

# Gender-specific risk factors for incident sarcopenia: 8-year follow-up of the English longitudinal study of ageing

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## ABSTRACT

**Background** The aetiology of age-related sarcopenia is not known.

**Objectives** To investigate if risk of developing sarcopenia differs by gender and to identify gender-specific risk factors of incident sarcopenia in a large population-based cohort of older English adults.

**Methods** The sample (n=3404; age 63.4 (SD 7.7) years; 54.1% women) comprised older community-dwelling adults recruited from the English Longitudinal Study of Ageing. Sarcopenia was defined as handgrip <26 kg in men and <16 kg in women. Handgrip strength was assessed at baseline (2004/2005) and repeated at follow-up (2012/2013). Analysed risk factors included baseline anthropometric measures, smoking, vigorous and moderate physical activity, depressive symptoms, chronic illnesses and wealth. After excluding participants with sarcopenia at baseline, multivariable logistic regressions were used to explore baseline risk factors for incident sarcopenia.

**Results** During 8-year follow-up, 208 and 287 cases of sarcopenia were identified in men (n=1564) and women (n=1840), respectively. Women were at 20% (age adjusted OR=1.20, 95% CI 0.98 to 1.47) higher risk of developing sarcopenia than men. The inverse association between physical activity and sarcopenia risk was observed at moderate (OR=0.44, 95% CI 0.27 to 0.67) and vigorous (0.53, 95% CI 0.31 to 0.82) intensities in men and only vigorous (OR=0.44, 95% CI 0.28 to 0.68) intensity in women. Social factors, such as wealth, and chronic health conditions appeared to be more strongly associated with sarcopenia in men.

**Conclusion** Women are at higher risk of developing incident sarcopenia than men, and this is likely explained by a range of gender-specific risk factors.

## INTRODUCTION

Age-related sarcopenia is one of the most deleterious effects of ageing. Presenting with loss of muscle mass, strength and function, sarcopenia has a major impact on quality of life in the elderly, development of physical disability and mortality.<sup>1,2</sup> The aetiology of sarcopenia is not well understood, but it is highly prevalent in older adults; up to 20% of the older population worldwide are thought to be living with sarcopenia, even among the apparently healthy.<sup>3</sup> Coupled with the rapidly growing ageing population worldwide, sarcopenia is projected to result in excessive healthcare and economic burden in the near future.<sup>4</sup>

Several mechanisms have been proposed to explain the development of sarcopenia, centering on protein synthesis, proteolysis, neuromuscular integrity and muscle fat content.<sup>5</sup> Recent epidemiological studies support the role of physical activity as a protective factor against sarcopenia development, yet the basis of current evidence is cross-sectional or retrospective investigations.<sup>6</sup> Moreover, only few investigations<sup>7</sup> have considered gender-specific risk factors in sarcopenia, despite the clear difference in immune response homeostasis between men and women and subsequent disease risks in their ageing process.<sup>8</sup>

To fill the knowledge gap, primary aims of the present study were: (1) to investigate if risk of prospectively developing sarcopenia differs by gender and (2) to identify gender-specific risk factors of incident sarcopenia in a large population based cohort of older English adults.

## METHODS

The English Longitudinal Study of Ageing (ELSA) is a cohort study of older, community-dwelling adults previously described.<sup>9</sup> Data on grip strength were first collected at wave 2 (2004/2005) and were thus used as the baseline for the present analyses. Handgrip assessments were repeated at wave 6 (2012/2013) in survivors. Participants gave full informed consent to participate in the study. Anthropometric data (waist and hip) and grip strength were collected by trained nurses. Participants were excluded from handgrip tests if they had swelling or inflammation, severe pain or a recent injury or surgery to the hand in the preceding 6 months. Handgrip strength (kg) of the dominant hand was assessed using the Smedley handheld dynamometer (Stoelting, Illinois, USA), using the average of three measurements from the dominant hand. Participants held the device at a right angle to their body and exerted maximum force for a couple of seconds when instructed. Waist circumference was recorded twice midway between the iliac crest and lower rib and hip circumference around the widest portion of the buttocks using measuring tape. Central obesity was defined using waist-to-hip ratio (WHR) WHO criteria (WHR  $\geq$  0.85 in women and WHR  $\geq$  0.90 in men).<sup>10</sup> Trained interviewers asked questions on cigarette smoking (current, ex-smoker or non-smoker), alcohol consumption (1–4/week, rarely and not in past 12 months), frequency of vigorous, moderate and low-intensity physical activity (>once a week, once



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a week, 1–3 times a month and hardly ever/never), depressive symptoms (using a score >3 on the eight-item Centre of Epidemiological Studies Depression scale), activity limiting illness (yes or no)<sup>11</sup> and diabetes (yes or no). Wealth was grouped into quintiles, comprising the total value of the participant's home (excluding mortgage) and other financial assets. Sarcopenia was defined as handgrip <26 kg in men and <16 kg in women.<sup>12</sup> After excluding participants with sarcopenia at baseline, we used multivariable logistic regression to explore longitudinal associations between psychosocial and clinical risk factors with incident sarcopenia. All analyses were conducted using SPSS V.22.

## RESULTS

At baseline, 7666 participants provided data on handgrip strength. After removing participants with sarcopenia at baseline (n=1265), those that died through follow-up (n=796) and those with missing covariates and follow-up data (n=2201), the analytic sample for multivariable logistic regression analyses comprised 3404 participants (mean age 63.4 (SD 7.7) years; 54.1% women). During 8-year follow-up, 208 and 287 cases of sarcopenia were identified in men (n=1564) and women (n=1840), respectively.

We observed an elevated risk of developing sarcopenia among women (OR=1.20, 95% CI 0.98 to 1.47) comparing to men in the age-adjusted model. In multivariable adjusted gender-specific models, age and physical activity level were significantly associated with incident sarcopenia in both genders. Such that older age was associated with higher risk of sarcopenia (men, OR=1.16, 95% CI 1.14 to 1.19; women, OR=1.12, 95% CI 1.10 to 1.14); physical activity of moderate (OR=0.44, 95% CI 0.27 to 0.67) and vigorous (0.53, 95% CI 0.31 to 0.82) intensities were protective of sarcopenia in men, but an association was only exhibited at vigorous intensity (OR=0.44, 95% CI 0.28 to 0.68) in women.

Activity limiting illness was associated with higher risk of developing sarcopenia in men (OR=1.49, 95% CI 1.03 to 2.18) but not in women (OR=1.29, 95% CI 0.94 to 1.77). Similarly, baseline diabetes diagnosis was associated with higher likelihood of incident sarcopenia in men (OR=2.43, 95% CI 1.50 to 3.95) but not in women (OR=1.49, 95% CI 0.83 to 2.68). Higher wealth status was associated with lower risk of sarcopenia in a dose–response manner, particularly in men. We observed no statistically significant associations in relation to incident sarcopenia with other risk factors, including smoking, alcohol consumption, depressive symptoms and central obesity (table 1).

## DISCUSSION

In the present population-based sample of older English adults, women were at 20% higher risk of developing sarcopenia than men over the 8-year follow-up. There appear to be a range of gender-specific risk factors for incident sarcopenia, notably, the benefit of physical activity at moderate and vigorous intensities in men and only vigorous intensity in women. In addition, social factors, such as wealth, appeared to be more strongly preventive of sarcopenia in men. Chronic conditions such as activity-limiting illness and diabetes may put men at higher risk of incident sarcopenia, likely owing to low levels of physical activity associated with such conditions.

Our findings support previous research on the role of physical activity in preventing sarcopenia.<sup>6</sup> The present study is one of the first to extend the beneficial influence of physical activity with longitudinal data. The greater benefit of physical activity engagement in men than in women has

**Table 1** Risk factors for incident sarcopenia\* over 8-year follow-up in men and women from ELSA

Baseline risk factor	Men OR (95% CI) (cases=208; n=1564)	Women OR (95% CI) (cases=287; n=1840)
Age	1.16 (1.14 to 1.19)	1.12 (1.10 to 1.14)
Physical activity		
Inactive	1.0 (Ref)	1.0 (Ref)
Moderate	0.44 (0.27 to 0.67)	0.85 (0.55 to 1.22)
Vigorous	0.53 (0.31 to 0.82)	0.44 (0.28 to 0.68)
Smoking		
None	1.0 (Ref)	1.0 (Ref)
Current	1.29 (0.75 to 2.19)	0.80 (0.53 to 1.21)
Alcohol		
Daily	1.0 (Ref)	1.0 (Ref)
1–4/week	1.17 (0.77 to 1.76)	1.13 (0.74 to 1.73)
Rarely	1.15 (0.75 to 1.92)	1.13 (0.74 to 1.73)
Not in past 12 months	1.02 (0.57 to 2.22)	1.30 (0.77 to 2.22)
Wealth		
1 (lowest)	1.0 (Ref)	1.0 (Ref)
2	0.75 (0.43 to 1.38)	1.26 (0.79 to 2.01)
3	0.63 (0.35 to 1.14)	0.60 (0.37 to 0.95)
4	0.52 (0.28 to 0.93)	0.77 (0.47 to 1.23)
5 (highest)	0.44 (0.24 to 0.81)	0.63 (0.38 to 1.02)
Depressive symptoms		
CESD <4	1.0 (Ref)	1.0 (Ref)
CESD ≥4	0.82 (0.45 to 1.51)	1.19 (0.81 to 1.75)
Activity limiting illness		
No	1.0 (Ref)	1.0 (Ref)
Yes	1.49 (1.03 to 2.18)	1.29 (0.94 to 1.77)
Central obesity		
No	1.0 (Ref)	1.0 (Ref)
Yes	0.84 (0.60 to 1.18)	1.12 (0.84 to 1.49)
Diabetes		
No	1.0 (Ref)	1.0 (Ref)
Yes	2.43 (1.50 to 3.95)	1.49 (0.83 to 2.68)

Participants with sarcopenia at baseline were removed.

OR are mutually adjusted for all presented variables.

\*Cases of sarcopenia at follow-up defined as handgrip <26 kg in men and <16 kg in women.

CESD, Centre of Epidemiological Studies Depression scale; ELSA, English Longitudinal Study of Ageing.

been previously reported in a cross-sectional study<sup>13</sup> that found associations of physical activity with muscle volume and functional parameters in men but null association in women. In that study, physical activity was defined using average metabolic equivalent value. This approach does not consider the intensity of physical activity, unlike the present approach that identified the benefit of vigorous physical activity in women. The stronger association of physical activity with incident sarcopenia in men than in women could also explain the higher risk of incident sarcopenia in men with activity-limiting illness and diabetes but not in women, since such conditions often restrict individuals from being physically active.

There is a growing interest in gender-specific differences in the development of sarcopenia, notably the role of androgens given that mechanistic studies found testosterone levels to be

associated with sarcopenia.<sup>14</sup> Moreover, recent in vivo and in vitro studies suggested that testosterone may enhance the benefit of low-intensity physical training on skeletal muscle mitochondrial function in elderly male mice.<sup>15</sup> Owing to different homeostasis between men and women, it is likely that muscle anabolic activity is more prone to external stimuli (such as physical activity) among men than women.<sup>16</sup>

Another protective factor of incident sarcopenia identified in men was a higher level of wealth. This finding is important because ageing is a complex process and not merely biological. Wealth is a key indicator of socioeconomic status in this population. We speculate that level of wealth may signify the quality of nutrition, yet it is unclear why the impact of wealth on incident sarcopenia differs between men and women. Future research should consider the inclusion of gender as a social and psychological factor to identify how social economics and contextual factors may later influence the risk of sarcopenia.

Strengths of the present study include the large population-based sample of older English adults and the longitudinal design. However, the data must be interpreted considering the following limitations. We used a single measure of muscle strength to assess sarcopenia. Although a unified geriatric assessment tool is yet to be widely implemented to diagnose sarcopenia, handgrip strength has been commonly used to measure muscle strength, which is a critical component of sarcopenia.<sup>5</sup> It has been widely used in research and clinical settings<sup>17 18</sup> and shown to be an independent predictor of all-cause mortality.<sup>19 20</sup> Other limitations include limited adjustment for subclinical disease process and severity of disease. Furthermore, participants retained in our analyses were generally healthier than the overall sample, thus bias may rise with likely lower incidental sarcopenia in the analysed sample.

In conclusion, the present longitudinal analyses suggest that women are at 20% higher risk of developing incident sarcopenia than men that may be explained by a range of gender-specific risk factors.

#### What is already known on this subject

- ▶ The aetiology of sarcopenia is not well understood, but it is highly prevalent in older adults.
- ▶ Previous investigations using cross-sectional and retrospective design suggested that physical activity may prevent sarcopenia.
- ▶ The aging processes differ between men and women.

#### What this study adds

- ▶ Women are at 20% higher risk of developing incident sarcopenia than men.
- ▶ Men benefit from physical activity of moderate and vigorous intensities in preventing incident sarcopenia, but this benefit requires vigorous intensity in women, which might be due to differed hormone production.
- ▶ Social factors and wealth appeared to be more strongly preventive of sarcopenia in men, suggesting gender as a social and psychological factor that is not merely biological.

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**Patient consent** Not required.

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