

Scientific Article

Feasibility of definitive chemoradiation therapy with nedaplatin and 5-fluorouracil in elderly patients with esophageal squamous cell carcinoma: A retrospective study

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Abstract

Purpose: This study was designed to retrospectively analyze the safety and efficacy of chemoradiation therapy with nedaplatin and 5-fluorouracil in elderly patients with esophageal squamous cell carcinoma.

Methods and materials: Eligible patients were aged 76 years or older, had a histopathologic diagnosis of esophageal squamous cell carcinoma, and were treated at the Kitasato University Hospital between January 2010 and March 2016. Chemotherapy consisted of nedaplatin in an intravenous dose of 90 mg/m² on day 1 and 5-fluorouracil in an intravenous dose of 800 mg/m² on days 1 to 5, repeated every 4 weeks for 2 cycles. Radiation therapy consisted of 50.4 Gy in 28 fractions for thoracic tumors and 61.2 Gy for cervical tumors.

Conflicts of interest: No conflicts of interest exist for any of the authors.

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Results: Twenty-five patients were studied. Patient characteristics were as follows: median age 79 years (range, 76-85 years), clinical stage I/II/III/IV (7/8/8/2, respectively), and surgically resectable/unresectable (17/8, respectively). The completion rates of radiation therapy and chemoradiation therapy were 100% and 84%, respectively. Grade ≥ 3 acute toxicities included neutropenia (76%), leukopenia (72%), thrombocytopenia (32%), anemia (28%), anorexia (32%), oral mucositis (20%), febrile neutropenia (12%), and esophagitis (8%). Grade ≥ 3 late toxicities included esophageal stenosis (12%) and pleural effusion (4%). The complete response rate was 64%. In the median follow-up period of 18.9 months, the 1-year overall survival rate was 68%.

Conclusions: Definitive chemoradiation therapy with nedaplatin and 5-fluorouracil may be a feasible treatment option for elderly patients with esophageal squamous cell carcinoma.

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Introduction

Esophageal cancer is a life-threatening disease and the number of patients in Japan has been increasing due to the rapid growth of the elderly population. Most cases of esophageal cancer develop in patients in their 60s to 70s and are advanced at the time of diagnosis. Among the estimated 21,965 new cases of esophageal cancer diagnosed in 2012 in Japan, 7497 (34.1%) were in elderly patients who were ≥ 75 years of age.¹

In Japan, the standard treatment for resectable advanced esophageal cancer is neoadjuvant chemotherapy followed by esophagectomy with 3-field lymph-node dissection. Chemoradiation therapy is also a curative treatment option for localized esophageal cancer, and 5-fluorouracil and cisplatin have been designated as key drugs.^{2,3} However, clinical trials supporting these standard treatments did not include elderly patients because patients who were aged ≥ 76 years were not eligible. In addition, outcomes after esophagectomy in elderly patients remain controversial.⁴⁻⁶ Moreover, a retrospective study reported that elderly patients with esophageal cancer had substantial morbidity from chemoradiation therapy, and long-term survival was low.⁷ Thus, the standard regimen of chemoradiation therapy for elderly patients with esophageal cancer remains to be established, and new treatment options with lower toxicity and higher efficacy must be developed.

Nedaplatin is a novel second-generation platinum compound that has shown promising antitumor activity with less nephrotoxicity, gastrointestinal toxicity, and neurotoxicity than cisplatin in some preclinical and clinical studies.⁸⁻¹² The combination of nedaplatin and 5-fluorouracil showed promising results in a phase 2 study of metastatic esophageal cancer.¹³ Moreover, a phase 1/2 study of definitive chemoradiation therapy with nedaplatin and 5-fluorouracil in patients with T4 disease showed that this regimen is active with acceptable toxicity.¹⁴ On the basis of these findings, nedaplatin seemed to be a new, less toxic anticancer drug in Japan.

We used nedaplatin and 5-fluorouracil combined with radiation therapy to treat esophageal squamous cell

carcinoma in elderly patients who were aged ≥ 76 years. To our knowledge, this is the first report to describe the results of a retrospective study evaluating the safety and efficacy of chemoradiation therapy with nedaplatin and 5-fluorouracil in elderly patients with esophageal squamous cell carcinoma.

Methods and materials

Patients

Between January 1, 2010 and March 31, 2016, a total of 25 patients with esophageal squamous cell carcinoma who were aged ≥ 76 years received definitive chemoradiation therapy with nedaplatin and 5-fluorouracil at our hospital. No patient with esophageal adenocarcinoma received this treatment. In patients with surgically resectable disease, we initially considered surgery-based treatments. However, if surgery was not performed because of the patient's refusal, poor performance status, or poor general condition, we administered chemoradiation therapy.

Endpoints

To assess safety, we retrospectively analyzed compliance with chemoradiation therapy, acute toxicity, and late toxicity. To assess effectiveness, we calculated complete response rates and overall and progression-free survival rates. To assess quality of life, we analyzed dysphagia scores. The dysphagia score was defined as 0 (able to eat a normal diet), 1 (unable to swallow certain solids), 2 (able to swallow semi-solid foods), 3 (able to swallow liquids only), and 4 (unable to swallow liquids).¹⁵ This retrospective study was approved by the ethics committee of our hospital.

Radiation therapy

Three-dimensional treatment planning was performed with the use of a computed tomography (CT) simulator.

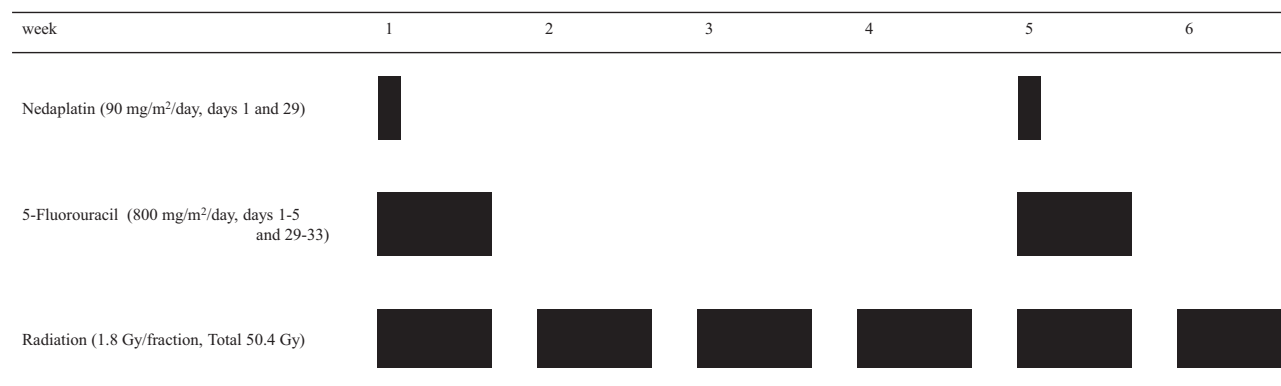


Figure 1 Treatment schema. Treatment consisted of 2 courses of chemotherapy with 5-fluorouracil (800 mg/m² on days 1-5) and nedaplatin (90 mg/m² on day 1) every 4 weeks. The total radiation dose was 50.4 Gy (28 fractions of 1.8 Gy per day, 5 times per week, starting on day 1) for thoracic tumors and 61.2 Gy (34 fractions of 1.8 Gy per day) for cervical tumors.

Four-dimensional CT simulation was also used for planning whenever possible. The total radiation dose was 50.4 Gy (28 fractions of 1.8 Gy per day) 5 times per week, starting on day 1 for thoracic tumors, and 61.2 Gy (34 fractions of 1.8 Gy per day) for cervical tumors (Fig 1).¹⁶ Radiation therapy was delivered with 6 or 10 megavoltage x-rays, using multiple fields, with at least 4 ports for middle and lower thoracic tumors. The primary tumor, metastatic lymph nodes, and subclinical regional lymph nodes were irradiated with 39.6 Gy or 41.4 Gy. A booster dose of 10.8 or 9.0 Gy then was delivered to the primary tumor and metastatic lymph nodes using oblique fields to spare the spinal cord.

The clinical target volume included the primary tumor with a 2 cm craniocaudal margin, metastatic lymph nodes, and regional lymph nodes. The planning target volume was defined as the clinical target volume plus a 0.5 to 1.0 cm margin in lateral and anteroposterior directions and a 1.0 to 2.0 cm margin in superoinferior direction to account for respiratory organ motion and daily setup error. In principle, regional lymph nodes were defined as the supraclavicular, cervical paraesophageal, and mediastinal lymph nodes (101, 104, 105, 106rec, 106pre, 106tb, and 107) to the carina for upper thoracic tumors, the mediastinal and perigastric lymph nodes (1, 2, 3, 7, 105, 106rec, 106pre, 106tb, 107, 108, 109, and 110) for midthoracic tumors, and the mediastinal, perigastric, and celiac lymph nodes (1, 2, 3, 7, 9, 105, 106rec, 106pre, 106tb, 107, 108, 109, and 110) for lower thoracic tumors.¹⁷ However, irradiation of regional lymph nodes was occasionally omitted because of the patient's general condition.

Chemotherapy

The treatment schema is outlined in Figure 1. Treatment consisted of 2 courses of chemotherapy with 5-fluorouracil (800 mg/m² on days 1-5) and nedaplatin (90 mg/m² on day 1) every 4 weeks.

Assessments

Tumor response was evaluated by CT and esophagogastroduodenoscopy in accordance with the Response Evaluation Criteria in Solid Tumors, version 1.1.¹⁸ CT and esophagogastroduodenoscopy were performed every 3 to 4 months after starting treatment during the first 3 years and every 6 months thereafter.

Acute toxicities were assessed weekly during chemoradiation therapy and up to 90 days after completion of radiation and chemotherapy. Late toxicity was defined as an adverse event that occurred beyond this time. Toxicities were evaluated in accordance with the Common Terminology Criteria for Adverse Events, version 4.0.¹⁹ Dysphagia score was evaluated on the basis of medical records, and the pretreatment score was compared with the best score after treatment.

Statistical analysis

Survival periods were calculated from the first day of treatment and were estimated using the Kaplan-Meier method. A Fisher's exact test was used to compare the complete response rates according to several patient factors. The analysis was performed with a statistical software package (IBM SPSS STATISTICS, version 17.0; IBM Japan, Tokyo, Japan).

Results

Patients

At our hospital, we have held an institutional cancer board to review all cases of esophageal cancer, excluding those for which endoscopic therapy is clearly indicated. Among the 591 patients who were reviewed between January 2010

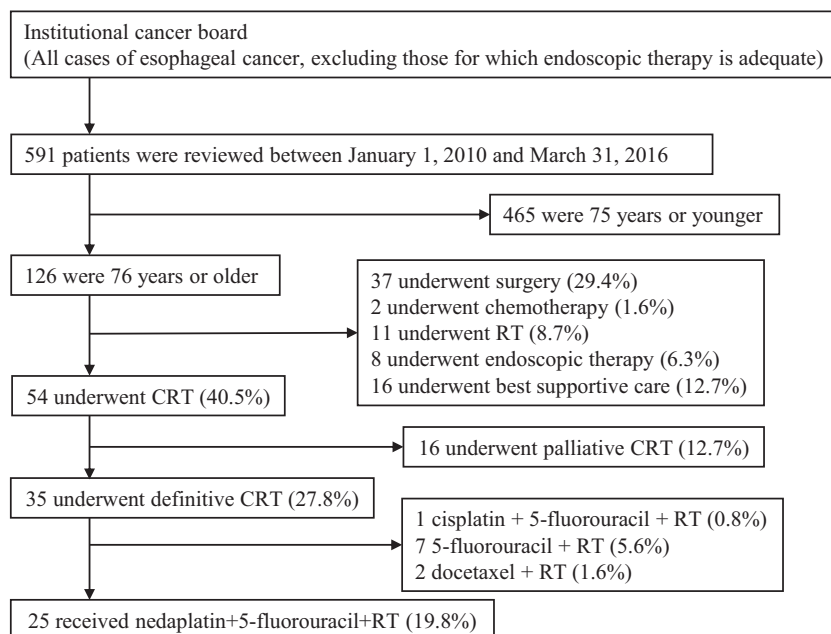


Figure 2 Patient flow chart. An institutional cancer board was held to review all cases of esophageal cancer, excluding those for which endoscopic therapy was clearly indicated. Of the 591 patients reviewed between January 2010 and March 2016, 126 (21.3%) were aged ≥ 76 years. Of the 126 elderly patients, 37 (29.4%) underwent surgery and 35 (27.8%) received definitive chemoradiation therapy. Twenty-five (19.8%) of the 35 elderly patients who received definitive chemoradiation therapy were included in this study. CRT, chemoradiation therapy; RT, radiation therapy.

and March 2016, 126 (21.3%) were aged ≥ 76 years. Among these 126 elderly patients, 37 (29.4%) underwent surgery, and 35 (27.8%) received definitive chemoradiation therapy. Of the 35 patients who received definitive chemoradiation therapy, 25 (19.8%) were included in this study (Fig 2).

Patient characteristics were as follows: 23 men and 2 women; median age 79 years (range, 76-85 years); primary tumors located in the cervical esophagus (3 patients), the upper thoracic esophagus (4 patients), the middle thoracic esophagus (15 patients), and the lower thoracic esophagus (3 patients). The clinical disease stage (International Union Against Cancer, 7th Edition) was I in 7 patients, II in 8 patients, III in 8 patients, and IV in 2 patients. Patients with stage IV disease had supraclavicular lymph node metastasis and no other organ metastasis. Seventeen patients had surgically resectable disease, and 8 had unresectable disease. Of the 17 patients with resectable disease, 6 refused surgery and 11 could not undergo surgery because of poor performance status, poor general condition, or both (Table 1).

Compliance

All 25 patients (100%) completed the scheduled radiation therapy, and 21 (84%) completed the scheduled chemoradiation therapy (all scheduled radiation therapy and 2 courses of chemotherapy). The median duration of

chemoradiation therapy was 43 days (range, 37-59 days). Of the 4 patients who could not receive the second cycle of chemotherapy, 2 had grade ≥ 3 hematologic toxicity. Two other patients refused the second cycle of chemotherapy

Table 1 Patient characteristics

Characteristic	All patients (n = 25)	Excluding T1bN0M0 (n = 21)
Age (y), median (range)	79 (76-85)	80 (76-85)
Sex, Male/female	23/2	20/1
Performance status, 0/1/2	11/14/0	7/14/0
Charlson comorbidity index, 2/3/4/5	11/10/2/2	10/8/1/2
Tumor location, Ce/ Ut/Mt/Lt	3/4/15/3	3/4/12/2
T factor, 1b/2/3/4 ^a	5/4/10/6	1/4/10/6
Clinical stage, I/II/III/IV ^a	7/8/8/2	3/8/8/2
Resectable/ unresectable	17/8	13/8
Creatinine clearance, >60/50-60/<50	13/6/6	9/6/6

Ce, cervical esophagus; Ut, upper thoracic esophagus; Mt, middle thoracic esophagus; Lt, lower thoracic esophagus.

^a International Union Against Cancer Staging System, 7th Edition.

Table 2 Acute toxicity

Toxicity	Grade (CTCAE version 4.0, n = 25)				
	1	2	3	4	≥3 (%)
Leukopenia	1	5	12	6	72
Neutropenia	2	3	11	8	76
Anemia	9	8	7	0	28
Thrombocytopenia	7	9	3	5	32
AST and/or ALT	14	1	0	0	0
Creatinine	6	6	1	0	4
Mucositis oral	4	5	5	0	20
Anorexia	7	6	8	0	32
Nausea	10	7	1	0	4
Vomiting	5	4	0	0	0
Fatigue	17	7	0	0	0
Diarrhea	5	0	1	0	4
Febrile neutropenia	0	0	3	0	12
Esophagitis	2	7	2	0	8
Dermatitis	11	8	0	0	0
Hyponatremia	0	0	0	1	4
Pneumonitis	0	0	1	0	4

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events.

because of grade 2 and 3 nonhematologic toxicity. Fifteen patients received chemotherapy in a decreased dose because of renal dysfunction or hematologic toxicity. Irradiation of regional lymph nodes was omitted in 9 patients. In the 10 patients who had residual tumors after chemoradiation therapy, we continued the same regimen of chemotherapy to achieve a complete response (CR).

Oncologists conducted additional chemotherapy in accordance with the patients' performance status and volume of residual disease. We additionally administered 1 course of chemotherapy to 4 patients, 2 courses of chemotherapy to 5 patients, and 4 courses of chemotherapy to 1 patient. All patients received best supportive care and routine surveillance, and no patient received an additional other regimen of chemotherapy.

Toxicity

There were no treatment-related deaths. Common adverse events that occurred during chemoradiation therapy are shown in [Table 2](#). Grade ≥3 acute toxicities included neutropenia (76%), leukopenia (72%), thrombocytopenia (32%), anemia (28%), anorexia (32%), mucositis oral (20%), febrile neutropenia (12%), esophagitis (8%), nausea (4%), diarrhea (4%), pneumonitis (4%), creatinine increased (4%), and hyponatremia (4%).

Late adverse events are summarized in [Table 3](#). No patient had grade 4 events. Grade 3 events included esophageal stenosis (12%), pleural effusion (4%), esophagobronchial fistula (4%), and dysphagia (4%).

Table 3 Late toxicity

Toxicity	Grade (CTCAE version 4.0, n = 25)				
	1	2	3	4	≥3 (%)
Pericardial effusion	–	4	1	0	4
Esophagobronchial fistula	0	0	1	0	4
Hoarseness	1	0	0	0	0
Pneumonitis	5	0	0	0	0
Dysphagia	0	0	1	0	4
Esophageal stricture	1	2	3	0	12

CTCAE, Common Terminology Criteria for Adverse Events.

Efficacy

As of September 30, 2017, the median follow-up was 18.9 months (range, 3.2–65.3 months). A CR was obtained in 16 patients, resulting in a CR rate of 64%. After excluding the 4 patients with T1bNOM0 disease, 12 patients achieved CR; the CR rate was 57.1%. Among the 16 patients with CR, 7 received only chemoradiotherapy. Among the 10 patients who received additional chemotherapy, 9 achieved CR.

The 1- and 2-year overall survival rates were 68% and 54.5%, respectively, and the 1- and 2-year progression-free survival rates were 64% and 50%, respectively. After excluding the patients with T1bNOM0 disease, the 1- and 2-year overall survival rates were 61.9% and 47.4%, respectively, and the 1- and 2-year progression-free survival rates were 57.1% and 42.1%, respectively ([Figs 3A, B](#)).

Among the 16 patients with CR, 12 were alive without failure, 1 died of locoregional recurrence, and 3 died of other causes (gastric adenocarcinoma, alcoholic cirrhosis, and hepatitis C virus cirrhosis). One of the 9 patients without a CR died of cerebral infarction, and the other 8 died of esophageal cancer ([Fig 4](#)).

The pattern of failure is shown in [Table 4](#). The 4 patients who died of other causes had a Charlson comorbidity index score of ≥3.

Among the 16 patients who had a CR, 15 survived for at least 1 year, and 11 survived for at least 2 years. The relation of CR rates to performance status, Charlson comorbidity index, T factor, clinical stage, creatinine clearance, and decreased lymphocyte count was investigated ([Table 5](#)).²⁰ A performance status score of 0 was significantly associated with a CR ($P = .0033$).

The dysphagia score was 0 in 9 patients, 1 in 5 patients, 2 in 3 patients, 3 in 7 patients, and 4 in 1 patient before treatment and 0 in 12 patients, 1 in 3 patients, 2 in 6 patients, 3 in 1 patient, and 4 in 3 patients after treatment. The dysphagia score improved in 10 patients (40%), remained unchanged in 10 patients (40%), and worsened in 5 patients (20%).

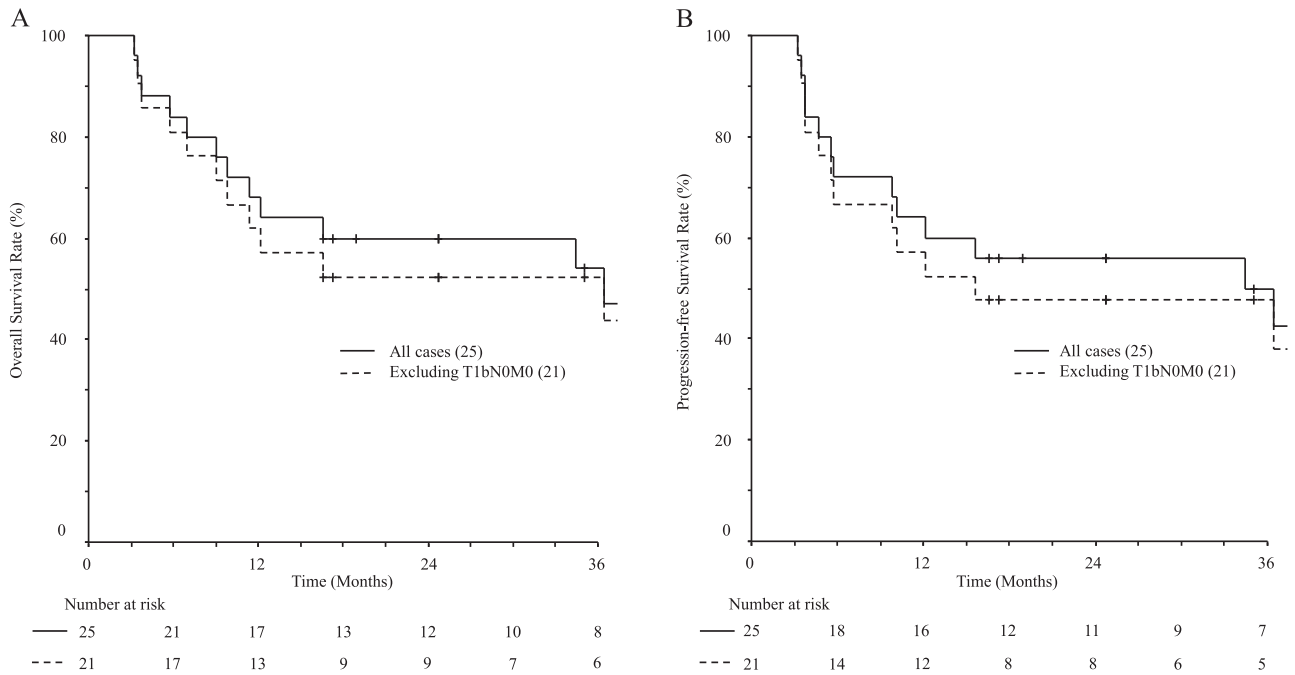


Figure 3 (A) Overall survival. As of September 30, 2017, the median follow-up was 18.9 months. The 1- and 2-year overall survival rates were 68% and 54.5%, respectively. After excluding patients with T1bN0M0 disease, the 1- and 2-year overall survival rates were 61.9% and 47.4%, respectively. (B) Progression-free survival. As of September 30, 2017, the median follow-up was 18.9 months. The 1- and 2-year progression-free survival rates were 64% and 50%, respectively. After excluding patients with T1bN0M0 disease, the 1- and 2-year progression-free survival rates were 57.1% and 42.1%, respectively.

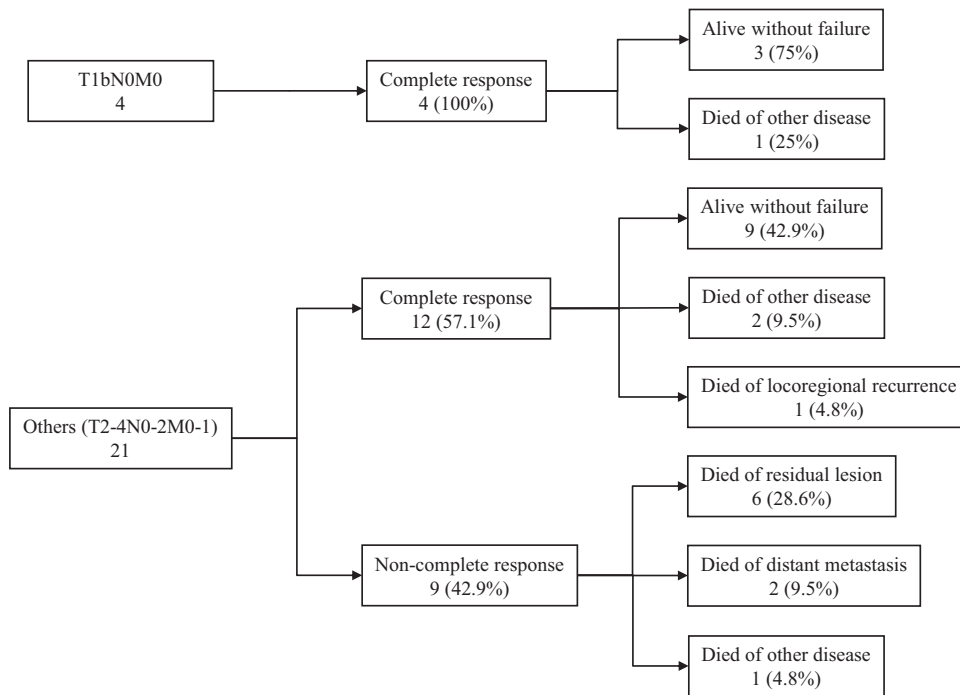


Figure 4 Clinical course. A complete response was achieved in all 4 patients with T1bN0M0 disease, resulting in a complete response (CR) rate of 100%. After excluding patients with T1bN0M0 disease, a CR was achieved in 12 patients (57.1%). Of the 16 patients with a CR, 12 were alive without failure, 1 died of locoregional recurrence, and 3 died of other causes. Of the 9 patients without a CR, 1 died of other causes, and the other 8 died of esophageal cancer.

Table 4 Pattern of failure

	n = 25	%
Alive/no failure	12	48
Any failure	13	52
Dead by other cause	4	16
Persistent failure	8	32
Only local failure	6	24
With distant failure	2	8
Recurrence after complete response	1	4
Only local recurrence	1	4
Only regional recurrence	0	0
Any distant recurrence	0	0
Total local/regional persistence/failure	10	40

Discussion

Very few studies have reported the outcomes of non-surgical treatment for esophageal cancer in elderly patients. Takeuchi et al retrospectively studied patients with clinical stage II or III esophageal cancer who received chemoradiation therapy with 5-fluorouracil and cisplatin and compared outcomes between 33 patients aged ≥ 71 years and 145 patients aged ≤ 70 years.²¹ The CR rates were similar in the groups (63.6% vs 63.4%). In the elderly patients, however, the median survival time was shorter (14.7 months vs 35.1 months; $P = .01$). The overall survival rate in the elderly patients was 60% at 1 year and 45% at 2 years.

The proportion of patients who did not receive chemotherapy as subsequent treatment was higher in the elderly patients (57.6% vs 17.3%; $P = .01$). Moreover, a high proportion of elderly patients had grade ≥ 3 hematologic toxicity. The rate of death from other causes did not differ between the groups. The dose intensity of chemotherapy should be improved to enhance efficacy, but this has been reported to be difficult to achieve because of toxicity.

Kawashima et al reported the outcomes in patients with clinical stage I or IIa esophageal cancer who were aged ≥ 80

years and received radiation therapy alone (66 Gy). The 2-year survival rate of patients with clinical T2 or T3 cancer was approximately 25%.²² These results suggest that regimens with adequate antitumor activity and low toxicity are likely to be effective for the management of esophageal cancer in elderly patients.

In the present study, we retrospectively evaluated the effectiveness and safety of definitive chemoradiation therapy with nedaplatin and 5-fluorouracil in elderly patients with esophageal cancer who were aged ≥ 76 years. The CR rate was 64% (57.1% excluding patients with T1bN0M0 disease), and the overall survival rates at 1 and 2 years were 68% and 54.5% (61.9% and 47.4% excluding patients with T1bN0M0 disease), respectively.

Anderson et al administered chemoradiation therapy with 5-fluorouracil and mitomycin-C (50.4 Gy) to 25 patients with stage II or III esophageal cancer (squamous cell cancer:adenocarcinoma, approximately 1:1) who were aged 66 to 88 years (median age, 77 years). In that retrospective study, the 1- and 2-year overall survival rates were 80% and 45%, respectively.²³ Ohba et al reported the results of a phase 2 study in which docetaxel-based chemoradiation therapy (60 Gy) was administered to patients with clinical stage II or III esophageal cancer who were aged 73 to 81 years (median age, 77 years). Although the study was prematurely terminated because of slow accrual, data from 16 enrolled patients were analyzed. The CR rate was 43.8%, and the 2-year overall survival rate was 62.5%.²⁴ The results of these 2 studies could not be directly compared because of different patient characteristics. However, definitive chemoradiation therapy with nedaplatin and 5-fluorouracil provided good local control in elderly patients with esophageal cancer who were aged ≥ 76 years, and the short-term outcomes were evaluated to be relatively good.

In our study, only 40% of patients received chemotherapy as subsequent treatment after definitive chemoradiation therapy. Moreover, salvage surgery or second-line chemotherapy was not administered to patients who had local recurrence or residual tumor. Although the rate of chemotherapy as subsequent treatment was low, the CR rate was good (64%). Only 1 patient had local recurrence after CR. Despite the fact that no patient received salvage surgery or second-line chemotherapy, the 1- and 2-year overall survival rates were 68% and 54.5%, respectively, and the 1- and 2-year progression-free survival rates were 64% and 50%, respectively. Therefore, definitive chemoradiation therapy with nedaplatin and 5-fluorouracil is expected to provide relatively good local control and short-term outcomes in elderly patients with esophageal cancer who are aged ≥ 76 years, even if the rates of subsequent chemotherapy, salvage surgery, and second-line chemotherapy are low.

In our study, there were no treatment-related deaths. The completion rate of radiation therapy was 100%, and the completion rate of chemoradiation therapy was 84%. The median duration of chemoradiation therapy was 43 days

Table 5 The relations of complete response rates to patients' factors

	Complete response rates (%)	<i>P</i> -value ^a
Performance status, 0/1	90.9/42.9	.033
Charlson comorbidity index, 2/3-5	63.6/64.3	1.000
T factor, 1b-2/3-4 ^b	88.9/50	.088
Clinical stage, I-II/III-IV ^b	80/40	.087
Creatinine clearance, ≤ 60 / >60	58.3/69.2	.688
Lymphocytopenia, Grade 1-3/4 ^c	58.3/69.2	.688

^a Fisher's exact test.

^b International Union Against Cancer Staging System, 7th Edition.

^c Common Terminology Criteria for Adverse Events, version 4.0.

(range, 37-59 days). Treatment was not markedly delayed or discontinued. Ishikura et al conducted phase 1 and 2 studies in which 26 nonelderly patients with T4 esophageal cancer received a combination of chemotherapy and 60 Gy radiation therapy, similar to the regimen administered in our study. They reported that the CR rate was 12%. Grade ≥ 3 acute toxicities were leukopenia in 35% of patients, neutropenia in 19%, thrombocytopenia in 15%, and esophagitis in 15%. Grade ≥ 3 late toxicities comprised pericardial effusion in 1 patient, pleural effusion in 1 patient, and esophageal stenosis in 2 patients.¹⁴ Our study included 6 patients with T4 disease, and 3 of these patients (50%) achieved CR. Although the incidence of hematologic toxicity was higher in our study than in the study by Ishikura et al, the treatment completion rate was good and delays in treatment were within the permissible range. The incidences of nonhematologic toxicity and late toxicity in the study by Ishikura et al were similar to those in our study.

Kato et al conducted a phase 2 trial to evaluate the efficacy and toxicity of cisplatin, 5-fluorouracil, and radiation in patients with stage II or III esophageal cancer. They reported that grade ≥ 3 acute toxicities were leukopenia (82.3%), neutropenia (78.4%), anemia (23.5%), thrombocytopenia (19.6%), anorexia (45%), and esophagitis (35%). The patients in that study were aged 42 to 70 years.³ Although they were younger than the patients in our study, the acute toxicities were similar to those in our study.

Ohba et al reported the results of a phase 2 study in which docetaxel-based chemoradiation therapy was administered to patients with stage II or III esophageal cancer who were aged 73 to 81 years. They reported grade ≥ 3 acute toxicities of leukopenia (6.3%), neutropenia (6.3%), anemia (0%), thrombocytopenia (6.3%), anorexia (12.5%), and esophagitis (31.3%). Grade ≥ 3 late toxicities were esophagitis (12.5%) and pleural effusion (12.5%).²⁴ The incidence of hematologic toxicity was higher and that of late toxicity was lower in our study.

Suntharalingam et al conducted a phase 3 trial evaluating the effect of adding cetuximab to paclitaxel, cisplatin, and radiation therapy in patients with esophageal cancer. They reported incidences of grade 3, 4, or 5 treatment-related adverse events of 46%, 23%, and 4%, respectively, in the experimental arm and 50%, 17%, and 1%, respectively, in the control arm.²⁵ Although the incidences of grade 3 and 4 events were higher in our study, there were no treatment-related deaths. On the basis of these findings, definitive chemoradiation therapy with nedaplatin and 5-fluorouracil can be evaluated as feasible in elderly patients with esophageal cancer who are aged ≥ 76 years.

Finally, we would like to stress that clinicians should consider all treatment modalities, even if patients are elderly. Vlacich et al provided a review of the National Cancer Database and reported that some elderly patients should be considered as candidates for more aggressive therapy, potentially including surgery, because trimodality therapy was associated with the largest survival benefit in their analysis.

They also reported that any therapy, including palliative care, was associated with improved survival.

The limitations of our study include a lack of assessment by positron emission tomography/CT and the inclusion of patients with stage I disease. Of the 16 patients with CR, 1 had local recurrence. The CR rate could be overestimated. In the future, positron emission tomography/CT should be used for pretreatment and posttreatment assessments. Moreover, our study was a retrospective study with a small study group. However, our regimen was evaluated to be effective and safe in elderly patients with esophageal cancer who are aged ≥ 76 years. Further multicenter, collaborative, prospective studies evaluating the quality of life using a detailed geriatric scale may be needed to verify the effectiveness and safety of our regimen.

Conclusions

Definitive chemoradiation therapy with nedaplatin and 5-fluorouracil is feasible and effective within a short period in elderly patients with esophageal squamous cell carcinoma. This therapy may be a treatment option for elderly patients with esophageal cancer, particularly for patients who are medically unfit for surgery or hydration followed by cisplatin therapy.

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