DOI: 10.1002/ncp.10780

CLINICAL RESEARCH

Calf circumference is an independent predictor of mortality in older adults: An approach with generalized additive models

Dalila Pinto de Souza Fernandes PhD[1] | **Leidjaira Lopes Juvanhol PhD**[1] | **Manuel Lozano PhD**[2] | **Andréia Queiroz Ribeiro PhD**[1]

[1] Department of Nutrition, Federal University of Viçosa, Viçosa, MG, Brazil

[2] Department of Preventive Medicine and Public Health, Food Sciences, Toxicology and Forensic Medicine, Faculty of Pharmacy, University of Valencia, Valencia, Spain

Correspondence
Dalila Pinto de Souza Fernandes, Nutrition Science Doctorate, Department of Nutrition, Federal University of Viçosa, PH Rolfs Avenue (no number), Viçosa, MG, 36570-000, Brazil.
Email: dalilaf.ufv@gmail.com

Funding information
Coordenação de Aperfeiçoamento de Pessoal de Nível Superior, Grant/Award Number: 23038.039412/2008-73; Conselho Nacional de Desenvolvimento Científico e Tecnológico, Grant/Award Number: 579255/2008-5; Fundação de Amparo à Pesquisa do Estado de Minas Gerais, Grant/Award Number: APQ-00594-17

Abstract

Background:There is a wide variation in the cutoff points of body mass index (BMI) and calf circumference (CC) , and it is necessary to assess their adequacy in predicting mortality, especially in the older adults in the community. This study aimed to investigate the association of low muscle mass and underweight with mortality in older adults, comparing different cutoff points.

Methods: This was a prospective study that included 796 older adults, not institutionalized, from a Brazilian city. Generalized additive models (GAMs) were used to identify cutoff points for CC and BMI, which were compared with values available in the literature. Survival analysis using Cox regression models was used to assess the independent association between these nutrition indicators and mortality.

Results: Over the 9 years of follow-up, 197 deaths (24.7%) occurred. Cutoff points established for CC and BMI as predictors of mortality were, respectively, <34.5 cm and <24.5. In the adjusted Cox models, older adults with a BMI <18.5 showed a significant increase in the risk of death (hazard ratio [HR], 2.57; 95% CI, 1.23–5.35). Higher mortality was observed among older adults with CC <34.5 cm (HR, 1.72; 95% CI, 1.27–2.33) and CC <31 cm (HR, 2.11; 95% CI, 1.44–3.10).

Conclusion: CC was an independent predictor of mortality, and the cutoff point identified by GAMs was higher than recommended by literature (31 cm). This study suggests a review of cutoff points for CC currently adopted to assess low muscle mass in older adults.

KEYWORDS
aging, body mass index, calf circumference, malnutrition, mortality, older adults

INTRODUCTION

The aging of the Brazilian population has increased rapidly. According to projections, the number of older adults must correspond to one-third of the population in 2060.[1] With the increase in life expectancy and epidemiologic transition, identification of modifiable risk factors responsible for early mortality in older adults should be central to public health.[2] Among these factors, nutrition can be modified to improve life expectancy and health, as well as preserve functional ability.[3]

Underweight in older adults is associated with higher mortality[4–10] and is a condition of malnutrition itself. This may be due to age-related factors, such as sensory loss of taste and smell, decreased masticatory capacity, and digestive problems,[11] as well as changes in body composition, with reduced fat and fat-free mass.[12] In particular, low muscle mass is associated with negative health outcomes, such as respiratory problems, sarcopenia, falls, fractures, longer hospital stays, disabilities, infections, and mortality.[13,14,15]

Among the tools available to study the association between nutrition status and mortality, anthropometric methods are commonly used, especially body mass index (BMI) [BMI= weight (Kg) / height^2 (m^2)].[16,17] However, body fat redistribution and muscle mass deficit, common in aging, can occur without significant changes in BMI.[18] Although BMI can be used to predict the risk of death,[19–21] calf circumference (CC) has been considered the most sensitive anthropometric index for assessing muscle mass in older adults to estimate their protein reserve and is an important measurement for assessing muscle mass loss.[22]

However, few studies have evaluated the relationship between low muscle mass from CC and the risk of death in older adults,[21,23–26] and studies with noninstitutionalized older adults in Brazil were not identified. In addition, a wide variation in the cutoff points have been adopted to estimate low muscle mass from CC[25,27–33] and underweight according to BMI.[4–10]

The hypothesis of the present study is that underweight (measured by BMI) and low muscle mass (measured by CC) are independent predictors of mortality in older adults. The aim was to investigate the association of underweight and low muscle reserve with mortality in older adults, comparing different cutoff points.

METHODS

Study design and participants

This prospective study was conducted with older adults aged ≥60 years, noninstitutionalized, living in a medium-sized city in the southeast region of Brazil (Viçosa). At the baseline of the study, the population of older adults in the city was 7980.

This population was identified through a census conducted during the National Older Adults Vaccination Campaign in 2008 (80% of vaccination coverage). From this census, a database was generated, which was supplemented with information from the records of the Universidade Federal de Viçosa servers, active and retired, from the Family Health Program, the Municipal Physiotherapy Service, the Women's Health Center, the Psychosocial Service, HiperDia, and Municipal Polyclinic. This database was organized in alphabetical order for sampling purposes. A 95% confidence level was considered to calculate the sample, with an estimated prevalence of the outcome of 50% and precision of 3.5%. This amount was increased by 20% for coverage of losses, totaling a sample of 858 individuals, selected by simple random sampling without replacement. The final sample of 796 older adults was obtained.

The inclusion criteria were interest in participating in the study, being ≥60 years old, and living in the community. Exclusion criteria were refusal to participate in the study, address not found, death, and older adults with physical limitations (wheelchair, amputated limb, or bedridden), which prevented the measurements of anthropometric measures.

Data collection

At the baseline (June 2009 to December 2010), home interviews were conducted by using a structured questionnaire and anthropometric assessment was conducted. To measure weight, a portable scale with a capacity of 199.95 kg and a precision of 50 g (model LC 200pp, brand Marte Balanças e Aparelhos de Precisão Ltda.®, Brazil) was used. The older adults wore light clothes and no adornments, warm clothing, or shoes. Height was measured with the aid of a stadiometer with a capacity of 2.13 m and an accuracy of 0.1 mm (Alturaexata®, brand, Brazil); the older adults stood barefoot, with their heels together, in an upright position, leaning against the wall and gaze fixed at the height of the horizon.[34] For the CC measurement, the older adults were seated with legs bent to form a 90° angle with the knee. A flexible and inelastic millimeter tape measure, with 1.80 m length and 0.1 mm precision, was wrapped around beneath the most protruding part of the left leg.[22]

The databases of the Mortality Information System, made available by the Viçosa Municipal Health Department, were consulted to obtain information on the deaths that occurred during the study period (June 2009 to July 2018). The death records and the basic cause of death of 185 baseline participants were identified.

When deaths were not registered in the system (n = 611), telephone calls and/or home visits were made to confirm the occurrence or not of death and basic cause of death, when relevant. At the end of the study, 197 deaths and 539 living participants were identified (7.5% were not found).

Study variables

Underweight and low muscle mass

The main explanatory variables of the study were underweight, assessed by BMI (calculated as the ratio between weight (kilograms) and height [meters squared]), and low muscle mass, assessed by CC. We considered the main cutoff points used for the BMI in studies with older adults, as follows. The Pan American Health Organization cutoff points (2001)[35] were adopted (underweight [<23] and without underweight [≥23]), as well as the cutoff points proposed by Lipschitz (1994)[36] (underweight [<22] and without underweight [≥22]) and nonspecific cutoff points for older adults adopted by the World Health Organization (WHO)[37] (underweight [<18.5] and without underweight [≥18.5]). The CC is used to estimate the protein reserve, an important measurement for assessing muscle mass loss in older adults.[22] For this anthropometric index, the cutoff points recommended by WHO (1995)[22] were adopted, which indicate a reduction in muscle mass when its value is <31 cm. In addition, considering the possibility of a nonlinear relationship between these anthropometric indices and the risk of death, a categorization was performed according to cutoff points obtained by generalized additive models (GAMs), as described below.

Covariables

- Sociodemographic (sex: male/female, age in years, and educational level: <4 years/≥4 years);
- Lifestyle (smoking habit: smoker, ex-smoker, or nonsmoker and physical exercise: yes/no);
- Food consumption (quality of the diet).

Food intake data were obtained by a usual dietary recall.[38] The estimation of the food consumption and the macronutrient and micronutrient value of the foods consumed were done with the DietPro version 5i software. Subsequently, the ingested portions of each food group were calculated according to the Food Guide for the Brazilian Population 2006.[39]

According to information found in the record, diet quality was assessed by using the Healthy Eating Index, revised[40] and validated for the Brazilian population (HEI-R) by Andrade et al (2013).[41] The score for food groups uses values from 0 to 100; the higher the score, the better the quality of the diet. Details can be seen in a previous publication.[42]

Statistical analysis

Descriptive data analysis was performed by using absolute and relative frequencies and estimation of central tendency and dispersion measures according to their distribution. The normality of quantitative variables was assessed by using the Kolmogorov-Smirnov test. In the bivariate analysis, the association of these variables with death was assessed by using Pearson chi-squared test for frequencies, Student *t*-test for means, and Mann-Whitney *U* test for medians.

GAMs were conducted to define the cutoff points of BMI and CC for the sample to predict risk of death. GAMs are an extension of generalized linear models, including nonparametric smoothing functions.[43] Smoothing parameters were selected by generalized cross validation by using the mgcv package in R.[44] Death, a dependent variable, presented a binomial distribution, and a smoothing function was included for each explanatory variable of interest.

Survival analyses were performed to assess the relationship between mortality and underweight and low muscle reserve. In these analyses, we used the variable time until the occurrence of death, defined in years, between the initial date (first interview) until the date of the event of interest (death) or end of the follow-up, that is, the date of the last contact (censoring). Participants whose death was not identified by the date of their last contact (July 2018) were censored.

Survival curves were used by the Kaplan-Meier method and the Peto log-rank test to compare the probability of survival according to interest groups. Cox regression models were used to estimate the independent association between low muscle mass and underweight and mortality, obtaining hazard ratio (HR) estimates and their respective 95% CIs. The assumption of proportionality of risk over time was assessed based on Schoenfeld residues.

The adjustment variables were identified by using a theoretical model and selected by using a directed acyclic graph, elaborated in the DAGitty program (http://www.dagitty.net/) (Supplementary Material). After that, three models were adjusted: model 1 (crude), model 2 (adjusted by sex, age, education, quality of diet, physical activity, and smoking), and model 3 (model 2 variables plus BMI). For all tests, the significance level was set at $\alpha = 0.05$. The analyses were performed by using Stata software, version 13.0 (Stata Corp, College Station, TX), and R software 3.5.2.

TABLE 1 Survival of the older adults according to baseline characteristics. Viçosa, MG, Brazil. 2009–2018

Characteristics	Total (N = 736)	Survivors (n = 539)	Nonsurvivors (n = 197)	*P*
Age, median (IQR), years	70.0 (64.0–77.0)	68.0 (64.0–74.0)	76.0 (69.0–82.0)	**<0.001**
Sex, female, n (%)	393 (53.4)	298 (55.3)	95 (48.2)	0.09
Educational level (<4 years), n (%)	595 (81.0)	425 (78.8)	170 (86.7)	**0.02**
Diet quality, average (SD)	64.5 (10.8)	64.76 (10.6)	63.8 (11.4)	0.30
No physical exercise, n (%)	522 (71.1)	362 (67.3)	160 (81.6)	**<0.001**
Smoker, n (%)	74 (10.1)	51 (9.5)	23 (11.9)	0.09
Ex-smoker, n (%)	237 (32.3)	165 (30.6)	72 (37.1)	
BMI, median (IQR)	26.5 (23.7–29.6)	26.5 (23.9–29.6)	25.9 (22.9–29.1)	0.06
BMI (according to WHO[37])				
Underweight (<18.5)	124 (19.8)	90 (14.4)	34 (5.4)	0.07
Normal weight (18.5–24.9)	272 (43.5)	215 (34.3)	57 (9.1)	
Overweight (>25)	230 (36.7)	187 (29.9)	43 (6.9)	
CC, median (IQR), cm	35.6 (33.1–38.2)	36.0 (33.5–38.5)	34 (31.3–36.8)	**<0.001**
CC, tertiles, cm				
Tertile 1 (<34)	258 (35.5)	157 (21.6)	101 (13.9)	
Tertile 2 (34–37)	226 (31.1)	182 (25.1)	44 (6.1)	**<0.001**
Tertile 3 (37.1–51)	242 (33.3)	196 (27.0)	46 (6.3)	

Abbreviation: BMI, body mass index; CC, calf circumference; IQR, interquartile range; WHO, World Health Organization.
Note: BMI is calculated as weight in kilograms divided by height in meters squared. We used the Pearson chi-squared test for comparison between proportions, Mann-Whitney *U* test for differences between medians, and Student *t*-test for differences between means.

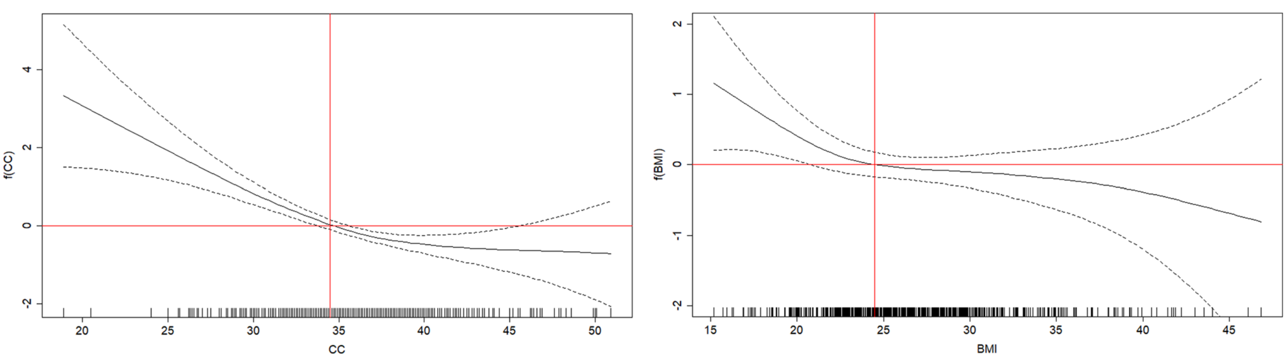

FIGURE 1 Smoothed function of mortality in older adults as a function of calf circumference (CC) and body mass index (BMI). Viçosa, MG, Brazil. 2009–2018. The solid black line represents the regression line, and the dotted lines represent the 95% CI

This study was directed according to the principles established in the Declaration of Helsinki and was approved by the Committee on Ethical Research of the Federal University of Viçosa (CAAE: 65782817.1.0000.5153). All participants who decided to participate in the study signed an informed consent form prior to their inclusion in the study.

RESULTS

Over the 9 years of follow-up, there were 197 deaths (24.7%), of which 51.8% were men, with a mean age of 76.1 ± 9.0 years. Compared with survivors, those who did not survive were older, had less education, did not exercise, and exhibited a lower median CC (Table 1) (Table S2).

According to the GAM, 34.5 cm was the cutoff point for CC, below which an increase in the risk of death is observed. In turn, the cutoff point identified for BMI was below 24.5 (Figure 1).

The probability of surviving, according to the survival curves, was statistically higher for older adults with a BMI of ≥18.5 and ≥22.0 (Figure 2) and with values of CC ≥ 31.0 cm and 34.5 cm (Figure 3).

Crude and adjusted HRs, with the respective 95% CIs, are presented in Table 2. Older adults with a BMI of <18.5 had a significant increase in the risk of death in the crude model (HR, 3.48; 95% CI, 1.70–7.12) and in

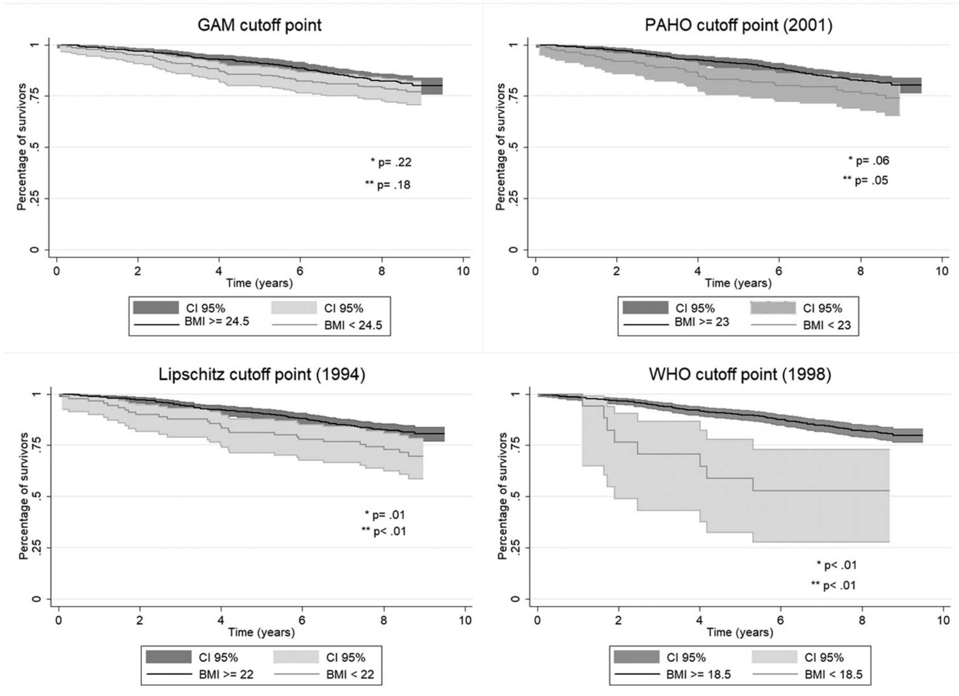

FIGURE 2 Survival curves (Kaplan-Meier) according to changes in BMI (calculated as weight in kilograms divided by height in meters squared). Viçosa, MG, Brazil. 2009–2018. *Log-rank test. **Peto test. BMI, body mass index; CC, calf circumference; GAM, generalized additive model; PAHO, Pan American Health Organization; WHO, World Health Organization

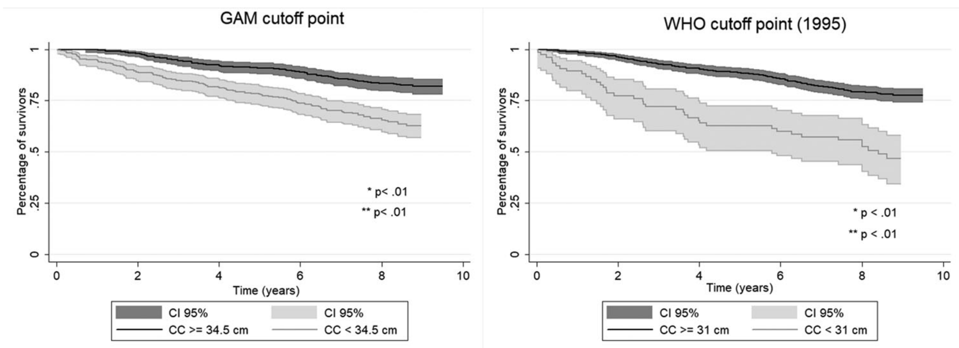

FIGURE 3 Survival curves (Kaplan-Meier) according to changes in CC. Viçosa, MG, Brazil. 2009–2018. *Log-rank test. **Peto test. CC, calf circumference; GAM, generalize additive model; WHO, World Health Organization

the adjusted model (HR, 2.57; 95% CI, 1.23–5.35). A significant association was observed for older adults with a BMI of <22.0 only in the crude model (HR, 1.71; 95% CI, 1.11–2.63). For the CC, significant associations were observed in both models considering the cutoff point of 34.5 (HR, 2.41; 95% CI, 1.81–3.20 and HR, 1.72; 95% CI, 1.27–2.33 for the crude and adjusted models, respectively). Likewise, significant associations were observed considering a CC of <31 cm, both in the crude model (HR, 3.11; 95% CI, 2.18–4.44) and in the adjusted model (HR, 2.11; 95% CI, 1.44–3.10). In model 3, after adjustments by model 2 and BMI, the risk of death increased significantly considering the cutoff points of the CC (<34.5 cm and <31.0 cm).

DISCUSSION

The main results of this study conducted with community-dwelling older adults show that underweight according to BMI (<18.5), and a probable low muscle mass measured by CC (<31.0 cm and <34.5 cm) was associated with higher

TABLE 2 HRs and 95% CIs for the association between underweight (assessed by BMI) and low muscle mass (assessed by CC) with mortality in older adults. Viçosa, MG, Brazil. 2009–2018

Variables	Model 1[a] HR (95% CI)	Model 2[b] HR (95% CI)	Model 3[c] HR (95% CI)
BMI, GAM cutoff			
≥24.5	1	1	NA
<24.5	1.25 (0.87–1.77)	0.90 (0.62–1.31)	NA
BMI, PAHO (2001) cutoff			
≥23.0	1	1	NA
<23.0	1.44 (0.98–2.13)	1.04 (0.68–1.57)	NA
BMI, Lipschitz (1994) cutoff			
≥22.0	1	1	NA
<22.0	1.71 (1.11–2.63)**	1.22 (0.79–1.92)	NA
BMI, WHO (1998) cutoff			
≥18.5	1	1	NA
<18.5	3.48 (1.70–7.12)*	2.57 (1.23–5.35)**	NA
CC, GAM cutoff, cm			
≥34.5	1	1	1
<34.5	2.41 (1.81–3.20)*	1.72 (1.27–2.33)*	2.36 (1.51–3.68)*
CC, WHO (1995) cutoff, cm			
≥31.0	1	1	1
<31.0	3.11 (2.18–4.44)*	2.11 (1.44–3.10)*	2.56 (1.47–4.49)*

Abbreviations; BMI, body mass index; CC, calf circumference; GAM, generalized additive models; HR, hazard ratio; PAHO, Pan American Health Organization; WHO, World Health Organization.
Note: BMI is calculated as weight in kilograms divided by height in meters squared.
NA: Not Applicable.
[a]Model 1: without adjustment.
[b]Model 2: adjusted for sex, age, education, quality of diet, physical activity, and smoking.
[c]Model 3: adjusted by model 2 and BMI.
*$P \leq .01$.
**$P \leq .05$.

mortality from all causes during the follow-up period. The cutoff point for CC identified through the GAM, from which there is also a significant increase in the risk of death in this population, was higher than that indicated in the scientific literature (31 cm). These results suggest that older adults with CC values of <34.5 cm already present a significant increase in mortality. Through aging, physiological changes occur in metabolic processes, sensory perception, and digestive functioning, in addition to changes in body composition.[45] These changes, in addition to socioeconomic factors, levels of physical activity, quality of diet, and functional capacity, interfere with nutrition status of older adults.[17,46,47]

Muscle mass influences energy and protein metabolism and is vital for maintaining good health, quality of life, and longevity.[48,49] Thus, among the changes in body composition resulting from aging, the loss of muscle can cause an increase in inflammation, which worsens muscle atrophy.[49] This process contributes to the development of sarcopenia, defined by progressive and generalized loss of strength and mass muscle, which is considered severe when there is also low physical performance[50].

CC, a simple anthropometric measurement, has been used as an indirect measurement of muscle mass in population studies[25,51,52] and has a good correlation with appendicular skeletal mass measured by dual-energy X-ray absorptiometry.[53] Therefore, international studies[21,23–26] consider CC to be an indicator of risk of death and a more effective measurement than other anthropometric indices, such as BMI. In the present study, low muscle mass, estimated by CC, was an independent predictor of mortality in older adults, as well as BMI.

Although CC is considered a good predictor of muscle mass reduction, studies have adopted different cutoff points, ranging from 29 cm to 35 cm;[5,30–33] among these, the WHO[22] cutoff point (31 cm) is the most used. According to the literature, lower CC indicates a reduction in leg muscle mass when subcutaneous fat is minimal, which is common in cases of malnutrition and chronic conditions.[31] Fat mass and leg strength, but not muscle mass, can independently predict physical function in older adults.[54] Considering the cutoff points obtained by the GAM, we observed a significant increase in the risk of death for CC values <34.5 cm. A higher cutoff point for this measurement compared with the WHO cutoff probably indicates that values below 34.5 cm (and not just below 31 cm) are already occurring loss of muscle mass or less muscle function. Thus, higher cutoff values should indicate the need to implement actions, such as dietary and physical activity interventions, with a view to improving muscle mass, strength, and physical performance, contributing to the reduction of early mortality in older adults.

The present study also observed a higher risk of death among older adults with low weight by BMI. Similar results were found in international[6–9,55] and national[10,19] studies. However, the different cutoff points, covariables used, and characteristics of the studied populations, which can affect the risk of death, make comparisons between studies difficult.[10,56] In addition, despite the fact that cutoff points for underweight/malnutrition in older adults are established in the literature (BMI < 22 and <23),[35,36] which indicate an association with higher mortality, we observe the association of BMI with mortality after adjustments for only a low cutoff point (BMI < 18.5), compatible with that established for adults.

CC has been considered a more appropriate measurement for clinical evaluation of older adults than BMI.[21,24] Considering that BMI, among its limitations, is not necessarily related to muscle mass, interventions related to low muscle mass are difficult. In addition, weight and height measurements are needed to calculate BMI, which can be difficult depending on the older person's assessment and their clinical condition. BMI is influenced by changes in aging, such as height reduction. In this sense, in addition to the CC being a sensitive measurement to assess muscle mass in older adults, it undergoes less changes with aging and can be obtained more easily, requiring only a tape measure and a trained health professional. The evaluation of CC can, therefore, be useful in clinical practice and in primary care to identify and monitor a probable reduction in muscle mass in older adults.

A limitation of the present study is that the weight, height, and CC measurements, as well as other characteristics of the sample, were obtained only at the baseline. Thus, it was not possible to assess changes over time in these measurements, as well as in eating habits, levels of physical activity, and smoking, and their influence on mortality. As strengths, we highlight that, in addition to using cutoff points from the literature, specific cutoff points were considered for the study population, allowing a more sensitive assessment of the association of anthropometric indices with mortality because changes resulting from aging differentiate the older population from other adults. Finally, only older adults living in the community were included in the study because the relationship between BMI and CC with mortality may be different for institutionalized older adults.

The CC was an independent predictor of mortality, and the cutoff point identified by the GAM was higher than that recommended by the literature (31 cm), indicating that there is an increased risk of death for values below 34.5 cm. In view of these results and considering CC as a simple measure for assessing early nutrition risk in older adults, this study suggests a review of the cutoff points for CC currently adopted to assess low muscle mass in older adults. This is essential to improve quality of life, prevent diseases, and promote healthy aging, postponing mortality.

ACKNOWLEDGEMENTS

We thank the older adults and their families for participating in the study. We also thank the team of researchers who collected the data and the Grupo de Estudo e Práticas sobre Envelhecimento, Nutrição e Saúde (GREENS) of the Department of Nutrition and Health of the Federal University of Viçosa.

CONFLICT OF INTEREST

None declared.

FUNDING INFORMATION

The present study was supported by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (Process no. 579255/2008-5). This work was also supported by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) (Process no. 23038.039412/2008-73) and the Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG) (Process APQ-00594-17). The funders had no role in the design, analysis or writing of this article.

AUTHOR CONTRIBUTIONS

Dalila Pinto de Souza Fernandes and Andréia Queiroz Ribeiro equally contributed to the conception and design of the research; Dalila Pinto de Souza Fernandes, Leidjaira Lopes Juvanhol, and Andréia Queiroz Ribeiro contributed to the acquisition and analysis of the data; Leidjaira Lopes Juvanhol, Manuel Lozano, and Andréia Queiroz Ribeiro contributed to the interpretation of the data; and Dalila Pinto de Souza Fernandes drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

ORCID

Dalila Pinto de Souza Fernandes PhD https://orcid.org/0000-0001-9683-7064

Leidjaira Lopes Juvanhol PhD https://orcid.org/0000-0001-8012-6006
Manuel Lozano PhD https://orcid.org/0000-0003-2046-5959
Andréia Queiroz Ribeiro PhD https://orcid.org/0000-0001-6546-1252

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Fernandes DPdS, Juvanhol LL, Lozano M, Ribeiro AQ. Calf circumference is an independent predictor of mortality in older adults: An approach with generalized additive models. *Nutr Clin Pract*. 2021;1–9. https://doi.org/10.1002/ncp.10780