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## Impact of Skeletal Muscle Measurements by Chest Computed Tomography on Survival and Postoperative Complications in Patients with Soft Tissue Sarcoma

Tugba Akin Telli<sup>a</sup> , Onur Bugdayci<sup>b</sup>, Ozkan Alan<sup>a</sup> , Nisanur Sariyar<sup>c</sup>, Selver Isik<sup>a</sup>, Rukiye Arikan<sup>a</sup> , Alper Yasar<sup>a</sup>, Nargiz Majidova<sup>a</sup>, Abdussamet Celebi<sup>a</sup>, Bulent Erol<sup>d</sup> , Zerrin Ozgen<sup>e</sup>, Osman Kostek<sup>a</sup> , Ibrahim Vedat Bayoglu<sup>a</sup>, Ozlem Ercelep<sup>a</sup>, Faysal Dane<sup>a</sup>, and Perran Fulden Yumuk<sup>a,f</sup> 

<sup>a</sup>Division of Medical Oncology, School of Medicine, Marmara University, Istanbul, Turkey; <sup>b</sup>Department of Radiology, School of Medicine, Marmara University, Istanbul, Turkey; <sup>c</sup>Department of Internal Medicine, School of Medicine, Marmara University, Istanbul, Turkey; <sup>d</sup>Department of Orthopaedic Surgery and Traumatology, School of Medicine, Marmara University, Istanbul, Turkey; <sup>e</sup>Department of Radiation Oncology, School of Medicine, Marmara University, Istanbul, Turkey; <sup>f</sup>Division of Medical Oncology, School of Medicine, Koç University, Istanbul, Turkey

### ABSTRACT

This study aims to evaluate whether sarcopenia, measured by chest computed tomography (CT), affects survival outcomes and postoperative complications in soft tissue sarcoma (STS) patients undergoing surgery. In this retrospective study, CT scans of 79 patients were reviewed to measure pectoralis and T12 vertebra muscle area. Both were then adjusted for height ( $\text{cm}^2/\text{m}^2$ ) as pectoralis muscle index (PMI) and T12 vertebra muscle index (TMI). Analyses were performed by dichotomizing muscle indices at gender-specific 50th percentile; PMI and TMI < 50th percentile were defined as low, and  $\geq 50$ th percentile as high. Overall postsurgical complication rate (PCR) was 16%. Median length of hospital stay (LOHS) was 10 days (3–90). PMI and TMI were significantly lower in women ( $p=0.02$ ,  $p=0.04$ ). Median body mass index was significantly higher in high PMI and TMI groups ( $p=0.01$  for both). PCR and LOHS were similar between low and high PMI and TMI groups. Median follow-up was 29 months, 37 patients had recurrence and 23 died. No significant difference was noted between low and high PMI and TMI groups, in terms of disease-free or overall survival. PMI and TMI as measured by chest CT had no impact on survival outcomes or postoperative complications in localized STS.



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## Introduction

Sarcopenia, defined as the progressive and generalized loss of skeletal muscle mass and function, has received much attention over the last years, particularly as a major component of cancer cachexia syndrome (1, 2). Various tools, each with its own set of advantages and disadvantages, have been proposed for objective screening of sarcopenia. Computed tomography (CT), as one of these tools, is advantageous because it can provide precise evaluation of muscle, fat and other tissues, and is used routinely in cancer patients for initial staging, assessment of relapse/metastasis and treatment response in the follow-up period. As a result, some investigators consider this modality the gold standard (2).

The third lumbar vertebra (L3) has long been used as an anatomical landmark for calculating muscle cross-sectional area, which was considered to reflect the whole-body muscle mass. Sarcopenia has been defined in several studies by measuring skeletal muscle mass at this level, and it has been demonstrated to be a predictor of poor survival in a variety of malignancies (3–7). However, evidence regarding to the predictor value of sarcopenia in soft tissue sarcomas (STSs) is conflicting (8–14). Given that STSs tend to metastasize to the lungs, patients routinely undergo chest CT rather than abdominal/pelvic CT for initial staging and surveillance, as recommended by international guidelines. As a result, measuring muscle area at the L3 level for all patients is extremely challenging (8). Furthermore, certain types of surgery,

**CONTACT** Tugba Akin Telli  [tugbaakintelli@gmail.com](mailto:tugbaakintelli@gmail.com)  Department of Medical Oncology, Marmara University Faculty of Medicine, 34899 Istanbul, Turkey.

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especially lower extremity amputations, create asymmetry in the psoas muscle area, making L3 level unsuitable for measuring sarcopenia in some STS patients (8). When compared to abdomen/pelvis CT, muscle measurements on chest CT are less investigated for sarcopenia in cancer. On chest CT, sarcopenia is commonly assessed at the level of thoracic vertebra 12 (T12) and the manubriosternal joint, by measuring the erector spinae muscle mass and pectoralis muscle mass, respectively. Only few studies investigated sarcopenia using muscle measurements on chest CT in lung cancer (15–17). Limited data with conflicting results exist on the association of sarcopenia with survival outcomes and surgical complications in STS patients; of these, only two studies examined chest CT muscle metrics (8, 9), whereas the majority used the L3 level with discordant results (10–14).

We conducted this study to assess the impact of preoperative sarcopenia detected by chest CT on survival outcomes and postoperative complications in patients with STS who underwent curative surgery.

## Materials and Methods

### Study Design, Patient Selection and Data Collection

This is a retrospective, single-center review of localized STS patients who were operated with curative intent between August 2011 and February 2020. Main inclusion criteria were as follows: 1—Patients aged 18 or older, 2—Having baseline staging chest CT performed within 90 day prior to surgery, 3—Pectoralis muscles and paravertebral muscles at the level of T12 vertebra could be measured in the available imaging, 4—Clinical, pathological and a minimum of 6 months, follow-up data were present. Patients without preoperative chest CT were excluded. Certain subtypes with different tumor behaviors and treatments such as gastrointestinal stromal tumor, Kaposi sarcoma, dermatofibrosarcoma protuberans, solitary fibrous tumor, and hemangioendothelioma were excluded from the study. Patients with metastatic disease at the time of diagnosis, as well as those who received preoperative chemotherapy or radiotherapy, were also excluded. Final study population included 79 patients.

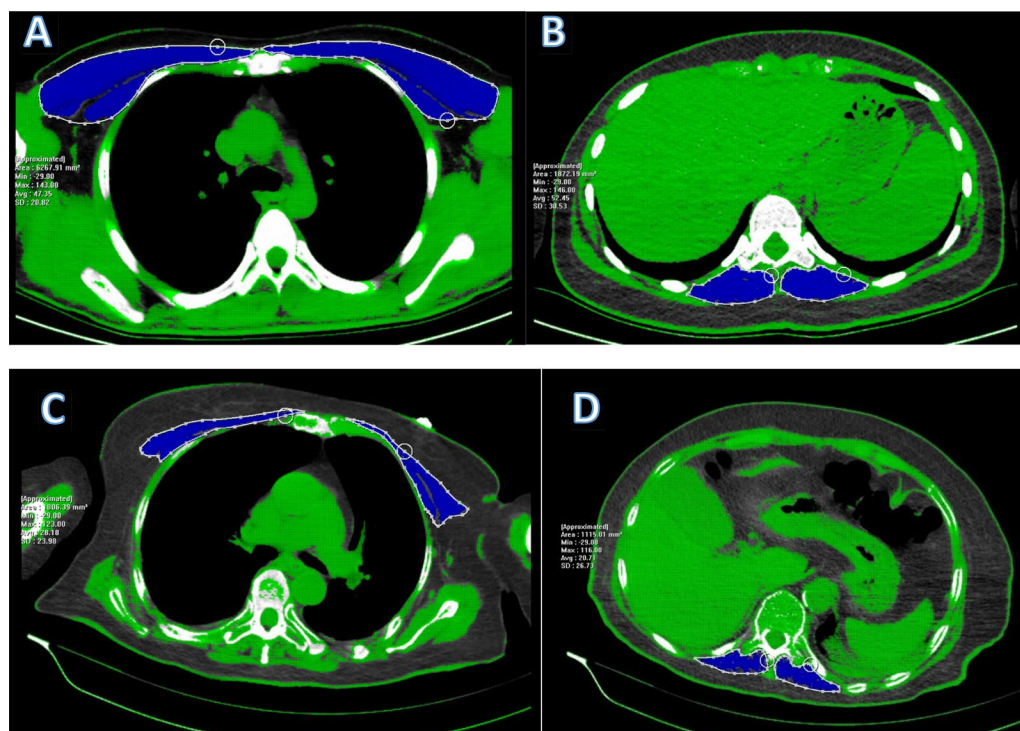
All demographic, clinical, operative, pathologic, and postoperative data were retrospectively extracted from medical records. Age, gender, Eastern Cooperative Oncology Group (ECOG) performance status (PS), comorbidities, weight (kg), height (m), body mass index [BMI, weight (kg)/square of height (m<sup>2</sup>)], date

of diagnosis, histological diagnosis, preoperative laboratory results were recorded. Date of surgery, re-resection status, primary tumor localization, size, grade (based on French Federation of Cancer Centers Sarcoma Group grading system), stage (according to the 8th edition (2017) of American Joint Committee on Cancer classification), resection margins were noted as operative and pathological details. Postoperative period data included length of hospitalization, postoperative complications, adjuvant chemotherapy or radiotherapy and survival outcomes. Postoperative complications included pneumonia, intensive care unit stay, hospital readmission, wound complications, wound infections, wound repair, abscess or hematoma drainage, intravenous antibiotics usage. This study was approved by the institutional ethics committee (Date of approval: 5 February 2021, Protocol Code: 09.2021.169).

### Chest CT Image Analysis and Evaluation of Sarcopenia

Routine chest CT imaging of patients was performed either on a 256-Channel Multislice Dual Source Scanner (Somatom Definition Flash, Siemens Healthineers, Erlangen, Germany) or 64-Channel Multislice Scanner (Somatom Definition AS, Siemens Healthineers, Erlangen, Germany) with or without IV contrast material with 1 mm slice thickness. Iodinated contrast material with an iodine concentration of 300 mg/ml was injected at 1.5 ml/kg dose.

Images were evaluated on the locum PACS (INFINITT PACS system, INFINITT Healthcare Co., Seoul, South Korea). Pectoralis muscles were evaluated at the level of the manubriosternal joint. In two patients this joint was not visible, and measurements were performed at the level of the aortic arch (last visible slice superiorly). In two patients only one side could be measured (in one patient due to previous surgery and in one patient only one side was included in the image) and this measurement was multiplied by two. Paravertebral muscle measurements were performed at the level of the transverse processes of the T12 vertebrae. Thresholding was applied to the images between  $-29\text{HU}$  and  $+150\text{HU}$  before measurement. Sum of bilateral pectoralis major and minor muscle areas as well as the total area of the paraspinal muscles on both sides were recorded as pectoralis muscle area (PMA) and T12 vertebra muscle area (TMA), respectively. Axial CT images demonstrating the measurements of PMA and TMA are presented in [Figure 1](#). Pectoralis and paraspinal (T12) muscle indices (PMI and TMI, respectively) were calculated by dividing



**Figure 1.** Preoperative axial computed tomography images demonstrating the measurements of cross-sectional areas in a non-sarcopenic (A and B) and sarcopenic patient (C and D) A/C) Cross-sectional area of pectoralis major and minor muscles at the level of the manubriosternal joint. B/D) Cross-sectional area of paraspinous muscles at the level of T12.

the total muscle area (in  $\text{cm}^2$ ) by the square of patient height (in  $\text{m}^2$ ). All skeletal muscle measurements and indices were categorized according to the gender-specific 50th percentile of each variable distribution; PMI and TMI  $<50$ th percentile was defined as low, and  $\geq 50$ th percentile as high.

### Statistical Analysis

Descriptive statistics were used to summarize the demographic and clinical characteristics and expressed as frequencies and percentages. Continuous variables were presented as median values with interquartile ranges (IQRs). The normality of data was tested by the Kolmogorov-Smirnov and Shapiro Wilks test and the parameters did not show normal distribution. Chi-square or Fisher's exact test was performed to compare categorical variables. Mann-Whitney U was used to compare the difference of medians between two independent groups. Disease-free survival (DFS) was defined as the time from surgery until recurrence of disease, death or last visit. Overall survival (OS) was defined as the time from diagnosis until death or last visit. Survival was estimated with Kaplan-Meier method and log-rank test. Cox proportional models were conducted to select prognostic factors for overall survival in univariate analysis. Variables which were

significant or close to significance ( $p < 0.1$ ) in univariate analysis were reassessed using a backward stepwise method in multivariate analysis. Confidence interval (CI) was accepted as 95% and  $p < 0.05$  was set as the level of significance. Statistical analyses were carried out using SPSS version 22.0 (SPSS Inc., Chicago, IL, USA).

### Results

#### Patient and Tumor Characteristics with Postoperative Details

Seventy-nine patients were eligible for the final analysis. Demographic and clinicopathologic characteristics of study population are presented in Table 1. Median age was 52 (range 18–86) years and 43 (53%) were male. ECOG-PS was 0 in 87% of the patients. Thirty-three of 79 patients (42%) had at least one comorbidity. Lower extremities were the most common primary tumor locations (65%). Median tumor size was 10 cm (range 1.2–38). The most common tumor histology was undifferentiated pleomorphic sarcoma (23%) followed by liposarcoma (18%) and myxofibrosarcoma (18%). Majority of the tumors (92%) were high-grade (grade 2–3). Three out of four patients had stage 3 disease (75%). Overall

**Table 1.** Baseline demographic and clinicopathologic characteristics of study population.

|                                 | Findings         | All patients, n=79 (%) |
|---------------------------------|------------------|------------------------|
| Gender                          | Female           | 36 (47%)               |
|                                 | Male             | 43 (53%)               |
| Age, median (range)             | 52 (18–86)       |                        |
| Body mass index, median (range) | 25.9 (15.7–40.4) |                        |
| ECOG-PS                         | 0                | 69 (87%)               |
|                                 | ≥1               | 10 (13%)               |
| Comorbidity                     | Yes              | 33 (42%)               |
|                                 | No               | 46 (58%)               |
| Re-resection                    | Yes              | 7 (9%)                 |
|                                 | No               | 72 (91%)               |
| Primary tumor location          | Upper extremity  | 16 (20%)               |
|                                 | Lower extremity  | 51 (65%)               |
|                                 | Others           | 12 (15%)               |
| Tumor histology                 | Leiomyosarcoma   | 6 (7%)                 |
|                                 | Liposarcoma      | 14 (18%)               |
|                                 | Synovial sarcoma | 9 (11%)                |
|                                 | Myxofibrosarcoma | 14 (18%)               |
|                                 | UPS              | 18 (23%)               |
|                                 | Others           | 18 (23%)               |
| Tumor grade                     | Grade 1          | 6 (8%)                 |
|                                 | Grade 2          | 19 (24%)               |
|                                 | Grade 3          | 54 (68%)               |
| Tumor stage at diagnosis        | Stage 1          | 6 (7%)                 |
|                                 | Stage 2          | 11 (14%)               |
|                                 | Stage 3          | 59 (75%)               |
|                                 | Unknown          | 3 (4%)                 |
| Surgical margins                | R0               | 69 (87%)               |
|                                 | R1-2             | 10 (13%)               |
| Postoperative complication      | Yes              | 13 (16%)               |
|                                 | No               | 66 (84%)               |
| Adjuvant chemotherapy           | Yes              | 39 (49%)               |
|                                 | No               | 40 (51%)               |
| Adjuvant radiotherapy           | Yes              | 55 (70%)               |
|                                 | No               | 24 (30%)               |
| Recurrence                      | Yes              | 37 (47%)               |
|                                 | No               | 42 (53%)               |
| Recurrence pattern              | Local            | 6 (16%)                |
|                                 | Distant          | 31 (84%)               |
| Status                          | Alive            | 56 (71%)               |
|                                 | Exitus           | 23 (29%)               |

ECOG-PS: Eastern Cooperative Oncology Group performance status, UPS: undifferentiated pleomorphic sarcoma.

**Table 2.** All group and gender-specific skeletal muscle measurements.

|  | All patients (n=79) | Gender           |                   | p       |
|--|---------------------|------------------|-------------------|---------|
|  |                     | Female (n=36)    | Male (n=43)       |         |
| PMA (cm <sup>2</sup> ), median (range)                 | 28.8 (11.6–67.7)    | 21.7 (11.6–61.9) | 33.5 (14.3–67.7)  | <0.001* |
| TMA (cm <sup>2</sup> ), median (range)                 | 34.7 (6.8–62.06)    | 28.4 (6.8–48.9)  | 37.7 (17.7–62.06) | 0.001*  |
| PMI (cm <sup>2</sup> /m <sup>2</sup> ), median (range) | 10.3 (4.7–20.4)     | 8.2 (4.7–20.4)   | 10.9 (5.2–19.8)   | 0.02*   |
| TMI (cm <sup>2</sup> /m <sup>2</sup> ), median (range) | 11.8 (2.7–18.9)     | 11.2 (2.7–18.9)  | 12.6 (6.2–18.3)   | 0.04*   |

PMA: Pectoralis muscle area, TMA: T12 vertebra muscle area, PMI: Pectoralis muscle index, TMI: T12 vertebra muscle index.

\*Significant values ( $p < 0.05$ ) are highlighted.

postsurgical complication rate (PCR) was 16%, and median length of hospital stay (LOHS) after surgery was 10 days (range 3–90). Adjuvant chemotherapy and radiotherapy were applied to 49% and 70% of the patients, respectively.

### Gender-Specific Skeletal Muscle Measurements

Median skeletal muscle measurements including PMA, TMA, PMI and TMI were significantly lower in women

than men ( $p < 0.001$ ,  $p = 0.001$ ,  $p = 0.02$  and  $p = 0.04$ , respectively). All group and gender-specific skeletal muscle measurements were shown in detail in Table 2.

### The Association between Skeletal Muscle Measurements (PMI and TMI) and Clinicopathologic Characteristics

None of the demographic and clinicopathologic features, except from BMI, showed statistically significant

difference between groups with low and high PMI, and low and high TMI. Median BMI was significantly higher in both high PMI and high TMI groups ( $p=0.01$  for both). Table 3 outlines the relationship between skeletal muscle measurements and clinicopathologic characteristics.

### The Association between Skeletal Muscle Measurements (PMI and TMI) and Postoperative Complications

Median LOHS was similar between low and high PMI and TMI groups ( $p=0.9$  for both). PCRs were not significantly different between groups, either ( $p=0.6$  and  $p=0.8$ , respectively) (Table 3).

### Survival Outcomes

During a median follow-up of 29 months (range 6–113), 37 (47%) patients experienced recurrent disease, the majority of which was distant metastasis. A

total of 23 (29%) patients died. In terms of DFS and OS, Kaplan-Meier survival analysis revealed no statistically significant difference between low and high PMI and TMI groups across the entire study population (Figure 2). DFS and OS were similar between groups when the analysis was rerun stratified by gender (Supplementary Table 1).

In univariate analysis, tumor grade ( $p=0.03$ ) and stage ( $p=0.03$ ) were found to be significant poor prognostic factors for OS. Multivariate analysis determined tumor stage ( $p=0.03$ ) as the only independent predictor of OS. Univariate and multivariate analyses of factors for predicting OS were summarized in Figures 3 and 4, respectively.

### Discussion

In this study, we aimed to show the impact of sarcopenia on survival outcomes and postoperative complications in patients with localized STS operated with curative intent. For this purpose, we used preoperative staging

**Table 3.** The association between skeletal muscle measurements and clinicopathologic characteristics/ postoperative complications.

| Findings  |                  | Pectoralis muscle index |                 |       | T12 vertebra muscle index |                 |       |
|---|------------------|-------------------------|-----------------|-------|---------------------------|-----------------|-------|
|   |                  | Low ( $n=41$ )          | High ( $n=38$ ) | $p$   | Low ( $n=40$ )            | High ( $n=39$ ) | $p$   |
| Gender  | Female           | 20 (48%)                | 16 (42%)        | 0.5   | 21 (52%)                  | 15 (38%)        | 0.1   |
|   | Male             | 21 (52%)                | 22 (58%)        |       | 19 (48%)                  | 24 (62%)        |       |
| Age, median (range)   |                  | 53 (18–82)              | 37 (27–69)      | 0.6   | 59 (18–82)                | 52 (29–74)      | 0.1   |
| Body mass index, median (range)                             |                  | 24.8                    | 29.8            | 0.01* | 22.3                      | 30              | 0.01* |
|   |                  | (15.7–40.4)             | (21.6–39.3)     |       | (20–31.9)                 | (18.3–38)       |       |
| Albumin (g/dL), median (range)                              |                  | 4.2                     | 4.1             | 0.4   | 4                         | 3.8             | 0.6   |
|   |                  | (3.7–4.6)               | (3.3–4.7)       |       | (3.3–4.6)                 | (2.9–4.7)       |       |
| C-reactive protein (mg/L), median (range)                   |                  | 9.2 (2–10)              | 14.8 (3–49)     | 0.09  | 7.9 (1–49)                | 8.8(3–25)       | 0.3   |
| Primary tumor location                                      | Upper extremity  | 9 (22%)                 | 7 (18%)         | 0.7   | 9 (22%)                   | 7 (18%)         | 0.7   |
|   | Lower extremity  | 26 (64%)                | 25 (67%)        |       | 26 (65%)                  | 25 (64%)        |       |
|   | Other            | 6 (14%)                 | 6 (15%)         |       | 5 (13%)                   | 7 (18%)         |       |
| Tumor histology   | Leiomyosarcoma   | 3 (7%)                  | 3 (8%)          | 0.6   | 2 (5%)                    | 4 (10%)         | 0.7   |
|   | Liposarcoma      | 4 (9%)                  | 10 (26%)        |       | 6 (15%)                   | 8 (20%)         |       |
|   | Synovial sarcoma | 5 (12%)                 | 4 (9%)          |       | 3 (7%)                    | 6 (15%)         |       |
|   | Myxofibrosarcoma | 9 (22%)                 | 5 (13%)         |       | 8 (20%)                   | 6 (15%)         |       |
|   | UPS              | 10 (25%)                | 8 (22%)         |       | 10 (25%)                  | 8 (20%)         |       |
|   | Others           | 10 (25%)                | 8 (22%)         |       | 11 (28%)                  | 7 (20%)         |       |
| Tumor grade   | Grade 1          | 3 (7%)                  | 3 (8%)          | 0.8   | 3 (7%)                    | 3 (7%)          | 0.9   |
|   | Grade 2          | 11 (27%)                | 8 (21%)         |       | 10 (26%)                  | 9 (21%)         |       |
|   | Grade 3          | 27 (66%)                | 27 (71%)        |       | 27 (67%)                  | 27 (72%)        |       |
| Tumor stage at diagnosis                                    | Stage 1          | 3 (7%)                  | 2 (5%)          | 0.8   | 3 (8%)                    | 3 (8%)          | 0.8   |
|   | Stage 2          | 6 (14%)                 | 5 (13%)         |       | 6 (15%)                   | 5 (13%)         |       |
|   | Stage 3          | 30 (75%)                | 29 (79%)        |       | 30 (75%)                  | 29 (74%)        |       |
|   | Unknown          | 2 (4%)                  | 1 (3%)          |       | 1(2%)                     | 2 (5%)          |       |
| Postoperative length of hospital stay (day), median (range) |                  | 9 (4–90)                | 10 (3–67)       | 0.9   | 9 (4–24)                  | 10 (7–29)       | 0.9   |
| Postoperative complication                                  | Yes              | 6 (15%)                 | 7 (18%)         | 0.6   | 7 (17%)                   | 6 (15%)         | 0.8   |
|   | No               | 35 (85%)                | 31 (82%)        |       | 33(83%)                   | 33 (85%)        |       |
| Adjuvant chemotherapy                                       | Yes              | 18 (44%)                | 21 (55%)        | 0.3   | 19 (47%)                  | 20 (51%)        | 0.9   |
|   | No               | 23 (56%)                | 17 (45%)        |       | 21 (53%)                  | 19 (49%)        |       |
| Adjuvant radiotherapy                                       | Yes              | 29 (71%)                | 26 (68%)        | 0.8   | 12 (30%)                  | 12 (31%)        | 0.6   |
|   | No               | 12 (29%)                | 12 (32%)        |       | 28 (70%)                  | 27 (69%)        |       |
| Recurrence  | Yes              | 21 (51%)                | 16 (42%)        | 0.4   | 18 (45%)                  | 19 (49%)        | 0.5   |
|   | No               | 20 (49%)                | 22 (58%)        |       | 22 (55%)                  | 20 (51%)        |       |
| Status  | Alive            | 29 (71%)                | 27 (71%)        | 0.9   | 28 (70%)                  | 28 (71%)        | 0.5   |
|   | Exitus           | 12 (29%)                | 11 (29%)        |       | 12 (30%)                  | 11 (29%)        |       |

UPS: undifferentiated pleomorphic sarcoma.

\*Significant values ( $p < 0.05$ ) are highlighted.

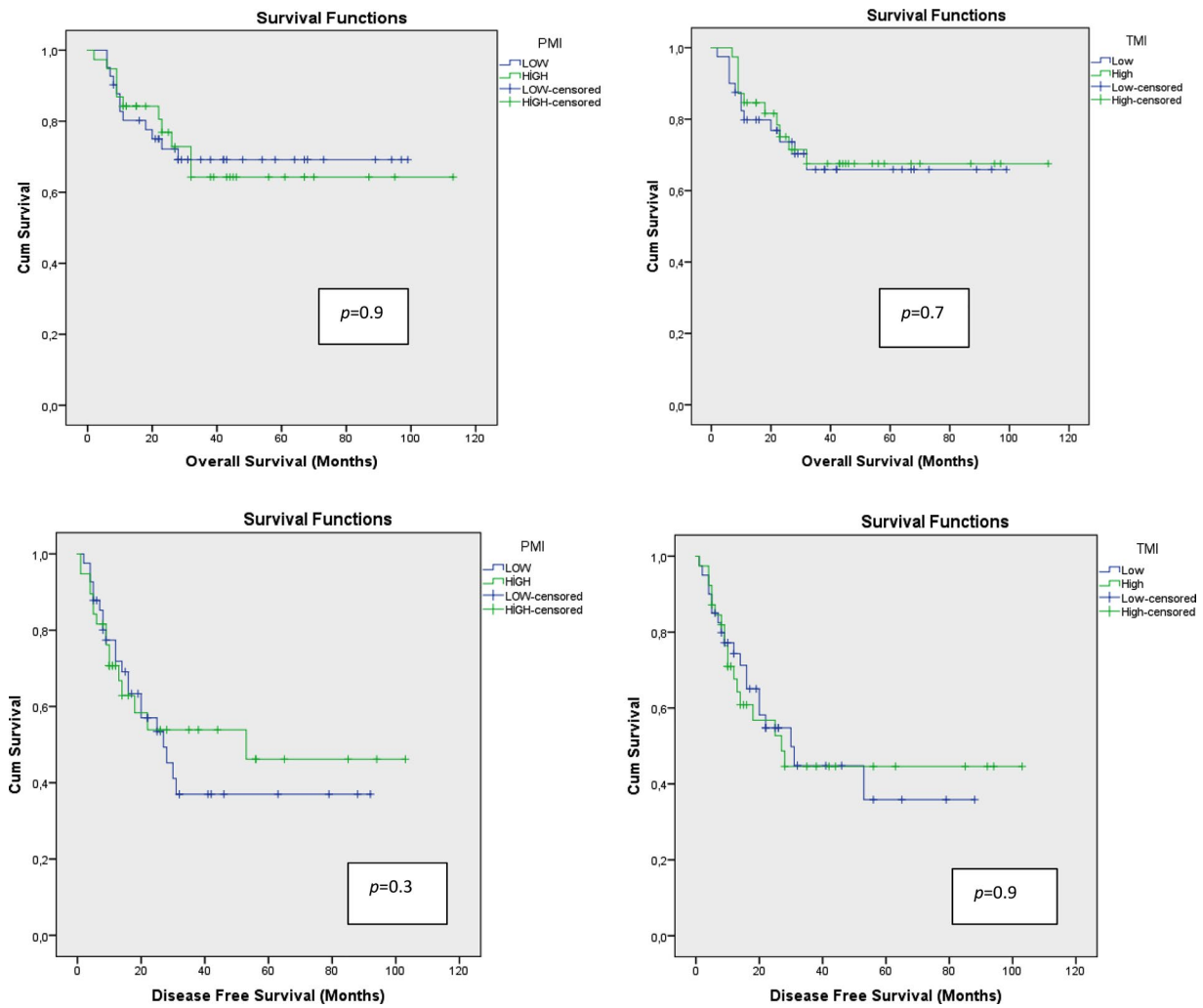


Figure 2. Kaplan-Meier curves showing overall and disease-free survival stratified by pectoralis muscle index (PMI) and T12 vertebra muscle index (TMI) across the entire study population.

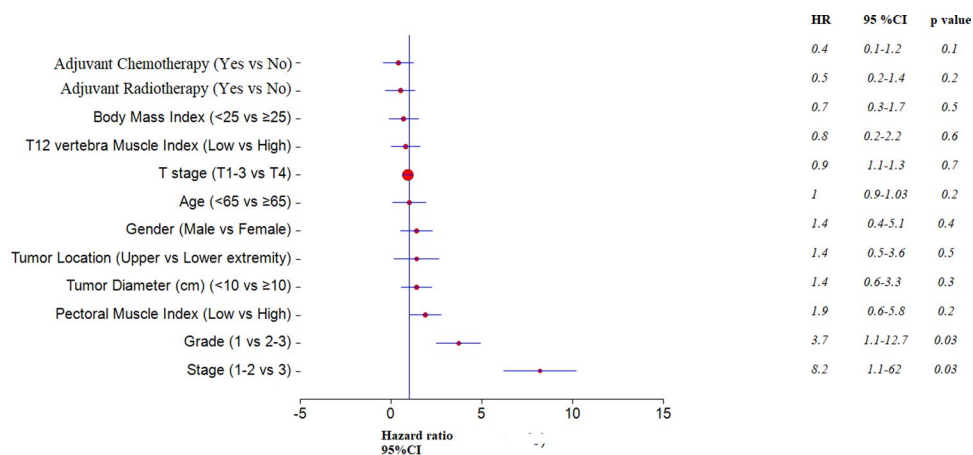
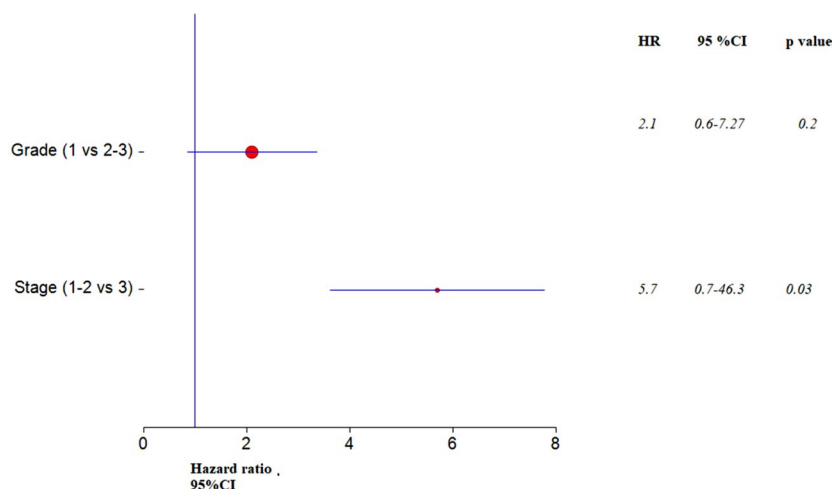


Figure 3. The forest plot shows the results of univariate analysis of factors for predicting overall survival.

chest CT, which is a routinely used imaging method in STS, since lungs are the most frequently metastasized sites. We simultaneously measured two separate indices,

PMI and TMI, both of which focus on the muscle quantity. Neither, however, were associated with survival outcomes or postsurgical complications.



**Figure 4.** The forest plot shows the results of multivariate analysis of factors for predicting overall survival.

A scarce amount of research exists regarding the effects of sarcopenia on STS, and the findings are often contradictory. In one study, sarcopenia was associated with mortality but not with postsurgical complications (11), whereas in another, sarcopenia predicted wound complications but not overall survival (13). Our results were in line with Wilson et al.'s findings from 137 patients with STS of extremities, which did not demonstrate any relation between sarcopenia and OS or wound complications (10). This apparent lack of correlation between studies can be clarified by several possible explanations.

First and foremost, findings need to be interpreted with caution, as the CT-derived muscle parameters differed between studies, since some focus on muscle quality while others focus on muscle quantity. As an indicator of muscle quality, skeletal muscle density (SMD) is calculated based on muscle adiposity. Skeletal muscle index (SMI) is measured based on muscle mass, which reflects muscle quantity. Both Hendrickson et al. (11) and Hirai et al. (13) used abdominal CT for evaluating sarcopenia, with measurements performed at the level of L3. The first group, on the other hand, selected to measure SMI of psoas, whereas the second used the skeletal muscle gauge, which was calculated by multiplying SMD and SMI. Wilson et al. (10) and Boutin et al. (12), reported two more studies that shared similar study designs, number of patients, imaging modalities, and level of measurements; nevertheless, their findings were contradictory. Sarcopenia was assessed in both studies by measuring total SMI at the level of L3/4 vertebra, but in Boutin's study, SMD was also evaluated. Unlike Wilson's study, Boutin et al. found a significant relation between SMD, SMI and mortality. Results of Veld et al. on SMD were consistent with

Boutin's study, they also reported the association between muscle quality and mortality, but they did not evaluate muscle area or index (14). In all the above-mentioned studies, the imaging modality used to assess sarcopenia was abdominal CT. Although most CT-derived muscle metrics are evaluated at the level of L3, measurements at the level of T10-L5 have recently been validated (18). To date, only two studies have addressed the utility of chest CT to assess sarcopenia in STS. Phan et al. (9) demonstrated that higher SMD but not SMI was associated with prolonged survival. Jo et al. (8), on the other hand, recently reported that both metrics had an impact on survival outcomes. They did in fact differ in muscle areas measured; one selected the paravertebral muscle at the level of T12 vertebra as a landmark (9), while the other used the pectoralis muscle (8). In the light of these findings, quality of muscle seems to be more related with survival outcomes but this hypothesis still needs to be further investigated. In our study, we evaluated muscle cross-sectional area and index at two different levels. However, we could not evaluate muscle density because some patients were scanned using IV contrast.

Secondly, the heterogeneity of STSs could also be a contributing factor to the discrepancies between studies. All studies, including ours, consisted of varied study populations in terms of sarcoma histologic subtype, tumor grade, stage and tumor depth, all of which could affect survival outcomes. Bone sarcomas were also included in two of the studies, which may have influenced the results due to differences in treatment strategies and prognosis (8, 11). Moreover, unlike our study, all others included metastatic patients. According to the international guidelines, tumor stage is one of the most important factors for

determining the severity of cancer cachexia (19). When compared to other study populations, ours had a more homogeneous distribution of histology and tumor stage, even though there were relatively few low-grade tumors.

Finally, it is important to keep in mind that, the pathogenesis of cancer cachexia, the relationship between systemic inflammation and muscle loss and prevalence of sarcopenia in early and metastatic stages may differ between sarcomas and carcinomas. As far as we know, no previous literature exists on this topic. Even the putative association between inflammatory markers and sarcopenia is still not fully understood. We evaluated the association between skeletal muscle metrics and C-reactive protein (CRP), but CRP levels were similar between sarcopenic and non-sarcopenic groups. Moreover, in our patient cohort, sarcopenia had no effect on albumin levels. Based on this finding, the hypothesis that this association arises in advanced stages of sarcomas may be a potential target for further studies.

Optimal threshold for each skeletal muscle measurement derived from chest CT is still a matter of debate. Geographic and ethnic variations in muscle mass are well defined in the literature (20). We conducted analyses in this study by dichotomizing muscle indices at the 50th percentile. With larger populations, however, lower cutoff values should be evaluated to define sarcopenia.

We acknowledge the limitations of our study. First, retrospective design in a single institution with relatively low number of samples might cause selection bias. Second, as some patients were imaged using IV contrast, the applied thresholding could have interfered with area measurements. However, no major omission or exclusion was noted on the color-coded images which marked the measured area. Third, heterogeneity of study population with a broad range of histologies may have affected outcomes.

## Conclusion

In our work, sarcopenia expressed by skeletal muscle measurements on preoperative chest CT did not predict survival or postoperative complications in localized STS. Previous data on the predictor value of sarcopenia in STS are still controversial. The variability of CT-derived muscle parameters to define sarcopenia, heterogeneity of STSs, uncertain optimal thresholds for skeletal muscle measurements, and the differences between sarcomas and carcinomas in terms of molecular, biological and pathological aspects seem to be the rationale behind this discrepancy. From this

point, this research has raised many questions in need of further investigation. Prospective studies with a larger sample size are needed to evaluate different skeletal muscle measurements focusing on muscle quality and quantity, to better define optimal cutoff values of sarcopenia and to investigate the correlation between sarcopenia and survival outcomes.

## Authors' Contributions

**T.A.T.:** Conceptualization, Data curation, Writing—Original draft, **O.B.:** Methodology, Resources, **O.A.:** Formal analysis, Investigation, **N.S.:** Data curation, **S.I.:** Data curation, Investigation, **R.A.:** Data curation, Investigation, **A.Y.:** Data curation, Investigation, **N.M.:** Data curation, Investigation, **A.C.:** Data curation, Investigation, **B.E.:** Supervision, **Z.O.:** Data curation, Investigation, **O.K.:** Formal analysis, **I.V.B.:** visualization, **O.E.:** Data curation, Investigation **F.D.:** Supervision, **P.F.Y.:** Supervision, Writing—Reviewing and Editing.

## Data Availability Statement

The data that support the findings of this study are available from the corresponding author, [T.A.T.], upon reasonable request.

## Disclosure Statement

The authors report no conflict of interest.

## Ethics Committee Approval

Ethical approval for this study was obtained from the Ethics Committee of Marmara University (Date of approval: 5 February 2021, Protocol Code: 09.2021.169).

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## ORCID

Tugba Akin Telli  <http://orcid.org/0000-0001-6535-6030>  
 Ozkan Alan  <http://orcid.org/0000-0002-6635-2012>  
 Rukiye Arıkan  <http://orcid.org/0000-0003-2688-1515>  
 Bulent Erol  <http://orcid.org/0000-0001-7099-6374>  
 Osman Kostek  <http://orcid.org/0000-0002-1901-5603>  
 Perran Fulden Yumuk  <http://orcid.org/0000-0001-8650-299X>

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