Original Article

Prognosis of patients with esophageal squamous cell carcinoma undergoing surgery versus no surgery after neoadjuvant chemoradiotherapy: a retrospective cohort study

Jiawei Li[1#], Baofu Chen[1#], Xia Wang[1#], Congcong Xu[1], Dong Chen[1], Kanghao Zhu[2], Zixian Jin[1], Hongbin Qiu[1], Jianfei Shen[1], Minhua Ye[1]

[1]Key Laboratory of Minimally Invasive Techniques & Rapid Rehabilitation of Digestive System Tumor of Zhejiang Province, Department of Cardiothoracic Surgery, Taizhou Hospital of Zhejiang Province Affiliated to Wenzhou Medical University, Linhai, China; [2]Key Laboratory of Minimally Invasive Techniques & Rapid Rehabilitation of Digestive System Tumor of Zhejiang Province, Department of Cardiothoracic Surgery, Taizhou Hospital, Zhejiang University, Linhai, China

Contributions: (I) Conception and design: J Shen, B Chen, J Li, C Xu, Z Jin; (II) Administrative support: M Ye, J Shen; (III) Provision of study materials or patients: B Chen, X Wang, J Li; (IV) Collection and assembly of data: X Wang, D Chen, K Zhu, H Qiu; (V) Data analysis and interpretation: J Li, X Wang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Jianfei Shen; Minhua Ye. Department of Cardiothoracic Surgery, Taizhou Hospital of Zhejiang Province Affiliated to Wenzhou Medical University, No. 150 Ximen Road, Linhai 317000, China. Email: jianfei051@163.com; ymh9889@163.com.

Background: Esophageal surgery is an invasive surgical method with high surgical risk, and seriously affects postoperative quality of life. This study compared the prognosis of patients with locally advanced esophageal squamous cell carcinoma (ESCC) treated with neoadjuvant chemoradiotherapy (Neo-CRT) plus surgery and Neo-CRT alone, in order to explore the necessity of continuing operation after Neo-CRT.

Methods: We retrospectively analyzed 223 patients who received Neo-CRT in Taizhou Hospital Affiliated to Wenzhou Medical University from June 2007 to December 2014. According to the treatment, the patients were divided into Neo-CRT plus surgery group (operation group, n=185) and single Neo-CRT group (non-operation group, n=38). Patients in both groups were followed up for a long time until death or deadline. The overall survival (OS), adverse reactions, recurrence and death results of the two groups were evaluated. The risk factors of poor prognosis were analyzed.

Results: The two groups were comparable. The median follow-up time was 23.5 months in non-operation group and 112.9 months in operation group. The 1-year survival rate, 2-year survival rate and 5-year survival rate in non-operation group were 69.9%, 47.7% and 31.8%, respectively. The rates in operation group were 94.0%, 79.3% and 65.0%, respectively. The incidence of low hemoglobin was 73.7% (non-operation group) and 53.0% (operation group). The infection rates were 15.8% and 2.7%, respectively. There was no significant difference in the incidence of leukopenia, neutropenia and thrombocytopenia between the two groups. Multivariate analysis showed that recurrence and treatment were independent risk factors affecting the prognosis of patients.

Conclusions: To sum up, no matter in terms of recurrence rate or OS rate, the prognosis of patients in the operation group was better than that in the non-operation group. Therefore, Neo-CRT combined with esophagectomy is recommended for locally advanced ESCC with acceptable surgical risk.

Keywords: Neoadjuvant chemoradiotherapy (Neo-CRT); esophageal squamous cell carcinoma (ESCC); surgical treatment; surgery avoidance; prognosis

Submitted Feb 22, 2022. Accepted for publication Jun 01, 2022.
doi: 10.21037/jgo-22-296
View this article at: https://dx.doi.org/10.21037/jgo-22-296

Introduction

Esophageal cancer (EC) is the sixth most common cancer and the fourth leading cause of cancer death in China (1). Cases originating in China account for about 53% of new cases of EC worldwide (2). At present, the clinical treatment of EC is mainly surgical resection, radiotherapy and chemotherapy. EC can be divided into two subtypes: esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC). EAC is dominant in the western population, but in China, more than 90% of EC is ESCC (2). ESCC has the characteristics of easy metastasis and recurrence. It's reported that 60–70% of Chinese patients are diagnosed with locally advanced EC that cannot be cured by surgery alone (1). Recent studies have confirmed that Neo-CRT combined with surgery is the standard treatment for locally advanced ESCC (3,4). It has been reported that the pathological complete response (pCR) rate may be up to 49% after ESCC (5). The relatively high rate of pCR, combined with the high invasive and risk of esophageal surgery, make some clinicians prefer a wait-and-see approach with close follow-up. Therefore, for patients with ESCC after Neo-CRT, whether to continue surgery has become a clinical problem. We believe that it is necessary to study the prognosis of patients undergoing surgery and non-operation after Neo-CRT. We present the following article in accordance with the STROBE reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-296/rc).

Methods

Study design and patient population

This was a retrospective cohort study. We retrospectively studied patients with locally advanced ESCC who were treated in Taizhou Hospital of Zhejiang Province Affiliated to Wenzhou Medical University from June 2007 to December 2014. Strict control of inclusion and exclusion criteria was required due to possible research selection bias. The inclusion criteria were as follows: Clinical stage T1-4N1M0/T4N0M0 (second stage B or third stage) according to American Joint Committee on Cancer (AJCC) cancer staging manual 8th edition; age 18–70 years; hematology, kidney, and liver function were normal; and the Karnofsky performance score of ≥90. We excluded patients with a history of other malignant tumors; those who were not suitable for surgery due to comorbidities. We collected data on 451 patients with locally advanced ESCC. A total of 227 patients who underwent surgery alone were excluded. In addition, 1 patient who received neither Neo-CRT nor surgery was excluded from the study. A total of 223 patients (189 males and 34 females) were enrolled (*Figure 1*). At the same time, 38 of these patients did not undergo surgery after Neo-CRT (non-operation group) and 185 patients underwent surgery after Neo-CRT (operation group).

The study was conducted in accordance with the Declaration Helsinki (as revised in 2013). This study was approved by Medical Ethics Committee of Taizhou Hospital of Zhejiang Province Affiliated to Wenzhou Medical University (No. K20220423). Individual consent for this retrospective analysis was waived.

Neo-CRT

All cases were administered intravenous infusion of vinorelbine 25 mg/m^2 on days 1 and 8, cisplatin 75 mg/m^2 within 3 hours on day 1 or cisplatin 25 mg/m^2 within 2 hours on days 1 to 4, every 3 weeks for 2 cycles. At the same time, radiation therapy was given at 2.0 Gy once, 5 times a week, with a total dose of 40.0 Gy. All cases received external irradiation using three-dimensional (3D) conformal radiotherapy.

Operation time

Patients in non-operation group did not undergo surgery for various reasons, and those in operation group underwent surgery 4–6 weeks after the end of radiotherapy and chemotherapy. Esophagectomy was performed on the right transthoracic (McKeown or Ivor Lewis), including thoraco and abdominal lymph node dissection.

Outcomes and follow-up

The primary outcome of this study was overall survival (OS), defined as the time from the date of enrollment to the date of death or last follow-up. Adverse reactions to Neo-CRT were assessed according to The National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 (https://ctep.cancer.gov). All patients were followed up regularly through outpatient appointments or telephone calls. Clinical follow-up is performed every 3 months for the first year and every 6 months thereafter until the patient dies or the deadline. Information on the first postoperative recurrence was used for this study. The data cutoff for the analysis presented

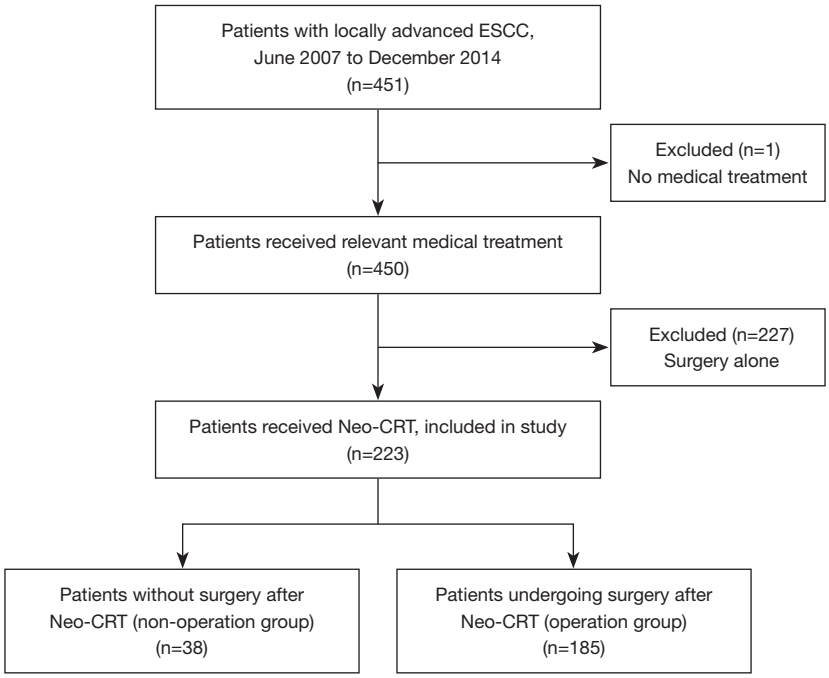

Figure 1 Study flow chart. ESCC, esophageal squamous cell carcinoma; CRT, chemoradiotherapy.

here was 31 December, 2019.

Statistical analysis

The software SPSS 24.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. We collected the clinical characteristics, adverse reactions of Neo-CRT, recurrence and survival, and evaluated the prognosis of the two groups. The baseline characteristics of the patients were compared with Student's *t*-test and Mann-Whitney U test. Clinical stages and adverse reactions were compared by chi-squared test. The OS was calculated by Kaplan-Meier method and compared by log-rank test. Cox proportional hazards model was used for univariate and multivariate analysis to evaluate the impact of different factors on survival, expressed as hazard ratios (HRs). Covariates included age, gender, tumor location, clinical T stage, N stage, surgery, and recurrence. All tests were set at 2-tailed P<0.05.

Results

Patient characteristics

A total of 223 patients with locally advanced ESCC treated in Taizhou Hospital of Zhejiang Province Affiliated to Wenzhou Medical University from June 2007 to December 2014 were included. The detailed clinical features of 223 patients are shown in *Table 1*. In non-operation group, 32 patients (84.2%) were male, and in operation group, 157 patients (84.9%) were male. The median age of patients in the two groups was 58 and 53 years old [interquartile range (IQR), 41 to 70 and 31 to 70], respectively. The average body mass index (BMI) was 21.88 [standard deviation (SD) =1.64] and 22.24 (SD=3.06) kg/m^2, respectively. Most patients were middle thoracic ESCC, with 28 cases in non-operation group (73.7%) and 129 cases in operation group (69.7%). There were 15 cases (39.5%) with clinic T3 and 19 cases (50.0%) with clinic T4 in non-operation group. Meanwhile there were 108 cases (58.4%) with T3 and 45 cases (24.3%) with T4 in non-operation group. Most patients had lymph node metastasis (27 *vs.* 163, 71.1% *vs.* 88.1% in non-operation group and operation group, respectively).

Among 223 patients with Neo-CRT, 38 cases did not undergo surgery, with a non-operative rate of 17.0%. There were many reasons for not undergoing surgery, including 29 patients who refused surgery, 2 patients with disease progression, 2 patients with poor general condition who could not tolerate surgery, 1 patient with cerebral infarction, and 4 patients who died of pneumonia, esophageal bleeding (n=2), and a car accident, respectively (*Table 2*).

Table 1 Baseline characteristics of both patient groups

Characteristic	Non-operation group (n=38)	Operation group (n=185)	P value
Age (years)			0.025
Median	58	53	
IQR	41–70	31–70	
Gender			0.919
Male	32 (84.2)	157 (84.9)	
Female	6 (15.8)	28 (15.1)	
BMI (kg/m^2)			0.300
Mean	21.88	22.24	
SD	1.64	3.06	
KPS			0.170
90	37 (100.0)	185 (100.0)	
100	1 (2.6)	0 (0.0)	
Tumor location			0.343
Proximal third	6 (15.8)	20 (10.8)	
Middle third	28 (73.7)	129 (69.7)	
Distal third	4 (10.5)	36 (19.5)	
Clinical T stage			0.006
T1–2	4 (10.5)	32 (17.3)	
T3	15 (39.5)	108 (58.4)	
T4	19 (50.0)	45 (24.3)	
Clinical N stage			0.007
N0	11 (28.9)	22 (11.9)	
N1	27 (71.1)	163 (88.1)	
Clinical stage			0.301
IIB	4 (10.5)	32 (17.3)	
III	34 (89.5)	153 (82.7)	

Data are presented as No. (%). IQR, interquartile range; BMI, body mass index; SD, standard deviation; KPS, Karnofsky performance score.

Table 2 Causes of patients without surgery

Discontinued surgery	n	Percentage (%)
Refused surgery	29	76.3
Disease progression	2	5.3
Could not tolerate surgery	2	5.3
Died before surgery		
Esophageal hemorrhage	2	5.3
Pneumonia	1	2.6
Accident	1	2.6
Cerebral infarction	1	2.6

Table 3 Comparison of incidence of adverse reactions between the two groups

Adverse reaction	Non-operation group (n=38)	Operation group (n=185)	P value
Low hemoglobin	28 (73.7)	98 (53.0)	0.019
Leukopenia	32 (84.2)	148 (80.0)	0.549
Neutropenia	31 (81.6)	134 (72.4)	0.242
Thrombocytopenia	20 (52.6)	69 (37.3)	0.079
AST or ALT increase	5 (13.2)	18 (9.7)	0.734
Anorexia	20 (52.6)	105 (56.8)	0.641
Vomiting	24 (63.2)	102 (55.1)	0.462
Diarrhea	3 (7.9)	12 (6.5)	1.000
Constipation	3 (7.9)	23 (12.4)	0.606
Mucositis	3 (7.9)	12 (6.5)	1.000
Radiation esophagitis	15 (39.5)	69 (37.3)	0.801
Radiodermatitis	2 (5.3)	13 (7.0)	0.968
Cough	4 (10.5)	18 (9.7)	1.000
Fatigue	1 (2.6)	35 (18.9)	0.013
Fever without infection	1 (2.6)	17 (9.2)	0.305
Infection	6 (15.8)	5 (2.7)	0.003

Data are presented as No. (%). AST, aspartate aminotransferase; ALT, alanine aminotransferase.

Adverse reactions

In non-operation group, 18.4% (7/38) of patients received only 1 course of chemotherapy, while 11.4% (21/185) of patients in operation group received only 1 course of chemotherapy. There was no statistical difference between the two groups in the course of chemotherapy (P=0.353). The most common adverse reactions after Neo-CRT in both groups were leukopenia (84.2% and 80%, respectively), followed by neutropenia (81.6% and 72.4%, respectively), with no statistical difference (P=0.549 and P=0.242). The hemoglobin hypoplasia rate was 73.7% (28/38) in non-operation group and 53.0% (98/185) in operation group, and the difference was statistically significant (P=0.019). There were significant differences in infection rate (15.8% and 2.7%, P=0.003) and fatigue rate (2.6% and 18.9%, P=0.013), respectively, between the two groups, while there were no significant differences in other adverse reactions (*Table 3*). Leucopenia was the most common grade 3 or above adverse reaction in both groups

Table 4 Distribution of adverse reactions in the two groups

Adverse reaction	Non-operation group			Operation group			P value
	Grade 0	Grade 1–2	Grade ≥3	Grade 0	Grade 1–2	Grade ≥3	
Low hemoglobin	10 (26.3)	24 (73.2)	4 (10.5)	87 (47.0)	93 (50.2)	5 (2.7)	0.007
Leukopenia	6 (15.8)	8 (21.1)	24 (63.2)	37 (20.0)	63 (34.1)	85 (45.9)	0.090
Neutropenia	7 (18.4)	9 (23.7)	22 (57.9)	51 (26.0)	54 (28.3)	80 (43.2)	0.099
Thrombocytopenia	18 (47.4)	13 (34.2)	7 (18.4)	116 (62.7)	60 (32.4)	9 (4.9)	0.027
AST or ALT increase	33 (86.8)	5 (13.2)	0 (0)	167 (90.3)	18 (9.7)	0 (0)	0.528
Anorexia	18 (47.4)	19 (50.0)	1 (2.6)	80 (43.2)	101 (54.6)	4 (2.2)	0.675
Vomiting	14 (36.8)	22 (57.9)	2 (5.3)	83 (44.9)	95 (51.4)	7 (3.8)	0.346
Diarrhea	35 (92.1)	3 (7.9)	0 (0)	173 (93.5)	12 (6.5)	0 (0)	0.753
Constipation	35 (92.1)	3 (7.9)	0 (0)	162 (87.6)	23 (12.4)	0 (0)	0.428
Mucositis	35 (92.1)	3 (7.9)	0 (0)	173 (93.5)	10 (5.4)	2 (1.1)	0.767
Radiation esophagitis	23 (60.5)	14 (36.8)	1 (2.6)	116 (62.7)	64 (34.6)	5 (2.7)	0.810
Radiodermatitis	36 (94.7)	2 (5.3)	0 (0)	172 (93.0)	13 (7.0)	0 (0)	0.693
Cough	34 (89.5)	3 (7.9)	1 (2.6)	167 (90.3)	18 (9.7)	0 (0)	0.843
Fatigue	37 (97.4)	1 (2.6)	0 (0)	150 (81.1)	34 (18.4)	1 (0.5)	0.013
Fever	37 (97.4)	1 (2.6)	0 (0)	168 (90.8)	15 (8.1)	2 (1.1)	0.176
Infection	32 (84.2)	4 (10.5)	2 (5.3)	180 (97.3)	4 (2.2)	1 (0.5)	0.001

Data are presented as No. (%). AST, aspartate aminotransferase; ALT, alanine aminotransferase.

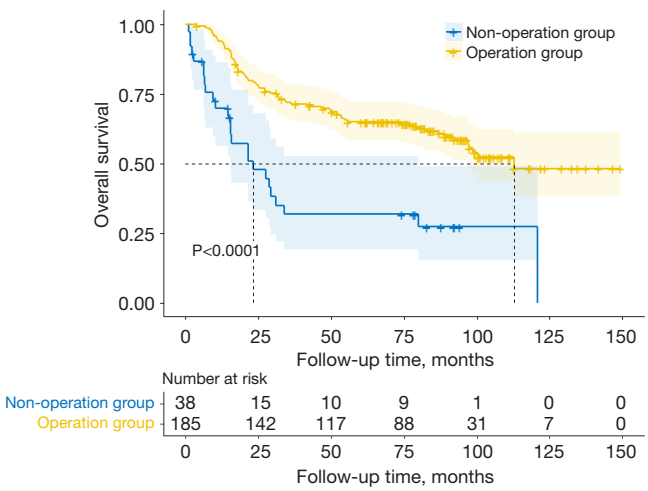

Figure 2 OS of two groups of patients with esophageal squamous cell carcinoma under different treatments. OS, overall survival.

(63.2% and 45.9%, respectively, P=0.090). In terms of the distribution of adverse reactions, there were differences in low hemoglobin, thrombocytopenia, fatigue, and infection between the two groups (*Table 4*).

The prognosis

In non-operation group, the 1-year survival rate was 69.9%, the 2-year survival rate was 47.7%, and the 5-year survival rate was 31.8%. The median follow-up time was 23.5 months [95% confidence interval (CI): 8.0 to 39.0]. At the same time, in operation group, the 1-year survival rate was 94.0%, the 2-year survival rate was 79.3%, the 5-year survival rate was 65.0%, and the median follow-up time was 112.9 months. The difference in survival curves between the two groups was statistically significant (*Figure 2*). During the follow-up period, there were 15 and 65 patients with disease progression in non-operation group and operation group, respectively, and 6 and 16 patients were lost to follow-up (*Table 5*). There were 25 deaths in non-operation group (65.8%) and 75 deaths in operation group (40.5%). The chi-square test showed that the difference in mortality between the two groups was statistically significant (P=0.004). Primary tumor was the main cause of death in

Table 5 Follow-up results of both patient groups

Follow-up results	Non-operation group (n=38)	Operation group (n=185)	P value
Disease progression			0.612
Locoregional progression	5 (33.3)	17 (26.2)	
Distant progression	7 (46.7)	40 (61.5)	
Overall progression	3 (20.0)	8 (12.3)	
Lost to follow-up	6	16	0.296
Alive	7	94	<0.001
Dead			0.004
Esophagus cancer death	18 (72.0)	56 (74.7)	
Other cancer-related death	3 (12.0)	18 (24.0)	
Perioperative death	4 (16.0)	1 (1.3)	

Data are presented as No. (%).

both groups (*Table 5*).

The results of multivariate analysis showed that the treatment method and recurrence had an impact on the survival of patients (*Table 6*), and the HR was 1.749 (P=0.018, 95% CI: 1.100 to 2.779) and 8.914 (P<0.001, 95% CI: 5.580 to 14.240), respectively. The OS of patients with recurrence was significantly lower than that of those without recurrence (*Figure 3*).

Discussion

In this retrospective analysis, the OS of patients without surgery was significantly shorter than that of patients after Neo-CRT, and the OS of patients with recurrence was shorter than that of patients without recurrence. Our results suggest that combination therapy is beneficial for patients with locally advanced ESCC. Patients with Neo-CRT alone

Table 6 Univariable and multivariable analysis of related factors for OS

Parameter	Univariable analysis		Multivariable analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age	1.020 (0.990–1.050)	0.197		
Gender				
M	1			
F	0.544 (0.290–1.019)	0.057		
Tumor location				
Pt	1			
Mt	0.868 (0.478–1.573)	0.640		
Dt	0.962 (0.479–1.935)	0.914		
cT				
T1-2	1			
T3	0.937 (0.526–1.670)	0.827		
T4	1.543 (0.842–2.829)	0.161		
cN				
N0	1			
N1	0.820 (0.486–1.384)	0.458		
Recurrence				
N	1		1	
Y	9.761 (6.157–15.476)	<0.001	8.914 (5.580–14.240)	<0.001
Treatment				
Neo-CRT + S	1		1	
Neo-CRT	2.993 (1.896–4.727)	<0.001	1.749 (1.100–2.779)	0.018

M, male; F female; Pt, proximal third; Mt, middle third; Dt, distal third; cT, clinical T stage; cN, clinical N stage; N, no; Y, yes; Neo-CRT + S, neoadjuvant chemoradiotherapy + surgery; Neo-CRT, neoadjuvant chemoradiotherapy; OS, overall survival; CI, confidence interval; HR, hazard ratio.

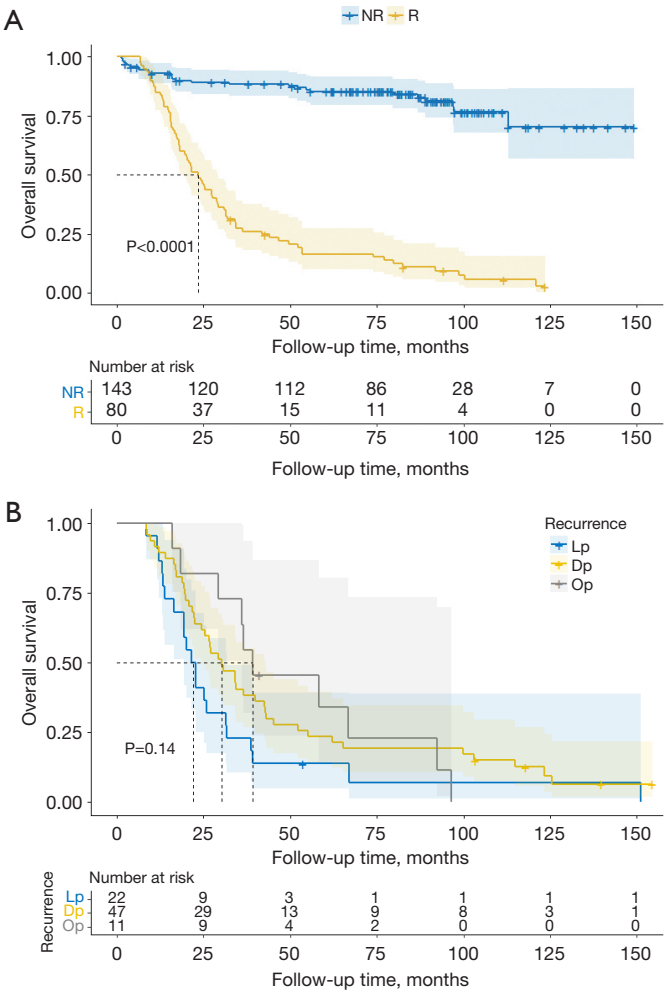

Figure 3 Kaplan-Meier survival plot of total population and subgroup population. (A) OS of patients with different prognosis; (B) OS of esophageal squamous cell carcinoma patients with different recurrence. NR, non-recurrence; R, recurrence; OS, overall survival; Lp, locoregional progression; Dp, distant progression; Op, overall progression.

and without surgery have poor prognosis.

Adverse events are adverse medical events that occur after patients or subjects in clinical trials receive a drug, but they do not necessarily have a causal relationship with treatment. Over the years, platinum-based therapies have been widely used in Neo-CRT for patients with ESCC and have achieved satisfactory results (4,6-9). However, the adverse reactions caused by chemotherapy have also attracted much attention. In this retrospective analysis, the most common adverse reaction after Neo-CRT was leukopenia, which is consistent with previous clinical trials of Neo-CRT for ESCC (10-12). In this data, we can clearly see that the infection rate of the 2 patient groups was significantly different, the infection rate of non-operation group was significantly higher than that of operation group. Whether the infection factor is the influencing factor of patients without surgery remains to be further studied.

According to the current data, for patients with locally advanced ESCC, the OS of patients treated with Neo-CRT combined with surgery was significantly better than that of those treated with Neo-CRT alone (without surgery), which was inconsistent with the previous literature (13). Advances in surgical techniques may be part of the reasons.

There were some limitations to this paper. Due to the retrospective analysis, the data were not sufficiently detailed for our purposes. In addition, this study did not include patients with poor general condition and those over 70 years old. Further study is required to investigate the

applicability of our finding to these patients. Some patients were followed up for too short a time and their ideal outcomes may have thus been overlooked. Additionally, the two groups patients are not completely comparable and need further study.

Conclusions

To sum up, no matter in terms of recurrence rate or OS rate, the prognosis of patients in operation group was better than that in non-operation group. Therefore, Neo-CRT combined with esophagectomy is recommended for locally advanced ESCC with acceptable surgical risk.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at Available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-296/rc

Data Sharing Statement: Available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-296/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-296/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration Helsinki (as revised in 2013). This study was approved by Medical Ethics Committee of Taizhou Hospital of Zhejiang Province Affiliated to Wenzhou Medical University (No. K20220423). Individual consent for this retrospective analysis was waived.

References

1. Chen W, Zheng R, Baade PD, et al. Cancer statistics in China, 2015. CA Cancer J Clin 2016;66:115-32.
2. Zheng RS, Sun KX, Zhang SW, et al. Report of cancer epidemiology in China, 2015. Zhonghua Zhong Liu Za Zhi 2019;41:19-28.
3. Yang H, Liu H, Chen Y, et al. Neoadjuvant Chemoradiotherapy Followed by Surgery Versus Surgery Alone for Locally Advanced Squamous Cell Carcinoma of the Esophagus (NEOCRTEC5010): A Phase III Multicenter, Randomized, Open-Label Clinical Trial. J Clin Oncol 2018;36:2796-803.
4. Yang H, Liu H, Chen Y, et al. Long-term Efficacy of Neoadjuvant Chemoradiotherapy Plus Surgery for the Treatment of Locally Advanced Esophageal Squamous Cell Carcinoma: The NEOCRTEC5010 Randomized Clinical Trial. JAMA Surg 2021;156:721-9.
5. van Hagen P, Hulshof MC, van Lanschot JJ, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. N Engl J Med 2012;366:2074-84.
6. Hayata K, Ojima T, Nakamori M, et al. Neoadjuvant Chemotherapy with Docetaxel, Cisplatin and S-1 for Resectable Advanced Esophageal Cancer. Anticancer Res 2018;38:5267-73.
7. Sasaki K, Uchikado Y, Omoto I, et al. Neoadjuvant chemoradiotherapy with docetaxel, cisplatin, and 5-fluorouracil (DCF-RT) for locally advanced esophageal squamous cell carcinoma. Cancer Chemother Pharmacol 2019;83:581-7.
8. von Döbeln GA, Klevebro F, Jacobsen AB, et al. Neoadjuvant chemotherapy versus neoadjuvant chemoradiotherapy for cancer of the esophagus or gastroesophageal junction: long-term results of a randomized clinical trial. Dis Esophagus 2019. doi: 10.1093/dote/doy078.
9. Wong IYH, Lam KO, Zhang RQ, et al. Neoadjuvant Chemoradiotherapy Using Cisplatin and 5-Fluorouracil (PF) Versus Carboplatin and Paclitaxel (CROSS Regimen) for Esophageal Squamous Cell Carcinoma (ESCC): A Propensity Score-matched Study. Ann Surg 2020;272:779-85.

10. Hashimoto M, Shirakawa Y, Maeda N, et al. Induction chemoradiotherapy including docetaxel, cisplatin, and 5-fluorouracil for locally advanced esophageal cancer. Esophagus 2020;17:127-34.
11. Boers J, Joldersma A, van Dalsen AD, et al. Intensified Neoadjuvant Chemoradiotherapy for Patients with Potentially Resectable Esophageal Cancer: A Retrospective Cohort Study. Ann Surg Oncol 2020;27:1520-8.
12. Goense L, van der Sluis PC, van Rossum PSN, et al. Perioperative chemotherapy versus neoadjuvant chemoradiotherapy for esophageal or GEJ adenocarcinoma: A propensity score-matched analysis comparing toxicity, pathologic outcome, and survival. J Surg Oncol 2017;115:812-20.
13. Stahl M, Stuschke M, Lehmann N, et al. Chemoradiation with and without surgery in patients with locally advanced squamous cell carcinoma of the esophagus. J Clin Oncol 2005;23:2310-7.

(English Language Editor: J. Jones)

Cite this article as: Li J, Chen B, Wang X, Xu C, Chen D, Zhu K, Jin Z, Qiu H, Shen J, Ye M. Prognosis of patients with esophageal squamous cell carcinoma undergoing surgery versus no surgery after neoadjuvant chemoradiotherapy: a retrospective cohort study. J Gastrointest Oncol 2022;13(3):903-911. doi: 10.21037/jgo-22-296

