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Research Article

Efficacy Analysis of Concurrent Chemoradiotherapy with TP and FP Regimens for Esophageal Squamous Cell Carcinoma Based on Propensity Score Matching

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Abstract

Objective: To evaluate the efficacy and toxicity of concurrent chemoradiotherapy with paclitaxel/cisplatinum versus 5-fluorouracil/cisplatinum in patients with esophageal squamous cell carcinoma.

Methods: The medical records of 348 patients with esophageal squamous cell carcinoma who received concurrent chemoradiotherapy in the Fourth Hospital of Hebei Medical University from January 1, 2005 to December 31, 2015 were retrospectively analyzed. Of the patients enrolled, 295 received 5-fluorouracil/cisplatinum regimen (FP group) and 53 received paclitaxel/cisplatinum regimen (TP group).Survival analysis was performed and PSM (Propensity Score Matching) was conducted to evaluate and compare the local control, overall survival and adverse reactions between TP and FP groups.

Results: A total of 98 patients with good balance in observed co-variables were enrolled. There was no significant difference in clinical data between the two groups after PSM ($P > 0.05$). After matching, the local control rate and overall survival rate of TP group were significantly better than those of FP group. The 1-year, 3-year, 5-year local control rates were 76.6%, 69.9%, 66.4% for patients in the TP group, respectively, and 71.7%, 36.6%, 27.4% for patients in the FP group, respectively ($\chi^2 = 6.123$, $P = 0.012$). The 1-year, 3-year, 5-year overall survival rates were 79.6%, 53.1%, 42.5% for patients in the TP group, respectively, and 65.3%, 20.4%, 12.2% for patients in the FP group, respectively ($\chi^2 = 12.246$, $P = 0.000$).The median survival time in the TP group was 41 months, significantly longer than 19 months in the FP group. In contrast, there was a trend towards increased acute radiation esophagitis toxicity among patients in TP group (77.56% vs 55.11%), mainly grade 2 esophagitis, no grade 3 esophagitis occurred, while 3 patients in the FP group had grade 3 acute radiation esophagitis. None experienced grade 5 and grade 4 acute oesophagitis. The TP group has a higher incidence of upper gastrointestinal toxicities, leukopenia and thrombocytopenia than FP group (71.43% vs 38.78%, 81.63% vs 71.43%, 28.57% vs 8.16%, respectively, $P<0.05$). Similar rates of acute radiation pneumonitis, lower gastrointestinal toxicities, and hemoglobin reduction were observed between patients in TP group versus FP group. Multivariate analysis of Cox regression model showed that different chemotherapy regimens and TNM stage were independent prognostic factors. Compared with the FP regimen, the TP regimen was a survival benefit factor (HR = 0.486, P = 0.002). Late clinical TNM stage is a prognostic risk factor for esophageal cancer (HR = 1.648, P = 0.008).

Conclusions: Patients with unresectable esophageal squamous cell carcinoma have obvious survival benefits from TP regimen during concurrent chemoradiotherapy, and the adverse reactions are tolerable, so TP regimen can be used as the optimal chemotherapy regimen during radiotherapy.

Keywords: Esophageal Cancer; Chemoradiotherapy; Paclitaxel; 5-Fluorouracil; Cisplatin; Survival

Introduction

Based on latest epidemiological researches, esophageal cancer (EC) is the 8th most common cancer worldwide, with more than 600,000 new cases reported in 2020, corresponding to an age-standardized incidence rate of 6.3 per 100,000. The global burden of esophageal cancer remains significant, with highest incidence rates observed in Eastern Asia and Southern Africa [1]. Esophageal squamous cell carcinoma (ESCC) is the primary subtype of esophageal cancer prevalent in the Asian region [2]. EC has strong invasive nature, and its early symptoms can be easily overlooked, therefore patients are frequently diagnosed at an advanced stage, resulting in relatively lower five-year survival rate, around 20% [3,4].

Current treatment strategies for esophageal cancer include surgery, radiotherapy, chemotherapy, targeted therapies and immunotherapy. For patients with operable esophageal cancer, surgery is the first choice for comprehensive treatment. At present, concurrent chemoradiation for non-operable esophageal cancer has become a consensus [5]. However, there is no consensus on which chemotherapeutic regiments to choose in combination with radiotherapy. There are few literature focusing on differences in the efficacy and adverse reactions between the fluorouracil plus platinum (FP) and taxane plus platinum (TP) regimens, which are widely used in clinical medicine. Thus, we collected information from 348 esophageal cancer patients who received concurrent chemoradiation in the Fourth Hospital of Hebei Medical University and reviewed the advantages and disadvantages of the two groups.

Materials and Methods

Patients

The initially diagnosed Esophageal cancer patients who received conformal intensity-modulated radiotherapy combined with FP or TP chemotherapy at The Fourth Hospital of Hebei Medical University from January 2005 to December 2015 were included in this study. Eligible participants were: 1. newly diagnosed and pathologically proven esophageal squamous cell carcinoma (ESCC); 2. karnofsky performance status ≥ 70; 3. radiotherapy dose ranges from 50 to 70 Gy; 4. conformal intensity-modulated radiotherapy combined with FP or TP chemotherapy was used as first-line treatment. Patients with previous cancer histories and distant metastasis were excluded. A total of 348 ESCC patients were identified as the research subjects, including 295 patients in FP group and 53 patients in TP group. The general clinical characteristics of the two groups were shown in Table 1. The clinical stage was evaluated based on the eighth edition of the American Joint Committee on Cancer (AJCC)/International Union against Cancer (UICC) tumor-node-metastasis (TNM) staging system for ESCC [6]. It is worth noting that several stage I and II ESCC patients are included in this study, which are usually considered resectable. However, in some rare cases, early stages patients could be unresectable due to following reasons, inoperability caused by complicated anatomical location, the lesion was too extensive to be operable assessed by surgeons, patients have multiple comorbidities, such as severe cardiac insufficiency, coronary artery disease, kidney failure and coagulopathy, hence can't tolerate surgery. Early stages patients enrolled in our study have been carefully reviewed by multidisciplinary team of gastroenterologists, oncologists, and radiologist. Proportion of early stages patients is no greater than 10% (28/348) [7].

	The FP Group (n = 295)	**The TP Group (n = 53)**	χ2/t value	**P value**
Gender				
Male	203(68.8)	48 (90.6)	10.574	0.001
Female	92(31.2)	5 (9.4)		
Age(year)				
Range	30-78	41-72	1.597[a]	0.111
Median	61	59		
the location of the lesions				

Cervical	19 (6.4)	6 (11.3)	1.968	0.579
Upper thoracic	103 (34.9)	19 (35.8)		
Middle thoracic	148 (50.2)	23 (43.4)		
Inferior thoracic	25 (8.5)	5 (9.4)		
barium meal imaging length (cm)				
Range	1.2-18.6	1.2-13.9	0.059[a]	0.953
Median	5.6	5.3		
T stage				
T1	3(1)	2(3.8)	5.224[b]	0.131
T2	68(23.1)	17(32.1)		
T3	43(14.6)	8(15.1)		
T4	181(61.4)	26(49.1)		
N stage				
N0	22(7.5)	6(11.3)	1.619[b]	0.661
N1	26 (8.8)	4(7.5)		
N2	190(64.4)	31(58.5)		
N3	57(19.3)	12(22.6)		
TNM stage				
Ⅰ	2(0.7)	0	4.273[b]	0.202
Ⅱ	20(6.8)	6(11.3)		
Ⅲ	73(24.7)	18(34.0)		
IVa	200(67.8)	29(54.7)		
GTV size(cm3)				
Range	4.1-275.85	4.3-279.03	0.071[a]	0.943
Median	41.62	38.55		
The number of chemotherapy cycles During radiotherapy				
1 cycle	141(47.8)	41(77.4)	29.234	0.000
2 cycle	154(52.2)	12(22.6)		
Consolidate chemotherapy				
Yes	164 (55.6)	36(67.9)	2.795	0.095
No	131(44.4)	17(32.1)		

Table 1: General clinical data of FP and TP groups in 348 patients with esophageal cancer before PSM (n(%)).

Note: a applies T test; b applies Fisher's exact test.

Treatment

Radiotherapy

All patients were located by CT simulation, and the target area of radiotherapy included esophageal lesions and regional lymph node involvement field irradiation. Gross tumor volume (GTV): The standard is that the thickness of esophageal wall is＞0.5 cm or the diameter of esophageal wall without air cavity is＞1.0 cm, and the length and position are determined with reference to the important examination results such as esophagography and gastroscopy.

Clinical tumor volume (CTV): it is 0.5 cm before and after GTV, and 2.0 cm up and down, and it is manually adjusted according to the anatomical barrier. The planned target volume (PTV) is 0.5 cm before and after CTV, and 1.0 cm up and down. The delineation criteria of mediastinal lymph nodes GTV-N are as follows: the short diameter of lymph nodes is ≥1.0 cm, and the long diameter of special parts such as para-esophageal, tracheoesophageal groove, pericardial horn, abdominal cavity and supraclavicular lymph nodes is ≥0.5 cm, or the lymph nodes are small but irregular in shape with annular enhancement. CTV-N of lymph nodes is 0.5 cm for GTV-N and 0.5 cm for PTV-N. Three-dimensional conformal intensity-modulated radiotherapy was used. The prescription dose was 50.4～66Gy (median 60Gy), and the routine division was 1.8 ~ 2.0 Gy/time, five times a week. The plan requires: 95% of PTV is irradiated with more than 100% of the prescribed dose, the whole lung V5 ≤ 55 ~ 60%, V20 ≤ 25 ~ 30%, V30≤18%, the average cardiac dose ≤ 26 ~ 30 Gy, and the maximum spinal cord dose < 45Gy.

Chemotherapy

All patients received 1-2 cycles of chemotherapy during radiotherapy and 1-2 cycles of consolidate chemotherapy was performed on part of the population. Chemotherapy regimens: FP[fluorouracil injection (Deyao Pharma, SFDA approval number: H20051619) 450~500 mg/m^2, intravenous drip, d1~d5 + cisplatin injection (Nanjing Pharma, SFDA approval number: H20030675) 25 mg/m^2, intravenous drip, d1~d3] and TP[paclitaxel injection (Cqlummy, SFDA approval number: H20054814) 135 mg/m^2, intravenous drip, d1 + Cisplatin injection (Nanjing Pharma, SFDA approval number: H20030675) 25 mg/m^2, intravenous drip, d2~d4] were used. Patients received chemotherapy in the first week and 4/5 weeks of radiotherapy.

Follow up and assessment

Patient's condition was evaluated by gastroscope, radiography, CT, PET/CT, MRI and patient's symptoms every 3-6 months. The National Cancer Institute Common Terminology Criteria for Adverse Events ver. 5.0 was used for the assessment of chemotherapy-related adverse events and the toxicity criteria of the Radiation Therapy Oncology Group was used for the assessment of acute radiation toxicity. The Local Control (LC), Overall Survival (OS), Progression-Free Survival (PFS) and Treatment-related adverse events were compared between the two groups.

Statistical analysis

Patients were matched using a 1:1 propensity score to eliminate baseline differences between groups based on age, gender, the length of esophageal lesions, the location of the lesions, T stage, N stage, TNM stage, GTV size, number of chemotherapy cycles during radiotherapy and consolidate chemotherapy. Probabilities of survival were estimated using the Kaplan-Meier method and compared using the log-rank test. Univariate analysis and multivariate analysis using a Cox proportional hazard regression model were performed to explore prognostic factors for survival. All statistical analyses were performed using SPSS (IBM SPSS 26.0, NY, USA). All p values are two-sided, and $p < 0.05$ was considered to indicate a statistically significant difference.

Results

Patient characteristics

There were statistically significant differences in gender and the number of chemotherapy cycles during radiotherapy between the two groups before PSM. As shown in Table 1, there were more male patients (90.6% vs 68.8%, P = 0.001) and more patients who received two cycles of concurrent chemotherapy (77.4% vs 47.8%, P = 0.000). After PSM, 49 pairs (98 cases) were successfully matched and there was no significant difference between the two groups (P > 0.05) (Table 2).

	The FP Group (n =4 9)	The TP Group (n= 49)	χ2/t value	P value
Gender				
Male	47 （95.9）	44 （89.8）	1.385	0.239
Female	2 （4.1）	5 （10.2）		
Age （year）				
Range	30-73	41-72	1.415[a]	0.160
Median	57	59		
the location of the lesions				

Cervical	4(8.2)	5(10.2)	1.118[b]	0.849
Upper thoracic	15(30.6)	18(36.7)		
Middle thoracic	26(53.1)	21(42.9)		
Inferior thoracic	4(8.2)	5(10.2)		
barium meal imaging length (cm)				
Range	2.1-13.6	1.2-13.9	1.365[a]	0.175
Median	6.3	5.5		
T stage				
T1	1(2)	2(4.1)	0.530[b]	1.000
T2	14(28.6)	14(28.6)		
T3	8(16.3)	7(14.3)		
T4	26(53.1)	26(53.1)		
N stage				
N0	5(10.2)	5(10.2)	0.937	0.816
N1	7(14.3)	4(8.2)		
N2	27(55.1)	29(59.2)		
N3	10(20.4)	11(22.4)		
TNM stage				
Ⅰ	0	0	0.481	0.786
Ⅱ	5(10.2)	5(10.2)		
Ⅲ	12(24.5)	15(30.6)		
IVa	32(65.3)	29(59.2)		
GTV size(cm^3)				
Range	8.2-164.76	4.3-279.03	0.352[a]	0.725
Median	39.6	41.19		
The number of chemotherapy cycles during radiotherapy				
1 cycle	25(51)	37(75.5)	1.271	0.223
2 cycle	24(49)	12(24.5)		
Consolidate chemotherapy				
Yes	25(51)	32(65.3)	2.055	0.152
No	24(49)	17(34.7)		

Table 2 : General clinical data of 98 patients with esophageal cancer in FP and TP groups after PSM[n(%)].

Note: a applies T test; b applies Fisher's exact test

Follow up and survival analysis

In our study, five patients were excluded because of loss of follow-up. The median follow-up period was 109 months until March 31, 2021. The Kaplan-Meier curves of LC and OS in the TP and the FP groups before PSM were shown. As shown in Figure 1, LC was 82.1%, 62.3% and 58.6% in the FP group and 76.3%, 70.0% and 66.6% in the TP group at 1, 3, and 5 years respectively, and there was no significant difference ($\chi 2 = 0.320$, $P = 0.572$). In addition, there was no difference in OS between the FP group and the TP group at 1, 3, and 5 years, which was 76.3%, 44.7% and

35.9% and 77.4%, 52.8% and 43.0%, respectively ($\chi2$ = 0.432, P = 0.511) (Figure 2). However, the 1-, 3- and 5- LC of the FP group was 71.7%, 36.6%, and 27.4% and the 1-, 3-, and 5-year LC of the TP group was 76.6%, 69.9%, and 66.4% after PSM, and the differences between the two groups were statistically significant ($\chi2$ = 6.123, P = 0.012) (Figure 3). As shown in Figure 4, it is obvious that the median OS of the TP group had obvious advantages compared with those of the FP group (median OS: 41 months vs 19 months), and the OS at 1-, 3-, and 5-year was 79.6%, 53.1%, and 42.5% in the TP group and 65.3%, 20.4% and 12.2% in the FP group, which indicated that the OS of the TP group was significantly better than that of the FP group ($\chi2$ = 12.246, P = 0.000).

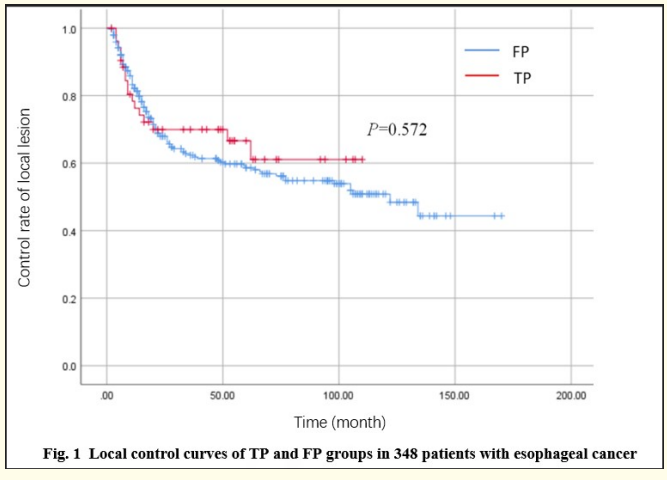

Fig. 1 Local control curves of TP and FP groups in 348 patients with esophageal cancer

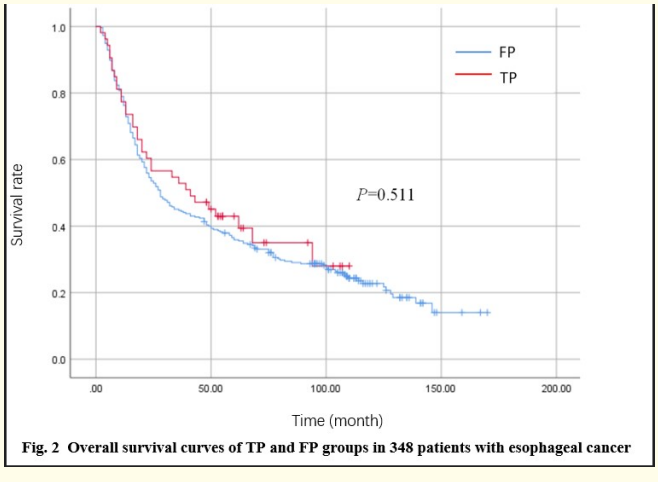

Fig. 2 Overall survival curves of TP and FP groups in 348 patients with esophageal cancer

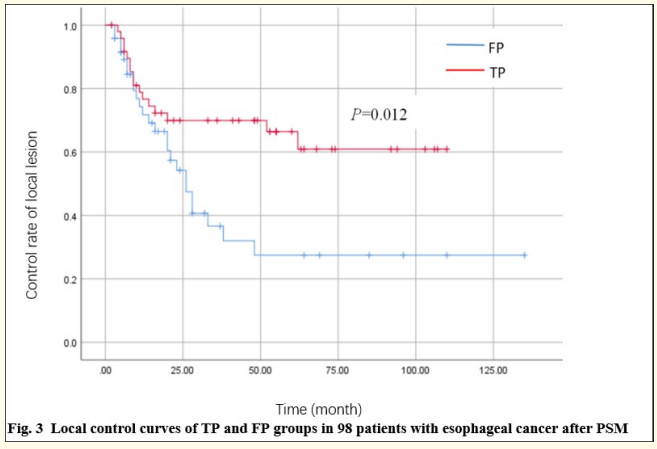

Fig. 3 Local control curves of TP and FP groups in 98 patients with esophageal cancer after PSM

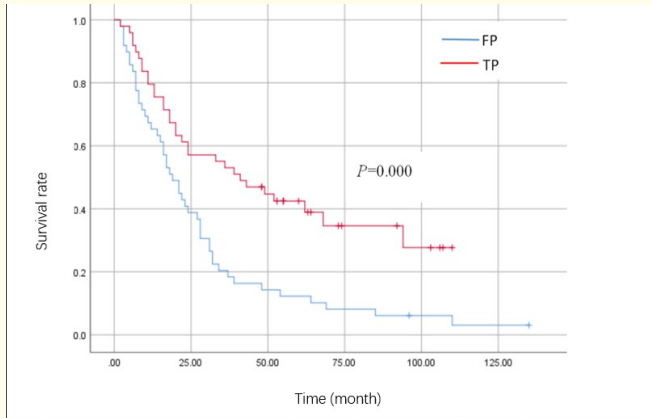

Fig. 4 Overall survival curves of TP and FP groups in 98 patients with esophageal cancer after PSM

Treatment-related adverse events

Details of the treatment-related adverse events were shown in Table 3. Among the 98 patients after PSM, the incidence of acute radiation esophagitis in the TP group was higher than that in the FP group (77.56% vs 55.11%, P = 0.007), with grade 2 being the predominant, and there was no acute radiation esophagitis above grade 3 occurring in the TP group. However, there were 3 cases experienced grade 3 acute radiation esophagitis in the FP group, and there was no grade 4 or above acute radiation esophagitis occurred in both groups. There was no significant difference in the incidence and severity of acute radiation pneumonitis between the two groups, but it seemed that the TP group had a higher incidence of grade 2 pneumonia, and one case of grade 3 acute radiation pneumonia occurred in the TP group. The incidence of upper gastrointestinal tract adverse events, such as nausea and vomiting, was higher in the TP group than that in the FP group (71.43% vs 38.78%, P = 0.011). Upper gastrointestinal tract adverse events

were mainly grade 1-2, but each group had one patient who developed grade 3 upper gastrointestinal tract adverse events. In addition, the TP group had a higher incidence of leukopenia and thrombocytopenia (81.63% vs 71.43% and 28.57% vs 8.16%, $P < 0.05$), of which 6 cases had grade 4 leukopenia. There was no statistically significant difference in the incidence and severity of lower gastrointestinal tract adverse events and hemoglobin reduction between the two groups.

Variables	Effective	Frequency %
HSG	N = 180	
Normal	84	46,67
Unilateral tubal blockage	18	10,00
Bilateral tubal blockage	63	35,00
Pelvic adhesions	5	2,78
Uterine synechia	10	5,56
ENDOMETRIAL BIOPSY	N = 121	
Normal	30	24,79
Functional abnormality	79	65,20
Organic abnormality	12	9,84
ULTRASOUND	N = 232	
Normal	98	42,24
Fibroids	67	28,88
Ovarian cyst	25	10,78
PCOS	42	18,10
SPERMOGRAM	N = 115	
Normozoospermia	22	21,09
Oligozoospermia	17	14,86
Asthenozoospermia	60	52
Leucospermia	16	11,56

Table 3: Paraclinical characteristics of women and men.

Prognostic analysis

As indicated in Table 4, the univariate analysis for prognosis manifested that barium meal imaging length, T stage, N stage and TNM stage were significantly associated with shorter survival at statistical level (HR = 2.033, 1.355, 1.319, 1.743, P = 0.002, 0.017, 0.003, 0.045), and chemotherapy was associated with longer survival (HR = 0.455, P = 0.001). In addition, the results of multivariate analysis showed that under the condition of concurrent chemoradiotherapy, chemotherapy regimens and TNM stage were independent factors affecting the patient's prognosis. The TP chemotherapy regimen was independently associated with a better prognosis (HR = 0.486, P = 0.002), and the TNM stage was a prognostic risk factor for ESCC (HR = 1.648, P = 0.008) (Table 5).

Variable	Effective=305	Frequency
AT TERM	212	69,51
LOSS	N = 93	
Early miscarriage	63	67,74
Missed abortion	26	27,95
Ectopic pregnancy	4	4,30

Table 4: Pregnancy outcomes.

	HR value	95.0% CI	P value
Chemotherapy regimens (TP vs FP)	0.486	0.287-0.721	0.002
Gender (Female vs Male)	0.647	0.647-2.153	0.096
barium meal imaging length	1.033	0.933-1.145	0.529
GTV size	1.002	0.995-1.009	0.501
T stage	1.119	0.7-1.787	0.638
N stage	1.239	0.797-1.927	0.341
TNM stage	1.648	1.140-2.383	0.008
Consolidate chemotherapy (Yes vs No)	1.391	0.829-2.333	0.211

Table 5: Multivariate Cox regression analysis of prognostic factor in 98 patients.

Note: HR: Hazard Ratio; CI: Confidence Interval.

Analysis of cause of death

A total of 78 patients died in our study until the last follow-up, among which 43 patients (55.12%) died of local tumor factors (uncontrolled, recurrence, bleeding, perforation), 27 patients (34.61%) died of distant metastasis. There was one treatment-related death in each group. One patient in the FP group died of lung infection 6 months after radiotherapy, with a survival time of 7 months, and another patient in the TP group died of shock during consolidation chemotherapy, with a survival time of only 3 months. Thus, local tumor factors are still the main cause of

death, followed by distant metastasis. There was no statistically significant difference in the distribution of causes of death between the two groups.

Discussion

Currently, for unresectable EC, the standard treatment model is chemoradiotherapy. This recommendation is based on the results of clinical trial of RTOG8501 [8] and RTOG9405 [9]. In European and North American countries, the most common pathological type of EC is adenocarcinoma (>70%), therefore, the preferred regimen is fluorouracil plus cisplatin, which has been recommended by National Comprehensive Cancer Network (NCCN) clinical guidelines for the first choice for many years [10]. However, for EC in Asian countries, squamous cell carcinoma has been the dominant pathological type (more than 90%) [11], therefore, in the clinical practice, paclitaxel plus platinum is preferable, which has been recommended by Chinese Society of Clinical Oncology (CSCO) [12]. However, it is still unclear which option can benefit patients more. Some studies indicate that for unresectable esophageal cancer, TP regimens is more effective than FP regimens [13], however, others indicate that FP is as effective as TP [14].

The results of this study showed that there was no statistically significant difference in LC rate and OS rate between FP group and TP group before PSM. PSM balanced baseline data according to the 1:1 principle, and 98 patients were finally successfully matched. The overall survival rate of the TP group after PSM was significantly better than that of the FP group, with the median OS benefit doubled (41 months vs 19 months), and the survival curve showed that the survival advantage of the TP group became more obvious as the follow-up time increased. The 1-, 3-, and 5-year OS rates of the two groups were 65.3%, 20.4%, 12.2%, and 79.6%, 53.1%, and 42.5%, respectively. The survival rate of the FP group after PSM was significantly lower than that before PSM, and was significantly lower than the 26% 5-year survival rate in the RTOG 85-01 study, which can be attributed to case selection bias caused by retrospective methods in this study. However, the 5-year survival rate of the TP group was significantly higher than FP with 26%, indicating that survival advantage of the TP program exists objectively. The results of a large clinical trial in the UK [15] are consistent with ours, showing that the median OS of the TP regimen was 24.28 months, and the 1- and 2-year OS rates were 81.9% and 50.6% respectively, suggesting that the TP weekly regimen has good efficacy and is tolerable. The performance is good, which is consistent with the results of this study. In a study comparing the survival outcomes and treatment toxicity of TP and FP regimens neoadjuvant chemotherapy had been used in 134 patients of locally advanced esophageal cancer (98% squamous cell carcinoma) [13]. The results showed that the incidence rate of non-hematological adverse reactions in the FP group was significantly higher than that in the TP group (69.45 vs 51.7%, P = 0.049). After neoadjuvant concurrent chemoradiotherapy, the surgical resection rate in the TP group was 49.4%, which was significantly higher than the 22.4% in the FP group (P <0.001), and the 1-year and 2-year OS rates of the TP group were also significantly higher than those of the FP group (71.2% vs 48.6% and 56.9% vs 28.7%, P = 0.001), indicating that in patients with locally advanced esophageal cancer, neoadjuvant concurrent chemoradiotherapy combined with TP regimen has better survival results, higher surgical resection rate and higher safety than FP regimen. In another retrospective study involving 229 patients of locally advanced esophageal squamous cell carcinoma [13], the objective response rate of patients in the TP group was 71.1%, which was significantly better than 51.4% in the FP group (P = 0.016), and the progression-free survival of patients in the TP group (median PFS: 16.5 months vs 8.4 months, P = 0.002) and overall survival (median OS: 18.6 months vs 10.9 months, P = 0.019) were significantly longer than those in the FP group, indicating the confirmed survival benefit brought by TP regimen. Therefore, TP regimen may be the prioritized chemotherapy regimen for radical concurrent chemoradiotherapy in patients with advanced ESCC. Well, in terms of toxicity and adverse effects, several studies reported that the main adverse effects of concurrent radiotherapy with paclitaxel combined with cisplatin is acute leukopenia, which can be controlled. At the same time, patients in these studies have experienced relatively less radiation-induced esophagitis, indicating that the combined therapy is slightly better tolerated [16,17]. The results of a meta-analysis [18] including 36 studies with total 3167 patients showed that the incidence of grade III-IV leukopenia (OR = 1.91, 95%CI 1.37-2.67, P < 0.001) was significantly higher with TP concurrent chemoradiotherapy. However, the incidence of grade III to IV nausea/vomiting (OR = 0.53, 95%CI is 0.32~0.86, P = 0.01) and radiation esophagitis (OR = 0.52, 95%CI is 0.39~0.70, P < 0.001) is lower than FP with concurrent chemoradiotherapy. This result from meta-analysis is consistent with ours, indicating that TP group had higher hematological toxicity (grade 3 or above), but the incidence of severe radiation esophagitis was lower than that of the FP group, and no fatal adverse effects has been observed.

Multivariate analysis shows that different chemotherapy regimens and clinical TNM staging are the independent prognostic

factors. TP regimens is more effective than FP regimens (HR = 0.486 , P = 0.002). Well, late clinical TNM stage is risk factor for esophageal cancer (HR = 1.648, P = 0.008). These results of our analysis have been consistent with other studies [13,14]. Analysis of causes of death revealed that treatment failure of local lesion is still the main cause of whole treatment failure, followed by distant metastasis, for locally advanced esophageal squamous cell carcinoma. Therefore, continuous exploring high-efficiency and low-toxic chemotherapy regimens and radiotherapy sensitizing drugs to further improve treatment efficacy for local lesion matters to effective survival benefit of patients with esophageal squamous cell carcinoma.

In summary, concurrent chemoradiation based on TP regimen as a first-line treatment option for unresectable esophageal squamous cell carcinoma can achieve long-term survival and can also be used as a preferred treatment option. This study was conducted retrospectively. Although patients were enrolled through PSM to reduce the impact of confounding factors on results, there is still the potential for biased selection. Therefore, this conclusion requires further verification by large cohort clinical studies.

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Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' Contributions

LHL and KM performed the conception and design of the study. LHL, KM, SHG performed the experiments. LHL, KM, and SHG analyzed and checked the data and drafted the manuscript. LHL and SHG prepared figures. LHL, KM edited and revised manuscript. SHG was primarily responsible for final content. LHL, KM, and SHG confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

Not applicable

Patient Consent for Publication

Not applicable

Competing Interests

The authors declare that they have no competing interests.

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