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Preoperative evaluation of sarcopenia in patients with colorectal cancer: a prospective study

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SUMMARY

OBJECTIVE: Colorectal cancer is the third most diagnosed malignant neoplasm in the world and the fourth leading cause of cancer mortality. The loss of muscle mass in oncological patients is the main aspect of cancer-related malnutrition. Associations between sarcopenia and poor outcomes, such as high postoperative mortality, chemotherapy toxicity, and reduced survival, have been recently described. The aim of this study was to prospectively assess the prevalence of preoperative sarcopenia in patients with colorectal cancer using validated methods to evaluate muscle strength, muscle mass, and physical performance.

METHODOLOGY: This study included patients with colorectal cancer undergoing oncological staging at a Cancer Center in Brazil from May 2019 to March 2020 who had images from abdominal computed tomography available for analysis of body composition. The muscle strength test, physical performance, referred fatigue, and clinical and nutritional data were evaluated.

RESULTS: A total of 31 patients were included, and most were diagnosed with colon cancer (77.4%) and clinical stage II in 41.9% of cases. The prevalence of probable sarcopenia was 22.6%; of these patients, sarcopenia was confirmed in 19.4%, and ultimately, 9.7% of the sample was classified as severe sarcopenia. We did not find a significant association between the presence of sarcopenia in our sample and age, sex, tumor staging, nutritional characteristics, referred patient fatigue, or postoperative complications.

CONCLUSION: Considering the criteria established by the EWGSOP, the prevalence of preoperative sarcopenia in colorectal cancer patients was 19.4%.

KEYWORDS: Sarcopenia. Colorectal neoplasms. Preoperative care. Computed tomography.

INTRODUCTION

Colorectal cancer is the third most diagnosed malignant neoplasm in the world and the fourth leading cause of cancer mortality. In cancer patients, cachexia and malnutrition are extremely important complications of clinical practice because of a variety of inherent tumor mechanisms, host response to the tumor, and oncological therapies[1].

Sarcopenia is directly responsible for functional impairment, increased risk of falls, loss of autonomy, reduced respiratory capacity, and reduced immunity[2]. The diagnostic criteria for sarcopenia include reduced muscle strength (criterion 1), low muscle quantity or quality (criterion 2), and poor physical performance (criterion 3). In addition, a classification into different stages is indicated: probable sarcopenia (criterion 1), sarcopenia (criteria 1 and 2), and severe sarcopenia (all criteria)[3].

The gold standard method to quantify muscle mass is a computed tomography (CT) scan to measure the skeletal muscle area at the L3 level and calculate the skeletal muscle index (SMI). Since abdominal CT is routinely performed in colorectal cancer patients for diagnosis, staging, and follow-up, it is suitable to use this method to measure muscle mass in this population[4,5].

Associations between sarcopenia and worse prognosis, such as high postoperative mortality, chemotherapy toxicity, reduced survival, higher infection rates, increased hospital length of stay, and increased mortality, have been pointed out recently[6-13]. Surgical resection in a patient with nonmetastatic colorectal cancer is an important aspect of cancer management, and including the evaluation of sarcopenia as a predictor of perioperative or postoperative morbidity risk can provide prognostic information for surgeons and patients. Thus, ideally, patients with colorectal cancer should be screened for sarcopenia from the beginning of their oncological treatment and be informed of its potential negative effects, highlighting the importance of sarcopenia prevention and treatment strategies[14].

The actual prevalence and impact of sarcopenia in this population are unknown, as most published studies classify sarcopenia solely by the presence of low muscle mass on CT, which may overestimate its prevalence. The aim of this study was to

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prospectively assess the prevalence of preoperative sarcopenia in patients with colorectal cancer using validated methods to evaluate muscle strength, muscle mass, and physical performance.

METHODS

This is a prospective, cross-sectional, single-center, Institutional Review Board-approved study evaluating patients with a diagnosis of colorectal cancer undergoing oncological staging at a cancer center from May 2019 to March 2020. All included patients were candidates for the institution's early recovery protocol after surgery and underwent a CT scan of the abdomen before the surgery. Patients with distant metastases (stage IV), those with previous cancer treatment or neoadjuvant therapy, who did not agree to participate in the study, who were unable to perform the muscle strength and/or physical performance test, those with physical deformities and reduced mobility, or who were bedridden were excluded.

The assessments of muscle strength, physical performance and fatigue, and nutritional status were carried out by the same physical therapist and a nutritionist, respectively, during the preoperative hospital stay. The Brief Fatigue Inventory (BFI) was used to classify the level of fatigue, which was considered mild from 1 to 3, moderate from 4 to 6, and severe from 7 to 10[15,16]. For the muscle strength test, the handgrip test was performed, obtained through manual dynamometry in kilograms (kg), using a manual hydraulic dynamometer brand Saehan®. The measure collected was from the dominant side. The reference values for identifying muscle weakness were below 16 and 27 kg for women and men, respectively[3,17].

The *short physical performance battery (SPPB)* was performed, and a better score represents a better physical performance of the patient. The highest score is 12 points, and values below 8 points are considered low physical performance[3].

The assessment of nutritional status was performed using the body mass index (BMI=weight/height²). The reference values that were used were the World Health Organization[18] for adults and the Pan American Health Organization (OPAS) for the elderly[19].

Muscle mass assessment was performed by the same radiologist. The analysis of CT images to obtain body composition data was performed using the OsiriX® software[4,20]. Axial CT images of the abdomen at the level of L3 were evaluated. To measure the skeletal muscle mass areas (skeletal muscles, including psoas, paravertebral, and abdominal wall muscles), a semiautomatic method with manual correction was used. To identify the skeletal musculature, a density of -29 to +150 Hounsfield units (HUs) was considered, and the SMI was calculated (skeletal muscle area [cm^2]/height [m]²), which is classified as low when the index is less than 55.4 cm^2/m^2 for men and 38.9 cm^2/m^2 for women[21].

The analysis of the presence of sarcopenia was carried out in accordance with the recommendation of the European Working Group on Sarcopenia (EWGSOP)[3]. Postoperative complications were assessed within 30 days after the procedure.

The information collected from the images and assessments was exported to a spreadsheet database using REDCap® Software. For data processing, the Statistical Packcage for Social Science (SPSS) software version 20 was used. Descriptive statistics parameters were used, adopting the usual measures of central tendency (average, median, and mode) and simple and relative frequency calculations. Statistical tests were used to correlate the variables, as indicated: for the correlation between the variables, the chi-square and Fisher's exact tests were used for frequencies of categorical variables; Student's *t*-test was used for continuous variables with normal distribution; and the Mann-Whitney test was used for continuous variables without normal distribution. The significance level adopted was 5%.

RESULTS

During the study period, 181 patients were eligible for the study, but 135 were excluded due to neoadjuvant treatment (n=46), previous treatment (n=30), and impossibility of performing evaluations before surgery (n=59). The remaining 46 individuals underwent preoperative evaluation; however, only 31 had CT images available for analysis and were included in the study.

The characteristics of the included patients are described in Table 1. Most of the patients were male (54.8%), with a mean age of 58 years. Most patients had cancer of the colon (77.4%), and clinical stage II was observed in 41.9% of the cases. Table 1 also shows the nutritional profile of the patients by BMI, muscle strength, physical performance, fatigue, and muscle mass. In the classification of BMI, most cases (41.9%) were classified as eutrophic, and no cases were classified as malnourished. Seven patients had low muscle strength (22.6%), and nine (29.0%) had low physical performance. Most patients had mild fatigue (41.9%), the mean skeletal muscle area was 137.5±33.3 cm^2 (75.2–231.0), and the SMI was 49.3±7.8 (35.3–68.0). Among the cases, 15 (48.4%) patients had a low SMI, and 16 (51.6%) had a normal SMI.

In Figure 1, the flowchart shows the classification of sarcopenia. The prevalence of probable sarcopenia was 22.6%, sarcopenia was confirmed in 19.4%, and 9.7% were classified as severe sarcopenia, while isolated low SMI on CT was observed in 48.4%.

Male patients had a higher rate of low SMI than female patients (p=0.018). There were no statistically significant differences between the presence of sarcopenia and low SMI with patient age, clinical staging, BMI, fatigue, or postoperative complications (Table 2). Postoperative complications were observed in 13 patients (41.9%); however, we did not observe a correlation between the presence of complications and the presence of sarcopenia or low SMI.

Table 1. Characteristics of the included patients (n=31).

Variable	Category	N (%)
BMI (kg/m²)	Min–Max	22.0–40.9
	Median	27.4
BMI (<60 years old)	Malnutrition Eutrophy Overweight Obesity	0 (0.0%) 10 (52.6%) 2 (10.5%) 7 (36.8%)
BMI (≥60 years old)	Malnutrition Eutrophy Overweight Obesity	2 (16.7%) 7 (58.3%) 3 (25.0%) 0 (0.0%)
Handgrip strength (kg)	Min–Max	14–52
	Average Average for women Average for men	28.4±9.6 20.9±4.2 34.7±8.3
SPPB	Min–Max Average	5–11 8.4±1.4
BFI	No fatigue Fatigue mild Fatigue moderate Fatigue severe	9 (29%) 13 (41.9%) 8 (25.8%) 1 (3.2%)
Muscle mass (cm²)	Min–Max Average	75.2–231.0 137.5±33.3
MMI (cm²/m²)	Min–Max Average	35.3–68.0 49.3±7.8

Min.: minimum; Max.: maximum; BMI: body mass index; SPPB: short physical performance battery; BFI: Brief Fatigue Inventory; MMI: muscle mass index.

DISCUSSION

Sarcopenia can be present in colorectal cancer patients at diagnosis, regardless of the presence of traditional nutrition risk factors[14]. The prevalence of sarcopenia in patients with colorectal cancer ranges from 11.9 to 60% in the literature. Miyamoto et al.[22] reported 25% sarcopenia in patients with stage I to stage III colorectal cancer; however, it is noteworthy that the authors used only low skeletal muscle mass as the definition of sarcopenia. Few studies present discussions about the need for an assessment of all aspects, as the consensus suggests[3]. The prevalence of sarcopenia in this study was 19.4% using the proper criteria, against 48.4% of patients with low SMI on CT.

Huang et al.[23] evaluated the impact of sarcopenia on postoperative outcomes in 142 recently operated colorectal cancer patients. They described that 17 patients (12%) were diagnosed with sarcopenia and concluded that including a functional aspect in addition to evaluating only skeletal muscle mass could result in a better prediction of postoperative complications. Nakanishi et al.[24] found a significant association between the higher prevalence of male colorectal cancer patients and the presence of sarcopenia, which was also observed in our results. Likewise, older age is associated with a greater chance of developing sarcopenia[25].

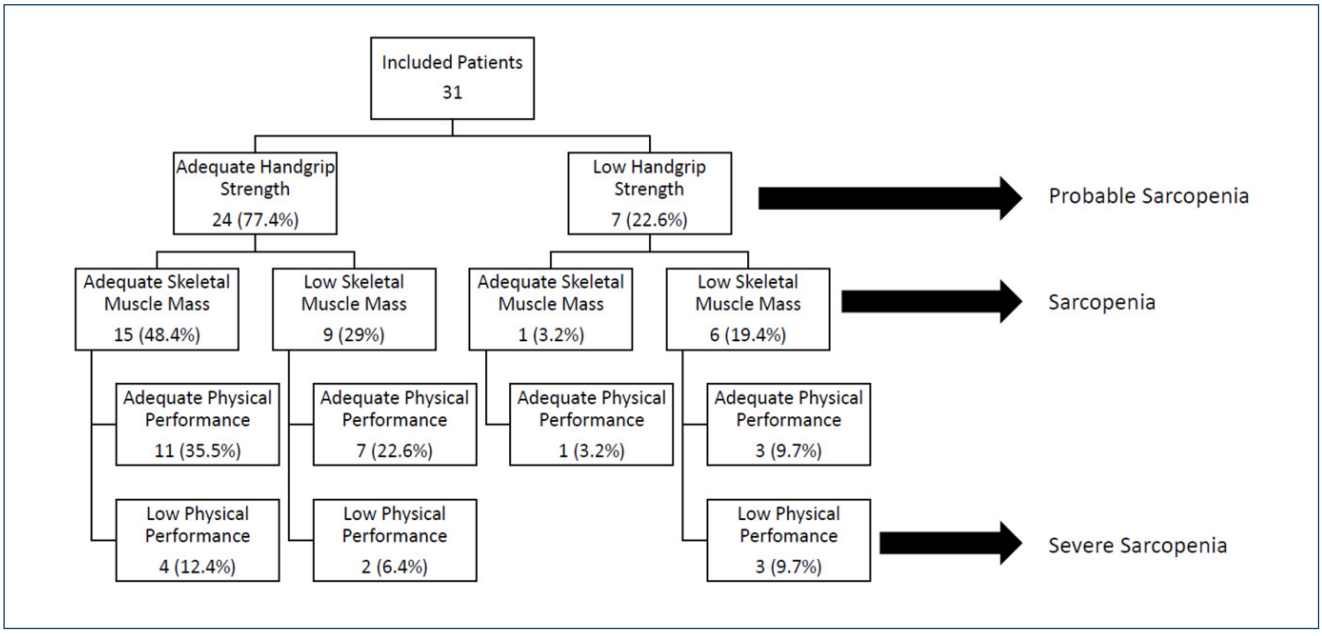

Figure 1. Flowchart of stages of sarcopenia for all patients included in this study.

Table 2. Correlation between the presence of sarcopenia/low muscle mass and evaluated variables.

Variables		Without sarcopenia	With sarcopenia	p	Adequate skeletal muscle mass	Low skeletal muscle mass	p
Gender	Female	12 (85.7%)	2 (14.3%)	0.664	11 (78.6%)	3 (21.4%)	0.018
	Male	13 (76.5%)	4 (23.5%)		5 (29.4%)	12 (70.6%)	
	All patients	25 (80.6%)	6 (19.4%)		16 (51.6%)	15 (48.4%)	
Stage	Stage I	9 (90.0%)	1 (10.0%)	0.439	7 (70.0%)	3 (30.0%)	0.388
	Stage II Stage III	11 (84.6%) 5 (62.5%)	2 (15.4%) 3 (37.5%)		5 (38.5%) 4 (50.0%)	8 (61.5%) 4 (50.0%)	
	All patients	25 (80.6%)	6 (19.4%)		16 (51.6%)	15 (48.4%)	
BMI	Malnutrition	2 (100.0%)	0 (0.0%)	0.157	1 (50.0%)	1 (50.0%)	0.209
	Eutrophy Overweight	11 (64.7%) 5 (100.0%)	6 (35.3%) 0 (0.0%)		6 (35.3%) 4 (80.0%)	11 (64.7%) 1 (20.0%)	
	Obesity	7 (100.0%)	0 (0.0%)		5 (71.4%)	2 (28.6%)	
	All patients	25 (80.6%)	6 (19.4%)		16 (51.6%)	15 (48.4%)	
Fatigue	Mild	11 (84.6%)	2 (15.4%)	0.888	7 (53.8%)	6 (46.2%)	0.849
	Moderate Severe	6 (75.0%) 1 (100.0%)	2 (25.0%) 0 (0.0%)		3 (37.5%) 1 (100.0%)	5 (62.5%) 0 (0.0%)	
	Without	7 (77.8%)	2 (22.2%)		5 (55.6%)	4 (44.4%)	
	Total	25 (80.6%)	6 (19.4%)		16 (51.6%)	15 (48.4%)	
Postoperative complications	Yes	12 (92.3%)	1 (7.7%)	0.359	6 (46.2%)	7 (53.8%)	0.879
	No	13 (72.2%)	5 (27.8%)		10 (55.6%)	8 (44.4%)	
	All patients	25 (80.6%)	6 (19.4%)		16 (51.6%)	15 (48.4%)	

Complications after surgical procedures in nonmetastatic colorectal cancer have been related to the presence of low muscle mass and sarcopenia in some studies. In our sample, 53.8% of patients with low muscle mass had postsurgical complications, compared to 44.4% of patients with normal muscle mass; however, this difference was not statistically significant. In other studies, postsurgical complications were observed in 32.8 to 60% of patients[26,27] with low skeletal muscle mass and were pointed out as an independent predictor of worse overall survival.

Souza et al.[28] evaluated sarcopenia in patients with colorectal cancer and observed a rate of 15% of patients with sarcopenia; among them, most patients were overweight and obese. In this study, most patients were eutrophic at the time of preoperative assessment, including patients with sarcopenia (35.5%) and patients with low muscle mass (64.7%).

Wang et al.[29] analyzed cancer-related fatigue reported in 187 stage III and stage IV patients with cancers at various sites. By using the BFI instrument, this study showed fatigue in 33.7% of the sarcopenic group, and the average score found on the BFI scale was 2.9. It was concluded that fatigue may result in changes in skeletal muscle, resulting in a feeling of tiredness, general weakness, and lack of energy.

On the contrary, in our results, we observed that moderate fatigue was more prevalent both in the population with diagnosed sarcopenia (25.0%) and in patients with isolated low muscle mass (62.5%). Few studies[30] performed a physical performance test in the population with cancer and advanced age, which makes it difficult to identify complications and compare them with frailty. The average score found in our population not testing physical performance (SPPB) was 8.4±1.4, taking into account that below 8 points on the scale, there is low physical performance. Nevertheless, we observed that severe sarcopenia, which in its classification adds poor physical performance, had a prevalence of 9.7% of the collected sample.

Some limitations of this study can be pointed out, such as the limited sample size, which may have impaired the statistical analysis performed. The limited sample was due to different reasons, including the logistical difficulty of performing all the necessary preoperative assessments, without compromising the therapeutic schedule, the nonavailability of CT images in some cases, and, finally, the limitations related to the COVID-19 pandemic during the final period of data collection. In this study, we only evaluated muscle quantity through the measurement of the muscle mass area by CT; however, we did not assess muscle

quality. Schneider et al.[31] recently showed that assessment of muscle quality through the measurement of muscle attenuation on CT can be a better predictor of adverse outcomes than muscle quantity, and it should be considered in future studies.

CONCLUSION

Our study showed that the analysis of muscle mass alone on CT may overestimate the prevalence of sarcopenia in preoperative colorectal patients. Considering the criteria established by the EWGSOP, the prevalence of preoperative sarcopenia in our study was 19.4%, against 48.4% if we consider only low muscle mass on CT. We did not find a significant association between the presence of sarcopenia and age, gender, tumor staging, nutritional characteristics, patient self-reported fatigue, or postoperative complications; however, the small sample size may have limited these analyses. As recommendations for future investigations, we emphasize the importance of reiterating the need to follow the updated sarcopenia consensus for sarcopenia assessment to determine the real impact of the three assessment pillars (muscle strength, muscle mass, and physical performance) in oncological patients.

AUTHORS' CONTRIBUTIONS

GDN: Conceptualization, Data curation, Investigation, Methodology, Writing – original draft, Writing – review & editing. **LZC:** Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **TMM:** Conceptualization, Formal Analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **AGVB:** Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **JOS:** Data curation, Formal Analysis, Methodology, Writing – original draft, Writing – review & editing. **LNC:** Writing – original draft.

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