Presence of dynapenia and association with anthropometric variables in cancer patients

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Abstract

Background: Dynapenia is defined as an age-related loss of muscle strength. There is little information on dynapenia in cancer patients and on how it relates to anthropometric variables. The aim of this study was to analyze the presence of dynapenia and its association with anthropometric variables in hospitalized cancer patients.

Methods: Participants comprised adult and elderly cancer patients evaluated within the first 48 h of hospital admission to a tertiary public hospital, a referral center for gastrointestinal tract surgery. Anthropometric variables were measured according to standardized protocols. Dynapenia was identified based on handgrip strength (HGS), according to the cutoff points defined by the European Working Group on Sarcopenia in Older People (EWGSOP2), with values for women < 16 kg and for men < 27 kg. Statistical analysis was performed using SPSS software, version 22.0, with a significance level of 5%.

Results: This study included 158 patients aged in average 59.5 ± 14.0 years; of these, 53.6% were elderly, 58.9% non-white and 59.5% had some degree of malnutrition. The most prevalent type of cancer was that of the lower gastrointestinal tract (33.5%). The presence of dynapenia was observed in 23.4% of the patients and cachexia in 36.1%. There was an association between dynapenia with age (p < 0.001), life stage (p = 0.002) and race/color (p = 0.027), and also with body mass index (BMI) (p = 0.001) and adductor pollicis muscle thickness (APMT) of both hands (p < 0.05). After logistic regression analysis, adjusted for the sociodemographic variables, the APMT of the dominant hand and the low weight determined by body mass index remained associated with the occurrence of dynapenia (p < 0.05).

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Conclusions: In this study we confirmed that dynapenia was present in cancer patients, being associated with APMT of the dominant hand and low weight. HSG was proven to be a reliable and complementary measure to be added to the process of assessing nutritional status, contributing to the nutritional diagnosis of these patients and to the detection of early muscle depletion.

Keywords: Dynapenia, Body composition, Muscle strength, Muscle mass, Cachexia

Background
The prevalence of malnutrition in cancer patients varies from 31 to 97% [1, 2] according to the location of the tumor, stage of the disease, and type of anticancer treatment adopted [3]. Patients with gastrointestinal tract cancer are the most affected, for about 15 to 66% of them are malnourished [3, 4].

Malnutrition is associated with a worse prognosis, the presence of complications and a reduced response to treatment, in addition to increasing the length of hospital stay and being an independent factor for shorter survival [4–6]. Anorexia is often observed, along with a rapid loss of adipose tissue, tissue loss, and skeletal muscle atrophy [7], which may or may not progress to cachexia [8].

Cancer cachexia is a multifactorial syndrome known for involuntary weight loss concomitant with reduced skeletal muscle mass, with or without loss of adipose tissue, being associated with decreased function, physical performance and a negative prognosis [8, 9]. It happens as a result of a negative energy-protein balance, reduced food intake and an increased catabolic process, being aggravated by the systemic inflammation syndrome that often takes place in cancer patients [8–12]. The worsening of the cachectic condition leads to a progressive impairment of muscle function, which may explain its association with dynapenia in these patients [13].

Dynapenia is defined as an age-related loss of strength and muscle function [14], having been considered an important predictor of functional disability and death related to the loss of isolated muscle mass [15, 16]. Its development varies according to the individuals’ pre-existing characteristics, such as nutritional status, body composition, physical activity, food intake, and comorbidities. When present simultaneously, these factors may lead to loss of muscle mass and, consequently, to the worsening of nutritional status [15].

Some studies have shown that dynapenia is more prevalent than sarcopenia [13, 17], which prompted an interest in investigating the relationship between muscle function, nutritional status and body composition.

The measurement of handgrip strength (HGS), which can be used to determine dynapenia, has been shown to reflect nutritional impairment even before changes in body composition could be detected through different anthropometric parameters that indicate muscle mass reserve [18, 19], such as the adductor pollicis muscle thickness (APMT), mid-arm circumference (MAC), corrected mid-upper arm muscle area (CAMA) and calf circumference (CC), all commonly used for the assessment of nutritional status and body composition in cancer patients [20, 21].

However, there is still a lack of evidence on how these measures are actually interrelated. A better understanding of this relationship would provide support for the assessment of more effective, practical and easier ways to diagnose the nutritional status of hospitalized patients earlier. Therefore, the aim of this study was to analyze the presence of dynapenia and its association with anthropometric variables in hospitalized cancer patients.

Methods
Design
This descriptive cross-sectional study was carried out in a public tertiary hospital – a referral center for gastrointestinal tract surgery – located in Vitória-ES, Brazil, from March 2017 to October 2019.

Study population
The study included patients of both sexes, aged 20 years or over, with a confirmed diagnosis of cancer, admitted to the General Surgery Unit to perform a curative surgical procedure to remove the neoplastic tumor. The recruitment was carried out by trained researchers, and, at first, all eligible patients were approached. Individuals with cognitive dysfunction predicted in medical records, in respiratory isolation, in palliative care, with full body edema or those who could not be evaluated by the researchers within the first 48 h of hospital admission were excluded.

Tumor location was categorized as follows: upper gastrointestinal tract (GIT), lower GIT, attached glands (liver, pancreas, and bile ducts), and others (lung and chest, hematological, skin, unknown behavior, ovary, gastrointestinal stroma, bladder, cervical, ganglia, parotid gland, breast, mediastinum, peritoneum, pleura, connective tissue, thyroid, submandibular and other locations). The length of hospital stay was categorized as follows: less than or equal to 7 days of hospitalization...
and greater than 7 days, according to the calculated median.

**Study variables**

Trained researchers applied specific protocols in order to collect sociodemographic (age, sex, and self-declared color) and anthropometric information, such as weight (kg), height (m), handgrip strength (HGS) (kg/f), arm circumference (AC) (cm), tricipital skinfold (TSF) (mm), calf circumference (CC) (cm) and thickness of the adductor pollicis muscle thickness (APMT) (mm), considered indicators of muscle mass and body composition [22–25]. Mid-arm circumference (MAC) (cm) and corrected mid-upper arm muscle area (CAMA) (cm²), which also evaluate the muscular compartments, were calculated from AC and TSF [22, 26]. All anthropometric variables were measured according to standardized protocols [27, 28].

For the classification of AC, TSF and MAC, we used the adequacy to the 50th percentile (%), according to Frisancho et al. Values < 90% were considered low and ≥ 90% adequate. For the classification of CAMA, values lower than the 15th percentile, according to sex and age, were considered reduced [22]. CC was classified according to the cutoff points proposed by Barbosa-Silva et al., who defined values ≤33 cm for women and ≤34 cm for men [24].

Body mass index (BMI) was calculated (weight (kg)/height² (m)) and classified according to the World Health Organization (WHO) [29] reference for adults, and to that proposed by the Pan American Health Organization (PAHO) [30] for the elderly. In the present study, the term “overweight” refers to individuals classified as overweight or obese, according to the BMI.

To identify cachexia, the patients were classified according to the following diagnostic criteria: (a) unintentional weight loss ≥5% in the last 6 months or (b) unintentional weight loss ≥2% in the last 6 months and BMI < 20 kg/m² [9].

APMT was measured according to the technique proposed by Lameu et al. [23] using a Lange® adipometer. The procedure was performed three times on both dominant (DAPMT) and non–dominant (NDAPMT) hands, and the mean value considered for the analysis [31]. The cutoff point of Bragagnolo et al. was used for surgical patients, with measures lower than 13.4 mm for the DAPMT and 13.1 mm for the NDAPMT indicating malnutrition [31].

To assess HGS we used the Jamar® handheld dynamometer. The test was performed according to the methodology recommended by the American Hand Therapy Association (ASHT) [32]. The procedure was performed three times on the dominant hand (DHGS) with maximum effort for about 5 s, with an interval of 1 min between measurements [32]. The outcome variable “dynapenia” was identified from the maximum HGS of the dominant hand, according to the cutoff points defined by the European Working Group on Sarcopenia in Older People (EWGSO), with values of < 16 kg for women and < 27 kg for men [33].

The Patient-Generated Subjective Global Assessment (PG-SGA) was collected through the application of a questionnaire translated and validated into Portuguese by Gonzales et al. [34], with permission to use the PG-SGA/Pt-Global Platform (www.pt-global.org) having been duly obtained. The PG-SGA is the subjective nutritional assessment and screening tool indicated by the Brazilian Consensus of Oncological Nutrition for the evaluation of cancer patients in Brazil [18]. It allows the classification of nutritional status into three categories: (A) well nourished, (B) suspected or moderate malnutrition, and (C) severe malnutrition.

**Statistical analysis**

Descriptive analysis was expressed in means and standard deviations to describe continuous variables and in percentages for categorical variables. Patients were grouped into adults (< 60 years old) and elderly (≥ 60 years old), according to the WHO classification for developing countries [35]. Race/color was grouped into whites and non-whites. Differences between the proportions were assessed by the Chi-square test. To determine the influence of independent variables in the presence of dynapenia (dependent variable) and anthropometric variables (independent ones), binary logistic regression analysis was performed. Crude Odds Ratios (ORs) were presented after adjustments for sociodemographic variables (sex, age range and race/color). The adjustment variables were inserted in blocks: model 1 (anthropometric variables and age), model 2 (anthropometric variables, age and sex) and model 3 (anthropometric variables, age, sex, and race/color) and model 4 (anthropometric variables, age, sex, color, malnutrition and cachexia). Only anthropometric variables with 5% statistical significance were selected for logistic regression in the chi-square test and that could have an influence on muscle strength (malnutrition and cachexia). Data were analyzed using SPSS 22.0 software. The level of significance adopted for all tests was 5.0%.

**Results**

A total of 158 patients aged in average 59.5 ± 14.0 years were evaluated. Of these, 56.3% were elderly, 51.3% were male, and 58.9% declared themselves non-white. As for tumor location, those on the lower gastrointestinal tract (GIT) were more prevalent, affecting 33.5% of patients. Most patients remained hospitalized for ≤7 days (54.4%). PG-SGA revealed that 59.5% of patients had some
degree of malnutrition (B + C). Moreover, cachexia was detected in 36.1% of the patients, while 23.4% presented dynapenia (Table 1).

We found significant differences between the presence and absence of dynapenia in relation to some sociodemographic variables, namely age \((p < 0.001)\), stage of life \((p = 0.002)\) and race/color \((p = 0.027)\) (Table 2).

Table 3 shows the association between anthropometric variables and the categories of dynapenia. We found the presence of dynapenia to be significantly affected by BMI \((p < 0.001)\), DAPMT \((p < 0.001)\) and NDAPMT \((p = 0.002)\) (Table 3).

In the logistic regression analysis, even after adjusting for age, sex and race/color, nutritional status by PG-SGA and cachexia, DAPMT and low weight remained associated with the occurrence of dynapenia. In relation to DAPMT, patients with reduced musculature were 5.54 times more likely to have dynapenia compared to individuals with adequate APMT (OR: 5.54 [95% CI: 1.04–29.39], \(p = 0.044\)). When analyzing by BMI, we found that those with low weight were approximately 4.55 times more likely to have dynapenia compared to eutrophic patients (OR: 4.55 [95% CI 1.47–14.08], \(p = 0.009\)). Despite the inclusion of malnutrition and cachexia in the regression model, we observed that DAPMT and low weight (BMI) remained associated with dynapenia. However, NDAPMT and overweight lost the strength of the association after adjusted analyses (Table 4).

### Discussion

This study identified dynapenia in 23.4% of the evaluated patients, who were mostly malnourished and had gastrointestinal tract cancer. Similar studies carried out in both adults and the elderly showed that dynapenia was present in 24.4% [36] and 44.9% [37] of cancer patients, respectively, while yet another study reported that 30.9% of the elderly population under evaluation presented dynapenia [13].

The incidence of malnutrition varies between 31 to 97% in cancer patients [1, 2], being more prevalent in cancers located in the GIT due to obstructions in this region and/or malabsorption of nutrients [38].

The metabolic changes resulting from cancer, physical inactivity, the adverse effects of treatment, and the presence of malnutrition, impair the maintenance of muscle mass and function, causing functional impairments, total physical disability and mortality [14, 38]. The impairment of the muscle’s ability to generate strength leads to dynapenia, which further aggravates clinical and nutritional aspects [13]. In our study the presence of malnutrition and cachexia did not influence dynapenia.

Dynapenia can be diagnosed through the HGS, a measure of functional capacity that complements the nutritional assessment for being associated with malnutrition [39–41], in addition to being recommended by the American Society for Parenteral and Enteral Nutrition (ASPEN) for the diagnosis of malnutrition in clinical practice [42].

Magnetic resonance imaging, computed tomography, biphotonic X-ray absorptiometry (DXA) and electrical bioimpedance are excellent methods for the estimation of muscle mass, for they allow the precise quantification

### Table 1

Sociodemographic characteristics, tumor location, length of hospital stay, nutritional status and presence of cachexia and dynapenia in hospitalized cancer patients

| Variable | n = 158 | Total |
|----------|---------|-------|
| Age (mean ± SD) | 59.5 ± 14.0 | 90.5 ± 14.0 |
| Min-Max | 20–88 | 20–88 |
| Stage of life n (%) | | |
| Adult | 69 (43.7) | 43.7 |
| Elderly | 89 (56.3) | 56.3 |
| Gender | | |
| Male | 81 (51.3) | 51.3 |
| Female | 77 (48.7) | 48.7 |
| Color | | |
| Non-white | 93 (58.9) | 58.9 |
| White | 65 (41.1) | 41.1 |
| Tumor Location | | |
| Lower GIT | 53 (33.5) | 33.5 |
| Attached glands | 39 (24.7) | 24.7 |
| Upper GIT | 27 (17.1) | 17.1 |
| Others\(^a\) | 39 (24.7) | 24.7 |
| Length of hospital stay | | |
| ≤ 7 days | 86 (54.4) | 54.4 |
| > 7 days | 72 (45.6) | 45.6 |
| PG-SGA | | |
| Well nourished (A) | 64 (40.5) | 40.5 |
| Moderately malnourished (B) | 64 (40.5) | 40.5 |
| Severely malnourished (C) | 30 (19.0) | 19.0 |
| Presence of Cachexia | | |
| Yes | 57 (36.1) | 36.1 |
| No | 101 (63.9) | 63.9 |
| Dynapenia | | |
| Yes | 37 (23.4) | 23.4 |
| No | 121 (76.6) | 76.6 |

\(^a\)Others (corresponding to cancers with a low prevalence within the sample): 6.33%: lung and thorax cancer; 3.80%: hematological cancer; 3.16%: skin cancer; 1.89%: cancer of unknown behavior; 1.26%: ovarian cancer; 0.63%: stromal gastrointestinal cancer; 0.63%: bladder cancer; 0.63%: cervical cancer; 0.63%: ganglion cancer; 0.63%: parotid gland cancer; 0.63%: breast cancer; 0.63%: mediastinal cancer; 0.63%: cancer from other locations; 0.63%: peritoneum cancer; 0.63%: pleural cancer; 0.63%: connective tissue cancer; 0.63%: thyroid cancer; 0.63%: submandibular cancer. PG-SGA: Patient-Generated Subjective Global Assessment
of muscle tissue and their use in research has increased the understanding of body composition [43]. This such methods are expensive, and only a few are accessible to clinical practice [36]. Thus, it is necessary to investigate tools capable of early identification of nutritional risk and possible changes in body composition, given the implications for the response to treatment, permanence and clinical outcomes in cancer patients [33].

In hospital practice, anthropometry is used to identify the risk and nutritional status of each patient and to assess the most appropriate nutritional and clinical interventions [21]. Despite the practicality of measurement, the use of HGS for such assessments is still limited. In this study, the presence of dynapenia was associated only with reduced values of DAPMT and BMI, even in the model adjusted for gender, stage of life and color/race. As for the other anthropometric variables studied here, those appear to depend on a more advanced picture of muscle impairment and on an association between different measures to yield results, depending also on the measurement techniques, the patient’s hydration status and applied equations.

Pereira et al., when evaluating 100 cancer patients in outpatient treatment, found an association of HGS with MAC and a weak correlation with CAMA only in the left hand. However, regression models were not used then, nor were cut-off points considered for HGS. The authors confirm the importance of using HGS as an auxiliary method in nutritional screening and as a complementary method in the nutritional diagnosis of cancer patients, in addition to the need for further studies [41].

Table 2  Distribution of sociodemographic variables, tumor location, length of stay, nutritional status and cachexia according to the categories of dynapenia in hospitalized cancer patients

| Variables (n = 158)           | Without dynapenia | With dynapenia | p value |
|------------------------------|-------------------|----------------|---------|
| Age (mean±SD)                | 57.4 ± 13.6       | 66.6 ± 13.3    | < 0.001 |
| n (%)                        |                   |                |         |
| Stage of life                |                   |                | 0.002   |
| Adult                        | 61 (88.4)         | 8 (11.6)       |         |
| Elderly                      | 60 (67.4)         | 29 (32.6)      |         |
| Gender                       |                   |                | 0.130   |
| Male                         | 58 (71.6)         | 23 (28.4)      |         |
| Female                       | 63 (81.8)         | 14 (18.2)      |         |
| Color                        |                   |                | 0.027   |
| Non-white                    | 77 (82.8)         | 16 (17.2)      |         |
| White                        | 44 (67.7)         | 21 (32.2)      |         |
| Tumor location               |                   |                | 0.566   |
| Lower GIT                    | 40 (77.5)         | 13 (24.5)      |         |
| Attached glands              | 28 (78.2)         | 11 (21.8)      |         |
| Upper GIT                    | 20 (71.4)         | 7 (28.6)       |         |
| Othersa                      | 33 (84.6)         | 6 (15.4)       |         |
| Length of hospital stay      |                   |                | 0.236   |
| ≤ 7 days                     | 69 (80.2)         | 17 (19.8)      |         |
| > 7 days                     | 52 (72.2)         | 20 (27.8)      |         |
| PG-SGA                       |                   |                | 0.308   |
| Well nourished (A)           | 46 (71.9)         | 18 (28.1)      |         |
| Moderately malnourished (B)  | 53 (82.8)         | 11 (17.2)      |         |
| Severely malnourished (C)    | 22 (73.3)         | 8 (26.7)       |         |
| Cachexia                     |                   |                | 0.518   |
| Yes                          | 79 (78.2)         | 22 (21.8)      |         |
| No                           | 42 (73.7)         | 15 (26.3)      |         |

GIT: gastrointestinal tract. Student’s t-test; aOthers (corresponding to cancers with a low prevalence within the sample): 6.33%: lung and thorax cancer; 3.80%: hematological cancer; 3.16%: skin cancer; 1.89%: cancer of unknown behavior; 1.26%: ovarian cancer; 0.63%: stromal gastrointestinal cancer; 0.63%: bladder cancer; 0.63%: cervical cancer; 0.63%: ganglion cancer; 0.63%: parotid gland cancer; 0.63%: breast cancer; 0.63%: mediastinal cancer; 0.63%: cancer from other locations; 0.63%: peritoneum cancer; 0.63%: pleural cancer; 0.63%: connective tissue cancer; 0.63%: thyroid cancer; 0.63%: submandibular cancer. PG-SGA: Patient-Generated Subjective Global Assessment.
As for the adductor pollicis muscle, it is the only muscle that can be directly measured by anthropometry, having been established as a good predictor of muscle mass loss [23, 44]. The measurement of APMT has been rather efficiently employed in the evaluation of the muscular compartment, being associated with muscle mass reduction, malnutrition and mortality [45–47]. Valente et al., observed significant correlations between APMT, anthropometric measurements and nutritional status, according to PG-SGA, in adult and elderly cancer patients [25].

Guerra et al. observed a positive correlation between HGS and APMT values in adult hospitalized patients [40], which demonstrates a relationship between such measures and the ability to assess strength and muscle mass.

The literature recognizes HGS as a sensitive, low-cost and easy-to-use method to assess functional muscle loss and nutritional risk [48, 49]. The present results suggest that it is also efficient for assessing muscle mass loss in cancer patients, both in adults and the elderly.

In cancer patients, lower HGS values are associated with unfavorable clinical outcomes, such as longer hospital stays, poor quality of life, postoperative complications and mortality [33, 36, 50]. However, the measure is still seldom used in hospital and outpatient clinical practice, as there are no specific cutoff points for cancer patients and for the evaluation of reduced HGS values in non-elderly subjects [39, 50].

The weight loss and reduced lean mass seen in cancer patients are associated with decreased food intake and the systemic inflammation syndrome induced by the presence of the tumor, which leads to increased pro-inflammatory cytokine activity [10, 11]. It also induces anabolic resistance, which decreases protein synthesis. Combined, all these mechanisms result in weight loss and lean mass depletion [8].

In the elderly, the mechanisms related to changes in muscle tissue may be attributed to a combination of neural factors, such as impaired neural activation and failures in neuromuscular and muscle transmission, accentuating the loss of muscle mass and strength with advancing age in cancer patients [14, 51].

Thus, identifying the presence of dynapenia in adult patients can reduce changes that would be enhanced by aging, which is confirmed by the association between dynapenia and stage of life: HGS was lower in elderly patients. Therefore, the interpretation of these results are limited by the absence of specific cutoff points for the classification of dynapenia in adults and in cancer patients.

Dynapenia is still a new concept that needs to be further investigated, especially in cancer patients. It is known that the loss of muscle mass affects 80% of these patients; however, that cannot be interpreted aside from muscle function, which is reflected by muscular strength [36].

A study conducted by Moreau et al. with 150 cancer patients revealed that the loss of muscle mass, assessed by computed tomography, was greater than the presence of dynapenia, what calls for further studies to elucidate the diagnostic criteria, the chronology of dynapenia and the loss of muscle mass, especially in this population [50].

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There are no studies associating the presence of dynapenia with anthropometric variables in cancer patients, what also limits this discussion. In addition, as the present study was carried out in a referral center for
surgical rather than antineoplastic treatment, tumor staging was not available for most patients, which hindered the conduction of analyses addressing this variable in relation to the presence of dynapenia. As a contribution, our study demonstrates clinical relevance in investigating dynapenia in cancer patients, both in adults and the elderly, adding to the knowledge on the subject. We believe our results stimulate further studies, and that definitions and cut-off points can be established with better precision.

Conclusion
In this study, the presence of dynapenia in cancer patients was confirmed through HSG, being associated with DAPMT and low weight. HGS was proven to be a reliable measure to be added – along with the other relevant variables – to the nutritional status assessment process, potentially contributing to the nutritional diagnosis of these patients and to the early detection of muscle depletion. However, it is still necessary to better elucidate dynapenia in cancer patients at different stages of life.

Abbreviations
AC: Arm circumference; ASPEN: American Society for Parenteral and Enteral Nutrition; ASTH: American Hand Therapy Association; BIA: Electrical bioimpedance; BMI: Body mass index; CC: Calf circumference; DAPMT: Dominant adductor pollicis muscle thickness, Non-dominant adductor pollicis muscle thickness; DXA: Dual energy x-ray absorptiometry; EWGSO: European Working Group on Sarcopenia in Older People; GIT: Gastrointestinal tract; HGS: Handgrip strength; MAC: Mid-arm circumference; NDAPMT: Non-dominant adductor pollicis muscle thickness; PG-SGA: Patient-Generated Subjective Global Assessment; TSF: Tricipital skinfold; TAPM: Thickness of the adductor pollicis muscle; WHO: World Health Organization

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Authors’ contributions
ABR, ILM and VRG: C: concept and design research; ABR, ILM, ECRMV, ISO, and VFS: conducted research; ABR, ILM, and VRG: analyzed data; ABR, ILM, GBP, JLMR and VRG: wrote paper; ABR, ILM and VRG: had primary responsibility for final content. The authors read and approved the final manuscript.

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Availability of data and materials
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Ethics approval and consent to participate
The study was conducted in accordance with the Resolution 466 of December 08, 2012, of the National Health Council of Brazil. Ethical approval for this study was obtained from the Research Ethics Committee of the Federal University of Espirito Santo - Protocol 2.141.932/2017. Patients participated voluntarily and provided written informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no conflict of interest.

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