Maryam Gharehkhani

The association between sedentary behavior in middle age and muscular structure and function at older age

HUNT study

Master's thesis in Physical activity and Health Supervisor: Beatrix Vereijken Co-supervisor: Turid Follestad May 2022

NTNU Norwegian University of Science and Technology Faculty of Medicine and Health Sciences Department of Neuromedicine and Movement Science

Master's thesis



Maryam Gharehkhani

The association between sedentary behavior in middle age and muscular structure and function at older age

HUNT study

Master's thesis in Physical activity and Health Supervisor: Beatrix Vereijken Co-supervisor: Turid Follestad May 2022

Norwegian University of Science and Technology Faculty of Medicine and Health Sciences Department of Neuromedicine and Movement Science



THE ASSOCIATION BETWEEN SEDENTARY BEHAVIOR IN MIDDLE AGE AND MUSCULAR STRUCTURE AND FUNCTION AT OLDER AGE

RESEARCH AIMS



The aim of this study was to answer these questions:

- How much time do middle-aged people spend in sedentary behavior?
- Is there an association between sedentary behavior in

2.

middle age and muscular structure and function at older age?



3.

METHODS

- study design: a prospective study
- participants: 7 281 individuals who had data on sedentariness in HUNT2 and were at least 70 years old at HUNT4
- exposure: sitting time in middle age
- outcome: muscle mass and chair rise time in older age
- statistical analysis: multiple linear regression & ordinal logistic regression



RESULTS

- The mean self-reported sitting time was 6.6 (SD 3.3) hours/day.
- The association between sitting time and skeletal muscle mass was statistically significant (p =0.002) with a regression coefficient of 0.034(95% CI: 0.009 to 0.059).
- The association between sitting time in middle age and chair rise time at an older age was not statistically significant (p=0.809) and the OR is 1.00 (95% CI: 0.99 to 1.08).



CONCLUSION

- The mean self-reported sitting time in middle-aged Norwegian adults is more than the average worldwide sitting time
- A statistically significant association between sitting time in middle age and muscle mass in older age but too small regression coefficient to be of clinical significance
- No evidence of any association between sitting time in middle age and muscular function at an older age

Acknowledgements

This research was supported by the Department of Neuromedicine and Movement Science, Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology (NTNU). I thank all the individuals who participated in the Nord-Trøndelag Health Study (HUNT).

I would like to thank my supervisor, Professor Beatrix Vereijken, for guiding me throughout this process, sharing her knowledge and insight, and for her invaluable guidance and encouragement throughout this process. I would also like to thank my co-supervisor, Turid Follestad, for guiding me in the process of data analyses and helping me in the writing process.

I wish to thank my husband and son for their support during this challenging period. I am very grateful to my parents whose love and positive vibes kept motivating me all the time.

Abstract

Background: The population of older adults is increasing exponentially. Promotion of healthy aging and prevention of chronic conditions has become an important issue in the world more than ever. Sarcopenia is a common condition in the older population and is defined as low muscle mass, low muscle strength, and/or low physical performance. Sedentary behavior is one of sarcopenia's risk factors, and has increased across the globe, especially among elderly people. The association between sedentary behavior and sarcopenia has been investigated in several studies, but it has not been investigated prospectively. The aim of this study is to assess the association between sedentary behavior in middle aged-people and muscular structure and function at older age.

Methods A total of 7281 older adults aged \geq 70 at HUNT4 and having sedentariness data at HUNT2 were included in this study. Sedentary behavior was assessed in a questionnaire in HUNT2 and muscle structure and function were assessed through associated variables including skeletal muscle mass (measured by Inbody 770) and the short physical performance battery (SPPB) in HUNT4. Linear regression models and ordinal logistic regression models were used to assess the association between sedentary behavior in middle aged-people and muscular structure and function at older age.

Results: The association between sitting time and amount of muscle mass was statistically significant (p = 0.008) with regression coefficient of 0.034 kg/hour (95% CI: 0.009 to 0.058). The association between sitting time and SPPB chair rise sub-score was not statistically significant (p=0.809) and the OR was 1.00 (95% CI: 0.99 to 1.08).

Conclusion: No evidence was found of an association between self-reported sitting time in middle-aged Norwegian adults and their muscular function at older age. A statistically significant association was found between sitting time in middle aged Norwegian adults and their muscle mass at older age after adjusting for age, sex, smoking status, educational levels, BMI, and physical activity levels. However, as the regression coefficient was low, this association is considered not be of clinical relevance.

Keyword: sedentary behavior, muscle mass, SPPB, elderly

Table of contents

Acknowledgements	01
Abstract	02
Table of contents	03
Introduction	04
Methods	07
Study design	07
Participants	07
Measurements and variables	08
Statistical analysis	10
Ethical consideration	10
Results	11
Participants' characteristics	11
Sitting time in middle-aged adults	12
Skeletal muscle mass and SPPB chair rise	13
Association between sitting time and skeletal muscle mass	14
Association between sitting time and SPPB (chair rise sub-score)	16
Discussion	17
Sedentary behavior in middle-aged people	17
Sitting time and muscle mass	18
Sitting time and muscle function	19
Strengths and limitations of this study	20
Conclusion	20
References	21

The association between sedentary behavior in middle age and muscular structure and function at older age

Introduction

Due to advances in the health care system, the rate of population aging is increasing exponentially around the world. The world's population aged 60 years and older is expected to be 2 billion by 2050 (1). The same holds for Norway, where it is estimated that in 2030, the elderly population will be larger than the children and young population for the first time, and it is expected that one in five people will be more than 70 years in 2060 (2). The increasing population of older adults can create an unsustainable burden on social and health care systems, and it is an important responsibility of governments to provide public services for older people (3). Promotion of healthy aging and prevention of non-communicable diseases and chronic conditions has attracted attention of health care systems in the world more than ever (2).

Sarcopenia is a common condition in the older population and is defined as low muscle mass, low muscle strength, and/or low physical performance by the European Working Group on Sarcopenia in Older People (4). Two main categories of sarcopenia are primary (age-related) and secondary (disease-related) sarcopenia (5). Recognized causes of primary sarcopenia include loss of motor units that are innervating muscles, systematic inflammation, decline in anabolic hormones, oxidative stress, and anorexia of aging coupled with a decrease in physical activity (5). The prevalence of sarcopenia is increasing, partly because of the growing population of the elderly. The overall prevalence of sarcopenia has been estimated to be 10% (6). Based on WHO population data, more than 50 million people are affected currently by sarcopenia, and more than 200 million people will be affected by sarcopenia over the next 40 years(7). Sarcopenia in aging people is an important issue for public health systems as it has several consequences including increased physical disability, poor quality of life, nursing home admission, and increased risk of death (8). Although sarcopenia is well known as a potential consequence of aging, it also seems to be associated with some lifestyle factors such as poor diet and low levels of physical activity (9).

Physical activity (PA) is defined as any bodily movement produced by skeletal muscles that requires energy expenditure above resting levels (10). PA can reduce body fat, blood pressure, and glycemic levels, increase muscle and bone mass, and preserve functional capacity and memory (11). There is a large body of evidence suggesting physical activity as a protective factor for sarcopenia in older adults (12, 13). In contrast, sedentary behavior is associated with several adverse effects such as development of various chronic diseases. Sedentary behavior has become an important focus area for public health. In general, sedentary behavior is defined as an

activity that requires less than 1.5 METs. Metabolic Equivalent of Task(MET) is defined as the ratio of oxygen consumed relative to mass, with 1 MET being roughly like energy expended while sitting quietly (14) in a sitting or reclined position during waking hours (such as using the computer or watching TV) (15). Sedentary behavior has been shown to be a risk factor independent of physical activity practice (16). It has been shown that sedentary behavior is associated with higher levels of deep adipose tissue and visceral adiposity which can lead to a catabolic effect in muscle by increasing protein degradation (17), hence it may be that sedentary behavior increases the risk of sarcopenia . Moreover, mechanical stimuli are essential for protein synthesis in the muscles. Without loading muscles which provide such stimuli, such as during exercise, protein degradation may exceed protein synthesis and objective signs of muscle atrophy will become visible (18).

In the last decades, sedentary behavior time has increased across the globe, and prevalence of sedentary behavior is especially high among elderly people (11). It has been shown that 60% of older adults reported sitting for more than 4 hours per day (19); However, when objectively measured, 67% of older adults were sedentary for more than 8.5 hours daily (9). Sedentary behavior results in reduced time participating in physical activity, (and can reduce the beneficial effects of physical activity on health and well-being). There is a large body of evidence showing that sedentary behavior is associated with poor health outcomes and all-cause mortality independently of levels of activity (19).

There are several studies that have investigated the association between sitting time, sleeping time and sarcopenia cross-sectionally. A systematic literature review and dose response meta-analysis carried out in 2019 concluded that both long and short sleep duration are associated with higher risk of sarcopenia (20). It has been shown that total daily sitting time is associated with higher risk of sarcopenia, lower percentage lean mass, and higher total body fat mass. However, more frequent breaks in sitting time are associated with a 45% reduced risk of having pre-sarcopenia (low muscle mass) (16, 21, 22). On the other hand, there are some studies that have investigated the association of sedentary behavior in general and sarcopenia. These studies have found that the prevalence of sarcopenia increased with more time spent in sedentary behavior, and that more hours per day spent in sedentary behavior is associated with higher days of sarcopenia (9, 13, 23).

Furthermore, a population-based cross-sectional study has concluded that an increase in moderate to vigorous physical activity that replaces sedentary behavior and light physical activity is associated with a reduction in sarcopenia prevalence and better performance across its determinants (muscle mass, gait speed and hand grip strength) (9). Although, sedentary behavior appears to have an important role in sarcopenia, a key gap in the literature includes the lack of studies that have investigated the association between sedentary behavior and sarcopenia longitudinally to be able to infer causal relationships.

There are some studies that indicate that muscle mass and strength vary across the lifespan, increasing up to ~40 years and beginning to decrease beyond the age of 50 (24). Therefore, maintaining muscle in middle age is of great importance to prevent or delay sarcopenia (25). The life course approach to sarcopenia prevention may enable public health to encourage a healthy lifestyle such as less sedentariness but requires documentations supporting this association.

To the best of our knowledge, the association between sedentary behavior in middle age and sarcopenia at older age has not been investigated prospectively yet. For this, long-term population studies tracking the same individuals over a long time are necessary. The aim of the current study is to investigate the association between sedentary behavior in middle age and muscular structure and function at older age prospectively. To achieve this aim, we use data from The Trøndelag Health Study (HUNT), which in the fourth wave examined the health status among older adults through the sub-study HUNT 4 70+. We obtained data about sarcopenia determinants including muscle mass and muscle function (SPPB) from the fourth wave of this study. We extracted the data of sedentary time (sitting and lying time) from the same participants from the second wave of HUNT study.

Objectives

The overall objective of the current study is to assess the association between sedentary behavior in middle aged people and muscular structure and function at older age. Specifically, this study will investigate the following research questions:

- How much time do middle-aged people spend in sedentary behavior?
- Is there an association between sedentary behavior in middle age and muscular structure and function at older age?

We also evaluated whether sex, age, physical activity levels, highest level of education, smoking status, and anthropometric characteristics (BMI) had an effect on this association.

Methods

Study design

The Trøndelag Health Study (HUNT) is the largest collection of health data from a population in Norway and one of the largest population-based health surveys globally. The study has enrolled about 230 000 participants in four different surveys so far: HUNT1 (1984-1986), HUNT2 (1995-1997), HUNT3 (2006-2008) and HUNT4 (2017-2019).

The current study is a prospective study in which we linked the data from HUNT2 and HUNT4.

Participants

The number of participants in HUNT2(1995-1997) and HUNT4(2017-2019) was 65 238 and 56 078 respectively. From these, 7 281 participants who had data on sedentariness in HUNT2 and were at least 70 years old at HUNT4 were included in the current study. Figure 1 presents a flow diagram outlining the selection process of the analysis dataset (participant inclusion and exclusion).



Figure 1. Flow diagram of the selection process for the analytical sample (inclusion, exclusion, and the number of participants) from HUNT2 and HUNT4.

Measurements and variables

Sedentary behavior as exposure variable

Sedentary behavior was assessed in a questionnaire in HUNT2 with two questions:

- How many hours do you usually spend lying down during a 24-hour period?
- How many hours do you usually spend sitting down during a 24-hour period?

For the current study, we used sitting time as the exposure variable. Answers given about hours lying down suggested that part of the participants included sleep time whereas others did not. Therefore, the current study used only sitting time as the exposure variable, as this variable is likely less influenced by sleep time.

Muscular structure and function as outcome variables

Muscle structure and function were assessed through associated variables including skeletal muscle mass and the short physical performance battery (SPPB). In HUNT4, skeletal muscle mass was measured using the Inbody 770 and muscle function was estimated using one of the SPPB sub scores. The SPPB includes a 4-meter gait speed test, 10-sec balance ability with feet side-to-side, in semi-tandem and in full tandem, and time needed to perform 5 rises from a chair. We used the latter sub score as an indication for muscle function. In this sub test, participants were asked to stand up and sit down as quickly as possible 5 times without stopping with their arms folded across their chest. The time needed to complete the task was scored as "0" if the participant was not able to complete 5 chair rises or completed rises in > 60 sec, "1" if chair rise time was 16.70 sec or more, "2" if chair rise time was 13.70 sec to 16.69, "3" if chair stand time was 11.20 sec to 13.69, and "4" if chair rise time was 11.19 sec or less.

Covariates

Covariates that could potentially bias the association between the exposure and outcome variables were recognized with a directed acyclic graph (DAG, see Figure 2), which provides a visual demonstration of causal assumptions by clarifying the underlying relations (26).



Figure 2. Directed acyclic graph (DAG) underlining associations between exposure, outcome variable and potential confounders.

All data on the covariates were collected in HUNT4 except for educational level, which was not collected in HUNT4 but available in HUNT2. As educational level is unlikely to change substantially between HUNT2 and HUNT4 in people 70 years and older, we decide to use educational level from HUNT2 as a covariate. Sociodemographic variables included age (continuous variable), and sex (female or male). In the original

data, educational level was categorized as 1: Primary school 7-10 years; continuation school, folk high school; 2: High school, intermediate school, vocational school, 1-2 years high school; 3: University qualifying examination, junior college, A levels; 4: University or other post-secondary education, less than 4 years, and 5: University/college, 4 years or more. We re-categorized it to years of education (<10, 10-12, \geq 13). BMI was calculated as weight divided by the square value of height (kg/m², used as a continuous variable). The lifestyle factor daily smoking was categorized in 5 levels in the original data as 0: never smoked; 1: previous smoker; 2: current daily smoker; 3: current occasional smoker; 4: previous occasional smoker. As the number of participants was very low in some of the categories, we merged them and categorized smoking status to never, former, and current smoker. In terms of physical activity levels, based on the original data, frequency of physical activity was categorized into 1: never; 2: less than once a week; 3: once a week; 4: 2-3 times a week; and 5: nearly every day. For this variable as well, we merged categories and divided participants into active and inactive groups: participants who reported that they exercised 2-3 days a week or more were considered to be active and participants who reported less than 2-3 days a week were considered to be inactive. This roughly corresponds to people who adhere to the WHO guidelines for physical activity and those who do not.

Statistical analysis

Descriptive statistics are presented for all participants and for males and females separately. The baseline characteristics are presented as percentages for categorical variables and mean ± standard deviation for continuous variables. T-tests and Pearson's chi-squared tests were used to evaluate differences between males and females in continuous and categorical variables, respectively.

The association between sitting time and muscle mass was evaluated using linear regression models. Crude and adjusted regression coefficients, with 95% confidence intervals (CIs) were estimated. The following potential confounders were controlled for by multivariable regression analysis: age, sex, BMI, education, smoking status, and physical activity level.

Ordinal logistic regression was used to investigate the association between sitting time and SPPB (chair rise sub-score). The model was adjusted for age, sex, BMI, education, smoking status, and physical activity level. Results are presented as odds ratios (ORs) of a category versus a lower category of SPPB (chair rise sub-score) with 95% Cls. Missing data were handled by using complete case analysis in all analyses.

SPSS version 28 was used to perform all the statistical analyses in this study.

Ethical considerations and risk assessment

The study was approved by the Regional Ethical Committee for Medical and Health Research Ethics, (REK), ref.nr. 2021/285704.

HUNT is licensed as registered data. License number for the HUNT2 and HUNT4 data collection wave was 15 / 01521-11 / GRA and 17 / 00426-7 / GRA, respectively. Before participating in the project, each participant provided informed consent, and they were informed that they could withdraw from the study at any time without stating a reason. All collected data is registered and stored in the HUNT Database, and deidentified before handing over for research. The HUNT Database is a closed data solution without possibility of connecting to the internet, which safeguards against hacking.

In the current project, researchers do not have access to any personal data nor to the identification key ('koblingsnøkkel'). The data needed for the current project is temporarily stored on NTNU's password-protected servers and deleted at the end of the project period.

Results

This section consists of three parts. Participants' characteristics are reported in the first part, the description of sedentary behavior in middle-aged people in the second part, and the association between sedentary behavior in middle-aged people and their muscular structure and function at older age in the third part.

Participants' characteristics

A total of 7281 older adults with age \geq 70 at HUNT4 and having sedentariness data at HUNT2 were included in this study, of which 3302(45.3%) males and 3979(54.7%) females. Table 1 presents the characteristics of the total study sample and per sex for continuous and categorical variables, as well as sex differences as tested by independent samples t-tests for continuous variables and Pearson's chi-squared test for categorical variables. All variables had some missing data. It can be seen in Table 1 that men were slightly younger, spent more hours in sitting position, had higher educational levels, were more active, had higher proportion of former smoker and lower proportion of both never and current smoker than women. There was no clear pattern for BMI.

	All		Males		Females		
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	p-value
Age, years	7281	78.3 (6.4)	3302	77.9 (6.1)	3979	78.6 (6.7)	<0.001
BMI, kg/m²	6957	27.2 (4.4)	3173	27.3 (3.8)	3784	27.1 (4.8)	0.08
		n (%)		n(%)		n(%)	
Education, years	7113		3245		3868		<0.001
1 <10		2957 (41.6%)		1064 (32.8%)		1893 (48.9%)	
2 10-12		2294 (32.3%)		1227 (37.8%)		1067 (27.6%)	
3 ≥13		1862 (26.2)		954 (29.4)		908 (23.5)	
PA level	6644		3082		3562		<0.001
1(inactive)		2143 (32.3%)		944 (30.6%)		1199 (33.7%)	
2(active)		4501 (67.7%)		2138 (69.4%)		2363 (66.3%)	
Smoking status	6814		3143		3671		<0.001
Never		2721 (39.9%)		1072 (34.1%)		1649 (44.9%)	
Former		3439 (50.5%)		1821 (57.9%)		1618 (44.1%)	
Current		654 (9.6%)		250 (8.0%)		404 (11.0%)	

 Table 1. Baseline characteristics of included participants overall and by sex.

Sitting time in middle-aged adults

The mean of self-reported sitting time in all participants (n=7 281) was 6.6 \pm 3.3 hours/day. Figure 3 illustrates the distribution of sitting time by sex. The range of sitting time was 0 to 20 hours/day in females and 0 to 19 hours/day in males. The average of sitting time was 7.3 \pm 3.4 hours/day in males (n=3 302) and 6.1 \pm 3.0 hours/day in females (n= 3 979).



Figure 3. Distribution of sitting time in males and females.

Skeletal muscle mass and SPPB chair rise

Among the 5 634 participants who had data on skeletal muscle mass, 2 933 persons were females and 2 701 were males. The range of skeletal muscle mass in males was 18.0 to 50.8 kg, while it was 13.8 to 37.0 kg in females. The mean of skeletal muscle mass was 23.16 ± 3.1 kg in females and 32.9 ± 4.2 kg in males. Figure 4 presents the distribution of muscle mass by sex.



Figure 4. Distribution of muscle mass in males and females.

Among the 7 049 participants who had data on the SPPB chair rise test, 3 845 persons were female and 3 204 persons were male. In the bar chart below (Figure5), it can be seen that the proportion of participants who received the best score, 4, in the chair rise test is higher in males than in females. In contrast, the proportion of participants who received the worst score, 0, in chair rise test was higher in females than males.





Association between sitting time and skeletal muscle mass

The association between sitting time and muscle mass was investigated using linear regression analysis (CMP statistical method) including only those participants who had complete data on all relevant variables.

A total of 5 388 participants were included in this analysis, of which 2 792(52%) were females and 2 596 (48%) were males.

In the first crude model, the association between sitting time and amount of skeletal muscle mass was investigated without adjusting for any potential confounders. The association was statistically significant (p < 0.001) and the regression coefficient was 0.347 kg/hour (95% CI: 0.301 to 0.394). After adjusting for age, sex, BMI, smoking status, educational level and physical activity level in the second model, the association between sitting time and amount of skeletal muscle mass was still significant (p = 0.003) and the regression coefficient was 0.037 kg/hour (95% CI: 0.012 to 0.062). We checked the adjusted model to confirm whether the assumptions of the multiple linear regression model were met or not. For this purpose, we drew a scatter plot with predicted values of amount of muscle mass and standardized residuals. The plot indicated that there might be some sex interactions not accounted for in the model. In the third model, we considered sex interactions with all continuous variables (age, BMI, sitting time), and again the association between sitting time and amount of 0.052(95% CI: 0.019 to 0.086). As the interaction between sex and sitting time was not significant in the third model, we

eliminated it in the fourth model. For checking the assumptions in the final model, we plotted the standardized residuals against the predicted values of amount of muscle mass (Figure 6) and we drew a histogram of residuals in order to check the normality of its distribution (Figure 7). It was acceptable that the assumptions were met.

 Table 2. Regression coefficient (B) and 95% CI for sitting time and muscle mass as outcome for all four linear regression models.

Models	Regression coefficient (kg/hour)	95% CI	p-value
Model 1	0.347	0.301 to 0.394	< 0.001
Model 2	0.037	0.012 to 0.062	0.003
Model 3	0.052	0.019 to 0.086	0.002
Model 4	0.034	0.009 to 0.058	0.008

Model 1: crude without any adjusting

Model 2: Adjusted for age, sex, BMI, smoking status, educational level and physical activity level

Model 3: Model 2 + sex interactions with age, BMI, and sitting time

Model 4: Model 3 without interaction between sex and sitting time



Figure 6. Standardized residual against predicted value of muscle mass





Association between sitting time and SPPB chair rise sub-score

The association between sitting time and SPPB chair rise sub-score was investigated using ordinal logistic regression analysis, including only those participants that had complete data on all relevant variables. A total of 6 164 participants were included in this analysis, of which 3 279 participants were female and 2 885 participants were male.

In the first model, the association between sitting time and SPPB chair rise sub-score was investigated without adjusting for any potential confounders. The association was statistically significant (p<0.001) and the OR was 1.06 (95% CI: 1.04 to 1.07). After adjusting for age, sex, BMI, smoking status, educational level and physical activity level in the second model, the association between sitting time and SPPB (chair rise sub-score) was not significant anymore (p = 0.681) and the OR was 1.00 (95% CI: 0.99 to 1.02). We checked the adjusted model to confirm whether the assumptions were met or not. For this purpose, we checked the linearity of the association between continuous variables with the log-odds of increasing one level in SPPB chair rise scores. In order to check the linearity, we categorized continuous variables (age, BMI, sitting time) and put them into the model to check whether the log-Odds have about the same difference between each other for those categories. The linearity of the association between BMI could not be assumed, so we categorized BMI as follow: underweight: BMI<18.5; normal: 18.5 $\leq BMI < 25$; overweight: 25 $\leq BMI < 30$; and obese:

BMI≥30. In the third model that was adjusted for BMI as a categorical variable, the association between sitting time and SPPB chair rise sub-score was not statistically significant (p=0.809) and the OR was 1.00 (95% CI: 0.99 to 1.08).

Table 3: Odds ratio (OR), 95% CI, and p-value for all three ordinal regression models. The response variable is SPPB (chair rise sub-score)

Model	OR	95% CI	p-value
Model 1	1.06	1.04 to 1.07	<0.001
Model 2	1.00	0.99 to 1.02	0.681
Model 3	1.00	0.99 to 1.02	0.809

Model 1: crude without any adjusting

Model 2: adjusted with BMI as a continuous variable

Model 3: adjusted with BMI as a categorical variable

Discussion

The aims of this study were to investigate how much time middle-aged people report that they spend in a sitting position per day, and to examine whether there is an association between sitting time in middle age and muscular structure and function at older age. In this study, muscular structure was assessed through amount of muscle mass which was measured by Inbody 770, and we considered chair-rise time which was measured by SPPB as an indication for muscular function.

Sedentary behavior in middle-aged people

The mean of self-reported sitting time in all participants was 6.6 ± 3.3 hours/day, with a range of 0 to 20 hours/day across participants. There were 32 participants who reported 0 hours/day sitting time that could be due to being bed bound. The average sitting time reported in the current study is higher than what reported recently in a scoping review of worldwide surveillance of self-reported sitting time. This study collected sitting time data from 62 countries representing 47% of the global adult population , and found that the daily sitting time was on average 4.7 h/day in adults aged 15-69 years (27). They also found higher sitting time in higher income countries than middle and lower income ones (27). This may be due to more people having sedentary occupations in higher income countries, which could have led to higher sitting times in the present study.

We found in the current study that the middle-aged Norwegian adults spend more time in a sitting position than in Australian middle-aged women (30), however the average reported time in sitting position in middle-aged Norwegian older adult was less than 15-65-year-old aged adults who lived in Latin American countries (31). A recent validation study, that aimed to compare self-reported and objectively measured sedentary time, it was found that self-reported sedentary time showed low correlation with objective data, low precision, and larger random error in comparison to objectively measured sedentary time. They found that all self-report measures under-reported sedentary time (28). Furthermore, another study in which objectively measured and self-reported sitting time was compared, showed a low and non-significant correlation between self-reported and objectively measured sitting time (29). As the sitting time which is reported in the current study is self-reported, it can be considered that it is underreported the actual sitting time in middle-aged people.

Considering adverse the many adverse effects of sitting time and its association with cardiovascular disease, type 2 diabetes, cancer and all-cause mortality (30), lower sitting time is preferred and to be recommended to all individuals in any age group, but particularly middle-aged adults.

Sitting time and muscle mass

In this population-based study of Norwegian older adults, we found that there is a statistically significant association between sitting time in middle age and muscle mass at older age, but the estimated regression coefficient was too small to have be meaningful. In the regression model, adjustments were made for the sociodemographic variables age, sex, BMI, smoking status, educational level and physical activity level.

There are several studies that have investigated the association between sitting time and muscle mass cross-sectionally and found no significant association (9, 16, 21, 31-34). This observation could be due to sitting time alone is not corresponding to the total sedentary behavior. Furthermore, the instrument which was used to assess the sitting time in the current study was a subjective self-reported measure and could have influenced the results. Another possible explanation for finding too small regression coefficient might be that physical activity is more related to the amount of muscle mass than sedentary behavior which is consistent with the significant association between moderate to vigorous physical activity(MVPA) and muscle mass found by Sanches et al. (9). They also found that 60 min/day replacement of sedentary behavior by MVPA is associated with a higher amount of muscle mass (9). In the current study, although we found a significant association between sitting time and muscle mass, the regression coefficient was very close to 0 and thus not meaningful, so what we found is in consistent with those who found no association between sitting time and muscle mass in their studies.

Sitting time and muscle function

In this population-based study of Norwegian older adults, we found no evidence of an association between sitting time in middle-aged people and muscular function at older age after adjusting for age, sex, BMI, education, smoking status, and physical activity level.

Consistent with these findings, no significant association was found between selfreported sedentary behavior and 30 second chair stand test which was adjusted for age, sex, smoking, diabetes, alcohol consumption, self-reported physical activity, and lean mass in an earlier Spanish study on adults 65±5 year-old adults (33). In another study on Australian community-dwelling older adults, no significant association was found between self-reported sitting time and 30-second chair stand test, and TUG (timed up and go test, the time that a person takes to rise from a chair, walk 3 meters at their normal pace, walk back to the chair and sit down again) after adjusting for smoking, chronic disease, fat mass, and MVPA (16). Another study on English community-dwelling older adults found no significant association between TV viewing time and time to complete 5 chair rises after adjustment for smoking status, alcohol intake, chronic ill nesses, socioeconomic status, BMI, and self-reported physical activity (35). Finally, there was no significant association between accelerometer-determined sedentary behavior and 3-meter gait speed in Spanish older adults (9). The latter was the only study that assessed sedentary behavior objectively and found no association between sedentary behavior and muscular function. In contrast, there are some other studies that did find a significant association between sedentary behavior and muscular function. Among those, in a study on community dwelling Swedish older adults, each 1 hour/week increase in accelerometer-determined sedentary behavior was significantly associated with 4% increase in likelihood of a high TUG (time up & go test) after adjustment for sex/ BMI, smoking status, and accelerometer-determined physical activity (32). A significant association was found between accelerometer determined sitting time with 30 second sit to stand test after adjustment for age, sex, ethnicity, education, employment status, marital status, vitamin D level, and prescription medication in a study on community dwelling Australian men and women (21). And finally, in a study on older adults, they found a significant association between objectively- measured (combined heart rate and movement monitor) sedentary behavior and TUG and chair rise speed after adjustment for sex, but after adjustment for BMI, educational level, smoking status, long term illnesses, and occupational classes the association between sedentary behavior and chair rise speed was no more significant.

Different methods of assessing muscle function and sedentary behavior in different studies may have resulted in this discrepancy between studies, as all the studies in which the association between sedentary behavior and muscular function was significant used an objective measurement of sedentary behavior which made them less prone to recall bias and resulted in more precise measurement. It is worth noting that these earlier studies have investigated the association cross-sectionally, while we assessed it prospectively, and this enable us to infer cause-and-effect relationship.

There are several possible factors that could explain the lack of a significant association in our study. A potential explanation may be that life-style factors can change over the years. As the follow-up time in this study was almost twenty years, the probability of changing sedentary behavior during this period is high. It may also be that the sedentary behavior assessed in this study, sitting time only, does not correspond to and underestimate the total daily sedentary behavior, since sedentary behavior is defined as any waking behavior characterized by an energy expenditure equal or less than 1.5 MET, while in a sitting, recline, or lying posture (15).

Strengths and limitations of this study

To the best of our knowledge, this is the first study that has investigated the association between sedentary behavior and muscular structure and function prospectively over 20 years which makes it less vulnerable to reverse causation. The other strength of this study is its large representative population-based sample and the inclusion of both men and women in almost equal numbers allowing us to generalize the results to the whole Norwegian adults.

The information about sedentary behavior was self-reported and therefore prone to recall bias. It has been shown that there can be lack of a significant correlation between self-reported and objectively measured sedentary behavior and that self-report measures under-report sedentary time (28, 29). Due to the data available we were unable to adjust our models for diseases and drugs which can affect muscle mass. In an earlier systematic review, observational evidence was provided the importance of diet to protect muscle mass and function (36). The data we used did not include dietary assessment, so the potential role of diet could not be considered in the investigated associations.

Conclusion

In conclusion, this is the first study that investigated the association between sedentary behavior and muscular structure and function prospectively over 20 years. We found no evidence of an association between self-reported sitting time in middle-aged Norwegian adults and their muscular function at older age. Furthermore, we did find a statistically significant association between sitting time in middle-aged Norwegian adults and their muscle mass at older age after adjusting for age, sex, smoking status, educational levels, BMI, and physical activity levels. However, as the regression coefficient was too low, this association is not considered to be of clinical relevance. Future epidemiological studies with more repetition of assessing sedentary behavior during the life and using objective measurement of sedentary behavior are recommended.

References

1. WHO. Ageing and health 2018 [Available from: <u>https://www.who.int/news-room/fact-sheets/detail/ageing-and-health</u>

2. skifte GREh. Snart flere eldre enn barn og unge 2020 [Available from:

https://www.ssb.no/befolkning/artikler-og-publikasjoner/et-historisk-skifte-flere-eldre-enn.

3. Nations U. World Population Ageing 2017. 2017.

4. Oliveira JS, Pinheiro MB, Fairhall N, Walsh S, Franks TC, Kwok W, et al. Evidence on Physical Activity and the Prevention of Frailty and Sarcopenia Among Older People: A Systematic Review to Inform the World Health Organization Physical Activity Guidelines. Journal of Physical Activity and Health. 2020;17(12):1247-58.

5. Bauer J, Morley JE, Schols AM, Ferrucci L, Cruz-Jentoft AJ, Dent E, et al. Sarcopenia: a time for action. An SCWD position paper. Journal of cachexia, sarcopenia and muscle. 2019;10(5):956-61.

6. Shafiee G, Keshtkar A, Soltani A, Ahadi Z, Larijani B, Heshmat R. Prevalence of sarcopenia in the world: a systematic review and meta-analysis of general population studies. Journal of Diabetes & Metabolic Disorders. 2017;16(1):1-10.

7. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosisReport of the European Working Group on Sarcopenia in Older PeopleA. J. Cruz-Gentoft et al. Age and ageing. 2010;39(4):412-23.

8. Beaudart C, Zaaria M, Pasleau F, Reginster J-Y, Bruyère O. Health outcomes of sarcopenia: a systematic review and meta-analysis. PloS one. 2017;12(1):e0169548.

9. Sánchez-Sánchez JL, Mañas A, García-García FJ, Ara I, Carnicero JA, Walter S, et al. Sedentary behaviour, physical activity, and sarcopenia among older adults in the TSHA: isotemporal substitution model. Journal of cachexia, sarcopenia and muscle. 2019;10(1):188-98.

10. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public health reports. 1985;100(2):126.

11. Lins-Filho OdL, Braga MM, Lima TMd, Ferreira DKdS. Low level of physical activity and sedentary behaviour in elderly: a systematic review of the parameters. Revista Brasileira de Cineantropometria & Desempenho Humano. 2020;22.

12. Lee S-Y, Tung H-H, Liu C-Y, Chen L-K. Physical activity and sarcopenia in the geriatric population: a systematic review. Journal of the American Medical Directors Association. 2018;19(5):378-83.

13. Smith L, Tully M, Jacob L, Blackburn N, Adlakha D, Caserotti P, et al. The association between sedentary behavior and sarcopenia among adults aged≥ 65 years in low-and middle-income countries. International journal of environmental research and public health. 2020;17(5):1708.

14. Lau M, Wang L, Acra S, Buchowski MS. Energy expenditure of common sedentary activities in youth. Journal of Physical Activity and Health. 2016;13(s1):S17-S20.

15. Tremblay MS, Aubert S, Barnes JD, Saunders TJ, Carson V, Latimer-Cheung AE, et al. Sedentary behavior research network (SBRN)–terminology consensus project process and outcome. International journal of behavioral nutrition and physical activity. 2017;14(1):1-17.

16. Gianoudis J, Bailey C, Daly R. Associations between sedentary behaviour and body composition, muscle function and sarcopenia in community-dwelling older adults. Osteoporosis International. 2015;26(2):571-9.

17. Smith L, Thomas EL, Bell JD, Hamer M. The association between objectively measured sitting and standing with body composition: a pilot study using MRI. BMJ open. 2014;4(6):e005476.

18. Narici M, Vito GD, Franchi M, Paoli A, Moro T, Marcolin G, et al. Impact of sedentarism due to the COVID-19 home confinement on neuromuscular, cardiovascular and metabolic health: Physiological and pathophysiological implications and recommendations for physical and nutritional countermeasures. European journal of sport science. 2021;21(4):614-35.

19. Harvey JA, Chastin SF, Skelton DA. How sedentary are older people? A systematic review of the amount of sedentary behavior. Journal of aging and physical activity. 2015;23(3):471-87.

20. Pourmotabbed A, Ghaedi E, Babaei A, Mohammadi H, Khazaie H, Jalili C, et al. Sleep duration and sarcopenia risk: a systematic review and dose-response meta-analysis. Sleep and Breathing. 2019:1-12.

21. Reid N, Healy G, Gianoudis J, Formica M, Gardiner P, Eakin E, et al. Association of sitting time and breaks in sitting with muscle mass, strength, function, and inflammation in community-dwelling older adults. Osteoporosis International. 2018;29(6):1341-50.

22. Tzeng P-L, Lin C-Y, Lai T-F, Huang W-C, Pien E, Hsueh M-C, et al. Daily lifestyle behaviors and risks of sarcopenia among older adults. Archives of Public Health. 2020;78(1):1-8.

23. Johansson J, Morseth B, Scott D, Strand BH, Hopstock LA, Grimsgaard S. Moderate-to-vigorous physical activity modifies the relationship between sedentary time and sarcopenia: the Tromsø Study 2015–2016. Journal of cachexia, sarcopenia and muscle. 2021.

24. Dodds RM, Syddall HE, Cooper R, Benzeval M, Deary IJ, Dennison EM, et al. Grip strength across the life course: normative data from twelve British studies. PloS one. 2014;9(12):e113637.

25. Sayer AA, Syddall H, Martin H, Patel H, Baylis D, Cooper C. The developmental origins of sarcopenia. The Journal of Nutrition Health and Aging. 2008;12(7):427-32.

26. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. Epidemiology. 1999:37-48.

27. McLaughlin M, Atkin A, Starr L, Hall A, Wolfenden L, Sutherland R, et al. Worldwide surveillance of self-reported sitting time: a scoping review. International Journal of Behavioral Nutrition and Physical Activity. 2020;17(1):1-12.

28. Chastin SF, Dontje ML, Skelton DA, Čukić I, Shaw RJ, Gill J, et al. Systematic comparative validation of self-report measures of sedentary time against an objective measure of postural sitting (activPAL). International Journal of Behavioral Nutrition and Physical Activity. 2018;15(1):1-12.

29. Lagersted-Olsen J, Korshøj M, Skotte J, Carneiro I, Søgaard K, Holtermann A. Comparison of objectively measured and self-reported time spent sitting. International journal of sports medicine. 2014;35(06):534-40.

30. Chau JY, Grunseit AC, Chey T, Stamatakis E, Brown WJ, Matthews CE, et al. Daily sitting time and all-cause mortality: a meta-analysis. PloS one. 2013;8(11):e80000.

31. Ribeiro Santos V, Dias Correa B, De Souza Pereira CG, Alberto Gobbo L. Physical activity decreases the risk of sarcopenia and sarcopenic obesity in older adults with the incidence of clinical factors: 24-month prospective study. Experimental aging research. 2020;46(2):166-77.

32. Scott D, Johansson J, Gandham A, Ebeling PR, Nordstrom P, Nordstrom A. Associations of accelerometer-determined physical activity and sedentary behavior with sarcopenia and incident falls

over 12 months in community-dwelling Swedish older adults. Journal of sport and health science. 2021;10(5):577-84.

33. Rosique-Esteban N, Babio N, Díaz-López A, Romaguera D, Martínez JA, Sanchez VM, et al. Leisure-time physical activity at moderate and high intensity is associated with parameters of body composition, muscle strength and sarcopenia in aged adults with obesity and metabolic syndrome from the PREDIMED-Plus study. Clinical nutrition. 2019;38(3):1324-31.

34. Gába A, Pelclová J, Štefelová N, Přidalová M, Zając-Gawlak I, Tlučáková L, et al. Prospective study on sedentary behaviour patterns and changes in body composition parameters in older women: a compositional and isotemporal substitution analysis. Clinical Nutrition. 2021;40(4):2301-7.

35. Luis de Moraes Ferrari G, Kovalskys I, Fisberg M, Gómez G, Rigotti A, Sanabria LYC, et al. Original research Socio-demographic patterning of self-reported physical activity and sitting time in Latin American countries: Findings from ELANS. BMC Public Health. 2019;19(1):1-12.

36. Bloom I, Shand C, Cooper C, Robinson S, Baird J. Diet quality and sarcopenia in older adults: a systematic review. Nutrients. 2018;10(3):308.



