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

Ishan Barotra[1]*, Ashish Katoch[2], Puneet Mahajan[3] and 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 progressive and generalised skeletal muscle disorder involving the accelerated loss of muscle mass and function that is associated with increased adverse outcomes including falls, functional decline, frailty, and mortality. Sarcopenia has become the focus of intense research aiming to translate current knowledge about its pathophysiology into improved diagnosis and treatment The aim of this study was to estimate the prevalence of sarcopenia in colorectal cancer patients using computed tomography. There is very limited data available from sub-Himalayan belt of northern India, hence the present study was planned to estimate the prevalence of sarcopenia in colorectal cancer 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 colorectal cancer were considered for the study. **Results:** Thirty nine patients were included in the study. Prevalence of sarcopenia was 38.46% (15 patients) based on EWGSOP2 (The European Working Group on Sarcopenia in Older People 2) recommendations. Patients had a mean age of 57.59± 16.51 years. The mean age was 59.58 years in the sarcopenic group (SG) and 55.6 years in the non-sarcopenic group (NSG). The mean SMI (Skeletal Muscle Index) was 47.54±7.65cm²/m² and 49.248±8.44cm²/m² in the SG and NSG, respectively. The mean body mass index (BMI) was lower in the sarcopenic group than in the nonsarcopenic group (20.86 ± 2.34 vs. 21.90± 2.8 kg/m^2). **Conclusions:** Prevalence of sarcopenia was 38.46% (15 patients) based on EWGSOP2 (The European Working Group on Sarcopenia in Older People 2) recommendations.

KEYWORDS: Sarcopenia _ Prevalance_ Colorectal cancer _Sub Himalayan Region.

INTRODUCTION

The term sarcopenia is derived from the Greek word meaning ‘poverty of flesh’ and is characterized by the progressive loss of skeletal muscle mass, muscle strength, and physical performance. This term was first coined by I.H. Rosenberg to denote “ageing related loss of skeletal muscle mass and strength”.[1] Sarcopenia has a biological component with the genes involved in skeletal muscle mitochondrial function, oxidative capacity, and glucose uptake showing reduced expression with ageing.[2] It affects women and men equally, starting from the fourth decade and accelerating from the 6th decade.[3] It was originally described in the elderly population, and is often now defined as a geriatric syndrome associated with functional impairment, increased risk of falls, fractures, and reduced survival. Sarcopenia has been found to be a predictor of chronic disease progression, poorer functional outcomes, and postoperative complications (both infections and non-infectious complications).[4] Sarcopenia can be divided into primary or secondary. Primary sarcopenia is caused by ageing, whereas secondary is triggered by illness, malnutrition, invasive procedures, organ failure, cancer and other diseases.[5] Both primary and secondary sarcopenia are of importance as they adversely affect patient’s functional status and can worsen prognosis of causative diseases. It is reported that 0.5–1.0% of skeletal muscle mass is lost per year beyond the age of 25 years.[6] Cancer is possibly the most notable pathological condition that promotes muscle atrophy, particularly in elderly patients.[7] The incidence of cancer and subsequent survivorship is observed to be greatest in patients >60 years of age.[8] The probability of developing gastrointestinal malignancies, lung, prostate, uterine, melanoma, breast cancer, non-Hodgkin lymphoma or leukaemia increases

with age. Therefore, the older the sarcopenia patient, the more likely they are to encounter a considerable reduction in body mass preceding and following a diagnosis of cancer. Regarding the evaluation of sarcopenia, diagnostic algorithms were proposed by the European Working Group on Sarcopenia in Older People (EWGSOP2)[9] in 2010 and by the Asian Working Group for Sarcopenia (AWGS) in 2014[10] EWGSOP2 (The European Working Group on Sarcopenia in Older People 2) defines sarcopenia as reduced muscle strength, low muscle quality and low physical performance and sarcopenia is considered severe if all three criteria are satisfied. The Asian Working Group for Sarcopenia (ASWG) defines this condition as ‘‘age-related loss of skeletal muscle mass plus loss of muscle strength and/or reduced physical performance” with population specific cut offs for measurements. Among the many definitions and criteria available, 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

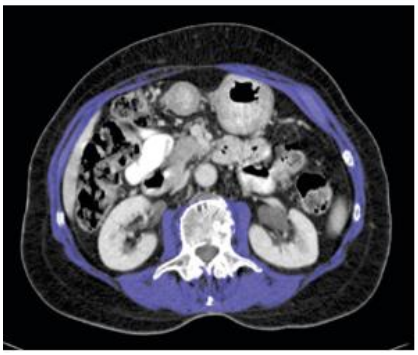
Various methods of measurement of skeletal muscle mass

Nowadays CT and MRI are increasingly used as research tools for assessment of body composition parameters as these imaging techniques are routinely used for staging purpose and assessment of respectability in malignant disease. The reduction of skeletal muscle mass can be assessed by the computed tomography (CT), magnetic resonance imaging (MRI), dual energy x-ray absorptiometry (DXA) or bioelectrical impedance analysis. But assessment of skeletal muscle index at L3 using CECT is the current gold standard for inferring total skeletal muscle mass The deterioration of muscle strength can be evaluated with the knee extension/flexion or handgrip strength. On the other hand, the decline in physical performance can be measured by 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 that there are no consensual cut-off points for sarcopenia definition in the literature and they also depend upon the evaluation technique selected. As CT is largely used for clinical tumour staging, it turns out to be an accessible method for the diagnosis of sarcopenia. Using a single abdominal cross-sectional CT image, at the third lumbar vertebrae (L3), it can be project the total body mass by assessing the skeletal muscle index (cm^2/m^2), that is calculated by the sum of skeletal muscle areas, at L3 level, and normalized for stature.[11,12] Results of several studies conclude that quantification of sarcopenia is possible through estimation of lumbar muscle mass in the 2 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 </=39 cm^2/m^2 in females and </=55 cm^2/m^2 in males according to EWGSOP2.[14] The prevalence of sarcopenia in patients undergoing surgery for gastrointestinal cancers (evaluated by the measurement of skeletal muscle mass by CT) was reported in some studies. The gastrointestinal malignancies are often diagnosed at an advanced stage and has a low 5-year survival rate.[15] Despite similar age and sex distribution between studies, there was an extensive variation in the prevalence of this condition. In healthy individuals, the prevalence of sarcopenia grows with ageing, oscillating from 9.0% at 45 years and up to 64.0% in individuals with 85 years old or more.[16] In Indian settings, prevalence of sarcopenia in patients with malignancy is an area of investigation as very limited Indian studies has evaluated the effect of sarcopenia on outcomes in cancer patients.. Therefore, we aimed to study the prevalence of sarcopenia in patients with colorectal malignancy.

Screening for sarcopenia

Sarcopenia was assessed by calculating Skeletal Muscle Index using CT scan at L3 vertebrae. In this study CECT ABDOMEN which is used for the diagnosis of the colorectal malignancy was used for calculating the SMI. No separate CECT ABDOMEN was done for calculating SMI. In this study patients were subjected for CT scan in 64 slice MDCT (Light speed VLT –XTE Gc medial

system) and the cross-sectional images at the level of L3 vertebral body at which both transverse processes were visualized. The area of the muscle's psoas, quadratus lumborum, erector spinae muscles, transversus abdominis, internal and external obliques and rectus abdominis muscles were evaluated manually by the area measurement tool using RadiAnt DICOM viewer. The threshold range for skeletal muscle was -30 to +150 Hounsfield units. The skeletal muscle area was normalized for height to calculate the skeletal muscle index.



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

Thirty nine patients were included in the study .Prevalence of sarcopenia was 38.46% (15 patients) based on EWGSOP2 (The European Working Group on Sarcopenia in Older People 2) recommendations. Patients had a mean age of 57.59± 16.51 years.

Among the 39 patients with diagnosis of colorectal cancer; 15 patients (38.46%) were diagnosed as sarcopenic and the remaining 24 patients (61.54%) were non sarcopenic based on EWGSOP2 (The European Working Group on Sarcopenia in Older People 2) recommendations. The mean age of patients with sarcopenia with colorectal malignancy was 59.58 years and the mean age of patients without sarcopenia with colorectal malignancy was 55.6 years. 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 (20.86 ± 2.34vs. 21.90± 2.8 kg/m^2). Nutritional parameters such as mean serum albumin was lower in the sarcopenic group than in the non sarcopenic group (sarcopenic, 3.22± .64g/dl vs. non-sarcopenic, 3.40± .63 g/dl). Mean skeletal muscle index (cm^2/m^2) in patients of colorectal carcinoma in sarcopenic patients was 47.54±7.65cm^2/m^2 while skeletal muscle index (cm^2/m^2) in patients of colorectal carcinoma in non sarcopenic patients was 49.24±8.44cm^2/m^2.

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

Clinicopathological features	Sarcopenic group(n=15)	Non Sarcopenic group(n=24)
Mean age(years)	59.58	55.6
Gender Men Women	8(61.1%) 7(31.8%)	14(52.17%) 10(47.82%)
BMI (kg/m ^{2})	20.86 ± 2.34	21.90± 2.8
Serum albumin(g/dl)	3.22± .64	3.40± .63
SMI(cm²/m²)	47.54±7.65	49.24±8.44

DISCUSSION

As the world population ages and lifespans increase, the number of elderly patients with gastrointestinal malignancy has been increasing significantly. Also with increasing age prevalence of sarcopenia also increases significantly in gastrointestinal malignancy. Surgical resection remains the most effective therapy for potentially curable gastrointestinal malignancy. However, surgeons sometimes hesitate to perform surgery on elderly patients due to the high frequency of complications and poor survival rates associated with aging. The role of sarcopenia in the management of patients with cancer is an evolving area of research. Numerous studies encompassing different tumour biologies have demonstrated that a low skeletal muscle index has an adverse effect on the outcomes of oncology patients. The aim of our study was to estimate the prevalence of sarcopenia in colorectal malignancy For defining sarcopenia cut-off points depend on the measurement technique and on the availability of reference studies and populations. The most widely used method for assessing muscle mass is computed tomography, with assessment of the skeletal muscle index at the level of the third lumbar vertebra and specific cutoff points for each sex. The current gold standard for determining total skeletal muscle mass is the assessment of the skeletal muscle index at L3 using CECT. Various studies have been used for assessing the sarcopenia by CT in various regions of the world and various cut offs have been devised by each of the study. In majority of studies done before, sarcopenia was defined using cut off used by Prado et al and Marti et al which defined sarcopenia as Lumbar skeletal muscle index by CT imaging (3rd lumbar vertebra) in Men < 52.4 cm^2/m^2 and in Women < 38.9 cm^2/m^2 and in men <53 cm^2/m^2 and in Women < 41 cm^2/m^2 respectively.[17] In our study, we used cut off introduced by EWGSOP2(The European Working Group on Sarcopenia in Older People 2) which defines sarcopenia, when Lumbar skeletal muscle index by CT imaging (3rd lumbar vertebra) in Men < 55 cm^2/m^2 and in Women < 39 cm^2/m^2. In the current investigation, we found that prevalence of sarcopenia in patients with colorectal cancer is 38.6%. According to research by Mourtzakis and colleagues,[18] there is a direct correlation between whole-body SM in cancer patients and the cross-sectional area of skeletal muscle at the level of the third lumbar vertebra. In another study done by Park, H, et al in 2018 in Korea, reported prevalence of sarcopenia as 32.4%.[19] In studies conducted by Hopkins, J, et al in 2019 in Canada,[20] and van Vugt, J, et al in 2018 in Netherlands,[21] reported prevalence of sarcopenia as 27.5% and 50.5% respectively. Fearon et al.[22] classified cancerous cachexia as precachexia, cachexia, and refractory cachexia, with the presence of sarcopenia as a key component of cachexia. In addition, involuntary weight loss and low BMI are frequently the first symptoms observed in cancer patients,[23] these symptoms place them in the first phase of cachexia.[22] In fact, preoperative sarcopenia was associated with lower BMI in previous studies[24–27, 28] as well as in the current study, it might be associated with more advanced disease stage and decreased food intake in our study. In contrast, serum albumin, routinely monitored as a nutritional parameter, was lower in the 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 move closer to the stage of refractory cachexia and that this decrease may not be observed 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 colorectal malignancy patients. In conclusion, prevalence of sarcopenia was 38.46% (15 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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