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PREVALANCE OF COMPUTED TOMOGRAPHY DETERMINED SARCOPENIA IN GASTRIC MALIGNANCY: A HOSPITAL BASED PROSPECTIVE OBSERVATIONAL STUDY IN SUB-HIMALAYAN REGION

Dr. Ishan Barotra[1]*, Dr. Ashish Katoch[2], Dr. Puneet Mahajan[3] and Dr. Rashpal Singh Thakur[4]

[1,2]Junior Resident, Department of General Surgery, Indira Gandhi Medical College Shimla Himachal Pradesh.
[3]Professor, Department of General Surgery, Indira Gandhi Medical College Shimla Himachal Pradesh.
[4]Assistant Professor(Surgical Oncology), Department of General Surgery, Indira Gandhi Medical College Shimla Himachal Pradesh.

***Corresponding Author: Dr. Ishan Barotra**

Junior Resident, Department of General Surgery, Indira Gandhi Medical College Shimla Himachal Pradesh.

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ABSTRACT

Background: Sarcopenia is a complex syndrome defined by progressive and generalized loss of skeletal muscle mass and strength. Sarcopenia is mostly related to age, however cancer is one of its causes as well. These days, sarcopenia is becoming recognized as a poor cancer prognostic factor. Sarcopenia is especially problematic in individuals with gastric cancer who also have eating problems, which frequently result in weight loss and muscle loss. However, the definition and assessment methodology differ throughout research, thus these must be standardized. The aim of this study was to determine the prevalence of sarcopenia in gastric malignancy patients using computed tomography. There is very limited data available from sub-Himalayan belt of northern India, hence the present study was planned the determine the prevalence of sarcopenia in gastric malignancy patients. **Methods:** A hospital based prospective observational study was conducted in the Department of General Surgery of a tertiary care hospital in Shimla, Himachal Pradesh. All patients who reported to Department of Surgery during the study period of 1st September 2021 to 30th September 2022 with diagnosis of gastric cancer were considered for the study. **Results:** Forty-one patients were included in the study. Prevalence of sarcopenia was 43.90% (18patients) based on EWGSOP2 (The European Working Group on Sarcopenia in Older People 2) recommendations. Patients had a mean age of 60.66± 12.93 years. Sarcopenia was detected in 18(43.90%) patients based on EWGSOP2 (The European Working Group on Sarcopenia in Older People 2) recommendations. The mean age was 65.94 years in the sarcopenic group (SG) and 55.49 years in the non-sarcopenic group(NSG).The mean SMI(Skeletal Muscle Index) was 44.08±8.93cm²/m² and 46.19±9.13cm²/m² in the SG and NSG, respectively. The mean body mass index (BMI) was lower in the sarcopenic group than in the nonsarcopenic group (19.64 ± 3.36 vs. 20.18± 3.38 kg/m^2). **Conclusions:** Prevalence of sarcopenia was 43.90% (18 patients) based on EWGSOP2 (The European Working Group on Sarcopenia in Older People 2) recommendations.

KEYWORDS: Sarcopenia _ Prevalance_ gastric malignancy _Sub Himalayan Region.

INTRODUCTION

The term sarcopenia, derived from the Greek word meaning "poverty of flesh," describes the progressive loss of skeletal muscle mass, strength, and physical performance. I.H. Rosenberg first coined this term to refer to the "ageing related loss of skeletal muscle mass and strength".[1] Sarcopenia has a biological aspect, with aging leading to reduced expression of genes involved in skeletal muscle mitochondrial function, oxidative capacity, and glucose uptake.[2] It affects both men and women equally, beginning in the fourth decade of life and accelerating in the sixth decade.[3] Initially identified in the elderly, sarcopenia is now often defined as a geriatric syndrome that includes functional impairment, increased risk of falls, fractures, and decreased survival. It is also a predictor of chronic disease progression, poorer functional outcomes, and postoperative complications, both infectious and non-infectious.[4] Sarcopenia can be classified as primary or secondary. Primary sarcopenia is age-related, while secondary sarcopenia results from illness, malnutrition, invasive procedures, organ failure, cancer, and other diseases.[5] Both types are significant as they negatively impact a patient's functional status and can worsen the prognosis of underlying conditions. It is estimated that individuals lose 0.5–1.0% of skeletal muscle mass per year after the age of 25.[6] Cancer is a particularly notable condition that exacerbates muscle atrophy, especially in older adults.[7] The incidence and survivorship of cancer are highest among those over 60 years old.[8] The likelihood

of developing cancers such as gastrointestinal malignancies, lung, prostate, uterine, melanoma, breast cancer, non-Hodgkin lymphoma, or leukemia increases with age. Therefore, older sarcopenia patients are more likely to experience significant muscle mass reduction before and after a cancer diagnosis. To evaluate sarcopenia, diagnostic algorithms were proposed by the European Working Group on Sarcopenia in Older People (EWGSOP2)[9] in 2010 and the Asian Working Group for Sarcopenia (AWGS) in 2014.[10] EWGSOP2 defines sarcopenia as reduced muscle strength, low muscle quality, and low physical performance, considering it severe if all three criteria are met. The AWGS defines sarcopenia as age-related loss of skeletal muscle mass plus loss of muscle strength and/or reduced physical performance, with population-specific cutoffs for measurements. Among the various definitions and criteria, EWGSOP2 is widely accepted. For diagnosis of sarcopenia as defined by the EWGSOP2 cut off values are:-

Assessing muscle strength cut off values are

Grip strength	<27 kg for men
	<16 kg for women
Chair stand test	>15 s for five rises

Assessing muscle mass/volume cut off values are

DEXA	<7.0 kg/m^{2}for men
	<5.5 kg/m^{2}for women
Bio-impedance analysis	8.87 kg/m^2 for men
	6.42 kg/m^2 for women
CT imaging	<55 cm^2/m^2 for men
	<39cm^2/m^{2}for women

Physical Performance tests

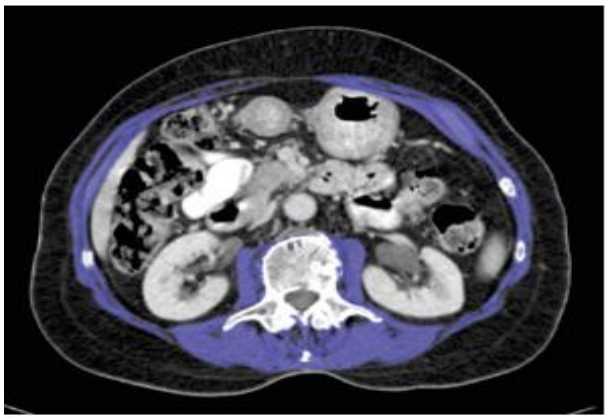
Short physical performance battery test	<8
400 m (Walk 20 m laps)	Non completion or > 6minutes
Gait speed (Over a 4 m course)	<0.8 m/s

Various methods of measurement of skeletal muscle mass

Nowadays, CT and MRI are increasingly utilized as research tools for assessing body composition parameters, as these imaging techniques are routinely employed for staging purposes and evaluating the resectability of malignant diseases. The reduction of skeletal muscle mass can be assessed using computed tomography (CT), magnetic resonance imaging (MRI), dual-energy x-ray absorptiometry (DXA), or bioelectrical impedance analysis. However, the current gold standard for estimating total skeletal muscle mass is the assessment of the skeletal muscle index at L3 using contrast-enhanced computed tomography (CECT). Muscle strength deterioration can be evaluated with knee extension/flexion or handgrip strength tests, while the decline in physical performance can be measured using the short physical performance battery test, the timed get-up-and-go test, gait speed, or the stair climb power test. An important limitation is the lack of consensus on cut-off points for defining sarcopenia, which also vary depending on the selected evaluation technique. Since CT is widely used for clinical tumor staging, it is a convenient method for diagnosing sarcopenia. By using a single abdominal cross-sectional CT image at the third lumbar vertebra (L3), total body mass can be projected by assessing the skeletal muscle index (cm²/m²). This index is calculated by summing the skeletal muscle areas at the L3 level and normalizing for stature.[11,12] Several studies have concluded that quantifying sarcopenia is possible by estimating lumbar muscle mass in two-dimensional planar CT scans taken at the level of the third lumbar vertebra (Third lumbar vertebra skeletal muscle index - L3SMI).[13] Radiologically significant sarcopenia is defined as a lumbar skeletal muscle index of ≤39 cm²/m² in females and ≤55 cm²/m² in males according to EWGSOP2.[14] The prevalence of sarcopenia in patients undergoing surgery for gastrointestinal cancers (evaluated by measuring skeletal muscle mass via CT) has been reported in several studies. Gastrointestinal malignancies are often diagnosed at an advanced stage and have a low 5-year survival rate.[15] Despite similar age and sex distributions between studies, the prevalence of this condition varied widely. In healthy individuals, the prevalence of sarcopenia increases with age, ranging from 9.0% at 45 years to up to 64.0% in those 85 years or older.[16] In India, the prevalence of sarcopenia in cancer patients is an area of investigation, as very few Indian studies have evaluated the effect of sarcopenia on outcomes in cancer patients . Therefore, we aimed to study the prevalence of sarcopenia in patients with gastric malignancy.

Screening for sarcopenia

Sarcopenia was assessed by calculating the Skeletal Muscle Index (SMI) using CT scans at the L3 vertebra. In this study, the contrast-enhanced CT abdomen (CECT) used for diagnosing gastric malignancy was used to calculate the SMI, with no additional CECT performed solely for this purpose. Patients underwent CT scans using a 64-slice MDCT (LightSpeed VLT – XTE, GE Medical System), with cross-sectional images taken at the L3 vertebral level where both transverse processes were visible. The areas of the psoas, quadratus lumborum, erector spinae, transversus abdominis, internal and external obliques, and rectus abdominis muscles were manually measured using the area measurement tool in RadiAnt DICOM viewer. The threshold range for identifying skeletal muscle was set between -30 to +150 Hounsfield units. The skeletal muscle area was then normalized for height to calculate the SMI.



The skeletal muscle index is calculated as follows

Cross-sectional area of the total skeletal muscles at L3 (psoas, quadratus lumborum, erector spinae, transversus abdominis, internal and external obliques and rectus abdominis muscles) in $[cm]^2$
Height $[m]^2$

Patients were categorized into sarcopenic and non-sarcopenic groups based on CT measurement of total skeletal muscle mass in cross sectional area at the level of L3. Based on EWGSOP2 (The European Working Group on Sarcopenia in Older People 2) recommendations, SMI < 55 cm^2/m^2 was considered the cutoff for men, compared to < 39 cm^2/m^2 for women.

Statistical analysis

The presentation of the Categorical variables was done in the form of number and percentage (%). On the other hand, the quantitative data were presented as the means ± SD and as median with 25th and 75th percentiles (interquartile range). The following statistical tests were applied for the results:

1. The association of the variables which were quantitative in nature were analysed using Independent t test (for two groups) and ANOVA (for more than two groups).
2. The association of the variables which were qualitative in nature were analysed using Chi-Square test. If any cell had an expected value of less than 5 then Fisher's exact test was used.

The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver 25.0. For statistical significance, p value of less than 0.05 was considered statistically significant. Ethical approval was obtained from institutional ethical committee.

RESULTS

Patient characteristics

Forty-one patients were included in the study. Prevalence of sarcopenia was 43.90% (18patients) based on EWGSOP2 (The European Working Group on Sarcopenia in Older People 2) recommendations. Patients had a mean age of 60.66± 12.93 years.

Among the 41 patients with diagnosis of gastric cancer; 18 patients (43.90 %) were diagnosed as sarcopenic and the remaining 23 patients (56.1%) based on EWGSOP2 (The European Working Group on Sarcopenia in Older People 2) recommendations. The mean age of patients with sarcopenia with gastric malignancy was 65.94 years and the mean age of patients without sarcopenia with gastric malignancy was 55.49 years. The prevalence of sarcopenia was remarkably higher among patients more than 60 years of age. Clinicopathological features of the two groups are shown in Table 1.

Regarding gender, the proportion of men was higher in the sarcopenic group than women in the non-sarcopenic group (61.1% vs. 38.8 %). Of body weight and composition, mean body mass index (BMI) was lower in the sarcopenic group than in the nonsarcopenic group (19.64 ± 3.36 vs. 20.18± 3.38 kg/m^2). Nutritional parameters such as mean serum albumin was lower in the sarcopenic group than in the non sarcopenic group (sarcopenic, 3.05± .42g/dl vs. non-sarcopenic, 3.24± .42 g/dl). Mean skeletal muscle index (cm^2/m^2) in patients of gastric carcinoma in sarcopenic patients was 44.08±8.93cm^2/m^2 while skeletal muscle index (cm^2/m^2) in patients of gastric carcinoma in non sarcopenic patients was 46.19±9.13cm^2/m^2.

Table 1: Clinicopathological features of sarcopenic and non-sarcopenic patients.

Clinicopathological features	Sarcopenic group(n=18)	Non Sarcopenic group(n=23)
Mean age(years)	65.94	55.49
Gender Men Women	 11(61.1%) 7(31.8%)	 12(52.17%) 11(47.82%)
BMI (kg/m^2)	19.64 ± 3.36	20.18± 3.38
Serum albumin(g/dl)	3.05± .42	3.24± .42
SMI(cm^2/m^2)	46.19±9.13	46.19±9.13

DISCUSSION

As the global population ages and lifespans increase, the number of elderly patients with gastrointestinal malignancies has been rising significantly. Additionally, the prevalence of sarcopenia also increases with age in gastrointestinal malignancy patients. Surgical resection remains the most effective treatment for potentially curable gastrointestinal malignancies. However, surgeons

sometimes hesitate to operate on elderly patients due to the high frequency of complications and poor survival rates associated with aging. The role of sarcopenia in cancer patient management is an evolving research area. Numerous studies on different tumor biologies have shown that a low skeletal muscle index adversely affects oncology patient outcomes. This study aimed to estimate the prevalence of sarcopenia in colorectal malignancy. Sarcopenia cut-off points depend on the measurement technique and the availability of reference studies and populations. The most widely used method for assessing muscle mass is computed tomography (CT), specifically by evaluating the skeletal muscle index at the third lumbar vertebra, with specific cut-off points for each sex. The current gold standard for determining total skeletal muscle mass is the skeletal muscle index assessment at L3 using contrast-enhanced CT (CECT). Various studies worldwide have used CT to assess sarcopenia and have established different cut-off points. Most previous studies defined sarcopenia using the cut-offs from Prado et al. and Marti et al., which classified sarcopenia as a lumbar skeletal muscle index by CT imaging (at the 3rd lumbar vertebra) of <52.4 cm^2/m^2 in men and <38.9 cm^2/m^2 in women, and <53 cm^2/m^2 in men and <41 cm^2/m^2 in women, respectively.[17] In our study, we used the cut-off points from EWGSOP2 (The European Working Group on Sarcopenia in Older People 2), which defines sarcopenia as a lumbar skeletal muscle index by CT imaging (at the 3rd lumbar vertebra) of <55 cm^2/m^2 in men and <39 cm^2/m^2 in women. Our findings indicated that the prevalence of sarcopenia in patients with colorectal cancer is 38.6%. According to research by Mourtzakis et al.[18], there is a direct correlation between whole-body skeletal muscle mass in cancer patients and the cross-sectional area of skeletal muscle at the third lumbar vertebra. Another study by Park, H., et al. (2018) in Korea reported a sarcopenia prevalence of 32.4%.[19] Studies by Hopkins, J., et al. (2019) in Canada[20] and van Vugt, J., et al. (2018) in the Netherlands[21] reported prevalences of 27.5% and 50.5%, respectively.

Fearon et al.[22] classified cancer cachexia as precachexia, cachexia, and refractory cachexia, with sarcopenia being a key component. Additionally, involuntary weight loss and low BMI are often the first symptoms observed in cancer patients[23], placing them in the initial phase of cachexia.[22] Preoperative sarcopenia has been associated with lower BMI in previous studies[24–28], and this was also observed in our study; it might be linked to a more advanced disease stage and decreased food intake. Conversely, serum albumin levels, routinely monitored as a nutritional parameter, were lower in both sarcopenic and non-sarcopenic groups. Although few studies have demonstrated a relationship between preoperative sarcopenia and serum albumin levels, we speculated that decreases in serum albumin are observed as patients progress to the refractory cachexia stage, which might not be evident early in cachexia. The current study has several limitations. This was a single-center prospective observational study and the sample size was small. A validation study with large sample size will be necessary to confirm the prevalence of sarcopenia in gastric cancer patients. In conclusion, prevalence of sarcopenia was 43.90% (18 patients) based on EWGSOP2 (The European Working Group on Sarcopenia in Older People 2) recommendations in our study.

Compliance with ethical standards

Ethical standards All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1964 and later versions. Informed consent was obtained from all patients for inclusion in the study.

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Conflict of interest: We declare that we have no conflicts of interest.

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