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Associations between sleep conditions and body composition states: results of the EPISONO study

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Abstract

Background Evidence suggests anthropometric indicators of obesity are associated with changes in sleep quality and quantity, and the presence of obstructive sleep apnoea (OSA). Investigations including diverse and objective evaluations of sleep and body composition are scarce. We aimed to evaluate the associations between indicators of sleep impairment and body composition states in a sample from a population-based study.

Methods Participants of the first follow-up of the EPISONO (São Paulo, Brazil) >50 years were cross-sectionally evaluated. Sleep was assessed through questionnaires, actigraphy, and polysomnography. Body composition was evaluated by bioelectrical impedance analysis. Appendicular skeletal muscle mass adjusted for body mass index defined sarcopenia (men <0.789 and women <0.512). Total body fat defined obesity (men >30% and women >40%). The overlap between both conditions defined sarcopenic obesity (SO). Final results were obtained by multinomial logistic regression analysis.

Results Three hundred fifty-nine adults [mean (standard deviation) age, 61 (8.8) years; 212 (59.1%) female] were enrolled. Obesity was detected in 22.6% of the sample, sarcopenia in 5.6%, and SO in 16.2%. After controlling for covariates, OSA was associated with SO [odds ratio = 3.14, 95% confidence interval (CI) = 1.49–6.61]. Additionally, nocturnal hypoxaemia was associated with both obesity (adjusted odds ratio = 2.59, 95% CI = 1.49–4.49) and SO (odds ratio = 2.92, 95% CI = 1.39–6.13). Other indicators of poor sleep/sleep disorders were not associated with body composition states.

Conclusions Sarcopenic obesity but not obesity alone was associated with OSA. Both obesity and SO but not sarcopenia were associated with nocturnal hypoxaemia. The findings suggest a complex pathophysiologic relationship between adverse body composition states and OSA. Upcoming research on risk factors and therapeutic interventions for OSA should target synchronically the lean and adipose body tissues.

Keywords Body composition; Obesity; Sarcopenia; Sarcopenic obesity; Obstructive sleep apnoea

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Introduction

Unfavourable body composition changes develop inexorably throughout adulthood due to lifelong interactions among endogenous, environmental, and lifestyle factors.[1,2] As a result, muscle loss and body fat accumulation lead to an increased risk of sarcopenia and obesity, contributing to adverse health-related outcomes in advanced ages.[3,4] More recently, the co-presence of sarcopenia and obesity, known as sarcopenic obesity (SO), has been considered a more deleterious body composition phenotype.[5] In addition to a myriad of cardiometabolic outcomes related to the effects of fat

tissue, higher proportions of fat mass might further affect muscle quality and increase the risk of disability and mortality.[6] The pathophysiological aspects explaining both muscle decline and body fat accumulation are multifactorial, and the mechanisms responsible for these changes are still under investigation.

Concurrently, sleep parameters worsen during adulthood, leading to an increased prevalence of sleep disorders from mid-life to late-life.[7] As an example, the majority of older adults complain of difficulty sleeping, and 36–69% of older adults report sleep disturbances.[8,9] Moreover, respiratory sleep parameters deteriorate with aging, and a remarkable age-related increased risk of obstructive sleep apnoea (OSA) is observed in population-based studies.[10–12] OSA has a multifactorial pathophysiology, and underrecognized risk factors may play a significant role in the development or worsening of this condition. Although obesity has a well-established association with OSA, more recently, indirect measurements have suggested that skeletal muscle mass reduction may be contributing to a higher risk of OSA.[13,14]

Likewise, other sleep-related measures have been isolatedly associated with either obesity or sarcopenia in middle-aged and older adults.[15–18] However, no study has evaluated the associations of sleep with obesity and/or sarcopenia using simultaneously different sleep assessment methods and including polysomnography (PSG), the gold-standard test for the diagnosis of OSA. Furthermore, to our knowledge, no study examined the potential relationships of sleep disorders with the co-occurrence of sarcopenia and obesity (SO). This study aimed to investigate the associations between sleep features indicating poor sleep/sleep disorder and different body composition patterns in a sample of middle-to-old age individuals living in the community.

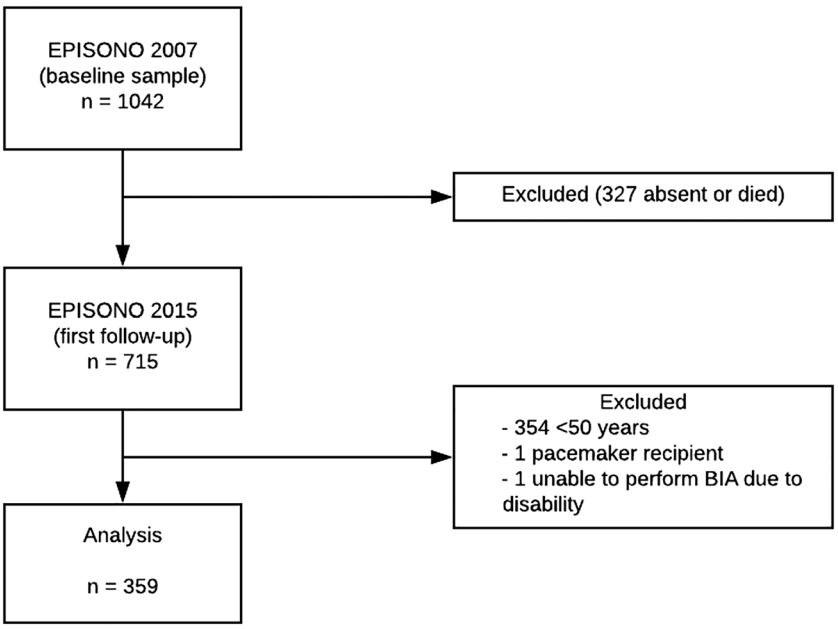
Materials and methods

Study population

Data from the first follow-up of the Sao Paulo Epidemiologic Sleep Study (EPISONO) from 2007, comprising a general population-based sample of Sao Paulo, Brazil, were analysed. Baseline's survey design was described in details elsewhere.[18] From July 2015 to April 2016, the second wave of this study was carried out and included 715 individuals of the baseline sample. Follow-up participants were community-dwelling adults from both genders and derived from a multi-ethnic population.

To our particular study analysis, individuals who were >50 years were included. Pacemaker recipients and those who were disable and could not undergo the body composition analysis were excluded from our analysis. Finally, we used a sample composed of 359 participants (*Figure* 1). The Ethical Committee of the Universidade Federal de Sao Paulo approved this study (registration number 610514/14), which was conducted according to the ethical standards defined in the 1964 Declaration of Helsinki as well as its subsequent amendments and was registered with ClinicalTrials.gov

Figure 1 Project EPISONO flowchart (from the 2007 baseline sample to the 2015 first follow-up) with the exclusion of participants according to exclusion criteria



(Identifier NCT00596713). Written informed consent was obtained from all volunteers.

Anthropometry and body composition measures

Height (stadiometer to the nearest 0.1 cm) and weight (electronic scale to the nearest 0.1 kg) were used to calculate the body mass index (BMI, kg/m^2). Body composition assessment was performed by a direct segmental multi-frequency bioelectrical impedance analysis (BIA) using InBody720 (Biospace Ltd, Seoul, Korea). Eight tactile electrodes (four in contact with the palm and thumb of hands and four in contact with the sole of feet) measured the impedance of each body segment at six different frequencies (1, 5, 50, 250, 500, and 1000 kHz) separately. The measurements were controlled by a microprocessor, and data output was calculated by a manufacturer's algorithm and included total and appendicular skeletal muscle and fat masses. Previous studies have validated the use of this instrument in different contexts.[19–21] Participants were submitted to anthropometric and body composition measurements right after waking up from an overnight laboratory-based PSG. They were using light clothes and fasting for more than 8 h. Voiding was recommended before the BIA.

Skeletal muscle mass index (SMI) for the morphological criteria definition of sarcopenia was applied according to the Foundation National Institute of Health, International Working Group on Sarcopenia.[22] More recently, guidelines have been recommended this criterion as one of the objective tools for the diagnosis of sarcopenia.[23] Appendicular skeletal muscle mass adjusted for BMI was generated for each participant, and pre-specified cut-offs for sarcopenia were established according to previous studies (men: $<$0.789 and women: $<$0.512).[23] Obesity was defined as total body fat $>$30% (men) and $>$40% (women).[24] SO was determined by the overlap between both definitions.

Sleep measures and definitions

During sleep evaluation, participants completed the Pittsburgh Sleep Quality Index (PSQI), which subjectively measures the sleep quality over a 1 month period. Global PSQI scoring ranges from 0 to 21. Scores $>$5 are considered as poor self-reported sleep quality and have a sensitivity of 89.6% and specificity of 86.5% in distinguishing good vs. poor sleepers.[25] The Epworth Sleepiness Scale, a questionnaire that classifies subjective daytime sleepiness, scoring from 0 to 24, with a score of $>$10 indicating excessive daytime sleepiness, was also completed.[26] A subjective sleep assessment using the 'Universidade Federal de São Paulo (UNIFESP)' Sleep Questionnaire additionally included questions related to insomnia symptoms.[19] Chronic insomnia complaint was defined as the report of regular insomnia symptoms (difficulties initiating/maintaining sleep and early morning awakenings, occurring at least three times a week, during at least 3 months).[27]

Nocturnal average sleep duration was objectively evaluated by actigraphy (Motionlogger Watch, Ambulatory Monitoring Inc., EUA). Volunteers were invited to use the device for 10 consecutive days. Similar to a wristwatch device monitoring, the actigraph was used in the non-dominant arm for at least three consecutive days for the assessment of the sleep–wake patterns. Collected data applied the *zero-crossing* mode, in 1 min epochs.[28] A sleep diary was filled out during this period to obtain information related to sleep and activity. A validated algorithm estimated the sleep-related variables.[29] Objective short sleep duration was defined as averaged nocturnal sleep duration measured by actigraphy $<$6 hr. The median registry of actigraphy data was nine 24 h periods [interquartile range (IQR), 4–10).

Additional objective sleep parameters were measured by an overnight laboratory-based PSG study, including sleep latency, sleep efficiency, wake time after sleep onset, sleep stages 3 (N3, %) and rapid eye movement (REM, %), periodic limb movement index (events/h), apnoea–hypopnoea index (AHI, events/h), and nocturnal hypoxaemia, defined as the per cent of time during sleep with percutaneous oxygen saturation (SpO_2) $<$90% (% of total sleep time with SpO_2 $<$90%). Sleep recording was performed by PSG technologist using a digital system (EMBLA® N7000, Embla Systems Inc., Broomfield, CO, USA). The following physiological tests were conducted: electroencephalography (EEG; F3-M2, F4-M1, C3-M2, C4-M1, O1-M2, and O2-M1), electrooculography (EOG; EOG-Left-M2 and EOG-Right-M1), electromyography (muscle of the submentonian region, tibialis anterior muscle, masseter, and temporal region), electrocardiography (derivation D2 modified), and airflow detection by both thermocouple and nasal cannula. Respiratory effort was assessed by inductance plethysmography belts. Snoring, body position, SpO_2, and pulse rate were evaluated by EMBLA® sensors (Embla Systems Inc., Broomfield, CO, USA). All PSGs were performed and scored by two technicians following guidelines for sleep studies and were reviewed by a sleep medicine physician. Sleep stages, EEG arousals, and leg movements were scored according to established criteria.[30]

Apnoea was defined as complete or close to complete airflow cessation for $\geq$10 s, and hypopnoea was identified as an evident reduction in the breathing amplitude (at least 30% below the baseline) for $\geq$10 s accompanied by either an EEG arousal or a SpO_2 drop $\geq$3%. OSA was defined according to AHI $>$15.[31,32]

Covariates

During the interview at the sleep laboratory, the application of the Socio-economics and Demographics Questionnaire

obtained general characteristics including age, gender, ethnicity (African–Americans, Caucasians, and others),[33] education level (college/graduate vs. lower education level), marital status (married/living together vs. single/divorced/widowed), social classification (high vs. lower level), smoking status (never, past, and current), alcohol intake (categorized into days per week of consumption: 0, 1–2, or ≥3), and recommended physical activity/week (>150 min of moderate-intensity exercise and/or 75 min of high-intensity exercise vs. lower exercise levels).[33,34] Participants were considered to have clinical comorbidity if they reported a previous physician diagnosis of one of the following: hypertension, diabetes, chronic osteoarticular disease, chronic pulmonary disease, cardiovascular diseases, and heart failure. The number of clinical comorbidities was categorized into a comorbidity index: 0, 1, or ≥2. The total score in the Beck Depression Inventory evaluated depression symptoms.[35] All current medications (prescription, over-the-counter, or vitamins) were registered and categorized according to their pharmacological class.

On the morning following the PSG exam, participants had a blood sample collected (12 h of fasting) for quantification of serum biochemical levels including total 25-hydroxyvitamin D (25(OH)D), insulin-growth factor 1 (IGF-1), free testosterone, leptin, adiponectin, interleukin 6 (IL-6), interleukin 10 (IL-10), tumour necrosis factor-alpha (TNF-α), and ferritin, which was quantified using standardized laboratory assay procedures described previously in detail.[19]

Statistical analyses

Characteristics of participants were described using means and standard deviations or counts and percentages. Skewed variables were summarized using medians and IQRs. One-way ANOVA or Kruskal–Wallis and χ^2 tests of homogeneity or Fisher's exact test were used when appropriate to compare participants' characteristics according to body composition definitions (normal, obesity, sarcopenia, and SO). Univariate analysis also compared normal and different adverse body composition patterns according to sleep features indicating poor sleep or sleep disorders: poor subjective sleep quality in the last month (PSQI >5 vs. ≤5),[25] excessive daytime sleepiness (Epworth Sleepiness Scale >10 vs. ≤10),[26] chronic insomnia complaint,[27] objectively measured short sleep duration (average nocturnal sleep duration from actigraphy <6 h),[36,37] prolonged sleep latency (>30 min vs. ≤30 min),[38] reduced sleep efficiency (<80% vs. >80%),[38] increased night-time wakefulness (wake time after sleep onset >60 min vs. ≤60 min),[39] reduced N3 sleep (% N3 sleep stage 1st vs. 4th quartile),[38] reduced REM sleep (% REM sleep stage 1st vs. 4th quartile),[38] periodic limb movements of sleep (periodic limb movement index >15 vs. ≤15),[40] OSA according to AHI (AHI >15 vs. <15),[41] and nocturnal hypoxia (>1% of sleep time with SpO_2 <90% vs. ≤1%).[38] Only sleep variables that were significantly associated with body composition status in the univariate analysis were considered to the subsequent multivariate modelling strategy.

Multinomial logistic regression models were applied to analyse the possible associations between each sleep variable as a main predictor and body composition categorized as adverse body composition patterns as the outcome (obesity, sarcopenia, and SO), using normal body composition category as the reference. Results were presented as adjusted odds ratio and 95% confidence interval (CI). For each one of the final multiple regression models including one of the sleep variables, known or suspected determinants of sleep predictors and body composition outcomes were examined for potential confounding. After evaluation according to biological plausibility, covariates in age and gender-adjusted models with $P < 0.20$ were considered for inclusion in the full multivariate models. Potential confounders tested for inclusion were ethnic group, social class, education, marital status, smoking status, alcohol consumption, recommended physical activity per week, number of comorbidities, Beck Depression Inventory score, psychotropic/hypnotic use, diuretic use, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers use, serum measures of 25(OH)D, IGF-1, free testosterone (gender-specific lower tertile), leptin, adiponectin, IL-6, IL-10, TNF-α, and ferritin. Before the covariate selection process, serum measures of 25(OH)D, IGF-1, free testosterone, leptin, adiponectin, IL-6, IL-10, TNF-α, and ferritin were examined as potential mediators using the Sobel–Goodman test followed by bootstrap with case resampling.

Because measures of sleep duration averaged over five nights of actigraphy recording were more likely representative of usual sleep duration pattern than only three nights, a sensitivity analysis excluding participants with <5 days of actigraphy registration was performed. As results were not significantly different after this exclusion, only results for the total sample were presented. Similarly, as a sensitivity analysis excluding eight participants with central sleep apnoea (central apnoea events >50% of total AHI >15) also did not affect the results, the entire sample was considered when testing the effects of OSA. All analyses were performed using STATA software, version 14.2 (Stata Corp., College Station, Texas, USA), and a P value <0.05 was considered statistically significant.

Results

General characteristics associated with adverse body composition patterns

Among the 359 participants [212 (59.1%) women], 164 (45.68%) were 60 years or more. *Table* 1 shows sample distributions according to body composition classification, from which 200 (55.71%) were classified as normal regarding SMI

Table 1 Relationships between body composition classification and participants characteristics

	Overall sample (n = 359)	Normal (n = 200)	Obese (n = 81)	Sarcopenic (n = 20)	Sarcopenic obese (n = 58)	P value[a]
Demographics						
Age, years—median (IQR)	59 (54–66)	57 (53–63)	59 (55–67)[c]	65 (56.5–73)[c]	64 (59–70)[c]	0.0001
Female gender—n (%)	212 (59.05)	117 (58.50)	59 (72.84)[c]	4 (20.00)[c]	32 (55.17)[c]	<0.0001
Ethnicity—n (%)						0.71
African–Americans—n (%)	45 (12.53)	26 (13.00)	9 (11.11)	3 (15.00)	7 (12.07)	
Caucasians—n (%)	208 (57.94)	116 (58.00)	51 (62.96)	8 (40.00)	33 (56.90)	
Others—n (%)	106 (29.53)	58 (29.00)	21 (25.93)	9 (45.00)	18 (31.03)	
Education (college/graduate school)—n (%)	106 (29.53)	65 (32.50)	29 (35.80)	2 (10.00)	10 (17.24)[c]	0.02
Marital status (married/living together)—n (%)	199 (54.43)	108 (54.00)	43 (53.09)	13 (65.00)	35 (60.34)	0.65
Social classification (high)—n (%)	218 (60.72)	127 (63.50)	51 (62.96)	11 (55.00)	29 (50.00)	0.27
Smoking status—n (%)						0.06
Never	158 (44.01)	85 (42.50)	33 (40.74)	11 (55.00)	29 (50.00)	
Past smoking	144 (40.11)	73 (36.50)	38 (46.91)	7 (35.00)	26 (44.83)	
Current smoking	57 (15.88)	42 (21.00)	10 (12.35)	2 (10.00)	3 (5.17)	
Alcohol intake, days/week—n (%)						0.32
0	194 (54.19)	99 (49.50)	50 (61.73)	10 (52.63)	50 (59.52)	
1–2	115 (32.12)	71 (35.50)	19 (23.46)	6 (31.58)	19 (32.76)	
>3	49 (13.69)	30 (15.00)	12 (14.81)	3 (15.79)	4 (6.90)	
Recommended physical activity per week—n (%)	214 (59.61)	125 (62.50)	51 (62.96)	11 (55.00)	27 (46.55)	0.15
Clinical/psychiatric data						
Number of clinical comorbidities—n (%)[b]						0.002
0	89 (24.79)	60 (30.00)[c]	16 (19.75)	4 (20.00)	9 (15.52)	
1	134 (37.33)	84 (42.00)[c]	28 (34.57)	5 (25.00)	17 (29.31)	
2+	136 (37.88)	56 (28.00)[c]	37 (45.68)	11 (55.00)	32 (55.17)[c]	
Beck Depression Inventory score (0–63)—median (IQR)	7 (3–14)	8 (3–15)	8 (4–15)	5 (1–11)	5.5 (2–11)	0.29
Psychotropic/hypnotic use—n (%)	52 (14.48)	29 (14.50)	15 (18.52)	2 (10.00)	6 (10.34)	0.53
Diuretic use—n (%)	66 (18.38)	17 (8.50)	24 (15.89)[c]	5 (25.00)[c]	21 (36.21)[c]	<0.0001
ACE inhibitor/ARB use—n (%)	108 (30.08)	42 (21.00)	38 (46.91)[c]	4 (20.00)[c]	24 (41.38)[c]	<0.0001
Serum measures						
25(OH) vitamin D3 (ng/mL)—mean (SD)	22.09 (7.74)	22.55 (8.04)	21.51 (7.167)	24.07 (6.58)	20.67 (7.72)	0.22
IGF–1 (ng/mL)—mean (SD)	138.51 (47.34)	145.36 (45.968)	126.16 (47.84)[c]	142.57 (38.13)	130.88 (50.57)[c]	0.01
Free testosterone (gender–specific lower tertile, ng/mL)—n (%)	85 (27.74)	87 (43.72)	30 (37.04)	11 (55.00)	24 (41.38)	0.29
Leptin (ng/mL)—median (IQR)	198.87 (61.16–397.38)	50.45 (109.59–330.25)	121.80 (304.16–628.11)[c]	58.18 (39.83–192.20)[c]	275.24 (96.51–680.60)[c]	0.0001
Adiponectin (ug/mL)—median (IQR)	93.05 (52.57–156.38)	54.52 (93.83–153.82)	44.87 (95.82–155.30)	93.90 (22.52–165.30)	89.45 (61.78–148.74)	0.94
IL–6 (pg/mL)—median (IQR)	7.76 (3.09–13.29)	7.00 (2.29–12.81)	5.60 (8.84–14.24)	8.18 (4.20–11.26)	7.72 (3.69–17.56)	0.09
IL–10 (pg/mL)—median (IQR)	0.28 (0.14–0.49)	0.13 (0.28–0.48)	0.27 (0.15–0.51)	0.30 (0.14–0.60)	0.27 (0.14–0.49)	0.85
TNF-α (pg/mL)—median (IQR)	1.42 (1.02–1.91)	0.92 (1.41–1.85)	1.38 (1.01–2.09)	1.32 (1.05–1.55)	1.53 (1.24–1.92)	0.39
Ferritin (mg/dL)—median (IQR)	102.55 (59.3–189.4)	105.3 (59.3–195.4)	96.7 (53.3–178.9)	125.35 (88.25–183.75)	97.85 (59.4–204.4)	0.66

ACE inhibitor/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; IGF-1, insulin-growth factor 1; IL-6, interleukin 6; IL-10, interleukin 10; TNF-α, tumour necrosis factor-alpha.

P value <0.05 was considered statistically significant.

[a]Differences according to body composition status in univariate analysis.

[b]Included comorbidities were hypertension, diabetes, chronic osteoarticular disease, chronic pulmonary disease, cardiovascular diseases and heart failure.

[c]Body composition categories that were considered significantly different from others.

Table 2 Poor sleep indicators and sleep disorders according to body composition status

	Overall sample	Normal	Obese	Sarcopenic	Sarcopenic obese	*P* value[a]
Poor subjective sleep quality in the last month (PSQI score >5)—*n* (%)	179 (49.86)	98 (49.00)	40 (49.38)	10 (50.00)	31 (53.45)	0.95
Chronic insomnia complaint (>3 times/week; >3 months)—*n* (%)	211 (58.77)	109 (54.50)	54 (66.67)	12 (60.00)	36 (62.07)	0.28
Excessive daytime sleepiness (ESS score >10)—*n* (%)	127 (35.38)	75 (37.50)	31 (38.27)	7 (35.00)	14 (24.14)	0.27
Objective short sleep duration—*n* (%)[b]	74 (20.61)	38 (19.00)	18 (22.22)	4 (20.00)	14 (24.14)	0.83
Prolonged sleep latency (>30 min)—*n* (%)	47 (13.24)	21 (10.55)	14 (17.72)	2 (10.00)	10 (17.54)	0.29
Reduced sleep efficiency (<80%)—*n* (%)	173 (48.73)	93 (46.73)	33 (41.77)	14 (70.00)	33 (57.89)	0.06
Increased night-time wakefulness (>60 min)—*n* (%)	219 (61.69)	117 (58.79)	44 (55.70)	16 (80.00)	42 (73.68)[d]	0.04
Reduced N3 sleep (%) (1st quartile)—*n* (%)[c]	96 (27.04)	66 (33.17)	14 (17.72)	8 (40.00)	12 (21.05)	0.06
Reduced REM sleep (%) (1st quartile)—*n* (%)[c]	126 (35.49)	58 (29.15)[d]	34 (43.04)	10 (50.00)	24 (42.11)	0.03
PLM (>15 events/h)—*n* (%)	57 (15.88)	25 (12.50)	20 (24.69)	4 (20.00)	8 (13.79)	0.08
Obstructive sleep apnoea (AHI > 15)—*n* (%)	186 (52.39)	86 (43.22)[d]	46 (58.23)	13 (65.00)	41 (71.93)[d]	<0.0001
Nocturnal hypoxaemia (>1% of TST with SaO_2 <90%)—*n* (%)	168 (47.32)	71 (35.68)[d]	52 (65.82)[d]	7 (35.00)	38 (66.67)[d]	<0.0001

AHI, apnoea–hypopnoea index; ESS, Epworth Sleepiness Scale; N3, sleep stage 3; PLM, periodic limb movements of sleep; PSQI, Pittsburg Sleep Quality Index; REM, rapid eye movements; TST, total sleep time during polysomnography.
P value <0.05 was considered statistically significant.
[a]Differences according to body composition status in univariate analysis.
[b]Nocturnal average sleep duration <6 h measured by actigraphy.
[c]4th quartile as a reference.
[d]Body composition categories that were considered significantly different.

and total fat mass, 20 (5.57%) were classified as sarcopenic, 81 (22.56%) were classified as obese, and 58 (16.16%) were considered SO. No significant differences were observed among the four categories according to ethnicity, marital status, social classification, smoking status, alcohol intake, recommended levels of physical activity, Beck Depression Inventory score, psychotropic/hypnotic use, 25(OH)D, free testosterone, adiponectin, IL-6, IL-10, TNF-α, and ferritin.

Age was higher among those with sarcopenia and SO. Contrasting with other body composition states, obesity status tended to be more observed in women. Sarcopenia and SO were less observed in people with higher education. Participants classified as normal tended to have a lower number of comorbidities. Diuretic use was more observed among those with SO. Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker use was more frequent among those with obesity and SO. IGF-1 was lower and leptin was higher among those with obesity and SO.

Indicators of poor sleep and sleep disorders associated with body composition states

Univariate associations between poor sleep indicators/sleep disorders and body composition states are displayed in *Table* 2. Increased night-time wakefulness, reduced REM sleep, OSA, and nocturnal hypoxaemia were significantly different among the body composition categories. A higher proportion of SO participants had increased night-time wakefulness. Among those with a normal body composition state, a lower proportion had reduced REM sleep. OSA was more observed in participants with SO, and nocturnal hypoxaemia was more frequent in those with obesity and SO.

Table 3 shows the selected indicators of poor sleep/sleep disorder as potential main predictors of adverse body composition states after multivariate analyses. After controlling for age and gender, OSA and nocturnal hypoxaemia were associated with an increased likelihood of obesity. OSA and nocturnal hypoxaemia were associated with SO. In the final multivariate models, OSA continued to be associated only with SO (OR = 3.14, 95% CI = 1.49–6.61) (*Figure* 2). Moreover, nocturnal hypoxaemia continued to be significantly associated with obesity (adjusted odds ratio = 2.59, 95% CI = 1.49–4.49) and SO (OR = 2.92, 95% CI = 1.39–6.13). None of the poor sleep indicators and sleep disorders was associated with sarcopenia.

Discussion

This study extensively explored the associations of sleep features derived from subjective and objective methodological sources with unfavourable body composition states in a sample of adults >50 years. After multiple confounding adjustments, OSA was only significantly associated with SO. Moreover, nocturnal hypoxaemia was associated with both obesity and SO. The final analysis did not find indicators of poor sleep/sleep disorders associated with sarcopenia exclusively. As far as we know, this is the first study to demonstrate the significant association between objective sleep parameters of OSA and SO in adults from the community.

Table 3 Age and gender-adjusted and multivariate[a] adjusted odds ratios (aORs)[b] (95% CI) for adverse body composition patterns[c] by poor sleep indicators[d]

	Obesity		Sarcopenia		Sarcopenic obesity	
	Age and gender adjusted	Multivariate adjusted	Age and gender adjusted	Multivariate adjusted	Age and gender adjusted	Multivariate adjusted
Increased night-time wakefulness (>60 min)	0.84 (0.49–1.46)	0.81 (0.44–1.51)	1.75 (0.54–5.69)	1.26 (0.31–5.06)	1.53 (0.78–3.02)	1.45 (0.70–3.21)
Reduced REM sleep (%) (1st vs. 4th quartiles)	1.80 (0.82–3.91)	1.57 (0.64–3.87)	5.03 (0.59–43.0)	2.33 (0.21–25.62)	2.57 (0.88–7.51)	2.11 (0.60–7.40)
Obstructive sleep apnoea (AHI > 15)	1.90 (1.09–3.32)[#]	1.65 (0.89–3.05)	1.32 (0.47–3.71)	1.74 (0.53–5.67)	2.69 (1.37–5.26)[#]	3.14 (1.49–6.61)[#]
Nocturnal hypoxaemia (>1% of TST with SaO_2 <90%)	3.61 (1.88–6.91)[#]	2.59 (1.49–4.49)[#]	0.58 (0.21–1.62)	0.47 (0.14–1.61)	2.91 (1.53–5.56)[#]	2.92 (1.39–6.13)[#]

AHI, apnoea–hypopnoea index; CI, confidence intervals; REM, rapid eye movement; TST, total sleep time measured by polysomnography.

[a]Potential confounders were considered a priori through biological and clinical plausibility, and their potential association with sleep, obesity, sarcopenia, and SO. They were included according to pre-specified criteria and for each PSG parameter. Final models included covariates among the following ones: age, gender, ethnic group, social class, education, marital status, smoking status, alcohol consumption, recommended physical activity per week, number of comorbidities, Beck Depression Inventory score, psychotropic/hypnotic use, diuretic use, ACE inhibitor/ARB use, 25(OH) vitamin D3, IGF-1, free testosterone, leptin, adiponectin, IL-6, IL-10, and TNF-α.

[b]aORs use as reference category the absence of both sarcopenia and obesity.

[c]Skeletal muscle mass index (SMI) applying the FNIH definition of sarcopenia was calculated using appendicular skeletal muscle mass (ASMM) and body mass index (BMI) (ASMM/BMI: men: <0.789; women: <0.512). Total body fat percentage defined obesity status (women: >40%; men: >30%). Participants simultaneously classified as sarcopenic and obese were defined as SO.

[d]Indicators of poor sleep/sleep disorders significantly associated with body composition categories in the univariate analysis were considered in multivariate models separately as the main exposure variable.

[#]*P* value <0.05 was considered statistically significant.

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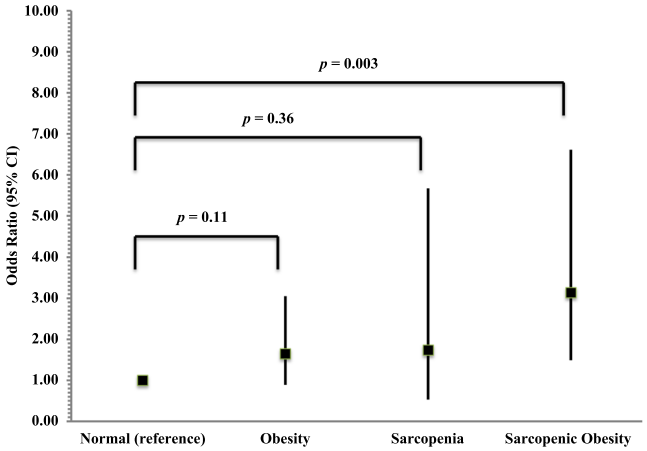
Figure 2 Multivariate adjusted odds ratios for adverse body composition states by OSA status



Other indicators of poor sleep, such as poor sleep quality, objective short sleep duration, reduced sleep efficiency, and increased night-time wakefulness were not associated with sarcopenia, obesity, or SO.

OSA is frequent among adults in all age groups. Previous studies found prevalence rounding 10%, although more recent population-based studies using updated measurement techniques and recommended criteria observed higher frequencies, achieving more than 30%.[10,42] Accordingly, using data from the follow-up of the EPISONO, 34.4% of participants in our sample had moderate-to-severe OSA. Additionally, aging is one of the most critical risk factors for OSA.[9] In our study, 186 (52.4%) participants (>50 years) had the diagnosis of OSA. This sleep disorder is related to a variety of health-related consequences across all age groups, including increased risk of cognitive impairment, depression, metabolic disorders, hypertension, cardiovascular disease, atrial fibrillation, and mortality.[43–45] Possibly, these outcomes might be in part explained by the association between OSA and SO.

In fact, disproportions between an excessive amount of fat mass relative to a reduced lean mass and a severe increase in the AHI are related to disruptions in inflammatory and metabolic pathways.[46,47] Pro-inflammatory cytokines, such as IL-6 and TNF-α, are both increased in people with SO and OSA.[48,49] Similarly, adverse hormonal profiles involving leptin, adiponectin, IGF-1, and testosterone, as well as increased insulin resistance, are commonly described in pathophysiological models explaining both SO and OSA.[6,50–52] For instance, our analyses showed IGF-1 levels tended to be lower among OSA participants and SO participants. Moreover, mediation analysis revealed IGF-1 as a potential mediator of the association between OSA and SO (data not shown). Indeed, OSA negatively impacts the growth hormone/IGF-1 axis among obese subjects.[53–55] The degree to which these analogies are related to our findings needs further research exploring potential common mechanisms between both conditions.

Participants with SO tended to have a higher frequency (71.9%) of OSA than those with obesity (58.2%) or sarcopenia (65.0%) alone. Previous literature has shown that OSA leads to a higher risk of adverse clinical consequences affecting multiple organ systems, including cardiometabolic comorbidities and mortality.[56] SO but not sarcopenia or obesity alone was associated with OSA in our study. Indeed, body fat accumulation adjacent to the neck may mechanically promote upper airway obstruction during sleep.[57] Likewise, central obesity diminishes lung capacity and alters airflow dynamics, increasing pharyngeal resistance.[58] Although these adiposity-related mechanisms are increasingly well-established factors related to the development of OSA, our data may further suggest that they might be insufficient to the development of established OSA states in people around old age.

Hence, not only fat mass gain but also skeletal muscle mass reduction may play a role in the pathophysiology of OSA. In a 20–30 years follow-up study, evidence of increased AHI was detected in community-dwelling middle-aged and elderly individuals after a significant decrease or maintenance in body weight, suggesting muscle decline might be related to apnoea occurrence.[13] Previous data indicated that airway anatomy/collapsibility has a greater pathogenic effect on the development of OSA as people age.[14] In contrasting this evidence with our results, it is possible to hypothesize that both the accumulation of fat tissue around the airway and the loss of pharyngeal/laryngeal muscle mass may explain the association of OSA with SO. The potential synergistic role of both obesity and sarcopenia characteristics in the mechanisms of OSA might endorse previous studies suggesting SO as a more harmful body composition phenotype.[59] Further prospective research looking at the morphologic and functional mechanisms of sarcopenia and SO in the airway collapsibility are required to confirm the relevance of muscle deterioration on the pathophysiology of OSA.

Among our findings, nocturnal hypoxaemia was associated with both obesity and SO. Obesity hypoventilation syndrome (OHS) is a sleep-related hypoventilatory condition frequently observed in obese subjects but with a disproportionate greater morbimortality in comparison with obesity alone.[27,60] Resting daytime hypercapnia is also recommended for the OHS diagnosis. In our study, although this criterion was not evaluated, the absence of an alternative cause for alveolar hypoventilation allows us to consider OHS as a possible cause for nocturnal hypoxaemia in individuals with obesity or SO, as results were controlled for potential differential diagnoses including pulmonary diseases. The pathophysiology of OHS remains not entirely characterized.[61] Restrictive lung physiology promoted by fat accumulation seems to be a mechanistic key factor for the development of OHS, resulting in breathing overload, oxygen consumption, and CO_2 production.[62]

Moreover, leptin resistance appears to affect the ventilatory control.[63] Accordingly, our analysis resulted in significant higher median leptin levels among those with obesity or SO, as well as in those with nocturnal hypoxaemia (data not shown). The similar associations of nocturnal hypoxaemia with both obesity and SO and the lack of association with sarcopenia suggest a preponderant role of fat deposition over the lean mass decline in the pathophysiology of the OHS. In fact, the potential role of muscle deterioration on respiratory dynamics remains elusive, even in chronic obstructive pulmonary disease patients.[64] On the other hand, some authors have suggested that hypoxia might negatively impact muscle mass and increase the risk of sarcopenia.[65,66] Therefore, future prospective studies focusing on the effects of nocturnal hypoxaemia on body composition and muscle function may elucidate the potential bidirectional relationships between nocturnal hypoxaemia and muscle deterioration.

Sarcopenia was not associated with indicators of poor sleep in our study. Otherwise, a few recent studies have suggested possible relationships between sleep and sarcopenia. A cross-sectional study evaluating 488 older adults found that subjectively assessed short sleep duration ($<$6 h) was associated with sarcopenia defined by BIA.[16] In contrast, our results did not find significant associations between objective-sleep duration and adverse body composition patterns. Differences in the study population, assessment methods, or even in the statistical analysis approach may justify this divergence. Nevertheless, additional studies are required to explore the relationship between more precise measurements of sleep duration and sarcopenia.

Another study including community-dwelling very old adults ($>$80 years) and applying actigraphy measures found that higher bedtime variability (a measure of sleep pattern variation) was independently related to reduced lean mass and increased fat mass.[17] Circadian rhythm disruptions are increasingly frequent with aging and can impact body composition negatively.[67] Our study included participants with a broader age range, and indicators of night-to-night sleep variability were not explored. Further research is also expected to investigate the role of different sleep pattern measures in the development of unfavourable body composition states across distinct age groups.

In contrast to our findings, a more recent epidemiological study showed that subjective-measured poor sleep quality (PSQI total score $>$5) was associated with sarcopenia in middle-aged adults.[18] More than 90% of participants were Caucasians, and older adults were not included. In contrast, our sample comprised a multi-ethnic and older group, with 57.9% of Caucasians and nearly 50% of aged persons. Our lower sample size did not allow us to perform subgroup analyses according to age group and ethnicity. Moreover, a greater number and diversity of potential confounders included in our final analysis might also explain the absence of subjective sleep quality effects on body composition states.

This study has some limitations. Among them, the cross-sectional design does not allow any conclusion towards a causal explanation for the findings. Although a large number of well-selected confounders included in the analysis reduced the risk of residual or unmeasured confounding effect, dietary pattern, which can impact on body composition, was not evaluated. Due to sample size limitations, we could not perform subgroup analysis regarding age-specific or gender-specific differences in the results. Moreover, low statistical power may explain the absence of some potential associations between sarcopenia and indicators of poor sleep or sleep disorders, as few participants were classified as sarcopenic. Although most of the sleep indicators were provided by objective measurement methods, they do not necessarily reflect the sleep pattern of participants. Sleep assessments were performed respecting habitual bedtimes, but the single night PSG recording might lead to a lack of habituation to this method. On the other hand, sleep duration, one of the variables that best reflects sleep pattern, expressed the mean sleep time during nine nights of actigraphy registry on average, generating a more reliable report of participant's sleep quantity.

Body composition was assessed by BIA (Inbody720, Biospace Ltd. Seoul, Korea), which has shown excellent agreement with the gold-standard dual-energy X-ray absorptiometry.[22] Although overestimations in the body composition measures are still a concern when using BIA, time and cost efficiency, as well as the lack of X-ray exposure of this modern BIA technique, offered a more favourable option to body composition analysis in a population-based study. Although sarcopenia and SO include decreased muscle mass as required diagnostic criteria, the majority of updated recommendations emphasize the importance of muscle function evaluations for supporting these diagnostics.[40,68] Despite the absence of performance measurements, our study applied validated cut-points and recommended diagnostic criteria for reduced lean mass that were previously able to predict significant weakness using a pooled sample originated

from nine different longitudinal cohorts or clinical trial studies.[23] Moreover, the relevance of our findings relies on the originality of revealing potential relationships between sleep and sarcopenia or SO, which are expected to be further explored in upcoming investigations.

Conclusions

The objective of this study was to investigate the possible associations between indicators of poor sleep/sleep disorders, focusing on OSA, and a broader number of adverse body composition phenotypes, including obesity, sarcopenia, and SO. Finally, the findings showed that OSA is associated with SO, and nocturnal hypoxia is associated with both obesity and SO. The growing coexistence of OSA and SO may further aggravate the consequences of each one of them isolatedly. Also, the intertwined pathophysiological mechanisms shared by OSA and SO are potential targets for future interventions aiming to reduce morbimortality in those suffering from these disorders. Upcoming prospective studies and clinical trials are expected to advance the elucidation of these findings.

Author contribution

All authors contributed equally to the conception and writing of the manuscript.

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Conflict of interest

Dalva Poyares has served as speaker for EMS, Takeda, and Sanofi pharmaceutical companies, which have no relationship with the current paper. There are no other conflict of interests to declare.

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