European Journal of Therapeutics
pISSN: 2564-7784
eISSN: 2564-7040

Eur J Ther. 2026;32(3):290–301.
https://doi.org/10.58600/eurjther2917

Original Research

Evaluation of Clinical, Pathological, and Treatment Effects on Prognosis in Non-Metastatic Esophagus Squamous Cell Carcinoma

Hatice Zeynep Dikici [1*], Nuriye Özdemir [2], Selma Özkan Karaahmetoğlu [3]

[1] Department of Hematology, Atatürk Sanatoryum Education and Research Hospital, Ankara, Türkiye
[2] Department of Medical Oncology, Gazi University, Ankara, Türkiye
[3] Department of Internal Medicine, Bilkent City Hospital, Ankara, Türkiye

Received: 2025–10–31 **Accepted:** 2026–03–07 **Published Online:** 2026–03–27

Corresponding Author
Hatice Zeynep Dikici, MD
Address: Department of Hematology, Atatürk Sanatoryum Education and Research Hospital, Ankara, Türkiye
E-mail: drzeynepdikici@hotmail.com

© 2026. The copyright of this article is retained by the author(s).

OPEN ACCESS

This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

This license permits the free sharing and adaptation of the work for non-commercial purposes, provided that appropriate attribution is given to the original author(s) and to its initial publication in this journal.

ABSTRACT

Objective: This study analyzed demographic, clinical, and pathological features, treatment responses, and survival outcomes in non-metastatic esophageal SCC patients.

Methods: A retrospective review of 74 patients was conducted. Performance status was assessed using ECOG, treatment response via RECIST 1.1, and staging via AJCC 7th edition TNM.

Results: The male-to-female ratio was 0.95, with a mean age of 50.6. Tumors were mainly distal (58%), and most patients (68.7%) presented at stage 2 (25%) or 3 (43.7%). Surgery was performed in 64.9% (47.3% surgery only, 35.1% CRT only, 17.6% CRT + surgery). Median overall and disease-free survival were 38 and 24 months, respectively. Female gender, middle/lower tumor location, fewer metastatic lymph nodes, and CRT + surgery correlated with better survival ($p < 0.05$).

Conclusion: Surgery was the most common treatment, but CRT + surgery yielded superior survival. Local recurrence was more frequent than distant metastasis. A combined approach is crucial for optimal outcomes.

Keywords: American Joint Committee on Cancer, Eastern Cooperative Oncology Group, non-metastatic esophageal cancer, response evaluation criteria in solid tumors, squamous cell carcinoma

INTRODUCTION

Cancer is the second cause of mortality after cardiovascular diseases, with a rate of 22% worldwide and in our country. Despite its low incidence, esophageal cancer has one of the highest mortality rates among cancers. It has a poor prognosis, with a five-year survival rate of 10%, and ranks 8th among all cancers in the world and 6th among causes of death from cancer [1]. In Türkiye, it accounts for 2% of all cancers and is most observed in the Eastern Anatolia region [2]. The fifth and sixth decades of life represent the peak incidence period for esophageal cancer, with a male-to-female ratio of 2–4 [3].

Esophageal squamous cell carcinoma (SCC) and esophageal adenocarcinoma are the most common primary esophageal malignancies, and their epidemiological characteristics differ significantly. SCC constitutes the vast majority of esophageal

tumors. Globally, SCC accounts for more than 90% of esophageal malignancies [4]. While esophageal cancer is uncommon in Turkey, the majority of cases are SCC. Alcohol and smoking are major risk factors for the development of squamous cell esophageal cancer. Esophageal SCC are poor prognostic tumors with a 5-year survival rate of 10%, and a cure can only be discussed in superficial cancers. The most important prognostic factor is the tumor stage [1].

In SCC, esophageal cancer, surgery, chemotherapy (CT), and radiotherapy (RT) are used as treatment modalities and combinations. The main factor determining the treatment method is the stage of the disease. Endoscopic treatment methods (Tis, T1a ≤ 2cm) and surgery are curative treatment options for resectable tumors. Neo-adjuvant, definitive chemoradiotherapy (CRT) is indicated depending on the level of invasion. Definitive CRT, CT, RT, and palliative treatments are used in unresectable, metastatic disease [5]. Within the scope of this research, we aimed to elucidate the demographic, clinical, and pathological characteristics, treatment methods, and responses to these treatments, as well as survival times and their impact on the prognosis of patients with non-SCC of the esophagus.

MATERIALS AND METHODS

A retrospective analysis was conducted on 74 patients diagnosed with non-metastatic esophageal SCC and followed at a research and training hospital's medical oncology clinic. Participants with non-metastatic esophageal SCC were monitored post-treatment. Procedures adhered to ethical standards and the Declaration of Helsinki. Ethics approval was given by Ethic Committee of Ankara Numune Training and Research Hospital (1155/2016, 29.06.2016). Informed consent was waived for this retrospective research study.

Main Points

- Combined chemoradiotherapy and surgery yielded the best survival outcomes.
- Female gender and distal tumor location were associated with improved prognosis.
- Lymph node involvement significantly affected overall and disease-free survival.
- Local recurrence was more frequent than distant metastasis.
- A multidisciplinary approach is essential in non-metastatic esophageal SCC.

Hospital records provided data on patient age at diagnosis, gender, smoking status and quantity, family history of cancer, comorbidities, performance status, and tumor site. From patient files, we obtained information regarding treatment modality (including chemotherapy regimen and number of cycles), treatment response, surgical details (including a number of lymph nodes resected and their pathological status), histological grade and stage, tumor size (macroscopic), and the presence of perineural and lymphovascular invasion. Laboratory characteristics (hemoglobin, lactate dehydrogenase, albumin), recurrence status and date, metastasis locations, updated last status, and last contact or date of death were recorded. Progression-free survival (PFS) and overall survival (OS) rates were determined. Tumors located within 25 centimeters of the incision were classified as proximal, those between 25 and 30 centimeters as middle, and those extending from 30 centimeters to the gastroesophageal junction as distal esophageal tumors.

Patient performance status and patient treatmen responses were assessed using the Eastern Cooperative Oncology Group (ECOG) and Response Evaluation Criteria In Solid Tumors (RECIST), respectively. Consequently, patient response was categorized as complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD). Staging of the patients was done using the 7th edition of the American Joint Committee on Cancer (AJCC) Staging System. In preclinical staging, early stage; lamina propria, muscularis mucosa, submucosa invasion (Tx, To, Tis, T1, T1a, T1b), locally advanced stage; muscularis propria, adventitia and surrounding anatomical structure invasion (T2, T3, T4, T4a, T4b) were evaluated. Determination of patient vital status was achieved through a combination of record review, national death registry data.

The OS time was determined by calculating the period between the diagnosis date and the date of mortality. Survival data for patients who remained alive at study conclusion were analyzed using the date of their final update. Progression-free survival was determined using the interval between diagnosis and either disease progression or death. In cases where patients died before progression could be assessed, their date of death served as the date of progression.

Statistical Analysis

IBM SPSS Statistics for Windows 29.0 was used to analyze patient data. Categorical data was described with frequency and percentage, while continuous data used mean and standard deviation. The presence of a relationship between categorical variables was determined using the Chi-Square test or Fisher's exact test. The Kaplan-Meier method was used to estimate OS and disease-free survival (DFS) times. Survival curves for different groups were compared using the log-rank test. Factors affecting the risk of death were determined using multiple stepwise COX regression analysis. The results were considered statistically significant when the p-value was less than 0.05.

RESULTS

Seventy-four patients with non-metastatic esophageal SCC comprised the retrospective study cohort. The mean age of the patients was 50.6 ± 10.2 years. The study included 74 patients: 38 (51.4%) female and 36 (48.6%) male. Smoking was present in 37 (50%) patients, and the mean amount of tobacco was 30.2±17.1. In terms of comorbidity, 17 (23%) patients had other accompanying diseases. The rate of having a family history of cancer was 21.6% (n = 16). Lower hemoglobin levels were observed in 25 (33.8%) patients, lower albumin levels in 7 (9.5%), and elevated LDH levels in 35 (53%) patients (Table 1).

Pathological and Staging Characteristics

Postoperative pathological staging (7th AJCC edition) demonstrated a heterogeneous distribution of disease, with 16.6% (n = 8) exhibiting T0N0M0 staging, while the majority presented with advanced T and N categories. Stage III disease was diagnosed in 43.7% of patients, stage II in 25%, and stage 0 in 16.7% (Table 2).

Among the patients, 36.5% had an ECOG performance status of 0, 48.6% had a status of 1, and 14.9% had a status of 2. The tumor was located distally in 58% of cases (n = 43), in the middle in 27% (n = 20), and proximally in 14.9% (n = 11). Preclinical staging classified 27% as early-stage and 73% as locally advanced. At the most recent follow-up, the survival rate was 52.7% (n = 39), while 47.3% (n = 35) had succumbed (Table 3).

Histopathological Findings

Perineural invasion (PNI) and lymphovascular invasion (LVI) were observed in 33.3% (n = 16) and 31.3% (n = 15) of the assessable patients, respectively. On average, 12.7 ± 10.6 lymph nodes were removed, which translates to an average of 1.4 ± 2.8 lymph nodes being removed per patient, showcasing significant variability in the procedure. The average tumor size was recorded as 4.2 ± 2.0.

Treatment

Treatment regimens determined the categorization of patients into groups. According to the treatments and responses, 39 patients (52.7%) were in the neoadjuvant group, and 35 patients (47.3%) were in the adjuvant group. Furthermore, neoadjuvant CRT was administered to 34 patients (45.9%), with the CF regimen used for the treatment of the majority (26 patients, 76.5%). The mean number of cycles was 2.4±1.0. There were 4 (5.4%) patients who received neoadjuvant RT and 10 (13.5%) patients who received neoadjuvant CT. When the response rates in patients who received neoadjuvant treatment were examined, 15 (38.5%) of the evaluable cases had a CR, 9 (23.1%) had a PR, 6 (15.4%) had SD, and 9 (23.1%) had PD.

Analysis of patient data stratified by the type of curative local treatment revealed that 17.6% (n = 13) received surgery and CRT, 35.1% (n = 26) received CRT only, and 47.3% (n = 35) received surgery only.

Surgical intervention was performed on 48 patients (64.9%), while 19 patients (25.7%) received adjuvant chemotherapy; all patients received the CF regimen. The mean number of cycles was 3.6±1.2. Of the 45 patients who had surgery, 93.8% had an r0 resection, 4.2% had a r1 resection, and 2.1% had palliative surgery. Differentiation analysis revealed tumor grades: 14.6% (n = 7) grade 1, 41.7% (n = 20) grade 2, 18.8% (n = 9) grade 3, and 2.1% (n = 1) grade 4. Comparatively, differentiation was undetermined for 22.9% (11 patients).

Survival Evaluation

The median OS time for our patients was 38 months. Respective OS probabilities at 1, 3, and 5 years were 79%, 51.9%, and 38.3%. Median DFS reached 24 months; 1-year, 3-year, and 5-year survival rates were 65.4%, 39.3%, and 34%. Among study participants, age, smoking history, comorbidities, family cancer history, tumor characteristics (stage, lymphovascular/perineural invasion, size, grade), performance status (ECOG), lymph node involvement, and blood markers (hemoglobin, albumin, LDH) showed no significant impact on OS.

Among females, survival rates reached 88.4%, 61.3%, and 51.4% at 1, 3, and 5 years, respectively. Male survival rates reached

69.2% at 1 year, 43.6% at 3 years, and 23.8% at 5 years. The results showed a statistically significant difference ($p < 0.05$). Proximal esophageal tumors had significantly lower survival rates than other tumor locations ($p < 0.05$). At one, three, and five years, survival rates were recorded as 50%, 20%, and 0%. The survival rate is impacted by the number of pathological lymph nodes, demonstrating a hazard ratio of 1.170 (95% CI: 1.012–1.352). DFS was impacted by the number of pathological lymph nodes affected, showing a hazard ratio of 1.189 (95% CI: 1.058–1.336).

When patients were evaluated according to the curative local treatment they received, the survival rate was significantly higher in the CRT + surgery group ($p < 0.05$), and 1-year, 3-year, and 5-year survival rates were 90.9%, 70.7%, and 70.7%, respectively.

Parameters such as age, smoking, presence of comorbidity, family history of cancer, preclinical stage, lymphovascular invasion, perineural invasion, tumor diameter, histopathological grade, ECOG performance status, total lymph node number, low hemoglobin, low albumin, and high LDH did not show a statistically significant effect on DFS.

For females, the 1-year, 3-year, and 5-year survival rates were 80.9%, 47.2%, and 43.3%, respectively. For males, the 1-year, 3-year, and 5-year survival rates were 48.4%, 30.8%, and 20.5%, respectively. The difference was statistically significant ($p < 0.05$). When patients were evaluated according to tumor location, the survival rate was statistically significantly lower in tumors located in the proximal esophagus as compared to OS ($p < 0.05$). The 1-year, 3-year, and 5-year survival rates were 50%, 0%, and 0%, respectively (Table 4). Treatment type impacted 1-year survival, resulting in rates of 81.8% (CRT + surgery), 50.9% (CRT), and 69.7% (surgery).

Patient grouping was determined by neoadjuvant and adjuvant treatments. OS and DFS showed no statistically significant difference between neoadjuvant and adjuvant treatment.

DISCUSSION

Our study revealed an average age of diagnosis of 50.6 years, highlighting a notable contrast with the international average of 67 years [6]. Age was not a factor in OS or DFS among participants aged 24–71 years, consistent with previous studies [7,8]. In contrast to global patterns showing higher esophageal SCC rates in men [9, 10], our study found an almost even gender distribution (M/F ratio: 0.95), with a slight female predominance. This corroborates findings from certain regional studies, including research conducted in Iran (male/female: 0.84) [11]. Notably, female gender showed a significant association with improved OS and PFS, corroborating previous research indicating gender as an independent prognostic factor [11, 12]. Despite smoking's established association with esophageal SCC [13, 14], it did not affect survival in the present cohort. However, our study found no significant effect of smoking status or amount on survival.

In 50–60% of cases, SCC of the esophagus is found in the middle third; the lower and upper thirds are affected less frequently (30% and 10–20%, respectively) [15]. Several studies in the literature have not demonstrated a significant effect of tumor localization on survival [16, 17]. Proximal tumor location was a significant predictor of poorer outcomes, a result of existing literature which documents diminished survival in cases of upper esophageal cancer because of the challenges associated with surgical intervention [18, 19]. Our observation contradicts prior literature, suggesting a negligible impact of localization. Proximal tumor location demonstrates poor prognostic value, potentially due to the inherent surgical difficulties in this region. Surgical resection being the primary curative treatment for esophageal cancer, the prospect of a cure is diminished. In our study, 52.7% of our patients received surgical treatment with or without CRT as curative local treatment.

A substantial majority (73%) of our patients presented with locally advanced disease at the time of diagnosis. The 5-year OS and DFS rates observed in our patient cohort (36.8% and 34.2%, respectively) aligned with those reported in prior studies [20]. Contrary to the assertions of previous research [20–22], ECOG performance status exhibited no significant impact on survival.

Postoperative assessment revealed that the majority of neoplasms exhibited grade 2 differentiation, signifying a moderate degree of cellular maturation, which is in accordance with prior literature [17]. The histological grade did not demonstrate a statistically significant association with survival in this study, corroborating previous findings by Kim et al. [20] and others [17].

LVI and PNI were present in 31.3% and 33.3% of patients, respectively, though one-third of cases lacked evaluable data. A lower survival rate was observed in the patient cohort exhibiting

Table 1. Demographic and Clinical Characteristics of Patients

Variables		**N**	**%**
Gender	Female	38	51.4
	Male	36	48.6
Smoking	Never	37	50.0
	Current	30	40.5
	Former	7	9.5
Comorbidities		17	23.0
Diabetes Mellitus		-	-
Hypertension		9	12.2
Coronary Artery Disease		5	6.8
Congestive Heart Failure		2	2.7
Hyperlipidemia		2	2.7
Other		9	12.2
Family History		16	21.6
Family History	1. Degree Relatives	5	6.8
	2. Degree Relatives	13	17.6
	3. Degree Relatives	4	5.4
ECOG	0	27	36.5
	1	36	48.6
	2	11	14.9
Tumor Localization	Superficial	11	14.9
	Medial	20	27.0
	Lower	43	58.1
Preclinical Stage	Early Stage	20	27.0
	Local Advanced Stage	54	73.0
Status	Alive	39	52.7
	Deceased	35	47.3
		Mean±SD	**Median [Min – Max]**
Age		50.6±10.2	50 [24 – 71]
Smoking	Smoker	32.0±16.5	32.5 [1 – 60]
	Ex-smoker	22.1±18.8	30 [3 – 50]
Blood sample measurements		**N**	**%**
Hemoglobin	Low	25	33.8
	Normal/High	49	66.2
Albumin	Low	7	9.5
	Normal	67	90.5
LDH	High	35	53
	Normal	31	47

Footnote: Hemoglobin levels <12 g/dL in women and <13 g/dL in men were defined as low, albumin levels <3.5 g/dL as low, and LDH levels >248 IU/L as high.

Table 2. Pathological Features of Patients

Variables		**N**	**%**
TNM	T0N0M0	8	16.6
	T1N0M0	5	10.4
	T2N0M0	1	2.1
	T2N1M0	1	2.1
	T3N0M0	12	25.0
	T3N1M0	10	20.8
	T3N2M0	6	12.5
	T3N3M0	1	2.1
	T4N0M0	1	2.1
	T4N2M0	1	2.1
	T4N3M0	1	2.1
	T4NXM0	1	2.1
Stage	0	8	16.7
	1a	2	4.2
	1b	5	10.4
	2a	9	18.8
	2b	3	6.2
	3a	12	25
	3b	5	10.4
	3c	4	8.3
Operation	r0	45	93.8
	r1	2	4.2
	Palliative	1	2.1
Grade	1	7	14.6
	2	20	41.7
	3	9	18.8
	4	1	2.1
	Unknown	11	22.9
Lymphovascular invasion	(+)	15	31.3
	(-)	16	33.3
	Unknown	17	35.4
Perineural invasion	(+)	16	33.3
	(-)	15	31.3
	Unknown	17	35.4
Quantitative Tumor and Nodal Parameters		**Mean±SD**	**Median [Min-Max]**
Number of removed lymph nodes		12.7±10.6	11 [0 – 55]
Number of pathological lymph nodes		1.4±2.8	0 [0 – 14]
Macroscopic tumor diameter		4.2±2.0	4 [0.2 – 11]

Table 3. Comparison of Clinical Features According to Local Treatment Status

Variables		Total (n=74) (%)	CRT + Surgery (n=13) (%)	CRT (n=26) (%)	Surgery (n=35) (%)
Age (years)*		50.6 ± 10.2	46.5 ± 9.2	54.9 ± 8.2	48.9 ± 11.0
Gender	Female	38 (51.4)	9 (69.2)	8 (30.8)	21 (60)
	Male	36 (48.6)	4 (30.8)	18 (69.2)	14 (40)
Comorbidity	(+)	17 (23)	3 (23.1)	7 (26.9)	7 (20)
	(-)	57 (77)	10 (76.9)	19 (23.1)	28 (80)
Smoking	(+)	37 (50)	7 (53.8)	9 (34.6)	21 (60)
	(-)	37 (50)	6 (46.2)	17 (65.4)	14 (40)
Family History	(+)	16 (21.6)	2 (15.4)	5 (19.2)	9 (25.7)
	(-)	58 (78.4)	11 (84.6)	21 (80.8)	26 (74.3)
Tumor Localization	Superficial	11 (14.9)	1 (8.7)	9 (34.6)	1 (2.9)
	Medial	20 (27)	5 (38.5)	4 (15.4)	11 (31.4)
	Lower	43 (58.1)	7 (53.8)	13 (50)	23 (65.7)
ECOG	≤1	63 (86.3)	13 (100)	23 (88.5)	27 (77.1)
	≥2	10 (13.7)	-	3 (11.5)	8 (22.9)
Preclinical Status	Early	20 (27)	4 (30.8)	4 (15.4)	12 (34.3)
	Local Advanced	54 (73)	9 (69.2)	22 (84.6)	23 (65.7)
Recurrence	(+)	41 (55.4)	5 (38.5)	18 (69.2)	18 (51.4)
	(-)	33 (44.6)	8 (61.5)	8 (30.8)	17 (48.6)
Blood sample measurements					
Albumin	Low	7 (9.5)	-	1 (3.8)	6 (17.1)
	Normal	67 (90.5)	13 (100)	25 (96.2)	29 (82.9)
Hemoglobin	Low	25 (33.8)	3 (23.1)	9 (34.6)	13 (37.1)
	Normal/High	49 (66.2)	10 (76.9)	17 (65.4)	22 (62.9)
LDH	High	35 (53)	6 (46.2)	12 (48)	17 (60.7)
	Normal	31 (47)	7 (53.8)	13 (52)	11 (39.3)

Footnote: Hemoglobin levels <12 g/dL in women and <13 g/dL in men were defined as low, albumin levels <3.5 g/dL as low, and LDH levels >248 IU/L as high.

Table 4. Survival Analysis

Parameter		Total
Overall Survival (OS)	**Mortality**	35 (47.3%)
	1-year survival probability	79%
	3-year survival probability	51.9%
	5-year survival probability	38.3%
	Median survival time	38 months
Disease-Free Survival (DFS)	**Mortality**	41 (55.4%)
	1-year DFS probability	65.4%
	3-year DFS probability	39.3%
	5-year DFS probability	34%
	Median DFS time	24 months

Table 5. Factors Affecting Disease-Free Survival

Factors		Recurrence (N)	1-year recurrence probability (%)	3-year recurrence probability (%)	5-year recurrence probability (%)	Median recurrence (months)	P
Gender	Female	18	80.9	47.2	43.3	36	0.030
	Male	23	48.4	30.8	20.5	12	
Smoking	(-)	20	77.7	43.5	39.9	35	0.137
	(+)	21	52	35.6	23.8	14	
Comorbidity	(+)	9	80	45.5	18.2	35	0.529
	(-)	32	61.1	37.3	37.3	19	
Family History	(+)	7	61.9	61.9	49.5	53	0.362
	(-)	34	66.3	33.6	30.8	22	
Tumor localisation	Superficial	9	50	0	0	11	0.025
	Medial	8	78.8	59.1	51.7	-	
	Low	24	63.3	39	34.1	24	
Preclinical stage	Early stage	11	61.5	34.2	34.2	27	0.948
	Local advanced	30	66.9	41.7	34.2	22	
Lymphovascular invasion	(+)	10	57.1	28.6	28.6	12	0.057
	(-)	6	93.8	55.8	37.2	40	
	Not available	6	93.3	66	57.8	-	
Perineural invasion	(+)	12	50	31.3	25	12	0.060
	(-)	4	85.1	66.2	66.2	-	
	Not available	6	93.3	66	57.8	-	
Tumor Size	<4	7	71.4	48.2	48.2	36	0.608
	≥4	13	67.4	47.6	35.3	32	
Grade	1-2	13	80.8	56.5	47.4	53	0.138
	3-4	7	42.4	31.8	31.8	12	
ECOG	0	13	76.6	43	43	24	0.248
	1	18	60.6	46.1	41	27	
	2	9	60	20	0	17	
Cure	CRT+surgery	5	81.8	0	0	36	0.014
	CRT	18	50.9	17.6	17.6	13	
	Surgery	18	69.7	51.2	44	40	

Table 6. Cox proportional hazards regression for DFS

Variables	Hazard ratio (HR)	95% Confidence Interval (CI)	p
Age	1.003	0.971 – 1.036	0.855
Removing lymph node	0.987	0.944 – 1.033	0.575
Pathological lymph node	1.189	1.058 – 1.336	**0.004**
Hemoglobin	1.070	0.898 – 1.274	0.450
Albumin	0.742	0.394 – 1.396	0.355
LDH	1.001	0.999 – 1.003	0.322

lymphovascular invasion (31%) and perineural invasion (34%) compared to the cohort without these features (65%), yet this difference failed to reach statistical significance. Previous studies, however, have established PNI as an independent predictor of poor prognosis, with particular relevance to post-radiotherapy outcomes [23, 24]. Analysis of LVI and PNI impact on prognosis demonstrated no influence on survival rates. Studies reporting comparable LVI rates (33.8% and 36.8%) demonstrated the independent prognostic effect of LVI on patient survival. In contrast to our study, these studies focused on particular groups, including those with "node-negative" status or only receiving "neoadjuvant treatment" [24, 25]. PNI's role as an independent prognostic factor was confirmed by a study of 433 post-surgery patients [25].

The role of tumor size in predicting esophageal cancer outcomes is still uncertain. Although several studies have established a 4 cm critical threshold [16,17,26], the results are inconsistent. While Wu et al. [16] and Ma et al. [26] identified tumor size as an independent prognostic factor, Wu et al. [16] highlighted its limited clinical value. Alternatively, other studies reported no significant correlation between tumor size and prognosis [27,28]. Five-year OS in our cohort was 66.3% for tumors < 4 cm and 36.7% for tumors ≥4 cm (4 cm cutoff), but this difference was not statistically significant. Importantly, the extent of lymph node involvement (AJCC 7th edition, N0–N3) is still a more reliable predictor of prognosis in esophageal cancer.

Our cohort exhibited a mean of 1.4 ± 2.8 pathological lymph nodes. This variable demonstrated a statistically significant influence on OS and DFS rates, consistent with the established literature. Previous literature, preceding the seventh edition of the AJCC, similarly highlighted the prognostic significance of categorizing nodal involvement based on the quantity of metastatic nodes [28].

A comparison of adjuvant and neoadjuvant treatment groups revealed a longer median survival in the adjuvant group (54 vs. 19 months for OS, 40 vs. 16 months for DFS); however, this difference lacked statistical significance. Xu et al. [29] conducted a review of clinical studies and meta-analyses comparing neoadjuvant and adjuvant CRT, revealing that neoadjuvant CRT enhances R0 resection rates and tumor control. However, the variability in randomized controlled trials made it difficult to conclude which approach is superior.

While surgery is the usual treatment for resectable esophageal cancer, 5-year survival is only 15–35% because of high recurrence, indicating suboptimal outcomes [30]. Guidelines now widely recommend a multidisciplinary approach where neoadjuvant CRT is followed by surgery [31]. Potential benefits of this approach include early micro metastasis treatment, tumor downstaging, and improved surgical removal. Numerous studies, including randomized controlled trials and meta-analyses, have investigated adding chemo and/or radiotherapy to surgery [32]. Preoperative concurrent CRT is preferred over chemotherapy alone by both the National Comprehensive Cancer Network (NCCN) and the European Society of Medical Oncology (ESMO) guidelines, given its superior outcomes [33]. In conclusion, our research findings bolster the accumulating evidence supporting a multidisciplinary approach to the management of non-metastatic esophageal SCC. Significant associations with survival were observed for certain prognostic markers (gender, tumor location, nodal involvement), while others (histologic grade, tumor size, ECOG performance status) failed to demonstrate consistent predictive capacity in the present cohort. These observed variations emphasize the prognostic complexities of esophageal cancer, thus demanding a more integrated, clinically driven approach to decision-making that surpasses the limitations of conventional staging. Additional rigorous research is required to elucidate the functions of novel biomarkers and refine personalized treatment strategies.

Limitations

This study has several limitations. Its retrospective, single-center nature may limit the generalizability of the results and introduce selection bias. The relatively small sample size reduced the statistical power for identifying weak prognostic effects. Incomplete documentation of some pathological parameters, such as perineural and lymphovascular invasion, restricted subgroup analyses. Furthermore, heterogeneity in treatment protocols (chemoradiotherapy regimens and surgical approaches) might have influenced survival outcomes. Future prospective, multicenter studies with larger populations and standardized treatment strategies are warranted to validate and expand these findings.

CONCLUSION

This study analyzed significant prognostic factors for non-metastatic esophageal SCC, namely gender, tumor site, local treatment method, and the extent of lymph node involvement. Although the majority of patients received surgery as a solitary

treatment, a multimodal approach of surgery, chemotherapy, and radiotherapy yielded substantially improved patient survival rates, thereby highlighting the significance of a multidisciplinary strategy. It is noteworthy that local recurrence occurred more frequently than distant metastasis. Considering the unfavorable prognosis for esophageal SCC, these results underscore the necessity of personalized treatment approaches. Subsequent multicenter studies with expanded patient populations are crucial for confirming these results and enhancing the precision of prognostication and treatment selection.

Acknowledgments: The authors thank all healthcare personnel involved in patient data collection.

Conflict of Interest: The authors declare that they have no conflicts of interest.

Informed Consent: As this was retrospective research, informed consent was not required.

Funding: This study received no external funding.

Data Availability Statement: The data supporting this study's findings are available on request from the corresponding author. The data is not publicly available due to privacy or ethical restrictions.

Disclosure of Relationships and Activities: The authors declare that they have no competing interests.

Author Statement Regarding the Use of Artificial Intelligence-Enhanced Tools: The authors used AI and AI-assisted Technologies (Grammarly and MS Word Editor) in the writing process. These technologies improved the readability and language of the work but did not replace key authoring tasks such as producing scientific or medical insights, drawing scientific conclusions, or providing clinical recommendations. The authors are ultimately responsible and accountable for the contents of the whole work.

Ethical Approval: Institutional approval was obtained from Ethic Committee of Ankara Numune Training and Research Hospital (No. 1155/2016, Date: 2016–06–29); the study was conducted in accordance with the Declaration of Helsinki.

Author Contributions:
Conception: HZD
Design: NO
Supervision: NO
Data Collection and/or Processing: HZD, SOK
Analysis and/or Interpretation: HZD, SOK
Literature Review: HZD
Writing: HZD, SOK
Critical Review: HZD, NO

REFERENCES

[1] Oshima K, Tsushima T, Ito Y, Kato K (2024) Recent progress in chemoradiotherapy for oesophageal squamous cell carcinoma. Jpn J Clin Oncol. 54:395–402. https://doi.org/10.1093/jjco/hyae005

[2] Türkay D, Vural Ç, Sayan M, Gürbüz Y (2016) Detection of human papillomavirus in esophageal and gastroesophageal junction tumors: A retrospective study by real-time polymerase chain reaction in an instutional experience from Turkey and review of literature. Pathol Res Pract. 212:77–82. https://doi.org/10.1016/j.prp.2015.10.007

[3] Qu HT, Li Q, Hao L, Ni YJ, Luan WY, Yang Z, Chen XD, Zhang TT, Miao YD, Zhang F. (2024) Esophageal cancer screening, early detection and treatment: Current insights and future directions. World J Gastrointest Oncol. 16:1180–1191. https://doi.org/10.4251/wjgo.v16.i4.1180

[4] Qi JH, Huang SL, Jin SZ (2024) Novel milestones for early esophageal carcinoma: From bench to bed. World J Gastrointest Oncol. 16:1104–1118. https://doi.org/10.4251/wjgo.v16.i4.1104

[5] Zhu LH, Yao J, Wu T, Wang Y, Wang CW, Xue CQ, Wu LG, Fan XW, Wu CY. (2020) Risk of Recurrence and Metastasis for Patients with T1N0M0 Esophageal Carcinoma Who Achieve Completed Resection via Endoscopic Submucosal Resection: Evidence for the Appropriateness of the Watch and Wait Follow-Up Strategy. Cancer Manag Res. 12:2427–2435. https://doi.org/10.2147/cmar.S227959

[6] Liu J, Wei Z, Zhang J, Hu W, Ma Z, Liu Q (2016) Which factors are associated with extremely short-term survival after surgery in patients with esophageal squamous cell carcinoma? Asia Pac J Clin Oncol. 12:308–313. https://doi.org/10.1111/ajco.12503

[7] Uchinami Y, Myojin M, Takahashi H, Harada K, Shimizu S, Hosokawa M (2016) Prognostic factors in clinical T1N0M0 thoracic esophageal squamous cell carcinoma invading the muscularis mucosa or submucosa. Radiat Oncol. 11:84. https://doi.org/10.1186/s13014-016-0660-4

[8] Yang H, Chen Y, Huang X, Gu Y, Chen Z, Mao W (2024) Bioinformatics Analysis Reveals a Novel Prognostic Model for Esophageal Squamous Cell Carcinoma. Int J Med Sci. 21:1213–1226. https://doi.org/10.7150/ijms.93423

[9] Liu M, Yang W, Guo C, Liu Z, Li F, Liu A, Yang H, Shen L, Wu Q, Duan L, Wang H, Tian H, Shi C, Pan Y, Liu Y, Liu F, Weiss NS, Cai H, He Z, Ke Y. (2024) Effectiveness of Endoscopic Screening on Esophageal Cancer Incidence and Mortality: A 9–Year Report of the Endoscopic Screening for Esophageal Cancer in China (ESECC) Randomized Trial. J Clin Oncol. 42:1655–1664. https://doi.org/10.1200/jco.23.01284

[10] Arnold M, Soerjomataram I, Ferlay J, Forman D (2015) Global incidence of oesophageal cancer by histological subtype in 2012. Gut. 64:381–387. https://doi.org/10.1136/gutjnl-2014-308124

[11] Bohanes P, Yang D, Chhibar RS, Labonte MJ, Winder T, Ning Y, Gerger A, Benhaim L, Paez D, Wakatsuki T, Loupakis F, El-Khoueiry R, Zhang W, Lenz HJ. (2012) Influence of sex on the survival of patients with esophageal cancer. J Clin Oncol. 30:2265–2272. https://doi.org/10.1200/jco.2011.38.8751

[12] Chen J, Zhu J, Pan J, Zhu K, Zheng X, Chen M, Wang J, Liao Z. (2010) Postoperative radiotherapy improved survival of poor prognostic squamous cell carcinoma esophagus. Ann Thorac Surg. 90:435–442. https://doi.org/10.1016/j.athoracsur.2010.04.002

[13] Freedman ND, Abnet CC, Caporaso NE, Fraumeni JF Jr, Murphy G, Hartge P, Hollenbeck AR, Park Y, Shiels MS, Silverman DT. (2016) Impact of changing US cigarette smoking patterns on incident cancer: risks of 20 smoking-related cancers among the women and men of the NIH-AARP cohort. Int J Epidemiol. 45:846–856. https://doi.org/10.1093/ije/dyv175

[14] Fahey PP, Page A, Stone G, Astell-Burt T (2020) Augmenting cancer registry data with health survey data with no cases in common: the relationship between pre-diagnosis health behaviour and post-diagnosis survival in oesophageal cancer. BMC Cancer. 20:496. https://doi.org/10.1186/s12885-020-06990-3

[15] Schuring N, van Berge Henegouwen MI, Gisbertz SS (2024) History and evidence for state of the art of lymphadenectomy in esophageal cancer surgery. Dis Esophagus. 37:4;doad065. https://doi.org/10.1093/dote/doad065

[16] Wu J, Chen QX (2016) Prognostic and predictive significance of tumor length in patients with esophageal squamous cell carcinoma undergoing radical resection. BMC Cancer. 16:394. https://doi.org/10.1186/s12885-016-2417-8

[17] Situ D, Wei W, Lin P, Long H, Zhang L, Fu J, Rong T, Ma G. (2013) Do tumor grade and location affect survival in esophageal squamous cell carcinoma? Survival analysis of 302 cases of pT3N0M0 esophageal squamous cell carcinoma. Ann Surg Oncol. 20:580–585. https://doi.org/10.1245/s10434-012-2656-0

[18] Wang Y, Wang L, Yang Q, Li J, Qi Z, He M, Yao J, Qiao X. (2015) Factors on prognosis in patients of stage pT3N0M0 thoracic esophageal squamous cell carcinoma after two-field esophagectomy. J Cancer Res Ther. 11 Suppl 1:C16–23. https://doi.org/10.4103/0973-1482.163833

[19] Bouvier AM, Binquet C, Gagnaire A, Jouve JL, Faivre J, Bedenne L (2006) Management and prognosis of esophageal cancers: has progress been made? Eur J Cancer. 42:228–233. https://doi.org/10.1016/j.ejca.2005.08.038

[20] Kim DE, Kim UJ, Choi WY, Kim MY, Kim SH, Kim MJ, Shim HJ, Hwang JE, Bae WK, Chung IJ, Nam TK, Na KJ, Cho SH. (2013) Clinical prognostic factors for locally advanced esophageal squamous carcinoma treated after definitive chemoradi-otherapy. Cancer Res Treat. 45:276–284. https://doi.org/10.4143/crt.2013.45.4.276

[21] Fakhrian K, Heilmann J, Schuster T, Thamm R, Reuschel W, Molls M, Geinitz H. (2012) Primary radiotherapy with or without chemotherapy in non-metastatic esophageal squamous cell carcinoma: a retrospective study. Dis Esophagus. 25:256–262. https://doi.org/10.1111/j.1442-2050.2011.01244.x

[22] Ordu AD, Nieder C, Geinitz H, Kup PG, Deymann LF, Scherer V, Combs SE, Fakhrian K. (2015) Radio (chemo) therapy for locally advanced squamous cell carcinoma of the esophagus: long-term outcome. Strahlenther Oncol.

191:153–160. https://doi.org/10.1007/s00066-014-0779-x

[23] Chen WH, Huang YL, Chao YK, Yeh CJ, Chang HK, Tseng CK, Liu YH. (2015) Prognostic significance of lymphovascular invasion in patients with esophageal squamous cell carcinoma treated with neoadjuvant chemoradiotherapy. Ann Surg Oncol. 22:338–343. https://doi.org/10.1245/s10434-014-3881-5

[24] Ning ZH, Zhao W, Li XD, Chen LJ, Xu B, Gu WD, Shao YJ, Xu Y, Huang J, Pei HL, Jiang JT. (2015) The status of perineural invasion predicts the outcomes of postoperative radiotherapy in locally advanced esophageal squamous cell carcinoma. Int J Clin Exp Pathol. 8:6881–6890.

[25] Chen JW, Xie JD, Ling YH, Li P, Yan SM, Xi SY, Luo RZ, Yun JP, Xie D, Cai MY. (2014) The prognostic effect of perineural invasion in esophageal squamous cell carcinoma. BMC Cancer. 14:313. https://doi.org/10.1186/1471-2407-14-313

[26] Ma MQ, Yu ZT, Tang P, Jiang HJ, Zhao XJ, Zhang JG, Qu DW, Jin QW, Zhang XZ. (2015) Is tumor length a prognostic indicator for esophageal squamous cell carcinoma? A single larger study among Chinese patients. Int J Clin Exp Pathol. 8:5008–5016

[27] Bollschweiler E, Baldus SE, Schröder W, Schneider PM, Hölscher AH (2006) Staging of esophageal carcinoma: length of tumor and number of involved regional lymph nodes. Are these independent prognostic factors? J Surg Oncol. 94:355–363. https://doi.org/10.1002/jso.20569

[28] Wijnhoven BP, Tran KT, Esterman A, Watson DI, Tilanus HW (2007) An evaluation of prognostic factors and tumor staging of resected carcinoma of the esophagus. Ann Surg. 245:717–725. https://doi.org/10.1097/01.sla.0000251703.35919.02

[29] Xu Y, Yu X, Chen Q, Mao W (2012) Neoadjuvant versus adjuvant treatment: which one is better for resectable esophageal squamous cell carcinoma? World J Surg Oncol .10:173. https://doi.org/10.1186/1477-7819-10-173

[30] Stahl M, Budach W, Meyer HJ, Cervantes A (2010) Esophageal cancer: Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 21 Suppl 5:v46–49. https://doi.org/10.1093/annonc/mdq163

[31] Matsuda S, Tsubosa Y,Sato H, Takebayashi K, Kawamorita K, Mori K, Niihara M, Tsushima T, Yokota T, Onozawa Y, Yasui H, Takeuchi H,Kitagawa Y. (2017) Comparison of neoadjuvant chemotherapy versus upfront surgery with or without chemotherapy for patients with clinical stage III esophageal squamous cell carcinoma. Dis Esophagus. 30:1–8. https://doi.org/10.1111/dote.12473

[32] Sjoquist KM, Burmeister BH, Smithers BM, Zalcberg JR, Simes RJ, Barbour A, Gebski V; Australasian Gastro-Intestinal Trials Group. (2011) Survival after neoadjuvant chemotherapy or chemoradiotherapy for resectable oesophageal carcinoma: an updated meta-analysis. Lancet oncol. 12:681–692

[33] Zagouri F, Liakou P, Bartsch R, Peccatori FA, Tsigginou A, Dimitrakakis C, Zografos GC, Dimopoulos MA, Azim HA Jr. (2015) Discrepancies between ESMO and NCCN breast cancer guidelines: An appraisal. Breast .24:513–523. https://doi.org/10.1016/j.breast.2015.02.031

How to Cite;

Dikici HZ, Ozdemir N, Ozkan Karaahmetoglu S (2026) Median Nerve Strain and Shear Wave Elastography in Hypothyroid Patients With Carpal Tunnel Syndrome Symptoms. Eur J Ther. 32(3):290–301. https://doi.org/10.58600/eurjther2917