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Original Article / Özgün Araştırma

Correlation of (18F) FDG PET/CT Parameters with Haematological Parameters in Esophageal Cancers and the Effect of These Parameters on Survival

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Abstract

Objective: In the present study, we aimed to investigate the relationship between metabolic (SUVmax) and volume-based (18F)FDG PET/CT parameters (metabolic tumour volume (MTV) and total lesion glycolysis (TLG)) and haematological parameters (neutrophil, lymphocyte, platelet,mean platelet volume(MPV) , neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (TLR)) with survival, and whether haematological parameters are correlated with metabolic and volume-based PET parameters.

Method: We included a total of 55 patients who underwent (18F)FDG PET/CT in our nuclear medicine clinic between January 2017 and December 2018 with a diagnosis of esophageal squamous cell carcinoma, had no distant metastasis, either had or did not have regional lymph node metastasis, whose imaging and laboratory data could be retrospectively accessed, who did not undergo an operation before imaging, did not receive chemo-radiotherapy.

Results: In multivariate regression analysis, we found esophageal MTV (OR 2.6; 95% CI 1.04–6.57, p: 0.041) and esophageal TLG (OR 2.7; 95% CI 1.2–6.2, p: 0.022) values to be independent variables in terms of survival. While we observed a negative correlation between PLR and esophageal MTV and TLG (p values were respectively p: 0.021, p: 0.03), we observed a positive correlation between lymphocyte counts and esophageal MTV and TLG (p values were p: 0.004, p: 0.001, respectively). We detected a positive correlation between the size and SUVmax of lymph node metastasis, on the one hand, and both neutrophil counts and NLR on the other.

Conclusion: We determined MTV and TLG values, which are volume-based metabolic PET parameters, to be independent prognostic factors for survival. MTV and TLG had a negative correlation with PLR and a positive correlation with lymphocyte counts.

Keywords: Survival, Volume-based PET/CT parameters, Esophageal cancer, neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (TLR).

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Özefagus Kanserlerinde (18F) FDG PET/BT Parametrelerinin Hematolojik Parametreler İle Korelasyonu ve Bu Parametrelerin Sağkalım Üzerine Etkisi

Öz

Amaç: Metabolik ve volüm tabanlı 18F-FDG pozitron emisyon tomografisi/bilgisayarlı tomografi (PET/BT) parametreleri (metabolik tümör volümü (MTV), total lezyon glikolizi (TLG), maksimum standardize tutulum değerleri (maksSTD)) ve hematolojik parametrelerin (nötrofil, lenfosit, trombosit, ortalama trombosit hacmi (OTH), nötrofil lenfosit oranı (NLO) ve trombosit-lenfosit oranı (TLO)) sağkalım ile ilişkisini ve ayrıca hematolojik parametreler ile metabolik volüm tabanlı PET parametreleri arasında korelasyon olup olmadığını incelemeyi amaçladık.

Yöntemler: Ocak 2017 ile Aralık 2018 tarihleri arasında özefagus skuamöz hücreli karsinom tanısı ile Nükleer Tıp Kliniğimizde PET/BT çekilen uzak metastazı olmayan, bölgesel lenf nodu metastazı olan veya olmayan retrospektif olarak görüntüleme ve laboratuar verilerine ulaşılabilen görüntüleme öncesi opere edilmemiş, kemo-radioterapi almamış, (18F)FDG PET/BT çekimi ile eş zamanlı tam kan parametrelerine ulaşılabilen 55 hasta dahil edildi.

Bulgular: Çok değişkenli regresyon analizinde özefagus MTV (OR 2.6; 95% CI 1,04-6,57, p:0,041) ve özefagus TLG (OR 2.7; 95% CI 1.2-6.2, p:0,022) değerleri sağkalım açısından bağımsız değişkenler olarak bulundu. TLO ile özefagus MTV ve TLG si arasında negatif korelasyon izlenirken (p değerleri sırasıyla p:0,021, p:0,03) lenfosit sayısı ile özefagus MTV ve TLG arasında pozitif korelasyon izlendi (p değerleri sırasıyla p:0,004, p:0,001). Lenf nodu metastazının boyutu ve maksSTD değeri ile hem nötrofil sayısı hem de NLO arasında pozitif korelasyon saptandı.

Sonuç: Volüm tabanlı metabolik PET parametreleri olan MTV ve TLG değerleri sağkalım için bağımsız prognostik faktörler olarak bulundu. MTV ve TLG ile TLO arasında negatif korelasyon izlenirken lenfosit sayısı ile pozitif korelasyon izlendi.

Anahtar kelimeler: Sağkalım, volüm tabanlı PET/BT parametreleri, Özefagus kanseri, , nötrofil lenfosit oranı (NLO) ve trombosit-lenfosit oranı (TLO).

INTRODUCTION

Esophageal cancer is the sixth-most prevalent cancer type, which is responsible for 5.8% of cancer deaths worldwide, and it is the third-most common malignancy in the gastrointestinal tract worldwide; it is more frequently fatal in males[1].

Squamous cell carcinoma (SCC) and adenocarcinoma, which are the two most common histological types that make up more than 95% of all esophageal cancers, have quite different aetiologies. Alcohol use, smoking and their synergistic effects are the primary risk factors for SCC. SCC has been the dominant histological type in Asian countries, especially in the twentieth century[2,3].

Patients with esophageal cancer often present with a locally advanced disease characterised by invasion into the surrounding structures or lymph node involvement[4]. Neo-adjuvant chemo-radiotherapy (CRT) and definitive CRT or radiotherapy treatment are among the important treatment strategies for locally advanced esophageal SCC. Despite recent advances in treatment methods, the prognosis for esophageal cancer is poor. Overall survival and local control rates are inadequate; the 2-year survival rate may reach 30%–40% and the local recurrence rate may reach 50%. Identifying the pre-treatment prognostic factors for esophageal cancer can improve treatment strategies and aid in the classification of risk[5,6]. C-reactive proteins and cytokines, a systemic inflammatory response that plays a key role in tumour growth and shows an inflammatory response, and leukocytes, their subtypes and platelets, which are easy to apply in daily practice, have been identified as promising prognostic factors[7,8].

Several markers in the blood—such as platelets, neutrophils, lymphocytes, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and mean platelet volume (MPV)—can serve as prognostic factors for esophageal cancer, especially for the squamous type[9,10].

Whole-body 18F-fluorodeoxyglucose ((18F) FDG) positron emission tomography/computed tomography (PET/CT) is used for pre-treatment staging of esophageal cancers, the evaluation of treatment response and both post-treatment regional recurrence and distant metastasis. In addition to the maximum standard uptake value (SUVmax), the most frequently used parameters in PET/CT, metabolic tumour volume (MTV) and total lesion glycolysis (TLG), which are volume-based metabolic PET parameters, reflect tumour load more accurately and are reportedly prognostic factors for many tumours, including esophageal cancer[11-14].

The present study aimed to investigate the relationship between volume-based PET/CT parameters (MTV, TLG, SUVmax) and haematological parameters (neutrophil, lymphocyte, platelet, MPV, NLR, and PLR) with survival and the correlation between haematological parameters and volume-based PET parameters.

METHODS

We included in our study a total of 55 patients who underwent PET/CT in our Nuclear Medicine Clinic between January 2017 and December 2018 with the diagnosis of esophagus SCC, had no distant metastasis, did or did not have regional lymph node metastasis in PET/CT, whose imaging and laboratory data could be accessed retrospectively, who were not operated on before imaging, did not receive chemo-radiotherapy and had no history of steroid use, and whose simultaneous complete blood parameters could be accessed with (18F)FDG PET/CT. We calculated times from the PET/CT scan to death dates. We carried out the study under local good clinical practice guidelines and current laws and obtained approval from the ethics committee of our hospital for the use of patient data (approval no: 401/2019).

(18F) FDG PET/CT protocol

We asked all patients not to eat for at least 6 hours before undergoing scans and to stop intravenous (IV) glucose intake. We confirmed blood glucose values to be ≤140 mg/dl by the finger-stick method before FDG injection. One hour after the (18F)FDG injection of 3.5 MBq/kg–5.5 MBq/kg, we obtained the CT images (120 kV, 80 mAs/slice, 700 mm transaxial FOV, no gap, 64xo. 625 mm collimation, pitch 1.4, 0.5 s rotation time, 3.3 mm slice thickness, 512x512 matrix) from the vertex to the middle of the thigh in the supine position with the Discovery IQ 4 ring 20-cm axial FOV PET/CT device (GE Healthcare, Milwaukee, WI, USA); we then obtained the bedside PET (3D FOV 20 cm, ordered subset expectation-maximisation algorithm (OSEM) 5 iterations/12 subset, full width at half maximum (FWHM) 3 mm) images 2.5 minutes thereafter.

Evaluation of the images

All (18F)FDG PET/CT images were evaluated by two specialist in nuclear medicine with 10 years of experience, using the PET Volume Computerised Assisted Reporting (PET-VCAR, GE, USA) (GE Advantage Workstation software version AW 4.7) program.

We drew volumetric regions of interests manually from the esophageal primary lesion to include the lesion in all three planes and obtained automatic MTV, TLG (MTV X SUVmean) and SUVmax values by the device for each lesion using a 40% SUV threshold value (Figure 1, Figure 2).

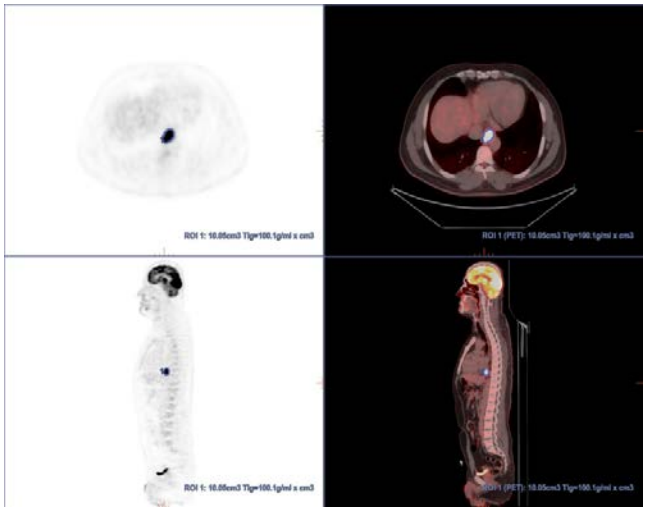

Figure 1. Male aged 45 years, survivor, survival time: 563 days; no lymph node metastasis; MTV: 10.05 cm3; TLG: 100.1g/ml.cm3; SUVmax: 11.2; NLO: 2.08; PLR: 82.00

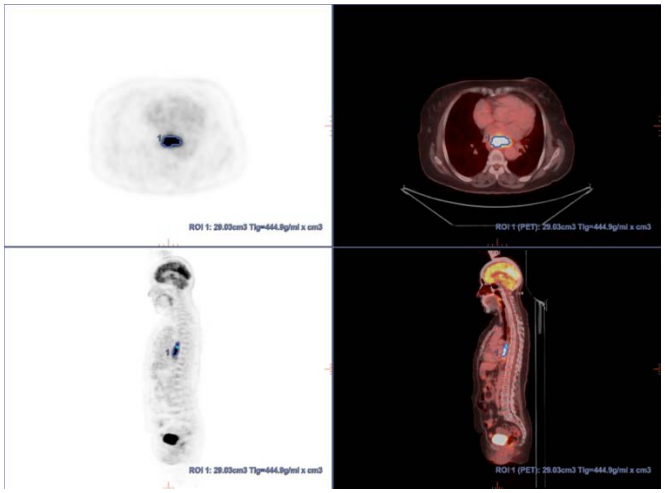

Figure 2. Female aged 63 years, non-survivor, survival time 338 days; no lymph node metastasis; MTV: 29.03 cm3; TLG: 444.9 g/ml.cm3; SUVmax: 19.3; NLR: 6.57; PLR: 438.5

Statistical Analysis

We used the SPSS 25.0 (IBM Corporation, Armonk, New York, United States) program to analyse the variables, and evaluated the conformity of univariate data to normal distribution by the Shapiro–Wilk and Francia tests, and variance homogeneity, by the Levene test. We used the independent samples T-test with the bootstrap results, and the Mann-Whitney U test with the Monte Carlo simulation technique in the comparison of two independent groups according to quantitative data. We used the Pearson Chi-square test with exact results in the comparison of categorical variables and compared column ratios with each other and expressed them according to the Benjamini–Hochberg corrected p value results. We analysed and expressed the sensitivity and specificity ratios by the ROC (receiver operating curve) curve analysis for the relationship between the classification by the cut-off value calculated for the independent variables according to mortality and the actual classification. We used the odds ratio with a 95% confidence interval to show how many times those with a risk factor were compared with those without. We used the Kaplan-Meier (product-limit method)–Log Rank (Mantel-Cox) analysis to examine the effects of factors on mortality and lifespan. We used the Cox regression analysis to measure the effects of prognostic variables on life span according to the main factor, and the Pearson correlation and Kendall's tau-b tests to examine the correlations of variables with each other. While we expressed quantitative variables as mean ± SD (standard deviation) and median (minimum/maximum), we showed categorical variables as n (%) in the tables. We analysed variables at a confidence level of 95% and considered them to be significant when the p value was less than 0.05.

RESULTS

Of the patients we included in the study, 29 (52.7%) were male and 26 (47.3%) were female. The mean age of the patients was 58.0+12.2 (57–91). The median survival of the patients was 365 (49–981) days (Table 1).

Table I: Comparison of PET and haematological parameters of survivors and non-survivors

	Total	Alive	Exitus	P
	(n=55)	(n=18)	(n=37)	
	Mean±SD.	Mean±SD.	Mean±SD.	
Age	57,98±12,16	55,44±10,25	59,22±12,94	0,284 t
	n (%)	n (%)	n (%)	
Gender				
Female	26 (47,3)	8 (44,4)	18 (48,6)	0,499 p
Male	29 (52,7)	10 (55,6)	19 (51,4)	
Lymph metastasis				
Absent	25 (45,5)	12 (66,7) B	13 (35,1)	**0,043** p
Exist	30 (54,5)	6 (33,3)	24 (64,9) A	3,7 (1,1-12,1) or
	Median (Min/Max)	Median (Min/Max)	Median (Min/Max)	
Survival	365 (49 / 981)	788,5 (359 / 981)	225 (49 / 935)	**<0,001** u
Esophagus MTV	34,79 (4,21 / 178)	22,015 (4,25 / 77,2)	46,83 (4,21 / 178)	**<0,001** u
Esophagus TLG	322 (15,6 / 1651)	128,55 (15,6 / 372,7)	410,5 (17,1 / 1651)	**<0,001** u
Esophagus SUVmax	10,8 (2,6 / 40,9)	9,65 (2,6 / 28,3)	11,3 (4,87 / 40,9)	0,223 u
Lymph node size	14,5 (6 / 63)	11,5 (9 / 19)	15,5 (6 / 63)	0,256 u
Lymph node SUVmax	5,65 (1,4 / 28,7)	5,3 (2,6 / 10,2)	5,65 (1,4 / 28,7)	0,933 u
NLR	2,72 (0,77 / 9,74)	2,79 (1,39 / 9,74)	2,72 (0,77 / 7,83)	0,927 u
PLR	158,4 (57,74 / 762)	156,37 (82,01 / 762)	160 (57,74 / 438,57)	0,654 u
	Mean±SD.	Mean±SD.	Mean±SD.	
MPV	8,69±1,59	8,50±1,83	8,79±1,47	0,601 t
Neutrophil	4,84±1,97	4,75±2,03	4,89±1,97	0,812 t
Neutrophil	1,69±0,70	1,64±0,67	1,71±0,72	0,726 t
Platelet	267,80±87,72	274,01±80,10	264,79±92,11	0,727 t

t Independent Samples t test(Bootstrap), p Pearson Chi-Square Test(Exact), u Mann Whitney U Test(Monte Carlo), or Odds Ratio %95 Confidence interval, A Significant for Alive , B Significant for Exitus, SD.:Standard deviation, Min.:Minimum, Max.:Maximum

Age and gender did not differ statistically significantly (p values were p: 0.284, p: 0.499, respectively), but the percentage of those with lymph node positivity was statistically significantly higher in non-survivors than in survivors (64.9% vs 33.3% p: 0.043) (Table 1).

We found the esophagus MTV median values (46.83 (4.21–138) cm3 vs 22.01 (4.25–77.2) cm3, p < 0.0019) and esophagus TLG median values (410.7 g/ml.cm3 (17.1–1651) vs 128.5 g/ml.cm3 (15.6–372.7), p < 0.001) to be significantly higher in those who died than in those who survived, respectively.

We detected no statistically significant difference between esophagus SUVmax, lymph node SUVmax, lymph node size, NLR and PLR median values among survivors and non-survivors. Additionally, platelet, lymphocyte, neutrophil, and MPV mean values did not differ statistically significantly between survivors and non-survivors (Table 1).

In the ROC curve analysis, we determined the sensitivity and the specificity to be 73% and 88.9%, respectively, for MTV (cut-off > 30.29 cm3) and 54% and 100%, respectively, for TLG (cut-off > 372, 7 g/ml.cm3) in predicting survivors and non-survivors; the area under the curve was found to be statistically significant in determining mortality (p values were p: 0.001, p < 0.001, respectively) (Table 2).

Table II: ROC curve analysis of esophagus MTV and TLG values: cut-off, sensitivity and specificity values

	Alive	Exitus	AUC±SE	Odds Ratio (95%G.A)	P Değeri [b]
	n (%)	n (%)			
Esophagus MTV					
≤30,29	16 (88,9) [sp]	10 (27,0)	0,781±0,065	21,6 (4,2 - 111,3)	**0,001**
>30,29	2 (11,1)	27 (73,0) [ss]			
Esophagus TLG					
≤372,7	18 (100,0) [sp]	17 (45,9)	0,824±0,055	43,3 (2,4-772,6)	**<0,001**
>372,7	0 (0,0)	20 (54,1) [ss]			

Roc Curve Analysis (Youden index J - Honley&Mc Nell), AUC: Area under the ROC curve, SE: Standard Error, ss Sensitivity, sp Specificity , [b] Cut Off için P Değeri

In the univariate analysis, there was no statistically significantly relationship between lymph node SUVmax value, lymph node size, primary tumor SUVmax value, haematologic parameters, presence or absence of lymph node metastasis and survival time (table 3). while the life span was shortened statistically significantly above cut-off values in esophagus MTV and TLG values (p values p < 0.001, p < 0.001, respectively) (Table 3) (Figure 3, Figure 4).

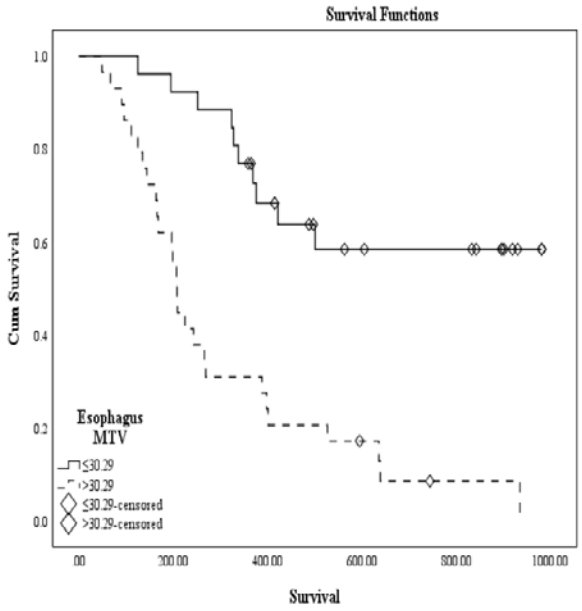

Figure 3. Survival curve esophagus MTV p<0.001

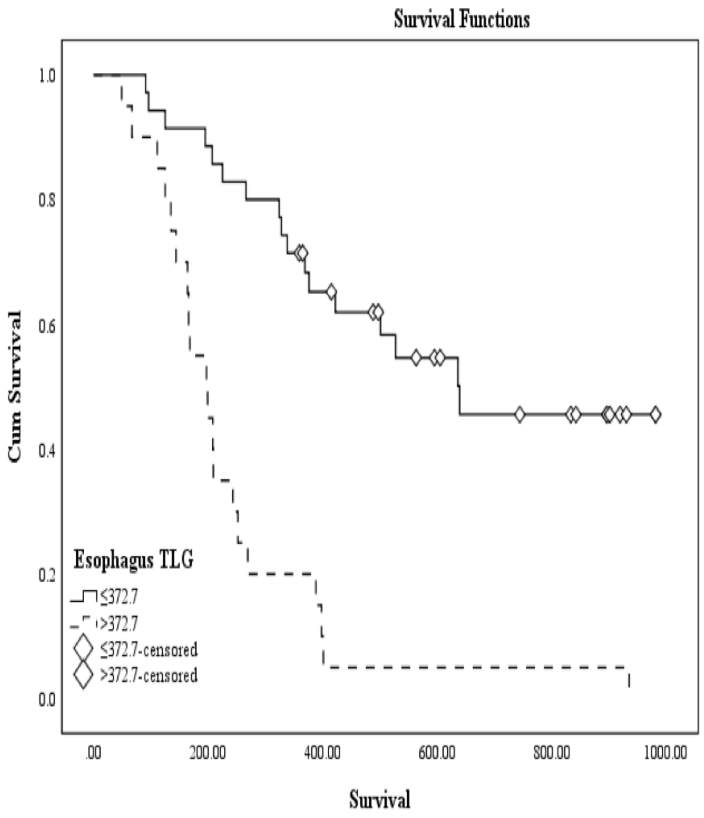

Figure 4. survival curve esophagusTLG p<0.001

Table III: Univariate analysis for survival

	Estimate Survival	Estimate Proportion Surviving at the 1 / 2 Year (%)	P Value
	Mean ± SE.		
Lymph node metastasis			
Absent	602,3±75,33	60 /48	0,063*
Exist	409,5±55,99	46,7 / 18	
Esophagus MTV			
≤30,29	711,7±66,72	76,9 / 58,5	**<0,001***
>30,29	309,8±47,51	31 / 8,6	
Esophagus TLG			
≤372,7	642,1±59,35	71,4 / 45,6	**<0,001***
>372,7	241,4±42,77	20 / 5	
	OR	**95%CI**	
Esophagus SUVmax	1,021	0,974-1,070	0,391**
Lymph node size	0,895	0,928-1,090	0,895**
Lymph node SUVmax	1,032	0,994-1,070	0,098**
Neutrophil	1,166	0,951-1,093	0,124**
Lympocyte	1,333	0,848-20,96	0,213**
Platelet	1,00	0,997-1,004	0,897**
MPV	1,073	0,856-1,344	0,543**
NLR	1,115	0,954-1,303	0,171**
PLR	1,115	0,997-1,003	0,847**

**Kaplan Meier Test ; Log Rank (Mantel-Cox) , ** Cox Regression , SE: Standard Error, OR:odds ratio , C.I. :Confidence interval 0,954-1,303*

In the multivariate regression analysis, esophagus MTV (OR 2.6; 95% CI 1.04-6.57, p: 0.041) and esophagus TLG (OR 2.7; 95% CI 1.2-6.2, p: 0.022) values were found as independent variables in terms of survival (Table4).

Table IV: Multivariate regression analysis

Independent variables	B±Sh	P Değeri	Odds Ratio (95%CI)
Esophagus MTV	-0,951±0,466	**0,041**	2,6 (1,04 - 6,5)
Esophagus TLG	-0,987±0,430	**0,022**	2,7 (1,2-6,2)
1/2 year survival rates (Sh): 55 (0,072) / 27,7 (0,073) - Base Line Hazard: 0,038			

Cox Regression-Enter Model, C.I. :Confidence interval B: regression coefficients SE: Standard error

When we compared parameters obtained from PET/CT and haematologic parameters, we detected a negative correlation between PLR and esophagus MTV and TLG (p values were p: 0.021, p: 0.003, respectively), while there was a positive correlation between lymphocyte and esophagus MTV and TLG (p values were p: 0.004, p: 0.001, respectively). We found a positive correlation between the size of lymph node metastasis and SUVmax value and both neutrophils and NLR (Table 5). We detected no statistically significant correlation between the haematologic parameters among those with and those without lymph node metastasis in PET/CT (Table 6).

Table V: Relationship between PET parameters of esophagus and lymph node and haematological parameters

	Esophagus MTV		Esophagus TLG		Esophagus SUVmax		Lymph node size		Lymph node SUVmax	
	r	P	r	P	r	P	r	P	r	P
NLR	-0,171	0,065	-0,141	0,127	-0,064	0,490	**0,342**	**0,009**	**0,270**	**0,037**
PLR	**-0,214**	**0,021**	**-0,273**	**0,003**	-0,105	0,260	-0,063	0,629	0,074	0,568
MPV	0,068	0,463	0,041	0,658	0,008	0,931	-0,090	0,496	0,007	0,957
Neutrophil	0,073	0,433	0,132	0,155	0,052	0,576	**0,464**	**<0,001**	**0,325**	**0,012**
Lymphocyte	**0,269**	**0,004**	**0,297**	**0,001**	0,101	0,282	0,135	0,307	0,098	0,453
Platelet	0,095	0,306	0,082	0,380	0,051	0,581	0,145	0,267	0,187	0,148

Pearson Correlation Test, Kendall's tau b Test, r: Correlation Coefficient

Table VI: Relationship between lymph node metastasis and haematological parameters

	Lymph node metastasis P		
	Absent	**Exist**	
	(n=25)	**(n=30)**	
	Median (Min/ Max.)	**Median (Min/ Max.)**	
NLR	3,04 (0,77 / 9,74)	2,69 (1,22 / 7,83)	0,740 [t]
PLR	192,25 (82,01 / 762,00)	140,84 (57,74 / 325,00)	0,068 [t]
	Mean±SD.	**Mean±SD.**	
MPV	8,71±1,85	8,67±1,37	0,927 [t]
Neutrophil	4,56±1,87	5,08±2,05	0,313 [t]
Lymphocyte	1,52±0,75	1,82±0,64	0,113 [t]
Platelet	276,68±91,14	260,41±85,61	0,525 [t]

t Independent Samples t test(Bootstrap), u Mann Whitney U Test(Monte Carlo), SD.:Standard deviation, Min.:Minimum, Max.:Maximum

DISCUSSION

The most important finding in our retrospective cohort is that esophageal MTV and TLG values are independent prognostic values for survival.

In the present study, we found no statistically significant difference between survivors and non-survivors in terms of age and gender, and neither were found as significant prognostic factors for survival.

Studies of prognosis in patients with esophageal cancer using (18F)FDG PET/CT frequently emphasised the SUVmax value and reported the SUVmax of the primary tumour to be significantly correlated with overall survival (OS), progression-free survival (PFS), local control and response to simultaneous CRT[15,16]. However, many studies reported that the SUVmax value was not a prognostic factor for OS and PFS[14,17-19]. In their study with simultaneous CRT in esophageal cancer, Song et al. reported that the SUVmax difference before and after treatment might show a pathological response, but the SUVmax value before treatment was not a prognostic value in showing the treatment response[20]. In the present study, we found that SUVmax median values of both the primary tumour and the lymph nodes not only did not show a statistically significant difference between survivors and non-survivors but also had no prognostic value for survival (p values were p: 0.223, p: 0.895, respectively). In addition, in this study, no statistically significant relationship was found between the SUVmax of the primary tumor and lymph node and the survival time in univariate analysis (p values were p: 0.391, p: 0,098, respectively).

Because it is a measurement based on a single pixel in the most active part of the tumour and does not fully reflect tumour heterogeneity except for solid tumours, the SUVmax value

causes excessive simplification. Since MTV and TLG—which are volume-based PET parameters—reflect the total tumour volume, metabolic activity and heterogeneity in the tumour in three dimensions, they may potentially be more sensitive than the single-pixel approach[21,22].

In their 151-patient study involving 146 squamous cancer cases, Hyun et al. found age, TNM stage, MTV and SUVmax as prognostic factors for survival in a univariant analysis (p < 0.001, p: 0.001 for MTV and SUVmax, respectively), whereas MTV and SUVmax values were not found as independent prognostic factors in the multivariant analysis, and the effect of MTV on survival was seen to be of greater prognostic power than the SUVmax value[14].

In a recent study of 38 patients with locally advanced esophageal cancer, TLG was found to be a prognostic value for OS, while MTV and SUVmax values were not prognostic factors. OS was significantly shorter in patients with TLG values higher than 232.98 g/ml.cm3 (p: 0.003)[23].

In their study investigating the prognostic values of MTV, TLG and SUVmax in patients with esophageal cancer who received definitive chemo-radiotherapy, Yıldırım et al. showed that for DFS and OS, MTV and TLG, regional lymph node metastasis and concomitant chemotherapy were major prognostic factors in patients with esophageal carcinoma. In addition, they reported that MTV and TLG were important in predicting nodal metastasis[24].

In the present study, we found MTV (cut-off > 30.29 cm3) and TLG (cut-off > 372.7 g/ml.cm3) values to be prognostic factors for survival in univariate analyses, and MTV (OR 2.6; 95% CI 1.04–6.57, p: 0.041) and TLG (OR 2.7; 95% CI 1.2–6.2, p: 0.022) to be independent prognostic values for survival. In distinguishing survivors and non-survivors by the ROC curve analysis for esophagus MTV and esophagus TLG, the sensitivity (73%, 54%, respectively) and specificity (88.9%, 100%, respectively) values were found to be quite high.

In the study by Hyun et all., the N phase was found to be a significant prognostic factor for survival in univariate analyses, but not in multivariate analyses (p < 0.001, p: 0.1, respectively)[14]. Other studies report lymph node positivity as the strongest prognostic factor in cases undergoing an operation[25,26]. In a study in which Ogino et all. Compared the localization of lymph node metastases to disease-free survival and mean survival in patients with esophageal cancers; While they found regional abdominal and left gastric lymph node metastases related to OS and PFS, they could not find a relationship between cervical and thoracic lymph nodes and OS and PFS[27]. In the present study, lymph node positivity in PET/CT was significantly higher in non-survivors than in survivors. However, we established in univariate and multivariate analyses that the presence of lymph node metastasis was not a significant variable for survival. The reason for this may be that the lymph nodes are evaluated only positively and negatively and due to the low number of cases, the evaluation could not be made according to the lymph node localizations.

It is widely accepted that the inflammation response plays a critical role in tumour progression and can affect the survival results in cancer patients. Among inflammatory markers, high neutrophil, platelet and macrophage counts, low lymphocyte counts and high NLR, PLR and low lymphocyte-to-monocyte ratio were considered to be associated with an adverse prognosis in solid tumours[28].

In a meta-analysis including 1540 patients, which evaluated the relationship between NLR and OS, a significantly worse OS (HR 1.40, 95% CI 1.08–1.81, P = 0.01) was found in patients

with a high NLR before treatment than that in those with a low NLR. High NLR and PLR were both found to be significant markers for a deeper tumour invasion and lymph node metastasis. However, neither high NLR nor high PLR was significantly associated with tumour differentiation or vascular invasion[29].

A recent meta-analysis demonstrated that a high NLR predicts negative survival in esophageal cancer, both in SCC and adenocarcinoma, and could, therefore, be a promising predictive factor[30]. In the present study, however, we found no statistical significance in the median and mean values of haematological parameters in survivors and non-survivors. We also found that haematological parameters were not a prognostic factor for survival. In addition, we did not find any statistically significant relationship between haematological parameters and survival time in univariate analysis.

There are very few studies comparing volume-based PET parameters and haematological parameters in patients with esophageal cancer. In a study comparing PET parameters and haematological parameters in 52 patients with esophageal cancer, Sürücü et al. found a positive correlation between MTV and NLR, while they did not find any correlation between MTV and MPV and NLR, nor between SUVmax and NLR, MPV and PLR. In addition, they found no correlation in haematological parameters in patients with or without lymph node positivity. However, they did not use the TLG value in their study[31]. In the present study, we observed a negative correlation between PLR and esophagus MTV and TLG (p values were p: 0.021 and p: 0.03, respectively), and a positive correlation between lymphocyte and esophagus MTV and TLG (p values were p: 0.004 and p: 0.001, respectively). We found a positive correlation between the size and SUVmax value of lymph node metastasis and both neutrophils and NLR. We also found a low, negative and statistically significant correlation between the lymph node size and MPV.

Our study had some limitations. First, this study is retrospective, but most studies in the literature have also been designed retrospectively. Since patients did not have post-treatment PET/CT evaluations, PET parameters were evaluated as pre-therapeutic metabolic index in all patients, and PET parameters and haematological parameters were associated with OS.

CONCLUSION

We found MTV and TLG values—the volume-based metabolic PET parameters—to be independent prognostic factors for survival. Both esophagus and lymph node SUVmax values and haematological parameters had no effect on survival. While we observed a negative correlation between both MTV and TLG and PLR, there was a positive correlation between MTV and lymphocyte counts We found a positive correlation between lymph node size and SUVmax value and both neutrophils and NLR. We established volume-based PET parameters as the most valuable parameters in terms of survival.

Ethics Committee Approval: We carried out the study under local good clinical practice guidelines and current laws and obtained approval from the ethics committee of our hospital for the use of patient data (approval no: 401/2019).

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