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ORIGINAL ARTICLE

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The effect of sarcopenia on survival in patients with metastatic colon cancer

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ABSTRACT

Introduction. Sarcopenia is a common loss of muscle mass in cancer patients. The aim of this study is to investigate the effect of sarcopenia on survival in patients with metastatic colon cancer.

Material and methods. The study was carried out retrospectively in patients diagnosed with metastatic colon cancer between January 2016 and December 2023. Sarcopenic patients were determined by total psoas area index and Hounsfield unit average calculation using computed tomography scan images obtained at the time of diagnosis. Statistical analyses were performed using Windows SPSS 20 package program. The effects of sarcopenia on survival were analyzed using the log-rank test, and univariate Cox regression analysis was applied to evaluate clinicopathological features. A p-value < 0.05 was considered statistically significant.

Results. A total of 70 patients with metastatic colon cancer were evaluated. Sarcopenia was detected in 18 patients (25.7%). The median age of the sarcopenic patients was 72 (53–83) years. A significant correlation was found between age and sarcopenia ($p = 0.002$). Median survival of sarcopenic patients was 11 months while non-sarcopenic patients had a median survival of 24 months. A difference was found in overall survival between the two groups ($p = 0.021$). There was no difference in progression free survival between sarcopenic and non-sarcopenic patients ($p = 0.615$).

Conclusions. In the present study, a significant prognostic effect of sarcopenia on survival was found in patients with metastatic colon cancer. The survival of sarcopenic patients was poorer.

Keywords: colon cancer, sarcopenia, metastasis

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Introduction

Sarcopenia and obesity are major public health problems in the aging population. The incidence of sarcopenia, associated with a sedentary lifestyle, poor nutrition, chronic disease, and medication use, increases with age [1, 2]. The easiest method of diagnosing sarcopenia is the measurement of mass, strength, and physical performance of muscle. Whole-body dual-energy X-ray absorptiometry, computed tomography (CT), or magnetic resonance imaging (MRI) can be used for muscle mass measurement [3]. The sarcopenia consensus, announced by The European Working Group on Sarcopenia in Older People (EWGSOP) in 2019, defined the third lumbar vertebra (L3) muscle mass measurement by CT as the gold standard method [1]. Colorectal cancers (CRC) are one of the cancers having most frequent mortality rate in the world [4]. Approximately 50–60% of all colorectal cancer cases are diagnosed as metastatic. Age, gender, performance status, tumor localization, site and number of metastases, RAS–BRAF mutations, and microsatellite instability (MSI) status are the main factors determining the prognosis. In addition to these factors, there are other factors affecting the patient's response to treatment [5]. In studies conducted with cancer patients,

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sarcopenia was determined as one of the factors affecting prognosis with a higher incidence in cancer patients [6]. In the EWGSOP sarcopenia consensus, the importance of sarcopenia in cancer patients as well as in the elderly was emphasized [1, 7].

In recent years, there has been an increasing awareness of the impact of sarcopenia on cancer prognosis. Particularly in populations such as solid cancer patients, the early detection of sarcopenia plays a critical role in planning personalized treatment and supportive care strategies, ultimately improving survival and quality of life [8]. However, the accessibility and practicality of the methods used to evaluate sarcopenia remain limiting factors. In this context, CT-based measurement methods, such as the Total Psoas Area Index (TPAI) and Hounsfield Unit Average Calculation (HUAC), can be easily applied without incurring additional costs or procedures by utilizing imaging data obtained during diagnosis. While TPAI normalizes the psoas muscle area based on the patient's height, HUAC measures the density of muscle tissue, allowing for the evaluation of muscle loss and fat infiltration. These methods stand out in clinical practice as cost-effective and time-efficient tools [9].

In the present study, the aim was to investigate the impact of sarcopenia on mortality and prognosis in patients with advanced colorectal cancer. For this purpose, sarcopenia was evaluated using TPAI and HUAC values calculated from abdominal CT scans obtained at the time of diagnosis. The aim of this study is to highlight the effects of sarcopenia on treatment response and survival in metastatic colorectal cancer patients, thereby addressing a gap in theexisting literature. Additionally, the aim to raise awareness of how early detection of sarcopenia can be integrated into personalized treatment approaches.

Material and methods

Eighty patients diagnosed with metastatic colon cancer in our oncology clinic were retrospectively screened between January 2016 and December 2023. Patients whose CT screening and clinicopathological information were not available in computer-based patient records at the time of diagnosis were excluded from the study. Additionally, to ensure a homogeneous treatment cohort, patients who did not receive systemic treatment with both chemotherapy and biological agents were excluded. Those who received monochemotherapy instead of doublet chemotherapy were also not included in the analysis. These exclusion criteria were applied to minimize treatment-related variability and provide a more accurate assessment of the prognostic impact of sarcopenia. A total of 70 patients were included in the study. Medical file records of patients, laboratory results, pathology reports, and CT scan and results at the time of diagnosis, were accessed by computer-based hospital records. Demographic and clinicopathological characteristics of the patients were recorded. Because ofthe study was a retrospective, informed consent could not be obtained from the patients. The study was conducted according to the principles of the Declaration of Helsinki and approval was obtained from the ethics committee of Health Sciences University Diskapi Yildirim Beyazit Training and Research Hospital.

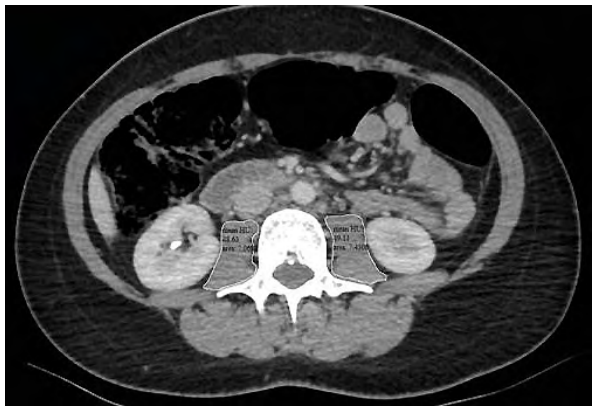

Figure 1. Abdominalaxial computed tomography images. At thelevel of thirdlombervertebra, outerboundaries of psoasmuscleswеredrawnmanually (whitelines) and psoasmusclecrosssectionalarea (cm^2) andattenuation (HounsfieldUnit, HU) weremeasured on bothsides

Assessment of sarcopenia

In the present study, sarcopenia was evaluated with TPAI and HUAC, similar to previous studies on this subject [10]. The lowest gender-specific cutoff point, 25%, was accepted as sarcopenia for the results obtained. In this study, CT scan images of the patients, at the time of diagnosis of metastatic colon cancer, were assessed by a single radiologist. Hounsfield Units (HU) is the radiation unit used in the classification of CT scan images according to tissue density. According to this, HUAC was calculated from the CT images of the patients by measuring areas of both psoas muscles (cm^2) at the level of the third lumbar (L3) vertebra and density (HU) (Fig. 1).

Right and left HU measurements were calculated by equations of Right Hounsfield Unit Calculation (RHUC) [(Hounsfield Unit right psoas × right psoas area)/(total psoas area)] and Left Hounfield Unit Calculation (LHUC) [(Hounsfield Unit left psoas × left psoas area)], respectively. Finally, the HUAC value was obtained with the HUAC = [(RUAC + LUAC)/2] equation. Total psoas area index was calculated by dividing the sum of the right and left psoas muscle areas by the square of the patient's height [TPAI = (right psoas area + left psoas area)/height^2].

Table 1. Results of gender-specific total psoas area, Total Psoas Area Index (TPAI) and Hounsfield Unit Average Calculation (HUAC)

	Male	Female	Sarcopenic	Non-sarcopenic
Total psoas area	17.37 ± **4.3**	10.05 ± **2.5**	**12.5** ± **4.9**	15.91 ± 5.02
TPAI [cm^2/m^2]	6.06 ± **1.5**	**22.0** ± 4.0	**4.8** ± **1.5**	5.64 ± 1.67
HUAC	22.44 ± 4.08	18.16 ± **5.3**	15.95 ± 4.57	22.93 ± 3.56

All patients included in the study were evaluated for sarcopenia and muscle mass after being diagnosed as metastatic and prior to the initiation of systemic therapy. This ensured that the assessments reflected the patients' baseline sarcopenia status at the time of systemic treatment initiation, without being confounded by the potential effects of previous chemotherapy regimens.

Statistical analysis

Windows SPPS 20 package program was used for statistical analysis (Chicago, Illinois, USA). Normal distribution of continuous variables was determined by the Kolmogorov-Smirnov test. Continuous variables were reported as mean ± standard deviation or median (minimum–maximum), according to the purpose. Categorical variables were analyzed by chi-square and the Fisher exact test. Univariate cox regression analysis was used to investigate the effects of clinicopathological features and sarcopenia on survival. The effect of sarcopenia on overall survival and disease-free survival was evaluated with the log-rank test. Cut-off values for TPAI and HUAC were determined as 25% percentile, the lowest threshold according to gender. P-value < 0.05 was considered statistically significant.

Results

Out of a total of 70 patients, 23 (32.9%) were female and 47 (67.1%) was male. The median age at diagnosis was 63 (31–83) years. There was right-sided colon tumor in 16 patients (22.9%) and left-sided colon tumor in 54 patients (77.1%). Forty-six patients (65.7%) had grade 1–2 and 24 patients (34.3%) had grade 3 tumors. The mean value of gender-specific body mass index (BMI) was 24 ± 3.83 kg/m^2 for women and 24.83 ± 3.28 kg/m^2 for men. Thirty-eight patients (54.3%) had KRAS mutation. All patients had stage 4 disease at the time of diagnosis. Metastases were inoperable and all patients received biologic agent treatment according to the mutation status and location of the tumor. The lowest threshold value of 25% was 3.2 cm^2/m^2 in women for diagnosing sarcopenia by TPAI, while it was found as 16.4 by HUAC. The lowest threshold value of 25% was 5.1 cm^2/m^2 in men for diagnosing sarcopenia by TPAI, while it was 19.2 by HUAC (Tab. 1).

According to these criteria, 18 patients (25.7%) were found compatible with sarcopenia (6 female, 12 male patients). No significant relationship was found between gender and sarcopenia (p = 0.960). The median age of sarcopenic patients was 72 (53–83) years, while it was 60 (31–83) years for non-sarcopenic patients. Out of 18 sarcopenic patients, 13 (72.2%) were over 65 years of age. As expected, a significant correlation was found between age and sarcopenia (p = 0.002). Of the sarcopenic patients, 10 were overweight/obese. No relationship was found between sarcopenia and location of the tumor (p = 0.536), KRAS mutation status (p = 0.221), BMI (p = 0.564), presence of liver metastasis (p = 0.558), tumor grade (p = 0.211), and Eastern Cooperative Oncology Group (ECOG) performance status (0.722) (Tab. 2).

Gender (p = 0.602), presence of liver metastases (p = 0.946), KRAS mutation status (p = 0.827), carcinoembryonic antigen (CEA) level (p = 0.159), tumor localization (p = 0.520), and ECOG performance status (0.751) were found to have no significant effects on survival (Tab. 3). The median survival time was 11 months for sarcopenic patients, and 24 months for non-sarcopenic patients (p = 0.021) (Fig. 2). The median survival of the patients was 21 months (0–61 months). During follow-up, progression developed in 65 patients (91.4%), and 57 (80%) patients died.

There was no difference in progression free survival (PFS) between sarcopenic and non-sarcopenic patients. During the follow-up, 17 of 18 sarcopenic patients developed progression. Progression developed in 47 of 52 non-sarcopenic patients. Median PFS was 9 months in both groups (p = 0.615) (Fig. 3).

Discussion

In the current study, sarcopenia was identified as the only significant factor affecting survival in metastatic colorectal cancer patients (p = 0.021). Patients with sarcopenia had a markedly shorter survival time compared to those without sarcopenia. Notably, 72.2% of sarcopenic patients were over 65 years old,

Table 2. Patient characteristics

Variables	Sarcopenic	Non-sarcopenic	p-value
Gender			
Female	6 (33.3)	17 (32.7)	0.623
Male	12 (66.7)	35 (67.3)	
Age [years]			
< 65	5 (27.8)	36 (69.2)	**0.002**
> 65	13 (72.2)	16 (30.8)	
ECOG			
0 or 1	17 (89.5)	44 (86.3)	0.722
2 or 3	2 (10.5)	7 (12.9)	
Grade			
1 or 2	14 (77.8)	32 (61.5)	0.211
3	4 (22.2)	20 (38.5)	
Tumor location			
Right sided	5 (27.8)	11 (21.2)	0.536
Left sided	13 (72.2)	41 (78.8)	
KRAS mutation			
Yes	6 (33.3)	26 (50)	0.221
No	12 (66.7)	26 (50)	
BMI [kg/m^2]			
Underweight (< 18.5)	0 (0)	3 (5.8)	0.564
Normal (18.5–24.9)	8 (44.4)	28 (53.8)	
Overweight (25–29.9)	8 (44.4)	18 (34.6)	
Obese (≥ 30)	2 (11.2)	3 (5.8)	
Liver metastasis			
No	3 (16.7)	10 (19.2)	0.558
Yes	15 (83.3)	42 (80.8)	

BMI — body mass index; ECOG — Eastern Cooperative Oncology Group performance status

Table 3. Effects of clinicopathologic factors and sarcopenia on survival: univariate analysis

Sarcopenia			
Present/none	0.511	0.288–0.907	0.022
Age [years]			
< 65/≥ 65	1.420	0.836–2.414	0.195
ECOG			
0 or 1/2 or 3	0.946	0.670–1.336	0.751
Gender			
Female/men	0.860	0.488–1.515	0.602
Liver metastasis			
Present/none	1.023	0.527–1.986	0.946
KRAS mutation			
Mutant/wild	1.061	0.626–1.798	0.827
CEA			
< 5/≥ 5	1.526	0.847–2.744	0.159
Tumor localization			
Right–sided/left–sided	1.227	0.657–2.291	0.520

CEA — carcinoembryonic antigen; ECOG— Eastern Cooperative Oncology Group performance status

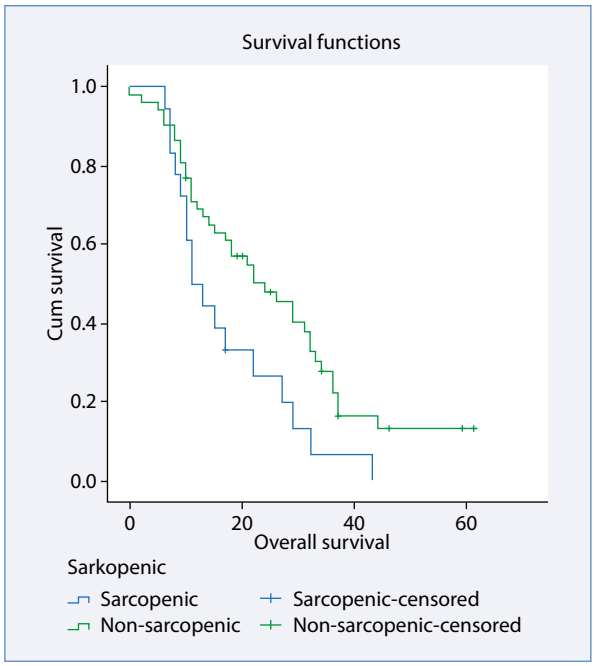

Figure 2. Survival time for sarcopenic and non-sarcopenic patients

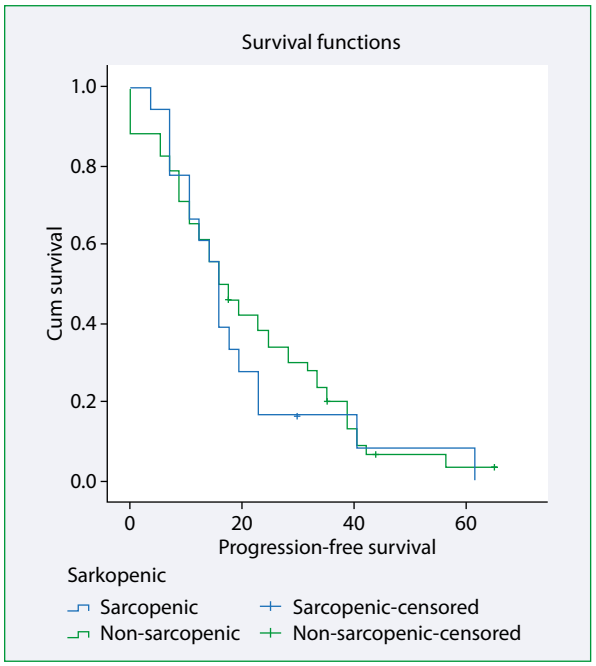

Figure 3. Progression-free survival for sarcopenic and non--sarcopenic patients

emphasizing the strong association between age and the development of sarcopenia. Sarcopenia is frequently observed in the elderly, with muscle mass decreasing by approximately 8–10% per decade after the age of 40. This age-related sarcopenia results from reduced muscle protein synthesis, hormonal alterations, and chronic low-grade inflammation, all of which contribute to decreased muscle mass and functionality. While age-related sarcopenia may not be entirely reversible, addressing modifiable factors such as nutritional deficits, systemic inflammation, and inactivity could help mitigate its impact and improve outcomes in this population [11]. Future research focusing on distinguishing age-related sarcopenia from secondary causes, such as cancer or treatment-related effects, could provide valuable insights for developing more targeted and effective interventions.

According to the review by Sun et al. [12], sarcopenia is highly prevalent in older cancer patients, with rates ranging from 18.5% to 83%, depending on the population and methods used. In the present study, the prevalence of sarcopenia was 25.7%, aligning with the lower end of this range. While Sun et al. [12] commonly identified sarcopenia using the skeletal muscle index (SMI) at the lumbar 3 level via CT scans, the current study employed TPAI and HUAC as practical and cost-effective alternatives. Both studies reached similar conclusions, demonstrating that sarcopenia significantly impacts survival, highlighting its critical role in the prognosis of cancer patients [12].

The meta-analysis by Jogiat et al. [13] highlights the significant prognostic value of sarcopenia in unresectable oesophageal cancer, demonstrating that sarcopenia, as assessed by skeletal muscle index (SMI) at the L3 vertebrae, is associated with decreased overall survival. In a similar vein, the present study identified sarcopenia, measured using TPAI and HUAC from CT scans, as a critical factor impacting survival in metastatic colorectal cancer patients. The prevalence of sarcopenia in their cohort (66%) aligns with the significant prevalence observed in this study (25.7%) [13].

The review by De Nardi et al. [14] highlights the prognostic relevance of skeletal muscle depletion in advanced rectal cancer patients undergoing neoadjuvant chemo-radiotherapy (NCRT), emphasizing that loss of muscle mass during treatment is associated with worse outcomes, particularly in terms of disease-free survival. Similarly, the current study demonstrates that sarcopenia significantly impacts survival in metastatic colorectal cancer patients [14].

The role of sarcopenic obesity warrants significant attention, as it represents a unique clinical challenge characterized by reduced muscle mass alongside increased adipose tissue [15]. In the present study, 10 sarcopenic patients were overweight or obese, highlighting the limitations of relying solely on BMI to evaluate nutritional status. A more comprehensive approach, such as assessing body composition through CT or bioelectrical impedance analysis, is necessary for accurate evaluation. While dual-energy X-ray absorptiometry (DEXA)

and bioelectrical impedance analysis are widely used for sarcopenia diagnosis, these methods involve complex devices that may not be available in all healthcare facilities [16].

In this context, evaluating psoas muscle area using CT or MRI scans has been recognized as the gold standard for assessing muscle mass, according to the revised European consensus on sarcopenia (EWGSOP) [1]. Computed tomography imaging, which is routinely performed during the staging of advanced colon cancer, eliminates the need for additional tests and associated costs, making it a more accessible and cost-effective method for sarcopenia evaluation. In this study, measurements of both the psoas muscle area and muscle density derived from CT scan images were utilized for the diagnosis of sarcopenia. This approach allowed us to distinguish fatty tissue infiltration, even in cases where the muscle area appeared normal, enabling a more accurate evaluation of muscle loss and its potential impact on clinical outcomes.

There are several limitations in the present study. First, it is a single-center retrospective study with a relatively small sample size, which may limit the generalizability and statistical power of the findings. Second, sarcopenia is not solely defined by measuring muscle mass but also requires the evaluation of muscle strength and physical performance. However, due to the retrospective nature of this study, data could not be collected on these parameters. Additionally, in the current study, sarcopenia was defined based on the lowest quantile of muscle mass within the patient population. This approach represents an internal classification rather than a universally accepted sarcopenia definition. Third, confidence interval calculations for hazard ratios were not performed, which could have provided greater insight into the precision and reliability of the results herein. Fourth, although CT-based methods for assessing sarcopenia are widely used and practical, they may not fully capture other aspects of sarcopenia, such as functional impairments or quality-of-life impact. Finally, the study did not evaluate the potential influence of nutritional interventions, physical activity, or other modifiable factors on the progression of sarcopenia, which might have provided a more comprehensive understanding of its impact on survival. Future prospective and multi-center studies with larger sample sizes, incorporating these additional factors, are necessary to validate and expand upon the present findings.

Conclusions

Sarcopenia significantly affects survival in metastatic colorectal cancer patients. This study highlights the practical application of CT-based measurements, such as TPAI and HUAC, as accessible and cost-effective tools for the early identification of sarcopenic patients. Incorporating these assessments into routine clinical care can help personalize interventions, improve treatment adherence, and enhance survival outcomes. Furthermore, the findings underscore the importance of integrating sarcopenia evaluations into oncology workflows to refine prognostic assessments and optimize resource allocation. Future research should focus on combining imaging-derived metrics with functional assessments and exploring the impact of early interventions on long-term outcomes in sarcopenic patients.

Article Information and Declarations

Data availability statement

Raw data were generated at Health Sciences University Diskapi Training and Research Hospital. Derived data supporting the findings of this study are available from the corresponding author O.D. on request.

Ethics statement

The study was conducted in accordance with the principles of the Helsinki Declaration and was approved by the Health Sciences University Diskapi Yildirim Beyazit Training and Research Hospital Ethics Committee on Apr 05, 2021, with protocol number 108/09.

Author contributions

O.D.: planning, data collection, ethics committee application, writing of the manuscript; H.S.: statistical analysis, writing of the data; E.Z.: planning, data collection of the manuscript; B.D.S.: evaluation and measurement of radiology images.

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Conflict of interest

The authors report no conflict of interest.

Supplementary material

None.

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