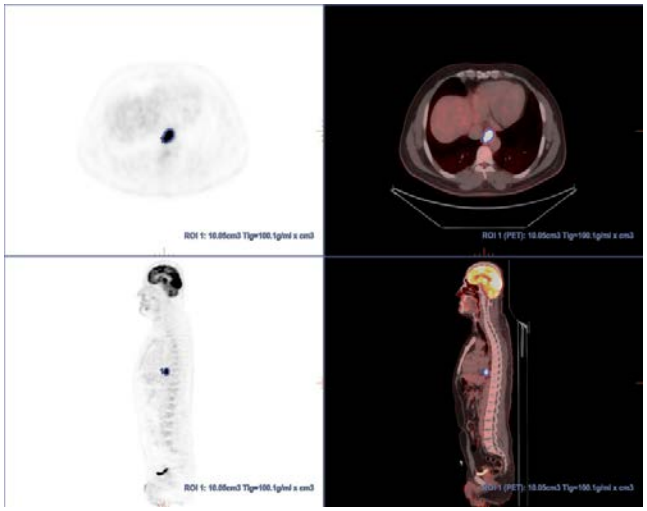

Figure 1. Male aged 45 years, survivor, survival time: 563 days; no lymph node metastasis; MTV: 10.05 cm3; TLG: 100.1g/ml.cm3; SUVmax: 11.2; NLO: 2.08; PLR: 82.00

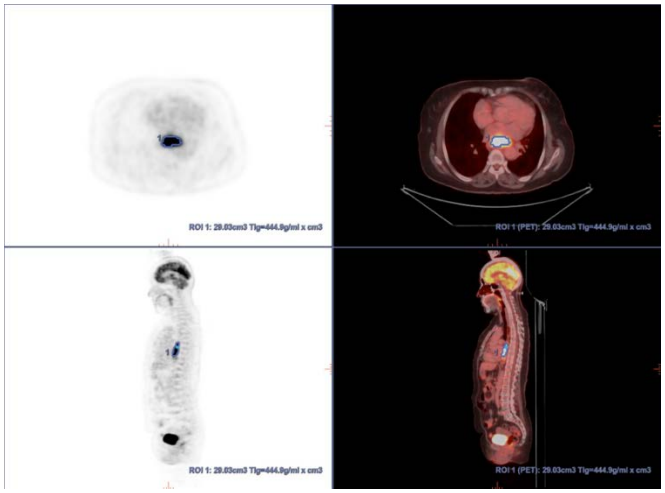

Figure 2. Female aged 63 years, non-survivor, survival time 338 days; no lymph node metastasis; MTV: 29.03 cm3; TLG: 444.9 g/ml.cm3; SUVmax: 19.3; NLR: 6.57; PLR: 438.5

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).

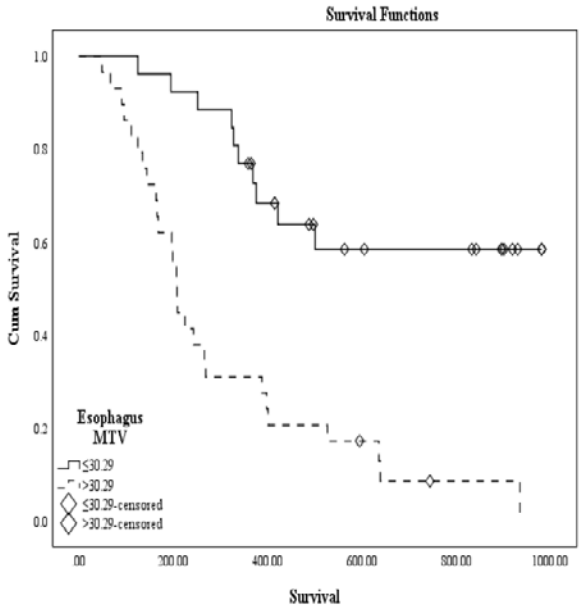

Figure 3. Survival curve esophagus MTV p<0.001

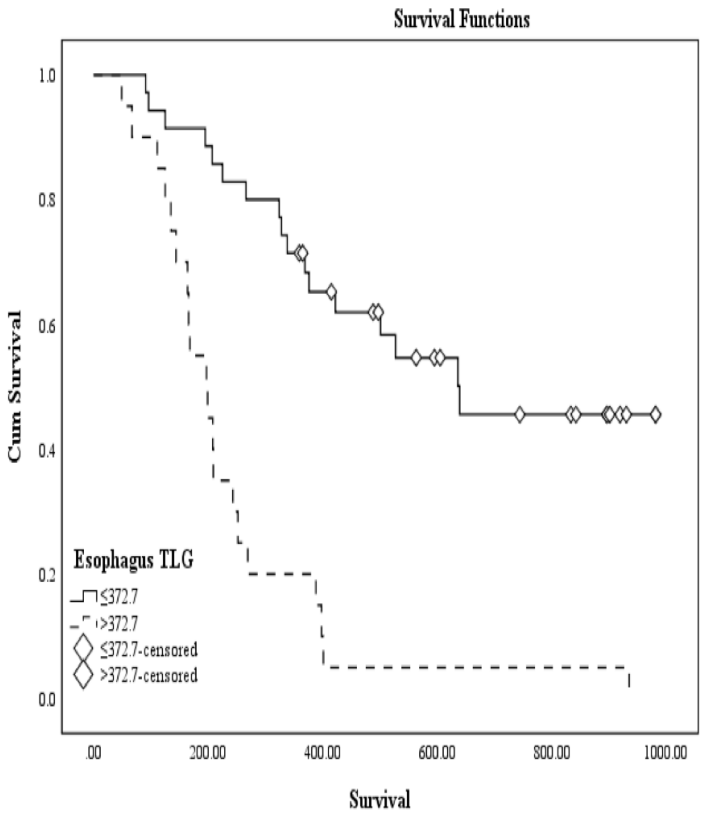

Figure 4. survival curve esophagusTLG p<0.001

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).

Declaration of Conflicting Interests: The authors declare that they have no conflict of interest.

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REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, et al. Global Cancer Statistics 2018: GLOBOCAN Estimates of

Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2018; 68: 394–424.

2. Blot WJ TR. Cancer Epidemiology and Prevention. 4th ed. Thun MJ, Linet MS, Cerhan JR, Haiman CA SD (eds). New york, Oxford University Press, 2018; 579–92.

3. Baquet CR, Commiskey P, Mack K, et al. Esophageal cancer epidemiology in blacks and whites: Racial and gender disparities in incidence, mortality, survival rates and histology. J Natl Med Assoc. 2005; 97: 1471–8.

4. Enzinger PC, Mayer RJ. Esophageal cancer. N Engl J Med. 2003; 349: 2241–52.

5. Shapiro J, van Lanschot JJB, Hulshof MCCM, et al. Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): Long-term results of a randomised controlled trial. Lancet Oncol. 2015; 16: 1090–8.

6. Stavrou EP, McElroy HJ, Baker DF, et al. Adenocarcinoma of the oesophagus: incidence and survival rates in New South Wales, 1972–2005. Med J. 2009; 191: 310–4.

7. Mantovani A, Allavena P, Sica A, et al. Cancer-related inflammation. Nature. 2008; 454: 436–44.

8. Matthews LM, Noble F, Tod J, et al. Systematic review and meta-analysis of immunohistochemical prognostic biomarkers in resected oesophageal adenocarcinoma. Br J Cancer. 2015; 113: 1746.

9. Templeton AJ, McNamara MG, Šeruga B, et al. Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: a systematic review and meta-analysis. J Natl Cancer Inst. 2014; 106: dju124.

10. Yang X, Huang Y, Feng JF LJ. Prognostic significance of neutrophil-to-lymphocyte ratio in esophageal cancer: a meta- analysis. Onco Targets Ther. 2015; 10: 789–94.

11. Liao S, Penney BC, Wroblewski K, et al. Prognostic value of metabolic tumor burden on 18F-FDG PET in nonsurgical patients with non- small cell lung cancer. Eur J Nucl Med Mol Imaging. 2012; 39: 27–38.

12. Dibble EH, Alvarez AC, Truong MT, et al. 18F-FDG metabolic tumor volume and total glycolytic activity of oral cavity and oropharyngeal squamous cell cancer: adding value to clinical staging. J Nucl Med. 2012; 53: 709–15.

13. Lin J, Kligerman S, Goel R, et al. State-of-the-art molecular imaging in esophageal cancer management: implications for diagnosis, prognosis, and treatment. J Gastrointest Oncol. 2015; 6: 3–19.

14. Hyun SH, Choi JY, Shim YM, et al. Prognostic value of metabolic tumor volume measured by 18F-fluorodeoxyglucose positron emission tomography in patients with esophageal carcinoma. Ann Surg Oncol. 2010; 17: 115–22.

15. Atsumi K, Nakamura K, Abe K, et al. Prediction of outcome with FDG-PET in definitive chemoradiotherapy for esophageal cancer. J Radiat Res. 2013; 54: 890–8.

16. Alie O, Michel P, Ménard JF, et al. The predictive value of treatment response using FDG PET performed on day 21 of chemoradiotherapy in patients with oesophageal squamous cell carcinoma. A prospective, multicentre study (RTEP3). Eur J Nucl Med Mol Imaging. 2013; 40: 1345–55.

17. Hatt M, Tixier F, Cheze Le Rest C, et al. Robustness of intratumour 18F-FDG PET uptake heterogeneity quantification for therapy response prediction in oesophageal carcinoma. Eur J Nucl Med Mol Imaging. 2013; 40: 1662–71.

18. Van Westreenen HL, Plukker JT, Cobben DC, et al. Prognostic value of the standardized uptake value in esophageal cancer. AJR Am J Roentgenol. 2005; 185: 436–40.

19. Omloo JM, Sloof GW, Boellaard R, et al. Importance of fluorodeoxyglucose-positron emission tomography (FDG-PET) and endoscopic ultrasonography parameters in predicting survival following surgery for esophageal cancer. Endoscopy. 2008; 40: 464–71.

20. Song SY, Kim JH, Ryu JS, et al. FDG-PET in the prediction of pathologic response after neoadjuvant chemoradiotherapy in locally advanced, resectable esophageal cancer. Int J Radiat Oncol Biol Phys. 2005; 63: 1053–9.

21. Kitajima K, Doi H, Kuribayashi K, et al. Prognostic value of pretreatment volume-based quantitative 18F-FDG PET/CT parameters in patients with

malignant pleural mesothelioma. Eur J Radiol. 26: 2287-96.

22. Choi ES, Ha SG, Kim HS, et al. Total lesion glycolysis by 18F-FDG PET/CT is a reliable predictor of prognosis in soft-tissue sarcoma. Eur J Nucl Med Mol Imaging. 2013; 40: 1836–42.

23. Hong JH, Kim HH, Han EJ, et al. Total lesion glycolysis using 18F-FDG PET/CT as a prognostic factor for locally advanced esophageal cancer. J Korean Med Sci. 2016; 31: 39–46.

24. Yildirim BA, Torun N, Guler OC, et al. Prognostic value of metabolic tumor volume and total lesion glycolysis in esophageal carcinoma patients treated with definitive chemoradiotherapy. Nucl Med Commun. 2018; 39: 553–63.

25. Rice TW, Apperson-Hansen C, DiPaola LM, et al. Worldwide Esophageal Cancer Collaboration: clinical staging data. Dis Esophagus. 2016; 29: 707–14.

26. Mariette C, Piessen G, Briez N et al. The number of metastatic lymph nodes and the ratio between metastatic and examined lymph nodes are independent prognostic factors in esophageal cancer regardless of neoadjuvant chemoradiation or lymphadenectomy extent. Ann Surg. 2008; 247: 365–71.

27. Ogino I, Watanabe S, Misumi T, et al. Lymph Node Metastases Diagnosed by 18F-FDG-PET/CT in Esophageal Squamous Cell Cancer Treated With Concurrent Chemoradiotherapy. Anticancer Res. 2019; 39: 4977-85.

28. Sun Y, Zhang L. The clinical use of pretreatment NLR, PLR, and LMR in patients with esophageal squamous cell carcinoma: Evidence from a meta-analysis. Cancer Manag Res. 2018; 10: 6167–79.

29. Yodying H, Matsuda A, Miyashita M, et al. Prognostic Significance of Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio in Oncologic Outcomes of Esophageal Cancer: A Systematic Review and Meta-analysis. Ann Surg Oncol. 2016; 23: 646–54.

30. Pirozzolo G, Gisbertz SS, Castoro C, et al. Neutrophil-to-lymphocyte ratio as prognostic marker in esophageal cancer: A systematic review and meta-analysis. J Thorac Dis. 2019; 11: 3136–45.

31. Sürücü E, Demir Y, Şengöz T. The correlation between the metabolic tumor volume and haematological parameters in patients with esophageal cancer. Ann Nucl Med. 2015; 29: 906–10.