Sarcopenia and mortality risk in frail older persons aged 80 years and older: results from iLSIRENTE study

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Abstract

Background and aims: sarcopenia has been indicated as a reliable marker of frailty and poor prognosis among the oldest individuals. We evaluated the impact of sarcopenia on the risk of all-cause death in a population of frail older persons living in community.

Methods: we analysed data from the Aging and Longevity Study, a prospective cohort study that collected data on all subjects aged 80 years and older residing in the Sirente geographic area (n = 364). The present analysis was conducted among those subjects who were between 80 and 85 years of age at the time of the baseline assessment (n = 197). The main outcome measure was all-cause mortality over 7-year follow-up. According to the European Working Group on Sarcopenia in Older People (EWGSOP) criteria, the diagnosis of sarcopenia required the documentation of low muscle mass and the documentation of either low muscle strength or low physical performance. Cox proportional regression models were used to estimate crude and adjusted hazard ratios and 95% confidence intervals of death by the presence of sarcopenia.

Results: using the EWGSOP-suggested criteria, 43 subjects with sarcopenia (21.8%) were identified. During the 7-year follow-up, 29 (67.4%) participants died among subjects with sarcopenia compared with 63 subjects (41.2%) without sarcopenia (P < 0.001). After adjusting for potential confounders including age, gender, education, activities of daily living (ADL) impairment, body mass index, hypertension, congestive heart failure, chronic obstructive pulmonary disease, number of diseases, TNF-α, participants with sarcopenia had a higher risk of death for all causes compared with non-sarcopenic subjects (HR: 2.32, 95% CI: 1.01–5.43).

Conclusions: our results obtained from a representative sample of very old and frail subjects show that sarcopenia is associated with mortality, independently of age and other clinical and functional variables.

Keywords: sarcopenia, mortality, frailty, older people

Introduction

The term sarcopenia describes the age-associated loss of muscle mass and muscle function [1]. Recently, a consensus definition for sarcopenia has been agreed upon by several, mostly European, geriatric and gerontological societies [2]. This consensus definition includes a mandatory measurement of the muscle mass and proposes the option to either measure muscle strength by hand grip or physical performance by gait speed [2].

According to Fried et al. [3], the loss of the muscle mass plays an important aetiological role in the frailty process of elderly subjects, being also a key player of its latent phase and explaining many aspects of the frailty status itself [4]. Sarcopenia is frequently associated with poor endurance,
physical inactivity, slow gait speed and decreased mobility [5, 6]. The age-related muscle mass loss is also associated with an increased risk of incident disability, all-cause mortality and higher health-care costs in the older people [1, 7].

Despite a growing interest of scientific community to such condition [1, 8, 9], information on sarcopenia among community living older subjects and its relation to survival is still lacking. In a previous study, the muscle mass was demonstrated to be a predictor of overall mortality after a follow-up of 4 years [10]. However, some recent studies suggested that muscle function may be a more powerful predictor of disability and mortality than the muscle mass [11, 12].

In the present study, we have evaluated the impact of sarcopenia—in term of low muscle function (strength or performance) and low muscle mass—on the risk of all-cause death in a large population of frail octogenarians living in community, enrolled in the ‘Invecchiamento e Longevità nel Sirente’ (Aging and Longevity in the Sirente geographic area, iSIRENTE study) study.

Methods

We used data from the iSIRENTE, a prospective cohort study conducted in the mountain community living in the Sirente geographic area (L’Aquila, Italy). The Catholic University of Sacred Heart ethical committee ratified the entire study protocol. All participants signed an informed consent at the baseline visit. The iSIRENTE study protocol has been described in details elsewhere [13].

Study population

A preliminary list of all persons living in this well-defined area was obtained at the end of October 2003 from the Registry Offices of the 13 municipalities involved in the study. From this preliminary list, potential study participants were identified by selecting all persons born in the Sirente area before 1 January 1924 and actually living in such area. Of the initial 514 subjects screened, 32 men and 53 women died or moved away from the area before the baseline assessment. Among those eligible (n = 429), the prevalence of refusals was low (16%). As a result, the overall study population consisted of 364 subjects (71% of the initial sample). To select a sample of individuals which would have been homogeneous with respect to life expectancy, the present analysis was conducted among those 197 subjects who were between 80 and 85 years of age at the time of baseline assessment.

Data collection

Participants’ baseline assessments began in December 2003 and were completed in September 2004 [13]. The Minimum Data Set for Home Care (MDS-HC) form was administered to all study participants according to the guidelines published in the MDS-HC manual [14]. The MDS-HC contains over 350 data elements including sociodemographics, physical and cognitive status variables, as well as major clinical diagnoses [14]. The MDS items have shown an excellent inter-rater and test–retest reliability when completed by nurses performing usual assessment duties (average weighted Kappa = 0.8) [15]. Additional information on family history, lifestyle and physical activity were collected using specific questionnaires shared with the ‘Invecchiare in Chianti Study’ [16].

Assessment of sarcopenia

For the present study, we adopted the European Working Group on Sarcopenia in Older People (EWGSOP) criteria [2]. The EWGSOP recommends using the presence of both low muscle function (strength or performance) and low muscle mass for the diagnosis of sarcopenia. Thus, the diagnosis of sarcopenia in the present study sample required the documentation of low muscle mass and the documentation of either low muscle strength or low physical performance.

Muscle mass assessment: mid-arm muscle circumference

The muscle mass was measured by the mid-arm muscle circumference (MAMC). The MAMC was calculated using the following standard formula [17]:

\[
\text{MAMC} = \frac{\text{mid - arm circumference} - (3.14 \times \text{triceps skin - fold thickness})}{C_0} 
\]

The measurement of triceps skin-fold thickness was made using Harpenden skin-fold calliper. Mid-arm circumference was made using a flexible steel measuring tape, on the right side of the participant’s body unless affected by disability or disease. In the absence of reliable cut-off points for European population, we considered the MAMC tertiles previously calculated on all subjects enrolled in the iSIRENTE study [10]. The lower tertile identified the subjects with the low muscle mass. As consequence, the low muscle mass was classified as MAMC <21.1 and 19.2 cm in men and women, respectively [10].

Physical performance assessment: four-meter walking test

Walking speed was evaluated measuring participants’ usual gait speed (in m/s) over a 4-m course. As suggested in the EWGSOP consensus paper [2], a cut-off point of <0.8 m/s identifies subjects with low physical performance. This cut-off point was similar to that obtained among 469 men and 561 women (age range from 20 to 102 years) from the InCHIANTI study population [16].

Muscle strength measure: hand grip

Muscle strength was assessed by hand grip strength which was measured using a dynamometer (North Coast Hydraulic Hand Dynamometer, North Coast Medical, Inc.,
Morgan Hill, CA, USA). One trial for each hand was performed and the result from the strongest hand was used for the present analyses. Using the cut-off points indicated in the EWGSOP consensus paper [2], low muscle strength was classified as hand grip < 30 and 20 kg in men and women, respectively. These cut-points were similar to that obtained from the InCHIANTI study population [18].

**Survival status**

The vital status of all study participants was ascertained by general practitioners and confirmed using the National Death Registry over a 7-year period of time after the baseline visit. The follow-up time was 7 years. Participants were censored at the time of their death using the date of death (for participants who died during the follow-up) or at the end of follow-up (for participants who did not die during the 7-year study follow-up).

**Covariates**

Medical diagnoses—directly collected by general practitioners—were defined as conditions that have a relationship with patients’ functional, cognitive, and behavioural status, medical treatment and risk of death.

Basic and instrumental activities of daily living (ADL) were assessed by the assessor using the MDS-HC instrument [13]. The ADL scale is based on seven levels of self-performance including dressing, eating, toilet use, bathing, mobility in bed, locomotion and transfer. Similarly, the IADL scale is based on seven levels of self-performance including meal preparation, house work, managing finance, phone use, shopping, transportation and managing medications. Cognitive performance was assessed using a six-items, seven-category scale [Cognitive Performance Scale (CPS)] [19]. The CPS was scored on a 7-point ordinal scale in which higher scores were associated with worse cognitive performance.

**Blood measurements**

Venus blood samples were drawn in the morning after an overnight fast. The samples were immediately centrifuged and stored at −80°C until the final analysis. Standard determinations of inflammatory markers (C-reactive protein, interleukine-6 and TNF-α) were performed by commercially available kits (Olympus, Italy) suitable on Olympus 2700 instrumentation.

**Statistical analysis**

Subjects with sarcopenia were identified using the algorithm developed and suggested by the EWGSOP [2] for sarcopenia case finding and screening in practice (Figure 1).

Characteristics of the study participants were described according to the sarcopenia status. Differences were assessed using Fisher’s exact test and ANOVA test statistics for categorical and continuous variables, respectively. A $P < 0.05$ level was chosen for statistical significance.

Time to death was calculated from the date of baseline assessment to the date of death. We examined all events which occurred during the 7-year follow-up. Crude and adjusted hazard ratios and 95% confidence intervals (CI) for mortality by sarcopenia were calculated using Cox proportional hazards models.

Also, survival curves of study participants were described according to the Kaplan–Meier method to explore the impact of sarcopenia on survival. Curves were adjusted for

![Figure 1. Study profile using the EWGSOP-suggested algorithm for sarcopenia case finding in older individuals.](image-url)
age and gender. Differences between curves were evaluated using the log-rank test.

All analyses were performed using the SPSS 10.0 package (SPSS, Inc., Chicago, IL, USA).

Results

The mean age of study participants was 82.2 (SD 1.4) years, and 131 subjects (66.5%) were women. Using the EWGSOP-suggested algorithm [2], 43 subjects (21.8%) with sarcopenia were identified (Figure 1). No difference between men and women was observed (25.7 versus 19.8%, \( P = 0.22 \), respectively).

The socio-demographic, functional, cognitive and clinical characteristics of study participants according to the presence of sarcopenia are summarised in Table 1. Compared with subjects without sarcopenia, those diagnosed with sarcopenia were more likely to be functionally impaired (ADL scale score: 1.3 versus 0.5, \( P < 0.001 \), respectively) and showed lower body mass index (mean BMI: 24.3 versus 26.7, \( P < 0.001 \), respectively). Overall, the mean number of diseases was higher among sarcopenic subjects compared with subjects without sarcopenia. Among inflammatory markers considered, only the TNF-\( \alpha \) serum level was higher among subjects with sarcopenia than subjects without sarcopenia (mean value 2.4 versus 1.5 pg/ml, \( P = 0.01 \), respectively).

A total of 92 deaths (38 men and 54 women) occurred during the 7-year follow-up. Twenty-nine (67.4%) participants died among subjects with sarcopenia compared with 63 subjects (41.2%) without sarcopenia (\( P < 0.001 \)). Results from unadjusted and adjusted Cox proportional hazard models are shown in Table 2. In the unadjusted model, there was a direct association between mortality and sarcopenia (HR: 2.95, 95% CI: 1.44–6.04). Similarly, this association was consistent both in male (HR: 3.12, 95% CI: 1.14–8.10) and female (HR: 2.77, 95% CI: 1.14–6.73) subjects.

After adjusting for potential confounders including age, gender, education, ADL impairment, BMI, hypertension, congestive heart failure, chronic obstructive pulmonary disease, number of diseases, TNF-\( \alpha \), such association remained statistically significant although somewhat less strong than that derived from the crude analysis (Table 2). In the fully adjusted model, participants with sarcopenia had a higher risk of death for all causes compared with non-sarcopenic subjects (HR: 2.32, 95% CI: 1.01–5.43).

The impact of sarcopenia on 7-year survival was also tested comparing the survival curves of study participants according to the presence of sarcopenia. Survival curves differed significantly at the log-rank test (\( P < 0.001 \)), both in men and women (data not shown).

Discussion

The evaluation of the impact of sarcopenia on survival among frail older subjects is an important and intricate issue. In the present study, we explored the association between sarcopenia and 7-year mortality in a sample of community-dwelling subjects aged 80 years or older. Our findings show that sarcopenia, as identified by the EWGSOP criteria (muscle mass, muscle strength and physical performance), is associated with mortality in older adults living in the community, independently of age and other clinical and functional variables.

Sarcopenia is usually the result of the combined effect of physiological alterations related to ageing and diseases [1, 20]. In fact, well-recognised risk factors for sarcopenia include increasing age, low levels of physical activity,
Sarcopenia and mortality risk in frail older persons

Table 2. Association between sarcopenia and all-cause mortality, after adjustment for various confounders (hazard ratios and 95% confidence intervals)

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted</th>
<th>Model 1 (95% confidence interval)</th>
<th>Model 2 (95% confidence interval)</th>
<th>Model 3 (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sarcopenia</td>
<td>2.95 (1.44–6.04)</td>
<td>2.89 (1.40–5.96)</td>
<td>2.40 (1.07–5.42)</td>
<td>2.32 (1.01–5.43)</td>
</tr>
<tr>
<td>Age</td>
<td>1.15 (0.93–1.42)</td>
<td>1.08 (0.85–1.36)</td>
<td>1.12 (0.87–1.43)</td>
<td></td>
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<tr>
<td>Gender (female)</td>
<td>0.55 (0.29–1.03)</td>
<td>0.49 (0.25–0.99)</td>
<td>0.49 (0.23–1.04)</td>
<td></td>
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<tr>
<td>Education</td>
<td>0.87 (0.72–1.04)</td>
<td>0.87 (0.72–1.05)</td>
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<tr>
<td>ADL impairment</td>
<td>1.91 (1.29–2.83)</td>
<td>1.75 (1.20–2.56)</td>
<td></td>
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<tr>
<td>Body mass index</td>
<td>0.92 (0.86–0.99)</td>
<td>0.93 (0.86–1.01)</td>
<td></td>
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<tr>
<td>Hypertension</td>
<td>0.60 (0.26–1.35)</td>
<td></td>
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<tr>
<td>Congestive heart failure</td>
<td>6.71 (0.70–64.1)</td>
<td>1.46 (0.50–4.21)</td>
<td></td>
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<tr>
<td>COPD</td>
<td>1.29 (0.92–1.80)</td>
<td>1.29 (0.92–1.80)</td>
<td></td>
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<tr>
<td>Number of diseases</td>
<td>0.99 (0.85–1.15)</td>
<td>0.99 (0.85–1.15)</td>
<td></td>
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</tr>
<tr>
<td>TNF-α</td>
<td>5.42 (1.15–23.2)</td>
<td>2.56 (1.05–6.1)</td>
<td>1.04 (0.87–1.26)</td>
<td>1.04 (0.87–1.26)</td>
</tr>
<tr>
<td>Hazard ratio</td>
<td>0.99 (0.93–0.99)</td>
<td>0.99 (0.93–0.99)</td>
<td>0.99 (0.93–0.99)</td>
<td>0.99 (0.93–0.99)</td>
</tr>
</tbody>
</table>

Model 1: adjusted for age, gender.
Model 2: adjusted for age, gender, education, ADL impairment, body mass index.
Model 3: adjusted for age, gender, education, ADL impairment, body mass index, hypertension, congestive heart failure, chronic obstructive pulmonary disease (COPD), number of diseases, TNF-α.

Age, education, ADL impairment, body mass index, number of diseases, TNF-α was treated as a continuous variable.

Inadequate nutrition, and comorbidities, such as congestive heart failure, chronic obstructive pulmonary disease, and type 2 diabetes [1]. Although sarcopenia itself is an adverse health outcome, it is also a risk factor for other adverse events [20]. Indeed, sarcopenia, independent of its causes, may predict negative outcomes, such as falls and/or subsequent difficulty in instrumental and basic ADL [21]. Furthermore, it has been associated with an increased risk of death, hospitalisation, need for long-term care and higher healthcare expenditures [1, 2, 22, 23].

The evidence that sarcopenia has a greater effect on survival than other clinical characteristics is significant for clinical practice among old and frail older persons. The traditional medical model should move from a disease-centred perspective to a functioning-centred view. In this respect, the prevention of sarcopenia is one of the major goals of public health professionals and clinicians. Greater emphasis is needed, therefore, to prevent or postpone as much as possible the onset of sarcopenia among older people, to enhance survival and to reduce the demand for long-term care.

On the basis of European guidelines, the diagnosis of sarcopenia requires impaired physical performance, characterised by slow gait speed, together with either by low muscle strength assessed by handheld dynamometry or low muscle mass measured, for example, by bio-impedance analysis or anthropometric measures [2]. The screening algorithm proposed by the EWGSOP group seems to be really useful to identify the subjects with sarcopenia and/or at risk to develop sarcopenia. Health education programmes, screening high-risk groups, might have an important role in promoting strategies to reduce the risk of worsening health and functional status. In terms of managing sarcopenia, many studies show that physical activity—in particular resistance exercise—and specific nutrition intervention—protein and vitamin D supplementation—can improve muscle mass and strength in older adults [24]. Some methodological issues may have influenced our results. As in all cohort studies, selective survival before entry the cohort has to be taken into account. Furthermore, in this observational study, results may be confounded by unmeasured factors. It is likely that there may be differences between the evaluation groups that may have biased the study results. For example, it can be hypothesised that subjects with sarcopenia received a lower level of medical care. However, our homogeneous population of old people born and living in a well-defined geographical area, minimises the possibility that subjects without sarcopenia had substantially better health care or health knowledge than those with sarcopenia. The data of the iSIRENTE study permitted to adjust measures of effect for many health and disease-related characteristics that are potentially associated with sarcopenia and survival. Second, another limitation of the present study is the lack of any documentation concerning the cause of death. However, we were interested in characterising the impact of sarcopenia itself on all-cause mortality. Third, many experts in sarcopenia believe that anthropometric measures are poor markers of muscle mass and cast doubts on their role in this kind of studies [25, 26]. However, as previously demonstrated by Wannamethee et al. [27], MAMC—as a marker of the muscle mass—provides a simple measure of body composition. Considering the type of study, it was not possible to assess the muscle mass using the DEXA or the bioelectrical impedance analysis. About the muscle strength assessment, the Southampton grip-strength measurement protocol suggests to perform three trials on each side, alternating sides, and to consider the maximal grip score from all six trials [5]. Using the maximal measurement of one trial for each hand may have led to an underestimate of strength. Finally, the iSIRENTE population included persons aged 80 years or older, so our results may not be applicable to other age groups.
In conclusion, sarcopenia is on the agenda for research on ageing and now needs to be recognised in routine clinical practice [28, 29]. Our results expand the knowledge that the presence of sarcopenia is associated with higher mortality. It is of particular importance to verify whether preventive strategies focusing on the early detection and treatment of sarcopenia could get better survival in the older people.

Key points

- Sarcopenia has been indicated as a reliable marker of frailty and poor prognosis among the oldest individuals.
- The European Consensus recommends using the presence of both low muscle function (strength or performance) and low muscle mass for the diagnosis of sarcopenia.
- Our findings show that sarcopenia is associated with mortality in older adults living in the community, independently of age and other clinical and functional variables.

Acknowledgements

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Conflicts of interest

None declared.

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Mortality in older care home residents in England and Wales

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Abstract

Background: mortality in UK care homes is not well described.

Objective: to describe 1-year mortality and predictors in older care home residents compared with community residents.


Results: a total of 2,558 (26.2%) care home and 11,602 (3.3%) community residents died within 1 year. The age and sex standardised mortality ratio for nursing homes was 419 (95% CI: 396–442) and for residential homes was 284 (266–302). Age-related increases in mortality were less marked in care homes than community. Comorbidities and identification as inappropriate for chronic disease management targets predicted mortality in both settings, but associations were weaker in care homes. The number of drug classes prescribed and primary care contact were the strongest clinical predictors of mortality in care homes.

Conclusions: older care home residents experience high mortality. Age and diagnostic characteristics are weaker predictors of risk of death within care homes than the community. Measures of primary care utilisation may be useful proxies for frailty and improve difficult end of life care decisions in care homes.

Keywords: nursing homes, mortality, primary care, older people

Introduction

Care home residents are a vulnerable group and high mortality has been reported in nursing homes in a number of countries [1–5]. Although, there have been large studies in the USA, there are few studies in the UK and no national studies in England and Wales [5]. The largest UK study to date is from Northern Ireland and uses census data that are limited in their measurements of clinical characteristics [6]. This paucity of studies reflects the limited information available on UK care homes residents in routine health data sources.