

ASSOCIATION OF SARCOPENIA AND DURATION OF POSTOPERATIVE HOSPITAL STAY IN RESECTABLE COLORECTAL CANCER PATIENTS UNDERGOING SURGERY FOR COLORECTAL CANCER: A HOSPITAL BASED PROSPECTIVE OBSERVATIONAL STUDY**Dr. Ishan Barotra^{1*}, Dr. Ashish Katoch², Dr. Puneet Mahajan³ and Dr. Rashpal Singh Thakur⁴**^{1,2}Junior Resident, Department of General Surgery, Indira Gandhi Medical College Shimla Himachal Pradesh.³Professor, Department of General Surgery, Indira Gandhi Medical College Shimla Himachal Pradesh.⁴Assistant Professor(Surgical Oncology), Department of General Surgery, Indira Gandhi Medical College Shimla Himachal Pradesh.***Corresponding Author: Dr. Ishan Barotra**

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ABSTRACT

Background: Sarcopenia is a common comorbidity in cancer patients. Skeletal muscle depletion(sarcopenia) is closely associated with limited physical activity and high mortality. The objective of this study was to determine the duration of postoperative hospital stay in patients with resectable colorectal cancer who underwent surgery for the disease, comparing those with sarcopenia to those without sarcopenia. There is very limited data available from sub-Himalayan belt of northern India, hence the present study was planned to know the association of sarcopenia with duration of postoperative hospital stay in resectable colorectal cancer patients who underwent surgery for colorectal cancer. **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 and had a mean age of 57.59± 16.51 years. Sarcopenia was detected in 15(38.46%) patients based on EWGSOP2 (The European Working Group on Sarcopenia in Older People 2) recommendations. The mean age was 59.58 years in the sarcopenic group (SG) and 55.6 years in the non-sarcopenic group. 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/m²). Postoperative duration of hospital stay was significantly higher in the sarcopenic group than in the non-sarcopenic group (11.6 days vs. 8.6days; p = 0.03). **Conclusions:** Postoperative duration of hospital stay was significantly higher in the sarcopenic group than in the non-sarcopenic group in resectable colorectal cancer patients who underwent surgery.

KEYWORDS: Sarcopenia _ Postoperative duration _ hospital stay _ Colorectal cancer.**INTRODUCTION**

Colorectal cancer (CRC) stands as the third most prevalent cause of cancer-related mortality worldwide.^[1] This devastating disease has a significant impact on public health, with millions of individuals affected each year. While surgical resection plays a crucial role in treating this condition, certain patients encounter postoperative complications that can have severe consequences.^[2-5] These complications, such as surgical site infections and anastomotic leakage, are strongly linked to both cancer recurrence and reduced survival rates in CRC patients, as well as increased duration of postoperative hospital stay.^[6-8] Addressing these complications is of paramount importance to improve

patient outcomes and reduce the burden on healthcare systems. Sarcopenia, initially conceptualized by Rosenberg and Roubenoff, characterizes a progressive and widespread decline in muscle mass and strength associated with aging.^[9] This condition is characterized by a significant loss of skeletal muscle volume, which can be accurately assessed using computed tomography (CT) imaging.^[10] Sarcopenia often coincides with aging, sedentary behaviour, and various comorbidities, such as chronic heart failure, pulmonary disease, cirrhosis, and renal failure.^[11,12] The presence of sarcopenia in CRC patients can further exacerbate the risk of postoperative complications, as reduced muscle mass and strength can impair the body's ability to recover from the surgical

intervention. Understanding the relationship between sarcopenia and postoperative complications in CRC patients is crucial for developing effective strategies to improve patient outcomes. By identifying and addressing sarcopenia early in the treatment process, healthcare providers may be able to implement targeted interventions, such as nutritional support, physical therapy, or pharmacological interventions, to mitigate the risk of these devastating complications. Additionally, further research is needed to elucidate the underlying mechanisms by which sarcopenia contributes to the increased risk of postoperative complications in CRC patients, which may lead to the development of novel therapeutic approaches. Sarcopenia, the age-related loss of muscle mass and strength, has emerged as a significant concern for cancer patients. Recent studies have highlighted the profound impact of this condition on cancer treatment outcomes.^[13-15] Despite its well-established association with functional limitations, physical disability, and reduced quality of life, the extent to which sarcopenia affects cancer patients remains a critical knowledge gap.^[2] Fortunately, this area has become the focus of extensive research in recent years. The findings are compelling – sarcopenia has been independently linked to poor outcomes following cancer surgery, both in the short and long term. Moreover, it has been shown to increase the risk of toxicity from chemotherapy.^[2] These insights underscore the importance of addressing sarcopenia as an integral part of cancer management. There is very limited data available from sub-Himalayan belt of northern India, hence the present study was planned to know the association of sarcopenia with duration of postoperative hospital stay in resectable colorectal cancer patients who underwent surgery for colorectal cancer.

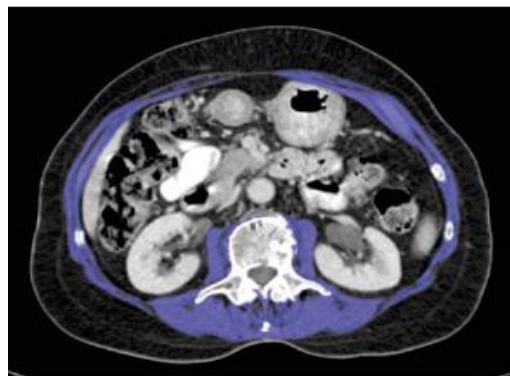
MATERIAL AND METHODS

A hospital based prospective observational study was conducted in the department of surgery of a tertiary care hospital in Shimla, Himachal Pradesh between

September 2021 to September 2022. A total of 39 colorectal cancer patients reported to Department of General Surgery IGMC SHIMLA. We excluded patients who were not willing for surgery in surgical operable cases and patients with spinal deformity, quadriplegia, spinal muscular atrophy.

Screening for sarcopenia

Sarcopenia was assessed by calculating Skeletal Muscle Index using CT scan at L3 vertebrae. In this study CECT ABDOMEN which was 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:-

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

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 cm²/m² was considered the cutoff for men, compared to < 39 cm²/m² 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 and 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 ± 2.34 vs. 21.90 ± 2.8 kg/m²). Nutritional parameters such as mean serum albumin was lower in the sarcopenic group than in the non sarcopenic group (sarcopenic, $3.22 \pm .64$ g/dl vs. non-sarcopenic, $3.40 \pm .63$ g/dl). Mean skeletal muscle index (cm²/m²) in patients of colorectal carcinoma in sarcopenic patients was 47.54 ± 7.65 cm²/m² while skeletal muscle index (cm²/m²) in patients of colorectal carcinoma in non sarcopenic patients was 49.24 ± 8.44 cm²/m².

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	8(61.1%)	14(52.17%)
Women	7(31.8%)	10(47.82%)
BMI (kg/m ²)	20.86 ± 2.34	21.90 ± 2.8
Serum albumin(g/dl)	$3.22 \pm .64$	$3.40 \pm .63$
SMI(cm ² /m ²)	47.54 ± 7.65	49.24 ± 8.44

Impact of sarcopenia on post operative duration of hospital stay in resectable colorectal cancer patients who underwent surgery

Of 39 patients who were diagnosed with colorectal cancer 11 patients were operable and they underwent surgery. Out of these 11 patients, 5 patients were sarcopenic and 6 were non sarcopenic. Postoperative duration of hospital stay was significantly higher in the sarcopenic group than in the non-sarcopenic group (11.6

days vs. 8.8 days; p = 0.03).

Table 2 and figure 2 shows the association of sarcopenia and duration of postoperative hospital stay in resectable colorectal cancer patients who underwent surgery. Although there significant difference in the mean duration of hospital stay (sarcopenic, 11.6 days, vs. non-sarcopenic, 8.6 days; p = 0.03).

Table 2: Mean duration of post operative hospital stay in resectable colorectal cancer patients with and without sarcopenia.

Mean duration of post operative hospital stay in resectable Colorectal Cancer patients (n=11)			
	Sarcopenic Group (n=3)	Non Sarcopenic Group (n=5)	P value
Post op duration of hospital stay	11.6 days	8.6	.03

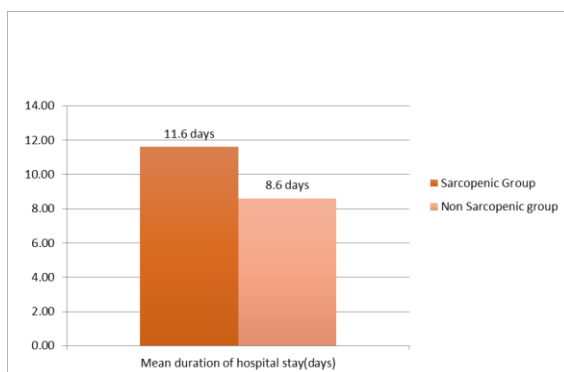


Figure 1: Mean duration of post operative hospital stay in resectable colorectal cancer patients with and without sarcopenia.

DISCUSSION

Surgical intervention continues to be the primary approach for treating and curing colorectal cancer. Despite advancements in alternative therapies, surgery remains the most effective and widely used method for addressing this type of cancer, as it offers the best chance of removing the tumour and achieving a complete cure. However, the challenges associated with surgery can have significant consequences, both for the patient and the healthcare system. Apart from diminishing adherence to postoperative care and increasing healthcare costs, the physical and psychological stress of surgery can exacerbate oncological results by impeding the maintenance of healthy lifestyles. One of the key concerns in the context of colorectal cancer surgery is the

issue of sarcopenia, a disease characterized by age-related muscle loss. The definition and standards of sarcopenia have evolved over time, reflecting the complex nature of this condition.^[16,17] Sarcopenia is now thought to be a syndrome in which a decrease in skeletal muscle mass, linked to a reduction in muscular strength or function, increases the probability of unfavourable outcomes, such as increased complications, longer hospital stays, and poorer overall survival.^[18] Accurately measuring muscle mass is crucial for the assessment and management of sarcopenia. Computed tomography (CT) is regarded as the "gold standard" for this purpose, as it provides an objective, repeatable, and precise evaluation of muscle mass, with errors ranging from 1 to 4%.^[19,20] The L3 muscle area is typically measured, as it has been shown to accurately reflect the "real" muscle mass and fat volume of the individual.^[22] Interestingly, patients undergoing elective gastrointestinal (GI) cancer surgery routinely undergo abdominal CT assessment for the purpose of tumor staging, without incurring additional costs. This presents a valuable opportunity to simultaneously evaluate the patient's muscle mass and identify those at risk of sarcopenia, which could inform personalized treatment strategies and improve overall outcomes. The process of aging involves a decline in every bodily function, including muscle mass and strength. This age-related deterioration can have significant implications for patients undergoing colorectal cancer surgery, as sarcopenia may compromise their ability to withstand the physical and metabolic demands of the procedure, leading to increased complications, prolonged recovery, and poorer long-term oncological outcomes. By recognizing and addressing sarcopenia in the context of colorectal cancer treatment, healthcare professionals can potentially optimize patient care and improve the overall quality of life for these individuals. As we age, our skeletal muscle mass starts to decline from around 30 years old, and the number of motor neurons decreases significantly in those over 70.^[16] Research indicates that the primary driver of sarcopenia is a reduction in type II muscle fibres, which can be as high as 40% in individuals older than 70.^[18] This may help explain why older people are more prone to falls. Our study found that preoperative sarcopenia increases the risk of total and major complications in colorectal cancer patients undergoing surgery. Sarcopenia can lead to weakness and reduced mobility, potentially hindering recovery after surgery. However, there is no evidence that increasing muscle mass before surgery can improve outcomes for colorectal cancer patients. This may be because improving nutritional status in the short time between diagnosis and surgery is challenging. Many elderly individuals have inadequate protein intake or absorption issues, and colorectal cancer patients often experience malnutrition and weight loss due to tumour-induced nutrient consumption. As a result, preoperative sarcopenia may be linked to postoperative complications. As people age, they often experience a gradual loss of muscle mass, known as sarcopenia. However, early intervention can help these individuals

retain their muscle strength and improve their health outcomes during medical treatment. Providing proper nutrition has the potential to enhance the prognosis of hospitalized patients, although there is ongoing discussion about its precise impact on muscle maintenance and function. Additionally, regular physical activity is widely acknowledged as an effective way to support overall physiological well-being. Here is an elaborated and longer version of the original passage. Factors contributing to age-related muscle decline include individual health, genetics, activity levels, muscle training, and nutritional intake.^[21] As people age, they naturally experience a gradual loss of muscle mass and strength, a condition known as sarcopenia. Notably, individuals with sedentary lifestyles exhibit a more pronounced decline in muscle fibres compared to those with regular activity, highlighting the potential of exercise in mitigating muscle atrophy. Emerging research suggests that the relationship between cancer and muscle health is multifaceted and complex. Cancer itself, along with the various treatments, can have a significant impact on a patient's muscle condition. Studies indicate that muscle depletion may signify heightened metabolism in malignant tumours, leading to increased systemic inflammation and muscle consumption.^[22] This vicious cycle of inflammation and muscle wasting can have detrimental effects on patient outcomes, as several studies have highlighted the link between systemic inflammation and poorer clinical outcomes.^[23,24] For instance, Richards et al. observed a clear association between muscle loss in patients with resectable primary colorectal cancer (CRC) and systemic inflammatory response.^[25] This finding underscores the need for a comprehensive approach to addressing muscle health in cancer patients. Recognizing the crucial role of maintaining muscle health, researchers and clinicians have explored various strategies to support muscle condition and address muscle deficiency in cancer patients. Combining active exercise with essential amino acid nutrition support presents a promising approach to improving muscle condition and mitigating the negative effects of muscle wasting.^[24] This integrated approach aims to provide the necessary building blocks for muscle growth and repair, while also stimulating the body's natural mechanisms to rebuild and maintain strong, healthy muscles. Most current studies primarily examine the correlation between sarcopenia and clinical outcomes, often neglecting to delve into its underlying causes. However, a deeper understanding of the complex interplay between cancer, inflammation, and muscle health is essential for developing more targeted and effective interventions. Aleman et al. have contributed to this field, providing valuable insights into the multifaceted nature of this challenge and the need for a comprehensive, patient-centered approach to addressing muscle-related issues in cancer care.^[26] This could elucidate the connection between sarcopenia's poor prognosis and the escalation of systemic inflammation. Sarcopenia, the age-related loss of skeletal muscle mass and strength, has been associated with a range of adverse

health outcomes, including increased risk of disability, hospitalization, and mortality. Understanding the underlying mechanisms behind this connection is crucial for developing effective interventions to address this growing public health concern. One potential link between sarcopenia and poor prognosis may be the role of systemic inflammation. Chronic low-grade inflammation, which is often observed in older adults, has been hypothesized to contribute to the development and progression of sarcopenia. Inflammatory cytokines, such as interleukin-6 (IL-6) and tumour necrosis factor- α (TNF- α), have been shown to promote muscle catabolism and impair muscle regeneration, leading to the loss of muscle mass and function. Additionally, genetic factors may play a significant role in the development of sarcopenia. A genome-wide association study (GWAS) has identified several genes that are associated with the risk of sarcopenia and osteoporosis, two conditions that often co-occur in older adults. These genes include growth differentiation factor 8 (GDF8), also known as myostatin, which is a negative regulator of muscle growth; myocyte enhancer factor 2C (MEF2C), a transcription factor involved in muscle development; and peroxisome proliferator-activated receptor gamma coactivator 1- α (PGC-1 α), a key regulator of mitochondrial biogenesis and function. The identification of these genetic factors provides valuable insights into the underlying biological pathways that contribute to the development of sarcopenia. Understanding the genetic predisposition to this condition may help researchers and clinicians develop personalized prevention and treatment strategies, tailored to an individual's genetic profile. This could include targeted interventions, such as exercise programs, nutritional supplementation, or pharmacological therapies, that aim to address the specific genetic and molecular mechanisms involved in the pathogenesis of sarcopenia. Further research is needed to fully elucidate the complex interplay between genetic, inflammatory, and other factors in the pathogenesis of sarcopenia. By unravelling these mechanisms, researchers can work towards developing more effective strategies to maintain muscle health and function in older adults, ultimately improving their overall well-being and quality of life. Nonetheless, there is still a dearth of knowledge on the genetics of sarcopenia, which calls for more research.^[27] Undoubtedly, the occurrence of sarcopenia is primarily determined by how the diagnostic cut-off point for sarcopenia is defined. This study employed the EWGSOP2 (The European Working Group on Sarcopenia in Older People 2) cut-off, which defines sarcopenia as a Lumbar skeletal muscle index $< 55 \text{ cm}^2/\text{m}^2$ in males and $< 39 \text{ cm}^2/\text{m}^2$ in women, as measured by CT imaging of the third lumbar vertebra. In the current investigation, we showed that postoperative duration of hospital stay was significantly higher in the sarcopenic group than in the non-sarcopenic group in patients of resectable CRC who underwent surgery. According to Mourtzakakis and colleagues^[28], the cross-sectional area of skeletal muscle at the third lumbar

vertebra is directly associated with whole-body SM in cancer patients. Sarcopenia is an important component of cachexia, according to Fearon et al.'s.^[29] Preoperative sarcopenia was associated with lower BMI in both the current study and previous research.^[30-31,32] Serum albumin, a commonly studied nutritional indicator, was shown to be lower in both the sarcopenic and non-sarcopenic groups. In our study postoperative duration of hospital stay was significantly higher in the sarcopenic group than in the non-sarcopenic group (11.6 days vs. 8.6days; $p = 0.03$).

CONCLUSION

Sarcopenia, as assessed by the EWGSOP 2 recommendations, is prevalent among colorectal cancer patients. Postoperative duration of hospital stay was significantly higher in the sarcopenic group than in the non-sarcopenic group (11.6 days vs. 8.6days; $p = 0.03$).

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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