Muscle mass and aerobic capacity in older women: Impact of regular exercise at middle age

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ABSTRACT

Background: The impact of regular exercise habits at middle-age on muscle mass and function at old age remains inconclusive. While regular exercise likely represents a primary source of health-enhancing physical activity (PA), the physical demand of occupation needs to be considered. Additionally, PA level at old age should be taken into account in order to elucidate true associations between past exercise behaviors and muscle mass and function at old age. Therefore, the aim of the study was to examine the impact of regular exercise habits during middle age years on muscle mass and physical function at old age, while considering occupation and objectively assessed PA level at old age.

Methods: Self-reported leisure-time PA during middle age years [35–65 years] and present accelerometer-derived PA level were assessed in a population of community-dwelling older women (65–70 years; n = 112). Participants who accumulated at least 600 MET-min of PA per week during middle age years were classified as physically active. Skeletal muscle mass index (SMI), aerobic fitness and maximal isometric arm and leg strength were determined. Analyses of differences in muscle mass and physical function between physically active and inactive at middle age were adjusted by present PA, adiposity level, and the physical demand of former occupation (sedentary vs manual).

Results: Participants accumulating at least 600 MET-min of exercise-related activities during middle-age years had higher aerobic fitness (P < 0.01) and SMI (P < 0.05) at old age compared to their less active peers. Notably, these beneficial impacts were driven by exercise habits during late middle-age period [50 to 65 years], and remained significant after further adjustment by the physical demand of former occupation and present PA behavior at old age. Finally, middle-age engagement in exercise-related activities had no influence on maximal arm and leg isometric strength at old age.

Conclusion: Our findings highlight the importance of engaging in regular PA of at least moderate intensity during middle age years in order to promote benefits at the level of muscle mass and aerobic fitness. This clearly supports the potential of PA in delaying aerobic capacity impairment and the occurrence of clinically manifest sarcopenia at old age.

1. Introduction

The age-related gradual loss of skeletal muscle mass accompanied by a decline in physical function represent key elements underlying the development of sarcopenia, a condition related to loss of independence, reduced quality of life and increased risk of institutionalization (von Bonsdorff et al., 2009). Given the worldwide increase in the number of older adults above 65 years (WHO, 2020), preventive strategies aiming to delay the age-related loss of muscle mass are warranted. Although physical function trajectories during aging is influenced by both sociodemographic and lifestyle factors, major health organizations currently endorse engagement in physical activity (PA) as a key measure for the promotion of healthy aging, including maintenance of muscle mass and physical function (WHO, 2020; ACSM, 2009). The promotion of muscle mass maintenance at old age has particular implications in older women, who typically have lower muscle mass than men (Suetta et al., 2019) and are more susceptible to develop sarcopenia and related morbidities (Holmes et al., 2009). Unfortunately, data examining the impact of PA habits performed between the ages 35 to 65 years on muscle mass at old age are inconclusive and remain scarce (Sims et al.,

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et al., 2012). In this respect, different occupations in terms of physical demand (i.e. sedentary or manual labor) may readily impact on the trajectory of physical function decline, where heavy manual labor has been shown to negatively affect physical function (Kulmala et al., 2016; Andersen et al., 2012). Thus, while leisure-time exercise habits likely represent a primary source of health-enhancing PA, the physical demand of occupation needs to be considered as it otherwise may moderate links between exercise habits and muscle mass and function throughout middle age years. Furthermore, PA level at old age should also be considered when exploring health benefits of past PA behaviors. Unfortunately, most previous studies have not accounted for moderating effects by present PA level or relied on self-reported data. Therefore, the aim of the present study is to explore the impact of regular exercise habits at middle age on skeletal muscle mass and function at old age in a sample of women, when also considering type of occupation and objectively assessed present PA level.

2. Material and methods

2.1. Participants and study design

In this cross-sectional study, 112 community-dwelling older women (65–70 years), living in an urban area in the middle of Sweden, were recruited through an advertisement in a local newspaper. All participants were examined by a physician. Inclusion criteria were: the absence of coronary heart diseases and diabetes mellitus, no disability concerning mobility, and being non-smoker. Written informed consent was obtained from all participants. The study was conducted according to the Declaration of Helsinki and approved by the regional ethical review board of Uppsala, Sweden (211/33).

2.2. Exercise-related activities and occupation type during middle age years

Engagement in exercise-related activities between 35 and 65 years of age was assessed based on the Historical Adulthood Physical Activity Questionnaire (HAPAQ). Previous studies have demonstrated sufficient validity for HAPAQ compared to objectively assessed PA when ranking individuals according to their past PA behavior (P < 0.001, R = 0.40) (Besson et al., 2010). Firstly, participants were asked to report on engagement in exercise-related activities requiring moderate intensity or higher and which had been performed at least once a week during one year. Activity duration (per session) and frequency during the year of each reported activity were assessed. Thereafter total activity time spent over all time periods was calculated for each reported activity. Based on the compendium of physical activities (Ainsworth et al., 2011) a metabolic equivalent score (MET-score) was allocated to each reported type of activity in order to adjust for differences in energy costs between activities. Only exercises requiring ≥3 METs, (for example jogging, cross-country skiing and different types of ball sports) were included in the final analysis. MET-minutes (MET-min) were expressed by multiplying total time reported in each activity with the allocated MET-score. Then, total amount of MET-min was summed and averaged per week. A weekly average of MET-min was derived for the whole middle age period (35–65 years), as well as for the early (35–50 years) and late middle age periods (50–65 years).

Given current guidelines endorsing at least 150 min of moderate-to-vigorous PA per week (WHO, 2020), a weekly average of at least 600 MET-min was set as threshold to be classified as having a physically active leisure time. Based on the reported occupations, participants were classified into three categories: (1) sedentary occupations, where participants spent most of the time sitting; (2) manual occupations, spending most of the time standing requiring moderate to vigorous physical efforts. To be classified into the sedentary occupation category, participants should have spent at least 20 years in sedentary occupations between ages 35 to 65 years.

2.3. Present physical activity level

Present physical activity was assessed with Actigraph GT3x accelerometers (Actigraph, Pensacola, FL, USA) during a week as previously described (Nilsson et al., 2017). In short, participants were instructed to wear the accelerometer on the right hip with an elastic belt during all waking hours, except for water activities. A minimum of at least four days with more than 10 h recorded per day was required for inclusion. Non-wear time was defined as periods of at least 60 consecutive minutes of zero values. Daily average PA level expressed as accelerometer counts per registered minute (CPM) was retrieved.

2.4. Physical function and body composition

A standardized submaximal exercise test on a cycle ergometer (model 874E; Monark, Varberg, Sweden) was used to assess cardiorespiratory fitness. Participants cycled for 6 min at 50 rpm with a constant workload (75 to 125 watts depending in subject’s current fitness level), and heart rate was measured throughout the test (Astrand and Ryhming, 1954). The average heart rate based on the last 2 min was used to predict maximal oxygen uptake (VO2max) expressed in relation to body weight (mL O2·min−1·kg−1) (Astrand and Ryhming, 1954).

Maximal isometric arm flexion and knee extension strength were measured in subjects seated on an adjustable chair with a 90° angle of elbow, hip and knee joints and with restraining straps crossing the torso, and the tested limbs using the same method as previously described (Edholm et al., 2017).

Briefly, subjects were instructed to exert maximal muscle force as “fast and forcefully” as possible and to maintain it for 3–5 s. Verbal encouragements were provided during each trial. All isometric measurements were performed on the dominant leg, and each subject performed three knee extensions at maximal voluntary effort separated by a rest period of 2.5 min.

The force sensor (K. TOYO 333A) was attached above the processus styloideus ulnae at one fourth of the distance between processus styloideus ulnae and olecranon and above the malleoli at one third of the distance between the lateral femoral epicondyle and lateral malleolus during the arm flexion and knee extension test respectively. Height was measured to the nearest 0.5 cm and body weight to the nearest 0.1 kg by a portable stadiometer and a digital scale, respectively. Skeletal muscle mass was measured using bioelectrical impedance analysis (BIA) (TANITA BC-420MA, Tanita Corporation, Japan) between 7:00 and 9:00 AM following an overnight fast. Skeletal muscle mass was calculated by using the equation of Janssen et al. (2002) (Janssen et al., 2002):

\[
\text{skeletal muscle mass (kg) } = \left[ \left( \text{height}^2 \times \text{BIA}^{-\text{resistance}} - 0.401 \right) \right. \\
+ \left( \text{gender} \times \text{3.825} \right) + \left( \text{age} \times -0.071 \right) \left. \right] + 5.102,
\]

where height is in cm; BIA-resistance is in ohms; gender = 0 for women; age is in years. Subsequently a skeletal muscle mass index (SMI) in percentage was calculated as: skeletal muscle mass / body mass × 100.

2.5. Statistics

Data are presented as means ± standard deviation unless otherwise noted. SMI and functional outcomes were checked for normality and log transformed if necessary to fit a normal distribution. Participants were
classified into two groups based on whether or not they reported a weekly average of at least 600 MET-min of leisure-time PA during middle age years (active vs. non-active). The participants were also categorized based on whether or not they reported a sedentary occupation during the middle age years. Factorial analysis of variance (ANOVA) was employed to investigate impact of engaging in regular exercise [Yes/No] and having a sedentary occupation [Yes/No] during middle age years on continuous outcomes of physical function and SMI. As no interaction effects (exercise - occupation) on dependent outcomes were evident, interaction terms were subsequently deleted from final models to retain statistical power. The models were further adjusted by present physical activity level (CPM). Analyses were conducted across the whole middle age period [35 to 65 years], followed by separate analyses of the early [35–50 years] and late [50–65 years] periods. When analyzing the early middle age period, data on PA and occupation during late middle age period was accounted for and vice versa. Statistical analyses were performed using SPSS ver. 24.0 (SPSS, Chicago, IL). Level of statistical significance was set to $P < 0.05$, which allowed detection of medium effect sizes ($f \lt 0.30$) with a power of $\geq 80\%$ when performing all ANOVA models.

3. Results

Basic characteristics of the study population are shown in Table 1. Participants wore the accelerometer for 14.9 ± 1.1 h per day. During middle age years, 59% of participants were classified as having sedentary occupations. A total of 46.7% of participants reported an average amount of at least 600 MET-min (median 487.0 METmin and IQR 771.8 METmin) during middle age years.

Regular engagement in exercise-related activities during middle age years [35–65] years had a beneficial impact on SMI (active: 31.4 ± 4.2 vs. inactive: 29.6 ± 3.5; $P < 0.05$ Table 1) and cardiorespiratory fitness (active: 30.5 ± 7.9 vs. inactive: 26.6 ± 6.8; $P < 0.01$; Table 1) at old age. Importantly, these beneficial influences remained significant after adjustment by occupation type (sedentary vs manual) and current amount of PA (CPM). We further sought to determine the separate influences of exercise-related activities performed during the early [35–50 years] and late middle age [50–65 years] periods. Interestingly, significant main effects of engagement in exercise-related activities during late middle age on SMI ($P < 0.01$) and cardiorespiratory fitness ($P < 0.01$) were observed, even after adjustment for occupation type and exercise habits performed during early middle age (Figs. 1A and 2A). No corresponding effects of exercise-related activities during early middle age on SMI or cardiorespiratory fitness were observed (Figs. 1B and 2B). Notably, occupation type did not impact on neither SMI nor cardiorespiratory fitness at old age. Finally, we did not observe any influences on maximal isometric strength in arms or legs at old age by exercise habits or occupation type during middle age years.

4. Discussion

The role of PA habits during middle age years for the maintenance of muscle mass and function holds important public health implications. Here we show that engagement in regular exercise activities during the late middle age period is associated with higher muscle mass and cardiorespiratory fitness level at old age. Notably, these beneficial impacts were independent of occupation during middle age and PA level at old age.

The present study highlights the importance of regular exercise habits at middle age for maintenance of muscle mass at old age. This finding supports previous cross-sectional (Nishiguchi et al., 2014) and longitudinal data covering 28 years (Sims et al., 2014), showing that self-reported leisure-time PA performed during middle age years is positively associated to lean mass at old age. In contrast, another study considering a shorter follow-up period (6 years) failed to demonstrate any influence of PA on age-related changes in lean mass (Sims et al., 2013). Notably, the authors of the latter study suggested that the lack of association between PA and lean mass could be because mostly aerobic activities were captured, thereby potentially masking specific impacts of strengthening activities on changes in lean mass over time. However, similar to this latter study, participants in our study mostly engaged in aerobic activities. Further studies are warranted in order to clarify the impact of exercise type on muscle mass trajectories during aging.

The mechanisms underpinning the development of sarcopenia are not fully understood. However, it may be hypothesized that engagement in exercise-related activities during middle age years will stimulate hypertrophy or at least maintenance of muscle mass. In addition, engagement in exercise-related activities during middle age years may diminish the catabolic effect of chronic age-related low-grade inflammation, which is a common condition linked to muscle wasting and reduction in muscle strength in older adults (Navab et al., 2008; Wahlin-Larsson et al., 2017). Indeed, recent reports demonstrated the beneficial impacts of time spent in different intensities of PA on clinical markers of systemic inflammation (Hamer et al., 2012; Nilsson et al., 2017). Additionally, physical exercise is related to improved metabolic control, including insulin sensitivity, and thus reduced risk of cardiometabolic diseases with documented detrimental effects on muscle mass and function (Myers, 2003). Importantly, the 2% unit difference in SMI between those reporting a physically active lifestyle at late middle age and their less physically active peers would in this sample correspond to approximately 1.5 kg of muscle, which represents a clinically important difference in lean body mass. However, to what degree such an impact on muscle mass would delay the occurrence of clinically manifest sarcopenia at old age remains elusive given previous research highlighting unclear relationships between muscle mass and force production (Manini and Clark, 2012).

In addition to links at the level of muscle mass, our study further reveals a beneficial impact of exercise-related activities at middle age on cardiorespiratory fitness at old age, which supports previous observations (Buchner et al., 1992; Paterson et al., 2004). Therefore, compared to physically active women, those who did not perform regular exercise at middle age are at higher risk to reach an aerobic threshold limiting such daily activities. Notably, the observed 3–4 ml/kg/min difference in VO$_{2\max}$ between the those engaging in exercise activities during middle-age years and those who did not would hypothetically imply that the threshold of aerobic capacity impairment is reached ca. 6 years earlier in the latter group given an annual general decline in VO$_{2\max}$ by 0.5 ml/kg/min (Paterson et al., 1999).

In contrast to findings observed at the level of aerobic capacity, there were no relationships between self-reported exercise-related activities at middle age and isometric strength at old age. Conflicting findings have previously been reported in women, where one study (Chang et al., 2017) found no difference in VO$_{2\max}$ between those engaged in exercise-related activities during middle age and those who did not, while another study (Paterson et al., 2004) reported a higher VO$_{2\max}$ in women who engaged in exercise-related activities during middle age.

Table 1 Subject characteristics, N = 112, Mean ± SD.

|                      | All participants | Engagement in regular exercise during middle age (35–65 years) | No | Yes |
|----------------------|------------------|---------------------------------------------------------------|----|-----|
| Age (years)          | 67.5 ± 1.7       | 67.5 ± 1.7                                                   | 67.5 ± 1.7 | 67.5 ± 1.7 |
| Height (cm)          | 164.5 ± 5.7      | 164.0 ± 5.6                                                  | 165.4 ± 5.7 | 165.4 ± 5.7 |
| Weight (kg)          | 68.3 ± 11.5      | 67.5 ± 10.6                                                  | 69.6 ± 12.9 | 69.6 ± 12.9 |
| Body mass index (kg/m$^2$) | 25.2 ± 4.0   | 25.1 ± 3.8                                                   | 25.4 ± 4.4  | 25.4 ± 4.4 |
| Body fat (%)         | 36.0 ± 6.3       | 36.1 ± 6.0                                                   | 36.0 ± 6.8  | 36.0 ± 6.8 |
| SMI (%)              | 30.4 ± 3.9       | 29.6 ± 3.5                                                   | 31.4 ± 4.2* | 31.4 ± 4.2* |
| VO$_{2\max}$ (mlO$_2$-min$^{-1}$-kg$^{-1}$) | 28.4 ± 7.4 | 26.6 ± 6.8                                                   | 30.5 ± 7.9* | 30.5 ± 7.9* |
| PA level (cmts-min$^{-1}$) | 314 ± 118 | 303 ± 117                                                   | 330.2 ± 119 | 330.2 ± 119 |
| Maximal isometric strength |                 |                                                              |                |
| Knee extension (N.kg$^{-1}$) | 2.7 ± 0.7 | 2.7 ± 0.6                                                   | 2.7 ± 0.8  | 2.7 ± 0.8 |
| Elbow flexion (N.kg$^{-1}$) | 1.2 ± 0.2 | 1.2 ± 0.2                                                   | 1.2 ± 0.2  | 1.2 ± 0.2 |

SMI: Skeletal muscle mass index; VO$_{2\max}$: Maximal oxygen consumption; PA: Physical activity.

* $P < 0.05$.

* $P < 0.01$.

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suggested an impact of PA behavior during adulthood on muscular strength at old age, whereas others did not observe such a relationship (Tikkanen et al., 2012; Dodds et al., 2013). The observed impact on muscle mass but not isometric strength in our study may reflect the fact that isometric strength is influenced by several factors other than muscle mass alone. In fact, it has been shown that age-related changes in muscle mass may explain as little as 5% of related changes in strength capacity (Hughes et al., 2001). Therefore, quantitative and qualitative changes at the level of muscle tissue are unlikely to directly reflect changes in capacity to generate isometric force. Moreover, it should be acknowledged that muscle mass assessed at whole-body level may not accurately reflect arm or leg muscle strength.

This study further demonstrates that engagement in exercise-related activities during late but not early middle age years is positively associated to muscle mass and aerobic capacity at old age. Although regular exercise habits likely elicit health-related impacts throughout adulthood, the lack of evidence regarding the early middle age period is likely due to the substantial time gap between the reported behavior and the

Fig. 1. Skeletal muscle mass index (SMI) (mean ± standard error, SE) in older women reporting weekly regular exercise (≥600 MET-min) (■) or not (□) at age intervals 50–65 years (A) and 35–50 years (B). All data are adjusted for occupation type and present PA level. # P < 0.01.

Fig. 2. Cardiorespiratory fitness (VO$_2$max) (mean ± standard error, SE) in older women reporting weekly regular exercise (≥600 MET-min) (■) or not (□) at age intervals 50–65 years (B) and 35–50 years (A). All data are adjusted for occupation type and present PA level. # P < 0.01.
hypothesized effect. This is also supported by previous studies who failed to demonstrate impacts of physical activity habits before the age of 50 on functional capacity at old age (Dodds et al., 2013; Stenholm et al., 2012). Thus, our findings highlight the importance of maintaining a physically active leisure-time beyond the age of 50 in order to infer significant health impacts on muscle mass and aerobic capacity at old age. However, it should be noted that despite the lack of observed health impacts at old age from early adulthood behaviors, promotion of regular exercise habits should still be encouraged throughout adulthood. In fact, a recent study on tracking of exercise behaviors across the life span concluded that exercise habits seem highly stable across adulthood (van der Zee et al., 2019), which would support efforts to promote adoption of regular exercise habits in early adulthood as they may be maintained into old age.

In this study, we hypothesized that having a sedentary occupation may moderate links between self-reported leisure-time exercise habits at middle age and health outcomes at old age. Interestingly, our data indicate that having a sedentary occupation at middle age does not alter the beneficial impacts of regular exercise habits on muscle mass and aerobic capacity at old age. Instead our findings, further point to the importance of regular engagement in exercise during middle age years for promotion of healthy aging.

Finally, the following aspects should be considered when interpreting the study findings; our sample of older women may not reflect more diverse populations in terms of age, biological sex, and different health conditions. Moreover, potential interaction with socio-economic factors cannot be excluded. Of note, average PA level in our sample of women is comparable to data previously reported in larger samples of older women (Berkemeyer et al., 2016). Additionally, similar to any retrospective assessment, recall bias is likely to occur, which would weaken the strength of any true association. Finally, further research is warranted to elucidate amounts and types of exercise activities required to elicit significant impact on strength at old age. In conclusion, exercise-related activities at middle age are beneficially linked to muscle mass and aerobic capacity in women at old age. Importantly, these benefits are evident regardless of physical demand of former occupation and present PA level.

In conclusion, little is currently known about the impact of physical activity during the early and late middle age years on muscle mass at old age. The present study highlights that regular engagement in exercise activities during the middle age period is associated with higher muscle mass and cardiorespiratory fitness level at old age, which holds important clinical and public health implications. These findings support efforts promoting regular exercise habits in order to combat development of clinically manifest sarcopenia and mitigate decline in cardiorespiratory function.

CRediT authorship contribution statement

Peter Edholm: Funding acquisition, Data curation; Formal analysis; Writing original draft; Review & editing the manuscript.
Jort Veen: Writing original draft; Review & editing the manuscript.
Fawzi Kadi: Conceptualization; Funding acquisition, Data curation, Review & editing the manuscript.
Andreas Nilsson: Conceptualization; Funding acquisition, Data curation, Review & editing the manuscript.

Declaration of competing interest

The authors have no conflict of interest to declare.

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