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ORIGINAL ARTICLE

Malnutrition, assessed by the Global Leadership Initiative on Malnutrition (GLIM) criteria but not by the mini nutritional assessment (MNA), predicts the incidence of sarcopenia over a 5-year period in the SarcoPhAge cohort

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Abstract

Background The capacity of malnutrition screening to predict the onset of sarcopenia is unknown.

Aim Our first objective is to explore the association between the screening of malnutrition and the incidence of sarcopenia and then, to assess the added value of the diagnosis of malnutrition to predict sarcopenia over a 5-year follow-up.

Methods Malnutrition was screened at baseline according to the MNA short-form (MNA-SF) and long-form (MNA-LF) and was diagnosed by the GLIM definition. Sarcopenia was defined using the European Working Group on Sarcopenia in Older People (EWGSOP2) criteria. Kaplan–Meier analysis and adjusted Cox regression were performed to explore the association between nutritional status and the incidence of sarcopenia.

Results A total of 418 participants were analyzed (median age 71.7 years (67.7 – 76.8), 60% women) for our first objective. Among them, 64 (15.3%) became sarcopenic during the follow-up period. In the adjusted model, the incidence of sarcopenia was nonsignificantly associated with the risk of malnutrition for both forms of the MNA (MNA-SF: HR of 1.68 (95% CI 0.95 – 2.99); MNA-LF: HR of 1.67 (95% CI 0.86 – 3.26)). However, among the 337 participants for which a GLIM assessment was possible and in which 46 participants became sarcopenic, malnourished subjects had a higher risk than well-nourished participants of developing sarcopenia after 5 years, with an adjusted HR of 3.19 (95% CI 1.56 – 6.50).

Conclusion A full diagnosis of malnutrition seems more useful than a simple malnutrition screening to predict the incidence of sarcopenia over 5 years.

Keywords Sarcopenia · EWGSOP2 · Malnutrition · GLIM · MNA · SarcoPhAge

Introduction

Skeletal muscles are crucial for maintaining physical ability and optimal health at every life stage [1]. However, a natural progressive decline in skeletal muscles occurs with age, with an age-related decline in muscle strength [2]. This process is known as sarcopenia and is defined by the presence of low muscle strength and low muscle mass according to the newest consensus on the diagnostic criteria published in 2019 by the European Working Group on Sarcopenia in Older People [3].

Throughout the past decade, clinicians and researchers have raised awareness of sarcopenia because it represents a burden on the health of people and the economy in an aging population. Sarcopenia has a worldwide prevalence estimated at 10% [4] and is associated with serious adverse

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events such as a higher risk of falls and fractures because of mobility disorders, a lower quality of life, a loss of independence and higher morbidity and mortality rates [1, 5–7]. These health-related consequences lead to higher healthcare costs for sarcopenic individuals compared to those without sarcopenia [8]. Furthermore, sarcopenia is now recognized as a geriatric disorder by the International Classification of Disease, Tenth revision, Clinical Modification (ICD-10-CM) [9].

Although the loss of muscle quantity and quality are a normal part of aging, malnutrition is a common pathological condition in older adults that can further influence and aggravate muscle health decline [10]. Deficient nutrient intake resulting from low dietary consumption, low nutrient bioavailability, or high nutrient requirements can lead to alterations in body composition that are characterized by a loss of muscle mass and muscle function [1]. Therefore, malnutrition augments the heavy burden of poor muscle health for both individuals and the public health system [11]. Furthermore, malnutrition is highly prevalent among older adults, with a pooled estimated risk of malnutrition ranging from 8.5% in community settings to 28% in hospital settings [12].

There is growing evidence that indicates the role of nutrition in the prevention and management of sarcopenia [13–18], suggesting that malnutrition can be one of its main risk factors. Given that nutrition and physical activity are modifiable lifestyle factors that affect sarcopenia [19, 20], it is important to promote research on these two factors and their mechanisms to support preventive and therapeutic measures, such as appropriate nutritional interventions [21].

In 2018, a new international definition of malnutrition was launched by the Global Leadership Initiative on Malnutrition (GLIM), constituted by major clinical nutrition societies [22]. The definition revised and updated the previous one from the European Society for Clinical Nutrition and Metabolism (ESPEN). Each criterion is taken into account separately in a two-step approach: first, individuals are screened to identify those at risk of malnutrition; second, a diagnosis of malnutrition requires the presence of at least one phenotypic (i.e., nonintentional weight loss, low body mass index or low muscle mass) and one etiologic criterion (i.e., reduced food intake or inflammation).

In a previous study of the SarcoPhAge (for "Sarcopenia and Physical Impairments with Advancing Age") cohort, a Belgian cohort composed of community-dwelling older adults, we observed a more than threefold risk of developing sarcopenia for malnourished individuals (as defined by the GLIM criteria) compared to well-nourished individuals after a 4-year follow-up [23]. However, in clinical practice, it is necessary to first apply the screening part of the GLIM definition [22], as the screening procedure is easier and faster to carry out. This avoids conducting the complete diagnostic assessment for individuals who are not at risk of malnutrition. Therefore, the primary objective of the present study was to analyze the capacity of the Mini Nutritional Assessment (MNA) questionnaire (the most widely used and specifically designed nutritional screening tool for older adults [10]) to predict the onset of sarcopenia in the SarcoPhAge cohort. The long form of the MNA was the original version developed to screen older adults in hospitals, nursing homes or in the community, and the short form was developed after to gain efficiency in the screening process [24]. As both versions are used in clinical practice and in research [25], we used both of them in the present study to assess the risk of malnutrition. In addition, since we had the data at 5-year of follow-up, we could measure the association between the diagnosis of malnutrition according to the GLIM criteria and the 5-year incidence of sarcopenia and then compare the capacity of the diagnosis and the screening of malnutrition to predict sarcopenia over a 5-year follow-up.

Methods

Population

The present study included participants from the SarcoPhAge cohort, a Belgian cohort composed of community-dwelling older adults over 65 years of age. The protocol and the complete methodology of the SarcoPhAge study have been detailed elsewhere [26]. Briefly, the SarcoPhAge study was initiated in 2013 and included a total of 534 volunteer older adults recruited from press advertisements and from an outpatient clinic in Liège, Belgium. The only exclusion criteria were those required for undergoing dual X-ray absorptiometry (DXA), which were individuals with an amputated limb or a BMI greater than 50 kg/m^2. Physical examinations and questionnaires were conducted annually by a clinical research assistant from baseline (T0) to the fifth year of follow-up (T5) and were completed in June 2019. The ethics committee of the University of Liege Teaching Hospital approved this study (reference 2012/277) with two amendments in 2015 and 2018, and all participants gave their written informed consent.

Nutritional status

First, the risk of malnutrition was assessed at baseline using both the short and the long forms of the MNA, a nutritional screening tool relevant for older adults [24, 27, 28]. The long form of the MNA was the original version developed to screen older adults in hospitals, nursing homes or in the community, and the short form was developed to gain efficiency in the screening process [24]:

- The short version of the MNA (MNA-SF) consists of six items [29]: involuntary weight loss, loss of appetite, loss of mobility, psychological stress, neuropsychological problems (i.e., dementia), and low BMI. The total score classifies individuals as well nourished (≥ 12 points), at risk of malnutrition (8 to 11 points) or malnourished (< 8 points).
- The long version of the MNA (MNA-LF) comprises 18 components [29], including the 6 items of the short form plus the following: autonomy, drug prescription, pressure sores or skin ulcers, number of meals per day, protein intake, fruit or vegetable consumption, fluid consumption, mode of feeding, self-view of nutritional status, self-view of health status in comparison to other people of the same age, and mid-arm and calf circumferences. The total score classifies individuals as well-nourished (≥ 24 points), at risk of malnutrition (17–23.5 points) or malnourished (< 17 points).

The standard procedure recommended for practice [25] was followed in the present study where only the individuals identified as at least at risk of malnutrition by the MNA-SF were then assessed by the MNA-LF. Therefore, individuals identified as well nourished by the short form were considered as well by the long form of the MNA. The risk of malnutrition was considered a dichotomous variable. Therefore, the participants were identified as either well nourished or at least at risk of malnutrition.

Second, the diagnosis of malnutrition was also performed at baseline according to the GLIM criteria, which require the presence of at least one phenotypic and one etiologic criterion meeting the thresholds. The thresholds were defined in this study in accordance with the guidance provided by the GLIM core leadership committee [22]:

- The phenotypic criteria were (1) an unintentional weight loss greater than 4.5 kg in the past year [27], (2) a body mass index less than 20 kg/m^2 or 22 kg/m^2 for those younger or older than 70 years, respectively [22], and (3) a low muscle mass identified as a fat-free mass index (FFMI) less than 17 kg/m^2 in men and 15 kg/m^2 in women or an appendicular lean mass index (ALMI) less than 7 kg/m^2 in men and 5.5 kg/m^2 in women [3, 22].
- The etiological criteria included (1) a reduced food intake determined according to the first item of the MNA-SF (moderate or severe loss of appetite in the past three months) [28] and (2) inflammation evaluated by interleukin-6 (IL-6) and insulin-like growth factor 1 (IGF-1) [30], where the highest or the lowest quartiles for IL-6 and IGF1, respectively, calculated for our data set in both sexes, was considered a sex-specific threshold (i.e., IGF-1 ≤ 88 ng/mL in men and ≤ 82 ng/mL in women and IL-6 > 3.84 pg/mL in men and > 2.99 pg/mL in women). Inflammation is considered to be present if the value of IL-6 is above, or IGF-1 is below, these thresholds, which are similar to previously published thresholds for community-dwelling older adults [31, 32]. Additionally, according to a comprehensive review conducted by a panel of experts, the biomarkers used in the present study were identified as robust, with a consistent ability to predict clinical and functional outcomes, are responsive to intervention, and can provide a reliable and feasible measurement [30].

A diagnostic assessment of malnutrition was performed for all the included participants without taking into account the results of the initial screening step. This was done to follow the same methodology as in our previous study to be able to compare the results of the two studies.

Sarcopenia

Sarcopenia was diagnosed according to the revised European definition of the EWGSOP, which includes the presence of both of the following criteria [3]:

- Low muscle strength was defined as < 27 kg for men and < 16 kg for women. Muscle strength was measured with a handgrip hand-held dynamometer (Saehan Corporation, MSD Europe Bvba, Brussels, Belgium) calibrated each year throughout the study. We followed the standardized procedures by asking participants to squeeze it with maximum strength. The test was repeated three times per hand, and the highest value of the six measures was considered in our analyses [33].
- Low muscle mass was defined as FFMI < 17 kg/m^2 in men and < 15 kg/m^2 in women or ALMI < 7 kg/m^2 in men and < 5.5 kg/m^2 in women. Fat-free mass (i.e., total body mass minus the fat mass) and the appendicular lean mass (i.e., the sum of the muscle mass in both arms and legs) were estimated from the whole body DXA scans (Hologic Discovery A, USA) calibrated daily. The values of these muscle parameters were then divided by height squared to obtain their index values.

Covariates

Sociodemographic and anamnestic data were gathered yearly through physical examinations and health questionnaires. The following variables were considered confounding factors for their potential impact on nutritional status and muscle health according to the literature and previous studies of the SarcoPhAge cohort [26, 34–40] (Locquet et al., in press): age, sex, number of comorbidities per individual, number of medications consumed per individual, mini-mental state

evaluation (MMSE) [41], self-reported physical activity level measured by the Minnesota questionnaire [42] and smoking status.

Statistical analysis

Sarcopenic participants diagnosed at baseline were excluded from the analyses to be able to measure the cumulative incidence of sarcopenia over time.

Binary variables were expressed as absolute (N) and relative frequencies (%). The quantitative variables were reported as the median (25th percentile – 75th percentile) because they did not follow a Gaussian distribution as evaluated by the difference between the mean and the median values, the histograms, the quantile–quantile plot and the Shapiro–Wilk test.

The malnutrition risk assessment was performed at baseline, and the sociodemographic and health characteristics of the participants at inclusion were compared according to nutritional status using the Mann–Whitney U test for continuous variables and the X^2 test for categorical binary variables. Additionally, Cohen's kappa was calculated (1) to measure the agreement between the two forms of the MNA for screening individuals at risk of malnutrition, and (2) to measure the agreement between the screening (MNA) and the diagnosis of malnutrition by the GLIM criteria. Cohen's kappa score can range between −1 and + 1. The agreement is considered null when the score is lower than 0, slight between 0 and 0.20, fair between 0.21 and 0.40, moderate between 0.41 and 0.60, substantial between 0.61 and 0.80, and almost perfect above 0.80 [43].

The number of new cases of sarcopenia was measured each year (i.e., the cumulative incidence) in a sample population who were free from the disease at baseline among participants who were assessed at least once over the 5-year follow-up period. This incidence rate was then compared against the nutritional status using the X^2 test. For the survival analysis, a Cox proportional hazards model, giving a hazard ratio (HR) and its 95% confidence interval (95% CI), was applied to measure the risk of developing sarcopenia over a 5-year follow-up, according to nutritional status. A crude and an adjusted hazard ratio were measured. The adjusted model included the following covariates: age, sex, number of comorbidities per individual, number of drugs consumed per individual, MMSE score, self-reported physical activity level and smoking status. The Kaplan–Meier method was used to create survival curves to estimate the impact of (the risk of) malnutrition on the incidence of sarcopenia, and log-rank tests were performed to statistically compare the survival curves according to nutritional status.

The results were considered statistically significant when the p value was less than 0.05. The SPSS Statistics 24 (IBM Corporation, Armonk, NY, USA) software package was used for the analyses.

Results

At baseline, the total SarcoPhAge population was composed of 534 participants, and 510 were free from sarcopenia. Among these 510 participants, 92 had no data available throughout the 5-year follow-up because they were unable to be contacted, were unable or refused to participate or died. Therefore, 418 participants for which we had data on the outcome "sarcopenia" constituted our baseline population for our primary objective. To confirm the association previously observed between malnutrition diagnosis and the incidence of sarcopenia (i.e., our secondary objective), we performed the analyses on a total sample of 337 participants for whom we had inflammation marker data, which was needed to diagnose malnutrition according to the GLIM criteria (Fig. 1).

The characteristics of the participants at inclusion are presented in Table 1. Out of the 418 participants that constituted our studied sample (median age of 71.7 years (67.7 – 76.8), 60% women), 75 (18%) were identified as at risk of malnutrition according to the MNA-SF and 44 (10.5%) according to the MNA-LF. Compared to the well-nourished participants, those at risk of malnutrition according to either MNA-SF or MNA-LF had a significantly lower BMI, took more drugs per day, had more comorbidities and had a slightly worse cognitive status, with all p values less than 0.05. For the participants at risk of malnutrition according to the MNA-SF specifically, they comprised more smokers than the well-nourished ones (p value of 0.01).

Regarding the muscle parameters, compared to well-nourished women, both the FFMI and the ALMI were significantly lower in women at risk of malnutrition (both p values of 0.004) while participants at risk of malnutrition using the MNA-LF had significantly lower SPPB and gait speed tests scores (p values of 0.001 and 0.003, respectively), lower muscle strength but in men only (p value of 0.01) and lower FFMI and ALMI in both men and women (all p values < 0.05).

Throughout the 5-year follow-up period, 64 participants (15.3%) were newly diagnosed with sarcopenia. The incidence of sarcopenia was significantly higher in the participants at risk of malnutrition than in the well-nourished participants regardless of the screening tool used, with log-rank p values of 0.008 for the MNA-SF and 0.003 for the MNA-LF Kaplan–Meier curves (Fig. 2a and b).

When the MNA-SF was used, 18 of the 75 participants at risk of malnutrition (24%) developed sarcopenia compared to 13.4% of the well-nourished participants (p value of 0.02), resulting in a crude HR of 2.05 (95% CI 1.19 – 3.54)

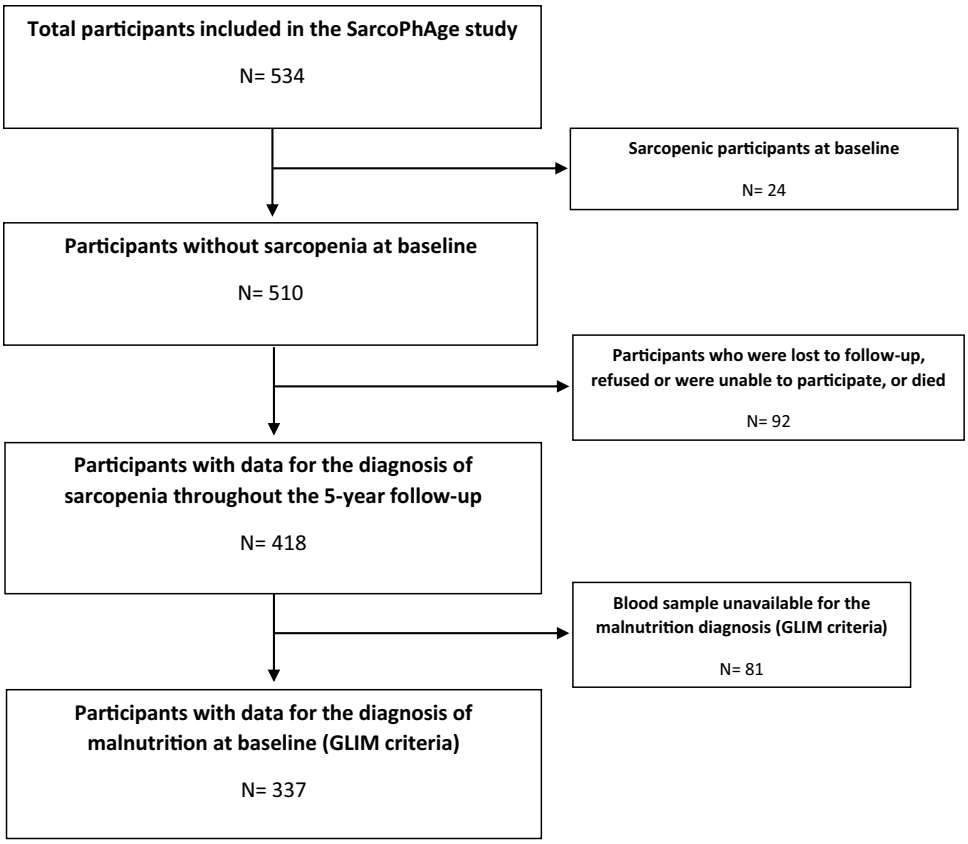

Fig. 1 Flow chart of the SarcoPhAge study. *GLIM* global leadership initiative on malnutrition

(Table 2). This means that participants at risk of malnutrition had a more than twofold risk of becoming sarcopenic over the follow-up period. In the model adjusted for the included covariates (age, sex, number of drugs per participant, number of comorbidities per participant, MMSE score, level of physical activity, and smoking status), the incidence of sarcopenia became non significantly associated with the risk of malnutrition according to the MNA-SF, with an HR of 1.68 (95% CI 0.95 – 2.99).

Regarding the long form of the MNA, 44 participants were identified as at risk of malnutrition at baseline, and 13 (29.5%) of them were diagnosed with sarcopenia during the 5-year follow-up compared to 13.6% of those with good nutritional status. In the crude model, the impact of nutritional status on the incidence of sarcopenia was significant, with an HR of 2.44 (95% CI 1.32 – 4.49). However, after adjusting for the covariates, the association was no longer significant, with an HR of 1.67 (95% CI 0.86 – 3.26).

There was strong agreement between the two forms of the MNA in the identification of participants who were at risk of malnutrition, with a Cohen kappa of 0.70 (95% CI 0.60 – 0.80).

The association between the 5-year incidence of sarcopenia and the diagnosis of malnutrition according to the GLIM criteria is displayed in Table 2. At baseline, 59 of the 337 participants included in the secondary analysis were diagnosed as malnourished. Among them, a total of 46 new events of sarcopenia were assessed after 5 years—20 events among the malnourished participants (34%) and 26 among the well-nourished participants (9.4%). The number of new cases of sarcopenia was significantly higher among the malnourished participants (p value < 0.001) than among the well-nourished participants, leading to an HR of 4.02 (95% CI 2.25–7.23). In the adjusted model, malnourished participants had also a higher risk than well-nourished participants of developing sarcopenia after 5 years, with an HR of 3.19 (95% CI 1.56–6.50).

There was low agreement between the diagnosis of malnutrition and the malnutrition screening for both versions of the MNA, with Cohen kappa values of 0.38 (95% CI 0.25–0.51) and 0.36 (95% CI 0.22–0.50) for the short and long versions, respectively.

Discussion

A significantly higher risk of developing sarcopenia for malnourished older adults diagnosed according to the GLIM criteria was observed in one of our previous studies [23]. The GLIM definition recommends that screening be conducted before attempting to diagnose malnutrition because the screening is easier and quicker to apply in clinical practice.

Table 1 Sociodemographic and health characteristics of participants at inclusion

Baseline characteristics	Studied Sample ($n=418$)	Malnutrition risk according to the MNA-SF			Malnutrition risk according to the MNA-LF		
		Yes ($n=75$)	No ($n=343$)	P value	Yes ($n=44$)	No ($n=374$)	*P* value
Age, years	71.7 (67.7 – 76.8)	72.0 (67.7 – 76.5)	71.7 (67.6 – 76.9)	0.90	73.6 (69.9 – 77.7)	71.5 (67.5 – 76.4)	0.05
Sex, women	252 (60.3)	52 (69.3)	200 (58.3)	0.08	32 (72.7)	220 (58.8)	0.08
Body mass index, kg/m^2	26.3 (23.8 – 29.8)	24.4 (20.3 – 28.0)	26.8 (24.2 – 29.9)	<0.001	23.8 (20.1 – 27.7)	26.6 (24.1 – 29.9)	<0.001
Smoking status, yes	39 (9.3)	13 (17.3)	26 (7.6)	0.01	8 (18.2)	31 (8.3)	0.05
Alcohol consumption, yes	213 (51.0)	34 (45.3)	179 (52.2)	0.28	18 (40.9)	195 (42.1)	0.16
Number of drugs	5.0 (3.0 – 8.0)	6.0 (4.0 – 9.0)	5.0 (3.0 – 7.0)	0.02	6.0 (4.0 – 10.0)	5.0 (3.0 – 7.0)	0.007
Number of comorbidities	4.0 (2.0 – 5.0)	4.0 (3.0 – 6.0)	4.0 (2.0 – 5.0)	0.002	5.0 (3.0 – 7.0)	3.5 (2.0 – 5.0)	<0.001
MMSE, max 30 points	29.0 (28.0 – 29.0)	28.0 (27.0 – 29.0)	29.0 (28.0 – 30.0)	0.002	28.0 (25.3 – 29.0)	29.0 (28.0 – 30.0)	<0.001
Physical activity level, kcal/day	791.0 (280.0 – 1536.5)	840.0 (112.0 – 1455.0)	779.5 (305.0 – 1582.0)	0.59	735.0 (0.0 – 1306.4)	815.5 (320.3 – 1582.0)	0.08
SPPB, max 12 points	10.0 (9.0 – 11.0)	10.0 (8.0 – 11.0)	10.0 (9.0 – 11.0)	0.12	9.0 (6.3 – 10.0)	10.0 (9.0 – 11.0)	0.001
Gait speed, m/s	1.0 (0.9 – 1.2)	1.0 (0.8 – 1.2)	1.0 (0.9 – 1.2)	0.09	0.9 (0.6 – 1.1)	1.0 (0.9 – 1.2)	0.003
Muscle strength, kg	40.3 (36.0 – 50.7)	38.0 (30.0—43.0)	41.0 (38.0 – 45.5)	0.05	32.0 (29.9 – 42.0)	40.9 (37.8 – 45.6)	0.01
Men	23.0 (18.0 – 27.0)	22.0 (18.0 – 27.0)	23.0 (18.0 – 26.6)	0.52	22.0 (18.0 – 25.5)	23.0 (18.0 – 27.0)	0.26
Women							
FFMI, kg/m^2	19.0 (17.4 – 20.7)	17.8 (16.1 – 20.8)	19.1 (17.5 – 20.7)	0.11	17.0 (15.7 – 18.7)	19.2 (17.5 – 20.58)	0.01
Men	15.2 (14.0 – 16.4)	14.6 (13.5 – 16.2)	15.3 (14.3 – 16.5)	0.004	14.0 (13.2 – 15.8)	15.3 (14.2 – 16.4)	0.002
Women							
ALMI, kg/m^2	8.0 (7.3 – 8.8)	7.4 (6.8 – 8.6)	8.1 (7.4 – 8.8)	0.07	7.1 (6.7 – 7.5)	8.1 (7.4 – 8.9)	0.004
Men	6.0 (5.5 – 6.6)	5.6 (5.1 – 6.5)	6.1 (5.6 – 6.6)	0.004	5.5 (5.0 – 6.2)	6.0 (5.6 – 6.6)	0.001
Women							

MMSE mini mental state evaluation, *SPPB* short physical performance battery test, *FFMI* fat-free mass index, *ALMI* appendicular lean mass index

Hence, the primary aim of the current study was to investigate the ability of both the MNA-SF and MNA-LF to predict sarcopenia during a 5-year follow-up using data from the SarcoPhAge cohort. The results of neither MNA form were found to be associated with the incidence of sarcopenia over the follow-up period in the fully adjusted models. However, the previously observed association between malnutrition diagnosis (according to the GLIM criteria) and the incidence of sarcopenia after 4 years of follow-up was confirmed at the 5-year follow-up in the present study, even after adjusting for all potential confounding variables, including smoking.

A growing number of studies have indicated that malnutrition represents an essential component of sarcopenia. Indeed, increasing evidence has highlighted the potential mechanisms by which an unbalanced diet can impact muscle health and lead to sarcopenia [14, 19, 44, 45]. Furthermore, improved diet quantity and quality has been found to be beneficial in the management of sarcopenia [46–48], and the synergistic effect of combination nutritional interventions, such as protein supplementation and exercise, may be even more effective in promoting muscle health by increasing muscle protein synthesis [47, 49, 50]. Because malnutrition likely plays a major role in the management of sarcopenia [51], the early identification of individuals at risk of malnutrition can be key to preventing sarcopenia and reducing its health burden. Thus, the screening part of the malnutrition diagnosis is important because it is the first step in the identification of individuals at risk of malnutrition.

The link between sarcopenia and screening for malnutrition risk using the MNA has mostly been explored in community-dwelling older adults in cross-sectional studies. The first study found a significant association between sarcopenia (as defined by EWGSOP1) and the risk of malnutrition as assessed by the MNA-SF [52]. In a second study, the same results were observed using the MNA-LF, but only for individuals identified as malnourished according to the MNA-LF and not for those established as simply at risk of malnutrition [53]. Their associations have

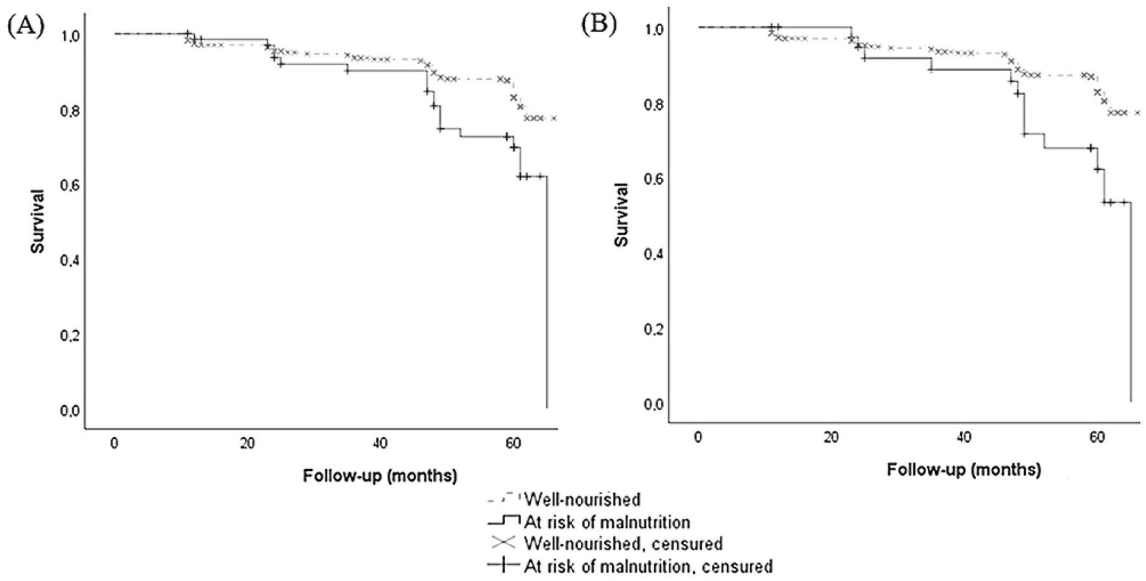

Fig. 2 **a** Incidence of sarcopenia in well-nourished participants and in those at risk of malnutrition according to the MNA-SF; **b** incidence of sarcopenia in well-nourished participants and in those at risk of malnutrition according to the MNA-LF

Table 2 Association between malnutrition risk ($n=418$) and malnutrition diagnosis ($n=337$) at baseline and the 5-year incidence of sarcopenia

	5-year incidence of sarcopenia		*p* value	Crude HR (95% CI)	Adjusted HR (95% CI)*
Malnutrition risk assessed according to the MNA short-form					
Malnutrition risk	Yes (n= 64)	No (n= 354)			
Yes (*n*= 75)	18 (24.0)	57 (76.0)	0.02	2.05 (1.19–3.54)	1.68 (0.95–2.99)
No (*n*= 343)	46 (13.4)	297 (86.6)			
Malnutrition risk assessed according to the MNA long-form					
Malnutrition risk	Yes (*n*= 64)	No (*n*= 354)	0.006	2.44 (1.32–4.49)	1.67 (0.86–3.26)
Yes (*n*= 44)	13 (29.5)	31 (70.5)			
No (*n*= 374)	51 (13.6)	323 (86.4)			
Malnutrition diagnosis according to the GLIM criteria					
Malnutrition diagnosis	Yes (*n*= 46)	No (*n*= 291)			
Yes (*n*= 59)	20 (33.9)	39 (66.1)	< 0.001	4.02 (2.25–7.23)	3.19 (1.56–6.50)
No (*n*= 278)	26 (9.4)	252 (90.6)			

MNA mini nutritional assessment, *HR* hazard ratio

*Adjusted for age, sex, number of drugs per participant, number of comorbidities per participant, MMSE score, and level of physical activity (Minnesota) and smoking status

also been investigated quantitatively using the MNA score in place of the nutritional status in the analyses, such as Wu et al. and Liguori et al. who concluded that sarcopenia (according to EWGSOP1) was associated with lower MNA-LF and MNA-SF scores, respectively [16, 54]. One longitudinal study explored the association between the MNA-LF score change and muscle parameters. The results showed that a decrease in the MNA score was associated with a decrease in physical performance (as assessed by the Short Physical Performance Battery test) but was not associated with muscle strength [55], which is considered to be the main criteria of sarcopenia in the EWGSOP2 definition [3]. However, these results are not comparable with ours, as it is well known that different sarcopenia diagnosis criteria (i.e., EWGSOP1 and EWGSOP2) will not identify the same sarcopenic individuals [56, 57]. This research used the newly formulated definition of sarcopenia as it is needed to support appropriate nutritional interventions and other relevant preventive measures for this pathology.

There is currently a lack of longitudinal research about the role of malnutrition in sarcopenia pathogenesis. The present study indicated that screening for malnutrition using the MNA could not predict the incidence of sarcopenia in the SarcoPhAge cohort. This is in contrast to the established diagnosis of malnutrition using the GLIM criteria, which was associated with a higher risk of developing sarcopenia after a 5-year follow-up. Risk screening is a process that must be rapidly performed and therefore includes minimal nutritional indicators [58]. Our results suggest that a more in-depth assessment of nutritional status is required to anticipate adverse health outcomes. The higher risk of becoming sarcopenic observed in malnourished individuals who are diagnosed by the GLIM criteria can be partly attributed to the overlap between the definitions of the two conditions—a low muscle mass is a criterion of both. Moreover, this overlap was also present with the previous definition of malnutrition, the definition of the European Society of Clinical Nutrition and Metabolism (EPSEN) [59]. Using this definition, a significantly higher risk of becoming sarcopenic was found in our previous study (HR of 4.28). The risk was lower than that found with the GLIM criteria, but we can assume that this is because low muscle mass was not a systematic criterion in the EPSEN definition.

The agreement between the two MNA forms was good (Cohen kappa of 0.70), but the agreement between the GLIM criteria and the MNA was poor, with Cohen kappas of less than 0.40 for both forms of the MNA. Among the 59 participants diagnosed as malnourished according to the GLIM criteria, 32 (54%) and 39 (66%) were not identified even as at risk of malnutrition by the MNA-SF and the MNA-LF, respectively. This means that if we had first screened the participants for being at risk of malnutrition and then diagnosed only those who were at least at risk, this would have led to an underestimation of the malnourished individuals. The MNA screening tool was used in the present study because it is the most validated tool in geriatric settings, but more than 30 validated screening tools exist [60] that include various criteria and nutritional factors. These tools could potentially lead to completely different populations being identified as at risk of malnutrition, both in research and in clinical practice. This highlights the importance of the criteria used for malnutrition risk screening and their validation in the targeted geriatric setting, as these could impact the optimal identification of individuals who most need early nutritional intervention.

Finally, the covariates included in the adjusted models indeed had an impact on the association between the risk of malnutrition and the incidence of sarcopenia, which became nonsignificant when adjusted for these covariates. Furthermore, this covariate impacted the analyses on the malnutrition risk but not those on the malnutrition diagnosis. This highlights the necessity to consider the global health status of the patient during malnutrition screening, as well as the hypothesis discussed earlier—that the association between the malnutrition diagnosis using the GLIM criteria and the incidence of sarcopenia was so strong owing to the overlap between the definitions (i.e., low muscle mass) that the adjustment for major confounding variables did not impact the association magnitude.

Strengths and limitations

This study is the first to investigate the capacity of both versions of the MNA screening tool to predict the incidence of sarcopenia according to the newest definition after a 5-year follow-up period. Nevertheless, there are several limitations to the present study.

First, we did not carry out the screening portion of the malnutrition diagnosis, as we had data to diagnose malnutrition according to the GLIM criteria for the entire population included in the secondary analyses. This allowed us to explore the agreement between the screening and the diagnosis of malnutrition and to compare the results obtained for the two steps. Regarding the criteria and threshold values used to diagnose malnutrition, we followed those recommended by the GLIM consensus, except for the unintentional weight loss criteria from the FRIED questionnaire, as we did not have these data available. However, evidence on how to assess each criterion and clear threshold values are currently lacking [61]. For example, the GLIM consensus report indicates that the thresholds for the "reduced food intake" and "weight loss" criteria can vary according to the malnutrition tool used [22]. This is also the case for inflammation for which clear measurement methods or threshold values are not communicated in the GLIM definition. This could have a large impact on the proportion of malnourished individuals identified across studies, e.g., a prevalence of 10.7% found in a study by Yeung et al. compared to 17.5% in the present study in which different measures and thresholds for the GLIM criteria were applied [62]. Therefore, a consensus regarding the assessment of the various malnutrition criteria is needed.

Second, our population study was composed of volunteer community-dwelling older adults. This could have brought a selection bias, as the included participants potentially had a better health status than the global geriatric community-dwelling population. Indeed, the prevalence of malnutrition risk was approximately 18% and 10.5% using the MNA-SF and MNA-LF, respectively, compared to a prevalence of 37.7% in the community setting according to the review by Kaiser et al. This could have impacted the statistical power of our analyses, resulting in a nonsignificant association. Additionally, no sample size or statistical power was determined because the analyses were performed using data

from a pre-existing database. We can assume that a greater number of individuals at risk of malnutrition in the current study could have influenced the significance of the results observed for the MNA and induced a higher risk of developing sarcopenia when diagnosed as malnourished. In addition, the patients lost to follow-up could have experienced a more severe health decline than those included in the analyses, leading to an attrition bias. Indeed, the participants lost to follow-up were older (75.2 years (71.1–78.6) versus 71.4 (67.5–76.5)), took more drugs per day (6 (4–8) versus 5 (3–7)), had a worse cognitive status according to the MMSE (28 points (26–29) versus 29 (28–29)), had a lower physical activity level (517.5 kcal per day (0.0–1335.0) versus 840.0 (310.0–1554.0)) and had a lower grip strength (25 kg (19.5–34.0) versus 28.0 (22.0–39.0)).

Finally, in addition to nutrition, resistance and aerobic training can potentially play a significant role in myofibrillar protein synthesis and, therefore, in maintaining muscle health [63]. Unfortunately, we could not adjust for types of physical activity because we did not have this data. However, a large number of confounding factors that could impact nutritional status or muscle heath were taken into account, including the level of physical activity [64].

Additional studies are needed to further explore and confirm our results because this is one of the first studies in this area. Investigating the association between the incidence of sarcopenia and other validated malnutrition screening tools could also be highly relevant.

Conclusions

In conclusion, the risk of malnutrition as assessed by either the MNA-SF or MNA-LF was not found to predict the incidence of sarcopenia after a 5-year follow-up period in the SarcoPhAge cohort. This suggests that the screening of the malnutrition risk alone is not sufficient to identify individuals at higher risk of sarcopenia and highlights the necessity of a more in-depth assessment using the GLIM criteria to implement appropriate nutritional preventive actions.

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Availability of data and material The datasets generated and/or analyzed in the current study are not publicly available due to GDPR policies and restrictions because the information could compromise the privacy of the participants. However, the data are available from the corresponding author on reasonable request.

Declarations

Conflicts of interest The authors declare no conflict of interest.

Ethics approval The guidelines of the Declaration of Helsinki were followed, and the present study was approved by the ethics committee of the University of Liege Teaching Hospital (reference 2012/277), with two amendments in 2015 and 2018.

Consent to participate and consent for publication Informed consent was obtained from all participants involved in the study.

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