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Significance of CT-Derived Sarcopenia Using L3 Skeletal Muscle Index in Lung Cancer Patients: A Prognostic Retrospective Study

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ABSTRACT

Introduction:

Sarcopenia, a progressive loss of skeletal muscle mass and strength, is increasingly recognized as a negative prognostic factor in cancer patients. In lung carcinoma, sarcopenia often coexists with cachexia and systemic inflammation, contributing to reduced treatment tolerance and poor survival outcomes. Computed tomography (CT)-based measurement of the skeletal muscle index (SMI) at the L3 vertebral level is a validated and non-invasive method for assessing sarcopenia.

Aim and Objective:

To evaluate the prognostic significance of CT-derived sarcopenia using L3 skeletal muscle index (L3SMI) and its correlation with survival in lung cancer patients.

Materials & Methods:

This retrospective cohort study was conducted in the Department of Radiodiagnosis, Govt. Kilpauk Medical College Hospital, from October 2020 to September 2021. Fifty lung cancer patients aged over 18 years who underwent CT including the L3 level within two months of diagnosis were included. Sarcopenia was defined as L3SMI <41 cm^2/m^2 in females and <53 cm^2/m^2 in males. Clinical and laboratory data were collected and survival outcomes were analyzed using Pearson correlation and ANOVA.

Results:

Out of 50 patients, 29 (58%) were sarcopenic, and 23 of them died during a follow-up period of 6–12 months. A strong positive correlation was observed between low L3SMI and mortality ($r = 0.726$, $p < 0.001$). Sarcopenia also showed a strong negative correlation with ECOG performance status ($r = –0.824$). Advanced cancer stage and low serum albumin levels were significantly associated with increased mortality.

Conclusion:

CT-derived L3SMI is an effective predictor of mortality in lung cancer patients. Early identification of sarcopenia allows for timely interventions to improve clinical outcomes and survival.

INTRODUCTION

Sarcopenia, characterized by the progressive loss of skeletal muscle mass and function, has emerged as a significant concern in clinical oncology due to its strong association with adverse outcomes, particularly in cancer patients. The term is derived from the Greek roots “sarx” meaning flesh and “penia” meaning loss, reflecting its central feature of muscle wasting. Originally recognized in the elderly as a natural part of aging, sarcopenia is now understood as a multifactorial syndrome that may develop in the context of chronic illness, inflammation, malnutrition, and malignancy. Unlike simple weight loss, sarcopenia can occur even in individuals with a normal or elevated body mass index (BMI), making it a silent but serious risk factor for treatment intolerance, prolonged hospitalization, and increased mortality. In oncologic patients, sarcopenia often forms

a component of cancer cachexia but may exist independently, progressing gradually and sometimes unnoticed in the absence of obvious clinical signs such as drastic weight loss (1, 2).

Traditionally, clinicians have relied on body weight and BMI to assess nutritional status and frailty in patients: However, these measures do not reliably reflect the presence or severity of muscle loss, especially in overweight or obese individuals. This has led to a growing awareness of the limitations of conventional anthropometric indices and a corresponding interest in more accurate tools for identifying sarcopenia. In this context, sarcopenia is now recognized as a physical manifestation of frailty—a concept that encompasses diminished strength, reduced endurance, and increased vulnerability to stressors. Frailty and sarcopenia frequently overlap, with sarcopenia often preceding and contributing to the onset of full-blown frailty. Recognizing sarcopenia as a precursor to functional decline has important implications for both prognostication and therapeutic planning. Objective assessment is essential, as subjective impressions or quick visual assessments, often referred to as the "eyeball test," are prone to error and inconsistency(3, 4)..

Advancements in diagnostic imaging have facilitated a more precise evaluation of body composition. Dual-energy X-ray absorptiometry (DXA) and bioelectrical impedance analysis (BIA) have been used to measure lean body mass, but both require specific equipment and can be influenced by hydration status or other variables. Among available methods, computed tomography (CT) has become the most widely accepted technique for evaluating sarcopenia in oncology. CT scans, routinely performed for cancer staging and treatment monitoring, can simultaneously provide data on muscle mass without exposing patients to additional radiation or cost. The muscle area at the level of the third lumbar vertebra (L3) on cross-sectional CT images has been shown to correlate strongly with total body skeletal muscle mass. This region has become the preferred site for analysis, as the muscle groups present there—including the psoas, paraspinal, and abdominal wall muscles—are representative of overall muscularity. The skeletal muscle index (SMI), calculated by normalizing the muscle area at L3 by height squared (cm^2/m^2), is used to classify sarcopenia and has been validated across multiple patient populations(5-8).

CT-based quantification of muscle mass has demonstrated high predictive value for a variety of clinical outcomes. In cancer patients, low SMI is associated with increased postoperative complications, poorer tolerance to chemotherapy, delayed wound healing, and decreased overall survival. The prognostic importance of sarcopenia has been observed in several malignancies, including gastrointestinal, hepatobiliary, pancreatic, and lung cancers. In addition to direct measurement, researchers have explored biochemical markers as indirect indicators of sarcopenia. One such marker is serum alanine aminotransferase (ALT), an enzyme traditionally considered liver-specific but also produced by skeletal muscle. Low ALT levels, in the absence of liver disease, have been linked to reduced muscle mass and increased mortality, suggesting a potential role as a cost-effective surrogate marker for sarcopenia in routine blood tests (9, 10).

Lung cancer is the most commonly diagnosed cancer worldwide and the leading cause of cancer-related mortality. Among its histological subtypes, non-small cell lung cancer (NSCLC) accounts for approximately 80% of all cases. The typical lung cancer patient is elderly and often has multiple chronic conditions such as ischemic heart disease, chronic obstructive pulmonary disease (COPD), diabetes mellitus, and chronic kidney disease. These comorbidities further compromise physiological reserves and contribute to systemic inflammation, accelerating muscle breakdown and functional decline. The combination of aging, cancer, and comorbid conditions creates a clinical profile that is highly susceptible to sarcopenia. Consequently, early identification and monitoring of muscle mass in this patient population are critical to optimizing therapeutic outcomes and minimizing complications(11-13).

The relevance of sarcopenia in lung cancer extends beyond its role as a marker of physical weakness. It has direct implications for clinical decision-making, influencing eligibility for surgery, tolerance to chemoradiotherapy, and suitability for immunotherapy. Patients with low muscle mass are more likely to experience treatment-related toxicities, dose reductions, treatment interruptions, and poor response rates. Moreover, sarcopenia has been associated with longer hospital stays, higher rates of infection, and increased readmissions, placing a greater burden on healthcare resources. Assessing sarcopenia at the time of diagnosis can help stratify patients according to risk and personalize care plans accordingly (14) (15).

Integrating sarcopenia assessment into routine cancer care provides significant clinical benefits, particularly in lung cancer patients where its subtle presentation often goes unnoticed. The widespread use of CT imaging allows for cost-effective and opportunistic screening through skeletal muscle index (SMI) measurements at the L3 vertebra, aided by automated software tools. Additionally, low serum ALT levels serve as useful biochemical adjuncts in identifying at-risk individuals. Interventions like nutritional support, resistance training, and anabolic therapies may improve functional status, treatment tolerance, and overall outcomes. As evidence grows, sarcopenia assessment is becoming a critical element of personalized oncology care(16, 17).

This study aims to evaluate the association between radiologically determined sarcopenia and overall survival in lung cancer patients. The objectives include assessing sarcopenia using CT imaging, specifically by calculating the L3 skeletal muscle index based on the cross-sectional area of muscles, and correlating this marker with patient survival outcomes. By identifying sarcopenia through imaging, the study seeks to determine its prognostic significance and contribution to clinical outcomes in individuals diagnosed with

with lung cancer.

MATERIALS AND METHODS

This retrospective cohort study was conducted in the Department of Radiodiagnosis, Govt. Kilpauk Medical College Hospital, from October 2020 to September 2021 on 50 lung cancer patients aged over 18 years. Patients who underwent CT scans including the L3 vertebra within two months of diagnosis were included. Exclusion criteria were incomplete CT images, missing height data, or lack of consent. L3 skeletal muscle index (L3SMI) was calculated to assess sarcopenia and correlated with survival. Ethical clearance was obtained from the Institutional Ethics Committee, and informed consent was secured from all participants prior to enrollment.

RESULTS

A total of 50 lung carcinoma patients were studied, comprising 32 males (64%) and 18 females (36%), with ages ranging from 40 to 80 years (mean 58.02). During a 6-month to 1-year follow-up, 27 patients died. Sarcopenia was present in 29 patients, of whom 23 died, indicating a strong mortality link. Low L3SMI (below 41 cm^2/m^2 in women and 53 cm^2/m^2 in men) significantly correlated with mortality. Stage 3 carcinoma was most common (34%). ECOG score 0 (40%) predominated. Co-morbidities were present in 22 patients, and key lab markers included albumin (3.526) and LDH (1132).

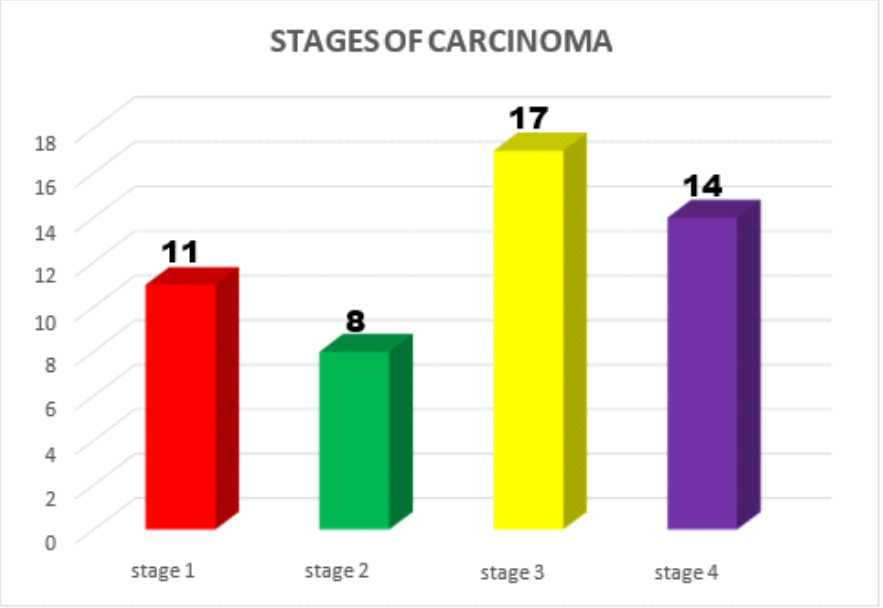

Figure 1: Stages of carcinoma

The bar chart shows the distribution of lung carcinoma stages among 50 patients. Stage 3 was most common (34%), followed by stage 4 (28%), stage 1 (22%), and stage 2 (16%). This suggests a higher proportion of patients presented with advanced disease. The predominance of later stages may indicate delayed diagnosis or aggressive tumor progression.

Table 1: Correlation Between ECOG Performance Status and L3SMI

		L3SMI<41-F & <53-M	ECOG
L3SMI<41-F & <53-M	Pearson Correlation	1	-.824**
	Sig.(2-tailed)		.000
	N	50	50
ECOG	Pearson Correlation	-.824**	1
	Sig.(2-tailed)	.000	
	N	50	50

The table shows a strong positive correlation (r = 0.726, p < 0.001) between low L3SMI (sarcopenia) and mortality in lung cancer patients. This indicates that patients with sarcopenia had (sarcopenia) is significantly associated with worse performance status. The correlation is statistically significant at the 0.01 level. Thus, sarcopenia negatively impacts patients' functional capacity.

Table 2: Correlation Between L3SMI and Mortality

		L3SMI<41 - F & <53 - M	DEATH=0, SURVIVED=1
L3SMI<41-F & <53 - M	Pearson Correlation	1	.726**
	Sig. (2-tailed)		.000
	N	50	50
DEATH=0, SURVIVED=1	Pearson Correlation	.726**	1
	Sig. (2-tailed)	.000	
	N	50	50

**. Correlation is significant at the 0.01 level (2-tailed).

The table shows a strong positive correlation (r = 0.726, p < 0.001) between low L3SMI (sarcopenia) and mortality in lung cancer patients. This indicates that patients with sarcopenia had a significantly higher risk of death. The correlation is statistically significant at the 0.01 level. Thus, low skeletal muscle mass is a strong predictor of poor survival.

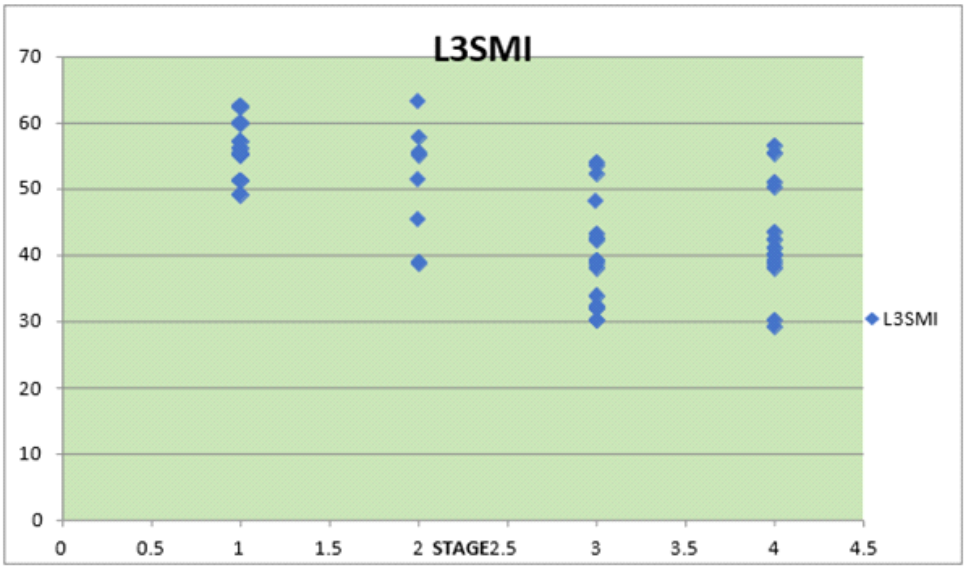

Figure 2: Correlation Between Carcinoma Stage and L3 Skeletal Muscle Index (L3SMI)

The scatter plot shows L3SMI values across different carcinoma stages, revealing a declining trend in muscle mass with advancing stage. Pearson's correlation coefficient (r = -0.579) indicates a moderate negative -lation between cancer stage and L3SMI. This suggests that higher tumor stage is associated with greater sarcopenia. The pattern emphasizes disease progression adversely impacting muscle status.

Table 3: Analysis of Variance (ANOVA) of ALT Levels in Relation to Mortality Outcomes

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	7.970	21	.380	2.388	.016
Within Groups	4.450	28	.159		
Total	12.420	49			

The ANOVA analysis shows a statistically significant difference in ALT values between patients who died and those who survived (p = 0.016). The F-value of 2.388 indicates moderate variability in ALT levels between the groups. This suggests that ALT levels may be associated with mortality outcomes. Thus, elevated or altered ALT could potentially serve as a prognostic marker in this patient cohort.

Table 4: Correlation Between Cancer Stage and Mortality Outcome

		cancer stage 1,2,3,4	YES=1, NO=0
cancerstage 1,2,3,4	Pearson Correlation	1	.671**
	Sig. (2-tailed)		.000
	N	50	50
YES=1, NO=0	Pearson Correlation	.671**	1
	Sig. (2-tailed)	.000	
	N	50	50

The Pearson correlation coefficient between cancer stage and death is 0.671, indicating a strong positive correlation. As the stage of cancer advances, the likelihood of death significantly increases. The correlation is statistically significant (p = 0.000), confirming a reliable association. This highlights cancer stage as a strong predictor of mortality in the studied cohort.

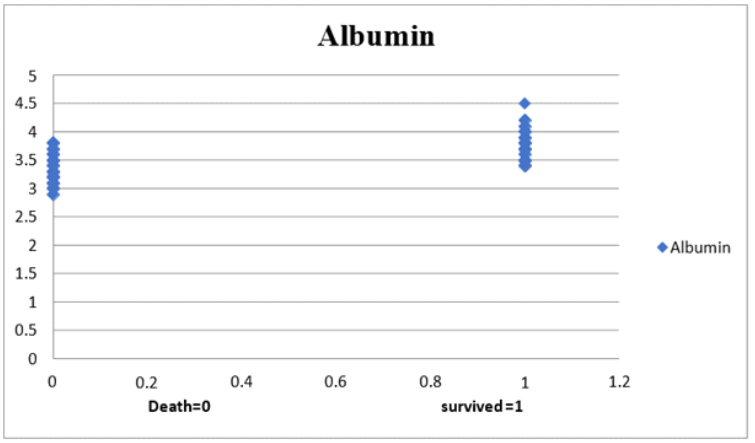

Figure 3: Comparison of Serum Albumin Levels Between Deceased and Surviving Patients

The scatter plot shows serum albumin levels in patients grouped by survival status. Patients who survived (survived = 1) generally had higher albumin levels, clustered around 4 g/dL or more. In contrast, those who died (death = 0) had lower albumin values, mostly below 3.8 g/dL. This indicates a potential association between higher albumin levels and improved survival outcomes.

DISCUSSION

Sarcopenia, characterized by the loss of skeletal muscle mass, is increasingly recognized as a negative prognostic factor in oncology. In the present study involving 50 lung carcinoma patients, sarcopenia was identified through the L3 Skeletal Muscle Index (L3SMI) calculated using CT scans obtained within two months of diagnosis. Patients were classified as sarcopenic or non-sarcopenic using threshold values from the criteria of Martin et al. Out of 50 patients, 29 were found to be sarcopenic, and among them, 23 died within a 6–12-month follow-up period, suggesting a strong correlation between sarcopenia and mortality(18).

This study demonstrated that lower L3SMI correlated with both higher mortality and advanced carcinoma stages. Among the sarcopenic group, 2 patients were in stage II, 12 in stage III, and 9 in stage IV. Importantly, the Eastern Cooperative Oncology Group (ECOG) performance status also correlated inversely with L3SMI: patients with higher ECOG scores (poorer functional status) had lower muscle mass, indicating that sarcopenia contributes to functional decline. In this cohort, 40% had an ECOG score of 0, while 34% and 26% had scores of 2 and 3, respectively.

The study found no significant correlation between mortality and comorbid conditions like diabetes mellitus (DM), chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), or ischemic heart disease (IHD). Similarly, serum ALT levels showed no association with mortality. However, reduced albumin levels were linked with increased mortality, highlighting hypoalbuminemia as a potential marker of poor prognosis.

Previous literature supports these findings. Kim et al. demonstrated that CT-defined sarcopenia in small cell lung cancer patients is associated with increased mortality, similar to the correlation observed in this study. They also found that higher ECOG scores and advanced cancer stages independently predicted worse outcomes. In contrast, Sjoblom et al. did not find a significant correlation between sarcopenia and prognosis in non-small cell lung cancer, though they acknowledged the potential role of muscle mass assessment and suggested further research (19, 20)..

N. Chargi et al., in a study on elderly patients with head and neck cancer, found that muscle mass alone was not predictive of survival. However, combining muscle mass with muscle strength or physical performance had significant prognostic value. Since the current study was retrospective, functional assessments like muscle strength or performance could not be incorporated, which is a limitation (21)..

Beyond oncology, sarcopenia has been shown to predict prognosis in chronic systemic diseases. Lee et al. found a significant inverse association between skeletal muscle mass and non-alcoholic fatty liver disease (NAFLD) over a 12-year follow-up, emphasizing muscle preservation as a therapeutic target in metabolic liver disease. Paternostro et al. highlighted the prognostic utility of different CT-based muscle indices in cirrhotic patients and identified transverse psoas muscle thickness (TPMT) as an independent risk factor for mortality (22, 23).

This study reinforces the relevance of sarcopenia—measured via L3SMI—as a non-invasive imaging biomarker that correlates with mortality and disease severity in lung cancer. Given its prognostic implications, incorporating muscle mass assessment into routine oncological evaluation could guide risk stratification and individualized care.

CONCLUSION

The L3 skeletal muscle index (L3SMI) is an effective surrogate marker for detecting sarcopenia in lung cancer patients and demonstrates a significant correlation with overall survival. Identifying patients with low L3SMI at an early stage enables timely intervention through nutritional support, physiotherapy, and medical management aimed at improving muscle mass. Such proactive measures may enhance treatment tolerance, reduce complications, and potentially improve survival outcomes. Routine assessment of L3SMI in clinical practice can aid in risk stratification, guiding personalized care plans that address muscle wasting and functional decline, thereby improving the overall prognosis in patients with lung cancer.

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