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ORIGINAL ARTICLE – OPEN ACCESS

Pretreatment Metabolic Tumor Volume of Primary Tumor and Total Lesion Glycolysis of Lymph Nodes are Predictive in Nasopharyngeal Cancer

Mete Gündoğ[1], Ümmühan Abdulrezzak[2]

ABSTRACT

Objective: Conventional prognostic factors are not yet sufficient to predict treatment outcomes factors in nasopharyngeal carcinoma (NPC). Parameters from PET/CT are still being investigated as a prognostic factor in nasopharyngeal cancer.

Materials and Methods: We retrospectively analyzed total lesion glycolysis (TLG), metabolic tumor volume (MTV), and maximum standardized uptake value (SUVmax) in patients with non-metastatic nasopharyngeal cancer treated with intensity-adjusted radiotherapy. According to the ROC analysis, we divided the whole cohort into two groups. Kaplan-Meier tests were used to evaluate survival differences between groups. Univariate and multivariate analyzes were performed to find the factors affecting the prognosis. P<0.05 was accepted as statistically significant.

Results: Ninety-one non-metastatic nasopharyngeal cancer patients were enrolled in this study. According to cut-off values, both MTVtumor and TLGnode were found as an independent prognostic factor for overall survival (OS). High MTVtumor (>21.5) and high TLGnode (>186.7) correlated with 4.9 and 4-fold increased mortality risk, respectively. Multivariate analyses showed high MTVtotal (>59.5) was associated with a 3.3 fold increased risk of locoregional recurrence. High TLGtotal (>181.56) was found to be independent prognostic factor for distant metastasis-free survival and it was associated with a 5.4 fold increased risk. The 5-years OS rate was 58.5% in high MTVtotal (>59.5) patients and 82.4% in low MTVtotal (<59.5) patients (p<0.01). The 5-years OS rates were 64.2% in patients with high TLGtotal (>181) and 88% in patients with low TLGtotal (p<0.01).

Conclusion: The results of our study showed that MTVtumor and TLGnode values are significant independent prognostic factors for OS.

Keywords: Metabolic tumor volume, total lesion glycolysis, PET-derived parameters, nasopharyngeal cancer

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[1]Department of Radiation Oncology, Erciyes University Faculty of Medicine, Kayseri, Turkey
[2]Department of Nuclear Medicine, Erciyes University Faculty of Medicine, Kayseri, Turkey

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Correspondence
Mete Gündoğ,
Department of Radiation Oncology, Erciyes University Medicine Faculty, Kayseri, Turkey
Phone: +90 352 207 66 66
e-mail: mgundog@erciyes.edu.tr

INTRODUCTION

Nasopharyngeal carcinoma (NPC) behaves differently from other head and neck cancers due to its ethnic variation, different geographical distribution and histopathological features (1). Radiotherapy (RT) is the treatment of choice for nasopharyngeal carcinoma because of anatomical location and high radio-sensitivity. The addition of chemotherapy to radiotherapy in locally advanced disease improved the treatment outcomes (2). TNM staging, gender, age, pre-treatment Epstein-Barr virus (EBV) DNA levels, serum lactate dehydrogenase (LDH), body mass index (BMI), and inflammatory biomarkers may be considered as individual-specific prognostic factors for survival (3–8). These prognostic factors may provide useful clinical information, but may be insufficient to predict the outcome of treatment in NPC. 18F- Fluorodeoxyglucose (18F-FDG) positron emission tomography (PET), which identifies tumors by measuring enhanced tumor glycolysis, has been widely used for the detection of recurrent disease and distant metastasis, as well as staging in patients with NPC. Also, maximum standardized uptake value (SUVmax) is a recommended factor to predict the prognosis of the primary tumor in some studies. There are some controversial thoughts that the SUVmax threshold provides accurate tumor delineation (9). In addition to SUVmax, SUVmean, metabolic tumor volume (MTV) and total lesion glycolysis (TLG) have been analyzed in the literature. Many studies have shown that the higher SUVmax, MTV, and TLG values are associated with worse treatment outcomes (10). There are few studies showing the meaning of parameters derived from PET for locally advanced NPC patients (11–13). More studies that evaluate the significance of PET-derived parameters concerning disease prognosis are needed. Therefore, we designed our study to investigate the prognostic value of PET-derived parameters in patients with locally advanced NPC.

MATERIALS and METHODS

The Study Design and Place

This study was designed as a retrospective study and carried out in the departments of radiation oncology and the nuclear medicine at Erciyes University. Written informed consent from the patients was obtained before treatment

Table 1. Comparison of the patient characteristics concerning MTV between groups

	*MTVtumor ≤21.5 54 (59.3)		MTVtumor >21.5 37 (40.7)			**MTVnode ≤93.4 84 (92.3)		MTVnode >93.4 7 (7.7)		
	n	%	n	%	p	n	%	n	%	p
Gender										
Female	17	31.5	11	29.7	1.00	28	33.3	0	0	0.09
Male	37	68.5	26	70.3		56	66.7	7	100	
Age										
50≤	32	59.3	23	62.2	0.83	54	64.3	1	14.3	**0.01**
50>	22	40.7	14	37.8		36	35.7	6	85.7	
T category										
T1-2	31	57.4	9	24.3	**<0.01**	35	41.7	5	71.4	0.23
T3-4	23	42.6	28	75.7		49	58.3	2	28.6	
N category										
Negative	10	18.5	6	16.2	1.00	16	19	0	0	0.34
Positive	44	81.5	31	83.8		68	81	7	100	
TNM stage										
II	14	25.9	4	10.8		18	21.4	0	0	0.25
III	22	40.7	10	27		30	35.7	2	28.6	
IVA	18	33.3	23	62.2	**0.02**	36	42.9	5	71.4	
Treatment response										
Complete	47	87	26	70.3	0.06	67	79.8	6	85.7	1.00
Partial	7	13	11	29.7		17	20.2	1	14.3	
Locoregional recurrence										
–	43	79.6	24	64.9	0.14	62	73.8	5	71.4	1.00
+	11	20.4	13	35.1		22	26.2	2	28.6	
Distant metastasis										
–	47	87	28	75.7	0.17	71	84.5	4	57.1	0.10
+	7	13	9	24.3		13	15.5	3	42.9	
Death										
–	48	88.9	23	62.2	**<0.01**	69	82.1	2	28.6	**<0.01**
+	6	11.9	14	37.8		15	17.9	5	71.4	

MTV: Metabolic tumor volume; *MTVtumor: The cut-off value of MTVtumor is 12.5 (AUC: 0.675, p<0.01); **MTVnode: The cut-off value of the MTVnode is 93.4 (AUC: 0.703, p<0.01); TNM: T and N categories are according to 8th edition American Joint Commission on Cancer staging system; p: Fisher's Exact test value

for the publication of results. This study was approved by the Erciyes University Medical School Ethics Committee (No: 2015/524).

Patient Selection

Patients with nasopharyngeal cancer who were treated with definitive chemoradiotherapy from January 2010 to January 2018 were included in this retrospective study. The inclusion criteria were defined as follows: (I.) age ≥18 years (II.) Karnofsky performance score ≥70, (III.) histologically proven non-keratinizing undifferentiated type carcinoma, (IV.) clinical and radiological proof of T1-4 and N0-3, (V.) no prior cancer history, (VI.) received platinum-based concurrent chemo-radiotherapy, (VII.) performed FDG-PET/CT scans before treatment. The exclusion criteria were defined as follows: (I.) age <18 years, (II.) Karnofsky performance score <70, (III.) presence of distant metastases, (IV.) previous history of cancer, (V.) uncontrolled diabetes mellitus, (VI.) no pre-treatment FDG-PET-CT scans, (VII.) insufficient liver and kidney function tests. One hundred and twenty-four patients were screened for this study and 91 patients who have been suitable for the inclusion criteria were analyzed. All patients were re-staged according to the 8th edition of the American Joint Committee on Cancer staging classification (14).

18F-FDG PET/CT Protocol

Philips Gemini TF PET/CT scanning system (Philips Medical Systems, Cleveland, Ohio, USA) was used for 18F-FDG PET/CT imaging. CT acquisition (70–120 mAs, 120 kV, slice thickness of 0.5 mm) was optimized for attenuation correction and improved ana-

Table 2. Comparison of the patient characteristics concerning TLG between groups

	*TLGtumor ≤142 53 (58.2)		TLGtumor >142 38 (41.8)			**TLGnode ≤186 69 (75.8)		TLGnode >186 22 (24.2)		
	n	%	n	%	p	n	%	n	%	p
Gender										
Female	14	26.4	14	36.8	0.35	24	34.8	4	18.2	0.18
Male	39	73.6	24	63.2		45	65.2	18	81.8	
Age										
50≤	33	62.3	22	57.9	0.82	45	65.2	10	45.5	0.13
50>	20	37.7	16	42.1		24	34.8	12	54.5	
T category										
T1-2	33	62.3	7	18.4	**<0.01**	26	37.7	14	63.6	0.04
T3-4	20	37.7	31	81.6		43	62.3	8	36.4	
N category										
Negative	10	18.9	6	15.8	0.78	16	23.2	0	0	0.01
Positive	43	81.1	32	84.2		53	76.8	22	100	
TNM stage										
II	15	28.3	3	7.9		16	23.2	2	9.1	
III	22	41.5	10	26.3		22	31.9	10	45.5	
IVA	16	30.2	25	65.8	**<0.01**	31	44.9	10	45.5	0.27
Treatment response										
Complete	49	92.5	24	63.2	**<0.01**	54	78.3	19	86.4	0.54
Partial	4	7.5	14	36.8		15	21.7	3	13.6	
Locoregional recurrence										
–	43	81.1	24	63.2	0.09	52	75.4	15	68.2	0.58
+	10	18.9	14	36.8		17	24.6	7	31.8	
Distant metastasis										
–	47	88.7	28	73.7	0.09	60	87	15	68.2	0.05
+	6	11.3	10	26.3		9	13	7	31.8	
Death										
–	46	86.8	25	65.8	**0.02**	57	82.6	14	63.6	0.07
+	7	13.2	13	34.2		12	17.4	8	36.4	

TLG: Total lesion glycolysis; *TLGtumor: The cut-off value of TLGtumor is 142.2 (AUC: 0.627, p=0.08); **TLGnode: The cut-off value of the TLGnode is 186.7 (AUC: 0.572, p=0.33), TNM: T and N categories are according to 8th edition American Joint Commission on Cancer staging system, p: Fisher's Exact test value

tomical localization. PET images (3D mode, 1 minute/bed position, axial field-of-view of 18 cm, mean axial resolution of 4–6 mm) were taken and evaluated by two different experts on nuclear medicine after reconstructed in trans-axial, sagittal and coronal slices according to LOR-OSEM algorithm. The regions of interest (ROI) for the imaged primary tumor lesions and pathological lymph node lesions were drawn from which the anatomical relations of the nasopharynx and the semi-quantitative index of the FDG uptake; SUVmax were obtained. SUVmax is normalized to body weight/surface area and injected activity. Thus, it is a semi-quantitative index determined by the ratio of the injected radiopharmaceutical dose to the mass of the subject. SUVmax=Maximum activity in ROI (mCi/ml)/Injected dose (mCi)/Body weight (g). Within a chosen ROI, SUVmax refers to a maximum pixel value in the tumor, and SUVmean refers to the mean pixel value in the ROI. MTV was calculated by Eclipse software (version 13.6) and was assumed by taking all the pixels of 50% SUVmax for the primary tumor. The unit of MTV was cm^3. TLG was defined by the product of metabolic volume times SUVmean. TLG was calculated as [SUVmean (tumor +node) × MTV (tumor +node)].

Definitive Treatment

Intensity-modulated radiotherapy was used as the basic radiotherapy technique for all patients. The delivered doses were described as follows: (I.) for the high-risk planning target volume (primary tumor volume and involved nodes), total 70 Gy with 2.12 Gy per fraction, (II.) for the intermediate-risk planning target volume, total 60 Gy with 1.8 Gy per fraction, (III.) for the low-risk planning target vol-

Table 3. Univariate and multivariate analysis for loco-regional recurrence-free survival, distant metastasis-free survival, and overall survival

Univariate analysis (LRRFS)	**The 5-years LRRFS (%)**	**HR**	**95% CI**	**p**
Age				
≤50	4.0	1		
>50	52.8	0.66	0.447–0.998	**0.04**
MTVtotal				
≤59.5	71.5	1		
>59.5	36.9	3.5	1.572–8.020	<0.01
MTVnode				
≤93.4	67.2	1		
>93.4	53.3	1.5	0.352–6.420	0.57
MTVtumor				
≤21.5	70.6	1		
>21.5	41.6	1.75	0.787–3.930	0.16
TLGtotal				
≤181.5	77.9	1		
>181.5	46.2	2.6	1.307–15.281	**0.03**
TLGnode				
≤186.7	69.0	1		
>186.7	60.3	1.93	0.796–4.706	0.13
TLGtumor				
≤142.2	67.1	1		
>142.2	48.2	2.08	0.924–4.687	0.06
Multivariate analysis (LRRFS)		**HR**	**95% CI**	**p**
MTVtotal				
≤59.5		1		
>59.5		2.82	1.095–7.288	**0.03**
Univariate analysis (DMFS)	**The 5-years DMFS (%)**	**HR**	**95% CI**	**p**
MTVtotal				
≤59.5	83.9	1		
>59.5	69.0	2.73	1.018–7.363	**0.03**
MTVnode				
≤93.4	80.6	1		
>93.4	57.1	3.59	1.023–12.659	**0.03**
MTVtumor				
≤21.5	85.4	1		
>21.5	68.6	1.97	0.737–5.315	0.16
TLGtotal				
≤181.5	93.4	1		
>181.5	68.6	5.4	1.228–23.804	**0.01**
TLGnode				
≤186.7	82.9	1		
>186.7	67.0	2.92	1.084–7.869	**0.02**
TLGtumor				
≤142.2	87.6	1		
>142.2	68.0	2.38	0.867–6.570	0.08
Multivariate analysis (DMFS)		**HR**	**95% CI**	**p**
TLGtotal				
≤181.5		1		
>181.5		5.4	1.228–23.804	**0.02**
Univariate analysis (OS)	**The 5-years OS (%)**	**HR**	**95% CI**	**p**
MTVtotal				
≤59.5	82.4	1		
>59.5	58.5	3.93	1.68–9.878	**<0.01**
MTVnode				
≤93.4	76.4	1		
>93.4	42.9	5.03	1.817–13.939	**<0.01**
MTVtumor				
≤21.5	87.0	1		
>21.5	55.3	3.66	1.402–9.571	**<0.01**
TLGtotal				
≤181.5	88.0	1		
>181.5	64.2	4.46	1.307–15.281	**<0.01**
TLGnode				
≤186.7	76.9	1		
>186.7	64.0	2.64	1.073–6.505	**0.02**
TLGtumor				
≤142.2	84.2	1		
>142.2	60.7	2.58	1.030–6.491	**0.03**
Multivariate analysis (OS)		**HR**	**95% CI**	**p**
MTVtumor				
≤21.5		1		
>21.5		4.95	1.840–13.369	**<0.01**
TLGnode				
≤186.7		1		
>186.7		4.01	1.569–10.274	**<0.01**

TLG: Total lesion glycolysis; MTV: Metabolic tumor volume; LRRFS: Locoregional recurrence-free survival; DMFS: Distant metastasis-free survival; OS: Overall survival; HR: Hazard ratio; CI: Confidence interval

ume (elective nodal areas), total 54 Gy with 1.65 Gy per fraction. Concurrent chemotherapy was performed using cisplatin with 100 mg/m^2 three-weekly scheme or 50 mg/m^2 weekly scheme, from the first day of treatment.

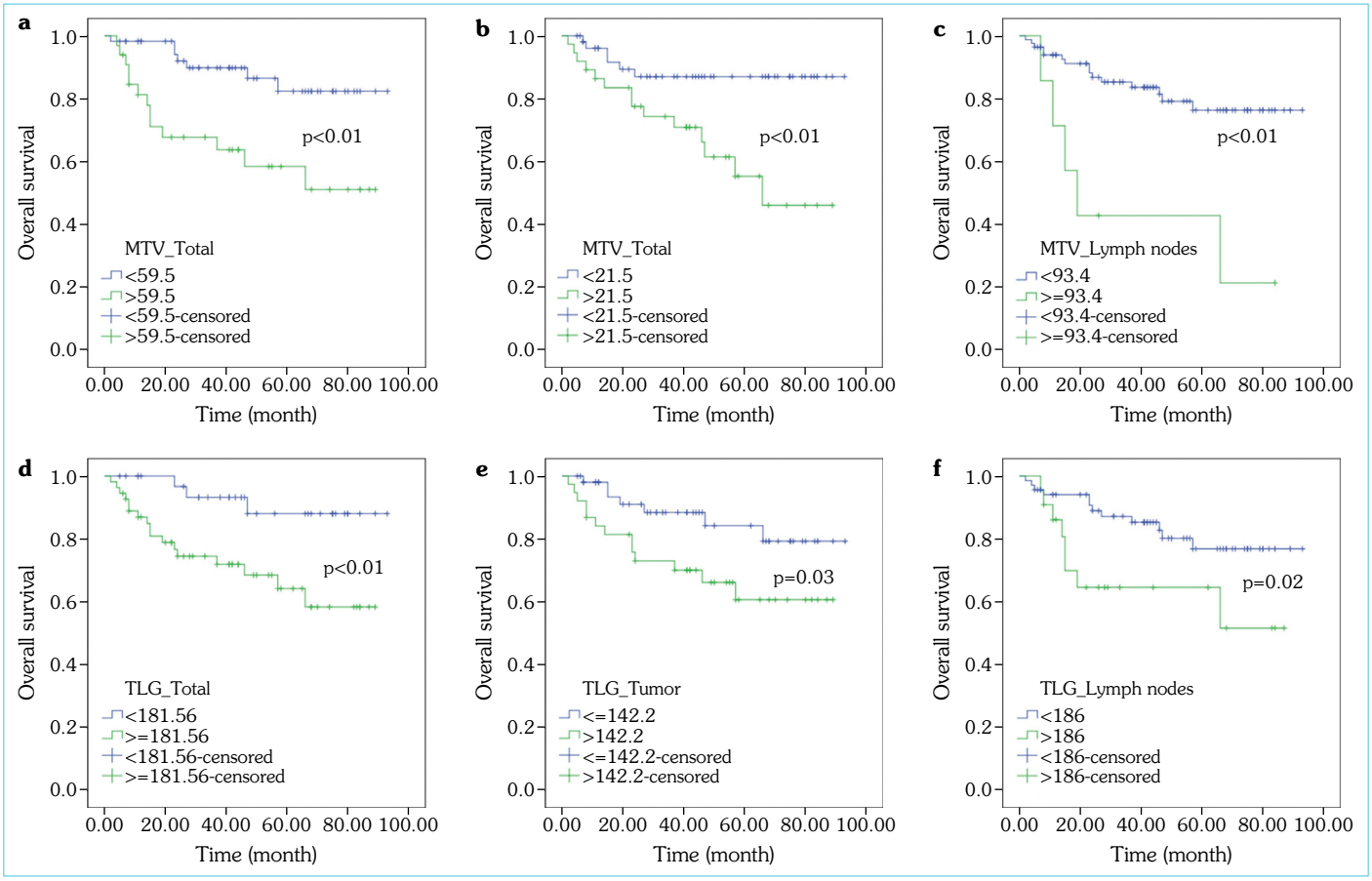

Figure 1. Overall survival curves for metabolic tumor volume (MTV) and total lesion glycolysis (TLG)

Follow up

The patient follows up was calculated from the first day of the treatment to the final examination or death, whichever came first. The response to treatment was evaluated by clinical examination, magnetic resonance imaging scans scan and PET/CT scan in the third month after the end of treatment and the assessment of treatment response was performed according to RECIST criteria. Locoregional recurrence-free survival (LRRFS) and distant metastasis-free survival (DMFS) were calculated from the first day of the treatment until the treatment failure is documented. Overall survival (OS) was calculated from the first day of the treatment until death or the last follow up.

Statistical Analysis

The statistical analysis of the data was performed using IBM SPSS Statistics 22.0 (IBM Corp., Armonk, New York, USA). Shapiro-Wilk test was used for normality tests of variables. Chi-square and Fisher exact tests were used to compare all categorical variables. Receiver operating characteristic (ROC) curves were used to find the cut-off values. Afterwards, the groups were divided into two according to the cut-off value. Survival differences between groups were evaluated using the Kaplan-Meier test. The effective factors on OS, LRRFS, and DMFS were analyzed using the univariate and multivariate Cox regression model (Backward-Wald method). P-values <0.05 were accepted as statistically significant.

RESULTS

Patient Characteristics

The mean age of the patients was 47 years (range 18–75 years). The complete response in 73 patients (80.2%) and the partial response in 18 (19.8%) were observed. Regarding the final examination, 23 patients (25.3%) had local recurrence, 10 patients (11%) had a regional recurrence, and 16 patients (17.6%) had distant metastasis. Seventy-one patients (78%) survived, 20 patients (22%) were exitus. Median follow up time was 42 months (range 2–93 months).

Cut-off Values for Parameters

ROC tests were performed to find out a cut-off value to examine the effects of MTVtumor, MTVtotal, MTVnode, TLGtumor, TLGnode, and TLGtotal on overall survival. Cut-off values for MTVtumor, MTVnode, MTVtotal, TLGtumor, TLGnode and TLGtotal were 21.5 (Area under the Curve (AUC): 0.675, p=0.01), 93.4 (AUC: 0.559, p=0.42), 59.5 (AUC: 0.703; p<0.01), 142.2 (AUC: 0.627; p=0.08), 186.7 (AUC: 0.572, p=0.33), 181.56 (AUC: 0.687, p<0.01), respectively. The patients were divided into two different groups based on the cut-off values. Differences between categorical variables are summarized in Table 1 and Table 2.

Survival Analysis

5-year OS was found to be worse in patients with high MTVtotal (>59.5), high MTVnode (>93.4), and high MTVtumor (>21.5)

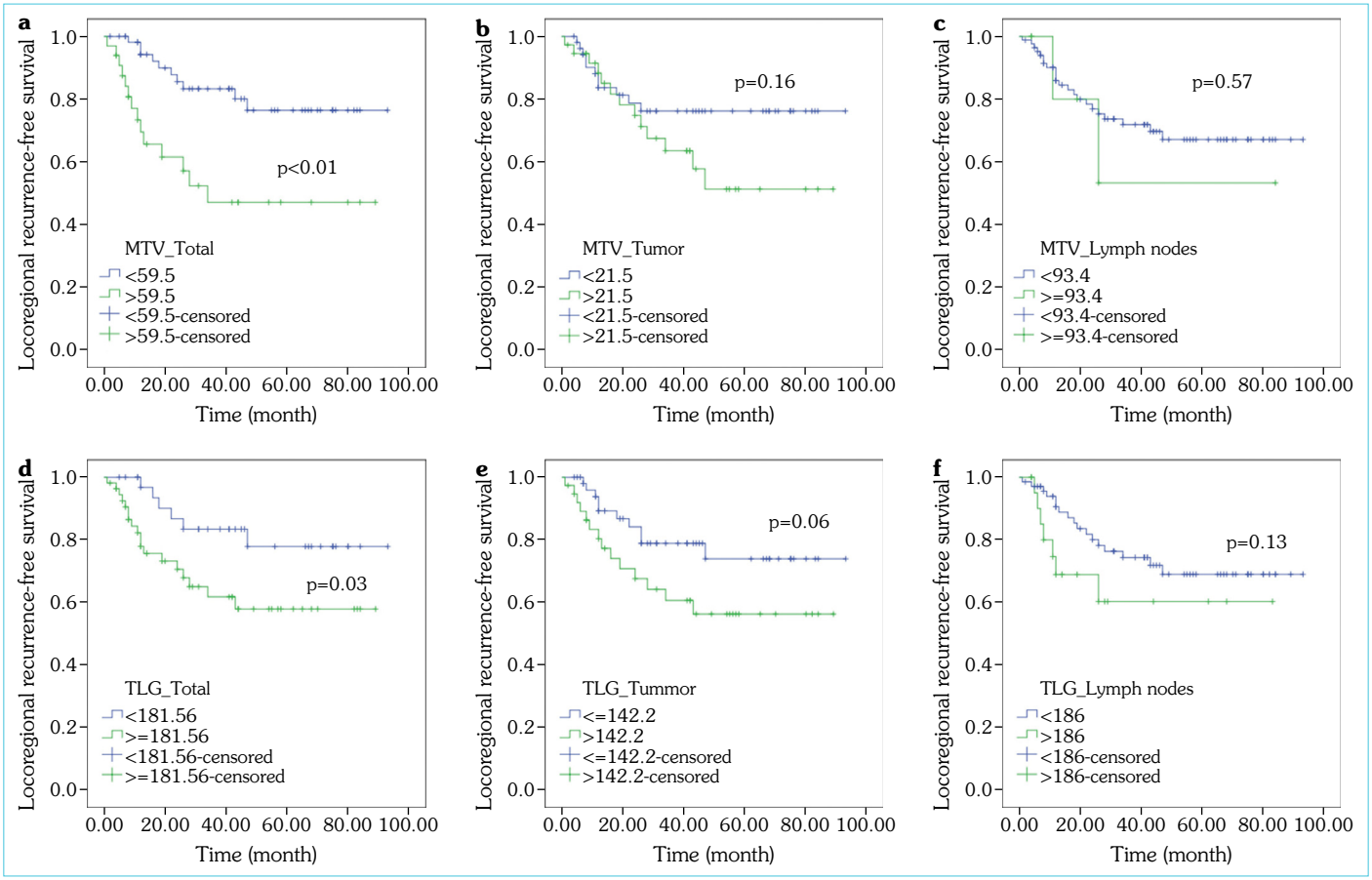

Figure 2. Locoregional recurrence-free survival curves for metabolic tumor volume (MTV) and total lesion glycolysis (TLG)

(Fig. 1). Similarly, 5-year OS was found to be worse in patients with high TLGtotal (>181.5), high TLGnode (>186.7), and high MTVtumor (>142.2) (Fig. 1). When groups are compared concerning LRRFS, no difference was found between high MTVnode and low MTVnode, and between high MTVtumor and low MTVtumor. However, in patients with high MTVtotal (>59.5), 5-year LRRFS was found to be worse (Fig. 2). There was no difference between high TLGnode and low TLGnode, and between high TLGtumor and low TLGtumor concerning 5-year LRRFS, whereas in patients with high TLGtotal (>181.5), worse 5-year LRRFS rate was detected (Fig. 2). The patients with high MTVtotal (59.5) and high MTVnode (>93.4) had worse 5-years DMFS rates. However, there was no difference between patients with high MTVtumor (<21.5) and low MTVtumor (<21.5) concerning 5-years DMFS (Fig. 3). Similarly, the patients with high TLGtotal (181.5) and high TLGnode (>93.4) had worse 5-years DMFS rates, while there was no difference between patients high TLGtumor and low TLGtumor concerning DMFS (Fig. 3).

Univariate and Multivariate Analysis

In the univariate analysis, MTVtotal, MTVnode, MTVtumor, TLGtotal, TLGnode, and TLGtumor values were found to be effective on OS (p<0.01; p<0.01; p<0.01; p=0.01; p=0.35; p=0.04, respectively). In the multivariate analysis, MTVtumor and TLGnode values were independent prognostic factors for OS. High MTVtumor and TLGnode values were correlated with 4.9 and 4-fold increased mortality risk, respectively. In the univariate analysis, MTVtotal, and TLGtotal values, as well as age (<50 vs. >50), were found to be effective factors for LRRFS (p=0.04; p=0.02; p=0.04, respectively). Only MTVtotal was observed as an independent prognostic factor for LRRFS in the multivariate analysis (Table 4). High MTVtotal value was correlated with 3.3 fold increased risk of locoregional recurrence. Concerning DMFS, MTVnode, MTVtotal, TLGtotal, and TLGnode values were found to be effective factors for survival in the univariate analysis (p=0.04, p=0.04, p=0.02, p=0.03, respectively, Table 4). In the multivariate analysis, only TLGtotal was found independent prognostic factor for DMFS. High TLGtotal value was correlated with a 5.4 fold increased risk of distant metastasis (Table 4).

DISCUSSION

FDG PET/CT is generally used for diagnosis, staging, and treatment planning for radiotherapy in patients with NPC. However, the prognostic value of parameters derived from FDG PET/CT is not clear. Concerning predicting treatment outcomes and tumor metabolic burden, TLG and MTV are generally considered more prognostic and optimal compared to SUVmax (15, 16). There are different methods used to measure MTV values in the literature. One of these methods is based on a fixed threshold value of SUVmax (>2.5), while the other method is based on a 40–50% threshold for SUVmax which is also used in this study (17).

Among all the PET parameters, SUVmax is one of the parameters cited as an important prognostic value in head and neck cancers.

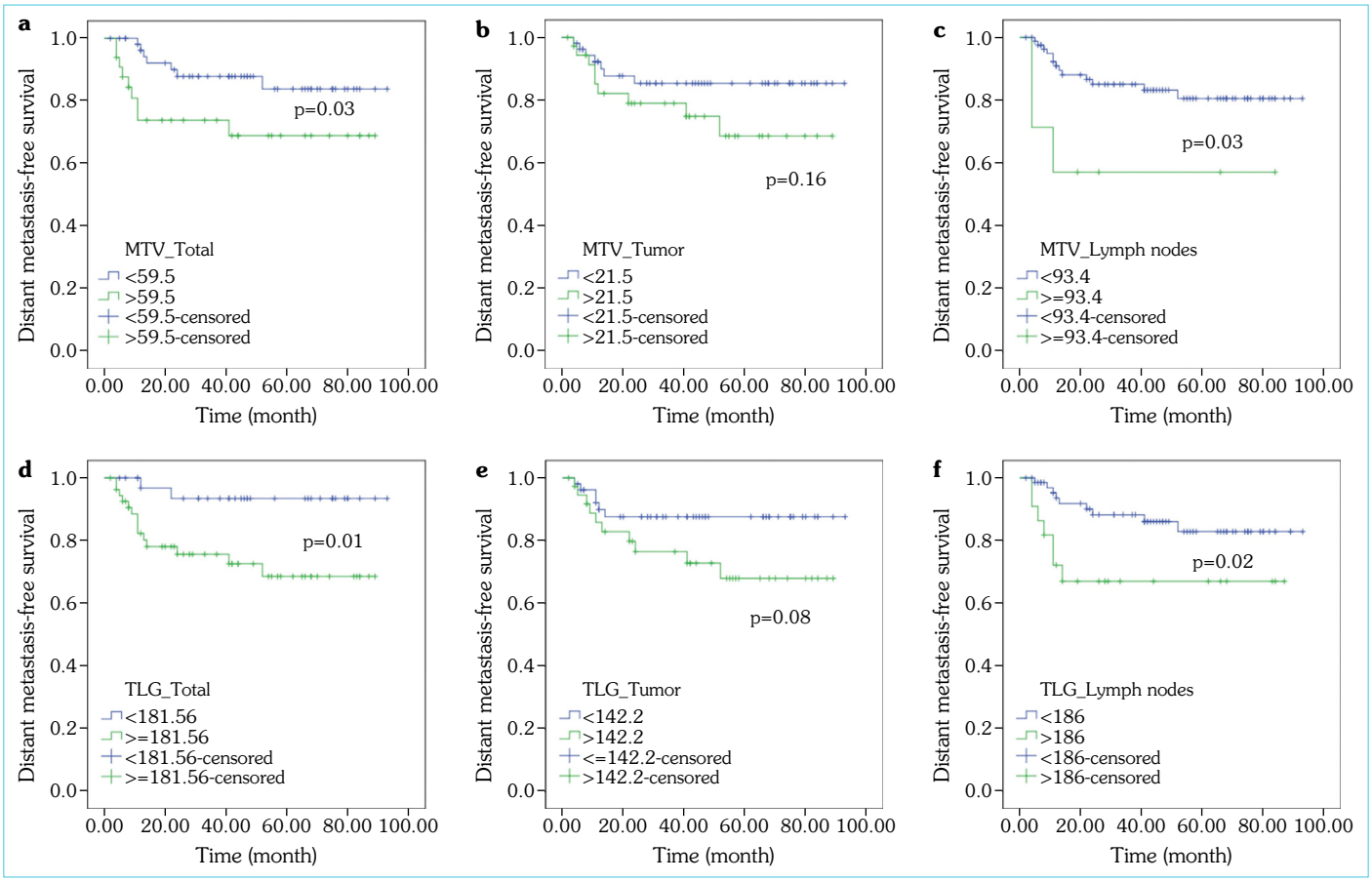

Figure 3. Distant metastasis-free survival curves for metabolic tumor volume (MTV) and total lesion glycolysis (TLG)

Chan et al. (18) declared that patients with >12 SUVmax values had lower DMFS compared to patients with <12 SUVmax values. Moreover, Hung et al. (10) showed that patients with high SUVmax values for both primary tumor and metastatic lymph nodes had poorer DMFS. Also, Lee et al. (19) showed that pretreatment high nodal SUVmax correlated with poorer survival and progression. Based on the ROC analysis in this present study, the most significant SUVmax values were found to be 19.3 and 4.9 for primary and lymph nodes, respectively. SUVmax of the primary tumor and SUVmax of lymph nodes were not predictive for OS, LRFS, and DMFS.

In recent years, MTV and TLG have been considered more commonly compared to SUVmax. MTV and TLG, which are metabolic-volumetric parameters, have been accepted as more important and effective parameters in the prognosis of head and neck cancers in comparison to SUV values, which are volumetric parameters (20, 21). Yang et al. (22) found that TLGtumor was effective for only local control in nasopharyngeal cancer patients. Chan et al. (18) observed that TLGtumor was an independent prognostic factor for OS in NPC patients. Moon et al. (23) found that high TNM staging and TLG values were independent prognostic factors for poor DFS in NPC patients. Alessi et al. (24) showed that both SUVmax of the primary tumor and TLG of the primary tumor were prognostic factors for OS. Yoon et al. (25) showed that TLG-total was independent prognostic factor for OS, LRFS, and DMFS. Lin et al. (26) showed in their trial, which included 30 patients with nasopharyngeal carcinoma, that the pre-treatment MTV and TLG values of the primary tumor were predictive for both OS and DMFS. However, the pre-treatment MTV and TLG values of lymph nodes were not associated with OS, while these values were prognostic concerning distant metastasis. In the same study, total TLG and MTV values were correlated with poorer DMFS when the primary tumor and lymph nodes were combined (26). TLG-total was found to be an independent prognostic factor for DMFS and this finding is consistent with the literature in this study (21). In addition, TLGnode was found to be an independent prognostic factor for OS. Similarly, SUVmax value for lymph node was found to be a prognostic factor in the literature (20). This present study showed for the first time that TLGnode was an independent prognostic factor for OS in nasopharyngeal cancer. In the literature, the assessment of MTV is not clear for NPC patients. In the study conducted by Yang et al. (22), MTVtumor and MTVnode were not associated with OS, PFS, and local control. Moon et al. (23) has found total MTV value to be independent factor correlated with DFS in the univariate analysis. However, MTV has not been shown as an independent factor in the multivariate analysis. Similarly, Shi et al. (27) showed that MTVtumor, MTVnode, MTVtotal values were not prognostic factors for survival. Lin et al. (26) pointed out that the pre-treatment high MTV for primary tumor (>11.2) was an independent prognostic factor concerning DMFS and OS. In the same study, MTV value for lymph node (>25.45) and MTV value for combined (>51.65) were shown as independent prognostic factors for DMFS. In the study of Yoon et al., (28) it was demonstrated that MTV3.0 might be a prognostic factor associated with OS. A meta-analysis involving 941 patients has been reported in

the literature in recent years, the study reported that SUVmax, TLG, and MTV are associated with a worse prognosis (29). In this present study, we found that MTVtotal value as an independent prognostic factor for LRRFS. In addition, MTVtumor value was the sole independent prognostic factor correlated with OS.

There are two main components of the treatment failure in nasopharyngeal cancer. The first component is a destructive progression of disease due to local failure in the head and neck area. The second component is organ failures due to distant metastasis. According to our results, MTVtotal is a significant independent factor for local failure, while TLGtotal is a significant independent factor for distant metastasis. Both of these parameters strongly point to the basic reasons for treatment failure in nasopharyngeal cancer. In addition, according to our data, MTVtumor and TLGnode values are the significant independent prognostic factors for OS. Interestingly, PET/CT derived volume-metabolic parameters are associated with survival although the TNM-derived T stage and N stage are not associated with survival. In the future, a PET/CT-based classification may be created specifically for nasopharyngeal cancer. TLG may be used to estimate that viability, aggressiveness, proliferation, and distant metastasis probability for both metastatic lymph node and primary tumor while MTV may be used as a predictor of tumor burden.

This current work has some limitations. Since this is a retrospective study, there may be problems in data completeness and comparability. It is still controversial in the literature that there is no standardized method to have PET-derived parameters and the threshold values are not yet clear.

CONCLUSION

It may be suggested that more aggressive systemic treatment practices are needed to reduce the risk of distant metastasis in patients with high TLG values according to the results of this study. Besides, patients with high MTV values could be treated more aggressively concerning local treatment to avoid locoregional failure. Finally, to evaluate the prognostic values of both TLG and MTV, more of those prospective, randomized studies with more patients are needed.

Ethics Committee Approval: This study has been approved by the local ethics committee (date: 04.12.2015, number: 2015/524).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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Author Contributions: Concept – MG; Design – MG; Supervision – ÜA; Resource – MG, ÜA; Materials – MG, ÜA; Data Collection and/or Processing – MG, ÜA; Analysis and/or Interpretation – MG; Literature Search – MG, ÜA; Writing – MG; Critical Reviews – MG.

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