EISEVIER

Contents lists available at SciVerse ScienceDirect

# Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu



# Original article

# Sarcopenia as a risk factor for falls in elderly individuals: Results from the ilSIRENTE study

Francesco Landi <sup>a,\*</sup>, Rosa Liperoti <sup>a</sup>, Andrea Russo <sup>a</sup>, Silvia Giovannini <sup>a</sup>, Matteo Tosato <sup>a</sup>, Ettore Capoluongo <sup>b</sup>, Roberto Bernabei <sup>a</sup>, Graziano Onder <sup>a</sup>

#### ARTICLE INFO

Article history: Received 21 November 2011 Accepted 17 February 2012

Keywords: Sarcopenia Falls Frail elderly

#### SUMMARY

Background & aims: Sarcopenia has been indicated as a reliable marker of frailty and poor prognosis among the oldest individuals. We evaluated the relationship between sarcopenia and 2-year risk of falls in a population of persons aged 80 years or older.

Methods: Data are from the baseline and follow-up evaluations of the Aging and Longevity Study in the Sirente Geographic Area (ilSIRENTE Study) ( $n\!=\!260$ ). According to the European Working Group on Sarcopenia in Older People (EWGSOP), sarcopenia was diagnosed in presence of low muscle mass (midarm muscle circumference) plus either low muscle strength (hand grip) or low physical performance (4-m walking speed). The primary outcome measure was the incident falls during the follow-up period of 2 years. The relationship between sarcopenia and incident falls was estimated by deriving hazard ratios (HRs) from multiple logistic regression models considering the dependent variable of interest at least one fall during the follow-up period.

Results: Sixty-six participants (25.4%) were identified as affected by sarcopenia. Eighteen out of 66 (27.3%) participants with sarcopenia and 19 out of 194 (9.8%) without sarcopenia reported incident falls during the two-year follow-up of the study (p < 0.001). After adjusting for age, gender, cognitive impairment, ADL impairment, sensory impairments, BMI, depression, physical activity, cholesterol, stroke, diabetes, number of medications, and C-reactive protein, participants with sarcopenia had a higher risk of incident falls compared with non sarcopenic subjects (adjusted hazard ratio [HR], 3.23; 95% confidence interval [CI], 1.25–8.29).

Conclusions: The present study suggests that sarcopenia — assessed using the EWGSOP algorithm — is highly prevalent among elderly persons without gender differences (25%). Sarcopenic participants were over three times more likely to fall during a follow-up period of 2 years relative to non sarcopenic individuals, regardless of age, gender and other confounding factors.

© 2012 Elsevier Ltd and European Society for Clinical Nutrition and Metabolism. All rights reserved.

#### 1. Introduction

Falls and their related injuries represent one major health care issue in the elderly population. Falls are a common event among older adults and are associated with increased morbidity and disability. The prevalence of falls in older community-dwelling elderly individuals is approximately  $30\%^2$  and such estimate increases to 40% among the "oldest-old". Moreover, older individuals have a high susceptibility to fall-related injuries. It has been estimated that, in such population, two-thirds of the death

E-mail address: francesco\_landi@rm.unicatt.it (F. Landi).

from unintentional injuries are related to a fall event.<sup>5</sup> Due to their high frequency and to their serious consequences on health and functional status, falls contribute substantially to the health care expenditure for elderly individuals. According to recent studies, about 6% of all medical expenditures for elderly persons in the United States are due to fall-related injuries.<sup>5</sup> Hospitalization is needed in 5% of elderly people who fall.<sup>5,6</sup>

Falls have many different causes. Several risk factors that predispose elderly individuals to falls have been identified. Risk factors can be classified as either intrinsic or extrinsic. The first category includes factors related to functional and health status (e.g., functional impairment, balance disorders); the second category includes adverse drug reactions, prostheses, use of restraints and environmental factors (e.g., poor lighting or lack of bathroom safety equipment).

<sup>&</sup>lt;sup>a</sup> Department of Gerontology and Geriatrics, Catholic University of Sacred Heart, Roma, Italy

<sup>&</sup>lt;sup>b</sup> Institute of Biochemistry and Clinical Biochemistry, Catholic University of Sacred Heart, Roma, Italy

<sup>\*</sup> Corresponding author. Centro Medicina dell'Invecchiamento (CEMI), Istituto di Medicina Interna e Geriatria, Università Cattolica del Sacro Cuore, Largo Agostino Gemelli 8, 00168 Roma, Italy. Tel.: +39 06 3388546; fax: +39 06 3051911.

Sarcopenia is a condition characterized by loss of muscle mass and strength and decreased physical performance. It may represent an important risk factor for falls. In fact, sarcopenia has been associated with poor endurance, physical inactivity, slow gait speed and decreased mobility. These factors represent common features of the frailty syndrome and may contribute to an increased risk of falling.<sup>8,9</sup>

To date, information on the association between sarcopenia and falls is limited. Also the underlying mechanisms of such association have yet to be clarified. In the present study, we estimated the effect of sarcopenia on increasing the 2-years risk of falls in a population of community-dwelling individuals aged 80 years or older enrolled in the "Invecchiamento e Longevità nel Sirente" (Aging and longevity in the Sirente geographic area, ilSIRENTE Study) study.

## 2. Methods

We used data from the *il*SIRENTE, a prospective cohort study conducted in the mountain community living in the Sirente geographic area (L'Aquila, Italy) and developed by the teaching nursing home Opera Santa Maria della Pace (Fontecchio, L'Aquila, Italy) in a partnership with local administrators and primary care physicians. The Catholic University of Sacred Heart ethical committee ratified the entire study protocol. All the participants signed an informed consent at the baseline visit. The *il*SIRENTE study protocol is described in details elsewhere.<sup>10</sup>

#### 2.1. 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 1st January 1924 and actually living in such area (inclusion criteria). No exclusion criteria were applied. General practitioners presented the ilSIRENTE study protocol to their clients, inviting them to participate to the study. Persons who refused to be enrolled were contacted at least two additional times by the study personnel before being considered as refusals. 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), prevalence of refusals was very low (16%), without significant differences across age or gender groups.

The resulting sample included 364 participants; ninety-nine of them were lost to follow-up (including 90 individuals who died during the follow-up period and 9 individuals who left the study area). The present analysis was conducted on 260 individuals, after excluding 5 additional participants with missing data respect to the main variables of interest (Fig. 1).

### 2.2. Data collection

Participants' baseline assessments began in December 2003 and were completed in September 2004. Assessors were trained on how to perform each component of the *ilSIRENTE* study protocol. 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. The MDS-HC contains over 350 data elements including socio-demographics, physical and cognitive status variables, as well as major clinical diagnoses. Moreover, the MDS-HC includes information on an extensive array of signs, symptoms, syndromes and treatments. 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). Additional information on family history,

lifestyle, physical activity and behavioral factors were collected using specific questionnaires shared with the "Invecchiare in Chianti Study". <sup>13</sup>

## 2.3. Assessment of incident falls

History of fall was assessed by a multidisciplinary team of professionals (general practitioner, nurses, and geriatrician) using the MDS-HC instrument. The assessors were instructed to ask simple and direct questions about whether the patients experienced falls. Participants (or proxy) were asked to report any fall event they had experienced during the follow-up period of 2 years. According to the MDS-HC manual,  $^{14}$  the "fall event" was considered to be a sudden loss of balance causing the contact of any part of the body above the feet with the floor. Independent, dual assessment of falls in a diverse sample of nursing home patients during the testing and revision of the MDS showed that the inter-rater reliability for fall assessment was excellent (weighted kappa correlation coefficient =0.90).  $^{11,15}$ 

## 2.4. Assessment of sarcopenia

For the present study we adopted the European Working Group on Sarcopenia in Older People (EWGSOP) criteria. <sup>16</sup> The EWGSOP recommends using the presence of both low muscle function (strength or performance) and low muscle mass for the diagnosis of sarcopenia. Thus, diagnosis of sarcopenia in the present study sample required the documentation of low muscle mass plus the documentation of either low muscle strength or low physical performance.

## 2.4.1. 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<sup>17</sup>:

MAMC = mid - arm circumference

 $-(3.14 \times triceps skinfold thickness)$ 

Measurement of triceps skinfold thickness (to the nearest 0.2 mm) was made using Harpenden skinfold caliper (range: 0.00–50.00 mm; minimum graduation: 0.20 mm). Mid-arm circumference (to the nearest 0.1 cm) was made using a flexible steel measuring tape, on the right side of the participant's body unless affected by disability or disease. For both these two variables the average of three measurements was computed. In a previous study,<sup>17</sup> the MAMC measure has shown an excellent reliability when performed by expert personnel. In the absence of reliable cut-off points, we considered the MAMC tertile previously calculated.<sup>18</sup> The lower tertile identified the subjects with low muscle mass. As consequence, low muscle mass was classified as MAMC less than 21.1 cm and 19.2 cm in men and women, respectively.<sup>18</sup>

## 2.4.2. Physical performance assessment -4-m walking test

Walking speed was evaluated measuring participants' usual gait speed (in m/sec) over a 4-m course. As suggested in the EWGSOP consensus paper,  $^{16}$  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.  $^{19}$ 

## 2.4.3. 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

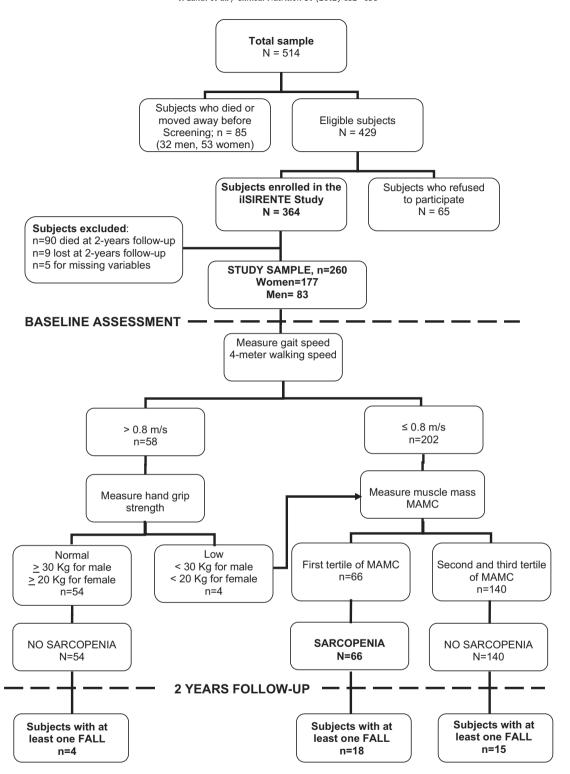


Fig. 1. Study profile using the EWGSOP-suggested algorithm for sarcopenia case finding in older individuals.

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, <sup>16</sup> low muscle strength was classified as hand grip less than 30 kg and 20 kg in men and women, respectively. These cut-points were similar to that obtained among 469 men and 561 women (age range from 20 to 102 years) from the InCHIANTI study population. <sup>19</sup>

## 2.5. Covariates

Basic and Instrumental Activities of Daily Living were assessed by the assessor using the MDS-HC instrument. The ADL scale is based on seven levels of self-performance including dressing, eating, toilet use, bathing, mobility in bed, locomotion, transfer. Cognitive performance was assessed using a six-items, sevencategory scale (Cognitive Performance Scale – CPS). The CPS was

scored on a 7-point ordinal scale in which higher scores were associated with worse cognitive performance.

Medical diagnoses and drugs were directly collected by general practitioners. Medical diagnoses were defined as conditions that have a relationship with patients' functional, cognitive, and behavioral status, medical treatment and risk of death. The diagnoses were listed on the MDS-HC form in a check-box section containing 27 specific diagnostic categories. General practitioner collected information on up to 18 different drugs received by each patient in the 7 days preceding the assessment. Drugs were coded using the Anatomical Therapeutic and Chemical (ATC) codes.

Body weight was measured while wearing light clothes using a calibrated bathroom scale. Body height was measured using a standard stadiometer. Body mass index (BMI) was defined as weight (kilograms) divided by the square of height (meters). As indicated in the MDS-HC manual, <sup>14</sup> hearing impairment was defined as difficulty to hear during normal conversational speech such as when using the telephone, watching television, responding to doorbells, and engaging group activities. Vision impairment was defined as difficulty to see regular print in newspaper and/or books. The alcohol consumption was assessed by asking the participants about the number of glasses of wine drunk during a standard day. Alcohol abuse was defined as consumption of more than half a liter of wine per day.

Physical activity was assessed by asking the participant to provide data on past and current activities involving energy expenditure, including recreational and work-related ones. For the present analyses, we considered as physically active those participants reporting light intensity activities (e.g. walking, dancing, and gardening) performed for at least 2–4 h per week during the last year.

Venus blood samples were drawn in the morning after an overnight fast. The samples were immediately centrifuged and stored at  $-80\,^{\circ}\text{C}$  until final analysis. Standard determinations of serum albumin, cholesterol and C-reactive protein were performed by commercially available kits (Olympus, Italy) suitable on Olympus 2700 instrumentation.

# 2.6. Statistical analysis

Characteristics of the study participants were described according to the presence of sarcopenia at baseline assessment and to the incident falls. Data were analyzed to obtain descriptive statistics. Continuous variables are presented as mean values  $\pm$  standard deviation. We evaluated trends of socio-demographic variables and indicators of disease severity using the Fisher exact test. Differences between continuous variables were assessed by ANOVA comparisons for normally distributed parameters; otherwise, the Kruskal—Wallis test was adopted. A level of p < 0.05 was chosen for statistical significance.

The relationship between sarcopenia and incident falls was estimated by deriving hazard ratios (HRs) from multiple logistic regression models considering the dependent variable of interest at least one fall during the follow-up period of two years. Variables showing significant differences (p < 0.05) between subjects with sarcopenia and without sarcopenia, and between subjects with incident falls and subjects without incident falls were included in the regression models. Final analyses were adjusted for age and gender (Model 1); age, gender, cognitive impairment, ADL impairment, sensory impairments, BMI, depression, physical activity, and cholesterol (Model 2); age, gender, cognitive impairment, ADL impairment, sensory impairments, BMI, depression, physical activity, cholesterol, stroke, diabetes, number of medications, and C-reactive protein (Model 3). Age, cognitive impairment, ADL scale score, BMI, number of medications, cholesterol, and C-reactive

protein were treated as a continuous variable. From these final models, we derived HRs and corresponding 95% confidence intervals (CIs).

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

#### 3. Results

Mean age of study participants was 86.7 (standard deviation 5.4) years, and 177 (68.0%) were women. Using the EWGSOP-suggested algorithm, <sup>14</sup> sixty-six participants (25.4%) were identified as affected by sarcopenia (Fig. 1). No difference between men (21/83) and women (45/177) was observed.

The socio-demographic, functional, cognitive and clinical characteristics of study participants according to the presence of sarcopenia are summarized in Table 1. Compared with participants without sarcopenia, those diagnosed with sarcopenia were more likely to be functionally impaired (mean ADL scale score 1.6 versus 0.6, p < 0.001, respectively), cognitively impaired (mean CPS scale

**Table 1**Characteristics of study population according to the presence of sarcopenia.

Characteristics	Sarcopenia n = 66	No sarcopenia $n=194$	p
Age, years	$86.7 \pm 5.4$	$84.7 \pm 4.3$	< 0.001
Gender Women Men	45 (68) 21 (32)	132 (68) 62 (32)	0.55
Marital status Married Widowed Never married	18 (27) 40 (61) 8 (12)	59 (30) 117 (61) 18 (9)	0.75
Education, years Cognitive performance scale score ADL scale score	$5.4 \pm 2.0$ $0.9 \pm 1.5$ $1.6 \pm 2.5$	$5.1 \pm 1.7$ $0.5 \pm 1.1$ $0.6 \pm 1.6$	0.15 0.01 <0.001
Sensory impairment Hearing Vision	19 (29) 22 (23)	28 (14) 34 (17)	<0.01 <0.01
Body mass index, kg/m <sup>2</sup> Alcohol abuse Smoking habit Physical activity	23.8 ± 4.2 6 (9) 1 (2) 32 (49)	$26.9 \pm 4.3$ 25 (13) 6 (3) 141 (73)	<0.001 0.28 0.16 <0.001
Diseases Ischemic heart disease Congestive heart failure Hypertension Stroke Diabetes Chronic obstructive pulmonary disease Parkinson's disease Cancer Osteoarthritis	8 (12) 3 (5) 44 (67) 2 (3) 20 (30) 9 (14) 3 (5) 1 (2) 17 (26)	21 (11) 4 (2) 148 (76) 2 (1) 45 (23) 21 (11) 2 (1) 7 (3) 39 (20)	0.48 0.25 0.08 0.26 0.16 0.33 0.10 0.35 0.21
Depression Number of diseases Number of medications	$20 (30)$ $2.1 \pm 1.0$ $3.1 \pm 1.8$	$42 (22)$ $2.0 \pm 1.2$ $3.0 \pm 2.0$	0.01 0.37 0.59
Hematological parameters Albumin, g/dl Cholesterol, mg/dl Reactive C protein, mg/dl	$4.1 \pm 0.3$ $190.7 \pm 50.1$ $3.8 \pm 3.2$	$4.2 \pm 0.2$ $208.6 \pm 42.1$ $3.3 \pm 2.9$	0.08 <0.01 0.59

<sup>&</sup>lt;sup>a</sup> Data are given as number (percent) for the following variables: gender, living alone, marital status, sensory impairment, alcohol abuse, smoking habit, physical activity, diseases; for all the other variables means ± SD are reported. Cognitive Performance Scale score: range 0–6, a higher number indicates higher impairment. ADL (Activity of Daily Living) and IADL (Instrumental Activity of Daily Living) scores: range 0–7, a higher number indicates higher impairment.

score 0.9 versus 0.5, p=0.01, respectively), and showed lower body mass index (mean BMI 23.8 versus 26.9, p<0.001, respectively). Relative to non sarcopenic individuals those with such condition resulted more likely to have vision impairment (23% versus 17%, p<0.01) and hearing impairment (29% versus 14%, p<0.01). Overall, the mean number of diseases was similar in sarcopenic and non sarcopenic subjects. Among the considered medical conditions, depression was more prevalent among sarcopenic than non sarcopenic participants (30% versus 22%, p<0.01). As it may be expected, physical activity was much more prevalent among non sarcopenic individuals relative to those with sarcopenia (73% versus 49%, p<0.001).

We also evaluated the baseline characteristics of the sample according to the incident falls to identify all the potential risk factors for falls (Table 2). We identified a significantly higher prevalence of stroke (11% versus 0%; p < 0.001), of diabetes (40% versus 22%; p = 0.01), and of hearing impairment (30% versus 16%; p = 0.04) in the group who fell during the follow-up period compared to the control group. Participants who fell were more likely to be functionally and cognitively impaired, too.

**Table 2**Characteristics of study population according to incident falls (2-years follow-up).<sup>a</sup>

Characteristics	Falls $n = 37$	No falls n = 223	р
Age, years	$86.5 \pm 4.6$	$84.9 \pm 4.6$	0.06
Gender Women Men	31 (84) 6 (16)	146 (65) 77 (35)	0.01
Marital status Married Widowed Never married	6 (16) 26 (71) 5 (13)	71 (32) 131 (59) 21 (9)	0.14
Education, years Cognitive performance scale score	$5.0 \pm 1.5 \\ 1.1 \pm 1.6$	$5.2 \pm 1.8 \\ 0.5 \pm 1.1$	0.82 0.01
ADL scale score	$\boldsymbol{1.7 \pm 2.6}$	$\textbf{0.7} \pm \textbf{1.8}$	< 0.001
Sensory impairment Hearing Vision	11 (30) 8 (21)	36 (16) 48 (21)	0.04 0.56
Body mass index, kg/m <sup>2</sup> Alcohol abuse Smoking habit Physical activity	$25.1 \pm 4.2$ 5 (13) 1 (3)	26.3 ± 4.5 26 (12) 6 (3)	0.16 0.46 0.39
Diseases Ischemic heart disease Congestive heart failure Hypertension Stroke Diabetes Chronic obstructive pulmonary disease	4 (11) 3 (8) 27 (73) 4 (11) 15 (40) 4 (11)	25 (11) 4 (2) 165 (74) 0 (0) 50 (22) 26 (12)	0.60 0.07 0.51 <0.001 0.01 0.57
Parkinson's disease Cancer Osteoarthritis Depression	1 (3) 1 (3) 9 (24) 11 (29)	4 (2) 7 (3) 47 (21) 51 (23)	0.53 0.68 0.39 0.23
Number of diseases Number of medications	$\begin{array}{c} 2.4 \pm 1.3 \\ 3.7 \pm 2.0 \end{array}$	$\begin{array}{c} 1.9 \pm 1.2 \\ 2.9 \pm 1.9 \end{array}$	0.06 0.02
Hematological parameters Albumin, g/dl Cholesterol, mg/dl Reactive C protein, mg/dl	$4.2 \pm 0.2 \\ 199.7 \pm 49.5 \\ 4.5 \pm 3.7$	$4.2 \pm 0.2 \\ 204.9 \pm 44.1 \\ 3.3 \pm 2.8$	0.48 0.52 0.02

<sup>&</sup>lt;sup>a</sup> Data are given as number (percent) for the following variables: gender, living alone, marital status, sensory impairment, alcohol abuse, smoking habit, physical activity, diseases; for all the other variables means ± SD are reported. Cognitive Performance Scale score: range 0–6, a higher number indicates higher impairment. ADL (Activity of Daily Living) and IADL (Instrumental Activity of Daily Living) scores: range 0–7, a higher number indicates higher impairment.

Thirty-seven subjects (6 men and 31 women) fell during the two-year follow-up of the study. As shown in Fig. 1, 18 out of 66 (27.3%) participants with sarcopenia and 19 out of 194 (9.8%) without sarcopenia reported incident falls (p < 0.001). Relative to participants without sarcopenia, those subjects with sarcopenia showed a significantly higher risk of incident falls during the follow-up period (hazard ratio [HR]: 3.45; 95% confidence interval [CI]: 1.68–7.09) (Table 3). Estimates derived from the fully adjusted model also indicated that after adjusting for age, gender, cognitive impairment, ADL impairment, sensory impairments, BMI, depression, physical activity, cholesterol, stroke, diabetes, number of medications and C-reactive protein, sarcopenic participants were over three times more likely to fall relative to non sarcopenic individuals and such measure of effect resulted statistically significant (HR 3.23, 95% CI: 1.25–8.29) (Table 3).

#### 4. Discussion

In the present study, we estimated the effect of sarcopenia on the risk of falling during a period of 2 years in a population of elderly persons aged 80 years and older living in community. According to our findings, sarcopenia — assessed using the EWG-SOP algorithm<sup>16</sup> — is highly prevalent among elderly persons. Also, the frequency of such condition does not change across gender. Individuals with sarcopenia are at increased risk of falling regardless of age, gender and other confounding factors.

Despite a recent scientific interest in such condition, information on sarcopenia among old-old subjects and its possible relation to falls is limited. Several observational studies have reported that reduced muscle strength, especially of the lower limbs, is one of the most important risk factors for falls. <sup>21–23</sup> Diminished muscle strength and low physical performance may enforce the impairment of postural reflexes and increase the risk of falls. On the contrary, the risk gets lower as the level of physical activity increases. This may be explained by the beneficial effect of physical activity on improving balance, co-ordination, muscle strength and reaction time. <sup>24–26</sup>

Moreland and colleagues<sup>27</sup> in a systematic review and metaanalysis indicated that lower extremity weakness is a clinically important and statistically significant risk factor for falls, even thought this association is stronger in institutionalized than in community-dwelling adults. Overall, the evidence that sarcopenia is a risk factor for falls derives from studies conducted on small samples of institutionalized elderly subjects, which adopted different measurement techniques (i.e. increased chair stand time, reduced knee extension strength) and that considered only the muscle strength.<sup>27</sup> At present, there are few data from large multicenter and/or multinational studies on the prevalence of sarcopenia among old-old subjects living in community. Furthermore, no research paper that relies on the accepted sarcopenia criteria has been published to address its role in determining the higher risk of falls. 16 The present study is the first attempt to estimate the correlation of sarcopenia with incident falls in the old-old individuals using the suggested EWGSOP-screening algorithm.<sup>16</sup>

Falls are the most important cause of morbidity and mortality for persons aged 75 and older.<sup>28,29</sup> When elders fall, they sustain such injuries as hip, spine, hand, and/or pelvic fractures. Even in case of no injury, falls cause a loss of confidence that results in reduced physical activity, increased dependency, and social withdrawal. Many authors have documented that a fall is a multifactorial syndrome involving the patient and the environment.<sup>5,10</sup> An accidental fall may be the consequence of an already existing impairment in physical function and, in a vicious cycle, responsible for further decline. This vicious cycle is generated and fed by several different mechanisms which may involve fall-related injuries and

**Table 3** Effect of sarcopenia on the risk of incident falls (hazard ratios and 95% confidence intervals).

	Unadjusted	Model 1	Model 2	Model 3		
	Hazard ratio (95% confidence interval)					
Sarcopenia	3.45 (1.68-7.09)	3.25 (1.54-6.88)	2.55 (1.06-6.14)	3.23 (1.25-8.29)		
Age		1.02 (0.93-1.13)	1.01 (0.92-1.10)	1.04 (0.94-1.14)		
Gender (female)		2.19 (0.98-6.53)	2.79 (1.00-7.76)	3.94 (1.97-9.99)		
Cognitive impairment (CPS)			1.22 (0.90-1.66)	1.21 (0.86-1.71)		
ADL impairment			1.01 (0.78-1.31)	0.94 (0.78-1.27)		
Hearing impairment			1.94 (0.71-5.30)	1.91 (0.63-5.74)		
Vision impairment			0.73 (0.27-1.97)	0.86 (0.31-2.42)		
Body mass index (BMI)			0.99 (0.91-1.08)	0.98 (0.89-1.09)		
Depression			1.24 (0.50-3.08)	1.10 (0.42-2.91)		
Physical activity			0.86 (0.30-2.39)	1.18 (0.39-3.54)		
Cholesterol			0.99 (0.98-1.00)	1.00 (0.98-1.01)		
Stroke				2.35 (1.92-3.10)		
Diabetes				1.35 (0.53-3.43)		
Number of medications				1.14 (0.92-1.42)		
Reactive C protein				1.11 (0.98-1.26)		

Model 1: adjusted for age, gender.

Model 2: adjusted for age, gender, cognitive impairment, ADL impairment, sensory impairments, Body mass index, depression, physical activity, and cholesterol.

**Model 3**: adjusted for age, gender, cognitive impairment, ADL impairment, sensory impairments, Body mass index, depression, physical activity, cholesterol, stroke, diabetes, number of medications, and reactive C protein.

Age, ADL scale score, CPS scale score, BMI, cholesterol, number of medications, and reactive C protein were treated as a continuous variable.

fear of falling. The progressive age-related changes affecting skeletal muscle mass, composition, structure, and physiology can play an important role in the activation and maintenance of such vicious cycle. In fact, the age-related muscle changes can be manifest in daily activities as slower gait speed, less endurance and difficulty performing simple tasks such as rising from a chair, stepping up a stair, or recovering posture to avert a fall.

A possible link between sarcopenia and falls is represented by the loss of muscle mass, strength and physical performance. In this respect, the relationship between sarcopenia and falls has important implications regarding the multi-factorial interventions to reduce the risk of falling. Many studies have hypothesized that specific programs of physical activity represent the most important approach to slow down the decline of muscle mass and muscle strength associated with aging and to treat sarcopenia. At the same time, adequate nutrition, with respect to amounts of energy, protein and micronutrients, such as vitamin D, has to be considered as an essential requisite for any successful therapeutic approach, in terms of prevention and treatment of sarcopenia. 33–35

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. However, our homogeneous population of old people born and living in a welldefined geographical area, minimizes the possibility that subjects without sarcopenia had substantially better health care or health knowledge that those with sarcopenia. Second, we cannot completely exclude that a reverse causation may play an important role in the relationship between sarcopenia and incident falls observed in our sample. However, because of the use of an extensive multidimensional assessment instrument, the present study could comprehensively investigate the different domains of elderly status influencing sarcopenia and incident falls. This made it possible to control for a large number of potential confounders. Despite this effort, it is possible that significant, not considered, differences between study groups may have biased the results and conclusions. Furthermore, 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. It is important to highlight that DXA is the preferred method for research and clinical use to distinguish fat, bone mineral and lean tissues. The bioelectrical impedance analysis (BIA) may be considered as a portable alternative to DXA,

especially for the nursing home residents. $^{36,37}$  However, some studies previously demonstrated that MAMC — as a marker of muscle mass — provides a simple measure of body composition in elderly subjects. $^{17,18}$  Finally, as the study sample was drawn from the ilSIRENTE population and it was composed of persons aged 80 years or older, our results may not be generalized to other age groups.

In conclusion, studies performed in specific and well-defined geographic regions - such as the Sirente Mountain Community can be particularly useful in interpreting and disentangling all the complex interactions involved in the development of disability status and longevity. 10 The potential relevance of these findings to clinical practice needs to be considered. At the population level. sarcopenia appears to be a risk factor for falls. The measurement of muscle mass, muscle strength and physical performance - as suggested by EWGSOP-screening algorithm – may contribute to risk stratification process for primary prevention of falls. A greater understanding of the mechanisms underlying the association between sarcopenia and risk of falls may also facilitate the development of beneficial interventions across the life course to preserve muscle function and prevent falls. In this respect, the most important treatment options include physical activity programs and nutritional interventions. 16 Further research is needed to establish the role of sarcopenia on determining clinical outcomes among oldold subjects and to provide evidence for specific interventions aimed at preventing and treating sarcopenia and its consequences.

# Statement of authorship

All authors have made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

# **Conflict of interest**

None.

# Acknowledgments

The "Invecchiamento e Longevità nel Sirente" (ilSIRENTE) study was supported by the "Comunità Montana Sirentina" (Secinaro,

L'Aquila, Italy). We thank all the participants for their enthusiasm in participating to the project and their patience during the assessments. We are grateful to all the persons working as volunteers in the "Protezione Civile" and in the Italian Red Cross of Abruzzo Region for their support. We sincerely thank the "Comunità Montana Sirentina", and in particular its President who promoted and strongly supported the development of the project.

The ilSIRENTE Study Group is composed as follows:

Steering Committee: R. Bernabei, F. Landi.

Co-ordination: A. Russo, M. Valeri, G. Venta.

Writing Panel: C. Barillaro, M. Cesari, P. Danese, L. Ferrucci, G. Onder, M. Pahor, V. Zamboni, E. Capoluongo.

Participants: Comune di Fontecchio: P. Melonio, G. Bernabei, A. Benedetti; Comune di Fagnano: N. Scarsella, A. Fattore, M. Fattore; Comune di Tione: M. Gizzi; Comune di Ovindoli: S. Angelosante, E. Chiuchiarelli; Comune di Rocca di Mezzo: S. Pescatore; Comune di Rocca di Cambio: G. Scoccia; Comune di Secinaro: G. Pizzocchia; Comune di Molina Aterno: P. Di Fiore; Comune di Castelvecchio: A. Leone; Comune di Gagliano Aterno: A. Petriglia; Comune di Acciano: A. Di Benedetto; Comune di Goriano Sicoli: N. Colella; Comune di Castel di Ieri: S. Battista; RSA Opera Santa Maria della Pace: A. De Santis, G. Filieri, C. Gobbi, G. Gorga, F. Cocco, P. Graziani.

### References

- 1. Thomas DR. Loss of skeletal muscle mass in aging: examining the relationship of starvation, sarcopenia and cachexia. Clin Nutr 2007;26:389–99.
- 2. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. *N Engl J Med* 1988;**319**:1701–7.
- Rossat A, Fantino B, Nitenberg C, Annweiler C, Poujol L, Herrmann FR, et al. Risk factors for falling in community-dwelling older adults: which of them are associated with the recurrence of falls? J Nutr Health Aging 2010;14:787–91.
- Verhage TL, Heijdra Y, Molema J, Vercoulen J, Dekhuijzen R. Associations of muscle depletion with health status. Another gender difference in COPD? Clin Nutr 2011;30:332–8.
- Guideline for the prevention of falls in older persons. American Geriatrics Society, British Geriatrics Society, and American Academy of Orthopedics Surgeons Panel on Falls Prevention. J Am Geriatr Soc 2001;49:664

  –72.
- Carroll NV, Slattum PW, Cox FM. The cost of falls among the communitydwelling elderly. J Manag Care Pharm 2005;11:307—16.
- Cesari M, Landi F, Torre S, Onder G, Lattanzio F, Bernabei R. Prevalence and risk factors for falls in an older community-dwelling population. J Gerontol A Biol Sci Med Sci 2002;57:M722-6.
- 8. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;**56**:M146–56.
- Cruz-Jentoft AJ, Landi F, Topinková E, Michel JP. Understanding sarcopenia as a geriatric syndrome. Curr Opin Clin Nutr Metab Care 2010;13:1–7.
- Landi F, Russo A, Cesari M, Barillaro C, Onder G, Zamboni V, et al. The ilSIRENTE study: a prospective cohort study on persons aged 80 years and older living in a mountain community of Central Italy. Aging Clin Exp Res 2005; 17:486–93.
- Morris JN, Fries BE, Steel K, Ikegami N, Bernabei R, Carpenter GI, et al. Comprehensive clinical assessment in community setting: applicability of the MDS-HC. J Am Geriatr Soc 1997;45:1017–24.
- 12. Landi F, Tua E, Onder G, Carrara B, Sgadari A, Rinaldi C, et al. Minimum data set for home care: a valid instrument to assess frail older people living in the community. *Med Care* 2000;**38**:1184–90.
- 13. Ferrucci L, Bandinelli S, Benvenuti E, Di Iorio A, Macchi C, Harris TB. Subsystems contributing to the decline in ability to walk: bridging the gap between epidemiology and geriatric practice in the InCHIANTI study. *J Am Geriatr Soc* 2000;48:1618–25.
- 14. Morris JN, Fries BE, Bernabei R, Ikegami N, Gilgen R, Steel K. RAI home care assessment manual. Washington, DC: InterRAI Coporation; 1996.

- 15. Bernabei R, Landi F, Onder G, Liperoti R, Gambassi G. Second and third generation assessment instruments: the birth of standardization in geriatric care. *J Gerontol A Biol Sci Med Sci* 2008;**63**:308–13.
- Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al, European Working Group on Sarcopenia in Older People. Sarcopenia: European consensus on definition and diagnosis: report of the European Working Group on Sarcopenia in Older People. Age Ageing 2010;39:412—23.
- 17. Antonelli Incalzi R, Landi F, Cipriani L, Bruno E, Pagano F, Gemma A, et al. Nutritional assessment: a primary component of multidimensional geriatric assessment in the acute care setting. J Am Geriatr Soc 1996;44:166–74.
- Landi F, Russo A, Liperoti R, Pahor M, Tosato M, Capoluongo E, et al. Midarm muscle circumference, physical performance and mortality: results from the aging and longevity study in the Sirente geographic area (ilSIRENTE study). Clin Nutr 2010;29:441–7.
- Lauretani F, Russo CR, Bandinelli S, Bartali B, Cavazzini C, Di Iorio A, et al. Ageassociated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. J Appl Physiol 2003;95:1851–60.
- Morris JN, Fries BE, Meher DR. MDS cognitive performance scale. J Gerontol 1994:49:M174–82.
- Blain H, Carriere I, Sourial N, Berard C, Favier F, Colvez A, et al. Balance and walking speed predict subsequent 8-year mortality independently of current and intermediate events in well-functioning women aged 75 years and older. I Nutr Health Aging 2010;14:595—600.
- 22. Muscaritoli M, Anker SD, Argilés J, Aversa Z, Bauer JM, Biolo G, et al. Consensus definition of sarcopenia, cachexia and pre-cachexia: joint document elaborated by special interest groups (SIG) "cachexia—anorexia in chronic wasting diseases" and "nutrition in geriatrics". *Clin Nutr* 2010; **29**:154—9.
- Visser M, Schaap LA. Consequences of sarcopenia. Clin Geriatr Med 2011;27:387–99.
- Hoekstra JC, Goosen JH, de Wolf GS, Verheyen CC. Effectiveness of multidisciplinary nutritional care on nutritional intake, nutritional status and quality of life in patients with hip fractures: a controlled prospective cohort study. Clin Nutr 2011;30:455–61.
- 25. Breedveld-Peters JJ, Reijven PL, Wyers CE, van Helden S, Arts JJ, Meesters B, et al. Integrated nutritional intervention in the elderly after hip fracture. A process evaluation. *Clin Nutr* 2011 Oct 27, in press.
- Mangani I, Cesari M, Russo A, Onder G, Maraldi C, Zamboni V, et al. Physical function, physical activity and recent falls. Results from the "Invecchiamento e Longevità nel Sirente (ilSIRENTE)" study. Aging Clin Exp Res 2008;20:234–41.
- 27. Moreland JD, Richardson JA, Goldsmith CH, Clase CM. Muscle weakness and falls in older adults: a systematic review and meta-analysis. *J Am Geriatr Soc* 2004;**52**:1121–9.
- 28. Landi F, Onder G, Cesari M, Barillaro C, Russo A, Bernabei R. Psychotropic medications and risk for falls among community-dwelling frail older people: an observational study. *J Gerontol A Biol Sci Med Sci* 2005;**60**:622–6.
- 29. Raguso CA, Kyle U, Kossovsky MP, Roynette C, Paoloni-Giacobino A, Hans D, et al. 3-Year longitudinal study on body composition changes in the elderly: role of physical exercise. *Clin Nutr* 2006;**25**:573–80.
- 30. Canavan PK, Cahalin LP, Lowe S, Fitzpatrick D, Harris M, Plummer-D'Amato P. Managing gait disorders in older persons residing in nursing homes: a review of literature. *J Am Med Dir Assoc* 2009;**10**:230–7.
- 31. Hui EK, Rubenstein LZ. Promoting physical activity and exercise in older adults. J Am Med Dir Assoc 2006;7:310–4.
- 32. Landi F, Russo A, Cesari M, Pahor M, Liperoti R, Danese P, et al. Walking one hour or more per day prevented mortality among older persons: results from ilSIRENTE study. *Prev Med* 2008;**47**:422–6.
- 33. Morley JE, Argiles JM, Evans WJ, Bhasin S, Cella D, Deutz NE, et al. Nutritional recommendations for the management of sarcopenia. *J Am Med Dir Assoc* 2010;**11**:391–6.
- 34. Onder G, Capoluongo E, Danese P, Settanni S, Russo A, Concolino P, et al. Vitamin D receptor polymorphisms and falls among older adults living in the community: results from the ilSIRENTE study. *J Bone Miner Res* 2008;**23**:1031–6.
- Landi F, Russo A, Liperoti R, Tosato M, Barillaro C, Pahor M, et al. Anorexia, physical function, and incident disability among the frail elderly population: results from the ilSIRENTE study. J Am Med Dir Assoc 2010;11:268–74.
- 36. Meeuwsen S, Horgan GW, Elia M. The relationship between BMI and percent body fat, measured by bioelectrical impedance, in a large adult sample is curvilinear and influenced by age and sex. *Clin Nutr* 2010;**29**:560–6.
- Landi F, Liperoti R, Fusco D, Mastropaolo S, Quattrociocchi D, Proia A, et al. Prevalence and risk factors of sarcopenia among nursing home older residents. J Gerontol A Biol Sci Med Sci 2012;67(1):48–55.