The evaluation of the affect of seventh staging system of esophagus cancers to the prognosis and survival

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Abstract

The exact staging of esophagus cancers are very important for the planning of treatment and analyse of prognosis. The aim of our study is the evaluation of last staging criteria of esophagus cancers and the comparison of sixth and seventh TNM staging systems. The eighty five patients who underwent resection due to esophagus cancer in the Thoracic Surgery Department of 19 Mayıs University, Faculty of Medicine between January 2003 and December 2014 were evaluated retrospectively. The clinical staging and the factors that effects the survival are evaluated both by the 6th and 7th TNM by using radiological imaging and upper gastrointestinal system endoscopy. The postoperative mean survival time is evaluated as 44.46 ± 6.71 months is measured for 85 patients who were resected by the diagnosis of esophagus cancer. The most common cause of admission to the hospital are dysphagia and weight loss. The 76.5 % of the patients are squamous cell carcinoma and 23.5 % of the patients are adenocarcinoma as a histopathological diagnosis of cancer. The most highest postoperative survival (57.50 ± 27.86 months) is reported after the McKeown surgery. According to the seventh staging system the tumor depth, the number of metastatic nodes and metastasis affect the postoperative prognosis and ratio of survival negatively.It is showed that the effected lymph nodes and the number of effected lymph nodes are the most valuable criterias in the seventh TNM staging system and it is evaluated that more powerful results are gained when it is compared with the sixth TNM staging system.

Keywords: esophagus cancer, stage, resection, survival

1. Introduction

Accurate staging, treatment planning, and prognosis determination are crucial in the management of esophageal cancer. Due to its anatomical features, esophageal cancer often remains asymptomatic in the early stages, leading to delayed diagnosis and presentation at advanced stages. Patients with esophageal cancer are frequently diagnosed at advanced stages, making early detection challenging. The patients with the longest survival in esophageal cancer are those with early-stage disease who undergo surgical treatment. Therefore, accurate staging, treatment planning, and prognosis determination are essential.

Currently, the 7th edition of the TNM classification system developed by the American Joint Committee on Cancer (AJCC) is used for staging esophageal cancers. This system incorporates major changes in TNM categories and takes into account histological grade, tumor localization and histopathological type.

Our study aims to evaluate the 6th and 7th editions of the TNM staging systems for esophageal cancer in terms of treatment, prognosis, and survival. Additionally, we seek to investigate and compare factors influencing survival.

2. Materials and Methods

This study was approved by The Medical Research Ethics Committee with the reference number: (Ref. No. OMU MREC 2015/289). 135 patients who were treated for esophageal cancer in our clinic between January 2003 and December 2014 were evaluated retrospectively. Fifty patients who underwent palliative treatment and were considered "unresectable as a result of preoperative examinations" were excluded from the study. Eighty-five patients who underwent anatomical resection and lymph node dissection were included in the study. Exclusion criteries are shown in table 1.

Table 1. Exclusion criteries

Patients with distant metastases
Presence of distant and/or multiple and/or unresectable extracapsular spread of lymph nodes,
Medically inoperable patients
Patients who refuse surgical treatment

Demographic data of the patients were obtained from the OMU Medical Faculty digital database. Preoperative PET-CT and Brain MRI, routine laboratory tests, pulmonary function tests (PFT), electrocardiograms (ECG), upper gastrointestinal tract endoscopy and esophagus stomach duodenum radiograph were performed in all patients. Patients were evaluated separately according to 6th and 7th TNM staging system according to Thorax CT, PET CT, Brain MRI results. In addition, the effects of gender, age, habits, additional systemic diseases, presence of second malignancy and stage on all outcomes were evaluated. Transhiatal esophagectomy, laparotomy, thoracotomy, mediastinal lymph node dissection, three-site esophageal resection, esophagogastrostomy lymph node dissection were applied to the patients who were evaluated as resectable tumors according to the results. The

definition of complete resection was evaluated according to the absence of microscopic or macroscopic tumor at the resection margins and complete mediastinal lymph node resection. The patients were called for outpatient clinic control every 3 months in the first year and every 6 months in the following years. In the controls, the patients were evaluated with complaints, physical examination findings, routine laboratory values, 2-way chest X-rays, thorax and abdominal computed tomography and/or PET CT.

The statistic analysis was done with SPSS for Windows 15.0 program. While evaluating the data, continuous variables were expressed as mean ± standard deviation, median (smallest-largest), number (%). Survival time after resection was calculated by Kaplan-Meier test. Log rank (Mantel – cox) analysis test was used to calculate survival times for different variables. Statistical significance level was accepted as p<0.05 for all tests.

3. Results

85 patients who underwent esophagectomy-esophagogastrostomy and lymph node dissection with the diagnosis of esophageal cancer between January 2003 and December 2014, were evaluated. All patients underwent open surgical procedures by the surgery types as Ivor lewis (49 patient), Orringer (17 patient), McKeown (4 patient), esophagolaryngectomy (7 patient), esophagojejunostomy (8 patients) were performed, respectively.

57.6% (n=49) of the patients were male and 42.4% (n=36) were female. Postoperative mean life expectancy was calculated as 44.46 ± 6.71 months for both genders (p>0.05). The mean age was calculated as 53.93 ± 11.72 (21-76) years. Survival for age was not statistically significant (p>0.05).

The most common complaint was dysphagia (95.3%, n=81). Other complaints were weight loss, pain, hoarseness and dyspeptic complaints. Survival according to symptoms was not statistically significant (p>0.05).

Although survival decreased in patients with comorbid disease and another primary malignancy, these results were not statistically significant in terms of esophageal cancer (p>0,05).

Squamous cell carcinoma was diagnosed in 76.5% (n=65) and adenocarcinoma in 23.5% (n=20) of the patients. The relationship between histopathological type, tumor location and survival (Table 2) was not statistically significant (p>0.05).

Table 2. The relationship between tumor location, histopathological type and survival

	Tumor Location	n=85	%	Postoperative mean survival time (month)	1 year survival (%)	5 year survival (%)
Squamous cell carcinoma	Cervical	9	13.8	29.55 ± 13.43	44	11
	Upper Thoracic	13	20.0	39.13 ± 12.09	53	28
	Middle Thoracic	22	33.8	40.49 ± 11.26	54	22
	Lower Thoracic	21	32.3	38.71 ± 11.32	43	28
Adenocarsinoma	Middle Thoracic	2	10.0	37.50 ± 10.96	-	-
	Lower Thoracic	18	90.0	44.72 ± 13.43	-	-

Postoperative mean life expectancy was the highest in patients who underwent McKeown's method. Survival was statistically significant according to the surgical treatment method (p<0,05). The most common postoperative complication in the patients in the study group was anastomotic stenosis. All of stenosis were treated by balloon and/or bugia dilatation. Other complications are fistula, infection and hernia. In our study, survival times according to complications were not statistically significant (p>0.05).

The patients in the study group were evaluated according to the 6th TNM staging to evaluate the effect of the tumor depth (T) factor on survival. When evaluated according to the 6th TNM staging based on the T factor and postoperative average survival time based on the T factor (Table 3, Fig. 1a), survival was found to be statistically significant (p<0.01). As the tumor depth increases, the postoperative average life expectancy decreases.
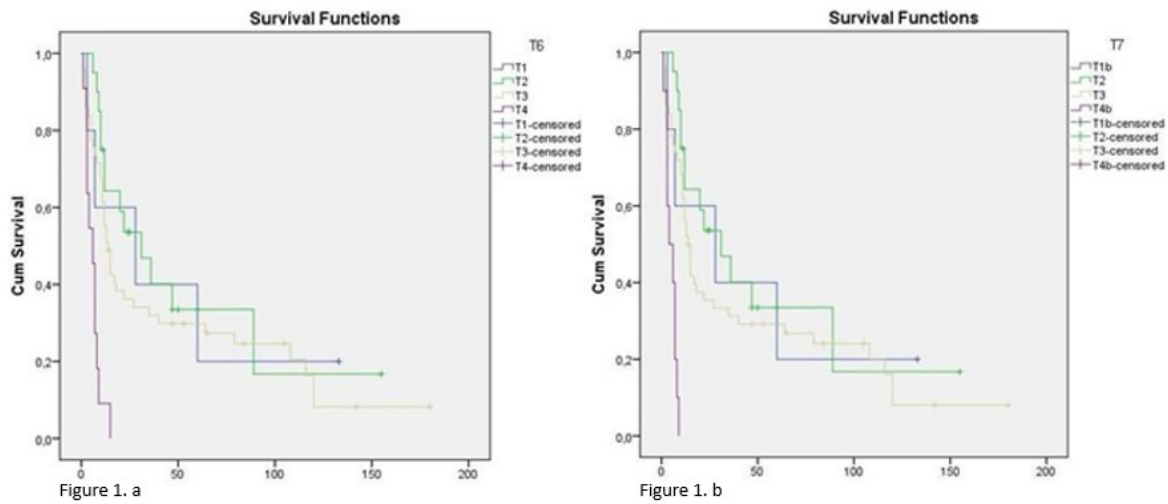
Table 3. T and survival by 6th TNM

6.TNM T Factor	n=85	%	Postoperative mean survival time (month)	1 year survival (%)	5 year survival (%)
T1	5	5.9	46.20 ± 21.40	60	20
T2	20	23.5	54.16 ± 14.16	64	33
T3	49	57.6	45.56 ± 8.51	75	29
T4	11	12.9	6.00 ± 1.17	9	0

Fig. 1. a. Survival by T in 6th TNM

b. Survival by T in 7th TNM

The patients in the study group were evaluated according to the 7th TNM staging to evaluate the effect of the tumor depth (T) factor on survival. When evaluated according to the 7th TNM staging based on the T factor and postoperative average

survival time based on the T factor (Table 4, Fig. 1b), survival was found to be statistically significant ($p<0.01$). As the tumor depth increases, the postoperative average life expectancy decreases.

Table 4. T and survival by 7th TNM

7.TNM T Factor	n=85	%	Postoperative mean survival time (month)	1 year survival (%)	5 year survival (%)
T1b	5	5.9	46.20 ± 21.40	60	20
T2	20	23.5	54.16 ± 14.16	64	33
T3	50	58.8	44.89 ± 8.35	56	29
T4b	10	11.8	5.1 ± 0.83	0	0

Patients in the study group were evaluated according to the 6th TNM staging to evaluate the effect of lymph node involvement (N) factor on survival. When evaluated according to the 6th TNM staging based on the N factor and postoperative

average survival time based on the N factor (Table 5, Fig. 2a), survival was found to be statistically significant ($p<0.05$). It can be seen that the postoperative mean life expectancy is significantly longer in those without lymph node involvement.

Table 5. N and survival by 6th TNM

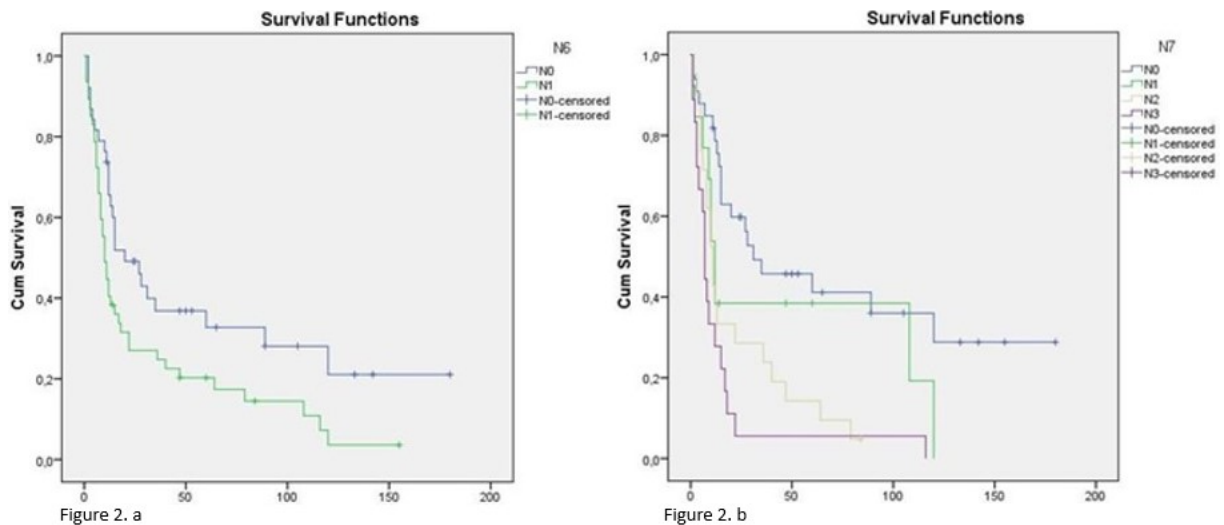| 6. TNM N Factor	n=85	%	Postoperative mean survival time (month)	1 year survival (%)	5 year survival (%)
N0	38	44.7	61.43 ± 12.23	73	32
N1	47	55.3	31.28 ± 6.40	40	20

Fig. 2. a. Survival by N in 6th TNM

b. Survival by N in 7th TNM

Patients in the study group were evaluated according to the 7th TNM staging to evaluate the effect of lymph node

involvement (N) factor on survival. When evaluated according to the 7th TNM staging based on the N factor and postoperative

average survival time based on the N factor (Table 6, Fig. 2b), survival was found to be statistically significant ($p<0.01$).The

postoperative mean survival time was calculated to be significantly longer in those without lymph node involvement.

Table 6. N and survival by 7th TNM

7. TNM N Factor	n=85	%	Postoperative mean survival time (month)	1 year survival (%)	5 year survival (%)
N0	33	38.8	76.21 ± 13.83	78	41
N1	13	15.3	48.61 ± 15.23	38	19
N2	21	24.7	22.90 ± 5.42	38	9
N3	18	21.2	14.33 ± 6.15	27	0

Patients in the study group were evaluated according to the 6th TNM staging to evaluate the effect of the metastasis (M) factor on survival. When evaluated according to the 6th TNM staging based on the M factor and postoperative average

survival time based on the M factor (Table 7, Fig. 3a), survival was found to be statistically significant ($p<0,01$). The postoperative mean survival time was found to be significantly longer in those without metastasis.

Table 7. M and survival by 6th TNM

6. TNM M Factor	n=85	%	Postoperative mean survival time (month)	1 year survival (%)	5 year survival (%)
M0	54	63.5	66.03 ± 9.41	70	41
M1a	15	17.6	9.26 ± 1.19	26	0
M1b	16	18.9	5.87 ± 1.39	12	0

Figure 3. a

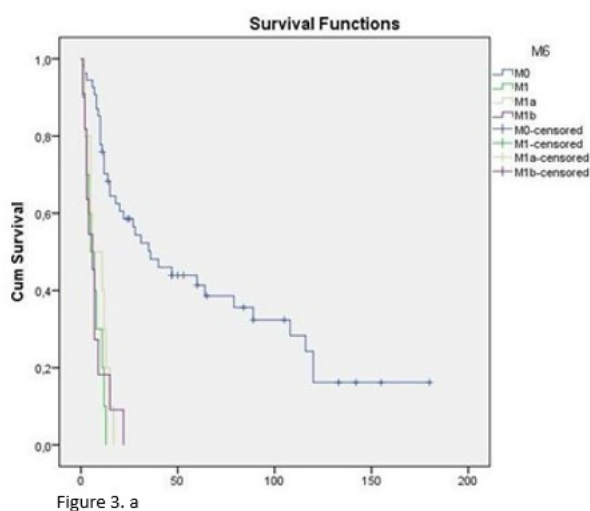Figure 3. b

Fig. 3. a. Survival by M in 6th TNM   **b.** Survival by M in 7th TNM

The patients in the study group were evaluated according to the 7th TNM staging to evaluate the effect of the metastasis (M) factor on survival. When evaluated according to the 7th TNM staging based on the M factor and postoperative average

survival time based on the M factor (Table 8, Fig. 3b), survival was found to be statistically significant ($p<0,01$). The postoperative mean survival time was found to be significantly longer in those without metastasis.

Table 8. M and survival by 7. TNM

7. TNM M Factor	n=85	%	Postoperative mean survival time (month)	1 year survival (%)	
M0	68	80	53.88 ± 8.0	60	32
M1	17	20	7.29 ± 1.33	17	0

The patients in the study group were evaluated according to the 7th TNM staging to evaluate the effect of the Grade (G) factor on survival. When evaluated according to the 7th TNM staging based on the G factor and postoperative average survival time based on the G factor (Table 9, Fig. 4), according to histological grade, although there are significantly longer differences in postoperative average survival times, statistical calculation couldn't be performed due to the low number of Grade 4 patients.

Table 9. Grade according to 7th TNM

Histological Grade	n=85	%
Well differentiated	53	62.4
Moderately differentiated	27	31.8
Poorly differentiated	4	4.7
Undifferentiated	1	1.1

The pathological stages of the patients were staged according to the 6th and 7th TNM by distinguishing the squamous cell carcinoma and adenocarcinoma. Because the tumor location is not taken into account in the staging of

adenocarcinoma according to the 7th TNM, while the stage changes according to the tumor location in squamous cell carcinoma.

The patients in the study group were evaluated according to the 6th TNM staging to evaluate the effect of pathological stages on survival of patients with squamous cell carcinoma. When evaluated according to the 6th TNM staging based on pathological stages and postoperative average survival time based on pathological stages (Table 10, Fig. 5a), it was found that the postoperative mean survival time decreased significantly as the stage increased, and a statistically significant difference was detected (p<0,01).
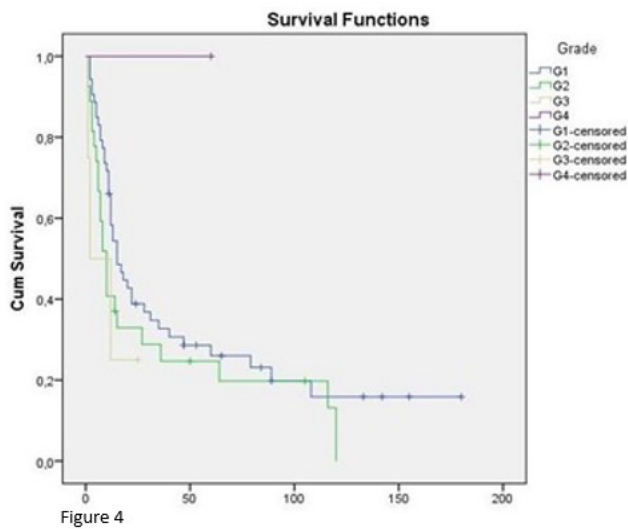

Figure 4

Fig. 4. Survival by grade in 7th TNM

Table 10. Stage and survival according to 6th TNM in patients with squamous cell carcinoma

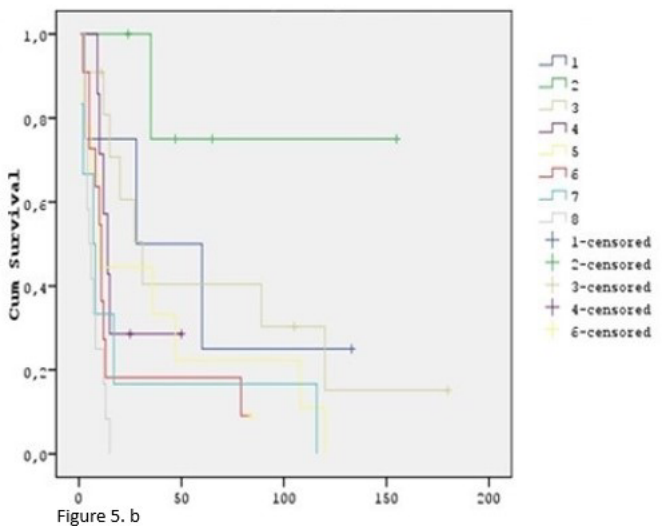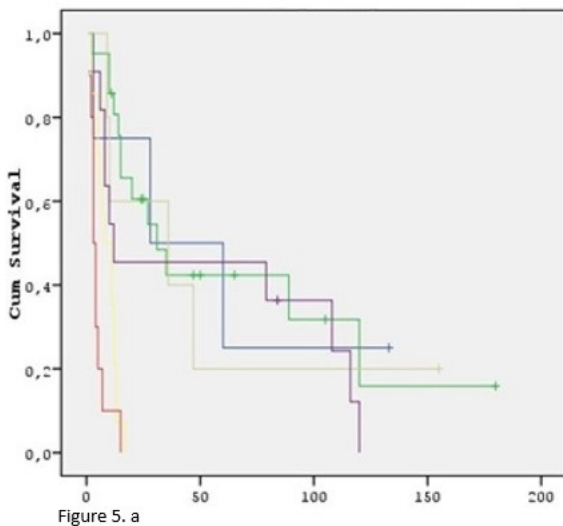| 6. TNM Stage	n=65	%	Postoperative mean survival time (month)	1 year survival (%)	5 year survival (%)
I	4	6.1	56.00 ± 24.41	75	25
IIA	21	32.3	67.57 ± 16.08	80	42
IIB	5	7.6	51.40 ± 24.08	60	20
III	11	17	52.97 ± 16.18	45	36
IVA	14	21.6	8.85 ± 1.20	21	0
IVB	10	15.4	4.70 ± 1.25	10	0

Figure 5. a

Figure 5. b

Fig. 5. a. Survival by stage in 6th TNM in patients with squamous cell carcinoma **b.** Survival by stage in 7th TNM in patients with squamous cell carcinoma

The patients in the study group were evaluated according to the 7th TNM staging to evaluate the effect of pathological stages on survival of patients with squamous cell carcinoma. When evaluated according to the 7th TNM staging based on pathological stages and postoperative average survival time based on pathological stages (Table 11, Fig. 5b), a significant difference was found (p<0.01).

Table 11. Stage and survival according to 7th TNM in patients with squamous cell carcinoma

7. TNM Stage	n=65	%	Postoperative mean survival time (month)	1 year survival (%)	1 year survival (%)
IA	4	6.2	56.00 ± 24.41	75	25
IB	5	7.7	125 ± 25.98	-	75
IIA	11	16.9	65 ± 20.53	80	40
IIB	7	10.8	22.85 ± 6.52	57	28
IIIA	9	13.8	37.77 ± 15.35	44	22
IIIB	11	16.9	21.81 ± 8.54	27	18
IIIC	6	9.2	25.16 ± 18.31	33	16
IV	12	18.5	6.91 ± 1.22	16	0

The patients in the study group were evaluated according to the 6th TNM staging to evaluate the effect of pathological stages on survival of patients with adenocarcinoma. When evaluated according to the 6th TNM staging based on pathological stages and postoperative average survival time based on pathological stages (Table 12, Fig. 6), it was found that the postoperative mean survival time decreased significantly as the stage increased and there was a statistically significant difference (p<0,05).

Table 12. Stage and survival according to 6th TNM in patients with adenocarcinoma

6. TNM Stage	n=20	%	Postoperative mean survival time (month)	1 year survival (%)	5 year survival (%)
IIA	4	20	109.25 ± 28.36	75	50
IIB	5	25	32.20 ± 10.37	60	40
III	5	25	34.25 ± 11.37	75	25
IVB	6	30	7.83 ± 3.09	16	0
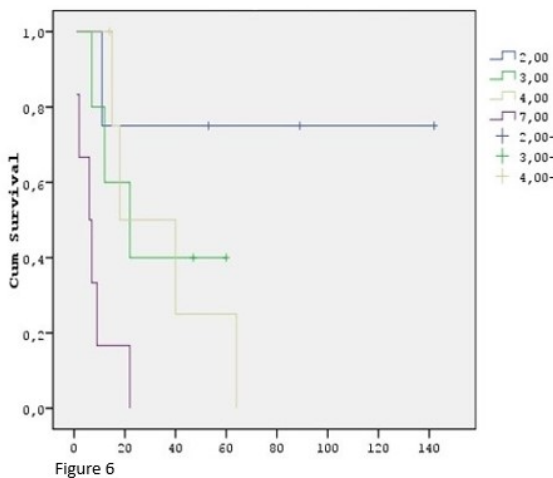
Figure 6

The patients in the study group were evaluated according to the 7th TNM staging to evaluate the effect of pathological stages on survival of patients with adenocarcinoma. When evaluated according to the 7th TNM staging based on pathological stages and postoperative average survival time based on pathological stages (Table 13), it is seen that the postoperative mean survival time decreases significantly as the stage increases, but it could not be calculated statistically in the groups with a low number of patients.

Fig. 6. Survival by stage in 6th TNM in patients with adenocarcinoma

Table 13. Stage and survival according to 7th TNM in patients with adenocarcinoma

7. TNM Stage	n=20	%	Postoperative mean survival time (month)	1 year survival (%)	5 year survival (%)
IIB	9	45	92.39 ± 21.81	88	50
IIIA	1	5	22 ± 0	-	-
IIIB	1	5	40 ± 0	-	-
IIIC	5	25	11.6 ± 2.29	40	20
IV	4	20	4.75 ± 1.93	0	0

4. Discussion

Correct staging in cancer treatment ensures the correct treatment protocol, and the correct treatment ensures successful results. Today, TNM staging system is used in staging of esophageal cancers, based on tumor invasion depth (T), lymph node involvement (N) and systemic metastasis (M).

The study conducted by Manzoni et al. on 116 esophageal adenocarcinoma patients, was demonstrated that advanced age, male gender, and an increased number of involved lymph nodes were negative prognostic factors (1). In our study, the postoperative mean survival time was found to be 57.31 ± 11.86 months in females, 33.42 ± 6.60 months in males, 53.11

± 9.30 months in patients under 60 years old, 28.13 ± 7.50 months in patients over 60 years old and 41.67 ± 7.22 months in patients diagnosed with squamous cell carcinoma, while it was 47.09 ± 13.15 months in patients diagnosed with adenocarcinoma. Although the differences were not statistically significant, similar survival times to the literature were determined.

In their study, Rice et al. Emphasized that previous staging systems based on TNM criteria for anatomical evaluation of T, N, and M were inadequate in terms of cancer biology. They highlighted that besides anatomical criteria, the evaluation of non-anatomical data is also important for survival and prognosis in esophageal cancer staging. The study emphasized that assessing tissue biological activity (histological grade), localization especially in esophagogastric junction tumors and histopathological cell type would lead to more accurate results in determining survival time (2).

In the staging of esophageal cancer concerning the T factor; T insitu was converted to high-grade dysplasia, and all non-invasive epithelial lesions were included in staging. In the 6th edition of TNM, patients classified as T1 were further divided into T1a and T1b. T4 tumors were classified as T4a and T4b. In the 6th TNM, tumors categorized as T4, thus Stage III and IV, were reassigned in the 7th TNM where T4a corresponds to Stage IIIA-Stage IIIC and Stage IV, and T4b corresponds to Stage IIIC and Stage IV. In our study, according to the T factor (independent from histological type), all patients classified as T1 in the 6th edition were classified as T1b in the 7th edition, hence the 5 patients classified as T1 according to the 6th TNM (46.20 ± 21.40 months) were also classified as T1b according to the 7th TNM (46.20 ± 21.40 months), and among the 11 patients classified as T4 (6.00 ± 1.17 months) according to the 6th TNM, 10 were classified as T4b (5.1 ± 0.83 months), and one was classified as T3. It was observed that changes in the T criteria in the 7th TNM from T1a to T1b and T4a to T4b did not make a difference in the number of patients, thus their survival remained the same. In the 6th staging, all patients classified as Stage I remained in Stage IA in the 7th staging, resulting in the same survival (56.00 ± 24.41 months). Therefore, while survival in the 6th staging was Stage IVA: 8.11 ± 1.76 months and Stage IVB: 6.40 ± 2.27 months, survival in the 7th staging was calculated as Stage IIIC: 25.16 ± 18.31 months and Stage IV: 6.91 ± 1.22 months. It was observed that as the T criterion increased, survival decreased, and statistically significant differences were found. In light of our results, when comparing the 6th and 7th stagings, it was observed that changes in the T criterion indicating the depth of tumor invasion did not have a sufficient effect on survival time in the staging system.

In T2-3 N0 M0 patients, survival remained the same according to the T criterion; however, in overall staging, it was observed that while patients were Stage IIA in the 6th staging, in the 7th staging, the stage changed based on grade for adenocarcinoma patients and based on grade and tumor location for squamous cell carcinoma patients. Increased histological grade is associated with decreased survival in early-stage cancers. For adenocarcinoma, differentiation into G1 (well) and G2 (moderate) in Stages I and IIA cancers is more important compared to G3 (poor) differentiation. Differentiation into G1, G2, G3 is also important for Stage I and II cancers for squamous cell carcinoma. Regarding tumor localization (upper-middle-lower thoracic), while T2 - T3 tumors in the lower thorax in the 6th staging shift one stage back in overall staging, the stage remains unchanged for tumors in the middle and upper regions. Although there is no difference in survival according to the T criterion between the 6th and 7th TNM, patients' stages change based on grade and location.

In their study, Kim et al. investigated 202 resected adenocarcinoma patients in terms of monotonicity (decreasing survival with increasing stage), different survival values between different stages, and homogeneity (presence of homogeneous survival values among patients in the same stage). They noted that in evaluations belonging to the 7th TNM system, survival rates decreased as the stage progressed. They also mentioned that although only Stage IIA was considered a more advanced stage compared to IA and IB, it could exhibit better survival values, which might be dependent on the tumor's histological grade. Despite evaluating that G3 had lower survival values compared to G1 and G2, they found that histological grade differences did not create a statistically significant difference according to the 7th staging system (3). In our study, according to tumor localization; when the survival values of 21 patients classified as Stage IIA in the 6th TNM were calculated in the 7th TNM, it was observed that 11 patients remained in Stage IIA and thus had similar survival values (65 ± 20.53 months), 5 patients shifted to Stage IB, resulting in increased survival (125 ± 25.98 months), and 5 patients classified as Stage IIA shifted to Stage IIB, leading to decreased survival (22.85 ± 6.52 months). In our study, survival according to histological grade and cancer localization, based on the obtained stage, exhibited contrasts to the literature as in similar studies (4,5,6).

However, the effects of histological grade on survival were not found to be statistically significant. It was observed that the survival of Stage IIA patients (65 ± 20.53 months) was higher than the survival of Stage IA patients (56 ± 24.41 months). The overall higher survival of patients in Stage IB may be attributed to the insufficient number of data for statistical evaluation. Similar to the results of Kim et al., monotonicity, homogeneity, and different survival rates according to stages were found in our study as well (107). Similar studies in the literature have also not considered histological grade and tumor localization as significant survival factors (4,7,8). Further investigations are required to evaluate the impact of histological grade and tumor localization on prognosis.

In our study, survival time in squamous cell carcinomas varied depending on tumor location, with median survival times observed in the midthorax, upperthorax, lowerthorax and cervical locations respectively. The shortest postoperative survival time was observed in cervical location (29.55 ± 13.43 months). While one-year survival rates showed similar durations, the 5-year survival was lowest in the cervical location. The shorter survival times in cervical and lower thoracic squamous cell carcinomas compared to other locations can be explained by the presence of closely located lymph nodes and a greater number of lymph nodes in these regions. Doki et al. demonstrated similar 5-10 year survival rates for upper, middle, and lower thoracic esophageal squamous cell carcinomas (9). While many studies indicate an increase in survival as tumors progress distally, these studies also include adenocarcinomas at the lower end and gastroesophageal junction, thus not reflecting the effect of localization on survival in patients with thoracic squamous carcinoma (6,10). Results based on cancer localization were not found to be significant (5,10,11).

In a study where Rice et al. evaluated 4627 patients who underwent esophagectomy for esophageal cancer, they found the 5-year and 10-year survival rates for adenocarcinoma and squamous cell carcinoma cases to be very similar according to the 7th staging. In this study, while squamous cell carcinomas and adenocarcinomas showed similar survival rates for Stage III (C, B, A) - II (A, B) and IB, in accordance with staging criteria for esophageal adenocarcinomas, the 5-year and 10-year survival rates for Stage IA and Stage 0 were found to be higher compared to squamous cell type. Unlike squamous cell carcinomas, Stage IA in squamous cell carcinomas has higher values both in terms of 5-year and 10-year survival rates compared to Stage 0 (2). In our study, the survival rates for adenocarcinomas were high (23.5%). According to our study, survival based on tumor cell type was found to be 47.09 ± 13.15 months for adenocarcinoma and 41.67 ± 7.22 months for squamous cell carcinoma.

In a study conducted by Hsu et al., they compared the 6th and 7th staging systems in 392 patients with esophageal cancer. When the 42 patients in Stage I were reclassified according to the new staging, 11 individuals were classified as Stage IA and 31 individuals as Stage IB. While survival was calculated as 70 months in the 6th staging, they reported 122 months for Stage IA and 70 months for Stage IB in the new staging. In Stage IIA, when 122 patients were re-staged, 7 patients were classified as Stage IB, 29 patients as Stage IIA, and 86 patients as Stage IIB. The survival of the 86 patients whose stage increased was calculated as 33 months, while the survival of the 7 patients whose stage decreased was reported as 70 months. The widest distribution of patients was observed in Stage IV; when 74 patients were classified according to the new staging, 9 patients were classified as Stage IIB, 19 patients as Stage IIIA, 20 patients as Stage IIIB, 26 patients as Stage IIIC and 9 patients as Stage IV (4).

In the 7th staging, the definition of regional lymph nodes has been restructured, including cervical and celiac lymph nodes in the paraesophageal lymph node definition. While in the 6th staging, celiac and similar non-regional lymph nodes considered metastases were evaluated as M1a; in the 7th staging, they were determined as N1, N2, N3 based on the number of metastatic lymph nodes. Thus, tumors classified as Stage IVA based on lymph node metastasis in the 6th staging regressed to Stage IIB, IIIA, IIIB, IIIC for N1 and N2 cases in the 7th staging and to Stage IIIC for N3 cases. Evaluation together with lymph node involvement and number allowed for a more precise assessment of patient survival. Retrospective studies have shown that evaluating the number of involved lymph nodes is a better criterion than classifying lymph node involvement as present or absent (12,13). When compared with the 6th TNM system, advanced stages in the 6th staging are corresponded to lower stages in the 7th staging, resulting in longer survival times than expected. Survival times obtained in the 7th TNM were found to be closer to reality. In our study, the survival of 12 patients classified as Stage IVA due to non-regional lymph node involvement in the 6th TNM (8.11 ± 1.76 months) was calculated as follows in the 7th TNM: 1 patient as Stage IIB (22.85 ± 6.52 months), 1 patient as Stage IIIA (37.77 ± 15.35 months), 6 patients as Stage IIIB (21.81 ± 8.54 months), and 4 patients as Stage IIIC (25.16 ± 18.31 months). The values obtained in our study are consistent with the literature and it is believed that the N criterion of the 7th staging is more effective in survival values. In a study conducted by Talsma et al., out of 64 patients classified as Stage 4 in the 6th TNM system due to celiac lymph node involvement being considered metastasis, it was observed that in the 7th staging, 6 patients were Stage IIB, 15 patients were Stage IIIA, 19 patients were Stage IIIB, and 16 patients were Stage IIIC. When survival values were calculated, it was observed that the 7th TNM staging more accurately reflected the survival values of the patients(14).

Xu et al. Reported that the presence and number of pathological lymph nodes are the most important criteria in both the 6th and 7th staging systems (15). Manzoni et al. Emphasized that among these criteria, the number of involved lymph nodes is the most important prognostic factor, and they highlighted the importance of the localization of involved lymph nodes in determining prognosis even when the number is equal. They also emphasized that in the presence of nodal involvement, the significance of tumor depth in assessing survival diminishes (1).

The similarity in survival between N2 and N3 patients explains why Stage IIIB (T3N2M0) and Stage IIIC patients show similar survival rates, which is not surprising. In the 7th staging, lymph node evaluation plays the most important role. Proper lymph node dissection and pathological examination help prevent discrepancies in lymph node staging (4). It has been observed that there is a wide difference in survival rates between N0 and N1 patients. This suggests that N1 patients

might actually include N2 or N3 patient groups due to inadequate lymph node sampling, resulting in significant differences in survival values between the two groups (14). A study by Peyre et al. reported that at least 23 regional lymph nodes should be sampled for the sampled lymph node count to be significant for survival (16). The Western Esophageal Cancer Consortium (WECC) stated that sampling at least 10 lymph nodes for T1, 20 for T2, and 30 or more for T3 and T4 would yield accurate results (17). This effect is not observed in N0 patients, so the number of removed lymph nodes does not create a significant difference in survival values (14).

In the 7th staging, the M factor was redefined, considering cervical and celiac lymph nodes as regional lymph nodes, which resulted in Stage IV patients transitioning to Stage III. In the 6th TNM staging, it was observed that the staging of M1a changed with the N factor, leading to a regression in stage and an increase in survival. On the other hand, in the 7th staging, M1b, indicating other distant metastases, was also considered as M1, resulting in no change in stage, which was consistent with the survival of Stage 4 patients. The survival value of Stage IVB patients in the 6th staging was found to be 6.40 ± 2.27 months, while in the 7th staging, the survival value of Stage IV patients was also 6.40 ± 2.27 months. The current results indicate that evaluating non-regional lymph nodes as M1a and M1b is unnecessary, and only patients with distant metastases should be considered Stage IV patients.

Patients who transitioned from Stage IV to early Stage III showed similar survival to Stage III patients. These patients were considered inoperable in the 6th TNM staging but became candidates for resection or neoadjuvant therapy in the 7th TNM staging (18). Patients with distant metastases were still considered inoperable (8).

Mehta et al. evaluated the prognostic and survival reliability of the 6th and 7th staging systems in 243 patients with esophageal cancer. They highlighted the importance of the TNM classification for both the 6th and 7th staging systems. They found that the changes in the 7th staging system provided more accurate values in determining treatment selection, prognosis and survival rates. They also observed that as the TNM classification worsened and the number of involved nodes increased, survival rates decreased (19). Both Hsu et al. and Gaur et al. confirmed that the 7th staging system was a better model in terms of survival values (4,20).

In our study, when esophageal squamous cell carcinomas were evaluated according to the 6th and 7th staging systems based on T status, grade, tumor localization, lymph node metastasis, and distant metastasis, it was observed that changes in T and M resulted in similar survival values, whereas changes in N factor leading to a decrease in stage prolonged survival time. It was also found that grade and tumor localization were not effective criteria for survival.

In conclusion, the 7th staging system is considered non-

anatomic cancer criteria. By incorporating tumor histopathology, localization, and grade into staging, the aim was to improve the quality of life of patients. The 7th staging system is believed to show similarities to the 6th staging system in many aspects. Nevertheless, it is considered superior to the previous staging system in terms of homogeneity, monotonicity and discriminability (4). The 7th staging system has been found to be more successful in determining treatment protocols and predicting prognosis and survival with proportional and accurate estimations. Additionally, we found that evaluating both the presence and the number of involved lymph nodes in the 7th staging system contributes to more accurate results. Cancer staging is a dynamic process and as our understanding of cancer biology improves, staging systems will need to be updated accordingly.

Conflict of interest
The authors declared no conflict of interest.

Authors' contributions
Concept: M.G.P., A.T.Ş., Y.B., A.B., Design: M.G.P., A.T.Ş., Y.B., A.B, Data Collection or Processing: M.G.P., A.T.Ş., Analysis or Interpretation: M.G.P., A.T.Ş., Literature Search: M.G.P., A.T.Ş., Writing: M.G.P., A.T.Ş., Y.B.,

Ethical Statement
This study was approved by The Medical Research Ethics Committee with the reference number:(Ref. No. OMU MREC 2015/289)

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