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Sarcopenia and its Association with the Timing of Metastasis in Breast Cancer: A Retrospective Cohort Study

Metastatik Meme Kanserinde Sarkopeninin Metastaz Zamanı ile İlişkisi: Retrospektif Kohort Çalışması

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Abstract

Objective: Sarcopenia is described as a progressive reduction that is increasingly recognized as a factor that can influence clinical outcomes in cancer patients. However, in metastatic breast cancer, its clinical significance remains unclear, particularly regarding when metastatic disease develops. This study therefore examines whether sarcopenia is related to the timing of metastasis and influences overall survival.

Methods: This study screened 530 female patients who were diagnosed with breast cancer between 2010 and 2020. Among them, 60 patients who developed metastatic disease and had available computed tomography imaging suitable for body composition analysis were included. Patients were categorized as having metastasis at initial diagnosis or during follow-up. Sarcopenia was quantified by measuring the psoas muscle area at the level of the L3 vertebra and normalizing these measurements to patient height. Survival outcomes were analyzed with Kaplan-Meier curves.

Results: Sarcopenia was present in 12 patients (20.0%). It was observed more often among patients who had metastatic disease at the time of diagnosis than among those who developed metastasis later during follow-up (42.9% vs. 13.0%, p=0.024). Over a median follow-up of 29.4 months, mortality was higher in the sarcopenic group (50.0% vs. 12.5%, p=0.009). Despite this, no significant difference was found in overall survival when analyzed using time-to-event methods.

Conclusion: Sarcopenia may be more common among patients presenting with metastatic disease and may be associated with higher mortality in metastatic breast cancer. However, its effect on overall survival is still unclear. Further evidence from larger, prospectively designed studies is required to better define its clinical relevance.

Keywords: Metastatic breast cancer, psoas muscle index, sarcopenia

Öz

Amaç: Sarkopeni, iskelet kas kütlesinde ilerleyici azalma ile karakterize olup kanser hastalarında sonuçları etkileyebileceği öne sürülmektedir. Metastatik meme kanserinde rolü, özellikle metastatik hastalığın zamanlaması ile ilişkisi açısından net değildir. Bu çalışmanın amacı, sarkopeni ile metastaz zamanlaması arasındaki ilişkiyi ve genel sağkalım üzerindeki olası etkisini değerlendirmektir.

Yöntem: Bu retrospektif çalışmada 2010-2020 yılları arasında meme kanseri tanısı almış 530 kadın hasta tarandı. Bunlardan metastatik hastalık gelişen ve vücut kompozisyon analizi için uygun bilgisayarlı tomografi görüntüleri bulunan 60 hasta çalışmaya dahil edildi. Hastalar metastazın tanı anında

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Öz

mevcut olması veya takip sırasında gelişmesine göre gruplandırıldı. Sarkopeni, üçüncü lomber vertebra düzeyinde ölçülen psoas kas alanlarının boya göre normalize edilmesi ile değerlendirildi. Sağkalım analizi Kaplan-Meier yöntemi ile yapıldı.

Bulgular: Sarkopeni 12 hastada (%20,0) saptandı. Tanı anında metastatik hastalığı olan hastalarda, takip sırasında metastaz gelişen hastalara göre daha sık bulundu (%42,9'a karşı %13,0; p=0,024). Medyan 29,4 aylık takip süresince sarkopenisi olan hastalarda mortalite daha yüksek bulundu (%50,0'a karşı %12,5; p=0,009). Ancak gruplar arasında genel sağkalım açısından istatistiksel olarak fark yoktu.

Sonuç: Sarkopeni, metastatik meme kanserinde hastalığın başlangıçtaki sunumu ve artmış mortalite ile ilişkili görünmektedir. Bununla birlikte genel sağkalım üzerindeki etkisi net olarak gösterilememiştir. Bu konuda geniş ölçekli prospektif çalışmalar gereklidir.

Anahtar Kelimeler: Metastatik meme kanseri, psoas kas indeksi, sarkopeni

Introduction

Loss of muscle mass or function-often termed sarcopenia-may influence patient outcomes. Prior research has linked sarcopenia to higher rates of morbidity and mortality across a range of solid tumors, suggesting that it may reflect diminished physiological reserve and a tendency toward less favorable oncological outcomes[1].

There has been growing interest in how body composition affects clinical outcomes in breast cancer. In particular, alterations in skeletal muscle mass have been linked to treatment tolerance and survival, especially in advanced disease settings. Metastatic breast cancer represents a biologically heterogeneous condition with variable clinical behavior and treatment responses, as emphasized in international consensus guidelines[2]. Therefore, identifying host-related factors that may influence disease course and outcomes remains of clinical importance.

Recent evidence suggests that sarcopenia may also have prognostic implications in metastatic breast cancer. Studies have reported that impaired muscle parameters, such as low muscle attenuation, are associated with poorer survival in patients receiving systemic therapy[3]. Recent cohort studies suggest that the presence of sarcopenia at baseline may adversely affect outcomes in certain subgroups of metastatic breast cancer, including patients receiving CDK4/6 inhibitor therapy[4]. Similarly, findings from a recent systematic review and meta-analysis indicate that sarcopenia is linked to higher mortality and disease progression in breast cancer, reinforcing its potential clinical importance[5]. Despite this growing body of evidence, the role of sarcopenia in metastatic breast cancer is not yet fully understood. In particular, the relationship between sarcopenia and the timing of metastatic disease-whether metastasis is present at initial diagnosis or develops during follow-up-has not been clearly elucidated. Moreover, data regarding the impact of sarcopenia on survival outcomes in this specific context remain limited.

In this context, we examined whether sarcopenia-defined using the psoas muscle index (PMI)-is related to the timing of metastatic disease and whether it influences overall survival for patients with metastatic breast cancer.

Materials and Methods

Study Design and Patient Selection

This study retrospectively reviewed the records of patients treated at Mersin University Faculty of Medicine. Between January 2010 and December 2020, 530 individuals with a diagnosis of breast cancer were evaluated. Of these, 60 patients who developed metastatic disease and had imaging data appropriate for body composition assessment were ultimately included.

Patients were categorized into two groups according to the timing of metastatic disease: those with metastatic disease at initial diagnosis and those who developed metastasis during follow-up (secondary metastatic disease).

Ethical Approval

Ethical approval was obtained from the Ethics Committee of Mersin University (approval no: 2026/110, date: 04.03.2026). All procedures were carried out in line with the principles outlined in the Declaration of Helsinki.

Data Collection

Clinical and pathological information was retrospectively obtained from the institutional electronic records. The dataset included age at diagnosis, histopathological subtype, and hormone receptor profile. The timing of metastatic

disease was determined based on imaging and clinical records. The date of diagnosis was defined as the date of the first positron emission tomography-computed tomography (CT) examination.

Assessment of Sarcopenia

Sarcopenia was evaluated using the PMI, derived from axial contrast-enhanced CT images obtained at the level of the third lumbar vertebra (L3), a widely used reference point for skeletal muscle assessment. The right and left psoas muscles were manually outlined at the L3 level, and the measured areas were adjusted for patient height squared (mm^2/m^2). PMI was determined using the following formula:

PMI (mm^2/m^2)= (left psoas muscle area+right psoas muscle area)/$height^2$

All measurements were performed on pre-treatment CT images using a standardized anatomical reference. All PMI measurements were performed by a single experienced observer using a standardized measurement protocol based on predefined anatomical landmarks at the L3 level. To minimize measurement variability, all assessments were conducted using the same methodology under consistent conditions. Formal intra- and interobserver reproducibility analyses were not performed because measurements were conducted by a single observer; this is acknowledged as a limitation. Sex-specific cut-off values derived from previously published studies were applied to define sarcopenia. Because the study cohort consisted exclusively of female patients, sarcopenia was defined using the previously published female-specific PMI threshold of <360 mm^2/m^2, which has been used in oncologic populations and validated in prior studies[6].

Outcome Measures

We examined whether sarcopenia is associated with the timing of metastatic disease onset. Overall survival was assessed and defined as the time from diagnosis to death from any cause or to the last available follow-up.

Statistical Analysis

Discrete variables are summarized as counts with corresponding percentages and are compared between groups using Fisher's exact test. Numerical data are described either by the mean and standard deviation or by the median and interquartile range, depending on their distribution.

Time-to-event outcomes were analyzed using Kaplan-Meier estimation, and group differences were assessed using the log-rank test. Statistical significance was set at a two-sided p-value below 0.05. All analyses were conducted using conventional statistical software.

Results

Patient Selection and Baseline Characteristics

Between January 2010 and December 2020, 530 patients with a diagnosis of breast cancer were evaluated. Among these, 60 patients who developed metastatic disease and had available imaging data suitable for body composition analysis were included in the final analysis. Of the 60 patients, 14 (23.3%) presented with metastatic disease at initial diagnosis, while 46 (76.7%) developed metastatic disease during follow-up. The mean age of the cohort was 53.6±12.8 years, with no significant difference between the *de novo* and secondary metastatic groups (p=0.86). Similarly, the estrogen receptor and human epidermal growth factor receptor 2 statuses were comparable between the two groups (p=0.49 and p=0.29, respectively). Baseline clinicopathological characteristics, stratified by timing of metastatic disease, are summarized in Table 1.

Association Between Sarcopenia and Timing of Metastatic Disease

Sarcopenia, as defined by PMI, was identified in 12 patients (20.0%) within the metastatic cohort. Among patients presenting with *de novo* metastatic disease, 6 of 14 (42.9%) were classified as sarcopenic. In contrast, among patients who developed metastasis during follow-up, 6 of 46 (13.0%) were sarcopenic. This difference was statistically significant (p=0.024), indicating a potential association between sarcopenia and *de novo* metastatic presentation. The distribution of sarcopenia according to metastatic timing is presented in Table 2.

Survival Outcomes

A mean follow-up of 31.5 months (median: 29.4 months), 12 patients (20.0%) died. Mortality was more frequent among patients with sarcopenia than among those without (50.0% vs. 12.5%, p=0.009). Even with this difference, there was no significant difference for overall survival between two groups (log-rank p>0.05), and median overall survival was not reached in either group. Survival data are summarized in Table 3.

Table 1. Baseline clinicopathologic characteristics according to timing of metastatic disease

Variable	Total (n=60)	*De novo* metastatic (n=14)	Metastasis during follow-up (n=46)	p-value
Age, years (mean ± SD)	53.6±12.8	53.1±12.1	53.8±13.0	0.86
Sarcopenia, n (%)	12 (20.0)	6 (42.9)	6 (13.0)	0.024
Non-sarcopenia, n (%)	48 (80.0)	8 (57.1)	40 (87.0)	
ER positive, n (%)	40 (66.7)	8 (57.1)	32 (69.6)	0.49
HER2 positive, n (%)	5 (8.3)	0 (0.0)	5 (10.9)	0.29

SD: Standard deviation, HER2: Human epidermal growth factor receptor 2, ER: Estrogen receptor

Table 2. Comparison of clinicopathologic characteristics according to sarcopenia status

Variable	Total (n=60)	Sarcopenic (n=12)	Non-sarcopenic (n=48)	p-value
Age, years (mean ± SD)	53.6±12.8	55.2±11.5	53.2±13.1	0.62
De novo metastasis, n (%)	14 (23.3)	6 (50.0)	8 (16.7)	0.024
Metastasis during follow-up, n (%)	46 (76.7)	6 (50.0)	40 (83.3)	
ER positive, n (%)	40 (66.7)	7 (58.3)	33 (68.8)	0.52
HER2 positive, n (%)	5 (8.3)	1 (8.3)	4 (8.3)	1.00
Death during follow-up, n (%)	12 (20.0)	6 (50.0)	6 (12.5)	0.009

Values are reported as mean ± standard deviation (SD) or as number (%). Fisher's exact test was used to calculate p-values HER2: Human epidermal growth factor receptor 2, ER: Estrogen receptor

Table 3. Overall survival outcomes according to sarcopenia status

Variable	Sarcopenic (n=12)	Non-sarcopenic (n=48)	p-value
Number of deaths, n (%)	6 (50.0)	6 (12.5)	0.009
Median follow-up, months	29.4	29.4	-
Mean follow-up, months	31.5	31.5	-
Median overall survival	Not reached	Not reached	-
Log-rank test	-	-	>0.05

Values are given as numbers (%) unless stated otherwise. Median overall survival was not reached in either group

Discussion

In this study including 60 patients metastatic breast cancer, sarcopenia-defined by the PMI-was identified in 12 patients (20.0%). Sarcopenia was significantly more frequent in patients with *de novo* metastatic disease than in those who developed metastasis during follow-up (42.9% vs. 13.0%, p=0.024). In addition, the proportion of deaths during follow-up was higher among sarcopenic patients than in non-sarcopenic patients (50.0% vs. 12.5%, p=0.009). Kaplan-Meier analysis did not show difference between 2 groups for overall survival. These findings suggest that sarcopenia may be associated with higher mortality, while its effect on overall survival (time-to-event) in this cohort remains uncertain, possibly because the limited number of events reduced the ability to detect differences in survival despite observed differences in crude mortality rates.

The observed association between sarcopenia and *de novo* metastatic presentation may reflect the broader clinical and biological significance of muscle depletion in breast cancer. Recent evidence suggests that sarcopenia is not merely a consequence of advanced disease but may represent an underlying host-related condition associated with more aggressive tumor behavior. In a analysis focusing on metastatic breast cancer, sarcopenia was associated with adverse clinical outcomes and poorer prognosis[7]. Similarly, Deluche et al.[8] highlighted that sarcopenia may be an under-recognized factor in the management of metastatic breast cancer, emphasizing its potential role in influencing disease course and patient outcomes. Taken together, this suggests that sarcopenia may be linked to an unfavorable disease phenotype and could contribute to the early manifestation of metastatic disease observed in our cohort.

The association between sarcopenia and survival has been widely reported, although the extent of its effect appears to differ across study populations. Evidence from a recent systematic review and meta-analysis indicates that sarcopenia is linked to increased mortality in patients with breast cancer, supporting its role as a negative prognostic factor[9]. Likewise, another meta-analysis focusing on muscle composition found that patients with sarcopenia experienced higher mortality, earlier disease progression, and greater treatment-related toxicity[10].

In the present cohort, mortality was numerically higher among patients with sarcopenia; however, this difference was not significance, may be attributable to the limited number of observed events. These observations suggest that although sarcopenia is generally associated with poorer survival, its effect may be less apparent in smaller datasets where statistical power is constrained.

The absence of a significant difference in overall survival between patients with and without sarcopenia in this cohort may reflect the complex, multifactorial determinants of prognosis in metastatic breast cancer. Clinical outcomes are influenced not only by muscle mass but also by a range of host-related factors, including inflammatory status and nutritional status. In line with this, previous studies have suggested that combining body composition parameters with systemic inflammatory markers provides a more comprehensive understanding of survival in metastatic breast cancer[11]. Reductions in muscle-related indices have been associated with not only survival outcomes but also with tumor progression dynamics. For example, lower pectoralis muscle index has been reported as an independent predictor of both distant metastasis-free survival and overall survival in breast cancer populations[12]. These observations indicate that muscle depletion should be interpreted within a broader biological context rather than as an isolated parameter and that PMI alone may not fully capture the interaction between host physiology and tumor behavior. The lack of a detectable effect on overall survival in the present study may therefore be related to methodological limitations, particularly the relatively small sample size and the limited number of events, which may have reduced the statistical power of the analyses. This should be considered when interpreting the lack of a significant difference in survival.

Study Limitations

The findings of this study have some limitations. The retrospective, single-center design might have led to selection bias. A small sample size and a limited number of survival events may reduce statistical power, particularly for overall survival analyses. Third, sarcopenia assessment was based solely on PMI and did not include functional measures of muscle performance. Measurements were performed by a single observer without formal reproducibility analysis.

Conclusion

In conclusion, our findings suggest that sarcopenia, as assessed by PMI, may be associated with *de novo* metastatic presentation and increased mortality in metastatic breast cancer. Despite these findings, a clear effect on overall survival could not be established. Further prospective studies with larger cohorts are required to better define its prognostic and clinical relevance.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Ethics Committee of Mersin University (approval no: 2026/110, date: 04.03.2026).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.G., Concept: E.G., M.B., Design: E.G., M.B., Data Collection or Processing: E.G., M.B., Analysis or Interpretation: E.G., M.B., Literature Search: E.G., M.B., Writing: E.G.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Prado CM, Lieffers JR, McCargar LJ, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. Lancet Oncol. 2008;9:629-35.
2. Cardoso F, Senkus E, Costa A, et al. 4th ESO-ESMO International Consensus Guidelines for advanced breast cancer (ABC 4)†. Ann Oncol. 2018;29:1634-57.
3. Rier HN, Jager A, Sleijfer S, van Rosmalen J, Kock MCJM, Levin MD. Low muscle attenuation is a prognostic factor for survival in metastatic breast cancer patients treated with first line palliative chemotherapy. Breast. 2017;31:9-15.
4. Karahan L, Akyildiz A, Sahin TK, et al. Prognostic value of baseline sarcopenia and adipose tissue indices in HR+/HER2- metastatic breast

cancer treated with CDK4/6 inhibitors: a retrospective cohort study. J Clin Med. 2026;15:1623.

5. Roberto M, Barchiesi G, Resuli B, et al. Sarcopenia in breast cancer patients: a systematic review and meta-analysis. Cancers (Basel). 2024;16:596.
6. Güler E, Gümüş T, Sayur V, et al. Preoperative psoas muscle index predicts long-term survival but not postoperative morbidity after curative-intent gastrectomy for gastric cancer. Int J Gen Med. 2026;19:581421.
7. Jang MK, Park S, Park C, Raszewski R, Park S, Kim S. Sarcopenia in patients with metastatic breast cancer: a systematic review and meta-analysis. Breast. 2025;82:104508.
8. Deluche E, Lachatre D, Di Palma M, et al. Is sarcopenia a missed factor in the management of patients with metastatic breast cancer? Breast. 2022;61:84-9.
9. Dai Y, Lan J, Li S, Xu G. Exploring the impact of sarcopenia on mortality in breast cancer patients: a comprehensive systematic review and meta-analysis. Breast Care (Basel). 2024;19:316-28.
10. Aleixo GFP, Williams GR, Nyrop KA, Muss HB, Shachar SS. Muscle composition and outcomes in patients with breast cancer: meta-analysis and systematic review. Breast Cancer Res Treat. 2019;177:569-79.
11. Yamanouchi K, Murakami S, Sato A, Ogawa S, Shinagawa H, Kamohara Y. Integrated evaluation of inflammatory, nutritional, and sarcopenia markers to predict survival in metastatic breast cancer patients. In Vivo. 2023;37:811-7.
12. Huang WJ, Zhang ML, Wang W, et al. Preoperative pectoralis muscle index predicts distant metastasis-free survival in breast cancer patients. Front Oncol. 2022;12:854137.