM sleep; all subjects with any REM sleep were included in the analysis. Sleep stages (REM, stages 1-4 NREM) were scored using standard criteria.[27,29] The reliability of indices of sleep architecture , determined by rescoring studies over time, indicates that the inter-scorer reliability (ICC) for the percent of sleep time spent in sleep stages 1, 2, slow wave sleep, and REM were 0.60, 0.91, 0.96, and 0.94, respectively.[2,30] AHI was calculated as the total number of apneas and hypopneas per hour of sleep. The inter-scorer reliability for AHI was high (ICC = 0.99).[30]

Apneas were identified if the amplitude of the airflow signal was flat or nearly flat for > 10 seconds. Obstructive apneas were scored if persistence of effort on abdominal or thoracic inductance plethysmography was noted, and central apneas were scored if there was no evident effort on either the abdominal and thoracic plethysmography bands. Hypopneas were scored using Sleep Heart Health Study criteria (requiring a ‟discernible" [> 30%] reduction in amplitude of respiratory effort or airflow) and, in secondary analyses, using the American Academy of Sleep Medicine (AASM) criteria (> 50% reduction in amplitude of signals), considered according to the following hierarchy: summed inductance plethysmography channel, abdominal or thoracic inductance plethysmography, nasal pressure, or thermistor.[28] For the current study, apneas and hypopneas associated with ≥ 4% oxygen desaturation were included, and the Sleep Heart Health Study definition was used for primary analyses.[30] The total AHI, as well as AHI-REM and AHI-NREM were computed as the number of apneas plus hypopneas per hour of total, REM, and NREM sleep, respectively.

Selection and Classification of Subjects

OSA was defined as AHI ≥ 15 during the entire sleep period. REM-predominant OSA was defined as AHI < 15, but AHI-REM ≥ 5 (**Figure 1**). From the entire population of MrOS study participants, men were first classified on the basis of OSA: AHI < 15 (absence of moderate to severe OSA group) and AHI ≥ 15 (OSA group). The 2,015 men with AHI < 15 (analytical cohort) were further subdivided based upon the AHI-REM sleep: AHI-REM < 5 (referent group) and AHI-REM 5 to < 15, AHI-REM

15 to < 30, and AHI-REM ≥ 30 (**Figure 1**). Baseline characteristics of men in the analytical cohort were compared across category of AHI-REM sleep (**Figure 1**, **Table 1**). The analysis was repeated defining OSA as AHI ≥ 5/h during the entire sleep period and REM-only OSA as AHI < 5/h and AHI-REM ≥ 5/h (supplemental material **Figure S1**, **Table S1**).

Sleepiness and Functional Outcome Measures

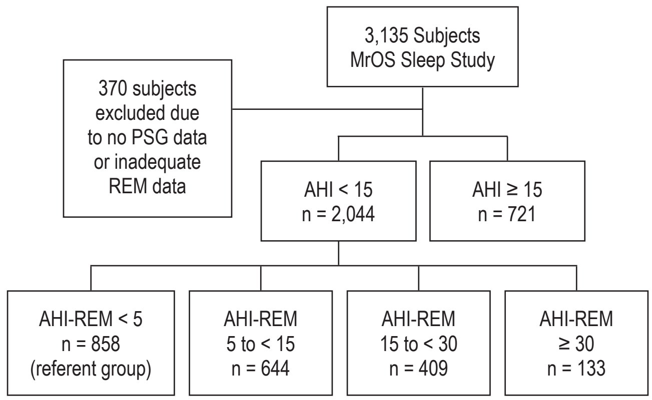
Subjective sleepiness was measured using the Epworth Sleepiness Score (ESS), a self-administered questionnaire which provides a measurement of the subject's general level of daytime sleepiness.[12] Individuals rate the chances that they would doze off or fall asleep when in 8 different situations commonly encountered in daily life on a 0- to 3-point scale. Possible scores range from 0 to 24. An ESS score > 10 is considered sleepy and correlates with sleep latency measured during the multiple sleep latency test and during overnight PSG.[12]

Sleep-related quality of life was measured using the Functional Outcomes of Sleep Questionnaire (FOSQ).[31,32] FOSQ is a 30-item disease specific self-reported measure designed to assess the impact of disorders of excessive sleepiness on multiple activities of everyday living.[31,32] Mean-weighted item scores are used to generate 5 subscales (activity level, vigilance, intimacy and sexual relationships, general productivity, and social outcome) that together produce a composite score.[31] The total score ranges from 5 to 20, and lower scores indicate greater dysfunction. FOSQ can successfully discriminate between normal subjects and those who should seek medical attention for a sleep problem.

Subjective sleep symptoms, disturbance, and patterns were assessed using the Pittsburgh Sleep Quality Index (PSQI).[33-35] PSQI is a self-reported questionnaire that assesses sleep quality and disturbances over a 1-month time interval.[33] Nineteen individual items generate 7 component scores (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction), the sum of which yields a global score. The total global score ranges from 0 to 21; greater scores indicate higher levels of sleep symptoms. A global PSQI score > 5 yielded a diagnostic sensitivity of 89.6% and specificity of 86.5% in distinguishing good and poor sleepers.[33]

General quality of life was measured using Short Form 12 (SF-12), a generic 12-question survey which is weighted and summed to provide interpretable scales for physical and mental health.[36] The physical and mental health composite summary

Figure 1—Distribution of subjects in MrOS Sleep Study with AHI < 15



AHI, apnea hypopnea index; AHI-REM, apnea hypopnea index-rapid eye movement sleep; PSG, polysomnography. REM-predominant OSA was defined as AHI < 15 but AHI-REM ≥ 5.

Table 1—Baseline subject characteristics based on AHI and AHI-REM sleep of subjects in MrOS Sleep Study

	AHI < 15					
Subject Characteristic	**AHI-REM < 5 (n = 858)**	**AHI-REM 5 to < 15 (n = 644)**	**AHI-REM 15 to < 30 (n = 409)**	**AHI-REM ≥ 30 (n = 133)**	**AHI ≥ 15 (n = 721)**	**p-value**
Age, mean (SD)	76.4 (5.6)	76.0 (5.6)	76.1 (5.4)	76.3 (5.3)	76.9 (5.5)	0.03
Caucasian, n (%)	801 (93.4)	586 (91.0)	375 (91.7)	128 (96.2)	654 (90.7)	0.09
BMI (kg/m^2), mean (SD)	25.8 (3.1)	26.7 (3.4)	27.9 (3.8)	29.0 (4.0)	28.4 (4.2)	< 0.001
Neck circumference (cm), mean (SD)	147.9 (70.5)	149.9 (72.2)	145.3 (70.7)	150.2 (71.1)	140.4 (71.1)	0.11
Waist circumference (cm), mean (SD)	38.5 (2.6)	39.3 (3.3)	39.9 (2.8)	40.0 (3.0)	40.2 (2.9)	< 0.001
PASE score, mean (SD)	96.1 (9.6)	98.4 (10.0)	101.5 (12.3)	104.1 (12.0)	102.7 (11.4)	< 0.001
Benzodiazepine use, n (%)	42 (4.9)	26 (4.0)	17 (4.2)	8 (6.0)	25 (3.5)	0.55
Diabetes, n (%)	88 (10.3)	78 (12.1)	59 (14.4)	20 (15.0)	119 (16.5)	0.005
Hypertension, n (%)	394 (45.9)	310 (48.1)	196 (47.9)	71 (53.4)	414 (57.4)	< 0.001
CVD, n (%)	342 (39.9)	264 (41.0)	169 (41.3)	43 (32.3)	340 (47.4)	0.004
Heart attack, n (%)	146 (17.0)	106 (16.5)	81 (19.8)	15 (11.3)	131 (18.2)	0.21
Stroke, n (%)	41 (4.8)	24 (3.7)	10 (2.4)	4 (3.0)	25 (3.5)	0.31
Respiratory Illness, n (%)	40 (4.7)	30 (4.7)	27 (6.6)	14 (10.5)	32 (4.4)	0.03
Alcohol (drinks/wk), mean (SD)	3.6 (4.2)	3.4 (4.2)	3.4 (4.4)	2.8 (4.1)	3.2 (4.0)	0.09
Current smoker, n (%)	22 (2.6)	15 (2.3)	5 (1.2)	2 (1.5)	9 (1.3)	0.25
Ever snored, n (%)	637 (83.6)	506 (88.3)	319 (87.9)	104 (88.9)	606 (90.7)	0.002

AHI, apnea hypopnea index; AHI-REM, apnea hypopnea index REM sleep; BMI, body mass index; CVD, cardiovascular disease; PASE, Physical Activity Scale for the Elderly; SD, standard deviation.

scores are computed using the scores of the 12 questions and range from 0 to 100, where a 0 score indicates the lowest level of health measured by the scales and 100 indicates the highest level of health. SF-12 does not target a specific age or disease group and the physical and mental summary scores tend to vary over the life span and for different age groups.

Depressive symptoms were assessed using the Geriatric Depression Scale (GDS).[37-39] GDS is a brief questionnaire in which participants are asked to respond to either 15 or 30 questions by answering yes or no in reference to how they felt on the day of administration.[37,38] GDS-15 was used in this study, and scores ≥ 6 on this scale indicates depression.[37,39]

Self-reported health status was scaled as excellent, good, fair, poor, or very poor; the responses were collapsed into 2 categories excellent/good health and fair/poor/very poor health.[40]

Other Measurements

Study participants completed an anthropometric evaluation and questionnaire assessment of medical history including self-reported provider–diagnosed disease which included hypertension, diabetes mellitus, cardiovascular disease (CVD), heart attack, respiratory illness, and stroke. All prescription and over-the-counter medications taken 30 days prior to the last visit were recorded by the clinics and stored in an electronic medications inventory database (San Francisco Coordinating Center, San Francisco, CA). Each medication was matched to its ingredient(s) based on the Iowa Drug Information Service (IDIS) Drug Vocabulary (College of Pharmacy, University of Iowa, Iowa City, IA).[41] Clinic visit examination and questionnaire measurements included age (years), body mass index (BMI = kg/m^2), race, neck and waist circumference (cm), tobacco smoking, and alcohol use status. Physical activity was assessed using Physical Activity Scale for the Elderly (PASE), a research instrument that measures the level of physical activity in individuals aged 65 years or older.[42]

Statistical Analysis

Participant characteristics were examined across AHI-REM categories. For categorical data, χ^2 test was used. Analysis of variance (ANOVA) was used for normally distributed continuous data and Kruskal-Wallis test for continuous data that were skewed. Similarly, sleep related variables were also explored across AHI-REM categories where p-value for trend was calculated.

Least square means linear regression was used to examine the relationship between continuous outcomes, such as sleepiness and quality of life, and AHI-REM categories. Logistic regression was used to assess the relationship between AHI-REM categories and similar dichotomized outcomes. All models were initially adjusted for age and study site. Since OSA has been associated with obesity[43] and weight loss has been associated with improvement in BMI, anthropometric measures, and OSA,[44] further adjustment was done for either BMI or waist and neck circumference. All analyses were performed using SAS software, version 9.1 (SAS Institute, Cary, NC).

RESULTS

Polysomnography data quality were excellent, with a failure rate < 4% and more than 70% of studies graded as being of excellent or outstanding quality using standardized criteria. Of the 2,765 men with technically adequate PSG data (**Figure 1**), 2,044 subjects had AHI < 15 (analytical cohort), while 721 subjects had AHI ≥ 15. Three hundred seventy subjects were excluded due to inadequate unreliable REM/NREM data or no PSG data. There were 858 subjects with AHI-REM < 5 who served as the referent group; there were 644 subjects with AHI-REM 5 to < 15, 409 subjects with AHI-REM 15 to < 30, 133 subjects with AHI-REM ≥ 30, and 721 subjects with AHI > 15. The average time spent in REM sleep time was 70.3 ± 28.2 min and in NREM 286.3 ± 55.5 min. The prevalence of REM-predominant OSA was 42.8% if OSA was defined as AHI ≥ 15 and 14.4% if OSA was defined as AHI ≥ 5.

Among our cohort of 2,041 older men without moderate or severe OSA (AHI < 15), there were no significant differences by age or race across AHI-REM categories. A higher AHI-REM was associated with higher BMI, neck circumference, and waist circumference (p value < 0.001) (**Table 1**). Subject-reported histories of respiratory illness and snoring were also associated with a higher AHI-REM (p < 0.05). There were no significant associations between PASE score, benzodiazepine use, smoking status, alcohol use, physician diagnosed and self-reported diabetes, stroke, cardiovascular disease, and heart attack across categories of REM-predominant OSA (**Table 1**). Results were similar when AHI ≥ 5 was used to define the presence of OSA (supplemental material **Table S1**).

There was a significant trend in decreasing total sleep time, sleep efficiency, and minutes and percentage of time in REM sleep across AHI-REM categories (**Table 2**). A higher AHI-REM was associated with a higher total and NREM AHI as well as a higher AHI-REM-to-AHI-NREM ratio and arousal index (**Table 2**). The trend was similar when AHI ≥ 5 was used as definition of OSA (supplemental material **Table S2**).

Adjusted for age, study site, and anthropometric measures, AHI-REM ≥ 30 was associated with worse self-perceived health status than AHI-REM ≤ 5 (**Tables 3** and **4**). After adjustment for age and site, there was no evidence that level of sleepiness or vitality (as measured by ESS, PSQI, and FOSQ) or quality of life (as assessed by SF-12 physical, mental summary scale, and GDS) varied across categories of REM-predominant OSA (**Tables 3** and **4**). Adjusting for BMI or neck or waist circumference did not change the results (data not shown). Results were not altered in analyses when OSA was defined as AHI ≥ 5 during the entire sleep period and REM-predominant OSA was defined as AHI < 5 with AHI-REM ≥ 5 (supplemental material **Table S3** and **S4**).

DISCUSSION

In a large, community-based sample of adults > 65 years old, we assessed the association between REM-predominant OSA, sleepiness and quality of life in subjects without OSA (using either AHI ≥ 15 or AHI ≥ 5 to define OSA). Our findings show that in this population of older men, an elevated AHI-REM sleep was highly prevalent even when the AHI was either low (< 5) or modest (< 15). Similar to what is known regarding total AHI levels, a higher AHI-REM was associated with a higher BMI, neck circumference, and waist circumference. Of note, even among those without an elevated AHI (overall AHI < 5 or < 15), a higher AHI-REM was associated with reduced total sleep time, sleep efficiency, and REM time and percentage. This suggests that even when the predominant number of respiratory disturbances occur in REM sleep, sleep architecture is disturbed. However, increasing REM-specific AHI levels were not linearly associated with increased sleepiness as determined

Table 2—Polysomnography characteristics of subjects in MrOS Sleep Study

	AHI < 15					
Subject Characteristics	**AHI-REM < 5 (n = 858)**	**AHI-REM 5 to < 15 (n = 644)**	**AHI-REM 15 to < 30 (n = 409)**	**AHI-REM ≥ 30 (n = 133)**	**AHI < 15 (n = 721)**	**p-value**
Total sleep time (min), mean (SD)	359.9 (67.0)	361.6 (65.7)	356.1 (68.0)	338.2 (75.6)	351.9 (67.9)	< 0.001
Sleep efficiency % , mean (SD)	75.5 (11.9)	75.5 (11.6)	74.1 (11.3)	72.8 (11.9)	71.4 (12.3)	< 0.001
REM time (min), mean (SD)	74.5 (28.4)	74.9 (27.9)	70.9 (28.2)	59.1 (28.3)	62.7 (26.1)	< 0.001
REM sleep (% TST), mean (SD)	20.4 (6.4)	20.5 (6.4)	19.6 (6.4)	17.0 (6.6)	17.5 (6.3)	< 0.001
Arousal index, mean (SD)	19.8 (9.3)	20.4 (9.5)	22.4 (10.1)	24.1 (11.3)	31.3 (12.5)	< 0.001
Total AHI (NREM+REM) events/h, mean (SD)	2.9 (3.3)	5.7 (3.5)	8.8 (3.2)	10.8 (2.9)	29.1 (12.9)	< 0.001
AHI events/h, median (25-75 IQR)	1.6 (0.7-3.9)	4.7 (2.9-7.7)	8.6 (6.5-11.4)	11.5 (8.8-12.8)	25.0 (19.2-35.6)	< 0.001
AHI REM events/h, median (25-75 IQR)	1.5 (0.0-3.1)	8.8 (6.6-11.6)	20.4 (17.3-24.2)	34.6 (31.6-40.0)	31.1 (18.1-42.1)	< 0.001
AHI NREM, events/h, median(25-75 IQR)	1.5 (0.3-4.5)	3.5 (1.3-7.4)	5.4 (2.7-8.9)	5.6 (3.3-7.6)	24.4 (18.2-35.6)	< 0.001
AHI REM/AHI NREM, median (25-75 IQR)	0.5 (0.0-1.8)	2.4 (1.3-6.2)	3.9 (2.4-7.5)	7.0 (4.8-10.8)	1.0 (0.7-1.6)	< 0.001

AHI, apnea hypopnea index; AHI NREM, apnea hypopnea index NREM sleep; AHI REM, apnea hypopnea index REM sleep; 25-75 IQR, 25^{th}-75^{th} percentile of interquartile range; min, minutes; SD, standard deviation; TST, total sleep time.

Table 3—Self-reported perceived health status, quality of life measures and sleepiness in subjects in MrOS Sleep Study

	AHI < 15					
Subject Characteristics	**AHI-REM < 5 (n = 858)**	**AHI-REM 5 to < 15 (n = 644)**	**AHI-REM 15 to < 30 (n = 409)**	**AHI-REM ≥ 30 (n = 133)**	**AHI ≥ 15 (n = 721)**	**p-value**
FOSQ score (5-20), mean (SD)	18.7 (1.4)	18.7 (1.4)	18.8 (1.5)	18.8 (1.7)	18.5 (1.7)	0.003
PSQI score (0-21), mean (SD)	5.5 (3.2)	5.3 (2.9)	5.8 (3.3)	5.9 (3.6)	5.9 (3.4)	0.002
SF12 mental summary scale, mean (SD)	55.2 (7.3)	55.6 (6.8)	55.3 (7.4)	55.2 (7.5)	54.6 (8.2)	0.18
SF12 physical summary scale, mean (SD)	49.7 (9.7)	49.5 (9.5)	49.1 (10.3)	47.8 (10.4)	47.2 (10.3)	< 0.001
ESS score, mean (SD)	5.9 (3.5)	6.2 (3.6)	5.9 (3.4)	6.2 (3.5)	6.6 (4.0)	0.02
ESS score > 10, n (%)	100 (11.7)	82 (12.7)	45 (11.0)	11 (8.3)	121 (16.8)	0.006
Geriatric Depression Scale ≥ 6 n (%)	46 (5.4)	31 (4.8)	28 (6.9)	9 (6.8)	57 (7.9)	0.12
Self-perceived health (excellent/good), n (%)	773 (90.1)	568 (88.3)	354 (86.6)	107 (80.5)	612 (84.9)	0.003

AHI, apnea hypopnea index; AHI-REM, apnea hypopnea index REM sleep; BMI, body mass index; ESS, Epworth Sleepiness Scale; FOSQ, Functional Outcomes of Sleep Questionnaire; GDS, Geriatric Depression Scale-15; PSQI, Pittsburg Sleep Quality Index; SD, standard deviation; SF-12, Short Form 12.

Table 4—Adjusted* means **(A)** and odds ratios **(B)** (95%CI) of functional outcome measures by AHI categories

	AHI < 15				
A	**AHI-REM ≤ 5**	**AHI-REM 5 to < 15**	**AHI-REM 15 to < 30**	**AHI-REM ≥ 30**	**AHI ≥ 15**
ESS	5.84 (5.60, 6.09)	6.16 (5.88, 6.44)	5.87 (5.52, 6.22)	6.33 (5.71, 6.95)	6.66 (6.39, 6.92)**
PSQI	5.49 (5.27, 5.71)	5.28 (5.03, 5.52)	5.75 (5.44, 6.06)	5.86 (5.32, 6.41)	5.88 (5.65, 6.12)**
FOSQ	18.8 (18.6, 18.9)	18.7 (18.6, 18.9)	18.8 (18.6, 18.9)	18.7 (18.5, 19.0)	18.5 (18.4, 18.6)**
Physical summary scale (SF-12)	49.6 (48.9, 50.2)	49.4 (48.6, 50.1)	49.2 (48.2, 50.1)	47.9 (46.2, 49.6)	47.4 (46.7, 48.1)**
Mental summary scale (SF-12)	55.1 (54.6, 55.6)	55.5 (54.9, 56.1)	55.3 (54.6, 56.0)	55.4 (54.2, 56.7)	54.7 (54.1, 55.2)
B					
ESS > 10	1.0 (reference)	1.13 (0.83, 1.55)	0.97 (0.67, 1.42)	0.77 (0.40, 1.49)	1.69 (1.26, 2.27)**
Self-perceived health (good/excellent)	1.0 (reference)	0.87 (0.62, 1.21)	0.76 (0.53, 1.10)	0.51 (0.31, 0.83)**	0.67 (0.49, 0.91)**
Geriatric Depression Scale ≥ 6	1.0 (reference)	0.88 (0.55,1.40)	1.23 (0.75, 2.01)	1.19 (0.56, 2.53)	1.38 (0.91, 2.08)

*Adjusted for age and study site, **different from REM AHI < 5 at p < 0.05 (adjustment of BMI, waist or neck circumference did not make any significant difference) in subjects with AHI < 15 in MrOS Sleep Study. AHI, apnea hypopnea index; AHI-REM, apnea hypopnea index REM sleep; BMI, body mass index; FOSQ, Functional Outcomes of Sleep Questionnaire; PSQI, Pittsburg Sleep Quality Index; SD, standard deviation; SF-12, Short Form 12.

by the ESS. In this elderly population, only adjusted AHI-REM ≥ 30 was associated with a decrease in self-perceived health status. There were no other associations between REM-predominant OSA and the behavioral measures studied.

Prior literature has provided conflicting reports regarding whether REM-predominant OSA is associated with excessive daytime sleepiness. Excessive daytime sleepiness can affect 10% to 33% of the elderly and has been associated with significant consequences, including an increased incidence of functional impairment, falls, cognitive deficits, and mortality.[13,45-47] The presence of OSA has been shown to be an important risk factor for mortality from excessive daytime sleepiness in older adults.[13,24] In our study, REM-predominant OSA was not associated with increased daytime sleepiness using the ESS. This is similar to two large studies which showed that OSA in NREM sleep was associated with excessive daytime sleepiness while patients with REM-predominant OSA did not have evidence of excessive daytime sleepiness.[17,22]

Similar to data from the Sleep Heart Health Study,[22] our results show that after adjusting for age, BMI, and study site, in subjects with either AHI < 15 or < 5, REM-predominant OSA did not have a significant association with quality of life measures as measured by FOSQ, PSQI, SF-12 physical and mental summary scale, or GDS-15. Worse self-perceived health, however, was associated with REM-AHI ≥ 30 (**Table 3** and **4**). Similar to our results, the Sleep Heart Health Study showed that REM-predominant SDB was not independently associated with daytime sleepiness, impaired health-related quality of life, or self-reported sleep disruption.[22] Self-perceived health status was not reported in the Sleep Heart Health Study.

We choose AHI ≥ 15 as the primary definition of OSA in our analysis because of the high prevalence of modestly elevated AHI levels in older adults that has no significant clinical consequences.[1-3,48,49] Morbidity and mortality in the elderly with lower AHI levels have been shown to be similar to those without OSA.[50,51] We further analyzed our data defining OSA as AHI ≥ 5 during the entire sleep period and defining REM-predominant OSA as AHI < 5 with AHI-REM ≥ 5 and the results were similar (supplemental material **Tables S3** and **S4**).

In our cohort, the average time spent in REM sleep time was 70.3 ± 28.2 min and in NREM 286.3 ± 55.5 min. It is possible that some of the effects of REM-predominant OSA were mitigated by a decrease in time spent in REM sleep with increasing AHI-REM (**Table 2**). This could be due to increased events in REM sleep leading to arousals and decreasing the time in REM sleep. The total AHI in all subgroups of AHI-REM was low, with the highest being 10.8 ± 2.9 in the subgroup with AHI-REM > 30. The total AHI in subjects with AHI ≥ 15 was 29.1 ± 12.9. This significant difference may have also been responsible for the lack of any effect of AHI-REM on sleepiness and quality of life measures.

AHI levels increase with age[1,48]; however, it has not been clear if REM-predominant OSA increases with age. The prevalence of REM-predominant OSA in our population was 42.8%, which is higher than the 14% in men ≥ 70 years old in another published trial with a similar definition of REM-predominant OSA.[16] More severe REM-predominant OSA was associated with a higher BMI, neck and waist circumference, and an increased prevalence of snoring. It has been suggested that narrowing of the upper airway in REM sleep due to REM-associated atonia may lead to changes in airway closing pressure in REM sleep.[52] It is possible that an increase in BMI or neck and waist circumference lead to an increased AHI-REM before any changes were observed in AHI-NREM which may explain some of our findings. The strength of our study is that we were able to evaluate the association of REM-predominant OSA with daytime sleepiness in a large, community-based sample of older adults, a population group that has not been evaluated before for the effects of REM-predominant OSA.

Our study has several limitations. This is an observational study and with associated limitations on inferences regarding causality. Our study population consists of community dwelling, ambulatory men aged 65 years or older with ability to walk without the assistance, who did not have either bilateral hip replacements or a medical condition that would result in imminent death at the time of enrollment.[25] There were no other exclusion criteria. Another limitation is that more than 90% of our subjects were Caucasian. Our data should be taken with caution while generalizing it to other populations and racial groups. We only studied male subjects and although we used validated instruments to measure subjective indices of sleepiness, these instruments may have lower levels of discrimination in older subjects, who may also have other competing causes of sleepiness.[53,54]

CONCLUSION

In a cohort of community dwelling males, 67 years or older, REM-predominant OSA was associated with small differences in objectively measured sleep quality: decreased total sleep time, sleep efficiency, minutes and percentage of time in REM sleep. However, increasing AHI-REM levels were not linearly associated with subjective measures of excessive daytime sleepiness or quality of life. Severe REM-predominant OSA was associated with worse self-perceived health status.

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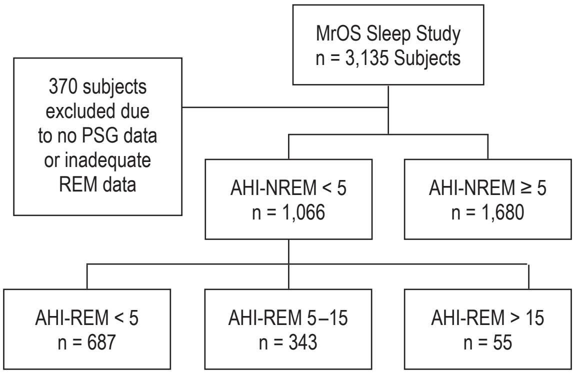
SUPPLEMENTAL MATERIAL

Figure S1—Distribution of patients in MrOS Sleep Study with AHI < 5 vs. AHI ≥ 5



AHI, apnea hypopnea index; AHI-REM, apnea hypopnea index REM sleep; PSG, polysomnography.

Table S1—Subject characteristics based on AHI and AHI-REM sleep in subjects with AHI < 5/h in MrOS Sleep Study

	AHI < 5				
Subjects Characteristics	**AHI-REM < 5 (n = 668)**	**AHI-REM 5–15 (n = 343)**	**AHI-REM > 15* (n = 55)**	**AHI ≥ 5 (n = 1680)**	**p-value**
Age, mean (SD)	76.4 (5.7)	75.8 (5.5)	76.9 (4.8)	76.4 (5.5)	0.26
Caucasian, n (%)	637 (92.7)	308 (89.8)	54 (98.2)	1545 (92.0)	0.13
BMI (kg/m^2), mean (SD)	25.6 (3.1)	26.7 (3.4)	28.5 (4.7)	27.8 (3.9)	< 0.001
Neck circumference (cm), mean (SD)	145.4 (70.9)	147.0 (71.9)	153.2 (76.5)	146.1 (71.0)	0.88
Waist circumference (cm), mean (SD)	38.4 (2.6)	39.2 (2.7)	40.2 (3.0)	39.9 (3.0)	< 0.001
PASE score, mean (SD)	95.8 (9.9)	98.2 (10.5)	103.5 (11.9)	101.2 (11.3)	< 0.001
Benzodiazepine use, n (%)	36 (5.2)	18 (5.3)	8 (9.1)	59 (3.5)	0.05
Diabetes, n (%)	62 (9.0)	43 (12.5)	10 (18.2)	249 (14.8)	0.001
Hypertension, n (%)	309 (45.0)	160 (46.7)	27 (49.1)	889 (52.9)	0.003
CVD, n (%)	268 (39.1)	137 (39.9)	22 (40.0)	731 (43.6)	0.18
Heart attack, n (%)	119 (17.3)	58 (16.9)	10 (18.2)	292 (17.4)	0.99
Stroke, n (%)	32 (4.7)	11 (3.2)	1 (1.8)	60 (3.6)	0.46
Respiratory illness, n (%)	32 (4.7)	20 (5.8)	4 (7.3)	87 (5.2)	0.76
Alcohol (drinks/wk), mean (SD)	3.7 (4.2)	3.1 (4.0)	2.7 (3.9)	3.3 (4.2)	0.06
Current smoker, n (%)	17 (2.5)	11 (3.2)	1 (1.8)	24 (1.4)	0.1
Ever snored, n (%)	498 (82.2)	265 (86.0)	42 (87.5)	1367 (89.9)	< 0.001

*Due to the small number of subjects, AHI-REM > 15 was not further subdivided into AHI-REM 15-30 and AHI-REM > 30. AHI, apnea hypopnea index; AHI-NREM, apnea hypopnea index NREM sleep; AHI-REM, apnea hypopnea index rapid eye movement sleep; BMI, body mass index; CVD, cardiovascular disease; PASE, Physical Activity Scale for the Elderly; SD, standard deviation; TST, total sleep time.

Table S2—Polysomnography Characteristics of subjects with AHI < 5/h in MrOS Sleep Study

Subject Characteristics	AHI < 5: AHI-REM < 5 (n = 668)	AHI < 5: AHI-REM 5–15 (n = 343)	AHI < 5: AHI-REM > 15* (n = 55)	AHI ≥ 5 (n = 1680)	p-value
TST (min), mean (SD)	362.7 (65.5)	364.3 (62.1)	329.0 (86.8)	353.4 (68.5)	< 0.001
Sleep efficiency % , mean (SD)	75.8 (11.7)	76.1 (10.8)	69.1 (13.4)	73.1 (12.1)	< 0.001
REM time (min), mean (SD)	75.8 (28.1)	76.0 (27.0)	50.2 (25.3)	67.5 (27.9)	< 0.001
REM sleep, % TST (SD)	20.5 (6.3)	20.6 (6.0)	14.5 (5.7)	18.8 (6.6)	< 0.001
Arousal Index, mean (SD)	18.9 (8.6)	18.7 (9.4)	22.1 (10.1)	26.4 (12.0)	< 0.001
Total AHI (NREM+REM) events/h, mean (SD)	1.5 (1.3)	3.0 (1.1)	3.8 (0.88)	17.8 (13.1)	< 0.001
AHI events/h, median (IQR)	1.1 (0.49-2.3)	3.0 (2.2-3.9)	4.1 (3.3-4.4)	13.2 (8.4-23.0)	< 0.001
AHI-REM events/h, median (IQR)	1.2 (0.0-2.7)	7.6 (6.1-10.3)	17.9 (16.1-22.9)	20.1 (10.3-32.6)	< 0.001
AHI-NREM, events/h, median (IQR)	0.94 (0.21-2.4)	1.4 (0.6-2.5)	1.1 (0.6-1.8)	11.8 (6.6-22.3)	< 0.001
AHI-REM/AHI-NREM, median (IQR)	0.8 (0.0-2.4)	5.8 (3.1-10.8)	15.0 (12.5-15.0)	1.4 (0.7-2.9)	< 0.001

*Due to the small number of subjects, AHI-REM > 15 was not further subdivided into AHI-REM 15-30 and AHI-REM > 30. AHI, apnea hypopnea index; AHI-NREM, apnea hypopnea index NREM sleep; AHI-REM, apnea hypopnea index rapid eye movement sleep; IQR, interquartile range; Min, minutes; SD, standard deviation; TST, total sleep time.

Table S3—Self-reported perceived health status, quality of life measures and sleepiness in subjects with the REM-only OSA vs. those with no OSA in patients with AHI < 5/h in MrOS Sleep Study

Subject Characteristics	AHI < 5: AHI-REM < 5 (n = 687)	AHI < 5: AHI-REM 5–15 (n = 343)	AHI < 5: AHI-REM > 15* (n = 55)	AHI ≥ 5 (n = 1680)	p-value
FOSQ score (5-20), mean (SD)	18.8 (1.5)	18.8 (1.3)	19.0 (0.98)	18.6 (1.6)	0.02
PSQI score (0-21), mean (SD)	5.5 (3.3)	5.1 (2.8)	6.2 (3.6)	5.7 (3.3)	0.003
SF-12 mental summary scale, mean (SD)	55.3 (7.3)	55.2 (7.2)	55.1 (7.7)	55.0 (7.6)	0.86
SF-12 physical summary scale, mean (SD)	49.6 (9.8)	50.0 (9.5)	47.2 (10.8)	48.3 (10.1)	0.001
ESS score, mean (SD)	5.9 (3.5)	6.2 (3.7)	5.5 (3.5)	6.3 (3.7)	0.11
ESS score > 10, n (%)	80 (11.6)	46 (13.4)	6 (10.9)	227 (13.5)	0.62
GDS ≥ 6, n (%)	36 (5.2)	18 (5.3)	6 (10.9)	111 (6.6)	0.24
Self-perceived health (excellent/good), n (%)	615 (89.5)	303 (88.6)	47 (85.5)	1449 (86.3)	0.14

*Due to the small number of subjects, AHI-REM > 15 was not further subdivided into AHI-REM 15-30 and AHI-REM > 30. AHI, apnea hypopnea index; AHI-REM, apnea hypopnea index REM sleep; BMI, body mass index; ESS, Epworth Sleepiness Scale; FOSQ, Functional Outcomes of Sleep Questionnaire; GDS, Geriatric Depression Scale-15; PSQI, Pittsburgh Sleep Quality Index; SD, standard deviation; SF-12, Short Form 12.

Table S4—Adjusted# means **(A)** and odds ratios **(B)** (95%CI) of functional outcome measures by AHI categories

	AHI < 5: AHI-REM < 5 (n = 687)	AHI < 5: AHI-REM 5–15 (n = 343)	AHI < 5: AHI-REM > 15* (n = 55)	AHI ≥ 5 (n = 1680)
A				
Epworth Sleepiness Score	5.84 (5.56, 6.11)	6.17 (5.78, 6.55)	5.51 (4.55, 6.47)	6.30 (6.13, 6.48)**
PSQI	5.55 (5.31, 5.79)	5.11 (4.77, 5.45)	6.22 (5.37, 7.07)	5.70 (5.54, 5.85)
FOSQ	18.8 (18.6, 18.9)	18.8 (18.7, 19.0)	19.0 (18.6, 19.4)	18.6 (18.5, 18.7)**
Physical summary scale (SF-12)	49.4 (48.7, 50.2)	49.8 (48.7, 50.8)	47.3 (44.7, 49.8)	48.4 (48.0, 48.9)**
Mental summary scale (SF-12)	55.2 (54.6, 55.8)	55.1 (54.3, 55.9)	55.0 (53.1, 57.0)	55.1 (54.7, 55.4)
B				
Epworth Sleepiness Score > 10	1.0 (reference)	1.20 (0.81, 1.78)	1.01 (0.42, 2.44)	1.26 (0.95, 1.66)
Self-perceived health (good/excellent)	1.0 (reference)	0.96 (0.63, 1.45)	0.71 (0.32, 1.57)	0.82 (0.61, 1.09)
Geriatric Depression Scale ≥ 6	1.0 (reference)	0.99 (0.55, 1.78)	2.10 (0.84, 5.26)	1.16 (0.78, 1.72)

#Adjusted for age and clinic, (adjustment of BMI, waist or neck circumference did not make any significant difference) in subjects with AHI < 5/h in MrOS Sleep Study. *Due to the small number of subjects, AHI-REM > 15 was not further subdivided into AHI-REM 15-30 and AHI-REM > 30. **Different from REM AHI < 5 at p < 0.05. AHI, apnea hypopnea index; AHI-REM, apnea hypopnea index REM sleep; BMI, body mass index; FOSQ, Functional Outcomes of Sleep Questionnaire; PSQI, Pittsburgh Sleep Quality Index; SD, standard deviation; SF-12, Short Form 12.