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Original Article

Validation of SARC-F-Proxy for the Screening of Sarcopenia in Older Patients with Cognitive Impairment

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Abstract

Objectives: The SARC-F is a validated questionnaire for the screening of sarcopenia in an older population. However, the clinical relevance of this self-reported questionnaire in patients with cognitive problems is questionable. This study aims to validate the SARC-F-Proxy as an alternative screening tool for sarcopenia in patients with cognitive impairment. **Methods**: This cross-sectional study included hospitalised community-dwelling older adults aged 60 years or older with confirmed cognitive impairment. Three SARC-F questionnaires were completed: one by patients, one by informal caregivers and one by formal caregivers. Muscle strength, mass and physical performance were measured by handgrip strength, anthropometric measurements, and gait speed respectively. The recently updated EWGSOP2 diagnostic criteria were used as the "gold standard" for diagnosis of sarcopenia. **Results**: The prevalence of sarcopenia using SARC-F-Proxy was 75.4% for SARC-F-Proxy-Formal caregiver and 66% for SARC-F-Proxy-Informal caregiver. SARC-F-Proxy had high sensitivity (85.9% for SARC-F-Proxy-Formal caregiver and 77% for SARC-F-proxy-informal caregiver) and low specificity (46.5% for SARC-F-Proxy-Formal caregiver and 54.7% for SARC-F-Proxy-Informal caregiver). **Conclusions**: the proxy-reported SARC-F questionnaire can be applied as a surrogate for the SARC-F in the screening of sarcopenia in hospitalised community-dwelling older people with known or suspected cognitive impairment. Second, the results in this study suggest a higher reliability when the proxy-reported questionnaire is performed by the formal caregiver.

Keywords: Cognition, Dementia, Geriatric population, SARC-F, Sarcopenia

Introduction

More than three decades ago, the concept of sarcopenia emerged, describing an age-related decline in muscle mass[1]. Since then, the term sarcopenia has undergone several changes, the definition finally being extended with muscle strength and function[2]. The prevalence of sarcopenia varies from 9.9 to 40.4%, depending on the definition that is used[3]. Currently, it is defined by the European Working Group on Sarcopenia in Older People (EWGSOP) as a generalized and progressive skeletal muscle disorder that is associated with negative health outcomes i.e., falls, fractures, physical disability, leading to a higher chance of mortality[4]. Taking into account the current global aging of population, the number of individuals with sarcopenia will significantly increase. By 2045, there will be an increase of 63.8-72.4% in prevalence making it a fundamental healthcare issue[5].

Another age-related major health problem is dementia, with a global prevalence of 46.8 million people in 2015, and

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an expected increase of 131.5 million people by 2050[6]. Weight loss due to malnutrition is a prominent clinical feature of dementia, which may present itself before the onset of apparent cognitive decline[7]. Weight loss and malnutrition are also major contributing factors for the development of sarcopenia[4]. This way, sarcopenia and dementia are interrelated. A causal relation was suggested by several studies in which low cognitive function was associated with accelerated loss of muscle strength and mass[8,9], whereas other studies found that a weak handgrip strength or slower walking speed at baseline were associated with more rapid cognitive decline[10,11]. The prevalence of sarcopenia in cognitive impaired patients is estimated between 54.4 and 70.1%[12].

Due to its low-to-moderate sensitivity and high specificity, the strength, assistance walking, rise from a chair, climb stairs, and falls (SARC-F) questionnaire has been used in clinical practice as an excellent test to exclude muscle function impairment. Therefore, it could be used as a rapid and inexpensive screening tool for sarcopenia that obviates the need for measuring muscle parameters[13,14]. However, the SARC-F questionnaire was not designed to be used in individuals with cognitive impairment since there is often an overestimation of one's own abilities[15]. It is hypothesized that the perception of the (in)formal caregivers on the patient's ability will be more correct, as they have a subjective, first-hand view on their daily activities. In this case, proxy-reported information of the SARC-F could be used as a more objective screening tool for sarcopenia in patients with cognitive decline. Maurus et al. already evaluated the use of a proxy-reported SARC-F questionnaire as a valid instrument for both ad-hoc as well as retrospective screening for sarcopenia-related functional impairment in patients who were assumed not be capable of adequate self-reporting[16]. However, no clear distinction was made in the patient's designated proxies who performed the SARC-F questionnaire.

The aim of this study is to investigate the validation of the proxy-reported SARC-F questionnaire as a surrogate for the SARC-F in the screening of sarcopenia in hospitalised community-dwelling patients with confirmed cognitive impairment.

Materials and Methods

Design, setting and study population

This cross-sectional study included hospitalised community-dwelling older adults aged 60 years or older with confirmed cognitive impairment (mild cognitive impairment or dementia) at the Joostens Psycho-Geriatric Hospital in Antwerp, Belgium. Patients were excluded when they were unable to undergo muscle evaluation due to physical and/or cognitive impairment, when the diagnosis of dementia was uncertain due to underlying comorbidities and/or incomplete cognitive evaluation, and in the situation of entering palliative care setting or dying.

Data collection and measurements

The data in the study were collected from the electronic medical records by two researchers. Demographics, pre-existing type/stage of dementia, Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) scores were collected. The ADL scores were divided into quartiles: normal (score of 6), mildly decreased (7-12), moderately decreased (13-18) and severely decreased (19-24)[17]. IADL score ranges from 0 (low function, dependent) to 8 (high function, independent) for women, and 0 to 5 for men[18].

Cognitive function in patients with suspected cognitive impairment was assessed using the Dutch version of Mini-Mental State Examination (MMSE), brain radiography and clinical presentation[19]. Patients underwent more comprehensive neuropsychological evaluation using the Dutch COTESS test (COgnitieve TEStbatterij voor Senioren)[20] when cognitive impairment was clinical still questionable after an acceptable MMSE evaluation. Diagnosis of dementia and subtyping was done using the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) criteria for major neurocognitive disorder by the same researcher with experience in this field. The stages of dementia were set by MMSE scores as mild (21-24), moderate (15-20), and severe (≤14).

Included patients underwent muscle assessment (hand grip strength, calf and mid-arm muscle circumference, gait speed) and were evaluated by the SARC-F questionnaire. More specifically, three SARC-F questionnaires were completed. One was completed by the patient (SARC-F-Patient), another by the patient's family (SARC-F-Proxy-Informal caregiver) and the last one by the attending nurses who took care of the patient for at least one consecutive week (SARC-F-Proxy-Formal caregiver). The proxy-reported version of the original SARC-F questionnaire was developed substituting 'you' with the respective patient's name within the questionnaire. A score≥4 points indicated possible sarcopenia. Patients were included if one of the proxies had filled in the SARC-F questionnaire. Patients who were not capable of performing the hand grip strength test or those within a palliative setting were excluded.

Anthropometric measurements were performed according to the reference manual for anthropometric standardization[21]. For measurements of body weight and height, individuals were wearing light clothing and were barefoot. Body mass index (BMI) was calculated by dividing the total body weight (kg) by height squared (m^2). The mid-arm circumference (MAC) was measured by a tape measure at the midpoint between the acromion process of the scapula and the olecranon process of the ulna in the right upper arm (cm) with the subject sitting and the elbow bent at 90° angle. Triceps skin fold thickness (TSF) was taken with a Harpenden skinfold calliper (Brit. Indicators Ltd, UK) to the nearest 0.1 mm. The site of measurement was located dorsally at the midpoint of the right upper arm. The average

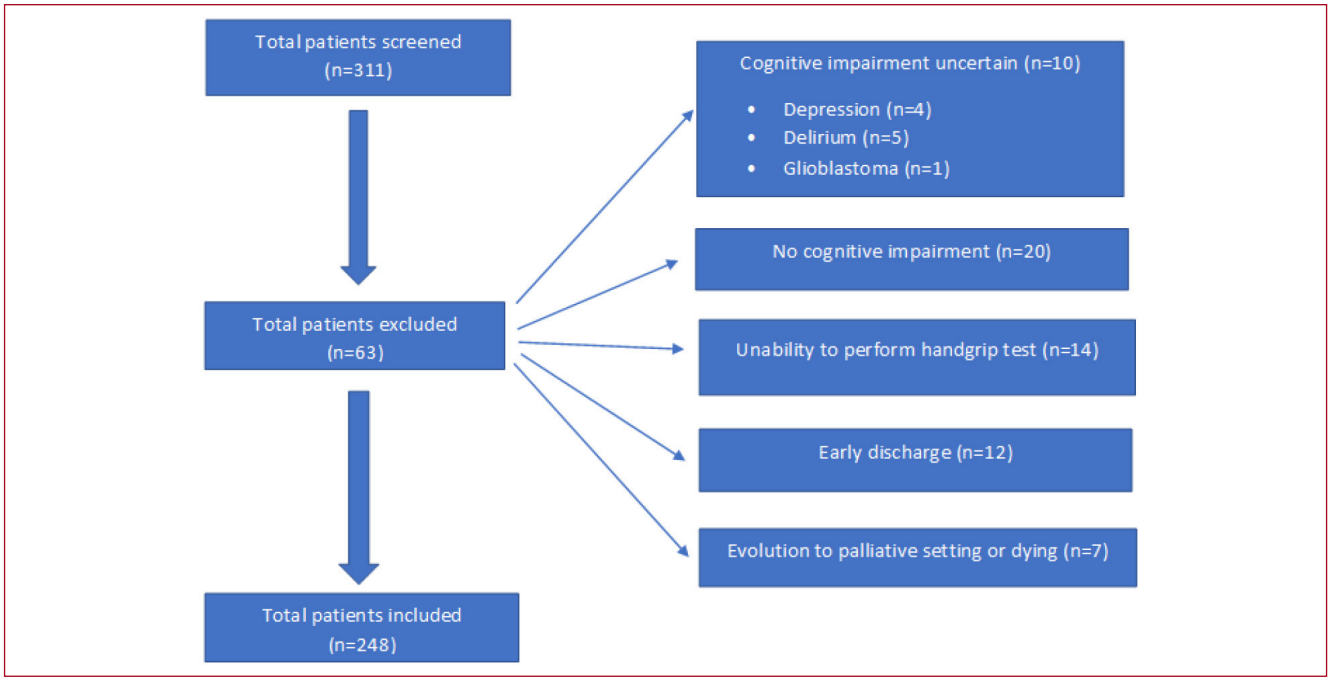

Figure 1. Overview patient inclusion.

value of three consecutive measurements was recorded. Calf circumference was measured by a tape measure at the point of calf's greatest girth while the subject standing upright or sitting with feet apart shoulder width and body weight evenly distributed between both legs[22].

Hand grip strength (HGS) was used to estimate muscle strength. Hand grip strength was measured with a mechanical JAMAR hand-held dynamometer (Lafayette, USA) adjustable to the width of the hand[23]. Patients were asked to stand with arms out stretched parallel to the trunk, take the dynamometer and apply maximum strength with each hand without support. In case the patient was not able to stand up, the task was performed in sitting or in supine position. The measurement was repeated three times in the dominant hand with separation of 1 minute to avoid fatigue. The maximum value was recorded in kg. Cut-off points of <27 kg for men and <16 kg for women were used to define low muscle strength[4].

Muscle mass (or muscle quantity) was estimated using calculations based on measurements of mid-arm muscle and calf circumferences. The mid-arm muscle circumference (MAMC) was calculated using the following equation[24]: MAMC (cm) = MAC (cm) − (π x 0.1 x TSF (mm)). Using reference data from Landi et al, the lowest tertiles for men (<21.1 cm) and for women (<19.2 cm) were used as cut-off points to indicate low muscle mass[25]. Calf circumference <31 cm was used as indicator of reduced muscle mass.

Four meters usual gait speed was measured as an estimation of physical performance. Patients were informed to walk a distance of 4 meters (patients were allowed to perform the task with assistance like parallel bars or walker). The best time of two attempts was recorded. The cut-off point used to evaluate low gait speed was ≤0.8m/s[4].

In this study, the recently updated EWGSOP2 diagnostic criteria were used as the "gold standard" for diagnosis of sarcopenia[4], although it needs to be emphasized that quantitative muscle evaluation was done by MAMC and CC due to absence of other conventional diagnostic tools like bioelectrical impedance analysis (BIA) or Dual X-ray absorptiometry (DXA)[26]. Patients with reduced muscle strength were considered to have probable sarcopenia. Those with reduced muscle strength and muscle mass were considered having confirmed sarcopenia and those with reduced muscle strength, mass and gait speed were considered to have severe sarcopenia.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics (Version 23.0, Armonk, New York). Descriptive statistics were used to describe the demographic data and baseline characteristics. Independent samples t-tests were used for normally distributed continuous data and chi-squared tests for categorical variables. In order to make the analyses the results of the SARC-F were dichotomized according to the cut-off score ≥4 points, which indicates

possible presence of sarcopenia. Results are presented as either mean ± standard deviation (SD) or as frequencies and percentages. In case of non-parametric data, the median with the interquartile range (IQR) are described. Correlations were calculated using the Pearson correlation coefficient (PCC). The level of statistical significance was set at alpha=0.05.

Results

Baseline characteristics

Three hundred and eleven patients were screened for the study during a period of 17 months. In total, 63 patients were excluded due to various reasons. Twelve patients were excluded because of early discharge from the hospital. Seven patients were excluded due to entering a purely palliative setting. Ten patients were excluded due to concurrent diagnosis of depression (n=4), delirium (n=5) and glioblastoma (n=1). Twenty patients were excluded because no cognitive impairment could be established. Another 14 patients who could not perform a hand grip test and were excluded (8 did not understand the test, 5 were agitated or aggressive during the test, 1 refused to do the test because of a painful wrist joint). An overview of the inclusion process is depicted in Figure 1. This study included N=248 patients, with a mean age of 84.1±6.4 years, of whom 60.9% were female (n=151). The sample included patients with mild cognitive impairment (MCI) and different types of dementia. In the total population, the mean MMSE score was 16.8±5.7. Baseline characteristics of the total population are presented in Table 1.

	Total (n=248)
Female	151 (60.9%)
Mean age (years) (SD)	84.1 (6.4)
Comorbidities ≥ 4	113 (45.6%)
Mean anthropometric measurements, (SD)	
- BMI (kg/m^2)	24.1 (4.9)
- MAC (cm)	27.4 (4.3)
- TSF (mm)	12.9 (6.1)
- CC (cm)	33.7 (3.8)
Type of cognitive impairment	
- Alzheimer dementia	139 (56.0%)
- Frontotemporal dementia	12 (4.8%)
- Parkinson's dementia	2 (0.8%)
- Korsakoff's dementia	4 (1.6%)
- Vascular dementia	18 (7.3%)
- Mixed dementia	62 (25.0%)
- Mild cognitive impairment	11 (4.4%)
Total type of cognitive impairment	248
Mean MMSE score, (SD):	16.8 (5.7)
- Mild dementia	65 (26.2%)
- Moderate dementia	106 (42.8%)
- Severe dementia	77 (31.0%)
Mean ADL score (N=223), (SD)	13.6 (3.7)
- Normal or mildly decreased	2 (0.9%)
- Moderately decreased	88 (39.5%)
- Severely decreased	106 (47.5%)
- Disable	27 (12.1%)
Mean IADL score (N=81), (SD):	3.7 (0.6)
- Female (N=46), (SD)	3.7 (0.5)
- Male (N=35), (SD)	3.7 (0.8)

SD standard deviation, BMI body mass index, MAC mid-arm circumference, TSF triceps skin fold thickness, CC calf circumference, MMSE Mini Mental State Examination, ADL activity of daily living, IADL instrumental activity of daily living.

Table 1. Baseline characteristics of the total population.

Assessment of sarcopenia

Sarcopenia was assessed by muscle measurements, gait speed, SARC-F-patient and SARC-F-Proxy (formal and informal caregivers), using the EWGSOP2 diagnostic criteria.

The muscle measurements (hand grip strength, calf circumferences and mid-arm muscle circumference) were executed in 220 patients. Mean values of these measurements in men and women are summarized in Table 2. The difference in mean HGS, CC and MAMC in men and women were all significant (p=0.001, p=0.007 and p<0.001 respectively). The gait speed was measured in 192 patients. Forty-nine patients could not perform the gait speed assessment (for 21 patients the gait speed was not measured, 11 had recent orthopaedic operation of the lower limb, 15 were wheelchair-bounded due to severe disability, 1 had fear of falling and 1 refused to do the test). Gait speed was found not to be significant different between men and women in this population (p=0.45). Seventy-one of the 220 patients had no sarcopenia. For the 149 patients who had sarcopenia, 106 had probable sarcopenia, 27 had confirmed sarcopenia and 16 had severe sarcopenia. The prevalence of sarcopenia in this cohort was 67.7% (n=220). The percentages and severity grade are presented in Table 2.

The SARC-F questionnaire was completed by 148 patients. The SARC-F-proxy was completed by the formal caregivers (n=220) and/or by informal caregivers (n=153). The SARC-F-Patient was predictive for sarcopenia in 77 patients (52.0%). The SARC-F-Proxy-Formal caregiver was predictive for sarcopenia in 166 patients (75.4%), while SARC-F-Proxy-Informal caregiver was predictive for sarcopenia in 101 patients (66%). See also Table 2.

There was a significant negative correlation between the

Mean HGS, (SD)	
- Total (N=220)	16.9 (9.2)
- Female (N=130)	12.5 (5.6)
- Male (N= 90)	23.1 (9.7)
Mean CC, (SD)	
- Total (N=253)	33.7 (3.8)
- Female (N=153)	33.2 (4.0)
- Male (N=100)	34.5 (3.4)
Mean MAMC, (SD)	
- Total (N=247)	23.3 (3.3)
- Female (N=148)	22.4 (3.1)
- Male (N=99)	24.7 (3.1)
Mean gait speed, (SD)	
- Total (N=192)	0.71 (0.3)
- Female (N=113)	0.69 (0.3)
- Male (N=79)	0.73 (0.3)
Assessment of sarcopenia with HGS, CC or MAMC and gait speed	**N=220**
- No sarcopenia	71 (32.3%)
- Probably sarcopenia	106 (48.2%)
- Confirmed sarcopenia	27 (12.3%)
- Severe sarcopenia	16 (7.2%)
SARC-F-Patient	N=148
- No sarcopenia	71 (48.0%)
- Sarcopenia	77 (52.0%)
SARC-F-Proxy-Formal caregiver	**N=220**
- No sarcopenia	54 (24.6%)
- Sarcopenia	166 (75.4%)
SARC-F-Proxy-Informal caregiver	**N=153**
- No sarcopenia	52 (34%)
- Sarcopenia	101 (66%)

SD standard deviation, HGS Hand grip strength, CC calf circumferences, MAMC mid-arm muscle circumference. ***SARC-F score≥4 points indicates sarcopenia.***

Table 2. Assessment of sarcopenia.

SARC-F-Proxy (≥4) and low physical performance (p<0.001; PCC= -0.525), and only a weak negative correlation between the SARC-F-Proxy and low muscle mass (p=0.12; PCC= -0.107).

The SARC-F-Patient had 63.2% sensitivity and a 70.0% specificity with a positive predictive value (PPV) of 80.5% and a negative predictive value (NPV) of 49.2%. The SARC-F-Proxy-Formal caregiver had a 85.9% sensitivity and a 46.5% specificity with a positive predictive value of 77.1% and a negative predictive value of 61.1%.

The SARC-F-Proxy-informal caregiver had a 77.0% sensitivity and a 54.7% specificity with a positive predictive value of 76.2% and a negative predictive value of 55.7% (see Table 3).

Discussion

This study aimed to validate the proxy-reported SARC-F as a surrogate for the SARC-F in the screening of sarcopenia in hospitalised community-dwelling patients with confirmed cognitive impairment and to evaluate a possible difference in reliability between a formal and informal caregiver.

The prevalence of sarcopenia using the EWGSOP2 diagnostic criteria in this cohort was rather high (67.7%) compared to the prevalence of sarcopenia in the literature. A recent systematic review has found that estimates of sarcopenia prevalence vary from 9.9 to 40.4%, depending on the definition used[3]. However, none of these studies have used the recent EWGSOP2 diagnostic criteria and did not include patients with cognitive impairment exclusively. One study investigating the prevalence of sarcopenia in institutionalized older people with dementia had found a similar percentage (68.7%)[27]. The prevalence of sarcopenia was 75.4% for the SARC-F-Proxy-formal caregiver and 66% for the SARC-F-Proxy-Informal caregiver. These are higher than the prevalence of sarcopenia according to the SARC-F in previous studies, but these had excluded patients with mental disorders or patients who could not communicate with the interviewer[28,29].

The SARC-F-Proxy was found to have a high sensitivity and low specificity. This is in contrast to previous studies, in which the SARC-F had a low sensitivity and a rather high specificity[14,29]. This is a very interesting finding. The SARC-F-Proxy reflects the perception of the caregivers on patient's muscular function, while the SARC-F in the previous studies reflected the patient's own perception on their muscular function. The caregivers in the current study were more inclined to judge patients as sarcopenic and physically frail. Furthermore, most studies exclude patients with disability and cognitive impairment. In the current cohort, patients were older and more malnourished, had comorbidities, were cognitively impaired, and had low ADL/IADL at baseline. These all are risk factors for the development or worsening of sarcopenia[4]. This would explain the high prevalence of sarcopenia in this cohort and also the high sensitivity of the SARC-F-Proxy.

In this cross-sectional study, the SARC-F-Proxy had a high sensitivity and low-to-moderate specificity when applying the EWGSOP2 diagnostic criteria as the 'gold standard'. Seventy-two patients (32.7%) in this cohort could not complete the SARC-F questionnaire, mostly due to communication problems related to reduced cognitive function. Therefore, because of the high sensitivity, the SARC-F-Proxy implies

	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
SARC-F-Patient	63.2%	70.0%	80.5%	49.2%	65.5%
SARC-F-Proxy-Formal caregiver	85.9%	46.5%	77.1%	61.1%	73.1%
SARC-F-Proxy-informal caregiver	77.0%	54.7%	76.2%	55.7%	69.2%

PPV positive predictive value, NPV negative predictive value.

Table 3. Sensitivity, specificity, PPV, NPV and diagnostic accuracy of the SARC-F and SARC-F-Proxy.

to be a good alternative in these patients with cognitive impairment and have the ability to detect possible underlying muscle impairment or sarcopenia. These results are in line with the study of Maurus et al. and confirm the possibility to use a proxy-reported SARC-F questionnaire as screening instrument in patients with cognitive impairment[16]. In addition, this study aimed to evaluate possible differences in reliability in proxy-reported SARC-F questionnaires when performed by formal and informal caregivers. The higher sensitivity when performed by formal caregivers (85.9%) versus 77.0% by informal caregivers may suggest a better judgment for possible underlying sarcopenia when evaluated by a formal caregiver. A possible explanation can be the difference in the patient's environmental adaptation. Functional decline might not be perceived by the informal caregiver as such if deficits are well compensated by the social environment and adaptation of lifestyle to deficits.

The SARC-F-Proxy (≥4) was strongly associated with low physical performance, but only weakly associated with low muscle mass. This weak association might be attributed to the use of anthropometric measures to estimate muscle mass and to the cut-off values that were used. In general, CC and MAMC have been shown to be correlated with appendicular muscle mass. They both reflect nutritional status and predict performance, health and survival in older people[25,30]. However, a consensus regarding the cut-off values of CC and MAMC that are associated with low muscle mass in a European population was not found. For CC, the value that was used was considered the best clinical indicator of sarcopenia, being associated with muscle-related disability and physical function[31]. In a non-European population, some variation was found in cut-off values of CC. In a recent study, CC ≤29 cm in women and ≤30 cm in men were validated as cut-off values for decreased skeletal muscle mass in a Japanese population[32]. These values were similar to the ones in this study. A Brazilian study suggested that the most accurate cut-off points for detecting decreased muscle mass in older persons were 34 cm for men (sensitivity 71.5%, specificity 77.4%) and 33 cm for women (sensitivity 80.0%; specificity 84.6%)[31].

In regard to MAMC, cut-off values by Landi et al were used[25]. Recently, two studies used the same cut-off values as indicator of reduced muscle mass[33,34]. However, these cut-off values are the lowest tertiles (<21.1 cm in males, <19.2 cm in females). This means that some patients with sarcopenia might be omitted due to MAMC values being higher than the cut-off values used here. The use of anthropometric measurements to estimate the muscle mass instead of the 'gold methods' (MRI, CT, DXA) can be seen as a limitation. However, no reference data with usable cut-off values for sarcopenia exist for MRI or CT. Also, DXA is known to have a very low availability in clinical practice[35]. These points limit the use of the recommended tools in clinical practice, and increase the need for a useful screening tool, certainly in specific populations. The phenomenon of acute sarcopenia secondary to hospitalization can influence the prevalence of sarcopenia in this cohort. In ideal conditions the muscle measurements should be retested after discharge. Moreover, to evaluate the psychometric performance of the proxy-reported SARC-F questionnaire there should be a reassessment after hospitalization to examine the test-retest reliability. As a strength of the study, a relatively large cohort size is used which provides sufficient statistical power.

The current study validates the proxy-reported SARC-F questionnaire as a surrogate for the SARC-F in the screening of sarcopenia in hospitalised community-dwelling older people with known or suspected cognitive impairment. Second, the results in this study suggest a higher reliability when the proxy-reported questionnaire is evaluated by the formal caregiver.

Ethical approval

The medical ethics committee of ZNA (Antwerp, Belgium) approved this study (OG 031-009).

Consent to participate

A written informed consent was obtained from all admitted patients or from an authorised family member for those who could not give consent due to cognitive impairment.

Authors' contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by SK, SP, WDRG and PK. The first draft of the manuscript was written by SL and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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