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Risk of Sarcopenia Identified by Sarc-Calf, Nutritional Status and Hand Grip Strength in Patients with Hematological Cancer

Lorraine Pires Avancini[1], Laís Freitas da Costa[2], Mariana de Souza Vieira[1], Vanusa Felício de Souza[1], Rayne de Almeida Marques[3], Jose Luiz Marques Rocha[1,3], Glenda Blaser Petarli[2], Valdete Regina Guandalini[1,3]

[1]Department of Integrated Health Education, Federal University of Espirito Santo, Vitoria, Espirito Santo, Brazil
[2]University Hospital Cassiano Antonio Moraes, Vitoria, Espirito Santo, Brazil
[3]Federal University of Espirito Santo, Vitoria, Espirito Santo, Brazil

Corresponding Author: Valdete Regina Guandalini, Department of Integrated Health Education, Federal University of Espirito Santo, Vitoria, Espirito Santo, Brazil.
E-mail: valdete.guandalini@ufes.br

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ABSTRACT

Background: Hematological cancer patients are prone to the development of sarcopenia and impaired nutritional and functional status. SARC-CalF is a screening tool for the risk of sarcopenia that has shown good results in this population. This study aimed to identify the risk of sarcopenia by SARC-CalF and to verify its association with nutritional status and Hand Grip Strength (HGS) in patients with hematological cancer.

Materials and Methods: Adult patients, of both sexes, with hematological cancer, and in outpatient care participated in the study. We measured the Hand Grip Strength of the Dominant Hand (HGSD) and the Adductor Pollicis Muscle Thickness of the Dominant Hand (APMTD). Moreover, we applied the Patient-Generated Subjective Global Assessment (PG-SGA) and SARC-CalF. Data were analyzed with SPSS® software, 22.0, with a significance level of 5.0%.

Results: Fifty-one patients aged an average of 60.4 ± 15.1 years were evaluated. Of those, 58.8% were elderly, 51% female, and 80.4% declared themselves non-white. The predominant diagnosis was Mature B Lymphoid Cell Neoplasia (37.7%), and 60.8% of the patients had a diagnosis time of ≤ 3 years. PG-SGA revealed that 35.3% of the patients were malnourished; APMTD and HGSD revealed that 60.8% and 25.5% had reduced muscle strength, respectively. SARC-CalF exposed that 39.2% of the patients were at risk for sarcopenia. Significant associations were found between SARC-CalF and diagnosis time ≤ 3 years ($p = 0.039$), PG-SGA ($p = 0.020$), APMTD ($p = 0.039$) and HGSD ($p = 0.002$). After binary logistic regression adjusted for age and sex, the reduced HGSD remained associated with the risk of sarcopenia.

Conclusion: SARC-CalF identified a risk of sarcopenia in 39.2% of patients. The reduced HGSD was associated with the risk of sarcopenia.

Keywords: Nutritional status; Muscle strength; Nutritional risk; Sarcopenia

INTRODUCTION

Hematological cancers are caused by changes in blood tissue, bone marrow and lymphatic system. Among the various types of hematological cancer, the most prevalent in Brazil are Hodgkin's lymphomas, not Hodgkin's, and leukemias[1].

Hematological cancer patients are prone to changes in body composition due to the course of the disease and its treatment. These changes include a reduction in the muscular compartment, which can progress to sarcopenia when associated to a compromised nutritional status[2-4].

Sarcopenia is defined by the European Working Group on Sarcopenia in Older People Revised (EWGSOP2)[5] as a reduction in muscle strength and muscle quality or quantity. Sarcopenia is associated with malnutrition[5,2], and both conditions are frequently encountered in cancer patients. Previous studies in individuals with hematological cancer showed that around 50.6% of these patients have sarcopenia and 50.4% have some degree of malnutrition[2,6].

The Patient-Generated Subjective Global Assessment (PG-SGA), indicated by the National Consensus of Oncological Nutrition, has been widely applied to assess the nutritional status of cancer patients[7]. PG-SGA it is a reliable and sensitive tool, as it evaluates nutritional status in a broader way and through different aspects. It combines parameters such as weight loss, changes in food intake, gastrointestinal symptoms, functional changes and physical examination, in addition to correlating them with anthropometric parameters[7].

One of the parameters proposed by EWGSOP2[5] to assess muscle strength and make up the criteria for the diagnosis of sarcopenia is the handgrip strength (HGS). It is an objective, viable and convenient method for identifying muscle strength, due to its low cost, availability and ease of use[8]. Reduced HGS is a predictor of poor prognosis, impaired functional capacity, longer hospital stay, and poorer quality of life[5, 9-11].

The presence of sarcopenia and malnutrition in cancer patients are powerful predictors of negative outcomes, such as reduced immunological competence, increased hospital stay, increased functional limitations, treatment toxicity, low quality of life, and death[5,12].

Calf circumference (CC) and the adductor pollicis muscle thickness (APMT) have been widely used in clinical practice to identify nutritional status and muscle mass in cancer patients, being considered simple, low cost, and obtainable measures[13]. However, these measures alone do not suffice to identify the risk of sarcopenia.

In view of the need to make sarcopenia screening more accessible, Malmstrom et al. [14] developed the SARC-F, a simple and quick questionnaire, currently recommended by the EWGSOP2 [5,14]. Barbosa-Silva et al.[15] validated the SARC-F for the Brazilian population and proposed a new version that included calf circumference, known as SARC-CalF. This version improved the instrument's sensitivity and ability to screen for the risk of sarcopenia[15].

Studies using SARC-CalF in elderly patients reported sensitivity from 66.7 to 77.4% and specificity from 82.9 to 89.8% in identifying the risk of sarcopenia[15,16]. Although these values are acceptable, there are still few such studies in patients with hematological cancer, as, unlike in those with solid tumors, the nutritional condition of hematological cancer patients remains little explored.

Based on the above, and in view of the complexity of the disease, the importance of nutritional status in its progress, and the need to identify sarcopenia early, this study aimed to identify the risk of sarcopenia by SARC-CalF and verify its association with nutritional status and handgrip strength (HGS) in patients with hematological cancer.

MATERIALS AND METHODS

Study population and study design

This cross-sectional, observational study was carried out in an outpatient clinic of a public university hospital in Vitória, Espirito Santo, Brazil, from August 2017 to October 2018. It included patients aged 20 years or older, from both genders, with clinical diagnosis of hematological cancer undergoing oral or venous chemotherapy. Patients who did not participate in all stages of the study were excluded.

This study was approved by the Research Ethics Committee of the Federal University of Espírito Santo under number 2.141.932. Patients participated voluntarily and provided written informed consent.

Data collection

Patients were recruited during their stay at the outpatient clinic, during medical pre-consultation. For those who agreed to participate, specific days and times were scheduled for data collection.

Personal information was collected, including: age, classified into adults (<60 years) and elderly (≥60 years) [17]; gender; race/color self-declared and classified into white and non-white (yellow, brown, black). Next, we applied the Patient-Generated Subjective Global Assessment (PG-SGA) and the SARC-CalF and measured the HGS of the dominant hand (HGSD) and the Adductor Pollicis Muscle Thickness of the Dominant Hand (APMTD).

Clinical data such as type of hematological cancer and time of diagnosis were collected from medical records. The types of cancer were grouped into Mature Lymphoid B Cell Neoplasms, Myeloproliferative Neoplasm, Non-Hodgkin's Lymphoma, and others – including Hodgkin's Lymphoma, Myelodysplastic Syndrome, and Acute Myeloid Leukemia. The time of diagnosis was classified as ≤ 3 years and > 3 years.

Handgrip strength (HGS)

To assess HGS, the Jamar® manual dynamometer was used. The test was performed according to the methodology recommended by the American Society of Hand Therapists (ASHT)[18]. During the procedure, the patient remained seated, with the spine erect, knees flexed at 90º, with the shoulder positioned in adduction, the forearm supported, and the elbow flexed at 90º. The test was performed on the dominant hand in triplicate, with maximum effort for about 5 seconds, with a 1-min interval between measurements[18]. The test was not performed if the participant underwent hand, arm or forearm surgery less than 60 days before, and / or suffered edema of the upper limbs. The cutoff point defined by the Revised European Sarcopenia Consensus was considered, with HGS <16 indicating reduced strength.

Nutritional sssessment

Patient-generated subjective global assessment (PG-SGA)

The PG-SGA assesses weight change, food intake, symptoms of nutritional impact, and functional capacity. It is divided into two parts: the first is completed by the patient himself and the second by the doctor or nutritionist. In this study, the evaluators helped the patients to read and understand the questionnaire. The PG-SGA classifies the patient in the following stages of nutrition: well-nourished (A), moderately malnourished or suspected of being so (B), and / or severely malnourished (C). The global classification of PG-SGA was grouped into two categories: well-nourished (A) and malnourished (B + C). In this study we used the Brazilian Portuguese version of the PS-SGA, translated and validated by Gonzalez et al.[7], and authorized by the PG-SGA/Pt-Global Platform (www.pt global.org).

Adductor pollicis muscle thickness (APMT)

The Adductor Pollicis Muscle Thickness (APMT) was measured according to Lameu et al.[19], using a Lange® adipometer with 10g / mm2 continuous pressure to pinch the adductor muscle at the apex of an imaginary triangle, formed by the extension of the thumb and index finger. The patient remained seated, with the arm flexed at approximately 90 °, with the forearm and hand resting on the knee. The procedure was performed on the dominant hand in triplicate. None of the patients had edema in the hands. The values obtained were classified according to Bragagnolo et al.[20], who considers values for APMT of the dominant hand (APMTD) <13.4 mm as a sign of malnutrition. The average of three measurements was used as a measure of APMT.

Risk assessment of Sarcopenia

The risk of sarcopenia was assessed using the SARC-CalF questionnaire. This instrument is structured in six components that assess: difficulty in relation to strength aspects; walking aid; getting up from the chair; climbing stairs; the number of falls, and the measurement of the circumference of the calf. At the end of the evaluation, a score ranging from 0 to 20 is obtained. Values between 0 and 10 are not suggestive of sarcopenia and values between 11 and 20 are suggestive of sarcopenia[15]. Calf circumference was measured with an inextensible measuring tape at the point of greatest horizontal protrusion of the right calf. The patient was instructed to stand up, with legs relaxed and feet 20 cm apart, as recommended by Barbosa-Silva et al.[15]. The cut-off points used, which consider the reduction in muscle mass, were calf circumference values below 34 cm for men and 33 cm for women[15].

Statistical analysis

A descriptive analysis was performed, expressed as means and standard deviations to describe continuous variables and percentage for categorical variables. The Kolmogorov-Smirnov test was used to verify the normality of the quantitative variables. Difference between the proportions was analyzed using the Chi-square and Fisher's exact tests. Binary logistic regression analysis was used to determine the influence of the variables of interest (independent variables) on the SARC-CalF score (dependent variable). Raw Odds Ratio was presented after adjustments for sociodemographic variables. Adjustment variables were inserted in blocks: model 1: age; model 2: age and sex. Variables that showed significance in the Chi-Square and Fisher's Exact tests were included in the regression model. The data were analyzed using SPSS 22.0 software. The level of significance adopted for all tests was 5.0%.

RESULTS

The characteristics of the studied population are shown in Table 1. The sample consisted of 51 patients aged in average 60.4 ± 15.1 years. There was a predominance of elderly (58.8%), women (51.0%) and individuals who declared themselves non-white (80.4%). The most prevalent diagnosis was mature B lymphoid cell neoplasm (37.7%). Regarding the time of diagnosis, 60.8% of the patients had been diagnosed less than or equal to three years before.

Table 1: Demographic and clinical characteristics of patients with hematological cancer in outpatient care

Age (mean ± SD)	60.4 ± 15.1 years
	n (%)
Sex	
Female	26 (51.0)
Male	25 (49.0)
Life stage	
Adult	21 (41.2)
Elderly	30 (58.8)
Race/Color	
White	10 (19.6)
Non-white	41 (80.4)
Diagnosis	
Mature B Lymphoid Cell Neoplasm	19 (37.7)
Non-Hodgkin's Lymphoma	11 (21.6)
Others*	21 (41.2)
Time of diagnosis	
> 3 years	20 (39.2)
≤ 3 years	31 (60.8)

Note. * Others: 5.9% Hodgkin's lymphoma; 5.9% Myelodysplastic Syndrome; 3.9% Acute Myeloid Leukemia; 25.5% Myeloproliferative Neoplasm

Nutritional status, HGSD and risk of sarcopenia are shown in Table 2. There was a higher proportion of well-nourished individuals (64.7%) according to PG-SGA, with reduced APMTD (60.8%), and adequate HGSD (74.5%). SARC-CalF identified a risk of sarcopenia in 39.2% of the patients.

Table 2: Nutritional status, HGSD and risk of sarcopenia in patients with hematological cancer in outpatient care

	n	%
PG-SGA		
Well nourished	33	64.7
Malnourished	18	35.3
APMTD		
Proper	20	39.2
Reduced	31	60.8
HGSD (kg)		
Proper	38	74.5
Reduced	13	25.5
SARC-CalF		
No risk sarcopenia	31	60.8
At risk sarcopenia	20	39.2

PG-SGA: Pacient-Generated Subjective Global Assessment; HGSD: Handgrip strength of the dominant hand. APMTD: Adductor Pollicis Muscle Thickness of dominant hand

There was a significant association between SARC-CalF categories with time of diagnosis (p = 0.039), HGSD (p = 0.002), APMTD (p = 0.039) and PG-SGA (p = 0.034) (Table 3).

Table 3: Association between the risk of sarcopenia according to the SARC-CalF and the diagnosis, time of diagnosis, nutritional status and hand grip strength of patients with hematological cancer in outpatient care

	With risk of sarcopenia	**Without risk of sarcopenia**	**p**
	n (%)	**n (%)**	
Sex[a]			0.153
Male	18 (72.0)	7 (28.0)	
Female	13 (50.0)	13 (50.0)	
Life Stage[a]			1,000
Adult	13 (61.9)	8 (38.1)	
Elderly	18 (60.0)	12 (40.0)	
Race/Color[b]			1,000
White	6 (60.0)	4 (40.0)	
Non-white	25 (61.0)	16 (39.0)	
Diagnosis[b]			0.401
Mature Lymphoid B Cell Neoplasm	11 (57.9)	8 (42.1)	
Non-Hodgkin's Lymphoma	5 (45.5)	6 (55.5)	
Others*	15 (71.4)	6 (28.6)	
Time of diagnosis (years [a]			0.039 *
≤ 3 years	15 (48.4)	16 (51.6)	
> 3 years	16 (80.0)	4 (20.0)	
HGSD (kg)[a]			0.002 *
Adequate	28 (73.7)	10 (26.3)	
Reduced	3 (23.1)	10 (76.9)	
APMTD[a]			0.039 *
Adequate	16 (80.0)	4 (20.0)	
Reduced	15 (48.4)	16 (51.6)	
PG-SGA[a]			0.034 *
Well nourished	24 (72.7)	9 (27.3)	
Malnourished	7 (38.9)	11 (61.1)	

Note. [a] Chi-square test; [b] Fisher's exact test. PG-SGA: Patient-Generated Subjective Global Assessment; HGSD: Handgrip strength of dominant hand. APMTD: Adductor pollicis muscle thickness of dominant hand. Others *: 5.9% Hodgkin's lymphoma; 5.9% Myelodysplastic Syndrome; 3.9% Acute Myeloid Leukemia; 25.5% Myeloproliferative neoplasm

In the logistic regression analysis (table 4), even after adjusting for life stage and sex, HGSD remained associated with the risk of sarcopenia. Patients with reduced strength were 9.64 times more likely to be at risk for sarcopenia than individuals with adequate HGS (OR: 9.64 [CI 95%: 1.79 - 51.96], p = 0.008). The other variables lost the strength of association after the adjusted analyzes.

Table 4: Logistic regression models for the SARC-CalF categories in patients with hematological cancer

	Crude OR (95% CI)	Model 1 OR (95% CI)	Model 2 OR (95% CI)
PG-SGA			
Well nourished	1	1	1
Malnourished	**4.20 (1.24 - 14.17)**	1.96 (0.44 - 8.82)	1.87 (0.41 - 8.51)
APMTD			
Adequate	1	1	1
Reduced	**4.26 (1.16 - 15.70)**	3.83 (0.79 - 16.65)	3.11 (0.59 - 16.41)
HGSD			
Adequate	1	1	1
Reduced	**9.33 (2.13 - 49.94)**	**8.91 (1.73 - 46.68)**	**9.64 (1.79 - 51.96)**
Time of diagnosis			
> 3 years	1	1	1
≤ 3 years	**4.26 (1.16 - 15.70)**	2.84 (0.61 - 13.30)	2.85 (0.61 - 13.40)

Note. Model 1: adjusted by age and stage of life. Model 2: adjusted for life stage and sex

DISCUSSION

The present study demonstrated that 39.2% of the evaluated patients were at risk for sarcopenia according to the SARC-CalF. The SARC-CalF categories were significantly associated with the time of diagnosis, HGSD, APMTD, and nutritional status defined by PG-SGA. However, only HGSD remained associated with the risk of sarcopenia after logistic regression analysis.

Morishita et al.[2] investigated the presence of sarcopenia in patients with hematological cancer and found that 50.6% of the patients were sarcopenic. Other studies have also shown that sarcopenia is high in this population[21-23], with prevalence ranging from 51.0% to 66.9%. Sarcopenia can occur in hematological cancer patients due to the hypercatabolism and anorexia caused by the disease and by antineoplastic treatment, which affect nutritional status, inducing muscle compartment reduction and fatigue[24]. Such conditions reinforce the importance of investigating the risk of sarcopenia, in order to avoid further depletion of nutritional status and associated complications, such as reduced quality of life, increased mortality and treatment costs [25].

As for the predominance of patients classified as well-nourished according to the PG-SGA, Krawczyk et al.[3], when evaluating patients with hematological cancer during treatment, have also identified an adequate nutritional status in 88.0% of them. Despite this preserved nutritional status, these patients are susceptible to nutritional risk, as evidenced by Rodrigues et al.[26], who observed that, although the majority of patients with oncohematological diseases were well-nourished, 70.1% were at nutritional risk according to NRS-2002. Taken together, these findings show that type of tumor, stage of the disease, and antineoplastic therapy are important factors that influence and determine the presence and degree of malnutrition[6]. Hébuterne et al.[27] found a higher prevalence of malnutrition in hospitalized cancer patients (44.1%) than in outpatients (27.7%), reinforcing this hypothesis.

After adjusted logistic regression analyses, HGSD was the only variable that remained associated with SARC-CalF. Patients with reduced HGSD were more likely to have a risk for sarcopenia than those with adequate HGSD. HGS is recommended by the EWGSOP2 to measure muscle strength, with its reduction being characterized as pre-sarcopenia[5]. SARC-CalF is an instrument that seeks to identify symptoms associated with this syndrome through patient reports, such as falling, feeling of weakness, slow walking speed, and difficulty in getting up from a chair, which are associated with reduction in muscle strength[5,15].

This relationship between sarcopenia and HGS has been already reported by previous studies on hematological cancer patients. Morishita et al.[2] observed that sarcopenic patients had significantly lower HGS of both hands compared to those without a diagnosis of sarcopenia. According to the authors, these patients are susceptible to a reduction in HSG due to the impairment of the muscular compartment caused by the disease and its treatment, as also evidenced by Silva et al.[28], who observed a significant reduction in HGS after hematopoietic stem cell transplantation.

This can be explained by cancer, regardless of its type and location, triggering significant changes in body composition, due to factors that mainly involve the state of systemic inflammation and its aggressive treatment[29]. In oncohematological patients, implications for the skeletal muscular system may occur, with consequent fatigue, reduced muscle strength and exercise capacity, and sarcopenia[30]. The reduction in HGS may also be associated with physical deconditioning and immobility during hospitalization[29], which may not interfere with muscle quantity, assessed in this study by APMT, but do so in muscle strength, obtained by HGS.

Muscle strength reflects nutritional depletion even before changes in body composition can be detected, due to different anthropometric parameters that indicate muscle mass reserve[31,32]. That explains the loss of the association of APMT in the final model applied here, and the importance of considering the measurement of HGS.

The non-association between nutritional status and SARC-CalF in the regression models is possibly due to PG-SGA assessing changes in body weight, food intake, functional and physical examination, and symptoms of nutritional impact associated with cancer, while SARC-CalF evaluates the patient's perception of signs that are characteristic of sarcopenia, thus aiming only at signs of reduced muscle quantity and quality[5,7].

The results of this study are relevant, as they show the feasibility of using SARC-CalF in the multimodal support of patients with hematological cancer. Another study that used this instrument to assess the risk of sarcopenia in patients with gastrointestinal tract cancer found SARC-CalF to be efficient also in this instance[25].

Sarcopenia is associated with muscle quantity and quality, but these parameters are used mainly in research, being more difficult to be accurately identified in clinical practice, since the diagnosis depends on more complex and costly tools, such as computed tomography and bone densitometry[5]. Therefore, SARC-CalF can be advantageous, since it is a low-cost instrument, with quick and easy application, with established cut-off points and efficient in detecting the risk of sarcopenia, favoring early treatment, reducing costs with hospitalization, medications, and specialized professionals[25].

SARC-CalF also has advantages over its original instrument. Measuring the calf's perimeter proved to be more efficient in predicting which patients were not at risk of sarcopenia, since SARC-F, being only subjective, may lead to misinterpretations[32].

Among the limitations of this study, we can highlight the cross-sectional design that does not allow the analysis of the temporality of the facts, and the absence of some information such as cancer staging and chemotherapy cycle. We must, however, state that all other information and measurements were collected by a trained team, with strict and controlled protocols.

CONCLUSION

SARC-CalF identified a 39.2% risk of sarcopenia in patients with hematological cancer, and this risk was associated with HGSD even after adjusted analyzes, showing that SARC-CalF is a promising instrument for use in clinical practice. The identification of the risk of sarcopenia by SARC-CalF may contribute to specific and early interventions, enabling a better prognosis for these patients.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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