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The effect of ibrutinib therapy on sarcopenia in patients with hematologic malignancies

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MAIN POINTS

- Ibrutinib therapy was not associated with a significant deterioration in skeletal muscle mass in patients with hematologic malignancies.
- Muscle density decreased during follow-up despite relatively stable muscle mass, suggesting a potential deterioration in muscle quality.
- These findings highlight the importance of considering sarcopenia-related parameters during treatment; however, larger prospective studies are required to clarify their clinical implications.

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ABSTRACT

Aim: Sarcopenia, characterized by progressive loss of skeletal muscle mass and function, is associated with poor prognosis in patients with hematologic malignancies. Given the potential musculoskeletal effects of Bruton tyrosine kinase inhibitors, this study aimed to investigate sarcopenia-related parameters in patients with hematologic malignancies receiving ibrutinib therapy.

Materials and Methods: This retrospective study included 55 patients diagnosed with hematologic malignancies. Using computed tomography (CT) images obtained before and after ibrutinib therapy, we calculated total abdominal muscle area (TAMA), skeletal muscle index (SMI), and muscle density in Hounsfield Units (HU). Changes in these imaging-based parameters, sarcopenia prevalence, and their associations with mortality were statistically analyzed.

Results: The mean age of the patients was 67.38 ± 8.66 years, and 72.7% were male. No significant difference in the prevalence of sarcopenia was observed between patients who received ibrutinib and those who did not ($p>0.05$). While SMI and TAMA values did not change significantly after treatment ($p>0.05$), muscle density (HU) decreased significantly ($p=0.001$). In the ROC analysis, baseline and follow-up SMI values in females, as well as follow-up SMI values in males, showed good discriminatory ability for predicting mortality (AUC>0.88).

Conclusion: In this retrospective cohort, ibrutinib therapy was not associated with significant changes in skeletal muscle mass; however, a decline in muscle density was observed, suggesting potential alterations in muscle quality. No restorative effect on pre-existing sarcopenia was demonstrated in this limited cohort. These findings should be considered exploratory; larger prospective studies that incorporate functional assessments are needed to clarify the clinical implications of sarcopenia in patients receiving ibrutinib.

Keywords: Sarcopenia, Skeletal muscle index, Computed tomography

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INTRODUCTION

Sarcopenia is a muscle disease characterized by progressive and generalized loss of skeletal muscle mass, strength, and function. Although traditionally considered a natural consequence of aging, it is now understood that sarcopenia can also emerge earlier in life, particularly in association with chronic illnesses such as hematologic malignancies. In its 2018 update, the European Working Group on Sarcopenia in Older People (EWGSOP2) emphasized low muscle strength as the principal determinant of sarcopenia, while identifying low muscle mass and reduced physical performance as confirmatory criteria for diagnosis and indicators of disease severity [1].

In cancer patients, sarcopenia has been associated with increased chemotherapy toxicity, higher risk of mortality, more

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frequent postoperative complications, and longer hospital stays. Sarcopenia is linked to poor prognosis across nearly all types of cancer, including hematologic malignancies [2]. In recent years, the prognostic relevance of sarcopenia in hematologic malignancies has received growing attention. Its high prevalence in this patient population is thought to be related to systemic inflammation, metabolic disturbances, and treatment-associated toxicities. A meta-analysis published in 2023 reported that the average prevalence of pre-treatment sarcopenia in patients with hematologic malignancies was 47%, rising to 51% in patients aged 60 years and older [3]. Furthermore, sarcopenia was independently associated with poorer overall and progression-free survival. Treatment response was also impacted, with notably lower complete response rates in male patients and those with a body mass index ≥25.

These observations suggest that sarcopenia represents a clinically relevant condition interacting with disease biology and treatment response, rather than being solely an age-related phenomenon. However, most available data are derived from heterogeneous patient populations and retrospective analyses, highlighting the need for further disease- and treatment-specific investigations.

Ibrutinib, a Bruton's tyrosine kinase (BTK) inhibitor, has been approved for the treatment of various hematologic malignancies, most notably chronic lymphocytic leukemia (CLL). Clinical studies have reported musculoskeletal adverse effects such as arthralgia and myalgia in approximately 30–40% of patients receiving ibrutinib therapy [4]. These side effects can impair quality of life and hinder treatment adherence. Although these adverse events are generally low grade, their potential impact on physical activity and muscle function may be particularly relevant in older patients and those with pre-existing vulnerability to sarcopenia.

Despite the widespread use of ibrutinib, its effects on skeletal muscle mass and muscle quality remain poorly characterized.

In this study, we aimed to evaluate the effect of ibrutinib therapy on sarcopenia-related parameters by comparing, using computed tomography (CT), changes in total abdominal muscle area (TAMA), muscle density expressed in Hounsfield Units (HU), and skeletal muscle index (SMI) before and after treatment in patients with hematologic malignancies. Given the retrospective design, this analysis was intended to be exploratory and hypothesis-generating.

MATERIALS AND METHODS

Study design and patient selection

This retrospective study included patients diagnosed with chronic lymphocytic leukemia (CLL) or mantle cell lymphoma (MCL) between 2020 and 2024 who had undergone at least two abdominal computed tomography (CT) scans. The study population consisted of 53 patients with CLL and 2 patients with MCL. Patients were required to undergo an abdominal CT scan at the time of diagnosis and a follow-up CT scan at least six months after treatment initiation or during a drug-free follow-up period. Skeletal muscle mass measurements were performed on CT images acquired at diagnosis and at least six months after treatment initiation, or during drug-free follow-up.

Patients without baseline or follow-up CT imaging and those whose image quality did not allow reliable muscle segmentation were excluded from the study. No additional exclusion criteria were applied. Due to the retrospective study design, informed consent was waived. The study was approved by the Samsun University Non-Invasive Clinical Research Ethics Committee (Decision No: 2025/10/17, Date: 14.05.2025).

Data collection

Sociodemographic and clinical data were retrieved from the hospital information system. Recorded variables included sex, diagnosis, age at diagnosis, height, laboratory values at diagnosis (e.g., white blood cell count, lactate dehydrogenase), presence of endocrine disorders, history of chemotherapy, and survival status. Treatment-related data included whether patients received ibrutinib, other chemotherapy regimens, or both. Chemotherapy exposure was recorded irrespective of disease stage at diagnosis because some patients initially diagnosed at early stages subsequently experienced disease progression requiring systemic treatment; this approach reflects real-world treatment practices and patients' prior treatment histories.

Imaging and muscle mass assessment

Sarcopenia assessment was performed using axial CT slices obtained at the level of the third lumbar vertebra (L3). A radiologist with 10 years of experience conducted the measurements using the Horos software. After the images were transferred to the Horos program, total abdominal muscle area (TAMA) was measured using a semi-automated segmentation method. The Hounsfield Unit (HU) threshold range was set between −29 and +130. The psoas major, erector spinae, quadratus lumborum, and abdominal wall muscles were included in the analysis.

The skeletal muscle index (SMI) was calculated as TAMA divided by the square of the patient's height in meters:

$SMI = TAMA(cm^2)/ height^2(m^2)$

Sarcopenia classification

Sarcopenia was classified using gender-specific SMI cut-off values determined by receiver operating characteristic (ROC) curve analysis of this study's dataset. Based on this analysis, optimal cut-off values were defined as $\leq 33.24\ cm^2/m^2$ for females and $\leq 38.25\ cm^2/m^2$ for males.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (Statistical Package for the Social

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Table 1. Distribution of sociodemographic and clinical variables.

Variable	N	%
Age		
Mean±SD	67.38±8.66	
Median (min-max)	68.0 (50-87)	
Age at diagnosis (years)		
Mean±SD	62.72±9.44	
Median (min-max)	64.0 (41-85)	
≤65	21	38.2
>65	34	61.8
Height (m)		
Mean±SD	1.68±0.08	
Median (min-max)	1.71 (1.50-1.81)	
Sex		
Female	15	27.3
Male	40	72.7
Diagnosis		
CLL	53	96.4
MCL	2	3.6
Disease stage at diagnosis		
0	2	3.6
1	15	27.3
2	21	38.2
3	6	10.9
4	11	20.0
Chemotherapy		
Not received	12	21.8
Received	43	78.2
Ibrutinib		
Not received	42	76.4
Received	13	23.6
Endocrine disease		
Absent	34	61.8
Present	21	38.2
WBC at diagnosis		
Mean±SD	60541.56±68821.22	
Median (min-max)	29740.0 (600.0-334000.0)	
LDH at diagnosis (U/L)		
Mean±SD	261.96±144.25	
Median (min-max)	225.0 (139.0-1129.0)	
Mortality		
Alive	44	80.0
Deceased	11	20.0

Sciences, IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as numbers and percentages for categorical variables and as mean ± standard deviation and median (minimum–maximum) for continuous variables. The assumption of normality was assessed using the Kolmogorov–Smirnov test, and a p-value <0.05 was considered statistically significant.

For non-normally distributed data, the Mann–Whitney U test was used for comparisons between two independent groups, and the Wilcoxon signed-rank test was applied for repeated measures. Pearson's chi-square test and Fisher's exact test were used to compare categorical variables. Relationships between continuous variables were evaluated using Spearman correlation analysis. A p-value <0.05 was considered statistically significant.

This study was a retrospective, observational analysis. Given the limited number of patients receiving ibrutinib therapy, a priori sample size calculation and power analysis were not planned. Accordingly, all statistical analyses were considered exploratory and hypothesis-generating rather than hypothesis-testing.

RESULTS

A total of 55 patients were included in the study. As presented in Table 1, the mean age was 67.38 ± 8.66 years, with a median of 68.0 (range: 50–87) years. The mean age at diagnosis was 62.72 ± 9.44 years, and 61.8% of the patients were aged ≥65 years. Of the participants, 72.7% were male and 27.3% were female. The mean height was 1.68 ± 0.08 m, with a median of 1.71 (range: 1.50–1.81) m.

The majority of patients were diagnosed with chronic lymphocytic leukemia (CLL, 96.4%), while 3.6% had mantle cell lymphoma (MCL). At diagnosis, the most frequent stage was stage 2 (38.2%), followed by stages 1 (27.3%), 4 (20.0%), 3 (10.9%), and 0 (3.6%). Chemotherapy was administered to 78.2% of patients, whereas 21.8% did not receive chemotherapy. 23.6% of the cohort received Ibrutinib therapy, while 76.4% did not.

Endocrine comorbidities potentially associated with sarcopenia were present in 38.2% of patients. The mean white blood cell (WBC) count at diagnosis was 60,541.56 ± 68,821.22/μL, with a median of 29,740.0 (range: 600.0–334,000.0). The mean lactate dehydrogenase (LDH) level was 261.96 ± 144.25 U/L, with a median of 225.0 (range: 139.0–1129.0) U/L. During follow-up, the overall mortality rate was 20.0%, while 80.0% of patients remained alive.

Receiver operating characteristic (ROC) analysis was used to evaluate the diagnostic performance of sarcopenia-related parameters for predicting mortality, as shown in Table 2. In female patients, both baseline skeletal muscle index (SMI1; AUC = 0.909, 95% CI: 0.752–1.000, p=0.019) and follow-up SMI (SMI2; AUC = 0.886, 95% CI: 0.710–1.000, p = 0.026) demonstrated strong discriminative ability. The optimal cut-off value for SMI1 in women was ≤33.24 cm^2/m^2, yielding a sensitivity of 75.0% and specificity of 72.7%.

In male patients, follow-up SMI2 showed a high discriminative performance (AUC = 0.903, 95% CI: 0.808–0.997), with 85.7% sensitivity and 84.8% specificity (p=0.001). Similarly, baseline and follow-up total abdominal muscle areas (TAMA1 and TAMA2) demonstrated significant predictive value for mortality in female patients (TAMA1: AUC = 0.932, p = 0.013; TAMA2: AUC = 0.826, p = 0.010). In male patients, TAMA2 also showed significant discriminative ability (AUC = 0.883, 95% CI: 0.765–1.000), with 71.4% sensitivity and 72.7% specificity (p = 0.002). In contrast, baseline and follow-up muscle density values (HU1 and HU2) did not

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Table 2. Analysis of the predictive value of various clinical parameters in differentiating mortality.

Variables	AUC	%95 CI	Cut-off	Sensitivity (%)	Specificity (%)	p
SMI1-Female	0.909	0.752-1.000	≤33.24	75.0	72.7	**0.019**
SMI1-Male	0.545	0.320-0.771	≤41.05	57.1	57.6	0.545
SMI2-Female	0.886	0.710-1.000	≤32.45	75.0	72.7	**0.026**
SMI2-Male	0.903	0.808-0.997	≤38.25	85.7	84.8	**0.001**
TAMA1-Female	0.932	0.787-1.000	≤80.38	75.0	72.7	**0.013**
TAMA1-Male	0.645	0.460-0.830	≤123.77	57.1	57.6	0.233
TAMA2-Female	0.826	0.699-1.000	≤82.74	75.0	72.7	**0.026**
TAMA2-Male	0.883	0.765-1.000	≤116.01	71.4	72.7	**0.002**
HU1	0.535	0.336-0.734	≥45.83	54.5	54.5	0.535
HU2	0.651	0.453-0.848	≤38.11	63.6	63.6	0.125

AUC: Area under the curve; 95% CI: Confidence interval; 1: measurements at diagnosis; 2: follow-up measurements.

Table 3. Development of sarcopenia.

	SMI-1		
Variables	Non-Sarcopenic N (%)	Sarcopenic N (%)	p
SMI-2			
Non-Sarcopenic	23 (85.2)	15 (53.6)	0.019
Sarcopenic	4 (14.8)	13 (46.4)	
	TAMA-1		
	Non-Sarcopenic N (%)	Sarcopenic N (%)	p
TAMA-2			
Non-Sarcopenic	23 (85.2)	13 (46.4)	0.049
Sarcopenic	4 (14.8)	15 (53.6)	
	HU-1		
	Non-Sarcopenic N (%)	Sarcopenic N (%)	p
HU-2			
Non-Sarcopenic	45 (90)	2 (40)	0.453
Sarcopenic	5 (10)	3 (60)	

McNemar test, p<0.05 considered statistically significant. 1: measurements at diagnosis; 2: follow-up measurements.

demonstrate a statistically significant predictive value for mortality (AUC = 0.535 and 0.651, respectively; p>0.05).

As presented in Table 3, significant associations were observed between baseline and follow-up measurements of SMI (SMI1 vs. SMI2, p=0.019) and of TAMA (TAMA1 vs. TAMA2, p=0.049). Among patients who were non-sarcopenic at baseline, 85.2% remained non-sarcopenic at follow-up, whereas 53.6% of those who were sarcopenic at baseline remained sarcopenic. No significant association was observed between baseline and follow-up HU values and sarcopenia status (p=0.453).

As shown in Table 4, no statistically significant changes were observed in SMI or TAMA values during follow-up in either female or male patients (all p > 0.05). In contrast, muscle density values demonstrated a significant decrease over time (p=0.001), with median HU declining from 45.3 (range: 10.9–65.6) at baseline to 39.6 (range: 10.3–60.0) at follow-up.

As presented in Table 5, no statistically significant differences were observed in sarcopenia prevalence—assessed by SMI, TAMA, or HU parameters—between patients who received ibrutinib therapy and those who did not (all p>0.05). In contrast, chemotherapy exposure was significantly associated with the prevalence of sarcopenia when sarcopenia was assessed using baseline SMI and HU values. Based on SMI1, sarcopenia was present in 58.3% of chemotherapy-naïve patients and in 86.0% of patients who received chemotherapy (p=0.049). According to HU1, sarcopenia was observed in 25.0% of chemotherapy-naïve patients and 4.7% of those who received chemotherapy (p=0.030).

As shown in Table 6, when patients were stratified by baseline sarcopenia status (SMI1), only the WBC count at diagnosis differed significantly between sarcopenic and non-sarcopenic groups (medians: 42,860.0 vs. 16,845.0; p=0.012). No significant differences were observed regarding age, age at diagnosis, LDH levels, endocrine comorbidities, disease stage, or mortality (all p>0.05). When sarcopenia status was defined using follow-up SMI2 values, a significant association with mortality was observed (p<0.001); mortality occurred in 52.9% of sarcopenic patients compared with 5.3% of non-sarcopenic patients.

DISCUSSION

Sarcopenia has been shown to negatively impact survival and increase chemotherapy-related toxicity, particularly in elderly patients with hematologic malignancies such as diffuse large B-cell lymphoma (DLBCL). However, in other hematologic cancers, including leukemia and multiple myeloma, the association between sarcopenia and survival remains inconsistent. This heterogeneity suggests that the clinical impact of sarcopenia may vary according to the specific subtype of hematologic malignancy. The ability to assess sarcopenia using routine imaging modalities, such as computed tomography (CT), without incurring additional cost or radiation exposure, makes screening highly feasible in hematology clinics. When complemented by assessments of muscle strength and physical performance, such screening may facilitate more individualized treatment strategies and potentially reduce treatment-related toxicity. Nevertheless, the lack of prospective interventional studies targeting sarcopenia in

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Table 4. Pre- and Post-treatment changes in SMI, TAMA, and HU values.

Variables	SMI-1 Median (min-max)	SMI-2 Median (min-max)	p
SMI-Female (n=15)	36.3 (18.0-46.8)	35.1 (13.0-49.4)	0.394
SMI-Male (n=40)	43.2 (32.1-54.1)	40.6 (22.2-53.0)	0.528
	TAMA-1 Median (min-max)	TAMA-2 Median (min-max)	p
TAMA-Female (n=15)	87.7 (47.2-114.2)	87.1 (32.9-118.8)	0.394
TAMA-Male (n=40)	127.6 (99.4-169.3)	121.2 (62.7-157.2)	0.519
	HU-1 Median (min-max)	HU-2 Median (min-max)	p
HU (n=55)	45.3 (10.9-65.6)	39.6 (10.3-60.0)	0.001

1: measurements at diagnosis; 2: follow-up measurements. Wilcoxon test, p<0.05 considered statistically significant.

Table 5. Sarcopenia status by treatment group.

	Ibrutinib			Other Standard Regimens		
Variables	Not Received N (%)	Received N (%)	p	Not Received N (%)	Received N (%)	p
SMI-1						
Non-Sarcopenic	9 (21.4)	2 (15.4)	0.486[b]	5 (41.7)	6 (14)	0.049[b]
Sarcopenic	33 (78.6)	11 (84.6)		7 (58.3)	37 (86)	
SMI-2						
Non-Sarcopenic	30 (71.4)	8 (61.5)	0.511[b]	9 (75)	29 (67.4)	0.753[b]
Sarcopenic	12 (28.6)	5 (38.5)		3 (25)	14 (32.6)	
TAMA-1						
Non-Sarcopenic	23 (54.8)	4 (30.8)	0.130[a]	6 (50)	21 (48.8)	0.941[b]
Sarcopenic	19 (45.2)	9 (69.2)		6 (50)	22 (51.2)	
TAMA-2						
Non-Sarcopenic	29 (69)	7 (53.8)	0.336[b]	9 (75)	27 (62.8)	0.511[b]
Sarcopenic	13 (31)	6 (46.2)		3 (25)	16 (37.2)	
HU-1						
Non-Sarcopenic	37 (88.1)	13 (100)	0.324[b]	9 (75)	41 (95.3)	0.030[b]
Sarcopenic	5 (11.9)	0 (0)		3 (25)	2 (4.7)	
HU-2						
Non-Sarcopenic	35 (83.3)	12 (92.3)	0.664[b]	10 (83.3)	37 (86)	0.563[b]
Sarcopenic	7 (16.7)	1 (7.7)		2 (16.7)	6 (14)	

[a]: Pearson Chi-Square test, [b]: Fisher's Exact test, p<0.05 considered statistically significant. 1: measurements at diagnosis; 2: follow-up measurements.

hematologic populations continues to limit the translation of these findings into routine clinical practice [5].

In patients with DLBCL receiving R-CHOP therapy, sarcopenia has been shown to significantly impair treatment tolerance and adversely affect both overall survival and progression-free survival [6]. The markedly increased rates of early mortality and treatment discontinuation among sarcopenic individuals suggest that sarcopenia may function as an active prognostic marker rather than a passive clinical finding. Similar associations between sarcopenia and treatment-related toxicity have been consistently reported in studies involving patients with solid tumors [7,8].

Ibrutinib, a Bruton's tyrosine kinase (BTK) inhibitor, is widely used to treat chronic lymphocytic leukemia and mantle cell lymphoma. Musculoskeletal adverse effects associated with ibrutinib therapy are of particular relevance in the context of sarcopenia research. In a large analysis involving 1,178 patients, low-grade adverse events such as arthralgia, myalgia, and musculoskeletal pain were reported in a substantial proportion of patients receiving ibrutinib [9]. These symptoms typically occurred within the first year of treatment and resolved spontaneously in most cases and rarely necessitated treatment discontinuation or dose modification. While these findings suggest that ibrutinib-related musculoskeletal adverse effects are generally mild and manageable, whether ibrutinib exerts any direct effects on skeletal muscle tissue remains unclear.

In the present study, no significant changes in muscle mass parameters were observed in patients with hematologic malignancies treated with ibrutinib during follow-up. This finding may be related to the targeted mechanism of action of ibrutinib and its relatively favorable toxicity profile [10]. While

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Table 6. Comparison of clinical parameters between sarcopenic and non-sarcopenic patients.

	SMI-1			SMI-2		
Variables	Non-Sarcopenic N=11	Sarcopenic N=44	p	Non-Sarcopenic N=38	Sarcopenic N=17	p
Age	64.0 (51.0-74.0)	69.0 (50.0-87.0)	0.226[c]	66.5 (50.0-82.0)	70.0 (51.0-87.0)	0.325[c]
Age at diagnosis	63.0 (41.0-71.0)	64.0 (46.0-85.0)	0.424[c]	62.0 (46.0-77.0)	65.0 (41.0-85.0)	0.554[c]
WBC	16845.0 (6490.0-113000.0)	42860.0 (600.0-334000.0)	0.012[c]	26100.0 (600.0-334000.0)	37450.0 (3800.0-248000.0)	0.478[c]
LDH	219.5 (139.0-337.0)	232.0 (139.0-1129.0)	0.964[c]	214.0 (139.0-380.0)	271.0 (161.0-1129.0)	0.131[c]
Endocrine disease						
Absent	6 (54.5)	28 (63.6)	0.731[b]	21 (55.3)	13 (76.5)	0.135[a]
Present	5 (45.5)	16 (36.4)		17 (44.7)	4 (23.5)	
Stage at Diagnosis						
0	2 (18.2)	0 (0)		1 (2.6)	1 (5.9)	
1	4 (36.4)	11 (25)		11 (28.9)	4 (23.5)	
2	3 (27.3)	18 (40.9)	0.097[b]	13 (34.2)	8 (47.1)	0.416[b]
3	1 (9.1)	5 (11.4)		6 (15.8)	0 (0)	
4	1 (9.1)	10 (22.7)		7 (18.4)	4 (23.5)	
Mortality						
Absent	10 (90.9)	34 (77.3)	0.430[b]	36 (94.7)	8 (47.1)	<0.001[b]
Present	1 (9.1)	10 (22.7)		2 (5.3)	9 (52.9)	

[a]: Pearson Chi Square test, [b]: Fisher's Exact test,c: Mann Whitney U test. p<0.05 considered statistically significant. 1: measurements at diagnosis; 2: follow-up measurements. WBC: White Blood Cell Count, LDH: Lactate Dehydrogenase.

ibrutinib does not appear to exert a direct catabolic effect on skeletal muscle, the current data do not suggest a restorative effect on pre-existing sarcopenia. These findings underscore that the pathophysiology of sarcopenia cannot be attributed solely to pharmacologic toxicity but is instead shaped by multifactorial processes, including aging, physical inactivity, chronic inflammation, anorexia, and metabolic alterations [11].

Notably, despite the absence of significant changes in muscle mass, muscle density — expressed in Hounsfield Units — decreased significantly during follow-up. Muscle radiodensity is increasingly recognized as a surrogate marker of muscle quality and is closely associated with intramuscular fat infiltration (myosteatosis) [12,13]. Previous studies have demonstrated that reduced muscle density may reflect inflammatory and metabolic alterations within skeletal muscle and may occur independently of changes in muscle mass. Importantly, declines in muscle quality have been linked to impaired physical function, increased frailty, and adverse clinical outcomes, even in patients with preserved muscle mass [14]. In this context, our findings suggest that deterioration in muscle quality may occur in patients with hematologic malignancies who receive long-term therapy, despite relative stability in muscle quantity, and that this deterioration may have clinically relevant implications, particularly for older patients and those with comorbidities.

The lack of significant improvement in muscle mass among sarcopenic patients despite ibrutinib therapy suggests that pharmacological treatment alone may be insufficient to preserve muscle health in this population. Accordingly, management strategies focusing exclusively on oncologic treatment may not adequately address sarcopenia. Early identification of sarcopenic patients, combined with nutritional support, structured exercise programs, and, when appropriate, anabolic interventions, may improve overall clinical management and patient outcomes [15].

Few studies have evaluated the effects of ibrutinib on skeletal muscle parameters; to our knowledge, this study is among the first to investigate the association between ibrutinib therapy and sarcopenia-related parameters in patients with hematologic malignancies. An important limitation of this study is that sarcopenia assessment was based solely on CT-derived muscle parameters. Due to the retrospective design, direct assessments of muscle strength and physical performance, which are prioritized in the EWGSOP2 criteria, could not be performed. Although the retrospective design and relatively small sample size may limit the generalizability of our findings, the objective assessment of muscle area and muscle density using CT represents an important methodological strength and provides a valuable foundation for future large-scale prospective studies.

CONCLUSION

This study suggests that ibrutinib therapy is not associated with a significant deterioration in muscle mass in patients with hematologic malignancies. However, no improvement in pre-existing sarcopenia was observed during follow-up, indicating that sarcopenia may persist despite effective oncologic treatment. In addition, the observed decline in muscle

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density highlights the potential for deterioration in muscle quality even in the absence of measurable muscle mass loss. Together, these findings underscore the importance of considering sarcopenia-related parameters as part of a comprehensive clinical assessment. Although routine implementation in clinical practice cannot be recommended based on the present data alone, early identification of patients at risk and the use of supportive strategies, such as nutritional and physical interventions, may contribute to improved treatment tolerance and patient-centered outcomes. Further prospective studies are warranted to clarify the clinical implications of sarcopenia and changes in muscle quality during targeted therapies.

Ethics Committee Approval: The study was approved by the Samsun University Non-Invasive Clinical Research Ethics Committee (Decision No: 2025/10/17, Date: 14.05.2025).

Informed Consent: Because this study was conducted retrospectively using anonymized medical records, informed consent was not required.

Peer-review: Externally peer-reviewed.

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