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Original Article

The Impact of Multidisciplinary Approach on Survival in Esophageal Cancer

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ABSTRACT

Objective: Esophageal cancer, one of the most aggressive gastrointestinal malignancies, is the eighth-most common cancer in the world and the sixth among cancer-related deaths in men. In our study, we aimed to show the survival effect of the multidisciplinary approach in the treatment of esophageal cancer.

Methods: The records of 103 patients who were diagnosed with esophageal cancer pathologically by endoscopy and underwent curative resection between January 2010 and December 2020 were reviewed retrospectively. The patients were evaluated in the multidisciplinary tumor council and appropriate treatment (neoadjuvant therapy+surgery or only surgery) was planned for each patient according to the TNM stage.T1N0M0 and T2N0M0 patients underwent direct surgery, T2-T3 and those who were considered to be locally advanced with the suspicion of lymph node metastasis underwent surgery after neoadjuvant therapy. As the surgical method, Ivor-Lewis+D2 lymph node dissection or transhiatal esophagectomy surgery was applied in lower and middle localization tumors of the esophagus, whereas McKeown surgery was preferred in middle and upper esophageal tumors.

Results: Of the 103 patients included in the study, 51 (49.5%) were male and 52 (50.5%) were female. Neoadjuvant chemoradiotherapy (NCRT) was applied to 70 (67.9%) patients. While the 5-year survival rate of 70 patients who received NCRT was 69.7% (mean 56 months) of the 5-year survival rate of 33 patients who underwent direct surgery without neoadjuvant therapy was found to be 39.5 (mean 25 months), and there was a statistically significant difference observed ($p<0.05$). The recurrence rate in the 5-year follow-up of 70 patients who received NCRTwas 31.4% (mean 48 months). The recurrence rate in the 5-year follow-up of 33 patients who did not receive neoadjuvant treatment and underwent direct surgery was 60.6% (mean 21 months). The rate of recurrence was statistically significant between patients who received neoadjuvant therapy and those who did not receive neoadjuvant therapy ($p<0.05$).

Conclusion: We believe that NCRT+surgery with a multidisciplinary approach in the treatment of patients with esophageal cancer have better survival results than those who underwent direct surgery.

INTRODUCTION

Esophageal cancer, which is one of the most aggressive gastrointestinal malignancies, is the eighth most common cancer type in the world and the sixth among cancer-related deaths in men.[1] There are two main histological subtypes of esophageal cancer and differ between geographic regions. Squamouscell carcinoma (SCC) has a higher prevalence in Eastern Asia, Eastern and Southern Africa, and Southern Europe, whereas adenocarcinoma (AC) is much more common in other parts of North America and Europe.[2] In order to determine an appropriate method for each patient in the treatment, it should be planned individually according to the type of cancer, local or regional involvement, and the functionalstatus of the patient.[3] For all resectable cases, the main component of treatment is considered to be surgery.[4] Although esophagectomy is often the mainstay of treatment in esophageal cancer, it has a high incidence of morbidity and mortality.[5] In general, patients with esophageal cancer are diagnosed at an advanced stage where surgery alone is not curative, and a multidisciplinary approach is required to perform curative treatment in suchcases.[6] Despite surgical treatment, the overall 5-year survival rate is low and ranges from 31% to 55%.[7,8] Local recurrence in the anastomosis line is observed in 43–53% of these patients, whereas distant metastases are observed in the supraclavicular lymph nodes and mediastinal lymph nodes, and the median time to re-

currence varies between 10 and 12 months.[9,10]

Recent studies have shown that esophagectomy performed after the application of neoadjuvant chemotherapy (NCT) or neoadjuvant chemoradiotherapy (NCRT) reduces the development of local recurrence and distant metastasis.[6,11] Promising results of locally applied radiotherapy have been shown in controlling lymph node recurrence after curative resection.[12-14] In many studies conducted in recent years, it has been shown that concurrent chemoradiotherapy (CRT) is effective in eliminating micrometastases, reducing distant metastases by increasing radiosensitivity, and providing local control.[15-17] In this study, we aimed to evaluate the results of the multidisciplinary treatment approach applied to our patients with esophageal cancer and compare them with the literature.

MATERIALS AND METHODS

The records of 103 patients who were diagnosed and operated endoscopically for esophageal cancer between January 2010 and December 2020 were reviewed retrospectively. Approval for this study was obtained from the local ethics committee (1/253/514/2023).

Patients with distant organ metastases, previous history of other organ malignancies, patients who could not undergo curative resection, obstructed or perforated patients who underwent emergency surgery, patients with systemic diseases (such as leukemia and lymphoma), and patients who developed mortality due to complications in the early post-operative period were excluded from the study. In this single-center study, all patients were staged preoperatively according to tumor size, lymph node involvement, and metastasis (TNM) status. Computed tomography (CT), positron-emission tomography (PET/CT), and endoscopic ultrasound (EUS) were used for staging purposes. All patients were evaluated in the multidisciplinary tumor council, and appropriate treatment (neoadjuvant therapy + surgery or direct surgery) was planned according to the TNM stage. T1N0M0 and T2N0M0 patients underwent direct surgery, and T2-T3 patients who were thought to be locally advanced with the suspicion of lymph node metastasis underwent surgery after neoadjuvant therapy.

After NCRT treatment, patients were reevaluated with CT, PET/CT, and EUS before surgery and operated within 6–8 weeks. As the surgical method, Ivor-Lewis + D2 lymph node dissection or transhiatal esophagectomy surgery was preferred in lower and middle localized esophageal tumors, and McKeown surgical technique was preferred in middle and upper esophageal tumors. Follow-ups were performed with chest X-ray, complete blood count, and routine biochemical tests in the 1st month postoperatively and every 3 months thereafter. Abdominal and thorax CT and PET/CT were performed at 6-month intervals. The anastomosis line was visualized by endoscopy in patients who developed dysphagia or suspected recurrence in the follow-ups, and biopsies were taken from the necessary areas for a definitive pathological diagnosis.

Adjuvant CRT was planned for patients with high tumor burden, lymph node metastasis, and recurrence in the post-operative period. The demographic characteristics of the patients, the histological pathological subgroup of the tumor, the effects of NCRT and direct surgical treatment on 5-year survival and recurrence were evaluated.

Statistical Analyzes

The Statistical Package for the Social Sciences was used for Windows 10.0 software. Data were summarized as mean ± standard deviation, numbers (n), and percent (%). Categorical variables were compared using the Chi-square test or Fisher's exact test. All statistical calculations were two-sided, and $p<0.05$ showed statistical significance at the 95% confidence interval.

RESULTS

Of the 103 patients included in our study who were operated on with the diagnosis of esophageal cancer, 51 (49.5%) were male and 52 (50.5%) were female. The mean age was 58 years (19–79). While 89 (86.4%) patients had SCC tumor type, 14 (13.6%) patients had AC tumor type. NCRT was administered to 70 patients (67.9%). McKeown surgery was performed in 38 (36.8%) of the operated patients, Ivor–Lewis surgery was performed in 33 (32.1%), and transhiatal esophagectomy was performed in 32 (31.1%) patients (Table 1).

In the examination of tumor localizations of the patients, it was found that 1/3 of the upper esophagus was located in 6 (5.8%) patients, the middle esophagus in 28 (27.1%) patients, and 1/3 distal esophagus in 69 (67.1%) patients. The mean esophageal tumor length in pathology reports was 49.2 mm (r: 9–120 mm). The mean number of lymph nodes removed by surgery was 14±8. In clinical follow-ups, the mean 5-year survival rate of 103 patients was 60.2%, this rate was 62.4% in patients with SCC and 50.2% in patients with AC, but no statistically significant difference was detected ($p>0.05$). While the 5-year survival rate of 70 patients who underwent NCRT was 69.7% (mean 56 months), the 5-year survival rate of 33 patients who un-

Table 1. Demographic, tumor type, and treatment characteristics of the patients

	Study group, n=103 (%)
Gender	
Male	51 (49.5)
Female	52 (50.5)
Treatment	
Direct surgery	33 (32.1)
NCRT+surgery	70 (67.9)
Surgical Procedure	
McKeown	38 (36.8)
Ivor-Lewis	33 (32.1)
Transhiatal	32 (31.1)

Table 2. Five-year survival rates of the patients

n=103	N	5-year survival (%)	p-value
All patients	103	60.2	
SCC	89	62.4	
AC	14	50.2	p>0.05
NCRT+surgery	70	69.7	
Direct surgery	33	39.5	p<0.05

AC: Adenocarcinoma; NCRT: Neoadjuvantchemoradiotherapy; SCC: Squamous cell carcinoma.

derwent direct surgery without neoadjuvant therapy was 39.5% (mean 25 months), and there was a statistically significant difference (p<0.05) (Table 2).

Postoperatively, tumor recurrence was observed in 42 (40.7%) patients. Of these patients, 15 had local recurrence, 18 had distant metastases, and 9 had both local and distant metastases. The recurrence rate in the 5-year follow-up of 70 patients who underwent NCRT was 31.4% (mean 48 months). The recurrence rate in the 5-year follow-up of 33 patients who did not receive neoadjuvant treatment and underwent direct surgery was 60.6% (mean 21 months). The difference in recurrence rate between patients who received neoadjuvant therapy and those who did not receive neoadjuvant therapy was found to be statistically significant (p<0.05).

DISCUSSION

In the treatment of resectable esophageal cancer, NCRT+-surgery has been shown to be the most recommended and applied treatment method compared to surgery alone.[18-21] It has been reported that NCRT+surgery is superior to NCT+surgery or surgery alone in terms of overall survival and recurrence-free survival.

While some studies have indicated that therapeutic CRT may be an alternative to esophagectomy for patients who are unsuitable for surgery or refuse surgery, they have shown that survival outcomes are similar, especially for patients with clinical Stage I SCC.[22,23] In contrast to Stage I SCC patients, because of the significantly lower survival results of CRT compared to esophagectomy after NCRT in patients with Stage II/III SCC, it has been shown that CRT should not be used for treatment alone but should be included in multidisciplinary treatment together with esophagectomy as the main modality method.[24]

NCRT is the gold standard for the treatment of esophageal cancer with locally advanced resectable SCC in most Western countries, and although it provides better survival outcomes for patients with both histologic subtypes, the survival benefit is more pronounced in those with SCC than in those with AC. In these studies, a pathologically complete response was observed in 49% of patients with SCC and 23% of patients with AC in the pathology piece resected in the NCRT group.[19,20,25]

In our study, we found that the 5-year survival rate was higher in patients with SCC (62.4%), whereasit was 50.2% in patients with AC, which is consistent with the literature.

Recent studies have shown that 43–53% of patients operated for esophageal cancer develop local recurrence or distant metastasis, and the median time to recurrence ranges from 10 to 12 months, while the most common sites of local recurrence are the supraclavicular and mediastinal lymph nodes of the anastomosis line.[7-9] In studies showing that NCRT+surgery is superior to surgery alone in terms of survival in patients with SCC and AC, the recurrence rate after a 5-year follow-up was found to be 35% in the NCRT+surgery group, and 58% in the surgery-only group.[19,25,26] In our study, similar results were obtained with the literature, with a recurrence rate of 31.4% (mean 48 months) in patients who underwent NCRT+surgery after a 5-year follow-up, and 60.6% (mean 21 months) in patients who underwent only surgery.

In previous studies, the 5-year overall survival rate of patients who underwent surgery ranged from 31 to 55%.[7,8] In the study of Udagawa et al., it was shown that the 5-year survival rate increased up to 64.8% with lymph node dissection.[27]

In the follow-ups of our patients, the mean 5-year survival rate of 103 patients was found to be 60.2%, which was consistent with the literature, while the mean number of lymph nodes removed by surgery was 14±8.

In the study of Van Hagen et al.,[19] 5-year survival rates were shown in 366 patients with T1-3, N0-1, M0 esophageal cancer who underwent surgery. The rates were as follows: 47% (mean 49 months) in those who underwent NCRT + Surgery, and 37% (mean 24 months) in those who underwent surgery only. In another study, 5-year survival was found to be 54.8% in patients with stage II/III esophageal cancer who underwent surgery after NCRT.[24]

In our study, in the same stage patients who underwent curative resection, the 5-year survival rate was 69.7% in those who underwent NCRT + surgery, whereas it was found to be better at 39.5% in those who underwent only surgery. It is thought that technological developments both in the field of CRT and in surgical applications are effective in obtaining better results.

Conclusion

The multidisciplinary approach and NCRT+surgery applications in the treatment of patients with esophageal cancer offer better survival results than direct surgery. We believe that multidisciplinary treatment will come to the fore more in the treatment plans of esophageal cancer and that new studies supporting this view will be added to the literature.

Ethics Committee Approval

This study approved by the Kartal Dr. Lütfi Kırdar City Hospital Clinical Research Ethics Committee (Date: 12.07.2023, Decision No: 2023/514/253/I).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: M.M.A.; Design: R.D.; Supervision: M.M.A.; Fundings: A.Ç., R.D.; Materials: M.M.A., R.D.; Data: R.D., A.Ç.; Analysis: R.D., A.Ç.; Literature search: M.M.A., R.D.; Writing: M.M.A., R.D., A.Ç.; Critical revision: R.D., A.Ç.

Conflict of Interest

None declared.

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Özofagus kanserinde multidisipliner yaklaşımın sürviye etkisi

Amaç: Gastrointestinal malignitelerin en agresiflerinden biri olan özofagus kanseri, dünyada en yaygın görülen sekizinci kanser türü olup, erkeklerde kansere bağlı ölümlerin altıncı sırasındadır. Çalışmamızda, özofagus kanseri tedavisinde multidisipliner yaklaşımın sürviye etkisini göstermeyi amaçladık.

Gereç ve Yöntem: Hastanemizde Ocak 2010-Aralık 2020 yılları arasında endoskopi ile patolojik olarak özofagus kanseri tanısı alan ve küratif rezeksiyon yapılan 103 hastanın kayıtları retrospektif olarak incelendi. Hastalar multidispliner tümör konseyinde değerlendirilerek her hastaya TNM evresine göre uygun tedavi (Neoadjuvan tedavi + Cerrahi veya direk Cerrahi) planlandı. T1N0M0 ve T2N0M0 hastalara direk cerrahi, T2-T3 ve lenf nodu metastaz şüphesi ile lokal ileri evre olarak kabul edilenlere neoadjuvan tedavi sonrası cerrahi uygulandı. Cerrahi yöntem olarak, özofagusun alt ve orta lokalizasyon tümörlerinde Ivor-Lewis+D2 lenf nodu diseksiyonu veya transhiyatal özofajektomi ameliyatı, orta ve üst özofagus tümörlerinde ise McKeown ameliyatı tercih edildi. Hastaların demografik özellikleri ile tümörün histolojik alt gurubu, Neoadjuvan Kemoradyoterapi uygulanması ve direk Cerrahi tedavinin, beş yıllık sağ kalım ve lokal nüks üzerine etkileri irdelendi.

Bulgular: Çalışmaya alınan 103 hastanın 51'i (%49.5) erkek, 52'si (%50.5) kadındı. Yaş ortalaması 58/yıl (19-79) olarak bulundu. Hastaların 89'u (%86.4) skuamöz hücreli karsinom tümör tipine sahipken, 14'ü (%13.6) adenokarsinom tümör tipindeydi. Neoadjuvan kemoradyoterapi 70 (%67.9) hastaya uygulandı. Ameliyata alınan hastaların 38'ine (%36.8) McKeown ameliyatı, 33'üne (%32.1) Ivor-Lewis ameliyatı ve 32'sine (%31.1) transhiyatal özofajektomi uygulandı. Klinik takiplerinde hastaların beş yıllık ortalama sağ kalım oranı %60.2 iken, bu oran patolojik tip olarak skuamöz hücreli karsinom'lu hastalarda %62.4 ve adenokarsinom'lu hastalarda %50.2 sağlandı, istatistiksel olarak anlamlı bir fark tespit edilmedi ($p>0.05$). Neoadjuvan kemoradyoterapi alan 70 hastanın beş yıllık sağ kalım oranı %69.7 (ortalama 56 ay) bulunurken, neoadjuvan tedavi uygulanmadan direk cerrahi uygulanan 33 hastanın beş yıllık sağ kalım oranı %39.5 (ortalama 25 ay) olarak bulundu, istatistiksel olarak anlamlı fark görüldü ($p<0.05$). Postoperatif takip döneminde 42 (%40.7) hastada tümör nüksü görüldü. Neoadjuvan kemoradyoterapi alan 70 hastanın beş yıllık takipte nüks görülme oranı %31.4 (ortalama 48 ay) idi. Neoadjuvan tedavi almayan ve direk cerrahi uygulanan 33 hastanın beş yıllık takipte nüks görülme oranı %60.6 (ortalama 21 ay) olarak bulundu. Neoadjuvan tedavi alan hastalarla, neoadjuvan tedavi almayanlar arasında nüks görülme oranı istatistiksel olarak anlamlı bulundu ($p<0.05$).

Sonuç: Özofagus kanserli hastaların tedavisinde multidispliner yaklaşımla NKRT+Cerrahi uygulamalarının, direk Cerrahi uygulananlara göre daha iyi sağ kalım sonuçlarına sahip olduğu kanaatindeyiz.

Anahtar Sözcükler: Cerrahi; multidisipliner tedavi; özofagus kanseri.