Original Article

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The Prognostic Value of ^{18}F-FDG PET/CT Parameters in Mantle Cell Lymphoma: A Retrospective Single-Center Study

Mantle Hücreli Lenfomada ^{18}F-FDG PET/BT Parametrelerinin Prognostik Değeri: Retrospektif Tek Merkezli Bir Çalışma

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Abstract

Objectives: Mantle cell lymphoma (MCL) is an aggressive subtype of non-Hodgkin lymphoma for which accurate early prognostication is crucial. This study primarily investigated the potential of quantitative metabolic parameters derived from baseline and interim ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) scans to independently predict treatment response and survival outcomes in patients with MCL.

Methods: A total of 48 newly diagnosed MCL patients were retrospectively enrolled in a cohort; of these, 32 patients had interim PET/CT scans analyzed. Semi-quantitative parameters, including standardized uptake value (SUV) and its normalizations, alongside quantitative volumetric parameters such as total body metabolic tumor volume (tMTV) and total body total lesion glycolysis (tTLG), were measured. Independent prognostic factors were determined by Cox regression analysis.

Results: A strong reduction in SUV, tTLG, and tMTV values between baseline and interim PET/CT verified a significant metabolic response to treatment. Interim volumetric parameters, specifically tTLG and tMTV, demonstrated superior performance in predicting treatment response. Multivariate Cox regression analysis identified tMTV and SUV normalized to body surface area (SUV_{bsa}) as independent prognostic factors for progression-free survival (PFS). Kaplan-Meier analysis revealed that high baseline SUV_{bsa} and high interim SUV values were strongly associated with poor survival outcomes. Overall survival was not independently associated with any PET/CT parameter in the multivariate model.

Conclusion: In MCL patients, baseline SUV_{bsa} and quantitative parameters derived from interim PET/CT are powerful and independent biomarkers for PFS. These data can improve prognostic stratification and guide risk-adapted therapies by enabling the early identification of high-risk patients.

Keywords: Mantle cell lymphoma, PET/CT, SUV, MTV, TLG

Öz

Amaç: Mantle hücreli lenfoma (MHL), erken dönemde doğru prognostik değerlendirmenin büyük önem taşıdığı, agresif seyirli bir Hodgkin dışı lenfoma alt tipidir. Bu çalışmada, MHL hastalarında başlangıç ve ara değerlendirme ^{18}F-florodeoksiglukoz pozitron emisyon tomografisi/bilgisayarlı

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tomografi (^{18}F-FDG PET/BT) görüntülerinden elde edilen kantitatif metabolik parametrelerin tedavi yanıtını ve sağkalım sonuçlarını bağımsız olarak öngörme potansiyeli araştırılmıştır.

Yöntem: Yeni tanı almış toplam 48 MHL hastası retrospektif olarak çalışmaya dahil edilmiş; bu hastaların 32'sinin ara değerlendirme PET/BT görüntüleri analiz edilmiştir. Standardize tutulum değeri (SUV) ve normalize edilmiş türevleri gibi yarı kantitatif parametrelerin yanı sıra, tüm vücut metabolik tümör hacmi (tMTV) ve tüm vücut toplam lezyon glikolizi (tTLG) gibi kantitatif hacimsel parametreler ölçülmüştür. Bağımsız prognostik faktörler Cox regresyon analizi ile belirlenmiştir.

Bulgular: Başlangıç ve ara değerlendirme PET/BT incelemeleri arasında SUV, tTLG ve tMTV değerlerinde gözlenen belirgin azalma, tedaviye anlamlı bir metabolik yanıt alındığını göstermiştir. Ara değerlendirmedeki hacimsel parametreler, özellikle tTLG ve tMTV, tedavi yanıtını öngörmede daha yüksek performans sergilemiştir. Çok değişkenli Cox regresyon analizinde, tMTV ve vücut yüzey alanına göre normalize edilmiş SUV (SUV_{bsa}), progresyonsuz sağkalımın (PFS) bağımsız prognostik faktörleri olarak belirlenmiştir. Kaplan–Meier analizi, başlangıçtaki yüksek SUV_{bsa} ve ara değerlendirmedeki yüksek SUV değerlerinin olumsuz sağkalım sonuçlarıyla güçlü biçimde ilişkili olduğunu göstermiştir. Çok değişkenli modelde, hiçbir PET/BT parametresi genel sağkalım ile bağımsız olarak ilişkili bulunmamıştır.

Sonuç: MHL hastalarında başlangıç SUV_{bsa} değeri ve ara değerlendirme PET/BT incelemelerinden elde edilen kantitatif parametreler, PFS için güçlü ve bağımsız biyobelirteçlerdir. Bu veriler, yüksek riskli hastaların erken dönemde belirlenmesini sağlayarak prognostik risk sınıflandırmasını iyileştirebilir ve riske uyarlanmış tedavilere yön verebilir.

Anahtar Kelimeler: Mantle hücreli lenfoma, PET/BT, SUV, MTV, TLG

Introduction

Mantle cell lymphoma (MCL) is a subtype of non-hodgkin lymphoma (NHL) characterized by significant clinical heterogeneity, manifesting in cases that range from highly aggressive, necessitating immediate treatment, to indolent forms where intervention can be safely deferred for years (1,2). The patient demographic is predominantly comprised of elderly males (3). Nevertheless, MCL remains a disease with a persistently low likelihood of cure, regardless of patient age group, primarily due to its inherent propensity to relapse. Given that a substantial number of cases culminate in relapse or the development of refractory disease, the overall prognosis tends to be unfavorable. Specifically, the median progression-free survival (PFS) rates are reported to be approximately 2-3 years for elderly patients and 5 years for younger patients, with corresponding median overall survival (OS) figures cited as 4 years and 12 years, respectively (4).

To facilitate the stratification of these patients into distinct risk categories, extensive research has been conducted on various biological, pathological, and imaging markers, yielding results that have often been controversial. A dedicated prognostic index for MCL, the MCL international prognostic index (MIPI), has been formally established (5). This index has proven its efficacy as a robust predictor of survival outcomes. Furthermore, the prognostic significance of other critical factors, including the blastoid variant, a Ki-67 index exceeding 30%, and TP53 mutation/deletion, has been independently tested and found to be significantly associated with clinical outcomes (6,7,8).

The recurrent nature of MCL suggests that following primary treatment, residual disease often persists at levels undetectable by conventional diagnostic techniques. Metabolic imaging utilizing ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) scanning offers the potential to identify lesions containing this subclinical residual disease (9,10). However, a limitation of hybrid molecular imaging lies in its reduced sensitivity for detecting disease in the common sites of MCL involvement, such as the gastrointestinal (GI) tract and bone marrow (BM), which prevents it from adequately substituting for routine biopsy in these areas (11,12,13).

A growing body of preliminary evidence highlights the potential prognostic utility of ^{18}F-FDG hybrid molecular imaging in MCL. The evaluation of metabolic tumor burden features derived from baseline PET/CT and the assessment of post-treatment metabolic response are particularly emphasized (14,15,16). The metabolic response is formally evaluated using the Lugano classification of treatment response, which is based on the application of the Deauville five-point scale a standard tool for response reporting in Hodgkin lymphoma (HL) and certain NHL subtypes (17).

Notwithstanding this, the current literature presents conflicting data concerning the prognostic value of quantitative hybrid molecular imaging parameters in MCL (18). This inconsistency results in substantial ambiguity regarding the generalizability of these parameters across diverse patient populations and treatment protocols. Consequently, there is an imperative need for more refined prognostic stratification tools to appropriately guide patients toward risk-adapted treatment strategies. Such advancements would allow the precise identification of subgroups that stand to gain the maximum benefit from aggressive therapies, while mitigating the risk of unnecessarily intensive treatment for patients with a more favorable prognosis.

The primary objective of our study is to meticulously investigate the treatment response and prognostic power of metabolic PET/CT parameters in MCL. To address the identified limitations, our study, involving a single-center retrospective cohort of newly diagnosed MCL patients, aims to comprehensively evaluate the independent and combined prognostic value of baseline and interim ^{18}F-FDG PET/CT parameters for documented survival outcomes.

Materials and Methods

Study Population

This study was a retrospective analysis of patients histopathologically confirmed to have MCL and diagnosed at the Department of Hematology, Faculty of Medicine, Ege University between January 1, 2014, and July 1, 2024. Patients with a concurrent malignancy or those who did not have a baseline PET/CT scan available were excluded from the analysis. Consequently, a total of 48 patients were eligible for inclusion in the study.

All included patients had a baseline PET/CT scan performed at the time of diagnosis. However, only 32 patients had an interim PET/CT scan deemed suitable for analysis. This reduction in available interim PET/CT scans resulted primarily from patient loss to follow-up and from exclusion of scans performed at external centers often necessitated by PET/CT equipment malfunctions—because these external images could not be standardized for study analysis. Patients were ultimately grouped based on the availability of their respective PET/CT parameters.

A retrospective analysis of the medical records of the 48 patients was conducted, focusing on the following key parameters: epidemiological data (age at diagnosis and sex), morphological characteristics (splenomegaly and bulky disease), clinical indicators [lactate dehydrogenase (LDH) levels, B symptoms, and MIPI scores], and histopathological findings (Ki-67 index and classic versus pleomorphic/blastoid variants). Furthermore, metabolic profiles were evaluated using ^{18}F-FDG hybrid molecular imaging.

For statistical analysis, LDH levels and MIPI scores were categorized using threshold values of 245 U/L and 2, respectively. Bulky disease was identified if a mass reached a maximum width of at least 10 cm on any imaging modality or exceeded one-third of the internal transverse thoracic diameter. In accordance with the Lugano recommendations (17), splenomegaly was defined by a cranio-caudal diameter greater than 13 cm. Regarding cellular proliferation, the Ki-67 expression available for all 48 patients was stratified into two distinct groups based on a 30% cutoff point (≤30% vs. >30%).

The therapeutic management of the 48-patient cohort followed the established standard-of-care chemotherapy protocols for MCL at our center. Treatment selection was heterogeneous, with regimens individualized according to patients' ages and overall clinical status. Regarding first-line immuno-chemotherapy, the majority of the cohort (n=38) underwent treatment with R-CHOP (rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisone) or with an alternating R-CHOP/R-DHAP (Rituximab, dexamethasone, high-dose ara-c cytarabine, and cisplatin) cycle. Other induction strategies included R-Bendamustine in four patients and R-EPOCH (rituximab, etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) in two patients. Furthermore, two patients were treated with the HyperCVAD protocol (hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone, alternating with methotrexate and cytarabine). Finally, each regimen, R-FC (rituximab, fludarabine, and cyclophosphamide) and R-CVP (rituximab, cyclophosphamide, vincristine, and prednisone), was administered to a single patient. Approval from the local ethics committee Ege University Medical Research Ethics Committee was obtained prior to the study (date:

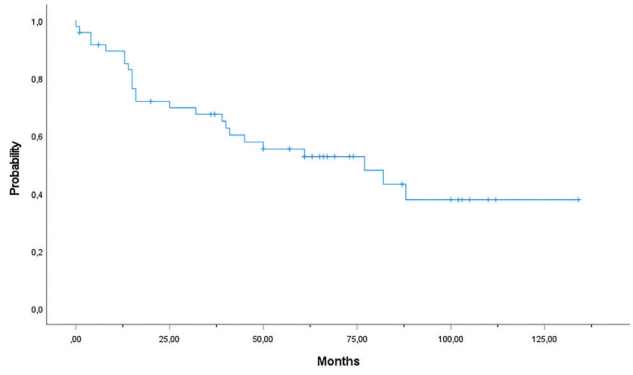

Figure 1. Overall survival curve for the entire cohort

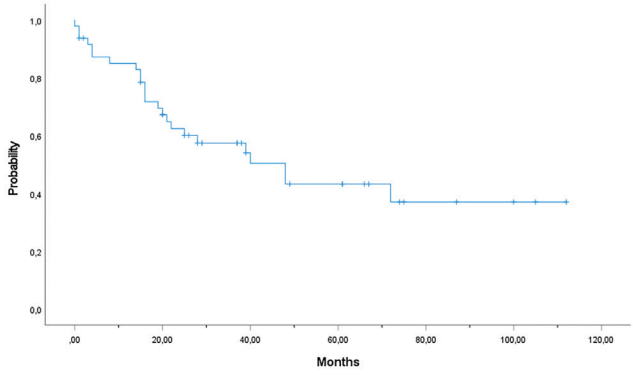

Figure 2. Progression-free survival curve for the entire cohort

31.10.2024, approval number: 24-10.2T/49).

PET/CT Acquisition Parameters and Image Assessment

The ^{18}F-FDG PET/CT procedures were initiated after a minimum 6-hour fasting period, ensuring that all patients had blood glucose levels below 200 mg/dL. In accordance with international protocols, ^{18}F-FDG was injected intravenously at a dose of roughly 3.7 MBq/kg. Prior to the examination, formal written consent was secured from each participant. A 60-minute post-injection rest period followed, during which physical exertion was prohibited, and patients were instructed to consume approximately 1 liter of water. Total-body scans (vertex to mid-thigh) were conducted in the supine position using a Siemens Biograph Truepoint 16 system. To facilitate anatomical correlation and attenuation correction, low-dose CT was performed (120 mA, 130 kV, 5 mm thickness) without contrast media. PET data were captured at a rate of 2 minutes per bed position.

Comprehensive image analysis was performed on specialized workstations using MIP, fusion PET/CT, and multi-planar (axial, coronal, sagittal) views. All identifiable nodal and extranodal lesions were assessed. Quantitative parameters, including maximum standardized uptake value (SUV_{max}) (normalized to body weight, lean body mass, and surface area), peak standardized uptake value, mean standardized uptake value (SUV_{mean}), MTV, and TLG, were extracted via Siemens Syngo.via software. Reference values for the liver (segment VIII) and the blood pool (aortic arch) were established using 10-mm circular regions of interest. For each patient, the lesion exhibiting the most intense ^{18}F-FDG avidity was designated as the reference lesion for calculating ratios (L-L SUV R and L-BP SUV R). MTV was determined using a 41% SUV_{max} threshold, while TLG was derived from the $SUV_{mean} \times$ MTV product. Total-body indices (tMTV and tTLG) represent the aggregate of all measured lesions, and total-body SUV_{mean} was calculated as tTLG/tMTV. Splenic involvement was defined as focal uptake or diffuse activity exceeding liver background by 150%. BM involvement (BMI) was recorded when focal uptakes were present that could not be attributed to benign etiologies or to the clinical history.

Statistical Analysis

Statistical analysis of the acquired data was performed using the Statistical Package for the Social Sciences (SPSS) version 27.0. Descriptive statistics, including median values and percentages, were utilized to summarize patient characteristics. Comparisons between independent groups and analyses of demographic data were conducted using the Mann-Whitney U test. The Wilcoxon signed-rank test was applied to compare dependent paired variables.

Survival outcomes, for both OS and PFS, were evaluated using the Kaplan-Meier method. Differences between the survival curves were analyzed using the log-rank test.

To determine the predictive power of baseline and interim PET/CT parameters for mortality and treatment response, and to identify the optimal cutoff values, receiver operating

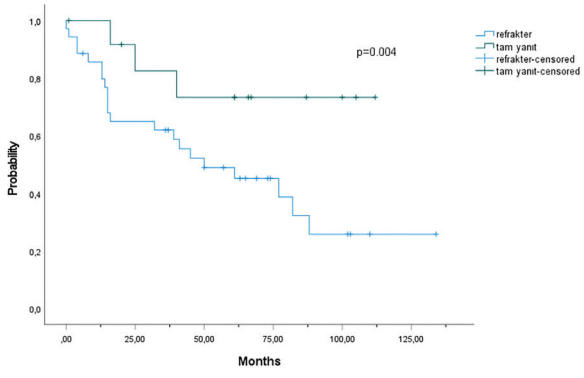

Figure 3. Overall survival stratified by treatment response

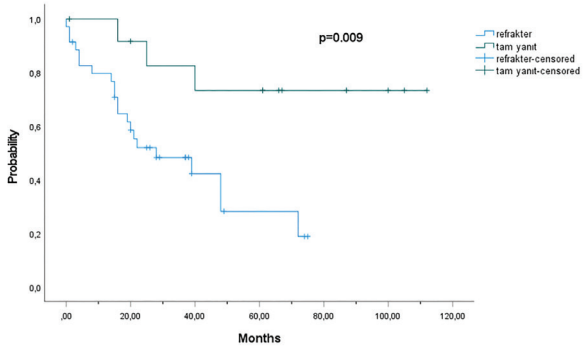

Figure 4. Progression-free survival stratified by treatment response

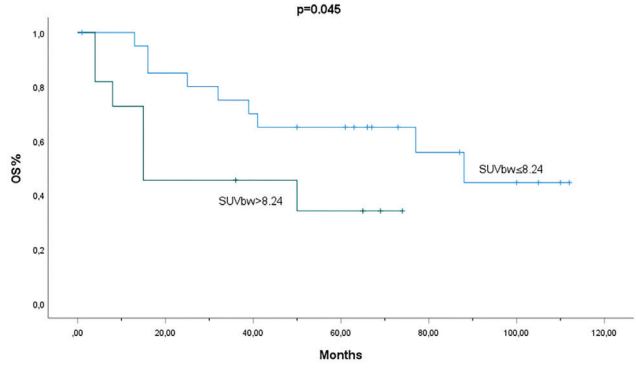

Figure 5. Overall survival stratified by interim SUV_{bw}
SUV_{bw}: Standardized uptake value normalized to body weight

Table 1. Patient characteristics		
Variables	**Patients n (%)**	**Median (range)**
Age (years)		71 (45-89)
Gender		
Female	4 (8 %)	
Male	44 (92%)	
Morphology		
Classic	29 (60 %)	
Blastoid and pleomorphic	19 (40 %)	
Ki67		26 (4-98)
<30%	25 (52%)	
≥30%	23 (48%)	
Bone marrow involvement		
No	12 (25%)	
Yes	36 (75%)	
Ann arbor stage		
II	3 (6%)	
III	9 (19%)	
IV	36 (75%)	
MIPI		
Low	13 (27%)	
Intermediate	17 (35%)	
High	18 (37%)	
First treatment response		
Refractory disease	17 (35%)	
Relapse	18 (37%)	
Complete response	13 (27%)	
AHSCT		
N/A	32 (67%)	
Yes	16 (33%)	
Allo-HSCT		
N/A	46 (96%)	
Yes	2 (4%)	
Comorbidity		
N/A	17 (35%)	
Yes	31 (65%)	
Extranodal involvement		
N/A	34 (71%)	
Yes	14 (29%)	
LDH		
≤245	35 (73%)	
>245	13 (27%)	
Bulky disease	1 (2%)	
Splenomegaly	18 (37%)	
Mortality		
Alive	24 (50%)	
Died	24 (50%)	

MIPI: Mantle cell lymphoma international prognostic index, AHSCT: Autologous hematopoietic stem cell transplantation, Allo-HSCT: Allogeneic hematopoietic stem cell transplantation, LDH: Lactate dehydrogenase

characteristic (ROC) curve analysis was performed. Univariate and multivariate Cox regression analyses were employed to identify variables independently associated with OS and PFS. Variables included in the multivariate analysis were those that reached statistical significance ($p<0.05$) in the preceding univariate Cox regression analysis. The level of statistical significance for all tests was set at $p<0.05$.

Results

Demographic and Clinical Characteristics of the Patient Cohort

Data from a total of 48 patients diagnosed with MCL were analyzed in our study. The median age of the patients was 71 years (range: 45-89), and 92% were male. The majority of patients (75%) were diagnosed at Ann Arbor Stage IV. The median Ki-67 proliferation index for the cohort was 26 (range: 4-98). According to the MIPI score, the patients were distributed into risk groups as follows: 27% low risk, 35% intermediate risk, and 37% high risk.

In the evaluation of response to first-line therapy, 27% of patients achieved a complete response, while the remaining 73% were classified as having relapsed/refractory disease. Detailed patient characteristics are presented in Table 1.

Comparative Analysis of PET/CT Parameters

Comparative Analysis of Baseline and Interim PET/CT Parameters

The differences between the baseline and interim evaluations of the PET/CT measurements were examined using the Wilcoxon signed-rank test. A statistically significant decrease was detected in the measured SUV, tTLG, and tMTV parameters ($p<0.05$). This finding confirms the metabolic response to the administered treatment. Furthermore, despite 75% (n=36) of patients being Stage IV based on BM biopsy, BM involvement (BMI) was detected by PET/CT in only 10.4% (n=5). BM metabolic activity (BM SUV_{max}, right iliac crest) showed a statistically significant increase from baseline (median: 2.79) to interim (median:

3.37) (p=0.009). All comparative statistics are presented in Table 2.

PET/CT Findings Predicting Treatment Response

Differences in PET/CT parameters between the relapsed/refractory and complete response groups were analyzed using the Mann-Whitney U test. Volumetric and clinical parameters, such as spleen size (p=0.032) and tMTV (p=0.046) on baseline PET/CT, were significantly higher in patients with relapsed/refractory disease than in those who achieved a complete response. On interim PET/CT, numerous parameters were significant predictors of treatment response. $SUV_{max\text{-}bw}$ (p=0.013), L-L SUV ratio (p=0.003), tMTV (p=0.004), and tTLG (p=0.001) were significantly higher in the relapsed/refractory group. BM SUV_{max} values on both baseline and interim PET/CT did not differ significantly between the complete response and relapsed/refractory groups. These findings are summarized in Table 3.

Analysis of Mortality Status

According to the Mann-Whitney U test results, baseline and interim hybrid molecular imaging metrics did not differ significantly by mortality status (p>0.05). Furthermore, the ROC curve analysis corroborated these findings, indicating that none of the investigated parameters had significant predictive value for mortality.

Survival Analyses and Prognostic Factors

The median follow-up duration for 48 patients included in the study, based on baseline PET/CT, was 47.5 months (min-max: 1-134 months). For the 32 patients whose interim hybrid molecular imaging was included in the analysis, the median follow-up duration was 12.1 months (range: 1-80 months).

Significance of Treatment Response in OS and PFS

The mean OS follow-up period for all patients was 73.99±8.32 months, with OS rates observed as 89% at 1 year, 72% at 2 years, and 67.5% at 3 years (Figure 1). The mean PFS duration for all patients was 57.93±7.34 months, with PFS rates observed as 85% at 1 year, 62% at 2 years, and 57.5% at 3 years (Figure 2).

The Kaplan-Meier log-rank test was used to examine the effect of treatment response groups on OS; the results indicated a significant effect (p=0.04). Patients with

Table 2. Comparison of baseline and interim ^{18}F-FDG PET/CT parameters in mantle cell lymphoma patients

Variables	Baseline median (range)	Interim median (range)	p-value
Spleen size	11.37 (5.4-31.03)	10.02 (7.14-23.45)	**0.002***
$SUV_{max\text{-}bw}$	12.45 (3.67-32.55)	4.62 (2.16-24.3)	**0.000***
$SUV_{peak\text{-}bw}$	9.27 (2.55-23.67)	3.46 (1.7-18.59)	**0.001***
$SUV_{mean\text{-}bw}$	6.11 (1.65-18.65)	2.82 (1.45-15.68)	**0.001***
$SUV_{max\text{-}lbm}$	8.43 (2.67-23.42)	3.62 (1.79-18.11)	**0.000***
$SUV_{max\text{-}bsa}$	2.72 (0.86-7.41)	1.21 (0.56-5.76)	**0.000***
Liver SUV_{max}	3.95 (2.43-6.06)	3.72 (2.88-6.3)	0.142
L-L SUV R	2.75 (0.76-8.46)	1.32 (0.57-6.83)	**0.000***
BP SUV_{max}	2.81 (1.56-5.40)	2.5 (1.62-4.59)	0.137
L-BP SUV R	3.88 (0.85-11.07)	2.01 (0.73-9.72)	**0.000***
Spleen SUV_{max}	4.34 (2.39-10.81)	3.28 (2.21-5.05)	**0.000***
tMTV	431,1 (7.71-2494,92)	55,93 (3.48-2081,76)	**0.000***
tTLG	1586,16 (16.15-15933,32)	119,46 (5.32-6453,74)	**0.000***
t SUV_{mean}	4.26 (2.06-10.05)	2.14 (1.12-10.83)	**0.000***
BM uptake suv_{max} (right iliac crest)	2.79 (1.33-5.15)	3.37 (2.03-7.59)	**0.009***
BM uptake suv_{max} (left iliac crest)	2.97 (1.54-6.08)	3.44 (2.06-8.47)	0.088
BM uptake suv_{max} (lumbar vertebra)	4.06 (2.12-6.6)	4.08 (2.77-11.5)	0.224

p: Wilcoxon rank testi p value. *p<0.05 indicates statistical significance.
SUV refers to the standardized uptake value, with SUV_{max}, SUV_{peak}, and SUV_{mean} representing the maximum, peak, and mean values, respectively. These values are normalized to body weight (bw), lean body mass (lbm), and body surface area (bsa). The metabolic tumor burden is measured by tMTV (total body metabolic tumor volume) and tTLG (total body total lesion glycolysis). Ratios include L-L SUV R (lesion-to-liver) and L-BP SUV R (lesion-to-blood pool), where BP SUV_{max} is the blood pool SUV_{max}. Other parameters are BM uptake (bone marrow uptake) and t SUV_{mean} (total SUV_{mean}). P-value was calculated using the Wilcoxon Signed Rank Test for paired sample, ^{18}F-FDG PET/CT: ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography

Table 3. Comparison of PET/CT measurements by treatment response				
		Treatment response		
	Parameters	Refractory/relapsed	CR	
		M (min -max)	M (min -max)	p
Baseline	Spleen size	12.2 (5.4-31.03)	9.5 (7.73-17.24)	**0.032**
	SUV_{max-bw}	11.4 (4.28-32.55)	12.66 (3.67-28.86)	0.831
	$SUV_{peak-bw}$	8.25 (2.97-23.67)	9.76 (2.55-23.45)	0.766
	$SUV_{mean-bw}$	5.96 (1.65-18.65)	6.72 (2.15-16.59)	0.849
	$SUV_{max-lbm}$	8.26 (2.88-23.42)	9.49 (2.67-20.01)	0.868
	$SUV_{max-bsa}$	2.65 (0.9-7.41)	3.05 (0.86-6.36)	0.943
	Liver SUV_{max}	3.93 (2.6-6.06):	3.96 (2.43-5.21)	0.908
	L-L SUV R	2.81 (0.76-8.46)	2.75 (0.93-8.0)	0.634
	BP SUV_{max}	2.77 (1.56-5.40)	2.94 (1.8-4.20)	0.676
	L-BP SUV R	3.76 (0.85-11.07)	4.37 (1.8-10.8)	0.887
	Spleen SUV_{max}	4.47 (2.39-10.81)	3.71 (2.87-5.99)	0.523
	tMTV	542.18 (16.62-2494.92)	227.72 (7.71-1344.83)	**0.046**
	tTLG	2958.08 (75.2-15933.32)	737.29 (16.15-6570.47)	0.051
	t SUV_{mean}	4.17 (2.27-10.05)	4.81 (2.06-5.42)	0.887
	BM uptake SUV_{max} (right iliac crest)	2.79 (1.33-5.15)	2.87 (1.58-4.84)	0.719
	BM uptake SUV_{max} (left iliac crest)	2.97 (1.54-6.08)	2.73 (1.72-5.54)	0.570
	BM uptake SUV_{max} (lumbar vertebra)	4.00 (2.12-6.60)	4.27 (3.15-6.02)	0.318
İnterim	Spleen size	10.98 (7.20-23.45)	8.90 (7.14-12.79)	**0.016**
	SUV_{max-bw}	7.54 (3.81–24.30)	3.50 (2.16-7.01)	**0.013**
	$SUV_{peak-bw}$	4.97 (2.29-18.59)	2.83 (1.70-4.13)	**0.027**
	$SUV_{mean-bw}$	4.35 (1.71-15.68)	2.50 (1.45-4.01)	**0.035**
	$SUV_{max-lbm}$	5.39 (2.0-18.11)	2.56 (1.79-5.26)	**0.011**
	$SUV_{max-bsa}$	2.05 (0.63-5.76)	0.82 (0.56-1.68)	**0.011**
	Liver SUV_{max}	3.67 (2.88-4.65)	3.82 (2.95-6.30)	0.425
	L-L SUV R	1.98 (0.77-6.83)	0.81 (0.57-1.82)	**0.003**
	BP SUV_{max}	2.50 (1.62-4.59)	2.96 (1.76-3.92)	0.711
	L-BP SUV R	2.57 (0.74-9.72)	1.26 (0.73-3.25)	**0.031**
	Spleen SUV_{max}	3.21 (2.21-5.05)	3.32 (2.67-4.48)	0.815
	tMTV	147.43 (4.63-2081.76)	7.66 (3.48-59.47)	**0.004**
	tTLG	359.11 (14.01-6453.74)	16.42 (5.32-119.46)	**0.001**
	t SUV_{mean}	2.50 (1.12-10.83)	1.86 (1.23-2.47)	**0.012**
	BM uptake SUV_{max} (right iliac crest)	3.37 (2.03-7.59)	3.42 (2.42-4.98)	0.755
	BM uptake SUV_{max} (left iliac crest)	3.31 (2.06-8.47)	3.45 (2.44-4.98)	0.559
	BM uptake SUV_{max} (lumbar vertebra)	4.03 (2.77-11.50)	4.47 (3.23-6.28)	0.785

SUV refers to the standardized uptake value, with SUV_{max}, SUV_{peak}, and SUV_{mean} representing the maximum, peak, and mean values, respectively. These values are normalized to body weight (bw), lean body mass (lbm), and body surface area (bsa). The metabolic tumor burden is measured by tMTV (total body metabolic tumor volume) and tTLG (total body total lesion glycolysis). Ratios include L-L SUV R (lesion-to-liver) and L-BP SUV R (lesion-to-blood pool), where BP SUV_{max} is the blood pool SUV_{max}. Other parameters are BM uptake (bone marrow uptake) and $tSUV_{mean}$ (total SUV_{mean}). A p-value was calculated using the Mann Whitney U test for independent samples

relapsed/refractory disease had a mean OS duration of 62.97±9.20 months, with OS rates of 68% at 1 year and 65% at 2 years. Conversely, patients achieving a complete response had a mean OS duration of 89.42±11.26 months, with OS rates of 100% at 1 year and 92% at 2 years (Figure 3).

Furthermore, patients' treatment response was found to significantly affect PFS (p=0.009). Patients with relapsed/refractory disease had a mean PFS duration of 36.48±5.14 months, with PFS rates of 71% at 1 year and 52% at 2 years. In comparison, patients achieving a complete response had a mean PFS duration of 89.42±11.26 months, with PFS rates of 100% at 1 year and 92% at 2 years (Figure 4).

Prognostic Role of PET Parameters and ROC Analysis

The Kaplan–Meier log-rank test was applied to investigate the effects of baseline and interim PET/CT measurements, categorized according to their cut-off values, on OS. Baseline PET/CT measurements were not found to be significant for OS based on these cut-off values (p>0.05). Conversely, interim PET/CT measurements, specifically SUV_{bw} (p=0.045) and SUV_{bsa} (p=0.045), were found to have a significant effect on OS. The mean survival time for patients with SUV_{bw} ≤8.24 was calculated as 75.97±9.04 months, compared to 36.45±9.07 months for those with SUV_{bw} > 8.24. The 2-year OS rate was 85% for patients with SUV_{bw} ≤ 8.24 versus 45% for those with SUV_{bw} >8.24. These findings are demonstrated in Figure 5.

The potential of PET/CT parameters to predict treatment response was evaluated by ROC curve analysis. The results indicated that interim PET/CT values, particularly tTLG (AUC: 0.889; p=0.001) and tMTV (AUC: 0.846; p=0.004), demonstrated very high predictive power. The highest AUC and optimal cut-off values are presented in Table 4.

Using the optimal cut-off values determined by these ROC analyses, the prognostic impact on survival was further evaluated using Kaplan-Meier curves and the log-rank test. Kaplan-Meier survival analyses using ROC-derived cut-off values are detailed in Table 5. The analyses demonstrated that both baseline and interim PET/CT parameters had a strong effect on patient survival in specific groups. High cut-off values of certain parameters obtained from baseline PET/CT were associated with significantly poorer survival outcomes. Specifically, elevated values of SUV_{lbm} (OS p=0.013; PFS p=0.006), SUV_{bsa} (OS p=0.006; PFS p=0.002), L-BP SUV R (OS p=0.013; PFS p=0.014), tMTV (PFS p=0.015), and tTLG (PFS p=0.037) were correlated with significantly shorter median OS and/or PFS and lower 2-year survival rates. For instance, the 2-year PFS rate for patients with a high baseline SUV_{bsa} >3.58(21.3%) was significantly lower compared to the low SUV_{bsa} (≤3.58) group (77.5%) (p=0.002).

Interim PET/CT parameters demonstrated a stronger and more pervasive significance in predicting survival. All interim parameters, including SUV_{bw}, SUV_{lbm}, SUV_{bsa}, L-L

Table 4. Receiver operating characteristic (ROC) curve analysis for treatment response prediction

	Parameter	**Cutoff**	**AUC (95%CI)**	**p-value**	**Sensitivity**	**Specificity**
Baseline	**SUV_{bw}**	14.58	0.466(0.236-0.696)	0.777	28%	89%
	SUV_{lbm}	11.07	0.469(0.238-0.700)	0.797	28%	89%
	SUV_{bsa}	3.58	0.488(0.256-0.719)	0.918	33%	89%
	L-L SUV R	4.24	0.481(0.255-0.708)	0.877	28%	89%
	L-BP SUV R	4.76	0.519(0.297-0.740)	0.877	22%	78%
	tMTV	393.2	0.815(0.633-0.996)	**0.009**	67%	89%
	tTLG	1623.3	0.802(0.619-0.986)	**0.012**	67%	89%
Interim	**SUV_{bw}**	6.3	0.809(0.645-0.972)	**0.010**	56%	89%
	SUV_{lbm}	4.78	0.815(0.652-0.977)	**0.009**	56%	89%
	SUV_{bsa}	1.56	0.821(0.661-0.981)	**0.007**	56%	89%
	L-L SUV R	1.75	0.883(0.744-1.00)	**0.001**	56%	89%
	L-BP SUV R	2.54	0.784(0.604-0.964)	**0.018**	56%	89%
	tMTV	58.67	0.846(0.699-0.993)	**0.004**	61%	89%
	tTLG	106.7	0.889(0.768-1.00)	**0.001**	72%	89%

AUC: Area under curve, CI: Confidence interval, SUV: Standardized uptake value, bw: Body weight, lbm lean body mass, bsa: Body surface area, L-L R: Lesion-to-liver ratio, L-BP R: Lesion-to-blood pool ratio, tMTV: Total body metabolic tumor volume, tTLG: Total body total lesion glycolysis

SUV R, L-BP SUV R, tMTV, and tTLG, were found to have significant prognostic value for both OS and PFS (range p≤0.025). Notably, the cut-off value for tTLG (106.7) showed the strongest association with OS (p=0.002) and PFS (p=0.004). The 2-year PFS rate for patients with high interim tTLG (>106.7) (42.9%) showed a marked decrease compared to the low tTLG (≤106.7) group (91.7%). Similarly, interim SUV normalizations (SUV_{bw}, SUV_{lbm}, and SUV_{bsa}) and the L-L SUV R parameter demonstrated a strong and significant prognostic effect on OS (p=0.004). The 2-year OS rate for patients with a high interim SUV_{bw} (>6.3) (72.7%) was lower than for the low SUV_{bw} (≤6.3) group (87.5%).

Independent Prognostic Factors (Cox Regression)

Potential predictors of OS were initially screened using univariate Cox regression analysis across the entire patient group. The analysis revealed that Ki-67, SUV_{lbm}, SUV_{bsa}, and

Table 5. Overall survival and progression-free survival based on baseline and ınterim ^{18F}-FDG PET/CT parameters

			OS				PFS			
	Parameters cut off		**Mean ± SE (months)**	**2-year rate (%)**	**3-year rate (%)**	**p**	**Mean ± SE (months)**	**2-year rate (%)**	**3-year rate (%)**	**p**
Baseline	SUV_{bw}	≤14.58	65.77±7.68	78.9	75.7	0.250	48.17±6.65	69.8	54.1	0.091
		>14.58	48.2±10.58	61.5	51.3		29.02±9.17	33.7	22.4	
	SUV_{lbm}	≤11.07	71.16±7.18	87.5	81.0	**0.013**	50.75±6.52	75.1	58.9	**0.006**
		>11.07	36.79±9.67	42.9	42.9		24.73±9.39	22.9	22.9	
	SUV_{bsa}	≤3.58	72.48±7.3	87.1	83.7	**0.006**	51.87±6.64	77.5	60.8	**0.002**
		>3.58	35.32±8.99	46.7	37.3		24.15±8.79	21.3	21.3	
	L-L SUV R	≤4.24	69.36±7.15	87.1	80.4	0.089	48.05±6.27	74.3	57.5	0.084
		>4.24	42.13±10.30	46.7	46.7		31.69±10.6	29.2	29.2	
	L-BP SUV R	≤4.76	73.13±7.80	89.7	82.2	**0.013**	52.06±7.02	72.3	60.9	**0.014**
		>4.76	39.06±8.34	47.1	47.1		28.4±8.03	33.1	33.1	
	tMTV	≤393.2	69.75±7.99	86.4	81.6	0.095	57.6±8.7	72.7	58.2	**0.015**
		>393.2	50.09±8.28	62.5	57.7		28.8±5.19	49.0	39.2	
	tTLG	≤1623.3	68.47±7.72	87.0	82.4	0.134	55.25±8.65	69.7	55.8	**0.037**
		>1623.3	50.52±8.68	61.9	55.8		30.06±5.27	51.1	40.9	
Interim	SUV_{bw}	≤6.3	80.16±9.07	87.5	87.5	**0.004**	70.23±10.25	81.3	81.3	**0.017**
		>6.3	45.14±7.31	72.7	54.5		32.09±6.75	45.5	27.3	
	SUV_{lbm}	≤4.78	80.16±9.07	87.5	87.5	**0.004**	70.23±10.25	81.3	81.3	**0.017**
		>4.78	45.14±7.31	72.7	54.5		32.09±6.75	45.5	27.3	
	SUV_{bsa}	≤1.56	80.16±9.07	87.5	87.5	**0.004**	70.23±10.25	81.3	81.3	**0.017**
		>1.56	45.14±7.31	72.7	54.5		32.09±6.75	45.5	27.3	
	L-L SUV R	≤1.75	80.16±9.07	87.5	87.5	**0.004**	70.23±10.25	81.3	81.3	**0.017**
		>1.75	45.14±7.31	72.7	54.5		32.09±6.75	45.5	27.3	
	L-BP SUV R	≤2.54	79.54±9.29	86.7	86.7	**0.005**	69.38±10.42	80.0	80.0	**0.025**
		>2.54	46.08±7.08	75.0	75.0		32.62±6.81	46.9	28.1	
	tMTV	≤58.67	77.75±10.8	78.6	78.6	**0.015**	70.45±11.14	78.6	70.7	**0.021**
		>58.67	50.87±6.61	83.3	66.7		34.08±6.63	50.0	41.7	
	tTLG	≤106.7	87.46±9.89	91.7	82.5	**0.002**	78.61±11.41	91.7	82.5	**0.004**
		>106.7	47.09±7.13	71.4	57.1		32.29±5.77	42.9	35.7	

The parameters presented in Table 5 assess the power of ^{18}F-FDG PET/CT variables to predict patient survival using Kaplan-Meier curves and the Log-Rank test. OS stands for Overall Survival, and PFS stands for progression-free survival. The survival time data is presented as Mean ± SE, representing the mean survival time ± standard error in months. SUV refers to the standardized uptake value, where parameters are normalized to body weight (bw), lean body mass (lbm), and body surface area (bsa). Ratios include the lesion-to-liver SUV ratio (L-L SUV R) and the lesion-to-blood pool SUV ratio (L-BP SUV R). The metabolic tumor burden is measured by tMTV (total body metabolic tumor volume) and tTLG (total body total lesion glycolysis). The p-value was calculated using the Log-Rank test. p<0.05 indicates statistical significance

L-BP SUV R values were statistically associated with OS. The subsequent Multivariate Cox regression analysis verified that the final model constructed for OS was statistically significant (χ^2=11.234; p=0.024).

The univariate analysis demonstrated that SUV_{lbm}, SUV_{bsa}, L-BP SUV R, tMTV, and tTLG values were significantly associated with PFS. The Multivariate Cox regression analysis for PFS also resulted in a statistically significant model (χ^2 =22.511; p=0.000). In this multivariate analysis, tMTV [hazard ratio (HR): 24.970; 95% confidence interval (CI): 2.242-278.056; p=0.009] and SUV_{bsa} (HR: 15.580; 95% CI: 1.511-160.632; p=0.021) emerged as independent prognostic factors for PFS. These findings are summarized in Table 6.

Discussion

The hallmark of MCL, which represents approximately 5-10% of NHL cases, is the chromosomal translocation t(11;14). This molecular event triggers the aberrant expression of cyclin D1, driving the aggressive nature of this NHL subtype (5,19). The prognosis of the disease is generally unfavorable due to its high risk of relapse and frequent tendency for extranodal involvement (4). Although powerful tools like the MIPI exist, improving prognostic prediction in MCL necessitates identifying more sophisticated prognostic indicators—in conjunction with biological markers like the Ki-67 index and TP53 mutations—to guide risk-adapted therapies (20).

While ^{18}F-FDG hybrid molecular imaging is widely used for staging and assessing treatment response, its prognostic value and routine clinical role specifically in MCL remain points of discussion in the literature (17,18,21). This debate focuses particularly on prognostic differences among SUV, tMTV, and tTLG. The findings of our study provide robust evidence supporting the strong and independent roles of SUV_{bsa} and volumetric metabolic burden parameters, particularly for predicting PFS in MCL patients.

MCL is generally considered an ^{18}F-FDG- avid histotype with high diagnostic performance in nodal lesions. The average sensitivity for detecting nodal disease has been reported to be 97.5% (21). The significant reductions in SUV, tTLG,

Table 6. Univariate and multivariate cox regression analysis for overall survival and progression-free survival

	OS			PFS		
	HR	**95% CI**	**p**	**HR**	**95% CI**	**p**
Univariate						
Gender	0.590	0.202-1.726	0.336	0.344	0.114-1.036	0.058
Age	1.027	0.993-1.061	0.118	1.014	0.983-1.046	0.377
Ki67	1.016	1.002-1.031	**0.022**	1.006	0.993-1.020	0.338
LDH	0.597	0.280-1.273	0.182	0.852	0.407-1.784	0.671
SUV_{bw}	1.545	0.728-3.278	0.209	1.883	0.886-4.005	0.100
SUV_{lbm}	2.475	1.178-5.197	0.017	2.736	1.297-5.771	**0.008**
SUV_{bsa}	2.673	1.286-5.555	**0.008**	2.966	1.419-6.200	**0.004**
L-L SUV R	1.866	0.895-3.891	0.096	1.882	0.901-3.931	0.092
L-BP SUV R	2.392	1.170-4.892	**0.017**	2.316	1.154-4.648	**0.018**
tMTV	1.680	0.843-3.348	0.141	2.040	1.023-4.071	**0.043**
tTLG	1.044	0.979-1.105	0.199	1.080	1.003-1.164	**0.042**
Multivariate						
Ki67	1.012	0.997-1.028	0.124			
SUV_{lbm}	0.367	0.034-3.987	0.410	0.228	0.017-3.093	0.267
SUV_{bsa}	4.803	0.598-38.567	0.140	15.580	1.511-160.632	**0.021**
L-BP SUV R	1.504	0.458-4.940	0.501	1.815	0.467-7.046	0.389
tMTV				24.970	2.242-278.056	**0.009**
tTLG				0.217	0.023-2.053	0.183

Table 6 presents the results of the Univariate and Multivariate Cox Regression Analysis used to determine the independent risk factors for overall survival (OS) and progression-free survival (PFS). HR stands for hazard ratio, which quantifies the risk of an event (death or progression) associated with a variable. 95% CI represents the 95% confidence ınterval for the HR. SUV refers to the standardized uptake Value. L-L SUV R is the lesion-to-liver SUV ratio, and L-BP SUV R is the lesion-to-blood pool SUV Ratio. tMTV stands for total body metabolic tumor volume, and tTLG stands for total body total lesion glycolysis. LDH is lactate dehydrogenase. A p-value less than 0.05 is considered statistically significant

and tMTV between baseline and interim PET/CT in our study further confirm a strong metabolic response to the administered treatment regimens.

Nevertheless, the use of hybrid molecular imaging for staging in MCL faces significant limitations due to its low sensitivity in detecting disease in frequent involvement sites like the BM and GI tract (12,15,21). A systematic review reported that the average sensitivity of PET/CT for GI tract involvement is 39% and for BMI is 36% (range: 12%-100%) (21). These limitations reinforce the indispensable role of BM biopsy in MCL staging. A recent cohort study demonstrated that the sensitivity of BM biopsy in detecting infiltration is significantly higher than that of PET/CT (22). These data clearly indicate that PET/CT cannot replace BM biopsy in MCL staging, particularly in patients who are negative for BM or GI involvement on imaging. Similarly, in our cohort, the observation that 75% of patients had BMI and were Stage IV based on biopsy, whereas PET/CT detected a lower rate of BMI, illustrates the limited contribution of PET/CT in non-nodal areas.

Although SUV_{max} is the most commonly used semi-quantitative parameter for assessing disease activity in lymphoma, its prognostic role in MCL remains controversial (23,24). While some studies have reported that high baseline SUV_{max} predicts poor survival, other large series found no significant correlation between SUV_{max} and survival outcomes or known poor prognostic factors (5,7,21,23,24). Our study demonstrates a strong association between a high baseline SUV_{bsa} value and poor PFS and OS. The emergence of SUV_{bsa} as an independent prognostic factor for PFS in the multivariate Cox regression analysis supports the prognostic potential of normalized parameters, which are less susceptible to the limitations of traditional SUV_{max} (such as variability due to radio-tracer uptake time and blood glucose levels).

Total body metabolic tumor volume and tTLG better represent the biological tumor burden by combining both the volume and metabolic aggressiveness of the tumor (25,26,27,28,29). Although the number of publications examining these parameters in MCL is limited (15,21), our study confirms that baseline tMTV and tTLG are strong independent prognostic factors for predicting treatment response and PFS. These results reinforce the critical importance of these quantitative parameters in estimating MCL aggressiveness.

Our study demonstrated that patients achieving a complete treatment response had significantly longer OS and PFS than those with relapsed/refractory disease. This supports the prognostic significance of the Lugano classification in MCL (17).

Generally, unlike for other lymphoma subtypes, no scientific consensus exists regarding the interim evaluation of PET/CT results in MCL. A systematic review by Albano et al. (21) noted only two studies evaluating interim PET/CT results, reporting conflicting outcomes. Accordingly, Kedmi et al. (30) reported that interim PET/CT results were not associated with PFS and OS, whereas Jeon et al. (31) demonstrated a significant correlation between metabolic response and both PFS and OS. The findings of our study strongly support the results of Jeon et al. (31), and provide robust evidence that the metabolic status during the interim period is highly predictive of survival. In our study, interim PET/CT parameters were more strongly and broadly associated with survival prediction than baseline parameters. Specifically, interim tTLG and tMTV values were highly predictive of treatment response. Kaplan-Meier analysis showed that all interim SUV normalizations and volumetric parameters had significant prognostic value for both OS and PFS.

The percentage change in SUV_{max} (ΔSUV_{max}), which is a strong prognostic indicator in lymphomas like diffuse large B-cell lymphoma, was found to be a weak predictor in analyses performed in MCL (32). Conversely, our study and other MCL studies suggest that the prognostic value of absolute metabolic burden (MTV and TLG) during the interim period is stronger (15,32). This highlights that the prognostic value of PET/CT parameters should be generalized with caution across different lymphoma subtypes.

In our multivariate Cox regression analysis, metabolic tumor burden parameters (tMTV and SUV_{bsa}) were identified as strong independent prognostic factors for PFS, whereas OS was not independently associated with any PET/CT parameter. Conflicts exist in the literature regarding the effect of end-of-treatment PET/CT results on OS (15,21,32). This often stems from the fact that effective salvage therapies and novel agents administered after relapse in MCL tend to prolong patients' OS.

Given the lack of independent prognostic factors for OS, researchers have begun investigating new PET variables focusing on the disease's dissemination pattern in MCL. A study by Albano et al. (33) examined two parameters: maximum tumor diameter (D_{max}) and D_{max} corrected for body surface area ($D_{max\text{-}bsa}$). This study showed that while D_{max} was not associated with PFS, $D_{max\text{-}bsa}$ was an independent prognostic variable for OS in multivariate analysis. This finding supports the hypothesis that long-term survival may be influenced not only by metabolic tumor burden but also by the anatomical extent of the disease. Similarly, the MCL-PET-I prognostic index proposed

by Ródenas Quiñonero et al. (22), which combines clinical factors (LDH > UNL, age > 70) with PET/CT-detected BMI information, was able to reliably risk-stratify patients for both PFS and OS. These results suggest that PFS and OS in MCL are driven by different biological processes: metabolic burden (MTV/TLG) plays a key role in determining initial treatment success and relapse risk, whereas tumor spread ($D_{max\text{-}bsa}$) may better reflect the patient's long-term survival potential.

Study Limitations

The most notable limitations of this study are its retrospective design and small sample size, which restrict the generalizability of the findings. Therefore, analysis of larger prospective cohorts with standardized protocols is essential to confirm the reliability of these data before incorporating PET/CT parameters into clinical decision-making.

Conclusion

This study demonstrates that high baseline SUV_{bsa}, high tMTV, and high tTLG values, together with early treatment response (interim PET), are strong and independent biomarkers for PFS in MCL. These quantitative parameters have the potential to improve prognostic stratification by complementing existing clinical tools such as MIPI and to enable early identification of high-risk patients with aggressive tumor biology. This provides a sound basis for directing these high-risk patients toward more intensive or risk-adapted regimens rather than standard treatment. The most notable limitations of this study are its retrospective design and small sample size, which restrict the generalizability of the findings. Therefore, analysis of larger prospective cohorts with standardized protocols is essential to confirm the reliability of these data before incorporating PET/CT parameters into clinical decision-making.

Ethics

Ethics Committee Approval: Approval from the local ethics committee Ege University Medical Research Ethics Committee was obtained prior to the study (date: 31.10.2024, approval number: 24-10.2T/49).

Informed Consent: Prior to the examination, formal written consent was secured from each participant.

Footnotes

Authorship Contributions

Surgical and Medical Practices: D.Ç.P., D.D., N.O., M.H., M.T., A.M.A., Concept: D.Ç.P., M.T., A.M.A., Design: D.Ç.P., M.T., A.M.A., Data Collection or Processing: D.Ç.P., E.E.T., E.M., D.D., N.O., M.H., M.T., A.M.A., Analysis or Interpretation: D.Ç.P., E.E.T., E.M., D.D., N.O., M.H., A.M.A., Literature Search: D.Ç.P., A.M.A., Writing: D.Ç.P., A.M.A.

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References

1. Armitage JO, Longo DL. Mantle-Cell Lymphoma. N Engl J Med. 2022;386:2495-2506.
2. Eyre TA, Cheah CY, Wang ML. Therapeutic options for relapsed/refractory mantle cell lymphoma. Blood. 2022;139:666-677.
3. Ye H, Desai A, Huang S, Jung D, Champlin R, Zeng D, Yan F, Nomie K, Romaguera J, Ahmed M, Wang ML. Paramount therapy for young and fit patients with mantle cell lymphoma: strategies for front-line therapy. J Exp Clin Cancer Res. 2018;37:150.
4. Al-Mansour M. Treatment landscape of relapsed/refractory mantle cell lymphoma: an updated review. Clin Lymphoma Myeloma Leuk. 2022;22:e1019-e1031.
5. Hoster E, Dreyling M, Klapper W, Gisselbrecht C, van Hoof A, Kluin-Nelemans HC, Pfreundschuh M, Reiser M, Metzner B, Einsele H, Peter N, Jung W, Wörmann B, Ludwig WD, Dührsen U, Eimermacher H, Wandt H, Hasford J, Hiddemann W, Unterhalt M; German Low Grade Lymphoma Study Group (GLSG); European Mantle Cell Lymphoma Network. A new prognostic index (MIPI) for patients with advanced-stage mantle cell lymphoma. Blood. 2008;111:558-565.
6. Tiemann M, Schrader C, Klapper W, Dreyling MH, Campo E, Norton A, Berger F, Kluin P, Ott G, Pileri S, Pedrinis E, Feller AC, Merz H, Janssen D, Hansmann ML, Krieken H, Möller P, Stein H, Unterhalt M, Hiddemann W, Parwaresch R; European MCL Network. Histopathology, cell proliferation indices and clinical outcome in 304 patients with mantle cell lymphoma (MCL): a clinicopathological study from the European MCL Network. Br J Haematol. 2005;131:29-38.
7. Hoster E, Rosenwald A, Berger F, Bernd HW, Hartmann S, Loddenkemper C, Barth TF, Brousse N, Pileri S, Rymkiewicz G, Kodet R, Stilgenbauer S, Forstpointner R, Thieblemont C, Hallek M, Coiffier B, Vehling-Kaiser U, Bouabdallah R, Kanz L, Pfreundschuh M, Schmidt C, Ribrag V, Hiddemann W, Unterhalt M, Kluin-Nelemans JC, Hermine O, Dreyling MH, Klapper W. Prognostic Value of Ki-67 Index, Cytology, and Growth Pattern in Mantle-Cell Lymphoma: Results From Randomized Trials of the European Mantle Cell Lymphoma Network. J Clin Oncol. 2016;34:1386-1394.
8. Hernandez L, Fest T, Cazorla M, Teruya-Feldstein J, Bosch F, Peinado MA, Piris MA, Montserrat E, Cardesa A, Jaffe ES, Campo E, Raffeld M. p53 gene mutations and protein overexpression are associated with aggressive variants of mantle cell lymphomas. Blood. 1996;87:3351–3359.
9. Cheson BD, Pfistner B, Juweid ME, Gascoyne RD, Specht L, Horning SJ, Coiffier B, Fisher RI, Hagenbeek A, Zucca E, Rosen ST, Stroobants S, Lister TA, Hoppe RT, Dreyling M, Tobinai K, Vose JM, Connors JM, Federico M, Diehl V; International Harmonization Project on Lymphoma. Revised response criteria for malignant lymphoma. J Clin Oncol. 2007;25:579-586.
10. Hosein PJ, Lossos IS. The evolving role of F-FDG PET scans in patients with aggressive non-Hodgkin's lymphoma. European J Clin Med Oncol. 2010;2:131-138.
11. Brepoels L, Stroobants S, De Wever W, Dierickx D, Vandenberghe P, Thomas J, Mortelmans L, Verhoef G, De Wolf-Peeters C. Positron emission tomography in mantle cell lymphoma. Leuk Lymphoma. 2008;49:1693-1701.

12. Hosein PJ, Pastorini VH, Paes FM, Eber D, Chapman JR, Serafini AN, Alizadeh AA, Lossos IS. Utility of positron emission tomography scans in mantle cell lymphoma. Am J Hematol. 2011;86:841-845.
13. Cohen JB, Hall NC, Ruppert AS, Jones JA, Porcu P, Baiocchi R, Christian BA, Penza S, Benson DM, Jr Flynn J, Andritsos LA, Devine SM, Blum KA. Association of pre-transplantation positron emission tomography/computed tomography and outcome in mantle cell lymphoma. Bone Marrow Transplantation. 2013;48:1212-1217.
14. Albano D, Laudicella R, Ferro P, Allocca M, Abenavoli E, Buschiazzo A, Castellino A, Chiaravalloti A, Cuccaro A, Cuppari L, Durmo R, Evangelista L, Frantellizzi V, Kovalchuk S, Linguanti F, Santo G, Bauckneht M, Annunziata S; Young Italian Association of Nuclear Medicine. The Role of ^{18}F-FDG PET/CT in staging and prognostication of mantle cell lymphoma: An Italian Multicentric Study. Cancers (Basel). 2019;11:1831.
15. Albano D, Bosio G, Pagani C, Re A, Tucci A, Giubbini R, Bertagna F. Prognostic role of baseline ^{18}F-FDG PET/CT metabolic parameters in Burkitt lymphoma. Eur J Nucl Med Mol Imaging. 2019;46:87-96.
16. Vergote VKJ, Verhoef G, Janssens A, Woei-A-Jin FJSH, Laenen A, Tousseyn T, Dierickx D, Deroose CM. [^{18}F]FDG-PET/CT volumetric parameters can predict outcome in untreated mantle cell lymphoma. Leuk Lymphoma. 2023;64:161-170.
17. Cheson BD, Fisher RI, Barrington SF, Cavalli F, Schwartz LH, Zucca E, Lister TA; Alliance, Australasian Leukaemia and Lymphoma Group; Eastern Cooperative Oncology Group; European Mantle Cell Lymphoma Consortium; Italian Lymphoma Foundation; European Organisation for Research; Treatment of Cancer/Dutch Hemato-Oncology Group; Grupo Español de Médula Ósea; German High-Grade Lymphoma Study Group; German Hodgkin's Study Group; Japanese Lymphorra Study Group; Lymphoma Study Association; NCIC Clinical Trials Group; Nordic Lymphoma Study Group; Southwest Oncology Group; United Kingdom National Cancer Research Institute. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. J Clin Oncol. 2014;32:3059-3068.
18. Bailly C, Carlier T, Touzeau C, Arlicot N, Kraeber-Bodéré F, Le Gouill S, Bodet-Milin C. Interest of FDG-PET in the management of mantle cell lymphoma. Front Med (Lausanne). 2019;6:70.
19. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele J, Vardiman JW, editors. WHO Classification of tumours of haematopoietic and lymphoid tissues. 4th ed. Lyon: IARC Press; 2008.
20. Maddocks K. Update on mantle cell lymphoma. Blood. 2018;132:1647-1656.
21. Albano D, Treglia G, Gazzilli M, Cerudelli E, Giubbini R, Bertagna F. ^{18}F-FDG PET or PET/CT in mantle cell lymphoma. Clin Lymphoma Myeloma Leuk. 2020;20:422-430.
22. Ródenas Quiñonero I, Marco-Ayala J, Chen-Liang TH, de la Cruz-Vicente F, Baumann T, Navarro JT, Martín García-Sancho A, Martin-Santos T, López-Jiménez J, Andreu R, Parra-Virto E, Usas A, Alonso D, Fernández-González M, Palomo Rumschisky P, Frutos L, Navarro JL, Alvarez-Perez RM, Sarandeses P, Cortes M, Tamayo P, Uña J, Martínez-Lorca A, Ruiz C, Lozano ML, Ortuño FJ. The value of bone marrow assessment by FDG PET/CT, Biopsy and Aspirate in the Upfront Evaluation of Mantle Cell Lymphoma: A Nationwide Cohort Study. Cancers (Basel). 2024;16:4189.
23. Jeon YW, O JH, Park KS, Min GJ, Park SS, Yoon JH, Eom KS, Min CK, Cho SG. Prognostic impact of interim positron emission tomography in mantle cell lymphoma patients treated with frontline R-CHOP. Br J Haematol. 2020;188:860-871.
24. Bodet-Milin C, Touzeau C, Leux C, Sahin M, Moreau A, Maisonneuve H, Morineau N, Jardel H, Moreau P, Gallazini-Crépin C, Gries P, Gressin R, Harousseau JL, Mohty M, Moreau P, Kraeber-Bodere F, Le Gouill S. Prognostic impact of ^{18}F-fluoro-deoxyglucose positron emission tomography in untreated mantle cell lymphoma: a retrospective study from the GOELAMS group. Eur J Nucl Med Mol Imaging. 2010;37:1633-1642.
25. Albano D, Bosio G, Camoni L, Farina M, Re A, Tucci A, Giubbini R, Bertagna F. Prognostic role of baseline ^{18}F-FDG PET/CT parameters in MALT lymphoma. Hematol Oncol. 2019;37:39-46.
26. Cottereau AS, Lanic H, Mareschal S, Meignan M, Vera P, Tilly H, Jardin F, Becker S. Molecular Profile and FDG-PET/CT total metabolic tumor volume improve risk classification at diagnosis for patients with diffuse large B-Cell lymphoma. Clin Cancer Res. 2016;22:3801-3809.
27. Toledano MN, Desbordes P, Banjar A, Gardin I, Vera P, Ruminy P, Jardin F, Tilly H, Becker S. Combination of baseline FDG PET/CT total metabolic tumour volume and gene expression profile have a robust predictive value in patients with diffuse large B-cell lymphoma. Eur J Nucl Med Mol Imaging. 2018;45:680-688.
28. Albano D, Bosio G, Pagani C, Re A, Tucci A, Giubbini R, Bertagna F. Prognostic role of baseline ^{18}F-FDG PET/CT metabolic parameters in Burkitt lymphoma. Eur J Nucl Med Mol Imaging. 2019;46:87-96.
29. Albano D, Bertoli M, Battistotti M, Rodella C, Statuto M, Giubbini R, Bertagna F. Prognostic role of pretreatment ^{18}F-FDG PET/CT in primary brain lymphoma. Ann Nucl Med. 2018;32:532-541.
30. Kedmi M, Avivi I, Ribakovsky E, Benyamini N, Davidson T, Goshen E, Tadmor T, Nagler A, Avigdor A. Is there a role for therapy response assessment with 2-[fluorine-18] fluoro-2-deoxy-D-glucose-positron emission tomography/computed tomography in mantle cell lymphoma? Leuk Lymphoma. 2014;55:2484-2489.
31. Jeon YW, O JH, Park KS, Min GJ, Park SS, Yoon JH, Eom KS, Min CK, Cho SG. Prognostic impact of interim positron emission tomography in mantle cell lymphoma patients treated with frontline R-CHOP. Br J Haematol. 2020;188:860-871.
32. Russler-Germain DA, Calhoun BR, Wu N, Watkins MP, Siegel BA, Bartlett NL, Mhlanga JC. FDG-PET/CT response assessment with qualitative Lugano criteria outperforms change in SUV_{max} as a predictive biomarker in frontline treatment of mantle cell lymphoma. Leuk Lymphoma. 2023;64:1870-1874.
33. Albano D, Bianchetti N, Talin A, Dondi F, Re A, Tucci A, Bertagna F. Prognostic role of pretreatment tumor burden and dissemination features from 2-[^{18}F]FDG PET/CT in advanced mantle cell lymphoma. Hematol Oncol. 2025;43:e70009.