AHOT Acta Haematologica Oncologica Turcica

Acta Haematol Oncol Turc 2025;58(2):110-114

Original Article

DOI: 10.4274/ahot.galenos.2025.2025-4-10

Prognostic Role of Sarcopenia in High-grade Lymphoma: A Retrospective PET/CT-Based Study

Özlem Beyler[1], Yunus Güzel[2], Cengiz Demir[1], Serdar Yıldırım[3], Canan Can[2], Halil Kömek[2]

[1]*University of Health Sciences Türkiye, Gazi Yaşargil Training and Research Hospital, Clinic of Hematology, Diyarbakır, Türkiye*
[2]*University of Health Sciences Türkiye, Gazi Yaşargil Training and Research Hospital, Clinic of Nuclear Medicine, Diyarbakır, Türkiye*
[3]*University of Health Sciences Türkiye, Gazi Yaşargil Training and Research Hospital, Clinic of Internal Medicine, Diyarbakır, Türkiye*

ABSTRACT

Aim: This study aimed to evaluate the impact of sarcopenia and myosteatosis on progression-free survival (PFS) in patients with aggressive non-Hodgkin lymphoma (NHL).

Methods: A retrospective analysis was conducted on 33 high-grade NHL patients diagnosed between 01.01.2018 and 31.12.2019, who had pre- and post-treatment ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (CT) imaging. Body composition was semiautomatically measured using axial CT slices at the lumbar L3 vertebral level, focusing on the psoas muscle (PM). The right and left average hounsfield unit (HU) values [right psoas HU corrected (RPHUc) and left psoas HU corrected (LPHUc)] were recorded as myosteatosis parameters. The cross-sectional area of the PM was adjusted for body size by dividing it by the square of the patient's height in meters, resulting in the PM index, expressed in cm^2/m^2.

Results: The average age of the patients was 57±16.2 years, and sarcopenia was identified in 39.4% of the cohort. During follow-up, relapse occurred in 9 patients (27.3%). A significant association was found between relapse and age (p=0.002), Eastern Cooperative Oncology Group (ECOG) performance status (p=0.003), and RPHUc (p=0.015). Receiver operating characteristic analysis for RPHUc (cut-off >33.550) in predicting PFS showed an area under the curve of 0.778 (p=0.015), with 66.7% sensitivity and 33% specificity. Univariate analysis identified age (p=0.001), ECOG score (p=0.000), and RPHUc (p=0.017) as significant prognostic factors for PFS. In multivariate analysis, only age remained an independent prognostic factor (p=0.04).

Conclusion: Our study demonstrated that age and RPHUc values have prognostic significance for PFS in aggressive lymphoma patients. These parameters, easily obtainable from routine imaging, may aid in guiding clinical management strategies.

Keywords: Lymphoma, sarcopenia, progression free survival, psoas muscle, myosteatosis

Introduction

Aggressive lymphomas are fast-growing subtypes of non-Hodgkin lymphoma (NHL) characterized by high proliferation rates. The most common type is diffuse large B-cell lymphoma (DLBCL). Others include mantle cell lymphoma (MCL), Burkitt lymphoma, high-grade B-cell lymphomas, primary mediastinal large B-cell lymphoma, and peripheral T-cell lymphomas [1]. Treatment typically involves intensive chemotherapy, targeted therapies, immunotherapy, and, in some cases, stem cell transplantation [2]. The heterogeneity in DLBCL's immunophenotype, genetic profile, and histology influences treatment response and long-term prognosis [3,4]. Although the MCL International Prognostic Index (IPI) has been introduced as a tool for risk stratification, its prognostic utility continues to be a subject of discussion [5,6]. Identifying new prognostic factors is crucial for disease management and survival. Established indices like the IPI, revised IPI, and National Comprehensive Cancer Network (NCCN)-IPI underscore the need for novel biomarkers to predict aggressive disease courses.

Address for Correspondence: Özlem Beyler MD, University of Health Sciences Türkiye, Gazi Yaşargil Training and Research Hospital, Clinic of Hematology, Diyarbakır, Türkiye
E-mail: drozlembeyler@gmail.com **ORCID ID:** orcid.org/0000-0002-2032-8877
Received: 30.04.2025 **Accepted:** 13.07.2025 **Epub:** 04.08.2025 **Publication Date:** 13.08.2025

Cite this article as: Beyler Ö, Güzel Y, Demir C, Yıldırım S, Can C, Kömek H. Prognostic role of sarcopenia in high-grade lymphoma: a retrospective PET/CT-based study. Acta Haematol Oncol Turc. 2025;58(2):110-114

Sarcopenia, defined as reduced skeletal muscle mass, quality, and function, is often age-related but may also result from an underlying disease or treatment side effects [7]. Studies in various malignancies suggest sarcopenia adversely impacts survival [8]. Current evidence supports low skeletal muscle mass as a prognostic biomarker in cancer patients [9], including hematologic malignancies [10]. Sarcopenia has been associated with an increased risk of adverse outcomes, including falls, bone fractures, functional impairment, and overall mortality [7,11]. Cancer patients may lose 15-50% of skeletal muscle mass, reducing chemotherapy tolerance and quality of life [12-14]. In recent years, it has also garnered attention as a potential prognostic marker in NHL [11,15].

This study aimed to expand the current literature by evaluating the prognostic significance of both sarcopenia and myosteatosis in patients with high-grade lymphoma.

Methods

This study was designed as a retrospective analysis of patients diagnosed with high-grade lymphoma between January 1, 2018, and December 31, 2022. Patients who had pre-treatment, post-treatment, and relapse, ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) imaging available were included in the study. Patients with missing data, incomplete treatment records, or insufficient follow-up information were excluded from the analysis. Patient data, including age, sex, disease stage, ECOG performance score, lactate dehydrogenase levels, sedimentation rate, treatment regimens, relapse dates, last follow-up dates, and other relevant clinical findings, were recorded. Body composition parameters were obtained from the CT component of each patient's ^{18}F-FDG PET/CT scans. The study was conducted according to the principles of the Declaration of Helsinki, and approval was obtained from the University of Health Sciences Türkiye, Gazi Yaşargil Training and Research Hospital (decision no: 345, date: 07.02.2025).

Body Composition Assessment

All ^{18}F-FDG PET/CT images were evaluated using the AW 4.7 workstation (Advantage Workstation software version 4.7; GE Healthcare, Milwaukee, WI, USA). The body composition of the psoas muscle (PM) was semiautomatically measured on axial CT slices at the level of the L3 lumbar vertebra from pre-treatment, post-treatment, and relapse ^{18}F-FDG PET/CT scans. The hounsfield unit (HU) thresholds for PM were set between -29 and +150 HU [16]. Separate regions of interest were manually drawn around the right and left PM, avoiding bone and adipose tissue, and the average HU values [right psoas hounsfield unit corrected (RPHUc) and left psoas hounsfield unit corrected (LPHUc)] were recorded as myosteatosis parameters. To calculate the PM index (PMI), the PM area was normalized by dividing it by the square of the patient's height in meters (m^2) (Figure 1) [17,18]. Sarcopenia was defined as PMI ≤5.1 cm^2/m^2 in men and ≤43 cm^2/m^2 in women [19].

Statistical Analysis

Statistical analysis was performed using Statistical Package for the Social Sciences 25.0 (IBM Corporation, Armonk, New York, United States). The normality of continuous variables was assessed using the Kolmogorov-Smirnov test. The Mann-Whitney U test was used to compare quantitative variables between two independent groups. The Kaplan-Meier (product-limit method) and log-rank (Mantel-Cox) tests were used to evaluate the impact of factors on progression-free survival (PFS). Cox regression analysis was applied to assess the prognostic effects of variables on PFS, with significant independent variables entered into the model both as single (individually) and multiple (collectively) variables. The relationship between predicted classification based on calculated cut-off values and actual classification was evaluated using sensitivity and specificity rates derived from receiver operating characteristic curve analysis. Variables were analyzed at a 95% confidence level, with a $p<0.05$ considered statistically significant.

Results

The study included 13 female and 20 male patients, with a mean age of 57±16.2 years (range: 20-85). Disease staging revealed one patient with stage 1, 5 with stage 2, 10 with stage 3, and 17 with stage 4 disease. ECOG performance status was 1 in 22 patients, 2 in 10 patients, and 3 in 1 patient. The median right psoas average HU (RPHUc) was 36.5±10.9. During follow-up, relapse occurred in 9 patients (27.3%), and one patient (3.03%) died. The median lactate dehydrogenase level prior to treatment initiation was 296.0 U/L, with values ranging from 139 to 4900 U/L. A statistically significant association was found

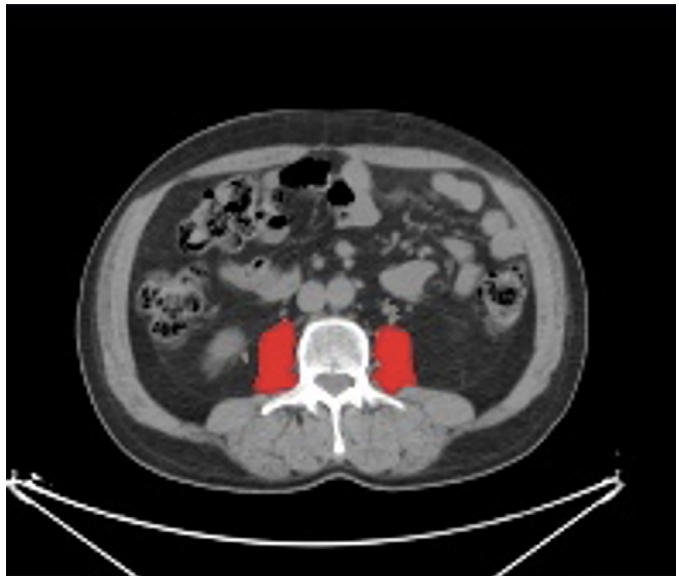

Figure 1. Axial PET/CT image demonstrating psoas muscle assessment
An axial PET/CT image from one of the cases included in our study, showing delineation of the right and left psoas muscles for radiodensity measurement. These measurements were used in the calculation of the psoas muscle index
PET: Positron emission tomography, CT: Computed tomography

between relapse and age (p=0.002), ECOG performance status (p=0.003), and RPHUc (p=0.015). Relapse was more frequently observed in patients of advanced age, with compromised ECOG performance status and reduced RPHUc levels. Among the 9 relapsed patients, 5 had sarcopenia in the PM, but no statistically significant relationship was found between relapse and sarcopenia. Other descriptive parameters are presented in Table 1. An RPHUc cut-off value of >33.55 predicted better PFS (area under the curve: 0.778, p=0.015) with 66.7% sensitivity, and 33.0% specificity (Figure 2). For RPHUc <33.550, the median PFS was 76.9 months at 1 year, while it was 27.4 months at 4 years. For RPHUc >33.550, the median 1-year and 4-year PFS were both 88 months. The median PFS was 10.03 months (range: 5-48) in relapsed patients and 22.72 months (range: 5-63) in non-relapsed patients (Figure 3). Univariate Cox regression analysis identified age (p=0.001), ECOG performance score (p=0.000), and RPHUc (p=0.017) as significant prognostic factors for PFS (Table 2). In multivariate Cox regression analysis, only age remained an independent prognostic factor for PFS (p=0.04).

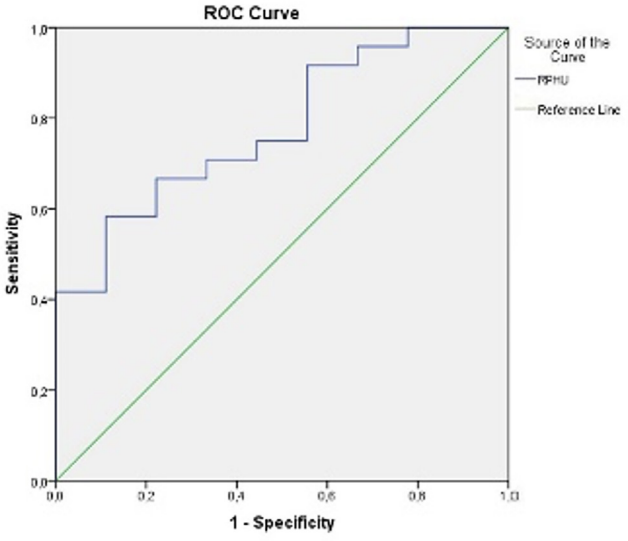

Figure 2. ROC curve of right psoas hounsfield unit cut-off value in predicting progression-free survival
ROC: Receiver operating characteristic

Table 1. Comparison of demographic and radiological sarcopenia-related parameters according to relapse status

Variable	Relaps	Median (min-max)
Age (years)	No	54 (20-80)
	Yes	72 (49-85)
Right psoas mean (HU)	No	38.1 (16.6-57.4)
	Yes	31.2 (14.6-43.1)
Left psoas mean (HU)	No	38.7 (22.3-56.8)
	Yes	32.7 (26.1-45.7)
PMI (cm²/m²)	No	5.34 (2.67-14.18)
	Yes	5.27 (3.43-7.08)

HU: Hounsfield unit, PMI: Psoas muscle index, min-max: Minimum-maximum

Discussion

Studies have demonstrated that NHL patients may lose up to 31% of their total body weight [20]. In advanced-stage cancers, including both solid tumors and hematologic malignancies, cancer cachexia affects approximately 60-80% of patients [7,10]. This condition can lead to adverse clinical outcomes such as reduced tolerance to chemotherapy and diminished quality of life [12,13].

Aging represents one of the most significant risk factors for sarcopenia development, contributing to progressive muscle mass loss. Additionally, various pro-inflammatory cytokines released by tumors, including interleukin-1, interleukin-6, tumor necrosis factor, and interferon gamma, accelerate muscle tissue catabolism [21]. Tumor-induced abnormalities in protein and amino acid metabolism, combined with malnutrition and reduced physical activity during treatment, result in more pronounced muscle mass reduction [22].

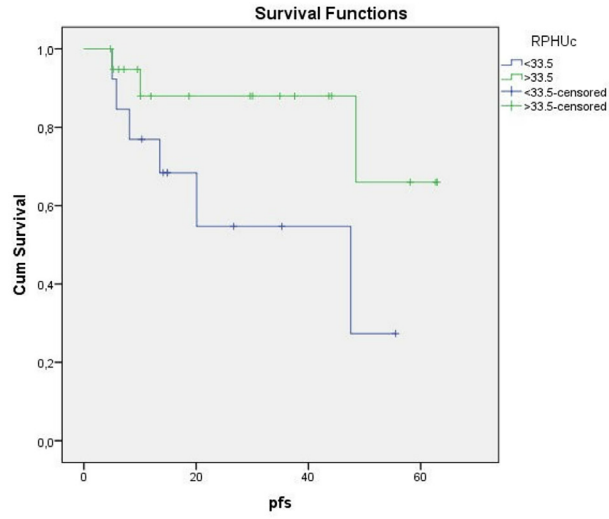

Figure 3. Kaplan-Meier curve for progression-free survival based on right psoas muscle HU cut-off value
RPHUc: Right psoas hounsfield unit corrected, HU: Hounsfield unit

Table 2. Cox regression analysis of clinical and radiological parameters for progression-free survival

Parameter	B	OR	95% CI	p
Age	0.127	1.135	1.051-1.226	**0.001**
Gender	0.779	2.179	0.451-10.538	0.333
Stage	0.143	1.154	0.506-2.634	0.734
ECOG	2.180	8.843	2.747-28.464	**0.000**
LDH	0.000	1.000	0.999-1.001	0.692
Sedimentation rate	0.005	1.005	0.980-1.030	0.717
PMI	1.029	2.799	0.742-10.552	0.128
Right psoas average	-0.085	0.919	0.857-0.985	**0.017**
Left psoas average	-0.022	0.978	0.909-1.052	0.548

B: Regression coefficient, OR: Odds ratio, CI: Confidence interval, PMI: Psoas muscle index, ECOG: Eastern Cooperative Oncology Group, LDH: Lactate dehydrogenase

Cancer treatments may also induce loss of fat and bone mass alongside muscle depletion [23]. The age-dependent increase in sarcopenia prevalence has been well-documented [24,25]. In our study of aggressive lymphomas, univariate analysis identified age as a prognostic factor for PFS (p=0.001), with multivariate analysis confirming its independent prognostic value (p=0.04). This finding contrasts with Albano et al. [26] study of older MCL patients (mean age 72.7±5.6 years), which found no significant association between age and PFS. Our study's inclusion of relatively younger patients provides valuable insights into the independent effect of age on PFS in sarcopenic patients.

While one MCL study in elderly patients reported significantly higher sarcopenia prevalence in women (93% vs. 47%, p=0.001) [25], Xu et al. [27] DLBCL study found no gender-specific association regarding gender differences between sarcopenia and prognosis. The lack of significant gender-PFS correlation in our study may reflect our inclusion of various high-grade lymphoma subtypes and relatively younger patients.

Saglam et al. [28] study of 112 patients identified ECOG performance status as a prognostic factor for PFS in both univariate and multivariate analyses. While our univariate Cox regression confirmed this association (p=0.000), multivariate analysis did not. This discrepancy may result from our limited sample size, cohort differences, or potential confounding effects of other variables in the model.

In our study, sarcopenia was identified in 36% of patients, aligning with the findings of Xiao et al. [29], who reported a prevalence exceeding 30% based on pretreatment CT evaluations in individuals with DLBCL. However, we found no significant association between PMI and PFS (p=0.128).

Myosteatosis, defined as muscle weakening due to fat infiltration and measured by HU [30,31], has been associated with worse OS in various malignancies including lymphoma [32]. In our cohort, PFS differed significantly based on RPHUc cut-off values: median PFS was 10.03 months in relapsed patients, versus 22.72 months in non-relapsed patients. These findings suggest that muscle quality rather than quantity may influence PFS. Univariate analysis confirmed RPHUc as a prognostic factor (p=0.017), aligning with reports of significantly worse PFS in patients with low skeletal muscle density (hazard ratio: 2.28, p=0.002) [33].

Sarcopenia assessment may prove particularly valuable when deciding between standard R-CHOP chemoimmunotherapy and dose-reduced regimens for elderly patients or those with poor performance status, comorbidities.

Study Limitations

One of the key strengths of this study is the use of an objective radiological parameter (RPHUc) to assess muscle quality and the investigation of its prognostic significance in a relatively younger and clinically heterogeneous high-grade lymphoma cohort. The limited number of prior publications exploring RPHUc in this setting enhances the novelty and potential clinical relevance of our results. Study limitations include the small sample size, retrospective design, lack of gender-specific analysis, and absence of DLBCL subtype and treatment toxicity data. Nevertheless, the study by Lanic et al. [34] reported no significant association between sarcopenia and the GCB or non-GCB subtypes.

Conclusion

Our findings suggest that both age and RPHUc are valuable prognostic indicators in high-grade lymphoma. This simple, routinely accessible imaging parameter may enhance risk stratification and guide individualized treatment approaches.

Ethics

Ethics Committee Approval: The study was conducted according to the principles of the Declaration of Helsinki, and approval was obtained from the University of Health Sciences Türkiye, Gazi Yaşargil Training and Research Hospital (decision no: 345, date: 07.02.2025).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept: H.K., Design: H.K., Data Collection or Processing: Ö.B., Y.G., Analysis or Interpretation: H.K., Literature Search: Ö.B., Y.G., C.D., S.Y., C.C., Writing: Ö.B., Y.G.

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

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Lenz G, Staudt LM. Aggressive lymphomas. N Engl J Med. 2010;362:1417-1429.
2. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology (NCCN Guidelines®): B-cell and T-cell lymphomas. Version [2.2025]. Published 2024. Last accessed date: 01.04.2025. Available from: https://www.nccn.org
3. Alaggio R, Amador C, Anagnostopoulos I, et al. Correction: "The 5th edition of the World Health Organization classification of haematolymphoid tumours: lymphoid neoplasms. Leukemia. 2023;37:1944-1951. Erratum for: Leukemia. 2022;36:1720-1748.
4. Silkenstedt E, Salles G, Campo E, Dreyling M. B-cell non-Hodgkin lymphomas. Lancet. 2024;403:1791-1807.
5. Hoster E, Dreyling M, Klapper W, et al. A new prognostic index (MIPI) for patients with advanced-stage mantle cell lymphoma. Blood. 2008;111:558-565.
6. Shah JJ, Fayad L, Romaguera J. Mantle cell international prognostic index (MIPI) not prognostic after R-hyper-CVAD. Blood. 2008;112:2583-2584.
7. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48:16-31.
8. Lopez P, Newton RU, Taaffe DR, et al. Associations of fat and muscle mass with overall survival in men with prostate cancer: a systematic review with meta-analysis. Prostate Cancer Prostatic Dis. 2022;25:615-626.
9. Wiegert EVM, de Oliveira LC, Calixto-Lima L, et al. Association between low muscle mass and survival in incurable cancer patients: a systematic review. Nutrition. 2020;72:110695.

10. Anabtawi NM, Pasala MS, Grimshaw AA, et al. Low skeletal muscle mass and treatment outcomes among adults with haematologic malignancies: a systematic review and meta-analysis. J Cachexia Sarcopenia Muscle. 2024;15:1084-1093.
11. Albano D, Dondi F, Ravanelli M, et al. Prognostic role of "radiological" sarcopenia in lymphoma: a systematic review. Clin Lymphoma Myeloma Leuk. 2022;22:e340-e349.
12. Aapro M, Rugo H, Rossi G, et al. A randomized phase III study evaluating the efficacy and safety of NEPA, a fixed-dose combination of netupitant and palonosetron, for prevention of chemotherapy-induced nausea and vomiting following moderately emetogenic chemotherapy. Ann Oncol. 2014;25:1328-1333.
13. Peterson SJ, Mozer M. Differentiating sarcopenia and cachexia among patients with cancer. Nutr Clin Pract. 2017;32:30-39.
14. Ryan AM, Prado CM, Sullivan ES, Power DG, Daly LE. Effects of weight loss and sarcopenia on response to chemotherapy, quality of life, and survival. Nutrition. 2019;67-68:110539.
15. Wang F, Chen Y, Tan X, et al. PET/computed tomography radiomics combined with clinical features in predicting sarcopenia and prognosis of diffuse large B-cell lymphoma. Nucl Med Commun. 2025;46:162-170.
16. Cushen SJ, Power DG, Murphy KP, et al. Impact of body composition parameters on clinical outcomes in patients with metastatic castrate-resistant prostate cancer treated with docetaxel. Clin Nutr ESPEN. 2016;13:e39-e45.
17. 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;9:629-635.
18. Mitsiopoulos N, Baumgartner RN, Heymsfield SB, Lyons W, Gallagher D, Ross R. Cadaver validation of skeletal muscle measurement by magnetic resonance imaging and computerized tomography. J Appl Physiol (1985). 1998;85:115-122.
19. Ebadi M, Wang CW, Lai JC, et al. Poor performance of psoas muscle index for identification of patients with higher waitlist mortality risk in cirrhosis. J Cachexia Sarcopenia Muscle. 2018;9:1053-1062.
20. Burkart M, Schieber M, Basu S, et al. Evaluation of the impact of cachexia on clinical outcomes in aggressive lymphoma. Br J Haematol. 2019;186:45-53.
21. Baracos VE, Martin L, Korc M, Guttridge DC, Fearon KCH. Cancer-associated cachexia. Nat Rev Dis Primers. 2018;4:17105.
22. Park S, Han B, Cho JW, et al. Effect of nutritional status on survival outcome of diffuse large B-cell lymphoma patients treated with rituximab-CHOP. Nutr Cancer. 2014;66:225-233.
23. Pin F, Couch ME, Bonetto A. Preservation of muscle mass as a strategy to reduce the toxic effects of cancer chemotherapy on body composition. Curr Opin Support Palliat Care. 2018;12:420-426.
24. Papadopoulou SK. Sarcopenia: a contemporary health problem among older adult populations. Nutrients. 2020;12:1293.
25. Iltar U, Sözel H, Sözel YK, et al. Prognostic impact of the psoas muscle index, a parameter of sarcopenia, in patients with diffuse large B-cell lymphoma treated with rituximab-based chemoimmunotherapy. Leuk Lymphoma. 2021;62:1098-1106.
26. Albano D, Pasinetti N, Dondi F, Giubbini R, Tucci A, Bertagna F. Prognostic role of pre-treatment metabolic parameters and sarcopenia derived by 2-[18F]-FDG PET/CT in elderly mantle cell lymphoma. J Clin Med. 2022;11:1210.
27. Xu XT, He DL, Tian MX, Wu HJ, Jin X. Prognostic value of sarcopenia in patients with diffuse large B-cell lymphoma treated with R-CHOP: a systematic review and meta-analysis. Front Nutr. 2022;9:816883.
28. Saglam B, Albayrak M, Yıldız A, et al. The prognostic impact of comorbidity, nutritional and performance status on patients with diffuse large B cell lymphoma. Niger J Clin Pract. 2023;26:1512-1518.
29. Xiao DY, Luo S, O'Brian K, et al. Impact of sarcopenia on treatment tolerance in United States veterans with diffuse large B-cell lymphoma treated with CHOP-based chemotherapy. Am J Hematol. 2016;91:1002-1007.
30. Aubrey J, Esfandiari N, Baracos VE, et al. Measurement of skeletal muscle radiation attenuation and basis of its biological variation. Acta Physiol (Oxf). 2014;210:489-497.
31. Martin L, Birdsell L, Macdonald N, et al. Cancer cachexia in the age of obesity: skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. J Clin Oncol. 2013;31:1539-1547.
32. Aleixo GFP, Shachar SS, Nyrop KA, Muss HB, Malpica L, Williams GR. Myosteatosis and prognosis in cancer: systematic review and meta-analysis. Crit Rev Oncol Hematol. 2020;145:102839.
33. Chu MP, Lieffers J, Ghosh S, et al. Skeletal muscle density is an independent predictor of diffuse large B-cell lymphoma outcomes treated with rituximab-based chemoimmunotherapy. J Cachexia Sarcopenia Muscle. 2017;8:298-304.
34. Lanic H, Kraut-Tauzia J, Modzelewski R, et al. Sarcopenia is an independent prognostic factor in elderly patients with diffuse large B-cell lymphoma treated with immunochemotherapy. Leuk Lymphoma. 2014;55:817-823.