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Risk of sarcopenia in women with breast cancer: a comparative analysis of screening tools

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Abstract

Background Sarcopenia is characterized by the loss of muscle strength and mass and is associated with poorer clinical outcomes in women with breast cancer. However, no specific tool is capable of assessing the risk of sarcopenia in this population. Therefore, the aim of the present study was to compare the performance of SARC-F, SARC-CalF, and BMI-adjusted SARC-CalF as screening tools for the risk of sarcopenia in women with breast cancer.

Methods An observational cross-sectional study was conducted involving women with breast cancer diagnosed in the previous 12 months. The risk of sarcopenia was identified by SARC-F, SARC-CalF, and BMI-adjusted SARC-CalF. As proposed by the EWGSOP2, sarcopenia was defined as low muscle strength (grip strength: <23.0 kg) and appendicular skeletal muscle mass index < 6.38 kg/m^2 (determined by dual-energy X-ray absorptiometry). The performance of the screening tools was assessed by calculating specificity, sensitivity, positive and negative predictive values, and area under the ROC curve (AUC). AUC values were compared using DeLong's test.

Results This study included 168 women with a mean age of 54.8 ± 11.3 years. The prevalence of sarcopenia risk ranged from 10.1 to 36.6%, depending on the screening tool employed. The prevalence of sarcopenia was 8.3%. Using the presence of sarcopenia as reference, the SARC-F had an AUC of 0.550 [(0.396–0.703) $p = 0.54$], sensitivity of 21.4%, and specificity of 85.7%; the SARC-CalF had an AUC of 0.790 [(0.654–0.927) $p < 0.001$], sensitivity of 42.8%, and specificity of 92.2%; the BMI-adjusted SARC-CalF had an AUC of 0.521 [(0.385–0.658) $p = 0.08$], sensitivity of 28.6%, and specificity of 63.0%. Therefore, the SARC-CalF tool had low sensitivity and high specificity.

Conclusion SARC-CalF performed the best compared to the alternatives provided. However, based on the current results, it may be necessary to reconsider the use of either of these instruments as a screening option for sarcopenia risk in women with breast cancer.

Keywords Muscle strength, Muscle mass, Sarcopenia, Screening, Diagnosis, Oncology

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Introduction

Breast carcinoma and antineoplastic treatment promote changes in body composition that include an increase in fat mass and a decrease in skeletal muscle mass, which can progress to sarcopenia [1]. Sarcopenia is correlated with negative clinical outcomes in individuals with cancer, such as an increased risk of infection and chemotherapy toxicity, postoperative complications, a poor response to antineoplastic treatment, an increased risk of recurrence/metastasis, and a lower overall survival rate [1, 2].

Despite the associated risks, sarcopenia is often overlooked or not assessed properly [1]. The SARC-F questionnaire was designed and validated as a screening tool for the risk of sarcopenia [3] and is endorsed by the European Working Group on Sarcopenia in Older People - revised version (EWGSOP2) [4]. However, previous studies assessing the risk of sarcopenia in healthy older adults of both sexes found that this tool has low sensitivity, which may compromise its effectiveness in detecting individuals at risk of sarcopenia [5, 6].

To improve the effectiveness of this tool, the inclusion of calf circumference (CC) has been proposed, which is considered an indicator of muscle mass reserve [7] not included in the original version [3, 4]. Comparing SARC-Calf to SARC-F in older adults, different studies have shown an average increase of 30.0% in the ability to identify the risk of sarcopenia [8–10]. However, the applicability of CC is problematic, as its sensitivity can be affected by sex, age, and muscle mass [9, 10].

The accumulation of subcutaneous fat in the lower region is notably greater in women, which, in some cases, may interfere with the results. This is especially true in patients with breast cancer, in whom an increase in adipose tissue and reduction in skeletal muscle mass can occur simultaneously [1, 9, 11]. However, studies investigating the accuracy of both tools under the current definition of sarcopenia [4] in women with breast cancer are scarce. Moreover, obesity, sarcopenia, or low weight/cachexia can coexist in this population group, which compromises the usefulness of CC [1, 12]. Despite the recognition of the impact of changes in body composition in women with breast cancer, gaps remain in the implementation of accessible tools for the early identification of the risk of sarcopenia in this population. The use of appropriate tools for this assessment can contribute to more effective nutritional and physical interventions, reducing the impact of the disease and prolonged treatment on the functioning and quality of life of affected individuals. To minimize this bias, we used CC adjusted by the body mass index (BMI), as proposed by Gonzalez et al. [10], hypothesizing that this adjustment could lead to more accurate predictions of muscle mass [10]. The risk of sarcopenia is under-investigated in women with breast cancer and the performance of the instruments proposed thus far has not been assessed in this population. Therefore, the aim of the present study was to compare SARC-F, SARC-CalF, and BMI-adjusted SARC-CalF as screening tools for the risk of sarcopenia in women with breast cancer.

Methods

Study design

A cross-sectional study with non-probabilistic, consecutive sampling was undertaken at the mastology outpatient clinic of a university hospital center in a capital city located in the southeastern region of Brazil from August 2021 to November 2023.

Study population

Women ≥ 30 years of age with a confirmed diagnosis of breast cancer in the previous 12 months, not having another malignant neoplasm or having received prior treatment for another type of tumor and without metastasis or recurrence were included in the study [13]. After confirming the diagnosis of breast cancer, eligible patients were contacted by telephone and invited to participate in the study or were referred by the medical team. At least four attempts were made to minimize the possibility of selection bias. The volunteers were instructed to be present at the place where they received care on a previously scheduled day and time based on the patient's availability on days of medical appointments and/or antineoplastic treatment.

Sample size calculation

The sample size was calculated with the aid of the G*Power software, considering an alpha of 5%, minimum power of 95%, and an effect size of 0.5 for the chi-square test, resulting in a minimum sample of 80 participants, to which 20% was added to compensate for possible losses or refusals, totaling a minimum of 116 participants.

Throughout the study, 265 women with breast cancer were assisted by the medical team and invited to participate in the research. Among those who agreed to participate in the assessment, 47 did not agree to participate in the study, 40 missed the appointment or could not be contacted by telephone, eight died before the interview, and ten did not perform the DXA exam, resulting in 168 participants (Fig. 1).

Data collection

Data were collected through face-to-face interviews based on a previously established protocol. All researchers involved in the study received training to administer the instruments as well as to measure the variables of interest.

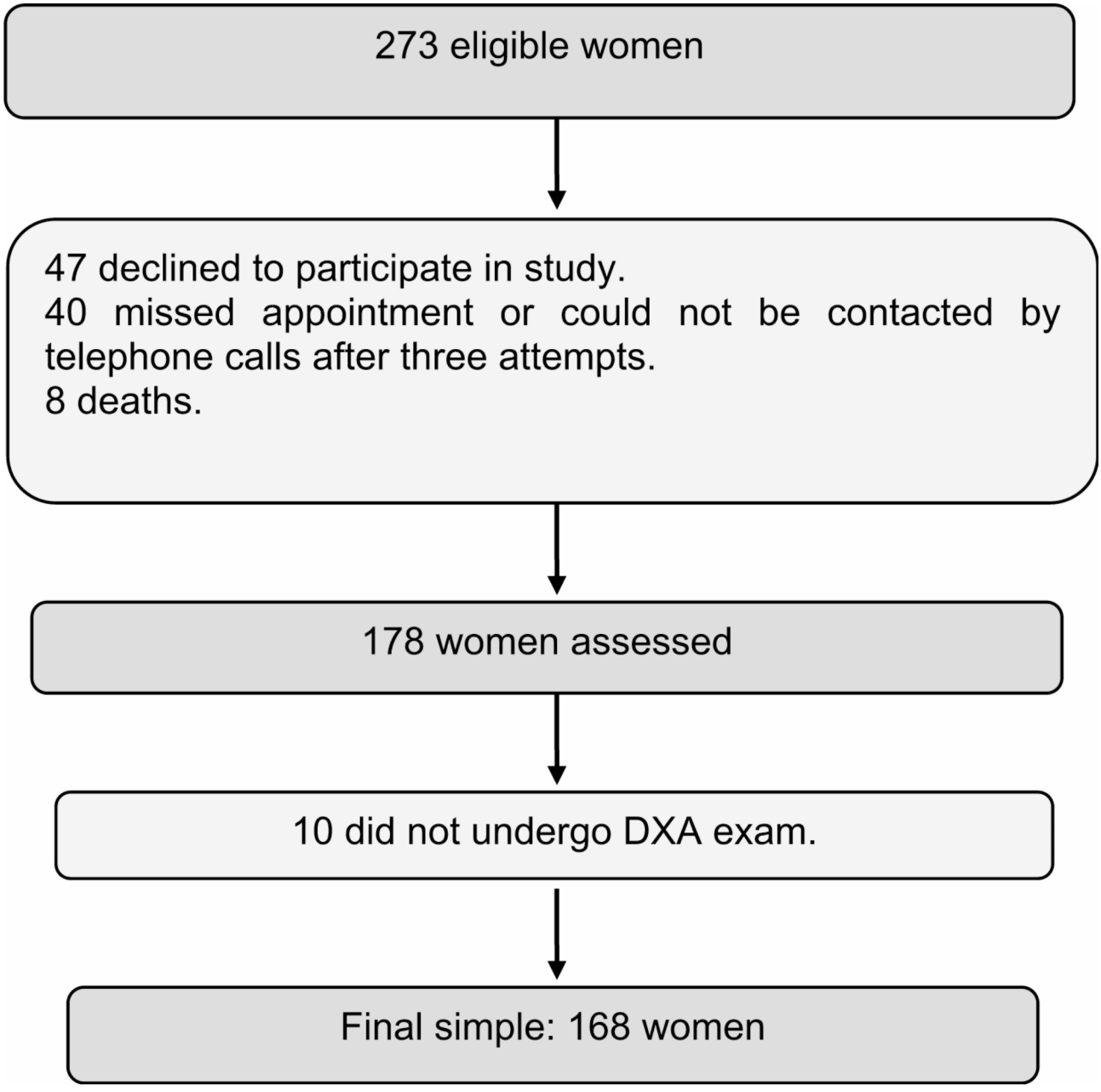

Fig. 1 Flowchart of sample

Sociodemographic and behavioral variables

The sociodemographic data considered for this study were age (in years) categorized into adults (30-59.9 years) and older adults (≥ 60 years) (the purpose of categorizing age was to determine a possible a difference in screening for the risk of sarcopenia between age groups and to ensure the adequate distribution of the sample in both groups); self-declared skin color categorized as "white", "black/brown", or "yellow" according to the Brazilian Institute of Geography and Statistics [14]; schooling (years); marital status (with married life and without married life); alcohol intake (never consumed, used to drink, or drinks); smoking (never smoked, used to smoke, or smokes); and level of physical activity (PA) assessed using the short version of the International Physical Activity Questionnaire for Brazilians [15] in accordance with standards established for physically active and sedentary individuals [16]. Women who reported performing 150 to 300 min of moderate PA or 75 to 150 min of intense PA/per week were classified as "sufficiently active" and those who did not meet this standard were placed in the "insufficiently active" category [16].

Clinical variables

Data on medical history, menopausal status, time since diagnosis (months), histological subtype, tumor staging (0, I, II, III), and treatment (surgery, radiotherapy, and chemotherapy) were collected from the medical records. Time since diagnosis was determined by the difference between the day of assessment by the researchers and the date of the medical diagnosis. The clinical variables were categorized based on the results. Type of treatment was categorized as "no previous treatment" when the participant had not undergone any treatment prior to the assessment, "neoadjuvant" for women who underwent neoadjuvant chemotherapy, "adjuvant" for those who underwent adjuvant chemotherapy, radiotherapy, or endocrine therapy, and "surgical" for those who had only been submitted to surgery. No participant had performed targeted therapy for HER2+. Histological subtypes were classified into invasive breast carcinoma of non-special type, invasive ductal carcinoma, in situ ductal carcinoma and special subtypes [13].

Anthropometric variables

Body mass (kg), height (cm), and calf circumference (CC) (cm) were measured. The body mass index (BMI) was obtained by the ratio between body mass and height squared (kg/m^2) and was classified according to the World Health Organization [17]: < 18.5 Kg/m^2 = underweight; 18.5–24.99 kg/m^2 = eutrophic; 25–29.99 kg/m^2 = overweight; > 30–34.99 kg/m^2 = grade I obesity; > 35–39.99 kg/m^2 = grade II obesity; ≥ 40 kg/m^2 = grade III obesity. CC was determined using an nonelastic measuring tape positioned horizontally around the calf at the largest perimeter [18]. Low muscle mass was indicated by ≤ 31.0 cm in adults and ≤ 33.0 cm in older adults, as proposed by Gonzalez et al. [10]. In women classified as underweight, overweight, or obese, CC values were adjusted by the BMI. For underweight participants, 4 cm was added to the measured value. For women with excess weight and those with grade I and II obesity, 3 and 7 cm were taken from the measured value, respectively. For those with grade III obesity, 12 cm were taken from the measured value [10].

Diagnosis of sarcopenia

The EWGSOP2 proposal was used to identify sarcopenia in the participants. Women with low muscle strength (based on the results of the handgrip test) and low skeletal muscle mass (determined by the appendicular skeletal muscle mass index) were considered sarcopenic [4].

Muscle strength was measured using a Jamar® hand dynamometer with a scale of 0 to 90 kg/f and a resolution of 2 kg/f. The test was performed following the protocol of the American Association of Hand Therapy [19], with three trials of maximum force of the dominant hand for about five seconds, with a one-minute interval between trials [19]. If a participant had undergone surgery on the dominant hand, arm, or forearm less than 60 days prior to the test, the non-dominant hand was used. The highest value among the three trials was considered for analysis. Grip strength < 23 kg/f was considered indicative of low muscle strength [20].

The appendicular skeletal muscle mass index (ASMI) was obtained by dual-energy X-ray absorptiometry (DXA). ASMI was calculated as the ratio between ASM (kg) and height (m) squared [ASM (kg/m^2)] to identify a low ASMI. The cutoff point was 6.38 kg/m^2 [20–22] and was defined based on the 20th percentile of the sample, which enables a more appropriate diagnosis, as it takes into account the characteristics of the population studied [21].

Risk of sarcopenia

The SARC-F and SARC-CalF tools were used to screen for the risk of sarcopenia. SARC-F is a questionnaire recommended by the EWGSOP2 used to investigate the loss of muscle strength and function based on five components: strength, need for assistance to walk, getting up from a chair, climbing stairs, and falls [23]. The score ranges from 0 to 10 points. A score of 0 to 3 points indicates no signs suggestive of sarcopenia, whereas scores from 4 to 10 indicate an increased risk of sarcopenia [5].

The SARC-CalF is an instrument validated for the Brazilian population that has the same components as the SARC-F plus the measurement of CC. The score ranges from 0 to 20 points. Scores between 0 and 10 indicate the absence of signs suggestive of sarcopenia, whereas scores between 11 and 20 indicate increased risk of sarcopenia [8]. In the present study, we also applied BMI-adjusted SARC-CalF in order to minimize bias related to low weight or obesity [23].

Ethical aspects

This study received approval from the Institutional Review Board of the Federal University of Espírito Santo, Brazil (certificate number: 34351120.1.0000.5060 protocol; reference ID: 4.142.391). All participants signed a statement of informed consent, as stipulated by the National Board of Health for research involving human beings.

Data analysis

The sample was characterized based on frequency distribution and the estimation of central and dispersion measures. The normality of the quantitative variables was determined using the Kolmogorov-Smirnov test. Differences in sociodemographic variables, lifestyle habits, clinical variables, menopausal status, nutritional status, calf circumference, muscle strength, the presence of

sarcopenia, and the risk of sarcopenia according to the different screening tools were tested using Pearson's chi-square test, Fisher's exact test, and the Student's t-test. Taking the diagnosis of sarcopenia as reference, we calculated the area under the ROC curve (AUC) with a 95% confidence interval (CI) and measures of diagnostic performance – sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). AUC values were interpreted as follows: 0.5–0.8 = poor; 0.8–0.9 = good; > 0.9 = excellent [24]. To determine the diagnostic efficacy of the SARC-F, SARC-CalF, and BMI-adjusted SARC-CalF tools, we calculated the Youden index, defined as (sensitivity + specificity − 1), with a value of 1 indicating a perfect test and 0 indicating no diagnostic value [25]. The AUC values of SARC-F, SARC-CalF, and BMI-adjusted SARC-CalF were compared using Delong's test [26]. Statistical analyses were performed using SPSS, version 22.0. The significance level was set at 5% ($p < 0.05$).

Results

One hundred sixty-eight women were included in the study. Mean age was 54.8 ± 11.3 years. Adults (66.1%), women who declared themselves to be black or brown (67.9%), those who consumed alcohol in the past (41.7%), those who had never smoked (72.0%), those classified as insufficiently active (57.1%), married women (55.4%), and those with four to eight years of schooling (42.9%) predominated in the sample. Comparing categories based on the cutoff points of the diagnostic tools, significant differences were found for age ($p = 0.005$) and stage of life ($p = 0.043$) when the SARC-F was used, education level when the BMI-adjusted SARC-CalF tool was used ($p = 0.005$), and alcohol intake when the SARC-CalF was used ($p = 0.016$) (Table 1).

When assessing the histological subtype and clinical staging of breast cancer, we found a predominance of invasive breast carcinoma of the non-special type (70.2%) and stage II (42.3%). Most of the women had time since diagnosis of up to three months (64.3%), had not undergone any antineoplastic treatment (51.8%), and were postmenopausal (69.0%) (Table 2). No participant had undergone targeted therapy for HER2+.

With regards to the BMI classification, women with obesity predominated in the sample (39.9%). Low muscle strength was found in 28.6% and the prevalence of sarcopenia was 8.3%. Furthermore, significant differences were found in grip strength between SARC-F categories ($p = 0.029$) and the presence of sarcopenia between SARC-CalF categories ($p < 0.001$) (Table 3).

The results of the use of SARC-F, SARC-CalF, and BMI-adjusted SARC-CalF for predicting the risk of sarcopenia in women with breast cancer are displayed in Table 4. Taking the diagnosis of sarcopenia as reference, the area under the ROC curve was 0.79 [(0.65–0.93); $p < 0.001$], sensitivity was 42.8%, specificity was 92.2%, PPV was 32.2%, NPV was 94.7%, and the Youden Index was 0.32 when SARC-CalF was used. SARC-F and BMI-adjusted SARC-CalF did not demonstrate acceptable accuracy. All instruments had lower sensitivity and PPV and higher specificity and NPV. However, the AUC value and its significance indicated that the SARC-CalF was the tool with the best diagnostic performance for predicting the risk of sarcopenia in the women with breast cancer assessed in the present study. The ROC curves of SARC-F, SARC-CalF, and BMI-adjusted SARC-CalF against the diagnosis of sarcopenia are shown in Fig. 2.

Comparison of SARC-F, SARC-CalF, and BMI-adjusted SARC-CalF

Delong's test indicated statistically significant differences ($p < 0.05$) between the AUC values of SARC-CalF vs. SARC-F and SARC-CalF vs. BMI-adjusted SARC-CalF, demonstrating that SARC-CalF performed better than both the SARC-F and BMI-adjusted SARC-CalF in screening for sarcopenia risk (Table 5).

Discussion

The results of the present study indicated that SARC-CalF had a low capacity for identifying the risk of sarcopenia in women of breast cancer compared to SARC-F and BMI-adjusted SARC-CalF. BMI-adjusted SARC-CalF did not exhibit the capacity to screen for the risk of sarcopenia.

The SARC-CalF tool was developed in Brazil as an adaptation of the SARC-F with the inclusion of the calf circumference (CC) measurement and has been shown to have better accuracy than SARC-F [10]. In our study, SARC-CalF had a significant AUC and was more suitable for screening sarcopenia risk, as confirmed by DeLong's test. However, sensitivity was low, which needs to be considered when administering this tool to women with breast cancer.

Studies conducted with Asian older adults in different settings and with different clinical conditions investigated the accuracy of SARC-F and SARC-CalF and also found increased sensitivity when including CC [27, 28]. This anthropometric variable is considered a sensitive indicator of low skeletal muscle mass, which is one of the components of sarcopenia and can be used when body composition determination methods are not available [29]. However, CC may not detect small changes in muscle mass in a short period the time [29], which may explain our results with regards to BMI-adjusted SARC-CalF.

In addition to the accumulation of adipose tissue, the CC cutoff point may affect the sensitivity and accuracy of SARC-CalF. Several factors influence the determination

Table 1 Sociodemographic and lifestyle variables of women with breast cancer according to different screening tools ($n = 168$)

		SARC-F		SARC-CalF		BMI-adjusted SARC-CalF	
	Total	**(< 4 points)**	**(≥ 4 points)**	**(< 11 points)**	**(≥ 11 points)**	**(< 11 points)**	**(≥ 11 points)**
n **(%)**		143 (85.1)	25 (14.9)	151 (89.9)	17 (10.1)	107 (63.7)	61 (36.3)
Age in years (mean ± SD)	54.8 ± 11.3	53.8 ± 10.7	54.8 ± 11.3	54.8 ± 11.3	57.0 ± 11.4	54.3 ± 10.4	55.7 ± 12.6
p-value		**0.005**[c]		0.396		0.434	
Variables	*n* **(%)**						
Stage of life (years)							
30–59.9	111 (66.1)	99 (89.2)	12 (10.8)	100 (90.1)	11 (9.9)	73 (65.8)	38 (34.2)
≥ 60	57 (33.9)	44 (77.2)	13 (22.8)	51 (89.5)	6 (10.5)	34 (59.6)	23 (40.4)
p-value		**0.043**[a]		1.000 [a]		0.499 [a]	
Skin color							
White	50 (29.8)	44 (88.0)	6 (12.0)	44 (88.0)	6 (12.0)	32 (64.0)	18 (36.0)
Black/Brown	114 (67.9)	97 (85.1)	17 (14.9)	104 (91.2)	10 (8.8)	73 (64.0)	41 (36.0)
Yellow	4 (2.4)	2 (50.0)	2 (50.0)	3 (75.0)	1 (25.0)	2 (50.0)	2 (50.0)
p-value		0.152 [b]		0.327 [b]		0.848 [b]	
Marital status							
With married life	93 (55.4)	66 (88.0)	9 (12.0)	69 (92.0)	6 (8.0)	48 (64.0)	27 (36.0)
Without married life	75 (44.6)	77 (82.8)	16 (17.2)	82 (88.2)	11 (11.8)	59 (63.4)	34 (36.6)
p-value		0.389 [a]		0.453 [a]		1.000 [a]	
Schooling (years)							
< 4	14 (8.3)	9 (64.3)	5 (35.7)	12 (85.7)	2 (14.3)	3 (21.4)	11 (78.6)
4–8	72 (42.9)	61 (84.7)	11 (15.3)	66 (91.7)	6 (8.3)	46 (63.9)	26 (36.1)
> 8–11	50 (29.8)	44 (88.0)	6 (12.0)	44 (88.0)	6 (12.0)	36 (72.0)	14 (28.0)
> 11	32 (19.0)	29 (90.6)	3 (9.4)	29 (90.6)	3 (9.4)	22 (68.8)	10 (31.3)
p-value		0.152 [b]		0.814 [b]		**0.005**[a]	
Alcohol intake							
Never drank	62 (36.9)	51 (82.3)	11 (17.7)	50 (80.6)	12 (19.4)	33 (53.2)	29 (46.8)
Used to drink	70 (41.7)	61 (87.1)	9 (12.9)	67 (95.7)	3 (4.3)	50 (71.4)	20 (28.6)
Drinks	36 (21.4)	31 (86.1)	5 (13.9)	34 (94.4)	2 (5.6)	24 (66.7)	12 (33.3)
p-value		0.755 [a]		**0.016**[b]		0.086 [a]	
Smoking							
Never smoked	121 (72.0)	103 (81.1)	18 (14.9)	108 (89.3)	13 (10.7)	75 (62.0)	46 (38.0)
Used to smoke	37 (22.0)	32 (86.5)	5 (13.5)	33 (89.2)	4 (10.8)	24 (64.9)	13 (35.1)
Smokes	10 (6.0)	8 (80.0)	2 (20.0)	10 (100)	0 (0.0)	8 (80.0)	2 (20.0)
p-value		0.858 [b]		0.813 [b]		0.544 [b]	
Physical activity level							
Insufficient	96 (57.1)	81 (84.4)	15 (15.6)	88 (91.7)	8 (8.3)	58 (60.4)	38 (39.6)
Sufficient	72 (42.9)	62 (86.1)	10 (13.9)	63 (87.5)	9 (12.5)	49 (68.1)	23 (31.9)
p-value		0.829 [a]		0.442 [a]		0.334 [a]	

[a] Pearson's chi-square test; [b] Fisher's exact test; [c] Student's t-test

of the cutoff point, such as sex, ethnicity, age, and environmental factors, which may cause the values to be underestimated [7]. Therefore, researchers or professional assessors must exercise caution when applying the tool to minimize such biases.

A study conducted by do Nascimento et al. [30] assessed and compared the predictive capacity of SARC-CalF and BMI-adjusted SARC-CalF in 206 older adults of both sexes diagnosed with all types of cancer (only 8.2% were diagnosed with breast cancer) and treated at a hospital in southern Brazil. The risk of sarcopenia by BMI-adjusted SARC-CalF was associated with a prolonged hospital stay and mortality at six and 12 months. However, SARC-CalF was also associated with 12-month mortality and revealed a higher risk compared to BMI-adjusted SARC-CalF.

BMI-adjusted SARC-CalF did not demonstrate screening ability in the present study. Our hypothesis for this poor performance is related to the characteristics the sample, which was predominantly composed of adult women with a short time since diagnosis (≤ three months) who had not yet started the treatment and did not yet have or had few changes in body composition, especially CC. There was also a predominance of adult women with excess weight or obesity and normal CC, even when considering adjusted CC. This point differs from previous

Table 2 Clinical variables and menopausal status of women with breast cancer according to different screening tools ($n = 168$)

		SARC-F		SARC-CalF		BMI-adjusted SARC-CalF	
	Total	**(< 4 points)**	**(≥ 4 points)**	**(< 11 points)**	**(≥ 11 points)**	**(< 11 points)**	**(≥ 11 points)**
n **(%)**		143 (85.1)	25 (14.9)	151 (89.9)	17 (10.1)	107 (63.7)	61 (36.3)
Variables	*n* **(%)**						
Histological subtype[1]	165						
Invasive breast cancer of non-special type	118 (70.2)	100 (84.7)	18 (15.3)	106 (89.8)	12 (10.2)	74 (62.7)	44 (37.3)
Invasive ductal carcinoma	23 (13.7)	19 (82.6)	4 (17.4)	22 (95.7)	1 (4.3)	15 (65.2)	8 (34.8)
In situ ductal carcinoma	12 (7.1)	10 (83.3)	2 (16.7)	9 (75.0)	3 (25.0)	7 (58.3)	5 (41.7)
Special subtypes	12 (7.1)	12 (100.0)	0 (0.0)	11 (8.3)	1 (8.3)	9 (75.0)	3 (25.0)
p-value		0.534[b]		0.295[b]		0.850[b]	
Clinical staging[2]	160						
0	15 (8.9)	12 (80.0)	3 (20.0)	12 (80.0)	3 (20.0)	9 (60.0)	6 (40.0)
I	42 (25.0)	33 (78.6)	9 (21.4)	36 (85.7)	6 (14.3)	29 (69.0)	13 (31.0)
II	71 (42.3)	64 (90.1)	7 (9.9)	65 (91.5)	6 (8.5)	44 (62.0)	27 (38.0)
III	32 (19.0)	27 (84.4)	5 (15.6)	30 (93.8)	2 (6.3)	18 (56.3)	14 (43.8)
p-value		0.310[b]		0.348[b]		0.727[a]	
Time since diagnosis (months)[3]	165						
≤ 3	108 (64.3)	93 (86.1)	15 (13.9)	98 (90.50)	10 (9.3)	70 (64.8)	38 (35.2)
> 3	57 (33.9)	48 (84.2)	9 (15.8)	50 (87.7)	7 (12.3)	35 (61.4)	22 (38.6)
p-value		0.817[a]		0.594[a]		0.734[a]	
Treatment[4]	161						
No previous treatment	87 (51.8)	75 (86.2)	12 (13.8)	77 (88.5)	10 (11.5)	59 (67.8)	28 (32.2)
Neoadjuvant	20 (11.9)	16 (80.0)	4 (20.0)	19 (95.0)	1 (5.0)	11 (55.0)	9 (45.0)
Adjuvant	28 (16.7)	24 (85.7)	4 (14.3)	24 (85.7)	4 (14.3)	15 (53.6)	13 (46.4)
Surgical	26 (15.5)	22 (84.6)	4 (15.4)	24 (92.3)	2 (7.7)	16 (61.5)	10 (38.5)
p-value		0.878[b]		0.738[b]		0.475[a]	
Menopausal status							
Pre-menopause	52 (31.0)	47 (90.4)	5 (9.6)	46 (88.5)	6 (11.5)	35 (67.3)	17 (32.7)
Post-menopause	116 (69.0)	96 (82.8)	20 (17.2)	105 (90.5)	11 (9.5)	72 (62.1)	44 (37.9)
p-value		0.246[a]		0.783[a]		0.604[a]	

[a]: Pearson's chi-square test; [b]: Fisher's exact test.[1]: $n = 165$; [2]: $n = 160$; [3]: $n = 165$; [4]: $n = 161$

studies, which mainly assessed and compared these tools in populations of older adults [30, 31]. Indeed, the aging process is associated with changes in body composition that contribute to the development of sarcopenia [32, 33].

In the BMI-adjusted SARC-CalF, the number of participants at risk of sarcopenia increased from 17 to 61 women. Among the 61 women, 50 (82%) had normal ASMI and 43 (70.5%) normal grip strength. Among the 17 women identified at risk of sarcopenia by SARC-CalF, seven (41.2%) had normal ASMI and nine (53%) had normal grip strength. Therefore, the BMI-adjusted SARC-CalF was not able to improve the screening for the risk of sarcopenia.

Women with breast cancer undergo changes in body composition, with reduced muscle mass and increased body fat due to hormonal changes, antineoplastic treatment, and lifestyle factors [1]. This increase in body fat may compromise the detection of sarcopenia risk by SARC-CalF and BMI-adjusted SARC-CalF, as these screening instruments have self-reported and subjective items. In agreement with our results, previous studies also showed that SARC-F had low sensitivity in detecting the risk of sarcopenia [34, 35]. Furthermore, no statistically significant differences in clinical characteristics, such as cancer stage, type of treatment, etc., were found between categories based on the cutoff points of the any of the instruments tested in the present study.

The sensitivity and specificity of a screening tool may vary depending on the population assessed. SARC-F and SARC-CalF have been validated in older adults and healthy populations [3, 8], whereas the population in the present study was composed of women (adults and older adults) diagnosed with breast cancer. Another factor that negatively interferes with the diagnostic capacity of the tools is the subjectivity of the responses, which can lead to self-assessment bias, inducing answers that may compromise the results [34, 35].

Another consideration is the questionnaire, which consists of questions related to the most advanced stage of sarcopenia and not milder symptoms that better reflect risk, which can lead to false negatives [34–36]. In view of this, it is possible that a large proportion of individuals in more advanced stages of the underlying disease are unable to perform the activities presented in the

Table 3 Nutritional status, calf circumference, muscle strength, and presence of sarcopenia in women with breast cancer according to different screening tools ($n = 168$)

		SARC-F		SARC-CalF		BMI-adjusted SARC-CalF	
	Total	**(< 4 points)**	**(≥ 4 points)**	**(< 11 points)**	**(≥ 11 points)**	**(< 11 points)**	**(≥ 11 points)**
n **(%)**		143 (85.1)	25 (14.9)	151 (89.9)	17 (10.1)	107 (63.7)	61 (36.3)
Variables	*n* **(%)**						
BMI							
Underweight	5 (3.0)	5 (100.0)	-	1 (20.0)	4 (80.0)	3 (60.0)	2 (40.0)
Eutrophic	40 (23.8)	35 (87.5)	5 (12.5)	30 (75.0)	10 (25.0)	31 (77.5)	9 (22.5)
Overweight	56 (33.3)	50 (89.3)	6 (10.7)	53 (94.6)	3 (5.4)	38 (67.9)	18 (32.1)
Grade I obesity	46 (27.4)	38 (82.6)	8 (17.4)	46 (100.0)	-	25 (54.3)	21 (45.7)
Grade II obesity	14 (8.3)	10 (71.4)	4 (29.6)	14 (100.0)	-	9 (64.3)	5 (35.7)
Grade III obesity	7 (4.2)	5 (71.4)	2 (28.6)	7 (100.0)	-	1 (14.3)	6 (85.7)
p-value		0.152 [b]		0.327 [b]		0.848 [b]	
Muscle strength	168 (100.0)	143 (85.1)	25 (14.9)	151 (89.9)	17 (10.1)	107 (63.7)	61 (36.3)
Normal	120 (71.4)	107 (89.2)	13 (10.8)	111 (92.5)	9 (7.5)	77 (64.2)	43 (35.8)
Low	48 (28.6)	36 (75.0)	12 (25.0)	40 (83.3)	8 (16.7)	30 (62.5)	18 (37.5)
p-value		**0.029**[a]		0.091[b]		0.860[a]	
Sarcopenia	168 (100.0)	143 (85.1)	25 (14.9)	151 (89.9)	17 (10.0)	107 (63.7)	61 (36.3)
No	154 (91.7)	132 (85.7)	22 (14.3)	143 (92.9)	11 (7.1)	97 (63.0)	57 (37.0)
Yes	14 (8.3)	11 (78.6)	3 (21.4)	8 (57.1)	6 (42.9)	10 (71.4)	4 (28.6)
p-value		0.441[b]		**0.001**[b]		0.580[a]	

[a]: Pearson's chi-square test; [b]: Fisher's exact test. BMI: body mass index

Table 4 Sensitivity/specificity analyses and area under receiver operating characteristic curve for SARC-F, SARC-CalF, and BMI-adjusted SARC-CalF to predict the risk of sarcopenia in women with breast cancer taking presence of sarcopenia as reference

Variables	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**	**AUC (CI 95%)**	***p*-value**	**Youden Index**
SARC-F	21.4	85.7	24.0	92.3	0.550 (0.396–0.703)	0.54	0.07
SARC-CalF	42.8	92.2	32.3	94.7	0.790 (0.654–0.937)	**< 0.001**	0.32
BMI-adjusted SARC-CalF	28.6	63.0	6.55	90.6	0.521 (0.385–0.658)	0.08	0.08

AUC: area under curve; BMI: body mass index

components of the SARC-F, SARC-CalF, and BMI-adjusted SARC-CalF questionnaires.

This study compared instruments used to identify the risk of sarcopenia. The EWGSOP2, which is one of the main references for the diagnosis of sarcopenia, recommends the use of SARC-F as a screening tool for the identification of individuals who should be submitted to muscle strength and skeletal muscle mass assessments for the diagnosis of the condition. Thus, the assessment of the accuracy of this instrument and its variations is necessary [4].

The tools analyzed here address muscle strength, mass, and performance. These are quick, low-cost questionnaires that can be administered by any trained healthcare provider [3, 7]. However, a screening method suitable for use in clinical practice must identify individuals positive for the outcome (i.e., must have high sensitivity), while maintaining the ability to avoid potentially unnecessary diagnostic investigations by identifying individuals at lower risk (i.e., high specificity). On the other hand, in this study the SARC-F and SARC-F-derived instruments exhibited low sensitivity and high specificity. These findings suggest a strong ability to exclude individuals without sarcopenia risk while demonstrating limited efficacy in detecting those at risk. In clinical practice, this reduced sensitivity may result in the underdiagnosis of a significant proportion of the target population, thereby delaying early intervention and the management of sarcopenia-related complications. Consequently, the involvement of a multidisciplinary team with specialized training is crucial for the comprehensive assessment of clinical signs and symptoms associated with sarcopenia. Furthermore, methodological refinements of these screening tools are necessary to enhance their sensitivity and overall diagnostic performance.

Our results demonstrate that a gap remains in identifying the risk of sarcopenia in women with breast cancer. Further studies are needed, as the performance diagnostic for assessing the risk of sarcopenia in women with breast cancer is essential to the implementation of preventive measures before the development of sarcopenia. One possibility would be to add anthropometric

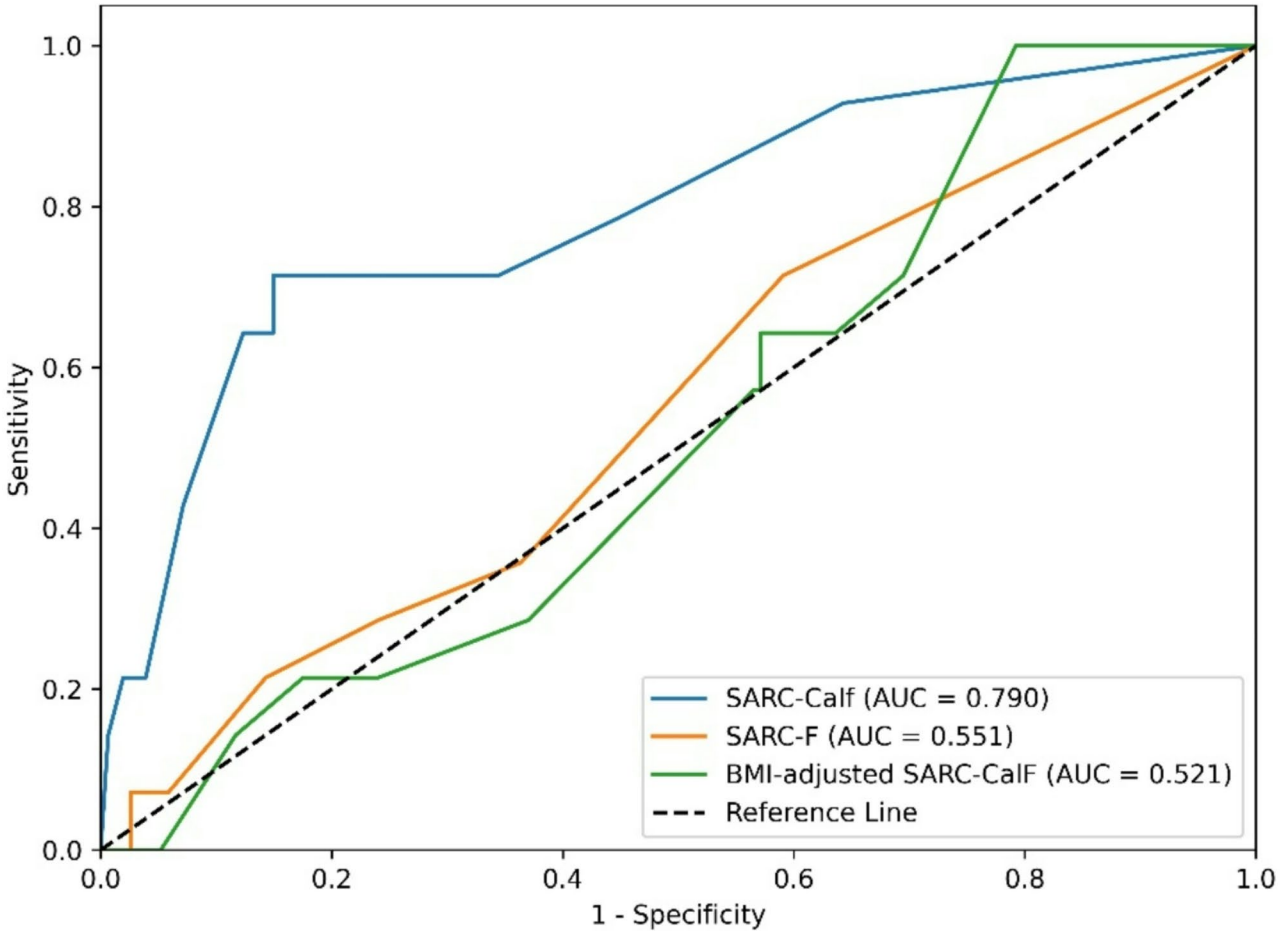

Fig. 2 Receiver operating characteristic (ROC) curves of SARC-F, SARC-CalF, and BMI-adjusted SARC-CalF to identify risk of sarcopenia in women with breast cancer taking presence of sarcopenia as reference

Table 5 Comparison of screening tools for risk of sarcopenia

Comparisons of tools	Difference between areas (95% CI)	Z test	*p*-value
SARC-CalF vs. SARC-F	0.239 (0.070–0.408)	2.78	0.005*
SARC-CalF vs. BMI-adjusted SARC-CalF	0.269 (0.124–0.414)	3.63	< 0.001*
SARC-F vs. BMI-adjusted SARC-CalF	0.029 (-0.134–0.193)	0.35	0.724

*$p < 0.05$

equations to estimate skeletal muscle mass in the screening phase. This procedure would play a key role in the prognosis of these patients, improving their quality of life.

Some limitations of this study must be recognized. We analyzed the performance of BMI-adjusted SARC-CalF in women with breast cancer. The CC adjustment proposed by Gonzalez et al. [10] was determined in individuals 18 years of age of older of both sexes, while we evaluated adult women and older women diagnosed with cancer.

There are also some limitations to our sample: (1) The participants came from a single comprehensive reference center in cancer care in Brazil; (2) the different types of antineoplastic treatments and clinical stages are factors that directly affect the body composition of this population [1, 13]; (3) the sample was composed of adult woman and older women in pre- and post-menopause, which also exerts an influence on body composition [13]. Lastly, the tools used were composed of subjective items and, even with the inclusion of the CC, SARC-CalF cannot differentiate and identify body fat and skeletal muscle mass. Thus, the present results cannot be generalized to the general population with cancer.

Conversely there are some strengths in our study that should be highlighted. As far as we know, this is the first study to assess the performance of SARC-CalF and BMI-adjusted SARC-CalF in women with breast cancer. The

instruments were administered by trained researchers and according to the protocols found in the literature. Furthermore, robust diagnostic performance measures were used, such as AUC, the Youden Index and DeLong's test.

Conclusion

The present results demonstrated that SARC-CalF was performed the best screening tool for the risk of sarcopenia in women with breast cancer compared to SARC-F and BMI-adjusted SARC-CalF. However, based on the current results, it may be necessary to reconsider the use of either of these instruments as a screening option for sarcopenia risk in women with breast cancer.

Abbreviations

ASM	Appendicular skeletal muscle mass
ASMI	Appendicular skeletal muscle mass index
AUC	Area under the ROC curve
BMI	Body mass index
CC	Calf circumference
DXA	Dual-energy x-ray absorptiometry
EWGSOP2	European Working Group on Sarcopenia in Older People Revised
NPV	Negative predictive value
PA	Physical activity
PPV	Positive predictive value
SPSS®	Statistical Package for the Social Sciences

Supplementary Information

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Supplementary Material 1

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Author contributions

VFSM: data collection, data curation, methodology, analyzed data, writing the original draft, manuscript revision and editing. RAMB: data collection, data curation, methodology, manuscript revision and editing. LLS and TGS: data collection. MSV: data collection and methodology.JLMR: manuscript revision and editing. VRG: conceptualization, project administration, supervision, writing the original.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethical approval and consent to participate

The individuals participated voluntarily and signed a statement of informed consent in compliance with Resolution 466/12 of the National Board of Health [28]. This study is part of a research project previously approved by the Research Ethics Committee of the Health Sciences Center of the Federal University of Espírito Santo (UFES) under certificate number 34351120.1.0000.5060 and opinion number 4.646.978.

Consent for publication

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Competing interests

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