



The Comparative Effect of Definitive Chemoradiotherapy and Neoadjuvant Chemoradiotherapy Plus Surgery on One-Year Survival Rate of Esophageal Cancer Patients

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Abstract

Background: Esophageal cancer is a malignancy with a poor survival rate, and the optimal management of esophageal cancer patients is still controversial. This study aimed to compare the one-year survival of patients who had received definitive chemoradiotherapy (DCRT) or neoadjuvant chemoradiotherapy plus surgery (NCRT + S).

Materials and Methods: In this cross-sectional descriptive study, the medical records of esophageal cancer were extracted from 2018 to 2019; the last survival status of patients was obtained one year after the end of the treatment course. Data were analyzed using SPSS (version 16), and survival was estimated by the Kaplan-Meier method with the log-rank test. A *P* value of less than 0.05 was considered significant for all the performed tests.

Results: Among 43 eligible patients, 39.5% were males and 60.5% were females. The mean age of the patients was 68.16 ± 12.03 years. In this population, 81.4% of cases had squamous cell carcinoma (SCC), and the rest had adenocarcinoma (ADC). In addition, 58.1% and 41.9% of cases were treated by DCRT and NCRT + S, respectively. The one-year survival rate was 68% and 66.67% in the DCRT and NCRT + S groups, respectively ($P > 0.05$). The one-year survival rate did not have significant relevance to the age of patients and histologic subtype. In terms of gender, there was no significant difference between males and females regarding the one-year survival rate.

Conclusion: There were no statistically significant differences in the one-year survival rate of the patients in the two treatment groups; thus, further studies are recommended to confirm the results.

Keywords: Esophageal neoplasms, Survival rate, Chemoradiotherapy, Surgery, Neoadjuvant therapy

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Introduction

Esophageal cancer is one of the most prevalent cancers and the sixth leading cause of death due to cancer in the world (1, 2). In some countries called “the Asian Esophageal Cancer Belt” such as Iran, Turkey, Kazakhstan, and China, the incidence rate of esophageal cancer is extremely high with an estimated rate of 100 cases per 100 000 persons annually. Esophageal cancer has two histological subtypes, squamous cell carcinoma (SCC), which is the predominant subtype globally, and adenocarcinoma (ADC) which is the most common subtype in some countries such as the USA, UK, Australia, Norway, Finland, and France (3). Surveys in different countries have shown that esophageal cancer has an extremely poor survival rate (4, 5); the one- and five-

year survival rates for patients diagnosed in early stages are nearly 70% and 31%, respectively. Unfortunately, most patients are diagnosed in advanced stages, which reduces the one- and five-year survival rates to 46% and 8%, respectively (5). Considering these facts, choosing a suitable treatment for esophageal cancer remains a challenge. There are various therapeutic modalities, but surgery and chemoradiotherapy are the two main treatment methods for esophageal cancer (6). The choice of the therapeutic approach is based on several factors, including the stage of the disease, tumor grade, tumor etiology, and presence of metastases (2, 6, 7).

Because of the limited success of single modality treatment, efforts have led to the exploration of multimodality therapies (8). Although esophagectomy

is one of the major treatments for esophageal cancer, the survival rate of patients treated with this method alone is reported to be poor (9). The five-year survival rate of patients, treated only by surgery, scarcely exceeds 20%, whereas some studies have shown that surgery, along with neoadjuvant chemoradiotherapy (NCRT) has better therapeutic outcomes (10). Performing NCRT prior to surgery may decrease the incidence of metastases, improve resectability, and control this systemic disease (11, 12).

Radiotherapy causes the palliation of symptoms in 70% of cases, but the survival rate and the local control of the disease in patients treated with radiotherapy alone are extremely poor (one-year survival rate of 30% and two-year survival of 3%) (13). In some cases, the combination of radiotherapy and surgery improves the survival rate of esophageal cancer patients (14). Considering the role of chemotherapy in reducing the systematic spread of the disease to other organs and the radiosensitizer effect, chemotherapy is added to therapies based on radiotherapy and surgery (15, 16). Some studies indicated that the overall survival rate of esophageal cancer patients was superior in the neoadjuvant chemoradiotherapy plus surgery (NCRT+S) group than in the definitive chemoradiotherapy (DCRT) group (17, 18). On the other hand, the findings of some studies demonstrated that the survival of esophageal cancer patients was not significantly different in the NCRT+S treatment group compared with the CRT treatment group (18, 19). Esophageal cancer is one of the most prevalent cancers in Zanjan province based on the epidemiologic study conducted in this province in 2019 (20). Moreover, the results of previous studies on effective treatment methods are somehow contradictory. Accordingly, it seemed necessary to conduct a study in this regard. Thus, this study aimed to compare the efficacy of DCRT to NCRT+S based on the one-year survival rate of esophageal cancer patients.

Materials and Methods

Patient Characteristics

In this cross-sectional descriptive study, 43 patients were eligible who had esophageal cancer based on computed tomography and/or pathologic reports and referred to the Radiotherapy Oncology Department of Vali-e-Asr Teaching Hospital in Zanjan province from February 2018 to October 2019. The inclusion criteria were patients older than 18 years and those who received DCRT or NCRT+S. The chemotherapy regime included 5fu and cisplatin or paclitaxel and carboplatin weakly. The therapeutic radiation dose of all patients was the same and equal to 50.4 Gy. Patients with incomplete medical records, metastatic diseases, and cervical esophageal cancer were excluded from the study.

Data Collection

The medical records of the patients were studied and the specifics of patients were extracted from the files. The obtained data were related to age, gender, treatment method (DCRT or NCRT+S), histology (SCC or ADC), location of the tumor (upper third [upper thoracic esophagus]), middle third [middle thoracic esophagus]), and lower third of the esophagus (lower thoracic), and the exact date of the treatment course ending.

Follow-up

Considering that the primary outcome of this survey was to assess the one-year survival rate of esophageal cancer patients, the survival status of patients was completed by contacting the patients or their families precisely one year after the treatment.

Ethical Considerations

Keeping privacy and not disclosing confidential information of patients was necessary. The procedure of this study was completely explained to the family members of the patients, and their permission was received for inquiring whether the patients have survived for one year.

Statistical Analysis

Data were analyzed by SPSS, version 16 (SPSS Inc. Chicago, USA), and the acquired data were categorized using tables and charts. The independent *t* test and chi-square test were used to compare the independent and categorical variables, respectively. The overall survival was estimated via the Kaplan-Meier method with the log-rank test. A *P* value of less than 0.05 was considered significant for all performed tests.

Results

Forty-three patients with esophageal cancer who referred to the Vali-e-Asr Hospital from February 2018 to October 2019 were recruited in this study. Overall, 39.5% of the studied population were males ($n=17$) and 60.5% of them were females ($n=26$). Patients were in the age range of 38-91 years. The mean age of the male and female patients was 67.17 ± 11.51 and 68.8 ± 12.55 years, respectively ($P=0.669$). The anatomical location of the lesion was recorded lower third in 39 cases (90.7%), the middle third in three cases (7%), and upper third in one case (2.3%). Histologically, there were 35 (81.4%) and 8 (18.6%) cases of the SCC type and ADC esophageal cancer, respectively. In general, 25 (58.1%) and 18 (41.9%) patients were treated by DCRT and NCRT+S, respectively. The mean age of the esophageal cancer patients receiving DCRT and NCRT+S was 69.92 ± 11.62 and 65.72 ± 12.5 years, respectively. The demographics of the patients are provided in Table 1.

Figure 1 represents a summary of the survival status of

Table 1. Patients' Characteristics (DCRT, NCRT+S, SCC, and ADC)

Characteristic	DCRT (n=25)	NCRT+S (n=18)	P Value ^a
Mean age (y)	69.92 ± 11.62	65.72 ± 12.5	0.264
Gender			
Male	9 (36%)	8 (44.4%)	0.576
Female	16 (64%)	10 (55.6%)	
Histological subtype			
SCC	18 (72%)	17 (94.4%)	0.062
ADC	7 (28%)	1 (5.6%)	
Tumor location			
Upper third	0 (0%)	1 (5.6%)	0.376*
Middle third	1 (4%)	2 (11.1%)	
Lower third	24 (96%)	15 (83.3%)	

Note. DCRT: Definitive chemoradiotherapy; NCRT+S: Neoadjuvant chemoradiotherapy plus surgery; SCC: Squamous cell carcinoma; ADC: Adenocarcinoma.

^a Fisher exact test.

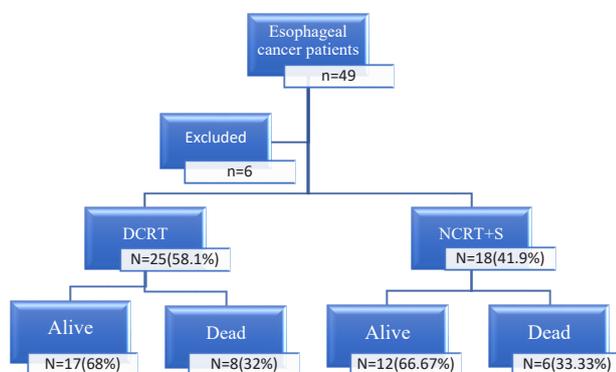


Figure 1. Diagram for Patients With Esophageal Cancer Receiving NCRT+S and/or DCRT. Note. DCRT: Definitive chemoradiotherapy; NCRT+S: Neoadjuvant chemoradiotherapy plus surgery.

patients in different treatment groups.

The survival in the two treatment groups was compared using the Kaplan-Meier method accompanied by the log-rank test, in which no significant difference was observed in the one-year survival rate ($P=0.395$, Figure 2). The one-year survival rate was 68% and 66.67% in the DCRT and NCRT+S groups, respectively. Further, no significant correlation was observed between the one-year survival rate of the patients and the histologic subtype ($P=0.741$). Twenty-nine patients (13 males and 16 females) were alive one year after the end of their treatment course. The one-year survival rate in males and females represented no significant difference ($P=0.307$, Table 2). The mean age of the patients with a one-year survival rate and those who died before one year was 67.1 ± 11.98 and 70.35 ± 12.30 years, respectively. No significant relevance was found between the one-year survival rate and the age of the patients ($P=0.413$). Similarly, there was no statistically significant relationship between the location of the tumor and the one-year survival of patients ($P=0.686$).

Discussion

Esophageal cancer is one of the most fatal cancers in the world that is extremely difficult to treat effectively (10, 21). Various factors can affect the survival rate of patients, including the choice of the therapeutic method (17). Considering the comparatively high surgical mortality (10) and morbidity (9, 10), researchers have investigated combination therapy. In this regard, multimodality therapy can result in better treatment by enhancing locoregional control and impeding systemic disease (21).

In this study, we compared the one-year survival rate between DCRT and NCRT+S. Overall, 25 (58.1%)

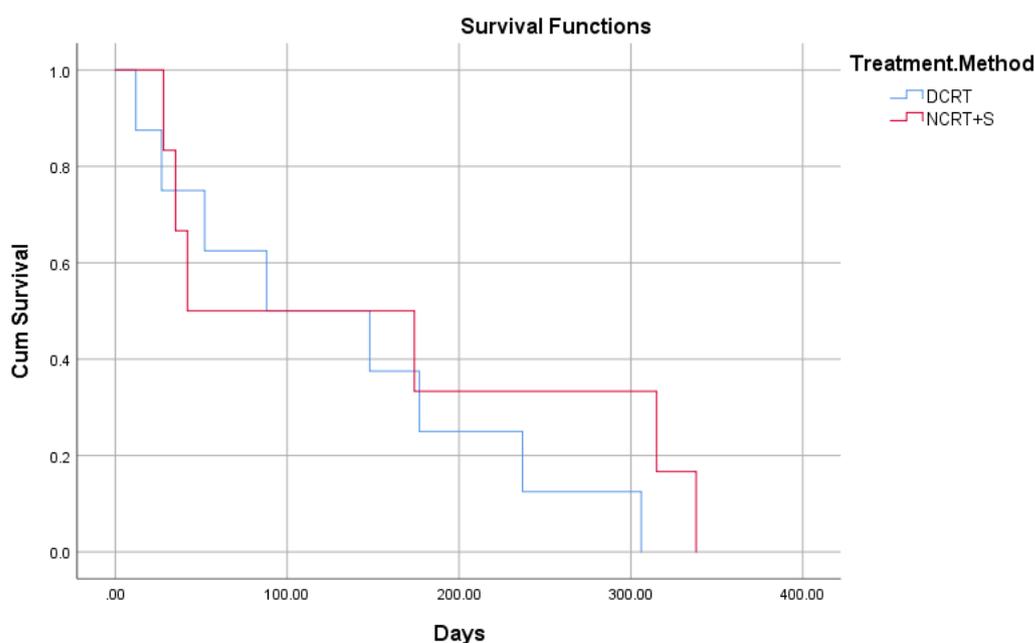


Figure 2. The Kaplan-Meier Curve of the Overall Survival of the Esophageal Cancer Patients According to the Treatment Method. Note. DCRT: Definitive chemoradiotherapy; NCRT+S: Neoadjuvant chemoradiotherapy plus surgery.

Table 2. The One-Year Survival Rate of the Esophageal Cancer Patients Based on Gender and Histology Type

One-Year Survival	Gender			
	Male		Female	
	SCC	ADC	SCC	ADC
Yes	11 (78.6%)	2 (66.7%)	13 (61.9%)	3 (60%)
No	3 (21.4%)	1 (33.3%)	8 (38.1)	2 (40%)

Note. SCC: Squamous cell carcinoma; ADC: Adenocarcinoma.

and 18 (41.9%) patients were treated via DCRT and NCRT+S, respectively, and the results revealed no significant difference in the one-year survival rate of the two treatment groups.

Bedenne et al (22) and Stahl et al (19) observed no significant difference in the overall survival (two-year and five-year survival, respectively) between DCRT and NCRT+S and concluded that adding surgery to chemoradiotherapy was not advantageous. In a study conducted in the Radiotherapy-Oncology Department of Razi Teaching Hospital in Guilan province, the survival of esophageal patients was examined based on treatment methods. In this study, 68% and 32% of patients received CRT and surgery followed by CRT (S-CRT), respectively. The overall survival in patients treated with CRT and S-CRT was 11.5 and 13 months, respectively, and there was no significant difference in this regard (23).

In a retrospective study by Neuhof et al, the survival of esophageal patients was 8, 9, and 20 months in RT (Radiotherapy), CRT, and NCRT+S, respectively (24). Preoperative therapy followed by surgery is the most accepted treatment method in patients with locally advanced esophageal cancer (2). Moreover, the reason for using CRT before surgery includes the removal of micrometastases and the betterment of tumor resectability (25). In medically unfit patients for surgery, DCRT should be given with a curative purpose (2). In a randomized controlled trial, the result of a comparison between NCRT+S and surgery alone demonstrated a significant increase in the five-year overall survival in the NCRT+S group. The overall survival was 81% at one-year interval for the NCRT+S group compared with 70% for the surgery group (26). Naik et al supported the addition of surgery to chemoradiotherapy for patients with locally advanced esophageal cancer (2).

Mirinezhad et al enrolled 331 esophageal cancer patients and evaluated four treatment methods (S+RT, CRT, RT, and NCRT+S). They reported that the five-year survival was significantly better in the NCRT+S group compared to the CRT group (35% and 11%, respectively, $P < 0.001$), and the survival rate was not associated with the histological subtype (27), which is consistent with the result of our study. The findings of a survey by Semrau et al (28) are consistent with those of the current study, indicating that gender and histological subtypes are not effective factors in the survival rate. Regarding survival, the advantages

of the collaboration of chemotherapy, radiotherapy, and surgery are unclear in multimodality therapy. In different studies, the radiation dose of radiotherapy, the type, and the dose of chemotherapy drugs are dissimilar (5fu and cisplatin or paclitaxel and carboplatin). Utilizing different radiotherapy protocols and chemotherapy drugs with varied doses alters the result of research. One cause for the breakdown of surgical treatment is the fact that most esophageal cancer patients are diagnosed at advanced stages of the malignancy (10); more specifically, almost 50% of esophageal cancer patients have distant metastases at the time of the initial diagnosis (29); furthermore, surgery may not be positively effective on survival because of surgical complications (10).

Among the limitations that the authors faced in this study were the relatively small number of patients available to enter the study, as well as access to the patients or their relatives to follow up on the survival status because some patients in this study moved after the end of the treatment and/or had changed their contact information.

Conclusion

In general, the efficacy of DCRT and NCRT+S on the one-year survival rate of esophageal cancer patients was evaluated, and no significant difference was observed in this regard. However, the results of previous studies are contradictory, and the choice of a competent treatment method is controversial. Accordingly, it is recommended that further investigations be conducted with a more appropriate treatment plan accompanied by a prolonged follow-up on a prospective larger population of patients with the same chemotherapy regimen.

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Author's Contribution

FKH, HCH, and HR: The original draft writing and investigation; ZKM and FS: Supervision and project administration; KK: Data analysis. All authors reviewed and confirmed the final manuscript.

Conflict of Interest Disclosures

There are no conflicts of interests.

Ethical Statement

This study was approved by the Ethics Committee of this Zanjan University of Medical Sciences (ethics code: IR.ZUMS.REC.1398.040).

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