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Calf circumference and 6-month survival in older patients with cancer

Circunferência da panturrilha e sobrevida em 6 meses em pacientes idosos com câncer

Circunferencia de la pantorrilla y supervivencia a 6 meses en pacientes mayores con cáncer

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ABSTRACT

Objective: To verify whether low CC (<31 cm) at the diagnosis is an independent risk factor for death in older persons with cancer. **Methods:** This study used secondary data from a cohort of older persons with cancer admitted from 2016 to 2020 in Northeast Brazil. Geriatric assessment and sociodemographic, background, and clinical data were collected upon admission. Inclusion criteria were patients who underwent MAN-based CC measurement. The primary outcome was death during the 180-day follow-up. Crude and adjusted hazard ratios (HR) were obtained from the Cox proportional hazard model, and the survival analysis used the Kaplan-Meier method according to CC. **Results:** From 414 included patients, 32.6% presented low CC. The overall mortality rate was 21.5% (89 deaths), 25.9% for the low CC group, and 19.7% for the adequate CC group. Low CC was not identified as an independent risk factor for death in the bivariate and multivariate analysis. The survival probability was not different among CC cutoff points. **Conclusion:** Low MM assessed using a CC cutoff point recommended by WHO and MNA did not present predictive value for death in older persons with cancer.

Keywords: Body composition, Calf circumference, Cancer, Older adults, Mortality.

RESUMO

Objetivo: Verificar se o CP baixo (<31 cm) ao diagnóstico é fator de risco independente para óbito em idosos com câncer. **Métodos:** Este estudo utilizou dados secundários de uma coorte de idosos com câncer internados de 2016 a 2020 no Nordeste do Brasil. Avaliação geriátrica e dados sociodemográficos, antecedentes e clínicos foram coletados na admissão. Os critérios de inclusão foram pacientes submetidos à medição de CP baseada em MAN. O desfecho primário foi morte durante o seguimento de 180 dias. As razões de risco (HR) brutas e ajustadas foram obtidas a partir do modelo de risco proporcional de Cox, e a análise de sobrevivência utilizou o método de Kaplan-Meier de acordo com CP. **Resultados:** Dos 414 pacientes incluídos, 32,6% apresentaram CP baixa. A taxa de mortalidade geral foi de 21,5% (89 óbitos), 25,9% para o grupo de CP baixo e 19,7% para o grupo de CP adequado. A baixa CP não foi identificada como fator de risco independente para óbito na análise bivariada e multivariada. A probabilidade de sobrevivência não foi diferente entre os pontos de corte do CP. **Conclusão:** A baixa MM avaliada através do ponto de corte de CP recomendado pela OMS e MAN não apresentou valor preditivo para óbito em idosos com câncer.

Palavras-chave: Composição corporal, Circunferência da panturrilha, Câncer, Idosos, Mortalidade.

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RESUMEN

Objetivo: Verificar si el CC bajo (<31 cm) en el momento del diagnóstico es un factor de riesgo independiente de muerte en personas mayores con cáncer. **Métodos:** Este estudio utilizó datos secundarios de una cohorte de personas mayores con cáncer ingresadas entre 2016 y 2020 en el Nordeste de Brasil. Al ingreso se recogió valoración geriátrica y datos sociodemográficos, antecedentes y clínicos. Los criterios de inclusión fueron pacientes que se sometieron a una medición de CC basada en MAN. El resultado primario fue la muerte durante el seguimiento de 180 días. Los índices de riesgo (HR) crudos y ajustados se obtuvieron a partir del modelo de riesgos proporcionales de Cox, y el análisis de supervivencia utilizó el método de Kaplan-Meier según CC. **Resultados:** De 414 pacientes incluidos, el 32,6% presentó CC baja. La tasa de mortalidad general fue del 21,5% (89 muertes), del 25,9% para el grupo de CC bajo y del 19,7% para el grupo de CC adecuado. El CC bajo no se identificó como un factor de riesgo independiente de muerte en el análisis bivariado y multivariado. La probabilidad de supervivencia no fue diferente entre los puntos de corte de CC. **Conclusión:** La MM baja evaluada mediante un punto de corte de CC recomendado por la OMS y la MNA no presentó valor predictivo de muerte en personas mayores con cáncer.

Palabras clave: Composición corporal, Circunferencia de la pantorrilla, Neoplasias, Anciano frágil, Mortalidad.

INTRODUCTION

Aging is a natural process that has led to changes in demographics and epidemiology, promoting an increased number of older individuals. Cheng X, et al. (2020), Chang AY, et al. (2017). Advanced age is closely associated with chronic conditions, including an elevated risk of cancer, which can be explained by the aging cellular process itself and its interaction with carcinogenesis. López-otín C, et al. (2013), Wildiers H, et al. (2014). Both cancer and advanced age can induce significant modifications in body composition, leading to nutritional syndromes such as sarcopenia and malnutrition. Jafari Nasabian P, et al. (2017). Consequently, older patients diagnosed with cancer accumulate risk factors for these abnormalities, particularly the loss of skeletal muscle mass (SM) and strength. Jafari Nasabian P, et al. (2017). As a result, they may experience a significant decrease in functionality, limited response to treatment, increased toxicity from chemotherapy at limiting doses, postoperative complications, and higher mortality rates (SOUSA IM, et al., 2020; PALMELA C, et al., 2017; KAZEMI SMR, et al., 2016; BARBALHO ER, et al., 2019).

Imaging techniques (e.g., magnetic resonance imaging and computed tomography) are opportunistically gold standard methods for assessing SM in patients with cancer. Castillo ML, et al. (2018). However, their widespread use is hindered by limited availability in some clinical scenarios. In this context, anthropometry emerges as an easy, and cost-effective alternative to estimate SM in clinical practice. Calf circumference (CC), an anthropometric marker, is a double-indirect method to estimate SM in older persons, addressing the issues in settings with limited technological resources (WORLD HEALTH ORGANIZATION (1995), CRUZ-JENTOFT AJ, et al., 2019; CHEN LK, et al., 2019; BARAZZONI R, et al., 2022). Previous evidence underscored the prognostic significance of CC, as an independent predictor of mortality in older persons with chronic diseases, including cancer (WEI J, et al., 2022; GONZALEZ MC, et al., 2021). Moreover, low CC has been highlighted as a prognostic factor, irrespective of considered individually and compared to body mass index (BMI), or combined with nutritional parameters (e.g., mini-nutritional assessment [MNA]) (KAISER MJ, et al., 2009; TSAI AC and CHANG T, 2011; GUIGOZ Y, et al., 2009; SALES LT, et al., 2017; SOUSA IM, et al., 2022).

The use of CC in clinical practice relies on the establishment of specific cutoff points to define low SM. The World Health Organization (WHO) recommends a CC cutoff point (<31 cm) to identify low SM and functionality in older individuals of both sexes. Consequently, other tools for assessing nutritional status, such as MNA – both in its full and short-form (MNA-SF), have adopted this value to classify low SM through CC (KAISER MJ, et al., 2009). It's important to note that this cutoff point was derived from a prospective study exclusively involving older females (>70 years) in France. Rolland Y, et al. (2003), thus caution is needed when applying it in clinical settings. Subsequent to this WHO recommendation, numerous studies have proposed higher cutoff points, accounting for differences in ethnicities and sex (CHEN LK, et al., 2019; BARAZZONI R, et al., 2022;

BARBOSA-SILVA TG, et al., 2016). However, determining the optimal cutoff point to define low SM using CC remains a subject of ongoing debate. Despite the issues presented, the revised European Working Group on Sarcopenia in Older People (EWGSOP 2) in 2019, still considers the WHO classification of CC <31 cm as an operational strategy for diagnosing sarcopenia (CRUZ-JENTOFT AJ, et al., 2019). Our hypothesis suggests that the adoption of the WHO CC classification may not adequately account for sex and clinical differences, potentially diminishing its prognostic value in other populations, such as Brazil.

A systematic review and meta-analysis including studies published until November 1, 2021, evaluated the prognostic value for death of low CC in adults and older persons with different cutoff points in diverse clinical contexts Wei J, et al. (2022);. It revealed that CC cutoff points of below or equal to 33 and 34 cm for women and men, respectively, were more accurate than the CC cutoff point of below 31 cm for both sexes (WEI J, et al., 2022).

Also, studies indicated that these CC cutoff points (≤ 33 cm for women and ≤ 34 cm for men) is as independent predictive values for death in adults and older persons with cancer Sousa IM, et al. (2020); Sousa IM, et al. (2022). Although a Chinese multicenter study established other CC cutoff points (< 30 cm for women and < 32.8 cm for men) for risk of death in individuals with cancer, the study did not indicate CC as an independent risk factor for death in persons older than 60 compared with those younger (WORLD HEALTH ORGANIZATION, 2019).

To date, there is no consensus regarding the optimal cutoff for defining low SM using CC that effectively predicts the risk of mortality in older patients with cancer. Therefore, this study aimed to evaluate whether the CC cutoff point for low muscle mass recommended by the WHO (< 31 cm) presents predictive value for mortality in older patients with cancer already at nutritional risk, during a 180-day follow-up period.

METHODS

Study design and subjects

This is a secondary analysis of a prospective cohort study Sales LT, et al. (2017) with data collection conducted between January 2016 and April 2020. Consecutive older patients (≥ 60 years) attending to consultations at *Instituto de Medicina Integral Prof. Fernando Figueira – IMIP* (Recife, Pernambuco, Brazil) were conveniently sampled. Additional inclusion criteria were cancer diagnoses confirmed by histology, cytology, or immunohistochemistry, who did not receive any oncological treatment, except for surgery. Given that the clinical protocol routine was adopted for this study, patient selection proceeded as follows: an initial screening was conducted using the MNA-SF. Only patients initially classified as being at nutritional risk underwent a comprehensive MNA evaluation and had their CC measured, thus being opportunistically included in this analysis. Patients with physical limitations resulting in lower limb atrophy were excluded. The study was approved by the Institution Ethics Committee in compliance with the Declaration of Helsinki, and Reolution no. 466/2012 of the National Health Council (CAAE: 53869221.9.0000.5201), opinion number (5.158.744). All patients provided their written informed consent.

Clinical characteristics and covariates

A trained multidisciplinary team performed the initial assessments, comprising a comprehensive geriatric assessment and sociodemographic, background, and clinical data collection. Patients were followed-up for up to 180 days, to access mortality as the main outcome. Details regarding clinical outcomes data collection can be found in our previous publication Sales LT, et al. (2017) .Data on age, sex, self-reported skin color, alcohol consumption, smoking, family income, and history of hospitalization in 30 days prior to data collection were accessed. Family income was the sum of the individual incomes of people living in the same household and was expressed as minimum wage (MW) for the collection year. One MW was set as the minimum family income, considering it is the closest to the poverty line in Brazil.

Clinical data encompassed information on metastatic disease and primary tumor site, including prostate, breast, lung, digestive system, gynecological system, or others. The geriatric assessment utilized established cutoff points. Wildiers H, et al. (2014); World Health Organization, (2019) for several parameters: Polypharmacy: defined as ≥ 5 medications (GNJIDIC D, et al., 2012). Comorbidities: accessed using the

Charlson Comorbidity Index (CCI), with a score > 2 indicating the occurrence of multiple comorbidities (CHARLSON ME, et al., 1987). Functionality: measured using the Karnofsky Performance Status Scale (KPS), with a score ≤50% representing reduced functionality (Karnofsky DA and Burchenal J, 1949). Risk of falls: determined using the Timed Up and Go test, classified as low (< 13.5 seconds), medium or high risk (≥13,5 seconds) (Podsiadlo D and Richardson S, 1991); and physical activity: estimated by the International Physical Activity Questionnaire (IPAQ) short version. For analysis, patients were categorized as sedentary (<10 min/week) or active (CRAIG CL, et al., 2003).

Nutritional assessment

Body weight (kg) and height (m) were used to calculate BMI (kg/m^2), classified according to the Pan American Health Organization (PAHO). CC measurements were taken at the largest point of the calf. Patients stood upright, barefoot, with feet apart and weight evenly distributed. An inelastic tape with a centimeter scale (CESCORF ®), was utilized. The tape was placed around the maximum circumference of the calf, which was determined by gently adjusting the tape up and down on a plane perpendicular to the longitudinal line of the calf (WORLD HEALTH ORGANIZATION, 1995). Low CC was classified according to the WHO classification, Guigoz Y, et al. (2009) <31 cm. Patients initially classified as at nutritional risk by MNA-SF, underwent full MNA evaluation and had their nutritional status redefined – being classified as it follows: malnourished (< 17 points), at risk of malnutrition (17 to 23.5 points), and well-nourished (24 to 30 points) (GUIGOZ Y, et al., 2009; CHRISTNER S, et al., 2016).

Statistical analysis

Data was analyzed using STATA 13.1SE (Stata Corporation, College Station, TX, USA). Categorical variables were presented as absolute (n) and relative frequencies (%), compared using Pearson's chi-squared test. Continuous variables were described as mean and standard deviation (SD) and compared using independent Student's "t" test. The association between low CC and overall survival (OS) was assessed by the Kaplan-Meier (KM) curves, considered significant if log-rank p <.05. Subsequently, assuming proportional hazards, Cox hazard regression analysis was conducted, utilizing both crude and multivariate models, to assess the independent association between low CC and 180-day mortality. Hazard ratios (HR) along with their corresponding 95% confidence intervals (CI) were estimated. Variables with a p-value below 0.20 in the crude analysis were included in the initial model for the multivariate regression using backward stepwise method. Those reaching a p value below 0.05, adjusted by CC, remained in the final model. For all analyses, statistical significance was set at 5%.

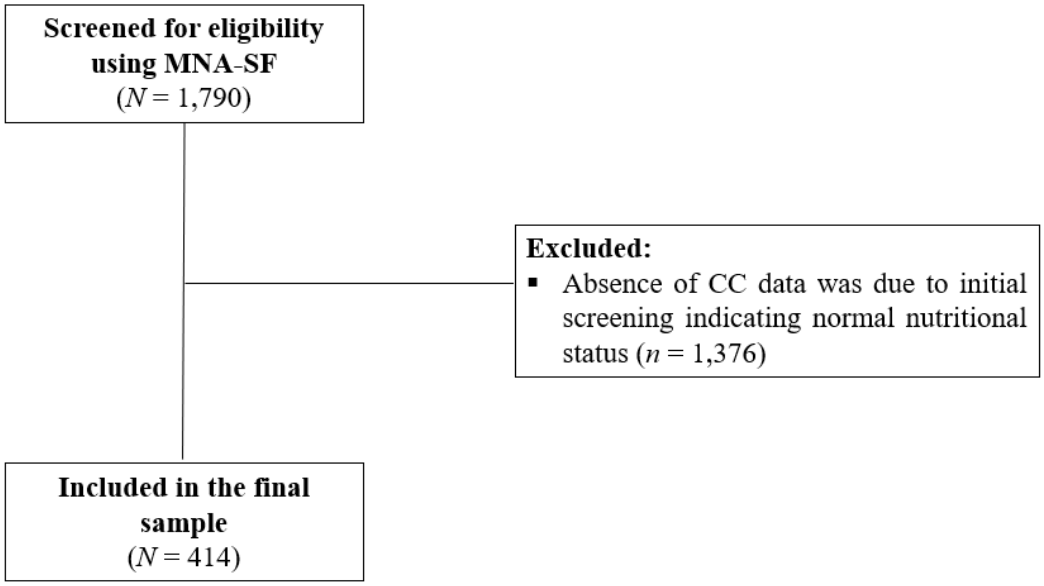
RESULTS

Figure 1 provides a study flowchart. Initially, 1,790 patients were screened for eligibility. After exclusions, the final sample included 414 patients, aged from 62 to 99 years, mostly males (52.4%). Gastrointestinal system tumors were the most common primary site (40.1%), followed by prostate (21.5%). Metastasis was reported in 38.9% of patients. Only 18.1% presented with polypharmacy. Most patients (91.8%) showed preserved functionality according to KPS, while 46.3% had a high or medium risk of falls. 40.6% were sedentary. 48% presented with underweight (BMI <23kg/m^2), and among these, 53.6% exhibited low CC. 32.6% (n = 135) had low CC. According to the MNA classifications, 66.2% were at risk of malnutrition, while 14% were already malnourished at the time of diagnosis. 6-month mortality occurred in the 21.5% of the sample (n = 89) (**Table 1**). **Table 1** additionally displays the comparisons between low and adequate CC (≥ 31 cm). 6-month mortality was observed in 25.9% *versus* 19.4% in the low and adequate CC groups, respectively, despite non-significant (p = 0.130). Except for the MNA full version and BMI, no differences were observed between groups.

Despite patients with low CC presenting a higher risk for mortality than those with adequate CC, in the bivariate analysis, no statistical significance was found (HR = 1.34; 95CI [0.88 - 2.06]; p= 0.173). The following variables were associated with early mortality with p< 0.20 (not shown in the tables): male sex; family income ≤ 1 MW; smoking or alcohol consumption (current or former); primary tumor site; metastatic disease; recent hospitalization; polypharmacy; comorbidities; reduced functionality; high and medium risk of falls; sedentary patients; and malnourished and at risk of malnutrition patients were included in the initial model for the

multivariate regression. The risk factors for mortality identified in the multivariate analysis adjusted by low calf circumference (<31 cm) were male, polypharmacy; poor functionality; primary tumor site, and metastatic disease (**Table 2**). **Figure 2** demonstrate de KM curve for association between low CC and OS. No significant differences were observed survival probability for low CC (0.74; [95% CI 0.66 – 0.81]) and adequate CC (0.81; [95% CI 0.76 – 0.85]) (log-rank $p = 0.171$).

Figure 1. Study flowchart.



Source: Santos PAA, et al., 2025.

Table 1. Characteristics of 414 older patients with cancer according to their calf circumference classification.

Variables	Overall (*N* = 414)	Calf circumference		*p*
		< 31 cm	≥ 31 cm	
Age (years)				
mean ± SD	75.3 ± 7.3	76.1 ± 7.3	74.8 ± 7.2	0.094
Sex, n (%)				0.318
Male	217 (52.4)	66 (30.4)	151 (69.6)	
Female	197 (47.6)	69 (35.0)	128 (65.0)	
Skin color, n (%)				0.119
White	126 (30.4)	47 (37.3)	79 (62.7)	
Black	48 (11.6)	19 (39.6)	29 (60.4)	
Brown	227 (54.8)	63 (27.7)	164 (72.3)	
Yellow or indigenous	13 (3.2)	6 (46.1)	7 (53.9)	
Family income, n (%)				0.881
≤ One minimal wage	137 (33.1)	44 (32.1)	93 (67.9)	
> One minimal wage	277 (66.9)	91 (32.8)	186 (67.2)	
Smoking, n = 408 (%)				0.860
Current and former smokers	240 (58.8)	78 (32.5)	162 (67.5)	
Non-smoker	168 (41.2)	56 (33.3)	112 (66.7)	
Alcohol consumption, n = 408 (%)				0.661
Current and former consumer	219 (53.7)	74 (33.8)	145 (66.2)	
Non-consumer	189 (46.3)	60 (31.7)	129 (68.3)	
Primary tumor site, n (%)				0.551
Lung	33 (8.0)	14 (42.4)	19 (57.6)	
Gastrointestinal tract	166 (40.1)	59 (35.5)	107 (64.5)	
Breast	48 (11.6)	12 (25.0)	36 (75.0)	
Gynecological	49 (11.8)	15 (30.6)	34 (69.4)	

Prostate	89 (21.5)	27 (30.3)	62 (69.7)	
Other	29 (7.0)	8 (27.6)	21 (72.4)	
Metastatic disease, n (%)				0.747
Yes	161 (38.9)	51 (31.7)	110 (68.3)	
No	253 (61.1)	84 (33.2)	169 (66.8)	
Recent hospitalization, n = 412 (%)				0.332
Yes	69 (16.8)	19 (27.5)	50 (72.5)	
No	343 (83.2)	115 (33.5)	228 (66.5)	
Polypharmacy (≥ 5 medications), n (%)				0.225
≤ 5	339 (81.9)	115 (33.9)	224 (66.1)	
> 5	75 (18.1)	20 (26.7)	55 (73.3)	
Comorbidities (CCI), n (%)				0.241
<2	272 (65.7)	94 (34.6)	178 (65.4)	
≥ 2	142 (34.3)	41 (28.9)	101 (71.1)	
Functionality (KPS), n = 412 (%)				0.261
≤ 50%	34 (8.2)	14 (41.2)	20 (58.8)	
> 50%	378 (91.8)	120 (31.8)	258 (68.2)	
Risk of falls (TUG), n = 408 (%)				0.578
Low	221 (54.7)	71 (32.1)	150 (67.9)	
Medium	129 (31.9)	39 (30.2)	90 (69.8)	
High	58 (14.4)	22 (37.9)	36 (62.1)	
Physical activity (IPAQ), n = 411 (%)				0.375
Sedentary	167 (40.6)	59 (35.3)	108 (64.7)	
Insufficiently active, active, or very active	244 (59.4)	76 (31.1)	168 (68.9)	
MNA – full version, n (%)				<0.001
Normal nutritional status (> 23.5)	82 (19.8)	9 (10.9)	73 (89.1)	
At risk of malnutrition (17 to 23.5)	274 (66.2)	83 (30.3)	191 (69.7)	
Malnourished (< 17.0)	58 (14.0)	43 (74.1)	15 (25.9)	
Body mass index (BMI), n=408 (%)				<0.001
Underweight (<23.0)	196 (48.0)	105 (53.6)	91 (46.4)	
Normal range (23.0 to 28.0)	127 (31.1)	21 (16.5)	106 (83.5)	
Overweight (>28 to 30)	33 (8.1)	3 (9.1)	30 (90.9)	
Obesity (≥ 30)	52 (12.8)	5 (9.6)	47 (90.4)	

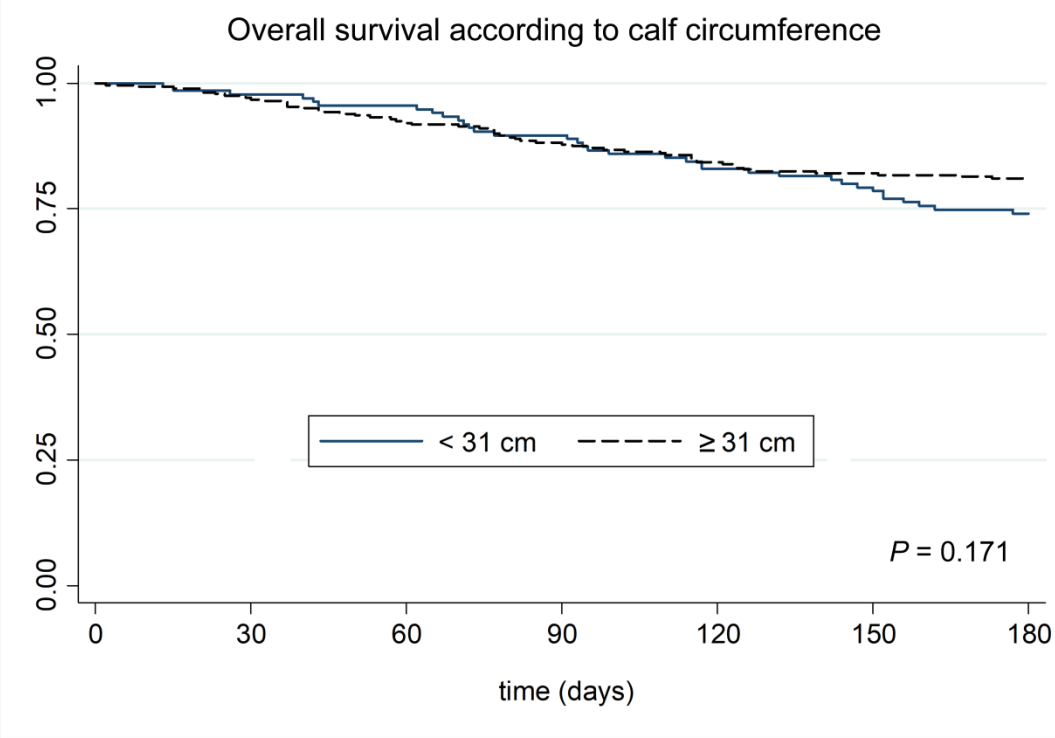
CCI: Charlson Comorbidity Index; IPAQ: International Physical Activity Questionnaire; KPS: Karnofsky Performance Status Scale; MAN: Mini Nutritional Assessment; Other: (bladder, kidney, retroperitoneum, ureter, urethra, adrenal, skin and annexes, epiglottis, nasal region, larynx, nasopharynx, ear, soft tissues, mediastinum, central nervous system, melanoma, neuroendocrine, thyroid, non-Hodgkin lymphoma, and testicle); *p*: Pearson's chi-square test or Student t-test; TUG: Timed Up and Go 8.

Table 2. Cox Regression Analysis: Multivariate model adjusted for calf circumference and its relation to the risk of 180-day mortality of older patients with cancer.

Variable	Bivariate			Multivariate		
	HR	(95% CI)	*P*	aHR	(95% CI)	*p*
Male	1.51	(0.99- 2.32)	0.059	1.81	(1.11 – 2.96)	**0.017**
Polypharmacy	1.68	(1,05-2.71)	**0.030**	1.89	(1.16 – 3.09)	**0.011**
Functionality	3.34	(1.94-5.75)	**< 0.001**	2.96	(1.70 – 5.16)	**< 0.001**
Primary tumor site			**< 0.001**			**< 0.001**
Lung	16.9	(5.73-49.63)		12.32	(4.05 – 37.51)	
Gastrointestinal tract	8.04	(2.90-22.24)		9.49	(3.37 – 26.70)	
Breast	2.41	(0.65-8.97)		4.42	(1.12 – 17.52)	
Gynecological	2.33	(0.63-8.68)		4.25	(1.05 – 17.24)	
Other	4.26	(1.14-5.86)		4.91	(1.31 – 18.47)	
Metastatic disease	3.36	(2.17-5.20)	**< 0.001**	2.43	(1.52 – 3.91)	**< 0.001**
Low calf circumference (<31 cm)	1.34	(0.88-2.06)	0.173	1.14	(0.73 – 1.79)	0.559

HR: hazard ratio; aHR: Adjusted HR; 95% CI: 95% confidence interval; Polypharmacy (≥ 5 medications); Functionality KPS [Karnofsky Performance Status Scale (KPS ≤ 50%)]; Other: bladder, kidney, retroperitoneum, ureter, urethra, adrenal, skin and annexes, epiglottis, nasal region, larynx, nasopharynx, ear, soft tissues, mediastinum, central nervous system, melanoma, neuroendocrine, thyroid, non-Hodgkin lymphoma, and testicle.

Figure 2. Kaplan-Meier curve: association between low calf circumference (<31 cm) and overall survival of older patients with cancer, during 180 days of follow-up.



Source: Santos PAA, et al.,2024.

DISCUSSION

To the best of our knowledge, this is the first study investigating the predictive value of WHO-derived low CC (<31 cm) in relation to 6-month mortality of geriatric patients with cancer. Our main findings revealed in both analysis (KM and Cox regression) that this CC classification was not associated with OS and mortality hazard in our cohort.

Beyond muscle mass, low CC also is an indicator of malnutrition, Sousa IM, et al. (2022); that t is a common geriatric syndrome with negative outcomes, including mortality, Wildiers H, et al. (2014). In a cohort with 180 patients with cancer who were ≥ 65 years were included in the study, Isleyen ZS, et al. (2023); also observed that malnutrition was associated with polypharmacy, frailty and a higher risk for all-cause mortality. In fact, malnutrition-sarcopenia syndrome is a predictor of worse clinical outcomes in hospitalized patients (SOUSA IM, et al., 2022).

Prior studies and guidelines have employed a range of different CC cutoff points to define low SM in diverse health and clinical populations, including cancer. For instance, EWGSOP 2 in their operational definition for sarcopenia, considers CC < 31 cm as a marker of low muscle mass. Cruz-Jentoft AJ, et al. (2019). In contrast, the Asian Working Group on Sarcopenia in Older People (AWGSOP) suggested different CC cutoff points (< 33 cm for women and < 34 cm for men) (CHEN LK, et al., 2020). Meanwhile, the 2022's Global Leadership Initiative on Malnutrition (GLIM) recommends CC cutoff points adjusted by BMI for adult malnutrition diagnosis (< 32 cm for women and < 33 cm for men) Barazzoni R, et al. (2022). Notably, there is an additional growing recognition of the need for identifying low CC in patients with excess weight, which adjustments based on BMI were proposed, Gonzalez MC, et al. (2021). This is now endorsed by the GLIM experts, which advocates that CC cutoff points should be population-specific and adjusted by BMI (Barazzoni R , et al., 2022).

This current scenario reflects a novel perspective on CC use as a marker of muscle mass in clinical practice. It has encouraged the growing evidence to rethink previously universally applied standardized values, such as WHO, recognizing the importance of adopting more tailored approaches. Contrastingly, previous studies using

higher cutoff values have shown the predictive significance of low CC concerning mortality in cancer. Sousa IM, et al. (2020); Sousa IM, et al. (2022); Silva JR, et al. (2019); Yin L, et al. (2022). In this context, we hypothesize that applying the universal cutoff value (<31 cm) in a Brazilian cohort of older patients with cancer, although convenient, may not accurately reflect the prognostic significance of muscle mass, as it is largely influenced by age, sex, and population-specific factors (D'ALMEIDA CA, et al., 2020; LIMA J and MORAES SF, 2022).

Our findings highlight additional concerns. It's important to note that patients were conveniently selected based on their initial classification using the MNA-SF (at risk), even if they were subsequently reclassified as having normal nutritional status following a full MNA evaluation. This suggests that we already had a population likely facing nutritional risk or even malnutrition. Indeed, nearly 70% of the sample was found to be from at risk-to-malnutrition after full MNA evaluations. This prompts us to question whether very low CC values, combined with the previously mentioned limitations, could indicate an additional risk factor, considering that impaired nutritional status (assessed by MNA) itself can independently predict mortality in older patients (SODERSTROM L and ROSENBLAD A, 2023; DACOSTA PEREIRA JP, et al., 2023). Furthermore, considering that older patients often experience redistribution of body composition, CC may not only reflect muscle mass but also intermuscular adiposity (FAYH APT and SOUSA IMGM, 2020), diluting its prognostic value.

Our additional findings revealed that functionality emerged as the clinical variable with the highest mortality hazard. Preserved functionality (KPS) not only ensures autonomy in older individuals but also correlates with muscle mass, sarcopenia, risk of falls, frailty (EDWARDS BJ, et al., 2020). In addition, functionality serves dual roles as it also presents prognostic value, being associated with OS of older patients with cancer (KÄSMANN L, et al., 2016). Furthermore, evidence demonstrates that approximately 50% of the whole body's muscle mass is concentrated in the lower limbs, Janssen I, et al., (2000) which tends to decline earlier than muscle mass in the upper limbs (CANDOW DG and CHILIBECK PD, 2005). Therefore, measuring CC may offer insights associated with other prognostic factors, such as frailty and prolonged length of hospital stay (LANDI F, et al., 2014; SOUSA IM, et al., 2023). Hence, we advocate for its inclusion in clinical assessments of older persons with cancer.

This study has limitations that warrant acknowledgments. The relatively small sample size and single-center, observational design preclude establishing causal relationships. The secondary nature of data collection, along with the initial screening method using MNA-SF, may introduce selection bias. Furthermore, our analysis was limited to the CC classification from MNA, preventing us from analyzing CC as continuous variables or employing alternative cutoff values, which is a significant limitation. It is also possible that our regression models overlooked residual effects of important variables influencing our findings. Limitations offer opportunities for future studies with larger and more representative sample sizes of older patients with cancer. Such studies could employ the WHO-derived low CC cutoff, investigate its prognostic significance, and compare to different CC cutoff points to further validate our findings.

CONCLUSION

In conclusion, this study demonstrated that the WHO-derived low CC (<31 cm) had limited predictive value during a 180-day follow-up for older patients with cancer. Our findings add to the expanding body of evidence highlighting the importance of using sex- and population-specific cutoff points, and more recently, adjustments for BMI, to accurately assess muscle mass through CC. By considering phenotypic individuality, these approaches enhance the clinical significance of CC in clinical practice. As a clinical recommendation, the utilization of CC is essential due to its simplicity and ease as an anthropometric measure. It could benefit individuals by contributing to personalized therapy, ultimately improving their care and prognosis.

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