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Original Research

Comparison of a Concurrent Fluorouracil-Based Regimen and a Taxane-Based Regimen Combined with Radiotherapy in Elderly Patients with Esophageal Squamous Cell Carcinoma☆,☆☆,★,★★

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ABSTRACT

Elderly patients with esophageal carcinoma may benefit from concurrent chemoradiotherapy (CCRT). However, the optimal concurrent chemotherapy regimen has not been determined. The aim of our study was to assess the efficiency and tolerance of treatment with a concurrent 5-fluorouracil (5-Fu)–based regimen and a taxane-based regimen combined with radiotherapy in elderly patients with esophageal squamous cell carcinoma (ESCC). A total of 46 patients with ESCC aged older than 65 years were included in this study. The patient population was divided into two treatment groups: 24 patients who received CCRT with a 5-Fu–based regimen were allocated to the PF group, and 22 patients who received CCRT with a taxane-based regimen were allocated to the DP group. The median overall survival (OS), median progression-free survival (PFS), overall response rate, and treatment-related toxicity were assessed. For patients in the PF group, the median OS time was 27.8 ± 9.1 months, and the median PFS time was 12.5 ± 2.7 months. Patients in the DP group had comparable survival outcomes, with a median OS time of 34.4 ± 6.4 months and a median PFS time of 21.1 ± 6.4 months ($P = .296$ and $P = .115$, respectively). Grade ≥3 leukocytopenia and grade ≥2 anemia occurred in 63.6% and 59.1% of patients in the DP group, respectively, and in 25.0% and 16.7% of patients in the PF group, respectively. Our results suggest that CCRT with a taxane-based regimen results in a higher incidence of treatment-related toxicity than CCRT with a 5-Fu–based regimen but comparable survival outcomes.

Introduction

The number of elderly patients with esophageal cancer is increasing as the number of elderly people increases. At present, in China, approximately 4,779,000 new cases are reported annually, and approximately 69.8% of male patients with esophageal cancer in China are older than 60 years [1]. Histologically, esophageal cancer can be divided into squamous cell carcinoma (SCC) and adenocarcinoma.

In Western countries, concurrent chemoradiotherapy (CCRT) using the cisplatin/5-fluorouracil (5-Fu) regimen has been considered the standard treatment option for patients with inoperable esophageal cancer [2,3]. However, the majority of patients enrolled in Western trials had adenocarcinoma, while most Asian patients suffered from SCC [4,5]. A number of published studies have reported that the prognosis and response to treatment seem to differ between patients with SCC and those with adenocarcinoma [6,7], suggesting that the clinical behaviors of SCC and adenocarcinoma are distinct. Therefore, the strategy used to treat esophageal cancer must be based on pathological features.

Taxane is one of the most promising drugs used for the treatment of esophageal cancer. Paclitaxel has been shown to temporarily arrest cells

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★ **Ethical approval:** All procedures performed in studies involving human participants conformed to the standards set by the Declaration of Helsinki and were approved by the Human Ethics Committee of the Affiliated Cancer Hospital & Institute of Guangzhou Medical University. All patients provided written, informed consent to participate in the study. All of the patient data were confidential.
★★ **Author contributions:** Yawei Yuan and Weijun Zhang designed this study. Chunyue Huang and Donglan Huang performed most of the experiments. Yujia Zhu, Hongmei Wang, and Guofeng Xie participated in the collection of data. Jianjun Shi and Baochang Jia provided helpful suggestions for the manuscript. The study was performed under the supervision of Yawei Yuan and Weijun Zhang. Chunyue Huang wrote the manuscript. Yujia Zhu performed the statistical analysis.
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Table 1
The Detailed Dosage of Fluorouracil-Based Regimen and Taxane-Based Regimen

	Drug 1	Drug 2	Frequency	Cases
PF group	5-Fu, 500-1000 mg/m^2 for 3-5 days	Cisplatin, 75-80 mg/m^2 for 1 day	q3W	6
	5-Fu, 500-1000 mg/m^2 for 3-5 days	Cisplatin, 20-30 mg/m^2 for 3-5 days	q3W	18
DP group	Docetaxel, 60 mg/m^2 for 1 day	Carboplatin, 200-400 mg/m^2 for 1 day	q3W	3
	Docetaxel, 60 mg/m^2 for 1 day	Cisplatin, 75-80 mg/m^2 for 1 day	q3W	10
	Docetaxel, 55-70 mg/m^2 for 1 day	Cisplatin, 20-25 mg/m^2 for 3 day	q3W	7
	Paclitaxel, 135-175 mg/m^2 for 1 day	Cisplatin, 75 mg/m^2 for 1 day	q3W	2

at the G2-M interface, the most radiosensitive cell cycle phase [8,9]. Docetaxel is a semisynthetic taxane that has also exhibited radiation-sensitizing effects *in vitro* [10]. Our previous study [11] demonstrated that elderly people with ESCC could benefit from double-agent-based CCRT, but the optimal concurrent chemotherapy regimen has not yet been determined. To date, no direct comparisons between 5-Fu–based and taxane-based CCRT have been conducted in elderly patients with esophageal cancer. To gain insight into the relative efficacy and toxicity of 5-Fu–based and taxane-based regimens in elderly patients with esophageal cancer, we performed a retrospective study to compare the feasibility and efficiency of 5-Fu and taxane in the treatment of elderly patients with ESCC by CCRT at our cancer center.

Patients and Methods

Patients

In our retrospective study, the target population was elderly patients with esophageal cancer who received CCRT with a 5-Fu–based regimen or a taxane-based regimen at the Affiliated Cancer Hospital & Institute of Guangzhou Medical University between January 2003 and June 2018. Patients fulfilled the following criteria: age ≥65 years; histologically proven SCC; treated with a concurrent 5-Fu–based regimen or a taxane-based regimen and radiotherapy; Karnofsky performance status (KPS) score ≥70; and total dose ≥50 Gy. Patients were excluded if they met the following criteria: 1) had multiple primary esophageal carcinoma; 2) had been treated with neoadjuvant chemoradiotherapy; 3) developed postoperative recurrence; or 4) had a past or current history of another malignancy. The TNM stage was based on barium esophagography, chest and abdominal computed tomography (CT), and esophageal ultrasonography when feasible. Tumors were staged according to the sixth edition of the American Joint Committee on Cancer staging manual.

Treatment

Patients who were treated with 5-Fu plus cisplatin with concurrent radiotherapy were allocated to the PF group. Patients who were treated with taxanes (including docetaxel or paclitaxel) plus platinum (including cisplatin or carboplatin) with concurrent radiotherapy were allocated to the DP group. Dosage details are shown in Table 1. The completion of two cycles of concurrent chemotherapy was achieved in 83.3% versus 81.8% of patients in the PF and DP groups, respectively (P = 1.000). One patient in the PF group suffered from dosage reduction in the second cycle of chemotherapy due to grade 3 leukopenia/neutropenia, while three patients in the DP group experienced dosage reduction in the second cycle of chemotherapy due to grade 3 or 4 leukopenia/neutropenia. 2D

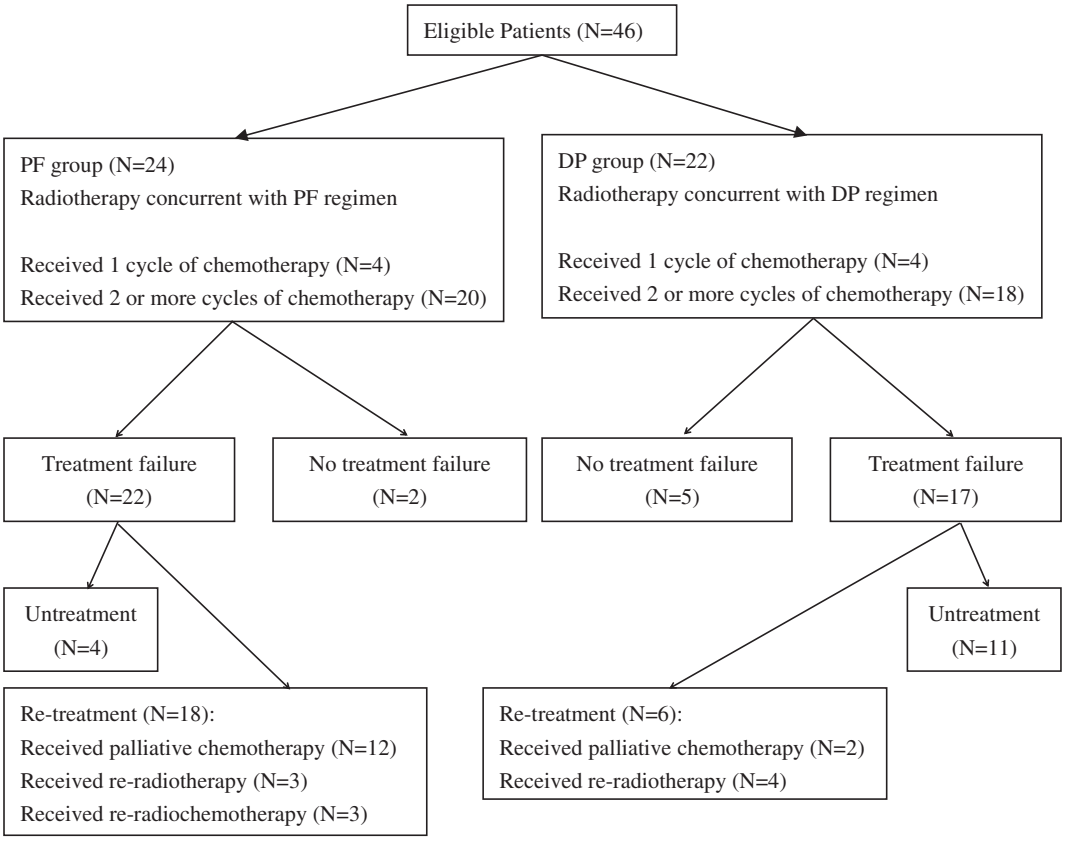

Figure 1. Trial profile. DP = docetaxel or paclitaxel plus platinum; PF = 5-Fu plus cisplatin.

radiotherapy (2D-RT), 3D conformal radiotherapy (3D-CRT), or intensity-modulated radiotherapy (IMRT) was used in the patients. A total dose of 50-66 Gy was designed to be delivered at 1.8-2.0 Gy with five daily fractions per week for 5-6.5 weeks.

Outcomes

The tumor response was assessed by barium esophagography or chest and abdominal CT at 1 month after the completion of treatment, and the response was classified according to the Response Evaluation Criteria in Solid Tumors version 1.1. Acute toxicity was graded according to the Radiation Therapy Oncology Group scale. Overall survival (OS) was defined as the time from diagnosis to death or the time of analysis. Progression-free survival (PFS) was defined as the time from diagnosis to recurrence or death from any cause or the time of analysis. The overall response rate (ORR) was defined as the proportion of patients who achieved a complete or partial response among all evaluated patients. Locoregional or distant relapse was confirmed by biopsy or fine-needle aspiration whenever possible. A clinical diagnosis was also accepted for lesions that were not accessible if classic features with or without clinical symptoms were present on examination by at least two imaging methods, including F-fluorodeoxyglucose positron emission tomography, bone scans, abdominal sonography, chest and abdominal CT, and chest radiography.

Statistics

OS and PFS were calculated according to the Kaplan-Meier method and compared using the log-rank test. Patient clinical characteristics and toxicity rates were determined and compared using the chi-squared test (χ^2 test). Factors with P values $< .150$ in the univariate analysis were included in the multivariate analysis. $P < .05$ was considered significant. Data were analyzed using SPSS 16.0 software (International Business Machines Corporation, Armonk, NY).

Results

Patient Characteristics

A total of 46 patients were enrolled in the current study (24 patients in the PF group and 22 patients in the DP group) (Figure 1). The final day of follow-up was in January 2019. At the time of analysis, 12 patients remained alive (6 in the PF group and 6 in the DP group).

Clinical Characteristics

The clinical characteristics are shown in Table 2. There were 38 men and 8 women, and the mean patient age was 68.3 ± 3.0 years (range, 65-75 years). 2D-RT, 3D-CRT, and IMRT were used in 41.3%, 32.6%, and 26.1% of patients, respectively. The middle thoracic esophagus was the most common tumor location ($n = 20$, 43.5%), followed by the upper thoracic esophagus ($n = 15$, 32.6%), the cervical esophagus ($n = 7$, 15.2%), and the lower thoracic esophagus ($n = 4$, 8.7%). The tumor length ranged from 2.0 to 11.0 cm, with a mean length of 5.7 ± 1.9 cm. The majority of patients had stage III (43.5%) or IV (41.3%) tumors. Upon admission, 41 patients had a body mass index (BMI) >18.5 kg/m^2. In total, 32 of the 46 patients had a history of smoking. In total, 26.1% of the patients had a family history of cancer, and 23.9% had comorbidities, including hypertension ($n = 6$), diabetes ($n = 3$), peptic ulcer disease ($n = 1$), liver disease ($n = 2$), or pulmonary tuberculosis ($n = 1$). The clinical characteristics were well balanced between the two groups except for smoking history.

OS and PFS

The median OS in all populations was 31.6 ± 4.4 months (95% CI: 22.8-40.4), with a 2-year OS rate of 62%. The median PFS in all populations was 14.8 ± 2.8 months (95% CI: 9.5-20.0), with a 2-year PFS rate of 35%. The ORR in the PF and DP groups was 66.7% and 81.8% ($P = .242$), respectively.

The median OS was 27.8 ± 9.1 months (95% CI: 10.0-45.6) in the PF group and 34.4 ± 6.4 months (95% CI: 21.7-47.0) in the DP group ($P = .296$, Figure 2). The OS rate was 92% at 1 year and 52% at 2 years in the PF group compared with 95% and 72%, respectively, in the DP group. The median PFS was 12.5 ± 2.7 months (95% CI: 7.2-17.7) in the PF group and 21.1 ± 4.3 months (95% CI: 12.7-29.5) in the DP group ($P = .115$, Figure 2). The 1- and 2-year PFS rates in the PF group were 54% and 29%, respectively, compared with 82% and 41%, respectively, in the DP group.

Univariate and Multivariate Cox Regression Analyses

The predictive factors of OS and PFS in the univariate analysis were age, sex, KPS score, smoking status, tumor length, tumor location, T stage, N

Table 2
Clinical Characteristics of Elderly Patients with ESCC in the PF and the DP Groups

Variable	Total (46)	PF Group (24)	TP Group (22)	*P* Value
Age (years)				.857
<70	35 (76.1%)	18 (75.0%)	17 (76.1%)	
≥70	11 (23.9%)	6 (25.0%)	5 (23.9%)	
Gender				.451
Male	38 (82.6%)	21 (87.5%)	17 (77.3%)	
Female	8 (17.4%)	3 (12.5%)	5 (22.7%)	
Karnofsky performance status				1.000
<80	2 (4.3%)	1 (4.2%)	1 (4.5%)	
≥80	44 (95.7%)	23 (95.8%)	21 (95.5%)	
BMI (kg/m^2)				.918
<18.5	5 (10.9%)	2 (8.3%)	3 (13.6%)	
≥18.5	41 (89.1%)	22 (91.7%)	19 (86.4%)	
Smoking status				**.034**
No	14 (30.4%)	4 (16.7%)	10 (45.5%)	
Yes	32 (69.6%)	20 (83.3%)	12 (54.5%)	
Tumor length (cm)				1.000
≤5.7	21 (47.7%)	11 (47.8%)	10 (47.6%)	
>5.7	23 (52.3%)	12 (52.2%)	11 (52.4%)	
Tumor location				.777
Cervical + upper thoracic	22 (47.8%)	11 (45.8%)	11 (50.0%)	
Middle and low thoracic	24 (52.2%)	13 (54.2%)	11 (50.0%)	
T stage				.700
T1-2	4 (8.9%)	3 (12.5%)	1 (4.8%)	
T3-4	41 (91.1%)	21 (87.5%)	20 (95.2%)	
N stage				.823
N0	9 (20.0%)	4 (16.7%)	5 (23.8%)	
N1	36 (80.0%)	20 (83.3%)	16 (76.2%)	
M stage				.198
M0	27 (58.7%)	12 (50.0%)	15 (68.2%)	
M1a	6 (13.0%)	5 (20.8%)	1 (4.5%)	
M1b	13 (28.3%)	7 (29.2%)	6 (27.3%)	
Tumor TNM stage				.109
I + II	7 (15.2%)	5 (20.8%)	2 (9.1%)	
III	20 (43.5%)	7 (29.2%)	13 (59.1%)	
IVa	6 (13.0%)	5 (20.8%)	1 (4.5%)	
IVb	13 (28.3%)	7 (29.2%)	6 (27.3%)	
Radiotherapy techniques				.125
2D-RT	19 (41.3%)	13 (54.2%)	6 (27.3%)	
3D-RT	15 (32.6%)	5 (20.8%)	10 (45.4%)	
IMRT	12 (26.1%)	6 (25.0%)	6 (27.3%)	
Radiation dose (Gy)				
Mean (range)	60 (50-66)	60 (50-66)	60 (50-66)	
Tumor early response				.337
CR	14 (30.5%)	6 (25.0%)	8 (36.4%)	
PR	20 (43.5%)	10 (41.7%)	10 (45.4%)	
SD	10 (21.7%)	6 (25.0%)	4 (18.2%)	
PD	2 (4.3%)	2 (8.3%)	0 (0.0%)	
Charlson Comorbidity Index				.697
Mean ± SD	0.28 ± 0.58	0.25 ± 0.44	0.32 ± 0.72	
Family history of cancer				.861
No	34 (73.9%)	18 (75.0%)	16 (72.7%)	
Yes	12 (26.1%)	6 (25.0%)	6 (27.3%)	

The *P* value in bold indicated that the difference between PF group and DP group was significant.

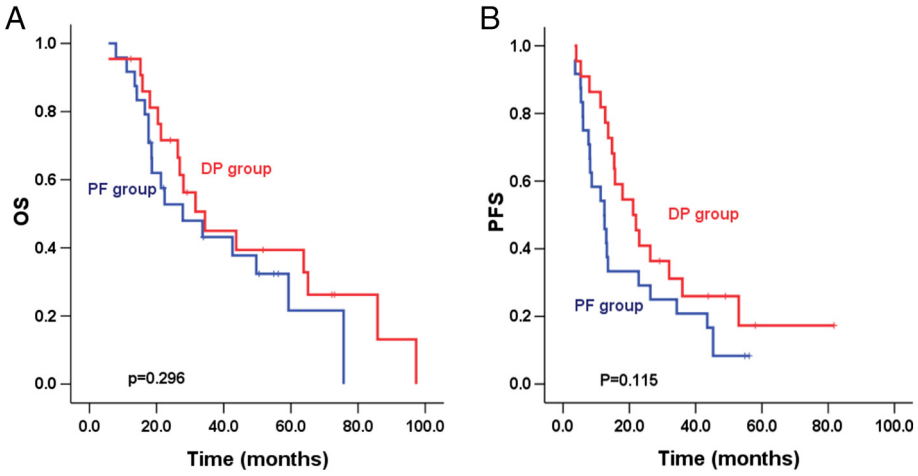

Figure 2. Overall survival (A) and progression-free survival (B) of the PF group (n = 24) and the DP group (n = 22).

stage, M stage, TNM stage, radiotherapy technique, radiation dose, concurrent chemotherapy, and early tumor response. In the multivariate analysis, tumor length (P = .042) and M stage (P = .009) were independent prognostic factors for OS. Moreover, the M stage (P = .031) was an independent prognostic factor for PFS (Table 3).

Treatment-Related Toxicity

Information related to acute treatment-related toxicity is listed in Table 4. The incidence of grade 3/4 total adverse events was higher in the DP group than in the PF group (68.2% versus 29.2%, P = .019). Leukocytopenia was the most common severe adverse event, and the incidence rate was higher in the DP group than in the PF group (63.6% versus 25.0%, P = .019). In addition, grade ≥2 anemia was also more frequently observed in the DP group than in the PF group (59.1% versus 16.7%, P = .008). The incidence and severity of other signs of toxicity, including thrombocytopenia, hypoalbuminemia, weight loss during treatment, esophagitis, radiation pneumonitis, liver enzyme elevation, and creatinine elevation, were all comparable between the two groups.

Patterns of Failure

In the PF group, 22 (91.7%) patients experienced treatment failure during the follow-up period, of whom 18 patients underwent retreatment, including 12 patients who underwent palliative chemotherapy, 3 patients who underwent re-radiotherapy, and 3 patients who underwent re-radiochemotherapy. In the DP group, 17 (77.3%) patients experienced treatment failure, and only 6 patients underwent retreatment (2 patients were treated with palliative chemotherapy, and 4 patients underwent re-radiotherapy).

Discussion

In the current retrospective study, we compared the efficacy and toxicity of CCRT with a 5-Fu–based regimen with those of a taxane-based regimen in elderly patients diagnosed with ESCC. Our findings show that CCRT with a 5-Fu–based regimen was comparable to that with a taxane-based regimen in terms of the ORR, OS, and PFS. In addition, a significantly higher incidence of grade ≥3 leukocytopenia or grade ≥2 anemia was observed in patients treated with a taxane-based regimen than in those treated with a 5-Fu–based regimen.

More than 90% of Asian patients suffer from SCC. Several studies have revealed that taxane is more efficient in patients with SCC than in patients with adenocarcinoma. In the CROSS trial [12], neoadjuvant chemoradiotherapy using carboplatin plus paclitaxel showed significant survival advantages in patients with SCC compared with patients with adenocarcinoma (median OS: 81.6 months versus 43.2 months). The results of a prospective multicenter trial [13] also showed that

Table 3
Univariate and Multivariate Analysis of Prognostic Factors on Treatment Results (n = 46)

Prognostic Factors	Univariate Analysis				Multivariate Analysis			
	OS		PFS		OS		PFS	
	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)
Age (<70 years vs. ≥70 years)	.743	0.87 (0.36-2.06)	**.072**	0.51 (0.24-1.06)				
Gender (male vs. female)	.320	1.57 (0.64-3.84)	.392	1.47 (0.61-3.52)				
KPS (<80 vs. ≥80)	.485	21.5 (0.76-1.46)	.600	0.68 (0.16-2.86)				
BMI (≤18.5 kg/m^2 vs. >18.5 kg/m^2)	.354	0.61 (0.21-1.75)	.876	0.92 (0.33-2.60)				
Smoking status (no vs. yes)	.395	1.40 (0.65-3.01)	.448	1.32 (0.65-2.67)				
Tumor length (≤5.7 cm vs. >5.7 cm)	**.054**	2.11 (0.99-4.51)	.525	1.23 (0.65-2.36)	**.042**	2.22 (1.03-4.82)		
Tumor location (cervical vs. thoracic)	.829	0.91 (0.37-2.22)	.980	0.99 (0.41-2.38)				
T stage (T1-2 vs. T3-4)	.610	0.73 (0.22-2.44)	.283	0.56 (0.19-1.62)				
N stage (N0 vs. N1)	.882	0.93 (0.38-2.31)	.171	0.58 (0.27-1.26)				
M stage (M0 vs. M1)	**.022**	2.28 (1.13-4.59)	**.031**	2.03 (1.07-3.84)	**.009**	2.59 (1.27-5.27)	**.031**	2.03 (1.07-3.84)
Tumor TNM stage (I + II vs. III + IV)	.231	0.55 (0.21-1.46)	.207	0.58 (0.25-1.35)				
Radiotherapy techniques (2D-RT vs. 3D-RT/IMRT)	**.032**	0.46 (0.23-0.94)	.183	0.62 (0.33-1.17)				
Radiation dose (≤60 Gy vs. >60 Gy)	.499	0.78 (0.37-1.61)	.344	1.36 (0.72-2.54)				
Concurrent chemotherapy (PF vs. DP)	.305	0.69 (0.34-1.40)	**.120**	0.60 (0.32-1.14)				
Tumor early response(CR/PR vs. SD/PD)	.446	0.74 (0.34-1.61)	.781	1.10 (0.55-2.22)				

The P value in bold indicated that the prognostic factor was associated with OS and PFS.

Table 4
Adverse Events of Elderly Patients with ESCC in the PF and the DP Groups

Variable	Total (46)	PF group (24)	TP group (22)	*P* Value
Total adverse events				**.019**
Grade 0-2	24 (47.8%)	17 (70.8%)	7 (31.8%)	
Grade 3-4	22 (52.2%)	7 (29.2%)	15 (68.2%)	
Leukocytopenia				**.019**
Grade 0-2	26 (56.5%)	18 (75.0%)	8 (36.4%)	
Grade 3-4	20 (43.5%)	6 (25.0%)	14 (63.6%)	
Thrombocytopenia				.702
Grade 0-1	38 (82.6%)	19 (79.2%)	19 (86.4%)	
Grade 2-4	8 (17.4%)	5 (20.8%)	3 (13.6%)	
Anemia				**.008**
Grade 0-1	29 (63.0%)	20 (83.3%)	9 (40.9%)	
Grade 2-3	17 (37.0%)	4 (16.7%)	13 (59.1%)	
Hypoalbuminemia				.178
Grade 0-1	41 (89.1%)	23 (95.8%)	18 (81.8%)	
Grade 2	5 (10.9%)	1 (4.2%)	4 (18.2%)	
Weight loss during treatment				.694
<10%	39 (84.8%)	21 (87.5%)	18 (81.8%)	
≥10%	7 (15.2%)	3 (12.5%)	4 (18.2%)	
Esophagitis				.925
Grade 0-1	30 (65.2%)	15 (62.5%)	15 (68.2%)	
Grade 2-4	16 (34.8%)	9 (37.5%)	7 (31.8%)	
Radiation pneumonitis				1.000
Grade 0	41 (89.1%)	21 (87.5%)	20 (90.9%)	
Grade 1-4	5 (10.9%)	3 (12.5%)	2 (9.1%)	
Liver enzyme elevation				.659
Grade 0	41 (89.1%)	22 (91.7%)	19 (86.4%)	
Grade 1-4	5 (10.9%)	2 (8.3%)	3 (13.6%)	
Creatinine elevation				.234
Grade 0	39 (84.8%)	22 (91.7%)	17 (77.38%)	
Grade 1-4	7 (15.2%)	2 (8.3%)	5 (22.7%)	

The *P* value in bold indicated that the difference between PF group and DP group was significant.

neochemoradiotherapy with docetaxel plus cisplatin was more efficient in patients with SCC than in patients with adenocarcinoma, with a pathological complete response rate of 38% and 16%, respectively. Moreover, the pathological complete response rate was identified as an independent prognostic factor of OS [14,15]. In a definitive setting for advanced ESCC, the promising efficacy of taxane has also been demonstrated, reaching a median OS time of 28.5 months and a PFS time of 14.7 months [16]. Based on the promising results for taxane in esophageal cancer, many prospective and retrospective studies have compared the efficacy and toxicity of concurrent 5-Fu/platinum and taxane/platinum in both a definitive and a neoadjuvant chemoradiotherapy setting in esophageal carcinoma patients but yielded controversial results. Some studies have indicated that taxane-based regimens are more effective than 5-Fu–based regimens[17–22], while other studies have shown a lower efficacy [23] or no difference [24,25]. Several factors might account for this discrepancy between studies. First, the dose intensity of the chemotherapy regimen varied among studies. For instance, in Zhang's study [18], patients in the PF group received a lower dose of cisplatin and 5-FU (cisplatin 60 mg/m^2 d1? + 5-FU 300 g/m^2/d d1-d3, Q4W) than did patients in Zhu's study [24] (cisplatin 80 mg/m^2 d1 + 5-FU 1000 g/m^2/d d1-d4, Q3W). Second, the radiation dose and pathological type also differed between studies. In Honing's study [21], 50% of patients with adenocarcinoma were enrolled, and more than 90% of patients received radiation doses less than 50.4 Gy, while in Zhu's study, all of the enrolled patients had SCC, and the radiation dose ranged from 60 to 64 Gy. Finally, patient selection bias might exist, especially for retrospective studies. All of the abovementioned factors substantially affected the clinical outcomes. However, more than 50% of patients enrolled in those trials were young (age ≤ 65 years), and no studies compared the treatment outcomes of a concurrent 5-Fu–based regimen to those of a taxane-based regimen combined with radiotherapy in elderly (age ≥ 65 years) patients with ESCC. To our knowledge, the present study is the first to focus on this particular issue.

Previous studies on the outcomes of radiotherapy combined with 5-Fu/platinum and taxane/platinum in ESCC patients are listed in Table 5. The results indicated that the taxane-based regimen was not inferior to the 5-Fu–based regimen in the definitive treatment of esophageal cancer by chemoradiotherapy. In the 5-Fu–based regimen group, survival showed great variation, with the median survival time ranging from 16 to 24 months, the 2-year OS rate ranging from 27% to 87%, and the median PFS time ranging from 11 to 20 months. The ORR ranged from 30% to 87%. In our study, patients in the PF group demonstrated a median survival time of 27.8 ± 9.1 months and a median PFS time of 12.5 ± 2.7 months, with an ORR of 66.7%, similar to previously reported results. On the other hand, in patients who underwent concurrent radiotherapy with a taxane-based regimen, the median survival time varied from 13 to 44 months, the 2-year OS rate varied from 35% to 70%, and the median PFS time varied from 9 to 26 months. The ORR varied from 52% to 85%. In our study, for patients in the DP group, the median OS, median PFS, and ORR was 34.4 ± 6.4 months, 21.1 ± 4.3 months, and 81.8%, respectively. These results are within the range of those reported in previous studies. Our results suggest that the survival in the DP group seemed better than that in the PF group; however, the statistical difference was not significant, which is contradictory with the results of three previous studies [17,18,26]. In a randomized trial reported in 2012 [17], CCRT with a docetaxel/cisplatin regimen led to a higher response rate and better survival than CCRT with a 5-Fu/cisplatin regimen in patients with esophageal carcinoma (median OS: 43.2 months versus 22.3 months). A previous retrospective study [26] also showed that patients treated with the cisplatin/paclitaxel regimen displayed a definitive advantage over those treated with the cisplatin/5-Fu regimen (median OS: 33.9 months versus 23.1 months; median PFS: 15.9 months versus 13 months). The authors postulated several possible reasons for the difference, including the dosage issue mentioned above. In Zhao's study, patients in the PF group were treated with the dose-reduced PF regimen (5-FU 250 mg/m^2/d for 4 days + cisplatin 75 mg/m^2 for 1 day, Q4W). In the current study, patients in the PF group were treated with a relatively high dosage (5-FU 500-1000 g/m^2/d for 3-5 days + cisplatin 75 mg/m^2 for 1 day, Q3W). Treatment compliance was another issue. In the present study, only 86.4% of patients in the DP group completed chemotherapy and radiotherapy at the full dosage as planned without treatment interruption, which was much lower than that in the PF group (95.8%). All of the abovementioned factors might have resulted in the discrepancy between studies. Although the patients in our study were older than those described in previous studies, the clinical efficacy after treatment with CCRT was similar to that observed in younger cohorts. This finding was also reported in a previous study [27]. Therefore, elderly patients should not be excluded from intensive treatments based on age alone.

Adverse events were the most notable issue in elderly patients. In our study, the most common sign of acute toxicity in the DP group, leukocytopenia, was observed in 63.6% of patients, which was higher than that previously reported (from 6% to 45%). This finding might be because aging is associated with a decreased bone marrow reserve and an increased risk of myelosuppressive-associated complications from chemotherapy [28]. Meanwhile, the 3-weekly docetaxel regimen in our study might also have resulted in a high rate of hematological toxicity. Studies on non–small cell lung cancer [29] and gastric cancer [30,31] showed that a weekly docetaxel schedule caused less bone marrow toxicity than a triweekly schedule. Therefore, weekly docetaxel may be a new therapeutic option to reduce the impact of this effect, and a head-to-head

Table 5
Previous Studies of Radiotherapy with a Fluorouracil-Based Regimen and a Taxane-Based Regimen in a Definitive Setting for Elderly Patients with ESCC

Study	Type	Pathology	*n*	Age	Stage	Treatment (*n*)	ORR (%)	OS (months)	2-y OS (%)	PFS (months)	2-y PFS (%)	≥ 3 Grade Leukocytopenia (%)	≥ 3 Grade Hematologic Toxicity (%)	Result
Hu, 2016 [26]	Retrospective	SCC	202	18-75	IIb-IIIc	CCRT with PF (97)	30.9	23.1	47.6	13	17*	12.3	16.5	PP>PF
						CCRT with PP (105)	52.4	33.9	61.9	15.9	21*	5.7	10.5	
Zhang, 2016 [18]	Retrospective	SCC	317	-	II-IVa	CCRT with PF (156)	-	21*	38*	20*	39*	35.3		DP>PF
						CCRT with DP (161)	-	29*	57*	25*	50*	45.1		
Zhao, 2012 [17]	Prospective	SCC	90	18-70	II-IVa	CCRT with PF (45)	53.3	22.3	42*	14	40*	-	24.4	DP>PF
						CCRT with DP (34)	73.3	43.2	59*	25.3	53*	-	35.6	
Zhu, 2017 [24]	Prospective	SCC	86	18-70	II-IVa	CCRT with PF (41)	87.3	Not rearch	86.2	Not rearch	55.0	19.5		DP = PF
						CCRT with DP (45)	84.4	Not rearch	69.1	Not rearch	69.4	68.9		
Honing, 2014 [21]	Retrospective	AC/SCC	102			CCRT with PF (47)	-	16.1	27*	11.1	21*	-	19	PC = PF
						CCRT with PC (55)	-	13.8	35*	9.7	28*	-	4	
Sun, 2016 [29]	Retrospective	SCC	179	42-76	II-IVb	CCRT with FB (96)	63.5	23	43*	18	42*	26	43.8	PC = PF
						CCRT with TB (83)	71.6	21	40*	17	40*	34.9	42.2	
Fang, 2017 [30]	Retrospective	SCC	82	-	II-IVa	CCRT with SC (41)	82.9	20*	40*	13*	32*	24.4	31.7	PP = SC
						CCRT with PP (41)	82.9	21*	43*	11*	40*	34.1	48.8	
Current	Retrospective	SCC	46	65-76	I-IVb	CCRT with PF (24)	66.7	27.8	52	12.5	29	25.0		DP = PF
						CCRT with DP (22)	81.8	34.4	72	21.1	41	63.6		

Abbreviations: *n* = number; AC = adenocarcinoma; dCCRT = definitive concurrent chemoradiotherapy; DP = docetaxel and cisplatin; PF = 5-fluorouracil and cisplatin; PC = paclitaxel and carboplatin; PP = paclitaxel and cisplatinum; SC = S-1 plus cisplatin; TL = paclitaxel and lobaplatin (TL); FB = fluorouracil-based regimen; TB = taxane-based regimen.
* Estimating from the survival curve.

comparison of weekly and 3-weekly docetaxel regimens in esophageal carcinoma is needed. Regarding anemia, the incidence of grade ≥2 toxicity was greater in the DP group than in the PF group (59.1% versus 16.7%, $P = .008$). On the other hand, in our study, 22 patients in the PF group suffered from treatment failure, and 18 patients accepted retreatment; therefore, the retreatment rate was 81.8%. However, in the DP group, only 6 of 17 (35.3%) patients underwent retreatment. This might be explained by the treatment toxicity observed from the initial treatment. Patients who initially underwent treatment with a taxane-based regimen had a low KPS score or were afraid to undergo re-chemotherapy or re-radiotherapy.

In conclusion, the results from the current trial indicate that CCRT with a taxane-based regimen does not improve the treatment response, OS, or PFS in elderly patients with ESCC compared with CCRT with a 5-Fu–based regimen. In addition, patients receiving treatment with a taxane-based regimen are more likely to develop severe (grade ≥3) leukocytopenia/neutropenia. However, further prospective clinical trials and retrospective studies on larger sample sizes are warranted.

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