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. 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
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 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 \(\geq\) 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 \(\geq\) 70; and total dose \(\geq\) 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.

Table 1

| Drug 1          | Drug 2                  | Frequency | Cases |
|-----------------|-------------------------|-----------|-------|
| **PF group**    |                         |           |       |
| 5-Fu, 500-1000 mg/m² for 3-5 days | Cisplatin, 75-80 mg/m² for 1 day | q3W       | 6     |
| 5-Fu, 500-1000 mg/m² for 3-5 days | Cisplatin, 20-30 mg/m² for 3-5 days | q3W       | 18    |
| **DP group**    |                         |           |       |
| Docetaxel, 60 mg/m² for 1 day | Carboplatin, 200-400 mg/m² for 1 day | q3W       | 3     |
| Docetaxel, 60 mg/m² for 1 day | Cisplatin, 75-80 mg/m² for 1 day | q3W       | 10    |
| Docetaxel, 55-70 mg/m² for 1 day | Cisplatin, 20-25 mg/m² for 3 day | q3W       | 7     |
| Paclitaxel, 135-175 mg/m² for 1 day | Cisplatin, 75 mg/m² for 1 day | q3W       | 2     |
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) 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 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

| Variable | Total (46) | PF Group (24) | TP Group (22) | P Value |
|----------|------------|---------------|---------------|---------|
| Age (years) | | | | |
| <70 | 35 (76.1%) | 18 (75.0%) | 17 (76.1%) | .857 |
| ≥70 | 11 (23.9%) | 6 (25.0%) | 5 (23.9%) | |
| Gender | | | | |
| Male | 38 (82.6%) | 21 (87.5%) | 17 (77.3%) | .451 |
| Female | 8 (17.4%) | 3 (12.5%) | 5 (22.7%) | |
| Karnofsky performance status | | | | |
| <80 | 2 (4.3%) | 1 (4.2%) | 1 (4.5%) | 1.000 |
| ≥80 | 44 (95.7%) | 23 (95.8%) | 21 (95.5%) | |
| BMI (kg/m²) | | | | |
| <18.5 | 5 (10.9%) | 2 (8.3%) | 3 (13.6%) | .918 |
| ≥18.5 | 41 (89.1%) | 22 (91.7%) | 19 (86.4%) | |
| Smoking status | | | | |
| No | 14 (30.4%) | 6 (25.0%) | 8 (36.4%) | .034 |
| Yes | 32 (69.6%) | 18 (75.0%) | 14 (63.6%) | |
| Tumor length (cm) | | | | |
| ≤5.7 | 21 (47.7%) | 11 (47.8%) | 10 (45.5%) | 1.000 |
| >5.7 | 23 (52.3%) | 12 (52.2%) | 11 (54.5%) | |
| Tumor location | | | | |
| Cervical + upper thoracic | 22 (47.8%) | 11 (45.8%) | 11 (50.0%) | .777 |
| Middle and low thoracic | 24 (52.2%) | 13 (54.2%) | 11 (50.0%) | |
| T stage | | | | |
| T1-T2 | 4 (8.9%) | 2 (8.3%) | 2 (9.1%) | .700 |
| T3-T4 | 41 (91.1%) | 21 (87.5%) | 20 (90.9%) | |
| N stage | | | | |
| No | 9 (20.0%) | 4 (16.7%) | 5 (22.7%) | .823 |
| Yes | 37 (80.0%) | 20 (83.3%) | 17 (77.3%) | |
| M stage | | | | |
| M0 | 27 (58.7%) | 12 (50.0%) | 15 (68.2%) | .198 |
| M1a | 6 (13.0%) | 5 (20.8%) | 1 (4.5%) | |
| M1b | 13 (28.3%) | 7 (29.2%) | 6 (27.3%) | |
| Tumor TNM stage | | | | |
| I + II | 7 (15.2%) | 5 (20.8%) | 2 (9.1%) | .109 |
| III | 20 (43.5%) | 10 (41.7%) | 10 (45.4%) | |
| IVa | 6 (13.0%) | 3 (12.5%) | 3 (13.6%) | |
| IVb | 13 (28.3%) | 7 (29.2%) | 6 (27.3%) | |
| Radiotherapy techniques | | | | |
| 2D-RT | 19 (41.3%) | 13 (54.2%) | 6 (27.3%) | .125 |
| 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) | .697 |
| Tumor early response | | | | |
| CR | 14 (30.5%) | 6 (25.0%) | 8 (36.4%) | .337 |
| 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 | | | | |
| Mean ± SD | 0.28 ± 0.58 | 0.25 ± 0.44 | 0.32 ± 0.72 | .697 |
| Family history of cancer | | | | |
| No | 34 (73.9%) | 18 (75.0%) | 16 (72.7%) | .861 |
| 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.
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 \((68.2\% \text{ versus } 29.2\%, P = .019)\). Leukocytopenia was the most common severe adverse event, and the incidence rate was higher in the DP group than in the PF group \((63.6\% \text{ versus } 25.0\%, P = .019)\). In addition, grade \(\geq 2\) anemia was also more frequently observed in the DP group than in the PF group \((59.1\% \text{ versus } 16.7\%, P = .008)\). 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-radiation).

**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 \(\geq 3\) leukocytopenia or grade \(\geq 2\) 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

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

**Table 3**

| 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. \(\geq 70\) years) | .743  (0.36-2.06) | .072  (0.24-1.06) | .042  (1.03-4.82) |
| Gender (male vs. female) | .320  (0.64-3.84) | .392  (0.61-3.52) | .009  (2.59-12.7)  |
| BMI (<18.5 kg/m\(^2\) vs. \(\geq 18.5\) kg/m\(^2\)) | .485  (0.76-1.46) | .600  (0.16-2.86) | .031  (2.03-10.7)  |
| Smoking status (no vs. yes) | .395  (0.65-3.01) | .448  (1.32-6.27) | .031  (2.03-10.7)  |
| Tumor early response(CR/PR vs. SD/PD) | .054  (0.99-4.51) | .525  (1.23-6.26) | .031  (2.03-10.7)  |
| Tumor location (cervical vs. thoracic) | .829  (0.91-2.22) | .980  (0.91-2.38) | .031  (2.03-10.7)  |
| T stage (T1-2 vs. T3-4) | .610  (0.73-2.24) | .283  (0.56-1.9)   | .009  (2.59-12.7)  |
| N stage (N0 vs. N1) | .022  (0.38-2.31) | .171  (0.58-2.71) | .009  (2.59-12.7)  |
| M stage (M0 vs. M1) | .022  (2.13-5.13) | .031  (2.03-10.7) | .031  (2.03-10.7)  |
| Radiation dose (<60 Gy vs. \(\geq 60\) Gy) | .022  (0.46-2.34) | .183  (0.62-3.17) | .031  (2.03-10.7)  |
| Concurrent chemotherapy (PF vs. DP) | .002  (0.78-1.61) | .344  (1.36-7.25) | .031  (2.03-10.7)  |
| Tumor early response(CR/PR vs. SD/PD) | .022  (0.74-1.61) | .781  (1.10-5.52) | .031  (2.03-10.7)  |

The \(P\) value in bold indicated that the prognostic factor was associated with OS and PFS.
received a lower dose of cisplatin and 5-FU (cisplatin 60 mg/m² d1 + 5-FU 300 g/m²/d d1-d3, Q4W) than did patients in Zhu's study [24] (cisplatin 80 mg/m² d1 + 5-FU 1000 g/m²/d d1-d4, Q3W). Second, the radiation dose and pathologic type also differed between studies. In Honig'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 cisplatin/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/m²/d for 4 days + cisplatin 75 mg/m² 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/m²/d for 3-5 days + cisplatin 75 mg/m² 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

| Variable                  | Total (46) | PF group (24) | TP group (22) | P Value |
|---------------------------|------------|---------------|---------------|---------|
| Total adverse events      |            |               |               | .019    |
| Grade 0-2                 | 24         | 17 (70.8%)    | 7 (31.8%)     |         |
| (47.8%)                   |            |               |               |         |
| Grade 3-4                 | 22         | 7 (29.2%)     | 15 (68.2%)    |         |
| (52.2%)                   |            |               |               |         |
| Leukocytopenia             |            |               |               | .019    |
| Grade 0-2                 | 26         | 18 (75.0%)    | 8 (36.4%)     |         |
| (56.5%)                   |            |               |               |         |
| Grade 3-4                 | 20         | 6 (25.0%)     | 14 (63.6%)    |         |
| (45.5%)                   |            |               |               |         |
| Thrombocytopenia           |            |               |               | .702    |
| Grade 0-1                 | 38         | 19 (79.2%)    | 19 (86.4%)    |         |
| (82.6%)                   |            |               |               |         |
| Grade 2-4                 | 8          | 5 (20.8%)     | 3 (13.6%)     |         |
| (17.4%)                   |            |               |               |         |
| Anemia                    |            |               |               | .008    |
| Grade 0-1                 | 29         | 20 (83.3%)    | 9 (40.9%)     |         |
| (63.0%)                   |            |               |               |         |
| Grade 2-3                 | 17         | 4 (16.7%)     | 13 (59.1%)    |         |
| (37.0%)                   |            |               |               |         |
| Hypoalbuminemia            |            |               |               | .178    |
| Grade 0-1                 | 41         | 23 (95.8%)    | 18 (81.8%)    |         |
| (89.1%)                   |            |               |               |         |
| Grade 2                   | 5          | 1 (4.2%)      | 4 (18.2%)     |         |
| (10.9%)                   |            |               |               |         |
| Weight loss during treatment |         |               |               | .694    |
| <10%                      | 39         | 21 (87.5%)    | 18 (81.8%)    |         |
| (84.8%)                   |            |               |               |         |
| ≥10%                      | 7          | 3 (12.5%)     | 4 (18.2%)     |         |
| (15.2%)                   |            |               |               |         |
| Esophagitis                |            |               |               | .925    |
| Grade 0-1                 | 30         | 15 (62.5%)    | 15 (68.2%)    |         |
| (65.2%)                   |            |               |               |         |
| Grade 2-4                 | 16         | 9 (37.5%)     | 7 (31.8%)     |         |
| (34.8%)                   |            |               |               |         |
| Radiation pneumonitis      |            |               |               | 1.000   |
| Grade 0                   | 41         | 21 (87.5%)    | 20 (90.9%)    |         |
| (89.1%)                   |            |               |               |         |
| Grade 1-4                 | 5          | 3 (12.5%)     | 2 (9.1%)      |         |
| (10.9%)                   |            |               |               |         |
| Liver enzyme elevation     |            |               |               | .659    |
| Grade 0                   | 41         | 22 (91.7%)    | 19 (86.4%)    |         |
| (89.1%)                   |            |               |               |         |
| Grade 1-4                 | 5          | 2 (8.3%)      | 3 (13.6%)     |         |
| (10.9%)                   |            |               |               |         |
| Creatinine elevation       |            |               |               | .234    |
| Grade 0                   | 39         | 22 (91.7%)    | 17 (77.38%)   |         |
| (84.8%)                   |            |               |               |         |
| Grade 1-4                 | 7          | 2 (8.3%)      | 5 (22.7%)     |         |
| (15.2%)                   |            |               |               |         |

The P value in bold indicated that the difference between PF group and DP group was significant.
Table 5

| Study | Treatment (a) | Pathology | Age | Stage | Grade | n | OS (months) | DFS (months) | 2-y OS (%) | PFS (months) | 2-y PFS (%) | Toxicity (%) | Leukocytopenia (%)
|-------|--------------|-----------|-----|-------|-------|---|-------------|-------------|------------|-------------|-----------|-------------|---------------|
| Hu, 2016 [26] | Retrospective SCC | 202 | 57 | IIIb-IIIc | IIb | 80 | 71.9 | 71.9 | 47.6 | 51.2 | 23 | 12 | 6.2 |
| Zhang, 2016 [18] | Retrospective SCC | 317 | 69 | II-IVa | IIb | 80 | 47.6 | 47.6 | 20 | 20 | 29 | 30 | 12 |
| | | | | | | | | | | | | | |
| Honing, 2014 [21] | Retrospective AC/SCC | 102 | 62 | IIb | IIb | 80 | 71.9 | 71.9 | 16.1 | 16.1 | 13.8 | 13.8 | 12 |
| Sun, 2016 [29] | Retrospective SCC | 179 | 42 | IIb | IIIb | 80 | 71.9 | 71.9 | 16.1 | 16.1 | 13.8 | 13.8 | 12 |

Abbreviations: AC = adriamycin; CCRT = chemoradiotherapy with a fluorouracil-based regimen; PC = paclitaxel and carboplatin; PP = paclitaxel and fluorouracil; TB = taxane-based regimen.

References

[1] Chen W, Zheng R, Baade PD, Zhang S, Zeng H, Bray F, Jemal A, Yu XQ, and He J (2016). Cancer statistics in China, 2015. CA Cancer J Clin 66, 115–132.
[2] Herlekovic A, Mance K, Al-Sarraf M, Leichman L, Bardwell J, Vázquez-Viciana V, Cooper J, Byrhardt R, Davis L, and Emami B (1992). Combined chemotherapy and radiotherapy compared with radiotherapy alone in patients with cancer of the esophagus. N Engl J Med 326, 1593–1598.
[3] Cooper JS, Guo MD, Herskovic A, Macdonald JS, Martenson JJ, Al-Sarraf M, Byrhardt R, Russell AH, Beitler JJ, and Spencer S, et al (1999). Chemoradiotherapy of locally advanced esophageal cancer: long-term follow-up of a prospective randomized trial (RT05-85). Radiation Therapy Oncology Group. JAMA 281, 1623–1627.
[4] Allen JW, Richardson JD, and Edwards MJ (1997). Squamous cell carcinoma of the esophagus: a review and update. Surg Oncol 6, 193–208.
[5] Wu X, Chen YW, Wu B, Andrews P, Su JI, and Corea P (2006). Incidence of esophageal and gastric carcinomas among American Asian/Pacific Islanders, whites, and blacks: subsite and histology differences. Cancer 106, 683–692.
[6] Udita SG, Orenstein MB, Torri A, Lassennet M, Fourrier A, and Stradmans M (2001). Randomized trial of neoadjuvant chemoradiation versus surgery alone in patients with locoregional esophageal carcinoma. J Clin Oncol 19, 305–313.
[7] Ruhani FR, Switzer SG, Gorria AM, Wu TY, Liao Z, Komaki R, Walsh GL, Vajtenjac AA, Rice DC, and Bresalier RS, et al (2006). Histologic subtypes as determinants of outcome in esophageal carcinoma patients with pathologic complete response after neoadjuvant chemoradiotherapy. Cancer 106, 552–558.
[8] Liebnam J, Cook JA, Fisher J, Teague D, and Mitchell JB (1994). In vitro studies of Taxol as a radiation sensitizer in human tumor cells. J Natl Cancer Inst 86, 441–446.
[9] Hennouq C, Giocanti N, and Favaudon V (1996). Interaction of ionizing radiation with paclitaxel (Taxol) and docetaxel (Taxotere) in HeLa and SQ20B cells. Cancer Res 56, 1842–1850.
[10] Mason KA, Hunter NR, Mills M, Abbruzzese JL, and Mills I (1997). Docetaxel enhances tumor radiosensitivity in vivo. J Natl Cancer Inst 89, 2431–2438.
[11] Huang C, Zhu Y, Li Q, Zhang W, Liu H, Zhang W, Hu Y, Yuan Y, and Liu M (2019). Feasibility of concurrent chemoradiotherapy with a single agent or double agents vs radiotherapy alone for elderly patients with esophageal squamous cell carcinoma: experience of two centers. Cancer Med 8, 28–39.
[12] Shapiro J, van Lanschot J, Hulshof M, van Hagen P, van Berge HM, Wijnhoven B, van Laarhoven AH, Beitler JJ, and Spencer S, et al (1999). Chemoradiotherapy of locally advanced esophageal cancer: a randomized clinical study. JAMA 281, 625–632.
[13] Jiang GL, et al (2016). A phase II study of concurrent chemoradiotherapy with paclitaxel and cisplatin in neoadjuvant chemoradiotherapy for locoregional esophagogastric adenocarcinoma (CROSS): long-term results of a randomized controlled trial. Lancet Oncol 17, 1090–1098.
[14] Ruhallah T, Widmer L, Schuller JC, Roth A, Hess V, Mingrone W, von Moos R, Bornier M, Pesenti BC, and Balhmayoja S, et al (2009). Multicenter phase II trial of neoadjuvant induction chemotherapy followed by chemoradiation with cisplatin and 5-fluorouracil for locally advanced esophageal cancer (CROSS)-long-term results of a randomized controlled trial. Lancet Oncol 10, 1952–1958.
[15] Huang TC, Hsu CH, Lin CC, and Tu YK (2015). Systematic review and network meta-analysis: neoadjuvant chemoradiotherapy for locoregional esophageal cancer. JPN J Clin Oncol 45, 1023–1028.
[16] Rizvi FH, Syed AA, Khutam S, Rizvi SS, Kamiss SA, and Khan MQ (2014). Complete pathological response after neoadjuvant treatment in locally advanced esophageal cancer predicts long term survival: a retrospective cohort study. Int J Surg Oncol 21, 621–625.
[17] Tang HB, Mu HF, An SM, Badakhshi H, Deng YF, Zhang JH, Chen Y, Zhang Z, Guo XM, and Jiang GL, et al (2016). A phase II study of concurrent chemoradiotherapy with paclitaxel and cisplatin for inoperable esophageal squamous cell carcinoma. Am J Clin Oncol 39, 350–354.
[18] Zhao T, Chen H, and Zhang T (2012). Docetaxel and cisplatin concurrent with radiotherapy versus concurrent cisplatin and 5-fluorouracil for locally advanced esophageal cancer: a propensity score-matched analysis. Onco Targets Ther 7, 4468–4474.
[19] Wang T, Yu J, Liu M, Chen Y, Zhu C, Lu L, Wang M, Min L, Liu X, and Zhang Z, et al (2019). The benefit of taxane-based therapies over fluorouracil plus platinum (FP) in the treatment of esophageal cancer: a meta-analysis of clinical studies. Drug Des Devel Ther 13, 559–573.

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 PF 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.
[20] Xi M, Zhang P, Zhang L, Yang YD, Liu SL, Li Y, Fu JH, and Liu MZ (2017). Comparing docetaxel plus cisplatin versus fluorouracil plus cisplatin in esophageal squamous cell carcinoma treated with neoadjuvant chemoradiotherapy. *Jpn J Clin Oncol* 47, 683–689.

[21] Honing J, Smit JK, Muijs CT, Burgerhof JG, de Groot JW, Paardekooper G, Muller K, Woutersen D, Logeurt MJ, and Fiers WE, et al (2014). A comparison of carboplatin and paclitaxel with cisplatinum and 5-fluorouracil in definitive chemoradiation in esophageal cancer patients. *Ann Oncol* 25, 638–643.

[22] Wang T, Yu J, Liu M, Chen Y, Zhu C, Lu L, Wang M, Min L, Liu X, and Zhang X, et al (2019). The benefit of taxane-based therapies over fluoropyrimidine plus platinum (FP) in the treatment of esophageal cancer: a meta-analysis of clinical studies. *Drug Des Devel Ther* 13, 539–553.

[23] Hailey KR, Hart KD, Nahavیدelb N, Bench KG, Vaccaro GM, Thomas CJ, Schipper PH, Hunter JG, and Dolan JP (2017). Neoadjuvant chemoradiotherapy with concurrent cisplatin/5-fluorouracil is associated with increased pathologic complete response and improved survival compared to carboplatin/paclitaxel in patients with locally advanced esophageal cancer. *Oncology* 30, 1–7.

[24] Zhu Y, Zhang W, Li Q, Li Q, Qiu B, Liu H, Liu M, and Hu Y (2017). A phase II randomized controlled trial: definitive concurrent chemoradiotherapy with docetaxel plus cisplatin versus 5-fluorouracil plus cisplatin in patients with esophageal squamous cell carcinoma. *J Cancer* 8, 3657–3666.

[25] Adelstein DJ, Rice TW, Rybicki LA, Larto MA, Ciezki J, Saxton J, DeCamp M, Vango JJ, Dumot JA, and Zuccaro G (2000). Does paclitaxel improve the chemoradiotherapy of locoregionally advanced esophageal cancer? A nonrandomized comparison with fluorouracil-based therapy. *J Clin Oncol* 18, 2032–2039.

[26] Hu G, Wang Z, Wang Y, Zhang Q, Tang N, Guo J, Liu L, and Han X (2016). Comparison of cisplatinum/paclitaxel with cisplatinum/5-fluorouracil as first-line therapy for nonsurgical locally advanced esophageal squamous cell carcinoma patients. *Drug Des Devel Ther* 10, 2129–2136.

[27] Xu C, Xi M, Moreno A, Shiraishi Y, Hobbs BP, Huang M, Komaki R, and Lin SH (2017). Definitive chemoradiation therapy for esophageal cancer in the elderly: clinical outcomes for patients exceeding 80 years old. *Int J Radiat Oncol Biol Phys* 98, 811–819.

[28] Hurria A, Mobile S, Gajra A, Klepin H, Mus H, Chapman A, Feng T, Smith D, Sun CL, and De Gla N, et al (2016). Validation of a prediction tool for chemotherapy toxicity in older adults with cancer. *J Clin Oncol* 34, 2366–2371.

[29] Camps C, Masutti B, Jimenez A, Maestro I, Gomez RG, Iba D, Gonzalez JL, Almenar D, Blasco A, and Rosell R, et al (2006). Randomized phase III study of 3-weekly versus weekly docetaxel in pretreated advanced non-small-cell lung cancer: a Spanish Lung Cancer Group trial. *Ann Oncol* 17, 467–472.

[30] Graziano F, Catalano V, Baldelli AM, Giordani P, Testa E, Lai V, Catalano G, Battelli N, and Cassinu S (2008). A phase II study of weekly docetaxel as salvage chemotherapy for advanced gastric cancer. *Ann Oncol* 11, 1263–1266.

[31] Piccinneti P, Durante E, Trolese A, Mercanti A, and Bonetti A (2012). Weekly Taxotere and cisplatin with continuous-infusion 5-fluorouracil for the treatment of advanced gastric and esophageal cancer: a prospective, observational, single-institution experience. *Gastric Cancer* 15, 106–110.