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Linear and non-linear associations of device-measured sedentary time with older adults' skeletal muscle mass

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ABSTRACT

Background: Time spent sitting is associated adversely with health outcomes in older adults. Nevertheless, it is not clear how sedentary time may be related to appendicular skeletal muscle mass (ASM) – a key attribute of sarcopenia. This cross-sectional study examined associations of total sedentary time with ASM among community-dwelling older Japanese males and females.
Methods: Participants ($n = 281$, 74.3 ± 5.2 yr) wore a tri-axial accelerometer for seven days. Body mass index-adjusted ASM (kg/BMI) was derived from bioimpedance measures. Multivariate linear and quadratic regression models examined the associations of ASM with total sedentary time, stratified by sex. Restricted cubic spline models were fitted to estimate non-linear associations. Isotemporal substitution (IS) models were used to estimate the impacts of replacing 30-minute of sedentary time with light physical activity (LPA) and moderate-to-vigorous physical activity (MVPA).
Results: After adjustment, total sedentary time had a significant linear and negative association with ASM among females ($\beta = -0.014$; $p = 0.023$). For males, total sedentary time had a significant quadratic association ($p = 0.020$). Spline models indicated a reverse U-shaped association ($p < 0.001$) with total sedentary time over 9.3 h/day being associated with lower ASM. The IS models indicated that replacing 30 min/day of sedentary time with LPA would be positively and significantly associated with older females' ASM ($\beta = 0.007$, $p = 0.022$).
Conclusions: In older Japanese adults, higher volumes of time spent sedentary were associated with lower ASM. For males, only very high volumes of sedentary time appeared to be detrimental. These adverse relationships may in part be offset by more time spent in either LPA or MVPA.

1. Introduction

In older adults, age-related loss of skeletal muscle mass has been reported to have deleterious associations with functional and health outcomes, including a decline in muscle strength (Goodpaster et al., 2006), frailty (Hirani et al., 2017), disability (Tyrovolas et al., 2015), loss of activities of daily living (Wang et al., 2020), and mortality (Srikanthan and Karlamangla, 2014). Also, such muscle atrophy is a key component of sarcopenia, the progressive and generalized loss of skeletal muscle mass and strength (Cruz-Jentoft et al., 2014). Sarcopenia is a highly prevalent geriatric syndrome worldwide (Cruz-Jentoft et al., 2014). For example, a Japanese cross-sectional study reported a 22 % prevalence of sarcopenia among community-dwelling older adults (Yamada et al., 2013). Sarcopenia contributes to increasing numerous health risks and health care costs (Cruz-Jentoft et al., 2019). In light of rapidly growing ageing populations in many countries, it is a global public health priority to prevent loss of skeletal muscle mass and the development of sarcopenia.

Older adults tend to spend a higher proportion of their waking hours in sedentary behaviors (Healy et al., 2011). Extensive epidemiological

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evidence shows that sedentary behavior is adversely associated with multiple health outcomes such as all-cause and cardiovascular mortality, the incidence of type 2 diabetes and cancer, including in older adult populations (Patterson et al., 2018; de Rezende et al., 2014a). The associations of sedentary behavior with physical function and/or muscle strength have also been explored in a small but growing number of cross-sectional studies, with deleterious associations reported (Copeland et al., 2017). However, evidence on sedentary behavior and skeletal muscle mass is limited and mixed. Total sedentary time has been reported to have a negative association with absolute total and percent lean tissue mass in older adults (Gianoudis et al., 2014; Reid et al., 2018). However, findings on appendicular skeletal muscle mass (ASM), which is a diagnostic index of sarcopenia (Cruz-Jentoft et al., 2019; Cruz-Jentoft and Sayer, 2019) and a better proxy measure of whole-body skeletal muscle mass (Walowski et al., 2020), have been inconsistent (Gianoudis et al., 2014; Reid et al., 2018; Foong et al., 2016), possibly due to differences in standardization of the ASM measures used, or the stratifications employed.

Most studies on sedentary behavior and health outcomes have focused on examination of linear relationships. However, recent evidence on associations of sedentary behavior with mortality suggests that they can be related in a non-linear manner (Matthews et al., 2016). Examining the shape of the association and whether there is an inflection in the slope of the relationship is relevant to better understand the nature of relationships and to identify a threshold that might be useful to inform future prevention initiatives. It is also possible that previous studies focusing on linear associations may have reported non-significant results due to the presence of non-linear, but meaningful relationships. However, no previous study has examined the shape of the relationship of sedentary behavior with skeletal muscle mass. Little is also known to what extent replacing time spent sedentary with physical activity can be beneficial for musculoskeletal health; such evidence would be valuable for informing public health guidelines and programs (Grgic et al., 2018).

Thus, we first examined linear and non-linear associations of total sedentary time with skeletal muscle mass among community-dwelling older Japanese adults. Thereafter, we used an isotemporal substitution (IS) approach to examine whether replacing sedentary behavior with light-intensity or moderate-to-vigorous intensity physical activity (LPA; MVPA) is associated with skeletal muscle mass.

2. Methods

2.1. Participants

The present study was conducted in 2013 in Matsudo, a suburban city east of Tokyo (population: approx. 0.5 million). Of the 107,928 community-dwelling older adults aged 65–84 years living in this city (as of April 2013), 3000 were randomly selected from the registry of residential addresses, stratified by sex and age (65–74 years, 75–84 years). Details of this data collection process have been published elsewhere (Shibata et al., 2019). Briefly, the postal surveys were mailed to 3000 potential participants. The response rate for the survey was 42 % ($n = 1250$). Those who agreed to take part in additional data collection of this study ($n = 951$) were invited to participate in on-site examinations via postal mail. At the testing site, participants' height and body composition were measured. They were also asked to wear an accelerometer except when sleeping or during water-based activities (i.e., bathing, showering, and swimming) for at least seven consecutive days. They also recorded their daily life activities (i.e. waking time, bedtime, and exercising time) during the seven-day period to confirm the date and time of their accelerometer wear.

The analytical sample of this study consisted of those who completed the postal survey and the on-site examinations ($n = 330$). After excluding those who had insufficient accelerometer data ($n = 30$) and missing data for relevant variables ($n = 25$) (numbers not mutually exclusive), the final sample size was 281. Written informed consent was obtained from all participants. The study was approved by the Waseda University Ethics Committee (2013-265).

2.2. Measures

2.2.1. Objectively measured sedentary behavior and moderate-to vigorous intensity of physical activity

Participants were asked to wear a tri-axial accelerometer (Active style Pro HJA 350-IT, Omron Healthcare Co. Ltd., Kyoto, Japan) on their left hip during waking hours for at least seven consecutive days. Data were recorded in one-minute epochs. Non-wear time was defined as intervals of at least 60 consecutive minutes of no activity, which was estimated to be 0.9 or less metabolic equivalents (METs) based on a validity study (Ohkawara et al., 2011), with allowance for up to two minutes of some limited movement ($\leq$1.0 METs). Days with at least 10 h of wear time were considered valid. Participants with at least four valid days, including at least one weekend day, were included in the analyses. Total sedentary time, LPA, and MVPA time were defined as all wear time for any activity with an estimated intensity of $\leq$1.5 METs, $>$1.5 to $<$3.0 METs, and 3.0 or more METs, respectively. MET values were determined by the built-in algorithms of the accelerometer. They have been reported to be closely correlated with METs calculated by the indirect calorimetry (Ohkawara et al., 2011). Mean weekday and weekend values for total sedentary, LPA, and MVPA time were first calculated on each valid weekday and weekend day. Then, the mean daily total value was computed by weighting five times for weekdays and two times for weekend days for each behavior.

2.2.2. Body composition

Skeletal muscle mass measures including total lean tissue mass (kg), percentage of lean tissue mass (%), and ASM (kg/BMI) and percentage body fat (%) were estimated using multi-frequency bioelectrical impedance analyzer (BIA; MC-980A, TANITA, Tokyo, Japan). This BIA instrument used six electrical frequencies (1, 5, 50, 250, 500, and 1000 kHz) and eight-point tactile electrodes with four in contact with the palm and thumb of both hands and the other four in contact with the anterior and posterior aspects of the sole of both feet. The accuracy of this whole-body BIA on estimating ASM has been validated against dual X-ray absorptiometry in the previous study (Heymsfield et al., 2015). The participants were asked to arrive at the measurement site with hydrated and rested state. Then, they were asked to stand barefoot on the analyzer platform and grasp the two handgrips. The analyzer was operated by trained staff and completed within 30 s. Data provided included weight, BMI, total and regional (arm, leg, trunk) lean tissue mass (kg), fat mass (kg), percentages of body fat (%) and total lean tissue mass (%). All skeletal muscle mass measures were estimated using the manufacturer's algorithm. Height was objectively measured and entered into the device prior to body composition assessment. ASM was calculated using the sum of arm and leg lean tissue mass. In this study, ASM (kg/BMI) was utilized as a skeletal muscle mass index because previous studies have reported that standardization by BMI may be more appropriate for discriminating clinically-related weakness and for predicting future mortality or disability than is the use of a measure of height (Hirani et al., 2017; Cawthon et al., 2014; Otsuka et al., 2018). The height-adjusted ASM, where skeletal muscle mass was divided by squared height (kg/m^2), was also examined as an alternative outcome, since this is another common and widely used measure (Chen et al., 2020; Cruz-Jentoft et al., 2019).

2.2.3. Covariates

The postal survey asked participants to report sex, age, educational attainment (university or further education; high school or less), marital status (married; single), living status (living alone; living others), employment status (employed; not employed), current smoking status, and the presence of chronic conditions (stroke, cardiovascular diseases, diabetes, dyslipidemia, hyperuricemia, peripheral vascular disease, osteoporosis, knee osteoarthritis, hip osteoarthritis, spondylosis, spinal canal stenosis, rheumatoid arthritis, collagenases, cancer). The total number of chronic conditions was used as a covariate.

2.3. Statistical analyses

Descriptive statistics (mean, standard deviation [SD]) were computed for all body composition variables, accelerometer-related variables, sociodemographic covariates in total and by sex. Multivariate linear ($y = a + b_1 * x$) and quadratic (curvilinear) regression models ($y = a + b_1 * x + b_2 * x^2$) were then utilized to examine the linear and non-linear associations between each skeletal muscle mass measure (total lean tissue mass, percentage of lean tissue mass, ASM) and total sedentary time for each sex. All models were adjusted for age, marital status, educational status, living status, working status, number of chronic diseases, current smoking, accelerometer-wearing time, and MVPA time. If a significant quadratic association was found between ASM and total sedentary time, restricted cubic spline models were fitted to describe the shape of the dose-response curves of total sedentary time with ASM. Knots corresponding to the 10th, 50th, and 90th percentiles of total sedentary time were utilized, given the distribution of the ASM values (Harrell, 2015).

If a significant linear association was found between ASM and total sedentary time, further three multiple linear regression models were fitted: a single-activity model; partition model; and IS models. The single-activity model assessed each activity component separately, only adjusting for accelerometer-wearing time and all covariates. The partition model examined all behaviors (sedentary behavior, LPA, MVPA) simultaneously, without adjusting for accelerometer-wearing time. The IS model was applied to estimate the "substitutional association" by statistically reallocating time from target behavior to an equal duration of another behavior with the outcome variable. This was accomplished by omitting the target behavior from the model and entering accelerometer-wearing time in the model. In this study, the effect of replacing a 30-minute of sedentary behavior with the same amount of LPA or MVPA with ASM was examined. Analyses were conducted with Stata 15.0 (Stata Corp, College Station, Texas, USA) and the level of statistical significance was set at $p < 0.05$.

3. Results

3.1. Descriptive characteristics of the sample

Table 1 and Supplementary Table 1 show the characteristics of the study sample including sociodemographic attributes, accelerometer-based sedentary behavior and physical activity, and body composition. They had a mean age of 74.4 (SD: 5.2) years, with three-fifths of them being male (61.5 %). The proportion of those who completed a tertiary or higher education was 40 %. More than four-fifths were married and lived with others. More than 70 % were not employed. Current smokers accounted for 7 % of all participants. The mean number of chronic diseases present was 1.2. Males were significantly older and more likely to be highly educated, married, and be current smokers than females.

Participants wore the accelerometer on average for 15.0 h/d, over a mean of 7.2 valid wearing days. Overall, they spent a mean of 8.8 h/d sedentary. The mean of total MVPA time was 49.6 min/d. Males had significantly less accelerometer-wearing time and wear days but longer sedentary time per day than females. There was no significant difference in total MVPA between males and females. For skeletal muscle measures, males had significantly higher total lean tissue mass, percentage of lean tissue mass and ASM than females.

3.2. Associations between skeletal muscle mass measures and sedentary behavior

The results for linear and quadratic associations of total sedentary time with the skeletal muscle mass measures in males and females are presented in Table 2. The total lean mass was not associated with sedentary time in males and females. In the linear models, total sedentary time was significantly negatively associated with percentage lean tissue mass (%) in both males and females. A negative association between total sedentary time and ASM was only observed in females ($p = 0.023$). In the quadratic models, a significant quadratic trend ($p = 0.020$) for the association of total sedentary time with ASM was observed among males. For them, spline models indicated a reverse U-shaped association of total sedentary time with ASM (p for nonlinearity <0.001, Fig. 1) with the peak point at total sedentary time per day of 8.8–9.3 h. The results for the height-adjusted ASM (kg/m^2) are shown in

Table 1
Characteristics of the study sample.

	Total N = 281		Males n = 173		Females n = 108		P[#]
Age (yr), mean (SD)	74.4	(5.2)	75.1	(5.4)	73.3	(4.8)	0.005
Educational attainment (≥university), n (%)	108	(38.4)	82	(47.4)	26	(24.1)	<0.001
Marital status (married), n (%)	234	(83.3)	153	(88.4)	81	(75.0)	0.003
Living status (with others), n (%)	249	(88.6)	157	(90.8)	92	(85.2)	0.153
Current employment status (not employed), n (%)	206	(73.3)	122	(70.5)	84	(77.8)	0.181
Current smoking, n (%)	20	(7.1)	19	(11.0)	1	(0.9)	0.001
Number of chronic diseases, mean (SD)	1.3	(1.2)	1.3	(1.2)	1.4	(1.1)	0.085
Accelerometer-based SB and PA, mean (SD)							
Total accelerometer wearing time (h/d)	15.0	(1.5)	14.9	(1.6)	15.4	(1.0)	0.004
Total accelerometer wearing day (d)	7.2	(0.9)	7.1	(1.0)	7.3	(0.7)	0.030
Total sedentary time (h/d)	8.8	(1.9)	9.2	(1.9)	8.1	(1.6)	<0.001
Total LPA time (h/d)	5.5	(1.7)	4.8	(1.5)	6.5	(1.4)	<0.001
Total MVPA time (min/d)	49.6	(32.4)	50.1	(35.5)	48.9	(27.0)	0.762
Body composition, mean (SD)							
BMI (kg/m^2)	23.4	(3.2)	23.6	(3.0)	23.1	(3.4)	0.173
Percentage body fat (%)	26.6	(7.5)	23.3	(5.7)	32.0	(7.0)	<0.001
Total lean tissue mass (kg)	41.3	(7.5)	46.2	(4.9)	33.5	(2.7)	<0.001
Percentage lean tissue mass (%)	69.5	(7.2)	72.7	(5.4)	64.3	(6.7)	<0.001
ASM (kg/m^2)	7.32	(1.00)	8.01	(0.55)	6.22	(0.39)	<0.001
ASM (kg/BMI)	0.78	(0.15)	0.88	(0.09)	0.62	(0.08)	<0.001

ASM = appendicular skeletal muscle mass; BMI = body mass index; LPA = light intensity of physical activity; MVPA = moderate-to vigorous intensity of physical activity; SB = sedentary behavior; SD = standard deviation.
Data are presented as mean (SD) for continuous data and as n (%) for categorical data.
[#] Statistical significance of sex differences.

Table 2
Linear and non-linear associations of total sedentary time with skeletal muscle mass measures.

	β	95%CI		p for linear	p for quadratic
Males					
Total lean mass (kg)	0.264	−0.263	0.790	0.324	0.159
Percentage lean tissue mass (%)	−0.807	−1.347	−0.267	0.004	0.836
ASM (kg/BMI)	−0.001	−0.010	0.008	0.794	0.020
Females					
Total lean mass (kg)	0.312	−0.116	0.740	0.151	0.640
Percentage lean tissue mass (%)	−1.663	−2.674	−0.652	0.002	0.334
ASM (kg/BMI)	−0.014	−0.025	−0.002	0.023	0.843

ASM: appendicular skeletal muscle mass; BMI = body mass index; CI = confidence interval.
β (unadjusted coefficient) corresponds to a 1 h/d increment of sedentary time.
All models adjusted for age, marital status, educational status, living status, working status, presence of chronic diseases, current smoking, accelerometer-wearing time, and moderate-to vigorous-intensity physical activity.

Supplementary Table 2. No significant associations were observed in the linear or quadratic models.

Based on the findings from the linear models, the IS model was applied only for females (Table 3). Replacing SB with LPA was significantly and favorably associated with ASM (β = −0.007; p = 0.022). On the other hand, the substitution of SB with MVPA was not significantly associated with ASM in the IS model.

4. Discussion

We examined linear and non-linear associations of total sedentary time with skeletal muscle mass among older adults. Our findings add to those of previous studies (Gianoudis et al., 2014; Reid et al., 2018; Foong et al., 2016) by identifying the magnitude and shape of associations for females and males distinctly. Total sedentary time per day was linearly and inversely associated with the percentage of total lean tissue mass among both older males and females. Furthermore, longer total sedentary time was associated adversely with ASM linearly in females but in a non-linear manner in males. It was found that the gradient of ASM was somewhat positive for the total sedentary time less than about 9 h/d and negative over 9 h/d in males. The associations we identified were largely independent of MVPA and potential confounding factors, including smoking and the presence of chronic diseases. From a public health perspective, these findings add to the currently modest body of evidence that supports the likely benefits of reducing sedentary time to prevent skeletal muscle loss and sarcopenia in older adults.

Our findings on the association of total sedentary time with total lean tissue mass percentage are consistent with those of two previous Australian studies that did not stratify by sex (Reid et al., 2018; Foong et al., 2016). Advancing age is accompanied by significant alterations in body composition, with declining lean tissue mass and increase in fat mass, even in those who are relatively stable in weight and healthy (Makizako et al., 2017). Thus, the evidence implies that longer time spent in sedentary behavior may accelerate such age-related alterations in body composition in both females and males. Fat and muscle mass can be interconnected via several pathways (Kim et al., 2014; Buch et al., 2016). For example, a decline in a basal metabolic rate by a loss of muscle mass may increase the risk of obesity and various metabolic disorders. Meanwhile, chronic subclinical inflammation induced by increased adiposity may contribute to the impairment of muscle mass and quality. A growing body of evidence has also revealed that longer sedentary time can be associated adversely with adiposity among older adults (de Rezende et al., 2014b). Considering such a deleterious interaction of muscle mass loss and fat mass accumulation, there is likely to be considerable health benefits from population-based strategies to reduce sedentary behaviors among older adults.

Appendicular skeletal muscle mass is the most common proxy measure of whole-body skeletal muscle mass in the diagnosis of sarcopenia, and various methods of adjustment with height or BMI have been applied (Cruz-Jentoft et al., 2019). Previously, only a small number of studies have examined the associations of sedentary behavior with ASM (Gianoudis et al., 2014; Reid et al., 2018; Foong et al., 2016). The present findings are inconsistent with previous studies in older adults, which found no significant associations with either height- or BMI-adjusted ASM for the whole sample without sex stratification. One possible explanation for this inconsistency may be related to sex differences in muscle pathology. During periods of sedentary behavior, skeletal muscle activity, especially in lower limbs, is greatly reduced, which could eventually lead to disuse atrophy. A previous study

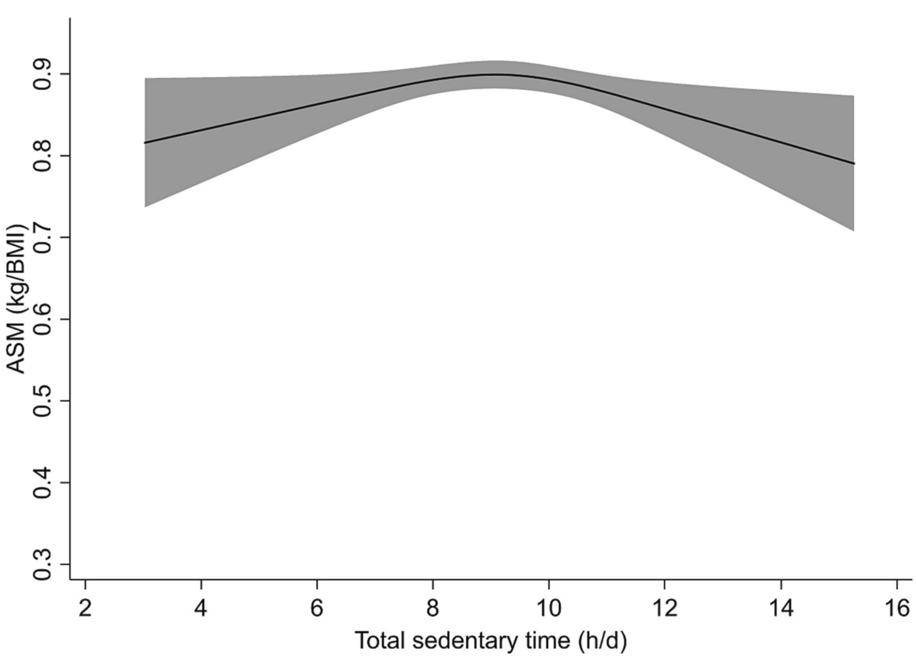

Fig. 1. Quadratic association of total sedentary time (h/d) with the BMI-adjusted ASM in males.
The solid line represents the estimated mean appendicular skeletal muscle mass (ASM; kg/BMI) and shaded area represents the 95 % confidence intervals. The restricted cubic spline with Harrell's knots (10th, 50th, and 90th percentile of total sedentary time per day) was fitted with adjustment for age, accelerometer-wearing time, marital status, educational status, living status, working status, presence of chronic diseases, current smoking, and MVPA time. ASM = appendicular skeletal muscle mass; BMI = body mass index; MVPA = moderate-to vigorous intensity of physical activity.

Table 3
Single, partition, and isotemporal substitution models examining the association of time spent in SB, LPA, and MVPA with the BMI-adjusted ASM in females.

Model	SB				LPA				MVPA			
	β	95% CI		p	β	95% CI		p	β	95% CI		p
Single	-0.006	-0.011	-0.002	0.011	0.007	0.002	0.013	0.012	0.010	-0.008	0.028	0.261
Partition	0.002	-0.006	0.010	0.559	0.009	0.001	0.017	0.020	0.007	-0.014	0.028	0.500
IS												
replace SB	Drop				0.007	0.001	0.013	0.022	0.005	-0.013	0.023	0.611
replace LPA	-0.007	-0.013	-0.001	0.023	Drop				-0.002	-0.023	0.018	0.839
replace MVPA	-0.005	-0.023	0.014	0.625	0.002	-0.018	0.023	0.822	Drop			

ASM = appendicular skeletal muscle mass; CI = confidence interval; IS = isotemporal substitution; LPA = light-intensity of physical activity; MVPA = moderate to vigorous intensity of physical activity; SB = sedentary behavior.
β (unadjusted coefficient) corresponds to a 30 min/d increment of each activity.
All models adjusted for age, marital status, educational status, living status, working status, presence of chronic diseases, and current smoking.
The single-activity and IS models also adjusted for accelerometer wear time.
Dropped (Omitted) activity from the model represents replacing time in that activity with an equal amount of time from another.

reported that mechanical stimulation by physical activity and resistance training can enhance protein synthesis and skeletal muscle hypertrophy (Boppart and Mahmassani, 2019). Longer time spent in sedentary behavior without such mechanical stimulation may cause reduced skeletal muscle mass and atrophy. The findings from a recent review suggest that females may be more susceptible to disuse atrophy relative to males (Rosa-Caldwell and Greene, 2019). This may imply that females' skeletal muscle mass could be more vulnerable to the detrimental impacts of sedentary behavior than males', even though the amount of time spent in sedentary behavior may be the same. On the other hand, muscle protein synthesis response to anabolic stimuli such as resistance exercise and dietary intake has been shown to be equivalent in females and males (Rosa-Caldwell and Greene, 2019; Smith et al., 2009). Age-related sex differences in muscle loss and weight loss (Makizako et al., 2017) due to sex-hormone changes (particularly in testosterone and estrogens) may partly contribute to the muscle-atrophy response to sedentary behavior, but the detailed mechanisms remain unclear. Thus, further evidence from prospective studies would be needed to better characterize the sex difference in the shape of the associations between sedentary behavior and ASM.

We observed that longer sedentary time was associated with greater ASM in males for daily sedentary time less than nine hours. Reasons or mechanisms for this unexpected relationship are unknown. However, the definition of non-wear time on the accelerometer in this study might be relevant. Prolonged sedentary behavior exceeding 60 min at a time without any body movement, such as watching TV and using computer could occur in older adults. If these prolonged unbroken sedentary periods are classified as non-wear time, it results in underestimation of sedentary time. This may have occurred more often for those with lower ASM. In addition, older males were reported to be more sedentary in total and the number/proportion of prolonged bouts (at least 30 consecutive minutes of sedentary time) (Shibata et al., 2019). Thus, this may have occurred more often in males than females. A recent study has recommended that a minimum of 90 min of zero counts per minute with an allowance of two minutes of interruptions (rather than 60 min) be used to identify a non-wear time for an ActiGraph GT3X (Migueles et al., 2017). Future studies may need to examine whether the current method to identify non-wear time can accurately capture non-wear periods among older adults.

A recent systematic review identified physical and cognitive health benefits of LPA, including flexibility, balance, lower limb muscle strength, and depressive symptoms for older adults (Tse et al., 2015). Our findings suggest that replacing sedentary time with time spent in LPA may be an effective and feasible approach for reducing appendicular skeletal muscle loss in older females. On the other hand, we did not observe favorable effects by replacing sedentary behavior with MVPA, which has been consistently associated with sarcopenia-related measures (Sánchez-Sánchez et al., 2019) and other health outcomes (Chodzko-Zajko et al., 2009). No associations of ASM with MVPA were found in both the single and partition models. A possible reason for this inconsistency is the patterns and amount of MVPA in older adults. In the present study, the mean total amount of MVPA in females was 49 min per day, which includes bouts of MVPA lasting <10 min in duration. A previous study among older Japanese adults reported that MVPA lasting 10 or more minutes in duration accounted for only 27 % of daily MVPA, whereas MVPA of 1–4 minute bouts accounted for 43 % (Machida et al., 2018). In the present study, the volume of bouts of MVPA that were 10 or more minutes in duration was only 14.7 % of daily MVPA in females (Supplementary Table 1). While the new WHO 2020 guidelines on physical activity and sedentary behavior removed the requirement of bouts of at least 10 min of physical activity to be counted toward the recommended levels (Bull et al., 2020), little is known whether short bouts of physical activity are related to skeletal muscle health (Jakicic et al., 2019). We found that MVPA was intermittent and accounted for only a small portion of time (approximately 5 %) in a day, which may be insufficient to provide benefits for skeletal muscle mass maintenance or improvement, especially in older Japanese females. Also, the accelerometer algorithm has been validated with younger adults (Ohkawara et al., 2011), which may be another possible reason for this unexpected result. Such algorithms may underestimate older adults' MVPA levels due to their lower resting metabolic rates (Barnett et al., 2016). Future studies ideally should use age-specific accelerometer algorithms to be more precise in examining the association between MVPA and skeletal muscle mass in older females.

Some limitations need to be considered in interpreting the present findings. First, the study design was cross-sectional, thereby precluding any determination of cause and effect. Longitudinal studies examining the contribution of sitting time to skeletal muscle loss are warranted. Further, the final sample size was reduced to <300. Even though a relatively large sample was initially recruited using random sampling, the reduced sample size may have resulted in potential selection bias. The present study utilized multi-frequency BIA to estimate muscle mass, which may be less accurate than other instruments, such as dual-energy X-ray absorptiometry, although BIA is inexpensive, easy to use, portable, and causing no radiation exposure. Furthermore, this study did not adjust for nutritional status such as protein and energy intake. Since it is possible that active and health-conscious older adults consume more healthy nutrients than sedentary ones (Hsueh et al., 2019), the consumption of protein may be a confounder involved in the associations observed. Another potential confounder not measured in the study was the amount of resistance exercise, which is known to influence muscle mass. Additionally, this study did not consider increased albuminuria and declined glomerular filtration rate, which have been reported to be associated with loss of muscle mass in those with more serious chronic kidney disease and type II diabetes (Chung et al., 2018; Zhou et al., 2018). Since they can be caused by prolonged sedentary behavior (Hannan et al., 2021), they may serve as potential pathways through which sedentary time can influence skeletal muscle mass. Understanding such biological mechanisms in future research can help reduce the possibility of reverse causality.

5. Conclusion

Building on existing studies that found detrimental associations of sedentary time with muscle strength (Copeland et al., 2017), this study added new evidence on how sitting time may contribute to sarcopenia. Our study found that higher volumes of sedentary time were generally associated with lower ASM in this sample of older Japanese adults, after accounting for MVPA and other potential confounding factors. We also found a sex difference in this relationship: It was linear among females but non-linear among males. For the latter, we observed an inverted U-shape relationship, in which the slope was positive for shorter total sedentary time (<9 h/d) and negative for longer sedentary time. Further studies are needed to examine male and female separately to better understand the role of sedentary time and bouts in older adults' musculoskeletal health.

CRediT authorship contribution statement

Ai Shibata: Conceptualization, Methodology, Formal analysis, Investigation, Data Curation, Writing-original draft, Funding acquisition; **Kaori Ishii:** Conceptualization, Methodology, Validation, Investigation, Data Curation, Writing-review and editing; **Mohammad Javad Koohsari:** Conceptualization, Writing-review and editing; **Takemi Sugiyama:** Conceptualization, Formal analysis, Writing-review and editing; **David W Dunstan:** Conceptualization, Writing-review and editing; **Neville Owen:** Conceptualization, Writing-review and editing; **Koichiro Oka:** Conceptualization, Methodology, Writing-review and editing, Supervision, Funding acquisition. All authors have read and approved the final manuscript.

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Declaration of competing interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.exger.2022.111870.

References

Barnett, A., van den Hoek, D., Barnett, D., Cerin, E., 2016. Measuring moderate-intensity walking in older adults using the ActiGraph accelerometer. BMC Geriatr. 16 (1), 211. https://doi.org/10.1186/s12877-016-0380-5.

Boppart, M.D., Mahmassani, Z.S., 2019. Integrin signaling: linking mechanical stimulation to skeletal muscle hypertrophy. Am. J. Physiol. Cell Physiol. 317 (4), C629–C641. https://doi.org/10.1152/ajpcell.00009.2019.

Buch, A., Carmeli, E., Boker, L.K., et al., 2016. Muscle function and fat content in relation to sarcopenia, obesity and frailty of old age–an overview. Exp. Gerontol. 76, 25–32. https://doi.org/10.1016/j.exger.2016.01.008.

Bull, F.C., Al-Ansari, S.S., Biddle, S., et al., 2020. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br. J. Sports Med. 54 (24), 1451–1462. https://doi.org/10.1136/bjsports-2020-102955.

Cawthon, P.M., Peters, K.W., Shardell, M.D., et al., 2014. Cutpoints for low appendicular lean mass that identify older adults with clinically significant weakness. J. Gerontol. A Biol. Sci. Med. Sci. 69 (5), 567–575. https://doi.org/10.1093/gerona/glu023.

Chen, L.K., Woo, J., Assantachai, P., Auyeung, T.W., Chou, M.Y., Iijima, K., et al., 2020. Asian working group for sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. J. Am. Med. Dir. Assoc. 21 (3) https://doi.org/10.1016/j.jamda.2019.12.012, 300-7.e2.

Chodzko-Zajko, W.J., Proctor, D.N., Fiatarone Singh, M.A., et al., 2009. American College of Sports Medicine position stand. Exercise and physical activity for older adults. Med. Sci. Sports Exerc. 41 (7), 1510–1530. https://doi.org/10.1249/MSS.0b013e3181a0c95c.

Chung, H.S., Hwang, S.Y., Choi, J.H., Lee, H.J., Yoo, H.J., Seo, J.A., et al., 2018. Effects of low muscle mass on albuminuria and chronic kidney disease in patients with type 2 diabetes: the Korean sarcopenic obesity study (KSOS). J. Gerontol. A Biol. Sci. Med. Sci. 73 (3), 386–392. https://doi.org/10.1093/gerona/glx055.

Copeland, J.L., Ashe, M.C., Biddle, S.J., et al., 2017. Sedentary time in older adults: a critical review of measurement, associations with health, and interventions. Br. J. Sports Med. 51 (21), 1539. https://doi.org/10.1136/bjsports-2016-097210.

Cruz-Jentoft, A.J., Sayer, A.A., 2019. Sarcopenia. Lancet 393 (10191), 2636–2646. https://doi.org/10.1016/S0140-6736(19)31138-9.

Cruz-Jentoft, A.J., Landi, F., Schneider, S.M., et al., 2014. Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the international sarcopenia initiative (EWGSOP and IWGS). Age Ageing 43 (6), 748–759. https://doi.org/10.1093/ageing/afu115.

Cruz-Jentoft, A.J., Bahat, G., Bauer, J., et al., 2019. Sarcopenia: revised european consensus on definition and diagnosis. Age Ageing 48 (1), 16–31. https://doi.org/10.1093/ageing/afy169.

Foong, Y.C., Chherawala, N., Aitken, D., Scott, D., Winzenberg, T., Jones, G., 2016. Accelerometer-determined physical activity, muscle mass, and leg strength in community-dwelling older adults. J. Cachexia. Sarcopenia Muscle 7 (3), 275–283. https://doi.org/10.1002/jcsm.12065.

Gianoudis, J., Bailey, C.A., Daly, R.M., 2014. Associations between sedentary behaviour and body composition, muscle function and sarcopenia in community-dwelling older adults. Osteoporos. Int. 26 (2), 571–579. https://doi.org/10.1007/s00198-014-2895-y.

Goodpaster, B.H., Park, S.W., Harris, T.B., et al., 2006. The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. J. Gerontol. A Biol. Sci. Med. Sci. 61 (10), 1059–1064. https://doi.org/10.1093/gerona/61.10.1059.

Grgic, J., Dumuid, D., Bengoechea, E.G., et al., 2018. Health outcomes associated with reallocations of time between sleep, sedentary behaviour, and physical activity: a systematic scoping review of isotemporal substitution studies. Int. J. Behav. Nutr. Phys. Act. 15 (1), 69. https://doi.org/10.1186/s12966-018-0691-3.

Hannan, M., Ricardo, A.C., Cai, J., Franceschini, N., Kaplan, R., Marquez, D.X., et al., 2021. Sedentary behavior and change in kidney function: the hispanic community health Study/Study of latinos (HCHS/SOL). Kidney360. 2 (2), 245–253. https://doi.org/10.34067/kid.00062.

Harrell, J.F.E., 2015. Regression Modeling Strategies: With Applications to Linear Models, Logistic and Ordinal Regression, and Survival Analysis. In: 2nd ed. Springer International Publishing, New York, pp. 24–28.

Healy, G.N., Clark, B.K., Winkler, E.A., Gardiner, P.A., Brown, W.J., Matthews, C.E., 2011. Measurement of adults' sedentary time in population-based studies. Am. J. Prev. Med. 41 (2), 216–227. https://doi.org/10.1016/j.amepre.2011.05.005.

Heymsfield, S.B., Gonzalez, M.C., Lu, J., Jia, G., Zheng, J., 2015. Skeletal muscle mass and quality: evolution of modern measurement concepts in the context of sarcopenia. Proc. Nutr. Soc. 74 (4), 355–366. https://doi.org/10.1017/S0029665115000129.

Hirani, V., Naganathan, V., Blyth, F., et al., 2017. Longitudinal associations between body composition, sarcopenic obesity and outcomes of frailty, disability, institutionalisation and mortality in community-dwelling older men: the Concord health and ageing in men project. Age Ageing 46 (3), 413–420. https://doi.org/10.1093/ageing/afw214.

Hsueh, M.C., Rutherford, R., Huang, Y.H., Chang Chien, H.Y., Chang, C.H., Park, J.H., et al., 2019. Are older adults without a healthy diet less physically active and more sedentary? Nutrients 11 (5), 1119. https://doi.org/10.3390/nu11051119.

Jakicic, J.M., Kraus, W.E., Powell, K.E., et al., 2019. Association between bout duration of physical activity and health: systematic review. Med. Sci. Sports Exerc. 51 (6), 1213–1219. https://doi.org/10.1249/MSS.0000000000001933.

Kim, T.N., Park, M.S., Ryu, J.Y., et al., 2014. Impact of visceral fat on skeletal muscle mass and vice versa in a prospective cohort study: the korean sarcopenic obesity study (KSOS). PLoS One. 9 (12), e115407 https://doi.org/10.1371/journal.pone.0115407.

Machida, M., Takamiya, T., Amagasa, S., et al., 2018. Descriptive epidemiology of accelerometer-measured moderate to vigorous physical activity in japanese older adults. Nihon Ronen Igakkai Zasshi. 55 (4), 584–593. https://doi.org/10.3143/geriatrics.55.584.

Makizako, H., Shimada, H., Doi, T., et al., 2017. Age-dependent changes in physical performance and body composition in community-dwelling Japanese older adults. J. Cachexia Sarcopenia Muscle 8 (4), 607–614. https://doi.org/10.1002/jcsm.12197.

Matthews, C.E., Keadle, S.K., Troiano, R.P., et al., 2016. Accelerometer-measured dose-response for physical activity, sedentary time, and mortality in US adults. Am. J. Clin. Nutr. 104 (5), 1424–1432. https://doi.org/10.3945/ajcn.116.135129.

Migueles, J.H., Cadenas-Sanchez, C., Ekelund, U., et al., 2017. Accelerometer data collection and processing criteria to assess physical activity and other outcomes: a systematic review and practical considerations. Sports Med. 47 (9), 1821–1845. https://doi.org/10.1007/s40279-017-0716-0.

Ohkawara, K., Oshima, Y., Hikihara, Y., Ishikawa-Takata, K., Tabata, I., Tanaka, S., 2011. Real-time estimation of daily physical activity intensity by a triaxial accelerometer and a gravity-removal classification algorithm. Br. J. Nutr. 105 (11), 1681–1691. https://doi.org/10.1017/S0007114510005441.

Otsuka, R., Matsui, Y., Tange, C., et al., 2018. What is the best adjustment of appendicular lean mass for predicting mortality or disability among Japanese community dwellers? BMC Geriatr. 18 (1), 8. https://doi.org/10.1186/s12877-017-0699-6.

Patterson, R., McNamara, E., Tainio, M., et al., 2018. Sedentary behaviour and risk of all-cause, cardiovascular and cancer mortality, and incident type 2 diabetes: a systematic review and dose response meta-analysis. Eur. J. Epidemiol. 33 (9), 811–829. https://doi.org/10.1007/s10654-018-0380-1.

Reid, N., Healy, G.N., Gianoudis, J., et al., 2018. Association of sitting time and breaks in sitting with muscle mass, strength, function, and inflammation in community-dwelling older adults. Journal article. Osteoporos. Int. 29 (6), 1341–1350. https://doi.org/10.1007/s00198-018-4428-6.

de Rezende, L.F., Rey-Lopez, J.P., Matsudo, V.K., do Carmo Luiz, O., 2014. Sedentary behavior and health outcomes among older adults: a systematic review. BMC Public Health 14, 333. https://doi.org/10.1186/1471-2458-14-333.

de Rezende, L.F., Rodrigues Lopes, M., Rey-Lopez, J.P., Matsudo, V.K., Luiz, Odo C., 2014. Sedentary behavior and health outcomes: an overview of systematic reviews. PLoS One. 9 (8), e105620 https://doi.org/10.1371/journal.pone.0105620.

Rosa-Caldwell, M.E., Greene, N.P., 2019. Muscle metabolism and atrophy: let's talk about sex. Biol. Sex Differ. 10 (1), 43. https://doi.org/10.1186/s13293-019-0257-3.

Sánchez-Sánchez, J.L., Mañas, A., García-García, F.J., et al., 2019. Sedentary behaviour, physical activity, and sarcopenia among older adults in the TSHA: isotemporal substitution model. J. Cachexia. Sarcopenia Muscle 10 (1), 188–198. https://doi.org/10.1002/jcsm.12369.

Shibata, A., Oka, K., Ishii, K., et al., 2019. Objectively-assessed patterns and reported domains of sedentary behavior among Japanese older adults. J Epidemiol. 29 (9), 334–339. https://doi.org/10.2188/jea.JE20180041.

Smith, G.I., Atherton, P., Reeds, D.N., et al., 2009. No major sex differences in muscle protein synthesis rates in the postabsorptive state and during hyperinsulinemia-hyperaminoacidemia in middle-aged adults. J Appl Physiol (1985) 107 (4), 1308–1315. https://doi.org/10.1152/japplphysiol.00348.2009.

Srikanthan, P., Karlamangla, A.S., 2014. Muscle mass index as a predictor of longevity in older adults. Am. J. Med. 127 (6), 547–553. https://doi.org/10.1016/j.amjmed.2014.02.007.

Tse, A.C., Wong, T.W., Lee, P.H., 2015. Effect of low-intensity exercise on physical and cognitive health in older adults: a systematic review. Sports Med. Open. 1 (1), 37. https://doi.org/10.1186/s40798-015-0034-8.

Tyrovolas, S., Koyanagi, A., Olaya, B., et al., 2015. The role of muscle mass and body fat on disability among older adults: a cross-national analysis. Exp. Gerontol. 69, 27–35. https://doi.org/10.1016/j.exger.2015.06.002.

Walowski, C.O., Braun, W., Maisch, M.J., et al., 2020. Reference values for skeletal muscle mass - current concepts and methodological considerations. Nutrients 12 (3), 755. https://doi.org/10.3390/nu12030755.

Wang, D.X.M., Yao, J., Zirek, Y., Reijnierse, E.M., Maier, A.B., 2020. Muscle mass, strength, and physical performance predicting activities of daily living: a meta-analysis. J. Cachexia. Sarcopenia Muscle 11 (1), 3–25. https://doi.org/10.1002/jcsm.12502.

Yamada, M., Nishiguchi, S., Fukutani, N., et al., 2013. Prevalence of sarcopenia in community-dwelling Japanese older adults. J. Am. Med. Dir. Assoc. 14 (12), 911–915. https://doi.org/10.1016/j.jamda.2013.08.015.

Zhou, Y., Hellberg, M., Svensson, P., Höglund, P., Clyne, N., 2018. Sarcopenia and relationships between muscle mass, measured glomerular filtration rate and physical function in patients with chronic kidney disease stages 3–5. Nephrol. Dial. Transplant. 33 (2), 342–348. https://doi.org/10.1093/ndt/gfw466.