Dataset: The Osteoporotic Fractures in Men (MrOS) Study

Association of Actigraphy-Measured Rest-Activity Rhythms with Obesity Phenotypes in the Osteoporotic Fractures in Men (MrOS) Study

Abstract

Background: Obesity in older adults presents as whole-body, abdominal, or sarcopenic obesity. Disruptions in rest-activity rhythms (RAR) are linked to metabolic disorders, but their role in obesity phenotypes among older men is unclear. This study examines the association between RAR and obesity phenotypes in older men from the Osteoporotic Fractures in Men (MrOS) Study.

Methods: This study utilized MrOS 2000-2016 data. A total of 2,989 men aged 65 and older with valid actigraphy, anthropometric, and physical function data, followed up at least once were included. RAR parameters were assessed using wrist-worn actigraphy. RAR variables were categorized into quartiles, where higher amplitude, mesor, interdaily stability (IS), F-statistics, and relative amplitude (RA), as well as lower intradaily variability (IV) and mid-range acrophase, reflect healthier activity rhythms. Obesity phenotypes were classified as whole-body obesity, abdominal, and sarcopenic obesity. Generalized estimating equations models were used to evaluate longitudinal associations between RAR and obesity phenotypes.

Results: Lower amplitude, mesor, F-statistics, IS, and RA, as well as earlier acrophase and higher IV, were associated with higher odds of whole-body and abdominal obesity. Associations were generally weaker and less consistent for sarcopenic obesity, though RA remained strongly associated across all obesity types. For example, the lowest quartile of RA compared to the highest quartile was associated with whole-body (OR = 5.62, 95% CI: 4.18-7.56), abdominal (OR= 3.93, 95% CI: 3.17-4.86), and sarcopenic obesity (OR = 3.39, 95% CI: 2.47-4.64).

Conclusion: Disrupted RARs may play a role in weight gain and metabolic dysfunction. Irregular activity patterns and reduced day-night variations could be linked to declines in muscle function. Enhancing activity levels and stabilizing RARs could help prevent and manage obesity in aging populations.

Background

Obesity is a well-established risk factor for multiple non-communicable diseases, including hypertension, type 2 diabetes, coronary heart disease, stroke, and certain cancers [1]. In the United States (US), the prevalence of obesity has risen at an alarming rate over the past few decades, with 40.3% of adults now classified as obese [2, 3]. In the older population, obesity represents a critical risk factor. With aging, body composition undergoes significant changes, including increased visceral, inter-, and intra-muscular fat deposition, along with reduced muscle mass and strength [4-6]. These conditions interplay intricately, manifesting in diverse obesity phenotypes such as whole-body, abdominal, and sarcopenic obesity.

Particularly beyond whole-body obesity identified by body mass index (BMI), older adults often experience a rapid rise in abdominal obesity and sarcopenic obesity, which is considered one of the most severe metabolic conditions in this demographic [7-9]. These obesity phenotypes substantially contribute to the development and progression of diverse geriatric diseases, including cardiovascular disorders, malignancies, falls, and fractures [9-11]. To effectively manage these chronic conditions, the importance of proactive lifestyle management, such as physical activity, diet, and sleep, is increasingly emphasized.

Circadian rhythms have recently gained attention as a key factor in obesity, as they regulate numerous physiological processes, including metabolism, hormone secretion, and energy balance [12]. Circadian rhythms are expressed behaviorally through rest-activity rhythms (RAR), which capture the daily fluctuations in movement and rest. By reflecting patterns of movement and rest over a 24-hour cycle, RAR provides insight into sleep-wake cycles, physical activity levels, and overall circadian rhythmicity in daily life. Given that RAR changes significantly with age and that prolonged disruptions to these natural rhythms can severely impact mortality, cardiovascular disease, and cognitive function, research focusing on RAR among older populations is particularly important [13-17].

Previous studies have found an association between RAR and increased likelihood of obesity [18-20]. For example, previous research has shown that accelerometry-generated RAR metrics, such as intra-daily variability (IV) and stability (IS), are associated with obesity in children, adolescents, and general adult populations [19-22]. However, those findings were limited by the poor reliability of BMI as an indicator of obesity, especially in older populations [23].

Therefore, in this study, we aimed to investigate the associations of actigraphy-measured RAR

with different obesity phenotypes in older men (aged 65 or older), including whole-body (BMI-based), abdominal (waist circumference-based), and sarcopenic (maximal grip strength combined) obesity, using the Osteoporotic Fractures in Men (MrOS) study from 2000 to 2016. We hypothesized that smaller amplitude, early or later acrophase, smaller mesor, smaller F statistics, smaller IS, larger IV, and smaller relative amplitude (RA) were associated with increased risks of whole-body, abdominal, and sarcopenic obesity, compared to the non-disrupted RAR group in older men living in the US.

Methods

Study Population

This study draws on data from the MrOS study, a large, multicenter cohort of community-dwelling older men aimed at identifying risk factors for osteoporosis and other age-related health outcomes. The six clinical sites included are Birmingham-AL (University of Alabama at Birmingham), Minneapolis-MN (University of Minnesota) Palo Alto-CA (Stanford University), Pittsburgh-PA (University of Pittsburgh), Portland-OR (Oregon Health and Science University), and San Diego-CA (University of California, San Diego). Over time, the study's scope broadened to encompass healthy aging, including detailed evaluations of musculoskeletal aging such as physical performance, falls, osteoarthritis, and sarcopenia. Additional data were gathered on sleep, cardiovascular outcomes (in a subset of participants), incident prostate cancer, and lower urinary tract symptoms [24].

Details of the MrOS study design and recruitment have been published elsewhere [24, 25]. The eligibility criteria included participants who had valid actigraphy data, complete anthropometric and physical function measurements, and necessary covariate information including age, race, education, physical activity, smoking status, alcohol consumption, caffeine intake, total sleep duration, and sleep medication use.

Exposure Assessment

RAR was assessed using wrist-worn actigraphy (Octagonal SleepWatch-O; Ambulatory Monitoring Inc., Ardsley, NY) during Sleep Visit 1. Participants were instructed to wear the actigraphy on their non-dominant wrist for a minimum of five consecutive days. Data was collected in 1-minute epochs and processed using the Proportional Integration Mode to quantify activity counts. To ensure data quality and consistency, participants with fewer than three valid days of actigraphy recordings were excluded from the analysis. Daily data were excluded if the watch was removed for more than 10% of the day, and nighttime data were excluded if the watch was removed for more than two hours during the night. Sleep and wake states were determined using the UCSD sleep-scoring algorithm, which classifies epochs as asleep or awake based on movement patterns.

RAR metrics were derived using the Extended Cosine Model, which fits a 24-hour sinusoidal function to the activity data under the assumption of a rhythmic pattern [26]. The model estimated amplitude (the difference between peak and baseline activity), acrophase (the timing of peak activity relative to clock time), mesor (the average activity level over 24 hours), and F-statistic, which quantifies how well the data fit the cosinor function. In addition to parametric modeling, non-parametric RAR metrics were calculated, characterizing rest-activity patterns without assuming a specific distribution. These included IS, which measures the consistency of activity patterns across days; IV, which quantifies the fragmentation of daily activity; and RA, defined as the difference between the most and least active periods. For analysis, RAR metrics were categorized into quartiles, except for acrophase, which was classified based on the mean ± 1.5 standard deviations. The reference group for each metric was selected based on expected healthier RAR patterns: highest amplitude, mesor, F-statistic, IS, and RA, as well as lowest IV and a mid-range acrophase.

Outcome Assessment

Anthropometric (weight and height), physical function (grip strength), and body composition (total body fat and muscle mass) measures were collected repeatedly in Sleep Visit 1 and 3. During home or clinic visits, body weight was recorded using a standard balance beam or digital scale, while height was measured with a wall-mounted Harpenden stadiometer (Holtain, England) to calculate the BMI. Grip strength was assessed using Jamar dynamometers (Sammons Preston Rolyan, Bolingbrook, IL) with two trials for each hand, excluding participants with recent hand pain, arthritis symptoms, or hand surgery within the past three months [26].

Three separate obesity phenotypes were included. Whole-body obesity was defined as BMI greater than or equal to 30 kg/m^2. Abdominal obesity was defined as waist circumference greater than or equal to 102 cm based on the World Health Organization standard cut-off point. Sarcopenic obesity was defined as having either whole-body or abdominal obesity criteria and having maximal grip strength <35.5kg.

Covariates

Potential confounders were selected based on biological plausibility and prior literature linking RAR and obesity. Given that multiple health and lifestyle factors fluctuate over time, key covariates were modeled as time-varying to account for within-individual changes across study visits. Demographic variables included age (continuous, time-varying), race (categorical, time-fixed), and education (categorical, time-fixed). Lifestyle factors included self-reported physical activity (measured by the Physical Activity Scale for the Elderly [PASE]; continuous, time-varying) [24, 27], smoking status (categorical, time-varying), alcohol consumption (drinks per week; categorical, time-fixed), and caffeine intake (continuous, time-fixed). Depression (continuous, time-varying) measured by 15-item Geriatric Depression Scale was adjusted to account for mental health status [28, 29]. Given the strong interplay between sleep and circadian rhythms, models also included total sleep duration (derived from actigraphy; continuous, time-fixed) and sleep medication use (categorical, time-fixed) as additional covariates.

Statistical Analysis

Descriptive analysis, including means and standard deviations (for continuous variables) or frequencies and percentages (for categorical variables), was used to summarize baseline characteristics overall and across three obesity phenotypes (whole-body obesity, abdominal obesity, and sarcopenic obesity). Differences between obese and non-obese groups within each phenotype were assessed using independent t-tests (for normally distributed continuous variables) or Wilcoxon rank-sum tests (for non-normally distributed continuous variables), Chi-square (or Fisher's exact) tests were used to compare categorical variables between the two groups.

To examine the associations between baseline RAR metrics and three binary obesity phenotypes, Generalized Estimating Equations (GEE) with a logit link function were used to identify longitudinal associations. Several correlation structures were tested in GEE, and the exchangeable structure was selected based on model fit criteria such as the Quasi-likelihood under the Independence model Criterion (QIC). Robust standard errors were used to account for potential model misspecification. The results were summarized as odds ratios (ORs) and corresponding 95% confidence intervals (95% CI). Interaction terms between RAR metrics and time were initially explored but excluded from the final models. This decision was based on (1) the primary focus on the overall effect of RAR rather than its time-varying effects, (2) higher Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) values for interaction models indicating poorer fit, and (3) likelihood ratio tests showing no significant improvement in fit ($p > 0.05$). Thus, interaction terms were omitted to maintain model parsimony and align with research objectives.

Covariates were sequentially added to the models. Model 1 was adjusted for demographic factors, including age, race, and education. Model 2 further incorporated lifestyle and health-related factors, including physical activity, smoking status, alcohol consumption, caffeine intake, depression, sleep duration, and sleep medication use. Multicollinearity was assessed using Variance Inflation Factors (VIFs) for continuous predictors and examining correlation matrices to identify highly correlated covariates before model inclusion. For the statistical analysis, SAS 9.4 and R 4.4.1 were utilized.

Results

Participant Characteristics

Descriptive statistics for baseline characteristics of the study population (N = 2,989) are presented in **Table 1**, overall and stratified by obesity phenotypes: whole-body obesity, abdominal obesity, and sarcopenic obesity. Participants with whole-body and abdominal obesity were younger compared to those without obesity ($p < 0.001$ for both), while no significant age difference was observed for sarcopenic obesity ($p = 0.3$). The majority of participants were White (92%), and racial distribution varied significantly within whole-body and abdominal obesity status ($p < 0.001$ for both) but not for sarcopenic obesity ($p = 0.11$). Smoking history varied by obesity phenotype: former smokers were more common among those with whole-body and abdominal obesity, but not with sarcopenic obesity. Physical activity was consistently lower in obese individuals across all phenotypes. Caffeine intake was higher in those with whole-body and abdominal obesity, while depression scores were elevated in whole-body and sarcopenic obesity. Sleep

duration did not differ, but individuals with sarcopenic obesity reported greater use of sleep medications (p = 0.031).

The prevalence of whole-body and abdominal obesity decreased between Visit 1 and Visit 3, while sarcopenic obesity showed a slight increase. Specifically, the proportion of participants with whole-body obesity declined from 20.7% to 16.5%, and abdominal obesity from 39.5% to 35.9%. In contrast, the prevalence of sarcopenic obesity increased from 9.6% to 11.9%.

Association between RAR and whole-body Obesity

All RAR parameters were significantly associated with higher odds of whole-body obesity and showed a dose-response relationship (**Table 2**). Individuals in the lowest (OR: 2.15, 95% CI: 1.65, 2.80) and second-lowest (OR: 1.45, 95% CI: 1.12, 1.89) quartiles of amplitude had significantly higher odds of whole-body obesity compared to those in the highest quartile in Model 2. Earlier acrophase (<12:30 PM) was associated with whole-body obesity compared to the 12:30 PM–4:06 PM category (OR: 1.57, 95% CI: 1.11, 2.23), although later acrophase did not show a significant difference.

The lowest quartiles of mesor, F statistic, IS were significantly associated with higher odds of whole-body obesity, compared to the highest quartile. For IV, the highest quartile had significantly higher odds of whole-body obesity compared to the lowest quartile (OR: 2.04, 95% CI: 1.57, 2.66). Additionally, the lowest RA quartile was strongly associated with whole-body obesity compared to the highest (OR: 5.62, 95% CI: 4.18, 7.56). While ORs in Model 2 were slightly attenuated compared to Model 1, statistical significance remained across quartiles.

Association between RAR and Abdominal Obesity

For abdominal obesity, the associations with RAR parameters were weaker than those observed for whole-body obesity but remained statistically significant (**Table 2**). A dose-response pattern was evident for all parameters except for acrophase. The lower quartiles of amplitude, mesor, F statistic, IS, and RA were associated with higher odds of abdominal obesity compared to the highest quartiles. For example, individuals in the lowest quartile of RA had nearly four times the odds of abdominal obesity compared to those in the highest quartile (OR = 3.93, 95% CI: 3.17, 4.86 in model 2). In contrast, earlier acrophase compared to the 12:30 PM–4:06 PM category and the higher quartile of IV compared to the lowest quartile was associated with higher odds of abdominal obesity. Although effect sizes were slightly attenuated in Model 2 compared to Model 1, the overall trends across quartiles remained consistent.

Association between RAR and Sarcopenic Obesity

In sarcopenic obesity, the magnitude of associations was slightly lower compared to the other obesity types, and some estimates were attenuated after covariate adjustments (**Table 2**). Although lower amplitude, F-statistics, and IS were still significantly associated with greater odds of sarcopenic obesity, the effect sizes were attenuated, and some trends across quartiles were less clear. Notably, mesor and acrophase were not significantly associated with sarcopenic obesity, and only the highest quartile of IV showed a significant association compared to the lowest quartile. Nevertheless, individuals in the lowest quartile of RA had more than threefold higher odds of sarcopenic obesity compared to those in the highest quartile (OR = 3.39, 95% CI: 2.47, 4.64), with a clear dose-response pattern observed across quartiles.

Table 1. Baseline Characteristics of the Study Population by Obesity Phenotypes

Characteristic	Overall	Whole-body Obesity			Abdominal Obesity			Sarcopenic Obesity		
		No	Yes		No	Yes		No	Yes	
	N = 2,989[1]	N = 2,370[1]	N = 619[1]	p-value[2]	N = 1,808[1]	N = 1,181[1]	p-value[2]	N = 2,702[1]	N = 287[1]	p-value[2]
Age (years)	76 (6)	77 (6)	75 (5)	<0.001	77 (6)	76 (5)	<0.001	76 (6)	78 (5)	<0.001
Race				<0.001			<0.001			0.07
White	2,699 (92%)	2,140 (92%)	559 (92%)		1,598 (90%)	1,101 (94%)		2,428 (91%)	271 (95%)	
African American	112 (4%)	77 (3%)	35 (6%)		65 (4%)	47 (4%)		103 (4%)	9 (3%)	
Asian, American Indian, or Alaska Native	2 (<0.1%)	2 (<0.1%)	0 (0%)		1 (<0.1%)	1 (<0.1%)		2 (<0.1%)	0 (0%)	
Native Hawaiian or other Pacific Islander	99 (3%)	92 (4%)	7 (1%)		90 (5%)	9 (1%)		95 (4%)	4 (1%)	
Other	32 (1%)	24 (1%)	8 (1%)		20 (1%)	12 (1%)		32 (1%)	0 (0%)	
Education				<0.001			<0.001			<0.001
Less than high school	161 (5%)	107 (5%)	54 (9%)		76 (4%)	85 (7%)		134 (5%)	27 (9%)	
High school graduate	477 (16%)	348 (15%)	129 (21%)		247 (14%)	230 (19%)		413 (15%)	64 (22%)	
Postsecondary	2,351 (79%)	1,915 (81%)	436 (70%)		1,485 (82%)	866 (73%)		2,155 (80%)	196 (68%)	
Site				<0.001			<0.001			<0.001
Birmingham	483 (16%)	366 (15%)	117 (19%)		255 (14%)	228 (19%)		423 (16%)	60 (21%)	
Minneapolis	523 (17%)	396 (17%)	127 (21%)		316 (17%)	207 (18%)		477 (18%)	46 (16%)	
Palo Alto	487 (16%)	430 (18%)	57 (9.2%)		388 (21%)	99 (8.4%)		464 (17%)	23 (8.0%)	
Pittsburgh	514 (17%)	359 (15%)	155 (25%)		242 (13%)	272 (23%)		441 (16%)	73 (25%)	
Portland	452 (15%)	383 (16%)	69 (11%)		264 (15%)	188 (16%)		414 (15%)	38 (13%)	
San Diego	530 (18%)	436 (18%)	94 (15%)		343 (19%)	187 (16%)		483 (18%)	47 (16%)	
Smoking				0.008			<0.001			0.04
No	1,175 (39%)	965 (41%)	210 (34%)		780 (43%)	395 (33%)		1,082 (40%)	93 (32%)	
Former smoker	1,755 (59%)	1,359 (57%)	396 (64%)		995 (55%)	760 (64%)		1,568 (58%)	187 (65%)	
Current smoker	58 (2%)	45 (2%)	13 (2%)		32 (2%)	26 (2%)		51 (2%)	7 (2%)	
Alcohol consumption				0.031			0.081			0.02
No drink in past 12 months	1,025 (34%)	795 (34%)	230 (37%)		589 (33%)	436 (37%)		904 (34%)	121 (42%)	
Less than 1 drk/wk	363 (12%)	276 (12%)	87 (14%)		222 (12%)	141 (12%)		328 (12%)	35 (12%)	
1-2 drks/wk	372 (13%)	293 (12%)	79 (13%)		222 (12%)	150 (13%)		336 (13%)	36 (13%)	
3-5 drks/wk	462 (16%)	370 (16%)	92 (15%)		288 (16%)	174 (15%)		425 (16%)	37 (13%)	
6-13 drks/wk	585 (20%)	491 (21%)	94 (15%)		380 (21%)	205 (17%)		546 (20%)	39 (14%)	
14 or more drks/wk	168 (6%)	135 (6%)	33 (5%)		99 (6%)	69 (6%)		149 (6%)	19 (7%)	
PASE Score[3]	145 (71)	148 (72)	137 (70)	0.001	150 (72)	139 (69)	<0.001	148 (72)	124 (63)	<0.001
Caffeine intake (mg/day)	235 (247)	228 (243)	262 (260)	0.004	214 (227)	267 (271)	<0.001	233 (245)	254 (266)	0.20
Depression Scale[4]	1.79 (2.18)	1.72 (2.14)	2.03 (2.32)	0.003	1.69 (2.13)	1.94 (2.25)	0.003	1.70 (2.08)	2.65 (2.86)	<0.001
Total sleep duration (hours)	7 (1)	7 (1)	7 (1)	0.2	7 (1)	7 (1)	0.093	7 (1)	7 (1)	0.50
Sleep medication use				>0.9			0.5			0.20
Not during the past month	2,359 (79%)	1,865 (79%)	494 (80%)		1,434 (79%)	925 (78%)		2,143 (79%)	216 (75%)	
Less than once a week	207 (7%)	166 (7%)	41 (7%)		121 (7%)	86 (7%)		185 (7%)	22 (8%)	
Once or twice a week	104 (4%)	82 (4%)	22 (4%)		56 (3%)	48 (4%)		88 (3%)	16 (6%)	
Three or more times a week	318 (11%)	256 (11%)	62 (10%)		196 (11%)	122 (10%)		285 (11%)	33 (11%)	
Height (cm)	174 (7)	174 (7)	174 (7)	0.8	173 (7)	175 (7)	<0.001	174 (7)	172 (6)	<0.001
Acrophase (clock time)	14.28 (1.21)	14.30 (1.19)	14.22 (1.28)	0.2	14.31 (1.13)	14.25 (1.31)	0.2	14.29 (1.20)	14.23 (1.30)	0.50

Amplitude (counts/minute)	3,607 (1,093)	3,649 (1,053)	3,447 (1,223)	<0.001	3,697 (1,058)	3,470 (1,131)	<0.001	3,643 (1,067)	3,270 (1,263)	<0.001
Mesor (counts/minute)	2,167 (503)	2,172 (490)	2,148 (548)	0.3	2,187 (485)	2,137 (527)	0.009	2,173 (491)	2,112 (599)	
F-statistics	1,049 (515)	1,087 (520)	904 (470)	<0.001	1,101 (510)	970 (514)	<0.001	1,064 (514)	902 (508)	<0.001
Interdaily Stability (0-1)	0.74 (0.11)	0.74 (0.10)	0.71 (0.12)	<0.001	0.75 (0.10)	0.72 (0.11)	<0.001	0.74 (0.10)	0.71 (0.11)	<0.001
Intradaily Variability (0-1)	0.65 (0.20)	0.64 (0.20)	0.67 (0.21)	<0.001	0.64 (0.20)	0.66 (0.21)	0.11	0.64 (0.20)	0.71 (0.23)	<0.001
Relative Amplitude (0-2)	0.83 (0.09)	0.84 (0.08)	0.79 (0.11)	<0.001	0.84 (0.08)	0.80 (0.10)	<0.001	0.83 (0.09)	0.78 (0.11)	<0.001

[1]Mean (SD); n (%)
[2]Welch Two Sample t-test; Fisher's exact test; Pearson's Chi-squared test
[3]PASE: Physical Activity Score for the Elderly
[4]15-item Geriatric Depression Scale adjusted for mental health status

Table 2. Longitudinal Associations Between Baseline RAR Metrics and Whole- body, Abdominal, and Sarcopenic Obesity

	Whole-body Obesity		Abdominal Obesity		Sarcopenic Obesity	
	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
Amplitude (counts/minute)						
Q1: 279 to <2895	**2.31 (1.79, 2.97)**	**2.15 (1.65, 2.80)**	**2.20 (1.80, 2.69)**	**2.20 (1.78, 2.71)**	**2.16 (1.61, 2.88)**	**1.78 (1.32, 2.41)**
Q2: 2895 to <3539	**1.50 (1.16, 1.94)**	**1.45 (1.12, 1.89)**	**1.62 (1.33, 1.97)**	**1.63 (1.34, 1.99)**	**1.56 (1.16, 2.09)**	**1.42 (1.05, 1.92)**
Q3: 3539 to <4191	1.18 (0.91, 1.54)	1.14 (0.87, 1.50)	**1.40 (1.15, 1.70)**	**1.39 (1.14, 1.70)**	1.20 (0.88, 1.63)	1.12 (0.82, 1.53)
Q4: 4191 to 12358	ref					
Acrophase						
< 12:30 PM	**1.60 (1.13, 2.26)**	**1.57 (1.11, 2.22)**	**1.50 (1.12, 2.02)**	**1.44 (1.07, 1.93)**	1.34 (0.91, 1.99)	1.26 (0.84, 1.87)
12:30 PM to 4:06 PM	ref					
> 4:06PM	1.16 (0.79, 1.70)	1.09 (0.74, 1.61)	1.23 (0.91, 1.67)	1.21 (0.89, 1.65)	1.45 (0.99, 2.14)	1.32 (0.89, 1.94)
Mesor (counts/minute)						
Q1: 641 to <1851	**1.66 (1.29, 2.13)**	**1.51 (1.17, 1.96)**	**1.56 (1.29, 1.90)**	**1.53 (1.25, 1.87)**	1.31 (1.00, 1.73)	1.07 (0.81, 1.43)
Q2: 1851 to <2135	1.19 (0.92, 1.53)	1.16 (0.89, 1.50)	1.21 (0.97, 1.47)	**1.23 (1.01, 1.49)**	1.23 (0.92, 1.63)	1.15 (0.86, 1.53)
Q3: 2135 to <2424	1.26 (0.98, 1.63)	1.25 (0.96, 1.61)	1.06 (0.87, 1.28)	1.05 (0.87, 1.28)	0.98 (0.73, 1.30)	0.96 (0.72, 1.28)
Q4: 2424 to 7592	ref					
F statistics						
Q1: 8.27 to <693.1	**3.05 (2.35, 3.96)**	**2.89 (2.21, 3.78)**	**2.25 (1.85, 2.75)**	**2.23 (1.82, 2.74)**	**2.14 (1.62, 2.83)**	**1.85 (1.39, 2.46)**
Q2: 693.1 to <964.64	**2.15 (1.64, 2.80)**	**2.12 (1.62, 2.78)**	**1.66 (1.37, 2.02)**	**1.67 (1.37, 2.04)**	**1.38 (1.03, 1.84)**	1.25 (0.93, 1.68)
Q3: 964.64 to <1317.6	**1.46 (1.11, 1.92)**	**1.45 (1.09, 1.91)**	**1.40 (1.15, 1.70)**	**1.42 (1.16, 1.73)**	1.22 (0.91, 1.65)	1.21 (0.89, 1.63)
Q4: 1317.6 to 4501.43	ref					
Interdaily Stability						
Q1: 0.166 to <0.68	**2.00 (1.55, 2.56)**	**1.90 (1.47, 2.45)**	**1.88 (1.54, 2.28)**	**1.89 (1.55, 2.31)**	**1.97 (1.49, 2.61)**	**1.81 (1.36, 2.40)**
Q2: 0.68 to <0.751	**1.53 (1.19, 1.98)**	**1.49 (1.14, 1.93)**	**1.50 (1.24, 1.83)**	**1.51 (1.24, 1.85)**	**1.56 (1.17, 2.09)**	**1.47 (1.09, 1.97)**
Q3: 0.751 to <0.812	1.16 (0.89, 1.51)	1.15 (0.88, 1.51)	1.17 (0.97, 1.42)	1.17 (0.96, 1.43)	1.29 (0.96, 1.73)	1.24 (0.92, 1.67)
Q4: 0.812 to 0.968	ref					
Intradaily Variability						
Q1: 0.218 to <0.499	ref					
Q2: 0.499 to <0.622	**1.32 (1.02, 1.71)**	**1.31 (1.01, 1.70)**	1.02 (0.84, 1.24)	1.03 (0.85, 1.25)	1.17 (0.88, 1.58)	1.13 (0.84, 1.5)
Q3: 0.622 to <0.761	**1.39 (1.07, 1.79)**	**1.37 (1.06, 1.78)**	**1.26 (1.04, 1.53)**	**1.29 (1.06, 1.57)**	**1.40 (1.05, 1.87)**	1.32 (0.98, 1.77)
Q4: 0.761 to 1.875	**2.12 (1.64, 2.74)**	**2.04 (1.57, 2.66)**	**1.69 (1.39, 2.07)**	**1.71 (1.39, 2.10)**	**1.92 (1.44, 2.55)**	**1.69 (1.26, 2.26)**
Relative Amplitude						
Q1: 0.204 to <0.791	**5.61 (4.20, 7.50)**	**5.62 (4.18, 7.56)**	**3.92 (3.19, 4.83)**	**3.93 (3.17, 4.86)**	**3.82 (2.80, 5.22)**	**3.38 (2.47, 4.64)**
Q2: 0.791 to <0.847	**3.15 (2.35, 4.23)**	**3.17 (2.36, 4.27)**	**2.51 (2.05, 3.07)**	**2.50 (2.03, 3.06)**	**2.27 (1.64, 3.14)**	**2.10 (1.51, 2.91)**
Q3: 0.847 to <0.89	**2.19 (1.62, 2.97)**	**2.21 (1.63, 3.00)**	**1.99 (1.63, 2.44)**	**1.98 (1.62, 2.43)**	**1.80 (1.29, 2.50)**	**1.72 (1.23, 2.40)**
Q4: 0.89 to 0.972	ref					

OR: Odds Ratio, 95% CI: Confidence Interval

Model 1 adjusted for age, race, and education.

Model 2 adjusted for age, race, education, physical activity, smoking status, alcohol consumption, caffeine intake, depression, sleep duration, and sleep medication use.

Q1-Q4: Quartiles were used to categorize RAR parameters, except for acrophase, which was classified using the mean ± 1.5 SD.

The reference group reflects healthier rest-activity rhythm patterns, characterized by the highest amplitude, mesor, F-statistic, IS, and RA; the lowest IV; and a mid-range acrophase.

Threshold for statistical significance was $p < 0.05$.

Discussion

In this large cohort of community-dwelling older men, we examined the associations between RAR metrics and three obesity phenotypes: whole-body, abdominal, and sarcopenic obesity. Nearly all RAR metrics were significantly associated with whole-body and abdominal obesity. Lower amplitude, mesor, F-statistics, IS, and RA, as well as higher IV and earlier acrophase timing, were associated with greater odds of whole-body and abdominal obesity. RA showed the highest associations across models. These RAR patterns—reflecting lower overall activity levels (amplitude and mesor), weaker circadian rhythmicity (F-statistics and IS), more fragmented activity patterns (IV), a reduced difference between the most and least active periods (RA), and earlier timing of peak activity (acrophase)—were also associated, though less consistently, with sarcopenic obesity.

Our findings build upon and extend a growing body of literature examining the role of RAR in obesity, particularly using actigraphy-based measures. Among population-based cross-sectional studies, those using the nationally representative National Health and Nutrition Examination Survey (NHANES) sample found that lower amplitude, mesor, RA, and IS, as well as higher IV, were consistently associated with greater odds of general and central obesity [15, 30]. Similar cross-sectional associations have been observed in community-based adult cohorts and adolescent populations, where fragmented or delayed rhythms were associated with greater adiposity, lower fitness, and higher metabolic risk [22, 31]. Additionally, a study integrating actigraphy with smartphone interaction data identified a subgroup with irregular rhythms that exhibited higher BMI [32]. While these studies provide important insights into the circadian correlates of excess adiposity, they focus exclusively on whole-body and/or abdominal obesity. In contrast, our study expands the phenotype definition to include sarcopenic obesity, a clinically relevant condition in older adults characterized by the co-occurrence of low muscle mass and high fat mass, enabling a more nuanced understanding of how disrupted rhythms may affect both fat accumulation and muscle deterioration in aging.

In contrast to these cross-sectional studies, longitudinal design and extended follow-up of MrOS allow for more robust insights into the role of RAR characteristics in predicting adverse changes in body composition. A prior study using the MrOS dataset employed a novel harmonic hidden Markov model to derive a rhythmicity index and demonstrated that lower rhythm strength was associated with higher BMI and increased odds of both prevalent and incident whole-body obesity over 3.5 years [23]. Our study builds on this by examining a broader range of RAR parameters and their associations with distinct obesity phenotypes (whole-body, abdominal, and sarcopenic obesity), using both traditional cosinor-derived measures and nonparametric rhythm metrics, analyzed within a longitudinal framework. Notably, both studies underscore the prospective significance of disrupted rhythms, affirming the role of circadian regulation in late-life metabolic health.

Disruptions in RAR, such as diminished amplitude, lower mesor, and increased IV, reflect irregular or dampened circadian activity patterns and have been linked to metabolic dysregulation [33, 34]. These alterations may lead to hormonal imbalances, such as increased ghrelin, decreased leptin, and elevated evening cortisol, that promote increased appetite, energy intake, and central fat storage [35, 36]. Furthermore, lower daytime activity and inconsistent sleep-wake cycles contribute to reduced energy expenditure and insulin resistance, key drivers of fat accumulation [37]. While these mechanisms broadly increase total adiposity, they may preferentially lead to abdominal obesity due to the unique sensitivity of visceral adipose tissue to stress hormones and inflammatory cytokines [38, 39]. Chronically disrupted RAR may also reflect behaviors such as late-night eating and sedentary lifestyles, which are particularly associated with visceral fat gain and cardiometabolic risk [40, 41].

In addition to promoting fat accumulation, disrupted RAR may contribute to declines in muscle strength and mass, thereby increasing the risk of sarcopenic obesity. Circadian rhythms play a critical role in regulating muscle metabolism, protein synthesis, and mitochondrial function; thus, RAR irregularities can impair muscle maintenance and recovery [42]. Reduced amplitude and mesor often reflect lower levels of physical activity, which is a key risk factor for both obesity and muscle atrophy in older adults [43]. Moreover, circadian misalignment has been associated with chronic low-grade inflammation and insulin resistance, biological processes that not only promote fat gain but also inhibit muscle regeneration and increase catabolism [44, 45]. The convergence of these factors may result in the dual burden of excess adiposity and compromised muscle strength, reinforcing the link between disrupted circadian patterns and sarcopenic obesity.

Several limitations should be considered. First, the number of follow-up time points for obesity phenotypes was limited (visits 1 and 3), as waist circumference was only available at two visits, restricting

our ability to assess long-term dynamic changes. Future studies with longer follow-up periods are needed to further assess a longer-term relationship. Second, RAR was assessed at a single time point, which also limited our ability to evaluate longitudinal changes in circadian activity patterns. Lastly, the study sample consisted exclusively of older men, predominantly White, which may limit the generalizability of findings to women or more diverse populations. Despite these limitations, this study has several notable strengths. First, we used a large, well-characterized cohort of older men from the MrOS study, allowing for assessment of temporally ordered associations between RAR and obesity phenotypes. Unlike prior studies that primarily relied on cross-sectional designs, our use of a semi-parametric longitudinal modeling framework (GEE) enhances the robustness of inference by accounting for within-subject correlation over time. Additionally, another key strength of this study was the inclusion of multiple clinically relevant obesity phenotypes, including whole-body, abdominal, and sarcopenic obesity, capturing distinct aspects of body composition that are particularly important in aging populations. This approach allows us to examine how circadian disruption may influence not just fat accumulation, but also muscle strength decline, which is often overlooked in circadian-metabolic research. Together, these strengths support the relevance of RAR patterns in understanding the risks of different obesity phenotypes in later life.

Conclusion

In summary, this study demonstrated that multiple aspects of disrupted RAR, including lower amplitude, mesor, F-statistics, IS, and RA, as well as higher IV and earlier acrophase timing, were significantly associated with whole-body, abdominal, and sarcopenic obesity. These findings highlight the potential value of increasing overall activity levels, strengthening day-to-day rhythmicity, reducing fragmentation, and enhancing the contrast between the most and least active periods as possible strategies to prevent and manage obesity in older adults.

Reference

1. National Heart, L., and Blood Institute, *Managing overweight and obesity in adults: Systematic evidence review from the Obesity Expert Panel*. 2013.
2. Emmerich, S.D., et al., *Obesity and Severe Obesity Prevalence in Adults: United States, August 2021-August 2023.* NCHS Data Brief, 2024(508).
3. *Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021.* Lancet, 2023. **402**(10397): p. 203-234.
4. Vincent, H.K., S.N. Raiser, and K.R. Vincent, *The aging musculoskeletal system and obesity-related considerations with exercise.* Ageing Res Rev, 2012. **11**(3): p. 361-73.
5. Ponti, F., et al., *Aging and Imaging Assessment of Body Composition: From Fat to Facts.* Front Endocrinol (Lausanne), 2019. **10**: p. 861.
6. Khanal, P., et al., *Sarcopenia, Obesity, and Sarcopenic Obesity: Relationship with Skeletal Muscle Phenotypes and Single Nucleotide Polymorphisms.* J Clin Med, 2021. **10**(21).
7. Batsis, J.A. and D.T. Villareal, *Sarcopenic obesity in older adults: aetiology, epidemiology and treatment strategies.* Nat Rev Endocrinol, 2018. **14**(9): p. 513-537.
8. Wannamethee, S.G. and J.L. Atkins, *Sarcopenic Obesity and Cardiometabolic Health and Mortality in Older Adults: a Growing Health Concern in an Ageing Population.* Curr Diab Rep, 2023. **23**(11): p. 307-314.
9. Roh, E. and K.M. Choi, *Health Consequences of Sarcopenic Obesity: A Narrative Review.* Front Endocrinol (Lausanne), 2020. **11**: p. 332.
10. Mirzai, S., et al., *Sarcopenic Obesity and Cardiovascular Disease: An Overlooked but High-Risk Syndrome.* Curr Obes Rep, 2024. **13**(3): p. 532-544.
11. Damluji, A.A., et al., *Sarcopenia and Cardiovascular Diseases.* Circulation, 2023. **147**(20): p. 1534-1553.
12. Laermans, J. and I. Depoortere, *Chronobesity: role of the circadian system in the obesity epidemic.* Obes Rev, 2016. **17**(2): p. 108-25.
13. Buysse, D.J., et al., *Circadian patterns of sleep, sleepiness, and performance in older and younger adults.* Sleep, 2005. **28**(11): p. 1365-76.
14. Paudel, M.L., et al., *Rest/activity rhythms and mortality rates in older men: MrOS Sleep Study.*

Chronobiol Int, 2010. **27**(2): p. 363-77.
15. Makarem, N., et al., *Rest-Activity Rhythms Are Associated With Prevalent Cardiovascular Disease, Hypertension, Obesity, and Central Adiposity in a Nationally Representative Sample of US Adults.* J Am Heart Assoc, 2024. **13**(1): p. e032073.
16. Rogers-Soeder, T.S., et al., *Rest-Activity Rhythms and Cognitive Decline in Older Men: The Osteoporotic Fractures in Men Sleep Study.* J Am Geriatr Soc, 2018. **66**(11): p. 2136-2143.
17. Hood, S. and S. Amir, *The aging clock: circadian rhythms and later life.* J Clin Invest, 2017. **127**(2): p. 437-446.
18. McGagh, D., et al., *Actigraphy-derived physical activity levels and circadian rhythm parameters in patients with psoriatic arthritis: relationship with disease activity, mood, age and BMI.* Ther Adv Musculoskelet Dis, 2023. **15**: p. 1759720x231174989.
19. Xiao, Q., et al., *Alignment Between 24-h Light-Dark and Activity-Rest Rhythms Is Associated With Diabetes and Glucose Metabolism in a Nationally Representative Sample of American Adults.* Diabetes Care, 2023. **46**(12): p. 2171-2179.
20. Qian, J., et al., *Blunted rest-activity rhythms link to higher body mass index and inflammatory markers in children.* Sleep, 2021. **44**(5).
21. Quante, M., et al., *Association of Daily Rest-Activity Patterns With Adiposity and Cardiometabolic Risk Measures in Teens.* J Adolesc Health, 2019. **65**(2): p. 224-231.
22. Garaulet, M., et al., *Fragmentation of daily rhythms associates with obesity and cardiorespiratory fitness in adolescents: The HELENA study.* Clin Nutr, 2017. **36**(6): p. 1558-1566.
23. Heckler, B., et al., *Cross-sectional and Prospective Associations of Rest-Activity Rhythms With Body Mass Index in Older Men: A Novel Analysis Using Harmonic Hidden Markov Models.* J Biol Rhythms, 2023. **38**(1): p. 87-97.
24. Orwoll, E., et al., *Design and baseline characteristics of the osteoporotic fractures in men (MrOS) study--a large observational study of the determinants of fracture in older men.* Contemp Clin Trials, 2005. **26**(5): p. 569-85.
25. Blank, J.B., et al., *Overview of recruitment for the osteoporotic fractures in men study (MrOS).* Contemp Clin Trials, 2005. **26**(5): p. 557-68.
26. Marler, M.R., et al., *The sigmoidally transformed cosine curve: a mathematical model for circadian rhythms with symmetric non-sinusoidal shapes.* Stat Med, 2006. **25**(22): p. 3893-904.
27. Washburn, R.A., et al., *The Physical Activity Scale for the Elderly (PASE): development and evaluation.* J Clin Epidemiol, 1993. **46**(2): p. 153-62.
28. Yesavage, J.A., et al., *Development and validation of a geriatric depression screening scale: a preliminary report.* J Psychiatr Res, 1982. **17**(1): p. 37-49.
29. Almeida, O.P. and S.A. Almeida, *Short versions of the geriatric depression scale: a study of their validity for the diagnosis of a major depressive episode according to ICD-10 and DSM-IV.* Int J Geriatr Psychiatry, 1999. **14**(10): p. 858-65.
30. Li, J., et al., *Rest-Activity Rhythm Is Associated With Obesity Phenotypes: A Cross-Sectional Analysis.* Front Endocrinol (Lausanne), 2022. **13**: p. 907360.
31. Cespedes Feliciano, E.M., et al., *Actigraphy-Derived Daily Rest-Activity Patterns and Body Mass Index in Community-Dwelling Adults.* Sleep, 2017. **40**(12).
32. Chen, I.M., et al., *Rest-Activity Rhythm Patterns and Their Associations With Depression and Obesity: A Study Using Actigraphy and Human-Smartphone Interactions.* Depress Anxiety, 2025. **2025**: p. 2617282.
33. Jones, S.E., et al., *Genetic studies of accelerometer-based sleep measures yield new insights into human sleep behaviour.* Nat Commun, 2019. **10**(1): p. 1585.
34. Reutrakul, S. and E. Van Cauter, *Sleep influences on obesity, insulin resistance, and risk of type 2 diabetes.* Metabolism, 2018. **84**: p. 56-66.
35. Taheri, S., et al., *Short sleep duration is associated with reduced leptin, elevated ghrelin, and increased body mass index.* PLoS Med, 2004. **1**(3): p. e62.
36. Adam, T.C. and E.S. Epel, *Stress, eating and the reward system.* Physiol Behav, 2007. **91**(4): p. 449-58.
37. Scheer, F.A., et al., *Adverse metabolic and cardiovascular consequences of circadian misalignment.* Proc Natl Acad Sci U S A, 2009. **106**(11): p. 4453-8.
38. Björntorp, P., *Body fat distribution, insulin resistance, and metabolic diseases.* Nutrition, 1997. **13**(9): p. 795-803.

39. Rosmond, R., M.F. Dallman, and P. Björntorp, *Stress-related cortisol secretion in men: relationships with abdominal obesity and endocrine, metabolic and hemodynamic abnormalities.* J Clin Endocrinol Metab, 1998. **83**(6): p. 1853-9.
40. Arble, D.M., et al., *Circadian timing of food intake contributes to weight gain.* Obesity (Silver Spring), 2009. **17**(11): p. 2100-2.
41. Knutson, K.L. and E. Van Cauter, *Associations between sleep loss and increased risk of obesity and diabetes.* Ann N Y Acad Sci, 2008. **1129**: p. 287-304.
42. Andrews, J.L., et al., *CLOCK and BMAL1 regulate MyoD and are necessary for maintenance of skeletal muscle phenotype and function.* Proc Natl Acad Sci U S A, 2010. **107**(44): p. 19090-5.
43. Cruz-Jentoft, A.J., et al., *Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People.* Age Ageing, 2010. **39**(4): p. 412-23.
44. Hotamisligil, G.S., *Inflammation and metabolic disorders.* Nature, 2006. **444**(7121): p. 860-7.
45. Dyar, K.A. and K.L. Eckel-Mahan, *Circadian Metabolomics in Time and Space.* Front Neurosci, 2017. **11**: p. 369.