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ASSOCIATION OF SARCOPENIA AND DURATION OF POSTOPERATIVE HOSPITAL STAY IN RESECTABLE GASTRIC CANCER PATIENTS UNDERGOING GASTRECTOMY: A HOSPITAL BASED PROSPECTIVE OBSERVATIONAL STUDY IN SUB-HIMALAYAN REGION

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ABSTRACT

Background: Malignancy is a secondary cause of sarcopenia, which is associated with impaired cancer treatment outcomes. The aim of this study was to determine the duration of postoperative hospital stay in patients with resectable gastric cancer who underwent gastrectomy, 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 gastric cancer patients undergoing gastrectomy. **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 and 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. 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). Postoperative duration of hospital stay was significantly higher in the sarcopenic group than in the non-sarcopenic group (15.66 days vs. 8.8days; p = 0.03). **Conclusions:** Postoperative duration of hospital stay was significantly higher in the sarcopenic group than in the non-sarcopenic group in resectable gastric cancer patients who underwent gastrectomy.

KEYWORDS: Sarcopenia _ Postoperative Duration _ Hospital Stay _ Gastrectomy.

INTRODUCTION

Aging is a complex and multifaceted process that brings about a myriad of physiological changes in the human body. One of the most prominent and well-studied aspects of this age-related transformation is the progressive, systematic loss of skeletal muscle mass (SM) and the gradual changes in body composition. This phenomenon, commonly referred to as "sarcopenia," was first coined by Rosenberg[1] in 1989, and since then, it has become a widely recognized concept in the field of geriatric medicine and public health. The understanding of sarcopenia has evolved over the years, and the definition has been expanded to encompass not only the loss of muscle mass but also the loss of muscle strength and functional impairment. This more comprehensive approach to sarcopenia was recently proposed by the European Working Group on Sarcopenia in Older People (EWGSOP)[2] and the Asian Working Group for Sarcopenia[3], who have designed a new algorithm for assessing this age-related condition. The prevalence of sarcopenia, as defined by the EWGSOP algorithm, has been extensively studied in various populations. In a study conducted among elderly community-dwelling residents in Japan (n = 4811), the prevalence of sarcopenia was reported to be 8.2% for men and 6.8% for women.[4] This highlights the significant impact of this condition on the aging population, particularly in terms of its potential to contribute to frailty, disability,

and reduced quality of life. Sarcopenia is a multifactorial condition, and several contributing factors have been identified. Malnutrition, physical inactivity, and a number of underlying illnesses can all play a role in the development and progression of sarcopenia.[5,6] Interestingly, the presence of excessive systemic inflammatory response, particularly in cancer patients, has been linked to the development of insulin resistance, hypercatabolism of proteins, and metabolic abnormalities, which can further exacerbate the loss of muscle mass and strength.[7,8] As a result, sarcopenia is expected to be more prevalent among cancer patients compared to the general senior population. The recognition of sarcopenia as a distinct clinical entity has led to a growing interest in the development of effective interventions and management strategies to address this age-related condition. On going research efforts are focused on understanding the underlying mechanisms, identifying risk factors, and exploring innovative approaches to prevent, delay, or even reverse the loss of muscle mass and function in the aging population. By addressing sarcopenia, healthcare professionals and researchers aim to improve the overall health, independence, and quality of life of older adults, ultimately contributing to the broader goal of healthy aging. The impact of sarcopenia, the age-related loss of skeletal muscle mass and strength, on cancer patients is not fully understood yet. However, it is well-established that sarcopenia is a significant risk factor for functional limitations, physical disabilities, decreased quality of life, and ultimately, higher mortality rates.[9] Recent research has focused extensively on investigating the influence of sarcopenia on cancer patients' treatment outcomes. These studies have consistently demonstrated that sarcopenia is an independent predictor of poor outcomes following surgical interventions, both in the short-term and long-term.[10–18] Patients with sarcopenia have been found to experience higher complication rates, longer hospital stays, and poorer overall survival compared to those without sarcopenia. Moreover, sarcopenia has also been linked to an increased risk of adverse reactions and toxicity from chemotherapy.[19–23] This is particularly concerning, as chemotherapy is a cornerstone of cancer treatment, and toxicity can significantly impact a patient's ability to tolerate and complete the intended course of treatment. The increased risk of toxicity in sarcopenic patients may be attributed to altered drug pharmacokinetics, reduced muscle mass, and compromised organ function, among other factors. Despite these concerning findings, the exact mechanisms by which sarcopenia affects cancer patients' treatment outcomes and overall prognosis are not yet fully understood. On going research is exploring the complex interplay between sarcopenia, tumour biology, and the host's response to various cancer therapies. As our understanding of this relationship continues to evolve, healthcare providers may be able to develop more personalized treatment strategies and interventions to address the challenges posed by sarcopenia in cancer care. 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 gastric cancer patients undergoing gastrectomy.

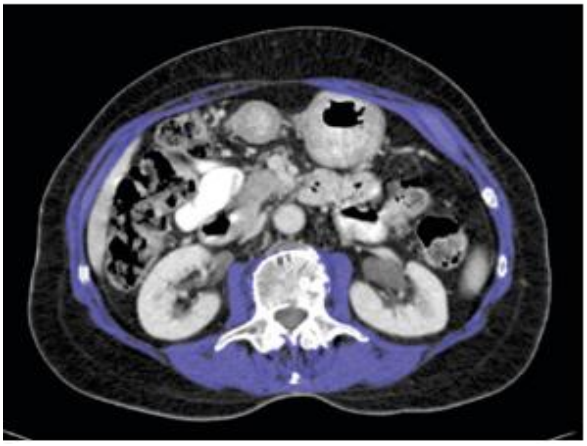
MATERIAL AND METHODS

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 41 gastric 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.

We investigated the duration of postoperative hospital stay in resectable gastric cancer patients undergoing gastrectomy between sarcopenic and non-sarcopenic patients.

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 gastrointestinal 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

Forty-one patients were included in the study and had a mean age of 60.66 ± 12.93years.

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

Impact of sarcopenia on post operative duration of hospital stay in resectable gastric cancer patients who underwent gastrectomy

Of 41 patients who were diagnosed with gastric cancer 8 patients were operable and they underwent gastrectomy. Out of these 8 patients, 3 patients were sarcopenic and 5 were non sarcopenic. Postoperative duration of hospital stay was significantly higher in the sarcopenic group than in the non-sarcopenic group (15.66 days vs. 8.8days; p = 0.03). Table 2 and figure 2 shows the association of sarcopenia and duration of postoperative hospital stay in resectable gastric cancer patients who underwent gastrectomy. Although there significant difference in the mean duration of hospital stay (sarcopenic, 15.66 days, vs. non-sarcopenic, 8.8 days; p = 0.03).

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

Mean duration of post operative hospital stay in resectable gastric cancer patients (n=11)			
	Sarcopenic Group (n=3)	Non Sarcopenic Group (n=5)	P value
Post op duration of hospital stay	15.66 days	8.8	.03

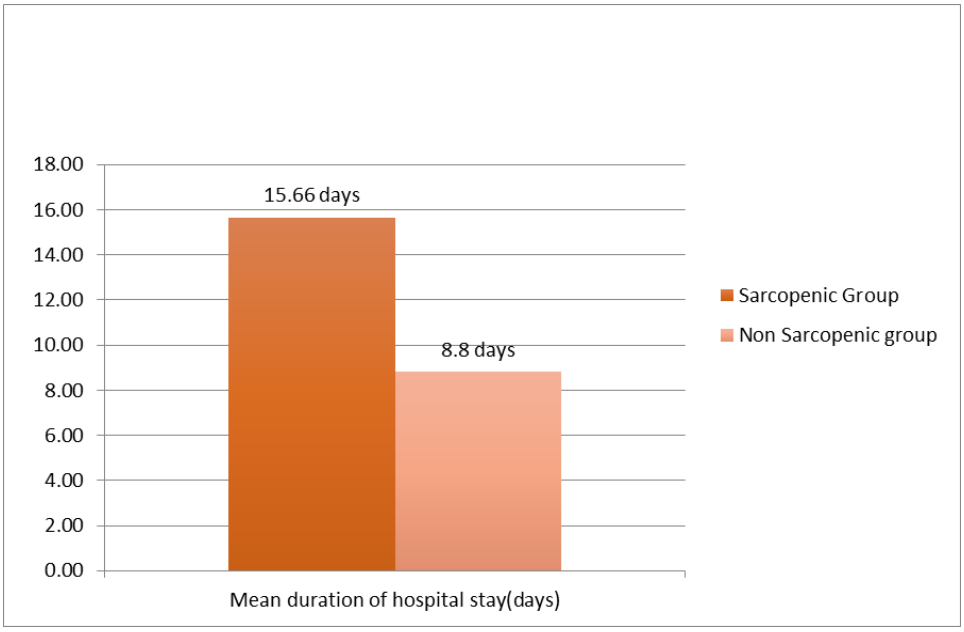


Figure 1: Mean duration of post operative hospital stay in resectable gastric cancer patients with and without sarcopenia.

DISCUSSION

Surgery remains the most common curative treatment option for patients diagnosed with gastric cancer. Despite advancements in surgical techniques and perioperative care, postoperative complications can still pose significant challenges. These complications not only lower patients adherence to subsequent adjuvant treatments, but they also lead to increased healthcare expenses.[24] More importantly, such postoperative difficulties can ultimately compromise patients' overall health and well-being, thereby worsening their long-term oncological outcomes. In this regard, it is crucial to carefully stratify surgical candidates based on their individual likelihood of experiencing postoperative problems. However, this process of risk assessment and patient selection remains a complex and challenging endeavour. Furthermore, with the global population rapidly aging, it is becoming increasingly imperative to comprehend the underlying etiologies and contributing factors associated with geriatric illnesses. One such condition that is closely linked to the aging process is sarcopenia, which is characterized by a progressive decline in skeletal muscle mass and physical function.[5] Importantly, sarcopenia can also be exacerbated by the presence of cancer and its associated metabolic derangements.[6] As a significant contributor to frailty in older adults, sarcopenia has been associated with adverse postoperative outcomes in various cancer types, including colorectal cancer[12,13], pancreatic cancer[17], hepatocellular carcinoma[11,15], metastatic liver cancer[14], and perihilar cholangiocarcinoma.[16] In the current investigation, the researchers sought to further elucidate the relationship between sarcopenia and postoperative outcomes in elderly patients diagnosed with gastric cancer. Their findings revealed that this patient population exhibited a higher prevalence of severe postoperative sequelae, which was concomitant with a greater prevalence of sarcopenia prior to undergoing surgical treatment. These results underscore the critical importance of comprehensive preoperative assessment and risk stratification, particularly in the elderly gastric cancer population, to optimize patient selection and ensure the best possible surgical outcomes. The original passage discusses the assessment of total skeletal muscle mass, which is considered the gold standard using the evaluation of the skeletal muscle index at the third lumbar vertebra (L3) through the use of contrast-enhanced computed tomography (CECT) imaging. The passage highlights that the most prevalent methods for predicting preoperative sarcopenia and examining the relationship between sarcopenia and postoperative outcomes have been through the utilization of computed tomography (CT) imaging. However, the passage also notes that various studies employ different methodologies when assessing the skeletal muscle index and determining the cut off points for sarcopenia diagnosis. This lack of standardization can lead to challenges in comparing and interpreting the results across different studies. To elaborate further, the assessment of the skeletal muscle index at L3 using CECT imaging is considered the gold standard because it provides a reliable and accurate measurement of the total skeletal muscle mass. This approach is advantageous as it allows for the quantification of muscle mass, which is a crucial factor in the evaluation of sarcopenia, a condition characterized by the progressive loss of skeletal muscle mass and strength. Sarcopenia is a significant concern in the preoperative and postoperative settings, as it is associated with various adverse outcomes, such as increased risk of complications, prolonged hospital stays, and higher mortality rates. Therefore, the accurate identification of sarcopenia using reliable methods is essential for effective patient assessment and management. CT imaging has become

the most common approach for predicting preoperative sarcopenia and examining its relationship with postoperative outcomes, the lack of standardized methodologies across different studies can hinder the comparability and interpretation of the findings. This variability in assessment techniques and sarcopenia cutoff points may lead to inconsistencies in the identification and diagnosis of sarcopenia, which can have implications for clinical decision-making and patient care. To address this issue, there is a need for the development of consensus guidelines or standardized protocols for the assessment of the skeletal muscle index and the diagnosis of sarcopenia using CT imaging. This would help to ensure that clinicians and researchers are using consistent and reliable methods, enabling more accurate comparisons and a better understanding of the impact of sarcopenia on surgical outcomes. The diagnosis of sarcopenia, a condition characterized by the progressive loss of skeletal muscle mass and strength, is a critical aspect in the assessment of an individual's overall health and physical function. The determination of appropriate cut-off points for the diagnosis of sarcopenia is a complex and crucial step, as it directly impacts the identification and management of this condition. Cut-off points depend on the measurement technique employed and the availability of reference studies and populations. Various studies have been conducted worldwide to assess sarcopenia using computed tomography (CT) imaging, and these studies have proposed different cut-off values to define sarcopenia. The European Working Group on Sarcopenia in Older People (EWGSOP2) has developed a widely recognized set of guidelines for the diagnosis of sarcopenia. In this study, the cut-off values introduced by EWGSOP2 were utilized. Specifically, the EWGSOP2 defines sarcopenia when the Lumbar Skeletal Muscle Index (LSMI), as measured by CT imaging at the level of the third lumbar vertebra (L3), is less than 55 cm^2/m^2 in men and less than 39 cm^2/m^2 in women. The use of these specific cut-off values is crucial, as it allows for the standardized and consistent identification of individuals with sarcopenia across different populations and healthcare settings.[25] By adopting these EWGSOP2-recommended thresholds, researchers and clinicians can ensure a systematic and evidence-based approach to the diagnosis and management of this condition, ultimately leading to improved patient outcomes and the development of targeted interventions to address the challenges associated with sarcopenia. Sarcopenia, or the progressive loss of skeletal muscle mass and strength, is conceptionally similar to the condition of cancerous cachexia, which is a complex metabolic syndrome associated with cancer progression and sequential dystrophy. Fearon et al.[26] have proposed a classification system for cancerous cachexia, identifying three distinct stages: precachexia, cachexia, and refractory cachexia. A key component of the cachexia stage is the presence of sarcopenia. In cancer patients, involuntary weight loss and a low body mass index (BMI) are frequently among the first observable symptoms, placing these individuals in the precachexia phase as described by Fearon and colleagues.[26] Previous studies[11–14,16] have consistently demonstrated an association between preoperative sarcopenia and lower BMI, as was also observed in the current study. This relationship may be indicative of more advanced disease progression and decreased food intake in these patients. In addition to the changes in body composition and weight, alterations in serum biomarkers are also commonly seen in cancer-related sarcopenia and cachexia. Serum albumin, a routinely monitored nutritional parameter, was found to be lower in both the sarcopenic and non-sarcopenic groups in the current study. While few studies have directly examined the relationship between preoperative sarcopenia and serum albumin levels, it is speculated that decreases in serum albumin may become more pronounced as patients progress closer to the refractory cachexia stage. This decrease in albumin may not be as readily observed in the earlier stages of the cachexia continuum.[27] The complex interplay between the development of sarcopenia, the progression of cachexia, and the associated changes in clinical and biochemical parameters highlights the importance of early identification and intervention in cancer patients. Understanding the nuanced relationships between these factors can guide the development of targeted therapeutic strategies to address the devastating consequences of cancer-related muscle wasting and metabolic derangements. In our study postoperative duration of hospital stay was significantly higher in the sarcopenic group than in the non-sarcopenic group (15.66 days vs. 8.8days; $p = 0.03$). The current study has several limitations. This was a single-centre prospective observational study and the sample size was small. A validation study with large sample size will be necessary to confirm the impact of preoperative sarcopenia on postoperative complications.

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

Authors' Biography.

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