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ORIGINAL RESEARCH

Long-term survival of patients with locally advanced esophageal squamous cell carcinoma receiving esophagectomy following neoadjuvant chemotherapy: a cohort study

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Purpose: The role of neoadjuvant chemotherapy and subsequent adjuvant therapy in the treatment of patients with locally advanced esophageal squamous cell carcinomas (ESCC) is not well established.

Patients and methods: We retrospectively reviewed 228 patients with locally advanced ESCC receiving esophagectomy following neoadjuvant chemotherapy from January 2007 through December 2016. The probabilities of disease-free survival (DFS) and overall survival (OS) were estimated by means of the Kaplan–Meier method and were compared with the use of the log-rank test. Univariate and multivariate analyses of predictors of DFS and OS were performed using a Cox proportional-hazards model. Propensity score matching analysis was performed for further analysis regarding the benefit of adjuvant therapy.

Results: The pathological complete response of neoadjuvant chemotherapy was achieved in 13 of 228 patients (5.7%). With a median follow-up of 59.6 months, the median DFS and OS were 35.4 and 45.4 months, respectively. The multivariate Cox model determined chemotherapy regimens (P=0.003) and ypT category (P=0.006) were significant independent predictors of DFS; and chemotherapy regimens (P=0.001), ypT category (P<0.001), and ypN category (P=0.013) were significant independent predictors of OS. Furthermore, patients who received adjuvant therapy seemed to be associated with poorer survival (both DFS and OS) compared with those who did not in full cohort (P=0.001 and P=0.184, respectively) and matched cohort (P=0.251 and P=0.374, respectively).

Conclusion: Surgery following neoadjuvant chemotherapy was applicable. Chemotherapy regimens and ypT category were significant independent predictors of both DFS and OS and ypN category was also a significant independent predictor of OS. However, these patients did not seem to benefit from subsequent adjuvant therapy. The necessity of adjuvant therapy requires further investigation.

Keywords: locally advanced esophageal squamous cell carcinoma, neoadjuvant chemotherapy, surgery, adjuvant therapy

Introduction

Esophageal cancer is the sixth most common cause of cancer deaths in the world, leading to 509,000 deaths occurred in 2018 worldwide. Moreover, it is the third most commonly diagnosed cancers of men, fifth of women, and one of the five leading causes of cancer death of both men and women in China. Additionally, 90% of cases are squamous cell carcinomas in China, compared with about 26% in the USA (among white individuals).[1,2]

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The role of neoadjuvant chemotherapy is equivocal because data supporting benefits are lacking and randomized trials comparing surgery alone with surgery following neoadjuvant chemotherapy in patients with locally advanced resectable esophageal cancer showed conflicting results.[3–6] Although several randomized trials showed significant disease-free survival (DFS) and overall survival (OS) benefit favoring neoadjuvant chemotherapy over surgery alone, the long-term results of these studies highly varied. The efficacy of adjuvant therapy has been demonstrated in INT-0116 trial (postoperative chemoradiotherapy) and MAGIC trial (perioperative chemotherapy) in patients with resectable adenocarcinoma of the stomach or esophagogastric junction cancers.[7,8] However, it is still unclear whether patients with esophageal squamous cell carcinoma (ESCC) will benefit from adjuvant therapy.

Therefore, we conducted this retrospective study to assess the influence of neoadjuvant chemotherapy and the subsequent adjuvant therapy, as well as the long-term survival of these patients.

Patients and methods

Patients

This study was approved by the Ethics Committee of the Peking University Cancer Hospital and Institute, Beijing, China. Written informed consent was obtained from all enrolled participants. All methods were applied according to the approved guidelines and regulations. We retrospectively reviewed all of the patients who underwent surgery following neoadjuvant chemotherapy for locally advanced resectable esophageal cancer at Department of Thoracic Surgery II, Peking University Cancer Hospital from January 2007 through December 2016. All patients underwent pretreatment staging, consisting of upper gastrointestinal endoscopy with histological biopsy and computed tomography (CT) scan of the neck, chest, and upper abdomen. Eligible patients were restaged according to the eighth American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) cancer staging system.[9] Locally advanced resectable esophageal cancer was defined as clinical stage T1 N+, T2 or higher, any N. R0 resection was defined as complete resection with no tumor within 1 mm of the resection margins. R1 and R2 resections were defined as microscopically confirmed tumor cell residual and macroscopically confirmed tumor cell residual or M1, respectively. Only patients who underwent R0 resection with histologically confirmed, locally advanced resectable ESCC were eligible for inclusion in the analysis. The main exclusion criteria were adenocarcinoma or large-cell undifferentiated carcinoma of the esophagus or esophagogastric junction, R1 or R2 resection, and previous chemotherapy and/or radiotherapy.

Treatment

The chemotherapy regimens were usually based on paclitaxel plus cisplatin or paclitaxel plus nedaplatin (TP), accounting for 82.5%, and 188 patients received these regimens. Meanwhile, the following chemotherapy regimens were also used: paclitaxel plus carboplatin, irinotecan plus cisplatin, etoposide plus cisplatin, and docetaxel plus nedaplatin. Administration of neoadjuvant chemotherapy would be delayed or withheld in case of severe toxic effects. Surgery was regularly scheduled within 4–6 weeks after the completion of two cycles of neoadjuvant therapy. Operative approaches included Ivor–Lewis and McKeown esophagogastrectomy with regional lymphadenectomy. The postoperative adjuvant therapy including chemotherapy and/or radiotherapy was usually performed >1 month after resection. Postoperative adjuvant chemotherapy was performed for two to four cycles according to the efficacy of neoadjuvant chemotherapy. The postoperative radiotherapy dose was usually 41.4–50.4 Gy (1.8 or 2 Gy/fraction). Postoperative chemotherapy and radiotherapy were conducted sequentially if both were administered. After surgery, patient's physical condition was assessed to see if he/she could tolerate postoperative treatment. Postoperative treatment was administered only in medically fit patients. For medically fit patients with downstaging, they were recommended to receive only postoperative chemotherapy with the same regimen as the preoperative one because chemotherapy is effective enough. For medically fit patients who had stable disease or progressive disease, postoperative chemoradiotherapy was recommended and these patients would receive another regimen of chemotherapy for the lack of response to the primary one. However, if these patients had acute toxicity toward preoperative chemotherapy, we recommended them to receive only postoperative radiotherapy for the sake of safety.

Follow-up

During the first 2 years after surgery, patients were reviewed every 3 months, and then every 6 months for 3–5 years. During follow-up, CT scan of thorax and ultrasonography of abdomen and neck were regularly carried out, and diagnostic investigation such as upper gastrointestinal endoscopy was carried out only when recurrence was suspected. Late toxic effects, disease recurrence, and death were documented meticulously. Additional examinations would be conducted,

if necessary, for patients with particular symptoms and signs. A combination of clinical service records, phone calls, and e-mails was used to determine every patient's status by September 2017.

Statistical analysis

In this analysis, the DFS was defined as the interval between the date of surgery and the date of recurrence or date of last follow-up. And OS was defined as the interval between the date of surgery and the date of death or the date of the last follow-up. The probabilities of DFS and OS were estimated by means of the Kaplan–Meier method and were compared with the use of the log-rank test. A Cox proportional-hazards model was used for univariate and multivariate analyses. To avoid overdetermination, the multivariable model included only highly significant ($P<0.20$) univariate factors. To better compare survival between patients with and without receiving adjuvant therapy, propensity score matching was performed in order to reduce imbalance in patients and treatment characteristics. A balanced cohort was then created using a 1:1 nearest neighbor matching algorithm with a caliper of 0.02 of the SD of the propensity score on the logit scale. Results of analyses were considered significant at a level of $P<0.05$. Statistical analysis was performed using SPSS software (IBM SPSS version 24, Chicago, IL, USA).

Results

Characteristics of the patients

From January 2007 through December 2016, a total of 1,123 patients with esophageal cancer underwent surgery, of whom 256 patients received esophagectomy following preoperative chemotherapy. R0 resection was achieved in 243 of 256 patients (94.9%). According to the inclusion and exclusion criteria, 15 patients were excluded: 9 esophageal adenocarcinoma; 3 esophageal large-cell undifferentiated carcinoma; 3 receiving preoperative chemoradiation therapy. Finally, 228 patients were included into this analysis (Figure 1). Baseline clinicopathological characteristics of these patients are shown in Table 1.

Follow-up and complications of surgery following neoadjuvant chemotherapy

During follow-up, 94 patients who underwent resection following neoadjuvant chemotherapy died after having been discharged, of whom 92 (97.9%) patients died from recurrent cancer and 2 (2.1%) from infection. In 37 of 228 patients (16.2%), postoperative complications were observed; among them, 17 patients developed anastomotic fistula, 22 developed postoperative infection, and 9 developed hemorrhage.

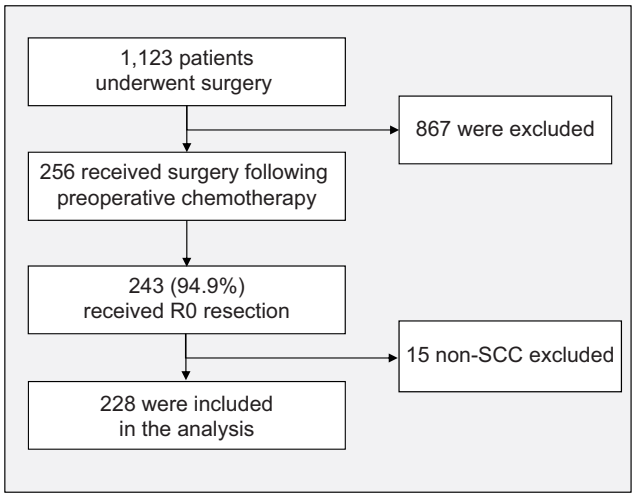

Figure 1 Study enrolment.
Abbreviation: SCC, squamous cell carcinoma.

Survival

For all patients, the median follow-up was 59.6 months. The median DFS was 35.4 months, and the estimated 3-, 5-, and 7-year DFS were 48.0%, 38.0%, and 36.0%, respectively. Separate curves for DFS according to clinical T category, clinical N category, ypT category, and ypN category are shown in Figure 2. The multivariate Cox proportional-hazards model determined that only chemotherapy regimens (others vs TP, HR =2.021, 95% CI =1.266–3.224, $P=0.003$) and ypT category (ypT3–4a vs ypT0–2, HR =2.035, 95% CI =1.230–3.368, $P=0.006$) were significant independent predictors of DFS (Table 2).

For the entire cohort, the median OS was 45.4 months and the estimated 3-, 5-, and 7-year OS were 55.0%, 46.0%, and 43.0%, respectively. Kaplan–Meier plots for OS according to clinical T category, clinical N category, ypT category, and ypN category are shown in Figure 3. Moreover, in the multivariate Cox proportional-hazards model, significant independent predictors of OS comprised chemotherapy regimens (others vs TP, HR =2.313, 95% CI =1.402–3.816, $P=0.001$), ypT category (ypT3–4a vs ypT0–2, HR =3.241, 95% CI =1.877–5.599, $P<0.001$), and ypN category (ypN1–3 vs ypN0, HR =3.653, 95% CI =1.312–10.174, $P=0.013$; Table 3).

Adjuvant therapy

There were no significant survival differences between groups with and without adjuvant therapy regarding OS

Table 1 Characteristics of patients

Variables	Number (%)
Age (years)	
≥60	117 (51.3)
<60	111 (48.7)
Sex	
Male	197 (86.4)
Female	31 (13.6)
Smoking history	
No	77 (33.8)
Yes	151 (66.2)
History of alcohol	
No	87 (38.2)
Yes	141 (61.8)
Downstaging	
No	153 (67.1)
Yes	75 (32.9)
Lesion location	
U	34 (14.9)
M	80 (35.1)
L	114 (50.0)
Chemotherapy regimen	
TP	188 (82.5)
Others	40 (17.5)
Surgery procedure	
Ivor–Lewis	149 (65.4)
McKeown	79 (34.6)
Tumor thrombus	
Negative	181 (79.4)
Positive	47 (20.6)
Adjuvant therapy	
No	103 (45.2)
Yes	125 (54.8)
Clinical T category	
cT1–2	11 (4.8)
cT3–4a	217 (95.2)
Clinical N category	
cN0	59 (25.9)
cN1–3	169 (74.1)
ypT category	
ypT0–2	91 (39.9)
ypT3–4a	137 (60.1)
ypN category	
ypN0	106 (46.5)
ypN1–3	122 (53.5)

Abbreviations: U, upper; M, middle; L, lower; TP, paclitaxel plus cisplatin or paclitaxel plus nedaplatin.

(*P*=0.184). Furthermore, patients who did not receive any adjuvant therapy seemed to have a better DFS compared with those who did (*P*=0.001). The results are shown in the Figure 4A,B. In order to further examine these findings, a secondary analysis using propensity score matching was performed to reduce imbalance in patients and treatment characteristics. Characteristics of patients in full cohort and propensity score matched cohort are shown in Table 4. Before propensity score matching, tumor downstaging (*P*=0.021), chemotherapy regimens (*P*=0.005), ypT category (*P*=0.009), and ypN category (*P*=0.007) were significantly different between patients with and without receiving adjuvant therapy. The matched cohort consisted of 81 patients in each arm, and all covariates included in the propensity score were well balanced after matching. In propensity matched cohort, there was no significant benefit found in either DFS (*P*=0.251) or OS (*P*=0.374; Figure 4C,D).

Discussion

In this retrospective analysis, we reviewed 228 R0 resected patients with esophageal squamous cell cancer who underwent esophagectomy following neoadjuvant chemotherapy. Surgery following neoadjuvant chemotherapy was applicable, associated with a low frequency of postoperative complications rate (16.2%). Furthermore, chemotherapy regimens and ypT category were significant independent predictors of both DFS and OS. We also found out that these patients did not seem to benefit from adjuvant therapy.

With a median follow-up of 59.6 months, the median DFS was 35.4 months, and the median OS was 45.4 months. The 5-year DFS rate and OS rate were 38% and 46%, respectively. It is noteworthy that the long-term results of the CROSS trial reported a survival outcome with a median progression-free survival of 74.4 months and a median OS of 81.6 months for patients with squamous cell carcinomas in the neoadjuvant chemoradiotherapy plus surgery group, albeit the population was small (41 patients).[10] This trial indicated that preoperative chemoradiotherapy may be more effective than preoperative chemotherapy. However, we need to note that currently there is no high-quality, multicenter, large-sample standard randomized trials directly comparing neoadjuvant chemoradiotherapy plus surgery and neoadjuvant chemotherapy plus surgery for patients with locally advanced resectable ESCCs. Thus, the best preoperative treatment strategy remains controversial, and further clinical randomized trials are needed.

There is controversy in the treatment of esophageal cancer for patients who have clinical complete response (cCR) after chemoradiotherapy. A standard treatment is to offer these patients an esophagectomy. However, there is a study indicating that cCR after chemoradiotherapy may mean surgery is not always needed because the addition of surgery to thoracic locally advanced esophageal carcinoma patients with a cCR after preoperative chemoradiotherapy did not benefit long-term survival.[11] Currently, this area remains controversial due to the lack of randomized controlled trials directly comparing surveillance to surgery in patients who have had a cCR to preoperative treatment.

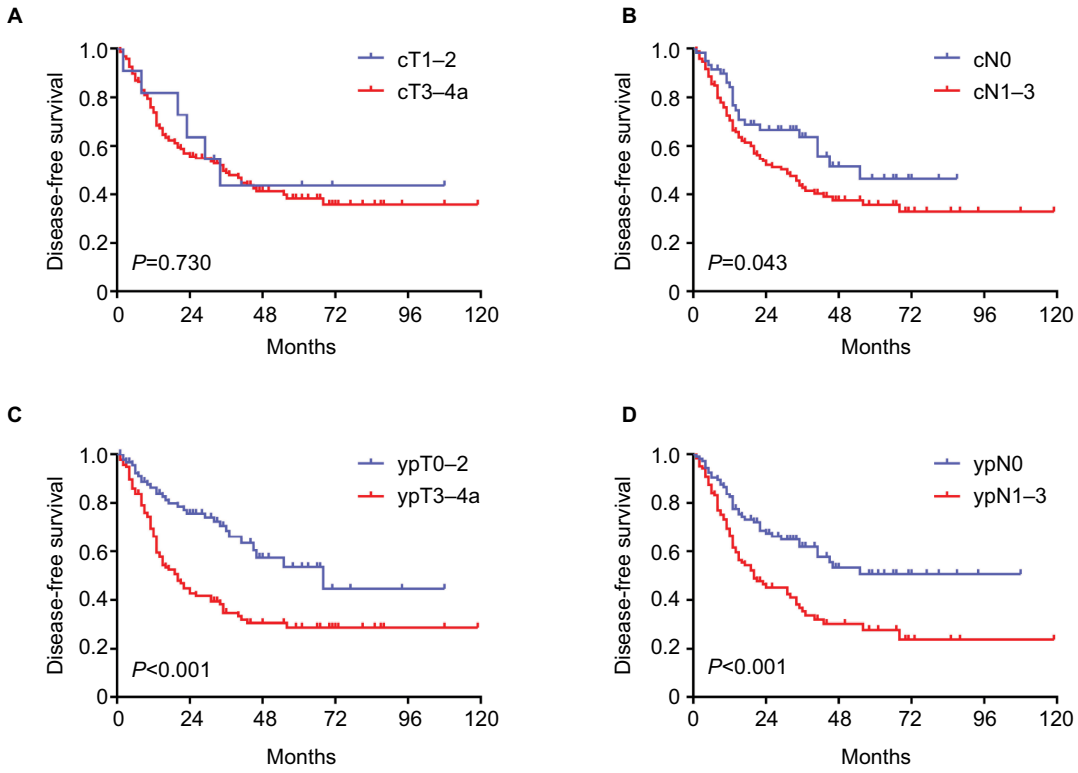

Figure 2 Curves of disease-free survival.
Notes: (**A**) By clinical T category. (**B**) By clinical N category. (**C**) By ypT category. (**D**) By ypN category.

Table 2 Univariable and multivariable analyses of disease-free survival

Variables	Univariable analysis		Multivariable analysis	
	HR (95% CI)	*P*-value	aHR (95% CI)	*P*-value
Age (years)				
≥60	Reference		Reference	
<60	0.913 (0.628–1.326)	0.632	1.009 (0.677–1.506)	0.963
Sex				
Male	Reference		Reference	
Female	0.906 (0.525–1.562)	0.721	1.124 (0.539–2.344)	0.755
Smoking history				
No	Reference			
Yes	0.755 (0.515–1.106)	0.149	0.795 (0.505–1.252)	0.322
History of alcohol				
No	Reference			
Yes	0.851 (0.583–1.243)	0.404		
Downstaging				
No	Reference		Reference	
Yes	0.53 (0.345–0.814)	0.004	1.204 (0.537–2.700)	0.653
Lesion location		0.186		
U	Reference		Reference	
M	1.663 (0.888–3.112)	0.112	1.487 (0.784–2.821)	0.225
L	1.749 (0.956–3.201)	0.07	1.594 (0.830–3.062)	0.161
Chemotherapy regimen				
TP	Reference		Reference	
Others	2.198 (1.418–3.407)	<0.001	2.021 (1.266–3.224)	0.003

(*Continued*)

Table 2 (*Continued*)

Variables	Univariable analysis		Multivariable analysis	
	HR (95% CI)	***P*-value**	**aHR (95% CI)**	***P*-value**
Surgery procedure				
Ivor–Lewis	Reference			
McKeown	0.794 (0.533–1.183)	0.256		
Tumor thrombus				
Negative	Reference		Reference	
Positive	1.835 (1.184–2.842)	0.007	1.224 (0.744–2.016)	0.426
Adjuvant therapy				
No	Reference		Reference	
Yes	1.892 (1.274–2.811)	0.002	1.498 (0.996–2.252)	0.052
Clinical T category				
cT1–2	Reference			
cT3–4a	1.154 (0.506–2.630)	0.733		
Clinical N category				
cN0	Reference		Reference	
cN1–3	1.592 (1.006–2.521)	0.047	0.999 (0.455–2.193)	0.998
ypT category				
ypT0–2	Reference		Reference	
ypT3–4a	2.359 (1.549–3.593)	<0.001	2.035 (1.230–3.368)	0.006
ypN category				
ypN0	Reference		Reference	
ypN1–3	2.028 (1.377–2.988)	<0.001	1.838 (0.736–4.593)	0.193

Abbreviation: aHR, adjusted hazard ratio.

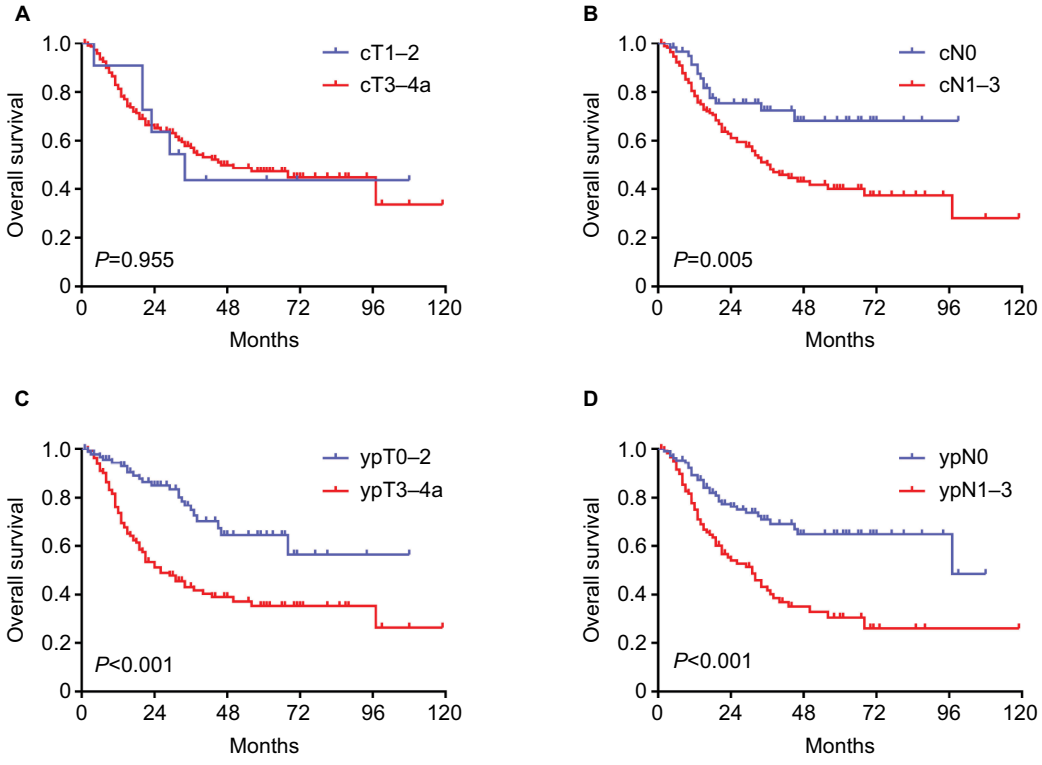

Figure 3 Curves of overall survival.
Notes: (**A**) By clinical T category. (**B**) By clinical N category. (**C**) By ypT category. (**D**) By ypN category.

Table 3 Univariable and multivariable analyses of overall survival

Variables	Univariable analysis		Multivariable analysis	
	HR (95% CI)	*P*-value	aHR (95% CI)	*P*-value
Age (years)				
≥60	Reference		Reference	
<60	0.998 (0.665–1.498)	0.992	1.211 (0.779–1.882)	0.394
Sex				
Male	Reference		Reference	
Female	0.946 (0.526–1.703)	0.853	1.681 (0.806–3.504)	0.166
Smoking history				
No	Reference			
Yes	0.864 (0.568–1.316)	0.496		
History of alcohol				
No	Reference			
Yes	0.911 (0.603–1.376)	0.657		
Downstaging				
No	Reference		Reference	
Yes	0.533 (0.334–0.849)	0.008	2.128 (0.875–5.171)	0.096
Lesion location				
U	Reference		Reference	
M	2.172 (1.045–4.515)	0.038	2.314 (1.090–4.912)	0.029
L	2.247 (1.101–4.586)	0.026	2.243 (1.039–4.843)	0.040
Chemotherapy regimen				
TP	Reference		Reference	
Others	2.077 (1.304–3.310)	0.002	2.313 (1.402–3.816)	0.001
Surgery procedure				
Ivor–Lewis	Reference			
McKeown	0.76 (0.494–1.171)	0.214		
Tumor thrombus				
Negative	Reference		Reference	
Positive	1.77 (1.092–2.869)	0.020	0.988 (0.571–1.707)	0.964
Adjuvant therapy				
No	Reference		Reference	
Yes	1.321 (0.871–2.003)	0.190	0.935 (0.609–1.437)	0.760
Clinical T category				
cT1–2	Reference			
cT3–4a	0.977 (0.426–2.238)	0.956		
Clinical N category				
cN0	Reference		Reference	
cN1–3	2.166 (1.247–3.763)	0.003	0.967 (0.397–2.357)	0.941
ypT category				
ypT0–2	Reference		Reference	
ypT3–4a	2.738 (1.707–4.392)	<0.001	3.241 (1.877–5.599)	<0.001
ypN category				
ypN0	Reference		Reference	
ypN1–3	2.503 (1.623–3.859)	<0.001	3.653 (1.312–10.174)	0.013

Abbreviation: aHR, adjusted hazard ratio.

With regard to chemotherapy regimens, the multivariate Cox proportional-hazards model demonstrated that patients administered with paclitaxel plus cisplatin or paclitaxel plus nedaplatin (TP) had a significantly better survival (both DFS and OS). Although the safety and efficacy of a single agent including paclitaxel, nedaplatin, carboplatin, irinotecan, etoposide, and docetaxel are confirmed,[12–19] adequately powered Phase III studies are lacking to determine the best combination of chemotherapy regimens. The value of this specific finding will need to be assessed in future randomized controlled studies.

ypT category was demonstrated to be the significant independent predictor of both DFS and OS. However, ypN category was not a significant independent predictor of survival. Obviously, the 7–8th AJCC/UICC cancer staging system[9,20] emphasizing on the number of nodes rather than their anatomic

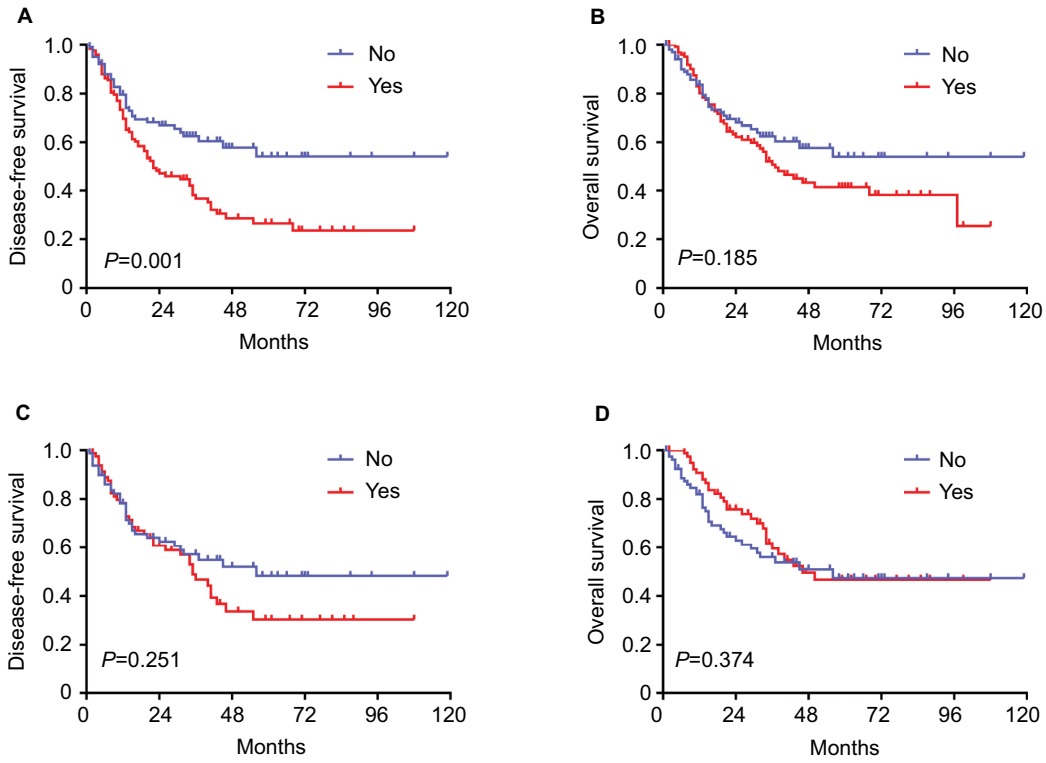

Figure 4 Curves of survival with and without adjuvant therapy.
Notes: (**A**) Curves of disease-free survival in full cohort. (**B**) Curves of overall survival in full cohort. (**C**) Curves of disease-free survival in propensity matched cohort. (**D**) Curves of overall survival in propensity matched cohort.

locations is controversial compared with 11th Japan Esophageal Society (JES) staging,[21,22] even though there is a study indicating that N staging for 7–8th AJCC/UICC cancer staging system and 11th JES staging system showed similar predictive power for DFS.[23] Besides, prognostication based on cT differed from that based on ypT reflects inaccuracies of obtaining cancer facts by current clinical staging modalities, including ineffectual use of clinical staging modalities, inaccurate evaluation of clinical cancers, and unpredictability of effectiveness of neoadjuvant treatment (downstaging) of advanced cancers. Therefore, a more accurate cancer staging system is needed.

The role of adjuvant therapy for patients with ESCC who have received preoperative therapy is not yet established.[24] In this study, we found that patients did not seem to benefit from adjuvant therapy. Moreover, the multivariate Cox proportional-hazards model demonstrated that patients who received adjuvant therapy had a worse DFS than those did not (yes vs no, HR, 1.498 [0.996–2.252], P=0.052). After using propensity score matching method to reduce imbalance in patients and treatment characteristics, still there was no significant benefit found in DFS (P=0.251) or OS (P=0.374). This finding needs further investigations and the reason for that remains unknown. However, our finding is comparable to some randomized trials of postoperative therapy[25–27] and a meta-analysis,[28] which came to a conclusion that postoperative chemotherapy did not add a survival benefit to surgery. Meanwhile, the National Comprehensive Cancer Network (NCCN) guidelines suggest that for patients with ESCC who have received preoperative therapy, no further treatment is necessary (irrespective of their nodal status) if there is no residual disease at surgical margins (R0 resection). This area remains an active subject of investigation.

A possible limitation of our study is that these patients with esophageal cancer receiving esophagectomy following preoperative chemotherapy did not receive totally consistent chemotherapy regimens. Besides, existence of confounding factors is inevitable due to the inherent nature of retrospective analysis. Therefore, results from this study might not be readily extrapolated. Nevertheless, this retrospective study provides an opportunity to assess the safety and long-term survival benefit for patients who underwent neoadjuvant chemotherapy followed by surgery. We believe this analysis will make a positive contribution given the lack of definitive evidence from randomized clinical trials.

Table 4 Characteristics of patients in full cohort and propensity score matched cohort

Variables	Full cohort		*P*-value	Matched cohort		*P*-value
	Adjuvant therapy			Adjuvant therapy		
	No	Yes		No	Yes	
	(n=103)	(n=125)		(n=81)	(n=81)	
Age (years)			0.568			0.875
≥60	55 (63.4)	62 (49.6)		40 (49.4)	41 (50.6)	
<60	48 (46.6)	63 (50.4)		41 (50.6)	40 (49.4)	
Sex			0.245			1.000
Male	86 (83.5)	111 (88.8)		69 (85.2)	69 (85.2)	
Female	17 (16.5)	14 (11.2)		12 (14.8)	12 (14.8)	
Smoking history			0.732			0.505
No	36 (35.0)	41 (32.8)		25 (30.9)	29 (35.8)	
Yes	67 (65.0)	84 (67.2)		56 (69.1)	52 (64.2)	
History of alcohol			0.311			0.515
No	43 (41.7)	44 (35.2)		28 (34.6)	32 (39.5)	
Yes	60 (58.3)	81 (64.8)		53 (65.4)	49 (60.5)	
Downstaging			0.021			0.867
No	61 (59.2)	92 (73.6)		54 (66.7)	55 (67.9)	
Yes	42 (40.8)	33 (26.4)		27 (33.3)	26 (32.1)	
Lesion location			0.586			0.498
U	18 (17.5)	16 (12.8)		14 (17.3)	11 (13.6)	
M	34 (33.0)	46 (36.8)		26 (32.1)	33 (40.7)	
L	51 (49.5)	63 (50.4)		41 (50.6)	37 (45.7)	
Chemotherapy regimen			0.005			0.807
TP	93 (90.3)	95 (76.0)		72 (88.9)	71 (87.7)	
Others	10 (9.7)	30 (24.0)		9 (11.1)	10 (12.3)	
Surgery procedure			0.518			0.329
Ivor–Lewis	65 (63.1)	84 (67.2)		48 (59.3)	54 (66.7)	
McKeown	38 (36.9)	41 (32.8)		33 (40.7)	27 (33.3)	
Tumor thrombus			0.288			1.000
Negative	85 (82.5)	96 (76.8)		65 (80.2)	65 (80.2)	
Positive	18 (17.5)	29 (23.2)		16 (19.8)	16 (19.8)	
Clinical T category			0.985			0.732
cT1–2	5 (4.9)	6 (4.8)		5 (6.2)	4 (4.9)	
cT3–4a	98 (95.1)	119 (95.2)		76 (93.8)	77 (95.1)	
Clinical N category			0.104			0.857
cN0	32 (31.1)	27 (21.6)		20 (24.7)	21 (25.9)	
cN1–3	71 (68.9)	98 (78.4)		61 (75.3)	60 (74.1)	
ypT category			0.009			0.749
ypT0–2	25 (24.3)	14 (11.2)		32 (39.5)	34 (42.0)	
ypT3–4a	78 (75.7)	111 (88.8)		49 (60.5)	47 (58.0)	
ypN category			0.007			0.875
ypN0	58 (56.3)	48 (38.4)		39 (48.1)	38 (46.9)	
ypN1–3	45 (43.7)	77 (61.6)		42 (51.9)	43 (53.1)	

Conclusion

Our results showed that neoadjuvant chemotherapy followed by esophagectomy was an applicable treatment strategy for locally advanced ESCC. Chemotherapy regimens and ypT category were significant independent predictors of both DFS and OS. The adjuvant therapy following neoadjuvant chemotherapy and R0 resection did not seem to show survival benefit and its necessity requires further investigations.

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Disclosure

The authors report no conflicts of interest in this work.

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