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Intensity modulated radiotherapy might be effective for locally advanced esophageal carcinosarcoma

A single center's experience and review of literature

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Abstract

Esophageal carcinosarcoma is a rare type of esophageal cancer; however, few studies have investigated the effects of radiotherapy in locally advanced patients. This study aimed to report experience of the safety and efficacy of intensity-modulated radiotherapy for locally advanced esophageal carcinosarcoma and review the literature. By searching the institutional database between January 2010 and December 2020, along with the literature review, 25 patients were eligible for the study. The clinical and radiologic information of all patients with esophageal carcinosarcoma who underwent radiotherapy were collected. Survival outcomes were calculated using Kaplan–Meier plots. In our series, 5 patients were in the curative/neoadjuvant radiotherapy group and 10 patients were in the adjuvant group. Most tumors were protruding (n = 10, 66.7%). All patients underwent intensity-modulated radiotherapy. In the curative/neoadjuvant radiotherapy group, 2 patients underwent concurrent chemoradiotherapy before surgery, and the other three received radiotherapy alone as the initial treatment. The median follow-up time was 43.1 months. All patients showed a partial response at the efficacy evaluation. The median time of overall survival and progression-free survival were 40.2 months (95% confidence interval [CI], 13.1–67.3 months) and 19.0 months (95% CI, 13.9 months—24.1 months) for the entire cohort, but were not reached for curative/neoadjuvant radiotherapy group. Overall survival (hazard ratio [HR] 0.81, 95% CI, 0.15–4.43; P = .805) and progression-free survival (HR 1.68, 95% CI, 0.35–8.19; P = .514) did not differ significantly between the 2 groups. When considering the literature review data in the final analysis, overall survival (HR 0.84, 95% CI, 0.25–2.81; P = .779) and progression-free survival (HR, 0.68; 95% CI, 0.26–1.76; P = .425) were also not different between the 2 groups. Treatment based on intensity-modulated radiotherapy with neoadjuvant or curative intent may be an option for patients with unresectable esophageal carcinosarcoma. Further research with a larger sample size is needed to validate the reliability.

Abbreviations: CRT = chemoradiotherapy, CI = confidence interval, EC = esophageal cancer, ECS = esophageal carcinosarcoma, HR = hazard ratio, IMRT = intensity-modulated technique radiotherapy, OS = overall survival, PFS = progression-free survival, RT = radiation therapy.

Keywords: curative radiotherapy, intensity modulated radiotherapy, locally advanced esophageal carcinosarcoma, neoadjuvant radiotherapy, survival

1. Introduction

Esophageal cancer (EC) mainly includes esophageal adenocarcinoma (EAC) and esophageal squamous cell carcinoma (ESCC), and ranks seventh and sixth with respect to tumor incidence and total tumor mortality worldwide[1]; the corresponding numbers are all sixth in China according to the most recent national research.[2] Carcinosarcoma is a rare malignant tumor that was first proposed in the middle of the 19th century[3] and occurs in different types of organs. Esophageal carcinosarcoma (ECS) is a rare malignant neoplasm that consists of both carcinomatous and sarcomatous components. It reportedly accounts for 0.5%

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to 2.8% of all EC.[4] Multiple designations such as carcinosarcoma and pseudo-sarcoma have been assigned to this neoplastic disorder, which reflects the different views regarding the heterogeneity of histogenesis and biology, as well as whether the spindle cell component is epithelial or mesenchymal in origin.[5]

Radical esophagectomy with adequate lymph node dissection is the standard treatment for ECS. However, for locally advanced potentially operable or inoperable patients, the efficacy of neoadjuvant or curative radiation therapy (RT) remains controversial because of the rather limited number of cases and difficulty in implementing a prospective trial. Few studies have reported the clinical treatment and outcome, most of which were case reports, retrospectively evaluated local medical databases in the early years to analyze cases diagnosed with ECS receiving RT as treatment with curative intent.[6–8] A total of 10 patients (6 men and 4 women) were reported. To date, the sensitivity of malignancies towards radiation and the containment of toxicities have not been proven in the era of intensity-modulated techniques.

Owing to the limited number of published cases, there is insufficient epidemiological evidence for the safety and effectiveness of neoadjuvant or definitive RT in ECS. With a case series and an overview of the literature, we increased the number of published cases and aimed to broaden the clinical knowledge on ECS and the possible role of neoadjuvant or definitive RT for patients with locally advanced ECS, and compared the clinical outcomes with the regimen of surgery combined with adjuvant RT. Here, we describe the experience of patients with ECS who received intensity-modulated radiotherapy (IMRT) or chemoradiotherapy (CRT) at our institution in the recent decade and summarize the existing literature.

2. Patients and methods

2.1. Patient eligibility and evaluation

From 2010 to 2020, we analyzed patients diagnosed with EC and enrolled patients pathologically confirmed with ECS. Data were retrospectively assessed from the institutional review board-approved databases: demographic characteristics, diagnosis (i.e., symptoms, workup, biopsy histology), treatment (curative treatment, neoadjuvant treatment, details of surgical resection, and adjuvant therapies), pathological results (type, quality of resection, involvement of lymph nodes), according to the American Joint Committee on Cancer (AJCC)/International Union against Cancer (UICC) TNM staging 8th edition, and long-term follow-up. Neoadjuvant treatment response was evaluated using the Mandard tumor regression grade (TRG).[9]

The literature study was performed in PubMed and Google Scholar with the following search terms: "neoadjuvant"/"preoperative," "curative"/"definitive," "radiotherapy"/"radiation therapy", and "chemoradiotherapy" in combination with "Esophageal carcinosarcoma," "Esophageal carcinoma," "Esophageal sarcoma," "Esophageal spindle cell carcinoma," "Esophageal squamous cell carcinoma," "Esophageal adenocarcinoma," "Esophageal cancer," and "complication," "toxicity," "side-effects," and "survival". In our overview of the literature (Table 1), we present all the papers published to date, with cases concerning ECS receiving neoadjuvant or curative RT (one patient without survival outcome). Because of the limited number of papers published on this topic, apart from the patients who received surgery combined with adjuvant RT, which was used to compare survival outcomes, there were no other inclusion criteria for the selection of the literature. The sources and methods of selection of participants were showed in flow chart (Fig. 1). The results of the literature search are summarized in tabular form.

2.2. Radiation regimens

Radiation was delivered by 6 MV photons with a conventional fraction (spinal cord dose, 40 Gy). A volumetric modulated arc technique was used in cases that received neo-/adjuvant or curative RT. The dose prescription consisted of primary tumor irradiation at 50 Gy and regional node irradiation at 40 Gy in 22 daily fractions over 4 weeks for pre-/postoperative RT. That dose was primary tumor irradiation at 60 Gy and regional node irradiation at 50 Gy in 28 fractions over 5 weeks for curative RT. Clinical target volume included the esophagus/tumor-bed (at least 3 cm superiorly and inferiorly from the esophageal

Table 1

Previous studies of preoperative or curative radiotherapy efficacy for esophageal carcinomsarcoma in recent years

Author	Case	Clinical stage	Treatments	Regimens	Pathological stage	Response*	PFS	OS
Zuiki et al, 2009	50 YO, M	III (cT-3N1M0)	CRT + surgery	FP + 40 Gy	II (pT1bN1M0)	PR	36 mo re-currence	36 mo alive
Zuiki et al, 2009	66 YO, M	I (cT1b-N0M0)	CCRT + surgery	FP + 40.8 Gy	I (pT1bN0M0)	PR	11 mo re-currence	19 mo alive
Kobayashi et al, 2010	64 YO, M	II (cT-2N1M0)	CCRT + surgery	FP + 38 Gy	II (pT1aN1M0)	2	4 mo metas-tasis	11 mo dead
Lokesh et al, 2010	55 YO, F	-	RT alone	66Gy/3 Gy per fraction for 2 wks followed by 2 Gy per fraction for 3 wks	-	CR	24 mo free of disease	24 mo disease-free alive
Cavallin et al, 2014	50 YO, F	I (cT-1N0M0)	NeoadjuvantRT + surgery + adjuvant RT	NA	-	NA	314 mo free of disease	314 mo alive
Ogasawara et al, 2014	69 YO, M	I (cT1b-N0M0)	RT + surgery	40 Gy	0 (pT1aN0M0)	PR	14 mo me-tastasis	16 mo dead
Nakao et al, 2015	87 YO, M	II (cT-2N0M0)	CCRT	TS-1 + 66 Gy	-	PR	3 mo free of disease	3 mo alive
Katsuya et al, 2017	67 YO, F	II (cT1b-N1M0)	CCRT + surgery	FP + 50.4 Gy	I (pT1bN0M0)	1	4.5 mo re-currence	10.9 mo dead
Katsuya et al, 2017	73 YO, F	III (cT-2N1M0)	CCRT + surgery	FP + 41.4 Gy	I (pT1bN0M0)	2	47 mo re-currence	47 mo alive
Kimura et al, 2019	89 YO, M	II (cT-2N0M0)	RT alone	45 Gy/ 15f	-	CR	25 mo free of disease	25 mo disease-free alive

CRT = chemoradiotherapy, CCRT = concurrent chemoradiotherapy, CR = complete response, F = female, FP = cisplatin+5-fluorouracil, M = male, NA = not available, OS = overall survival, PFS = progression-free survival, PR = partial response, RT = radiotherapy, TS-1 = tegafur, YO = years old.

*Pathological response: 0, No evidence of effect; 1, Viable tumor cells occupy more than 1/3 of the tumorous area; 2, Viable tumor cells remain in less than 1/3 of the tumorous area.

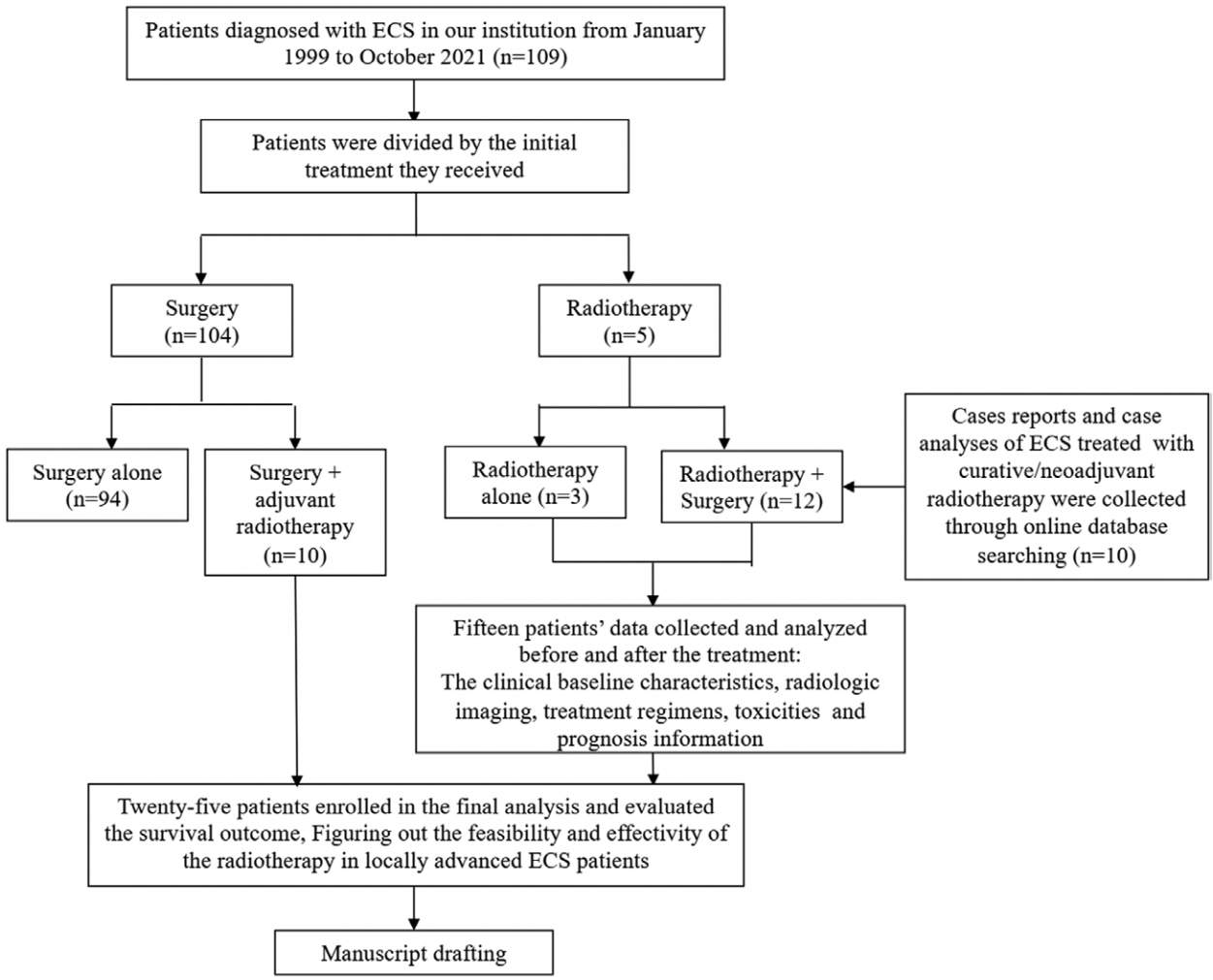

Figure 1. Flow diagram showing patient selection.

lesion) or tumor bed, with mediastinal and supra/infraclavicular lymph nodal area, and margin for planning target volume (PTV) was recommended as 1 cm superior-inferiorly and 0.5 to 0.7 cm in the other directions. The irradiation was delivered using inverse- or forward-planned (field-in-field) IMRT, with the prescribed dose covering 95% of the PTV.

2.3. Endpoints

The primary endpoint was local recurrence (PFS), defined as disease recurrence or newly diagnosed metastasis in the primary location and/or regional lymph nodes, or death due to any cause, whichever occurred first. The secondary endpoints were overall survival (OS) and toxicities. OS events included death from any cause.

Acute toxicity was assessed and scaled during and after treatment according to the Common Terminology Criteria for Adverse Events version 4.03. Late toxicity was assessed using NRG-Radiation Therapy Oncology Group criteria.

2.4. Statistical analysis

Categorical variables are expressed as frequencies, and continuous variables are expressed as maximum, minimum, and median values. Patient characteristics were compared using the chi-square test or Fisher exact test for categorical variables and Wilcoxon or Kruskal–Wallis H rank-sum test of variance for continuous data. Survival was calculated as the number of months from surgery to death or last follow-up visit for all patients. As no surgical treatment was performed, the time interval was calculated from the date of diagnosis. Categorical data are expressed as number and percentage, and continuous data are expressed as median and interquartile range (IQR). OS and PFS were calculated using the Kaplan–Meier plots. Patients with missing data were included in the study. All analyses were performed using SPSS version 26.0 (IBM Corporation, Armonk, NY) and R version 4.1.0 (The R Foundation for Statistical Computing, Vienna, Austria).

The authors are accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (revised in 2013). This study was approved by the institutional ethics committee, and the requirement for individual consent was waived. Written informed consent was obtained from all subjects involved in the study. The need for ethical approval was waived for this study because of its retrospective nature.

3. Results

3.1. Patient characteristics

Of the 11,682 patients diagnosed with EC at our institution, 64 (0.5%) were pathologically confirmed to have ECS. RT was performed in 15 patients, with 10 patients who underwent

adjuvant RT (adjuvant RT group) and 5 patients who underwent neoadjuvant or curative RT (curative/neoadjuvant RT group; Fig. 1). All 15 patients were men. The median age at diagnosis was 55 years (range: 39–70 years). The majority of tumors were located in the middle third (n = 10, 66.7%) of the esophagus, and 3 (20.0%) and 2 (13.3%) were located in the upper and lower thirds of the esophagus, respectively. As shown in Figure 2, the protruding type was the most common endoscopic type (n = 10; 66.7%). Near-or full-peripheral lesions were observed in most patients (n = 14, 93.3%). The endoscopic appearance also showed superficial erosion of the ulcerative lesion, which bled easily when touched. Esophageal ultrasound endoscopy revealed that the lesions were mostly moderate-to-hypoechoic, the internal echo was uneven, and the boundary was unclear. The depth of infiltration exceeded the fibrous membrane and reached peripheral structure invasion in only 2 patients (13.3%), while others were confined to the submucosa or muscularis propria layer or only involved fibrous membrane. X-ray barium meal revealed broken mucosal folds, niches, and limited filling defects. Computed tomography (CT) revealed irregular thickening of the esophageal wall and uneven enhancement. The median length of the focus was 6.0 (range: 4–11 cm). Mediastinal, supraclavicular, or cardia lymph node metastases were observed in most patients (n = 14, 93.3%), as shown in Figure 3. Nine (60.0%) and 3 (20.0%) patients had stage III and stage II disease, respectively, while three patients (20.0%) had stage IV disease for supraclavicular or abdominal lymph nodes. The most common clinical symptom was difficulty in swallowing (n = 15, 100%). Four patients (26.7%) experienced chest and back pain. Five cases (33.3%) were reported as squamous cell carcinoma on biopsy histopathological examination, but all patients were confirmed to have carcinosarcoma or spindle cell carcinoma on postoperative pathology.

Patient characteristics are shown in Table 2 when considering the data from the literature review. The median age at diagnosis was 63 years (range: 39–89 years). Most of the patients were men, with a protruding mass in the middle of the esophagus. As

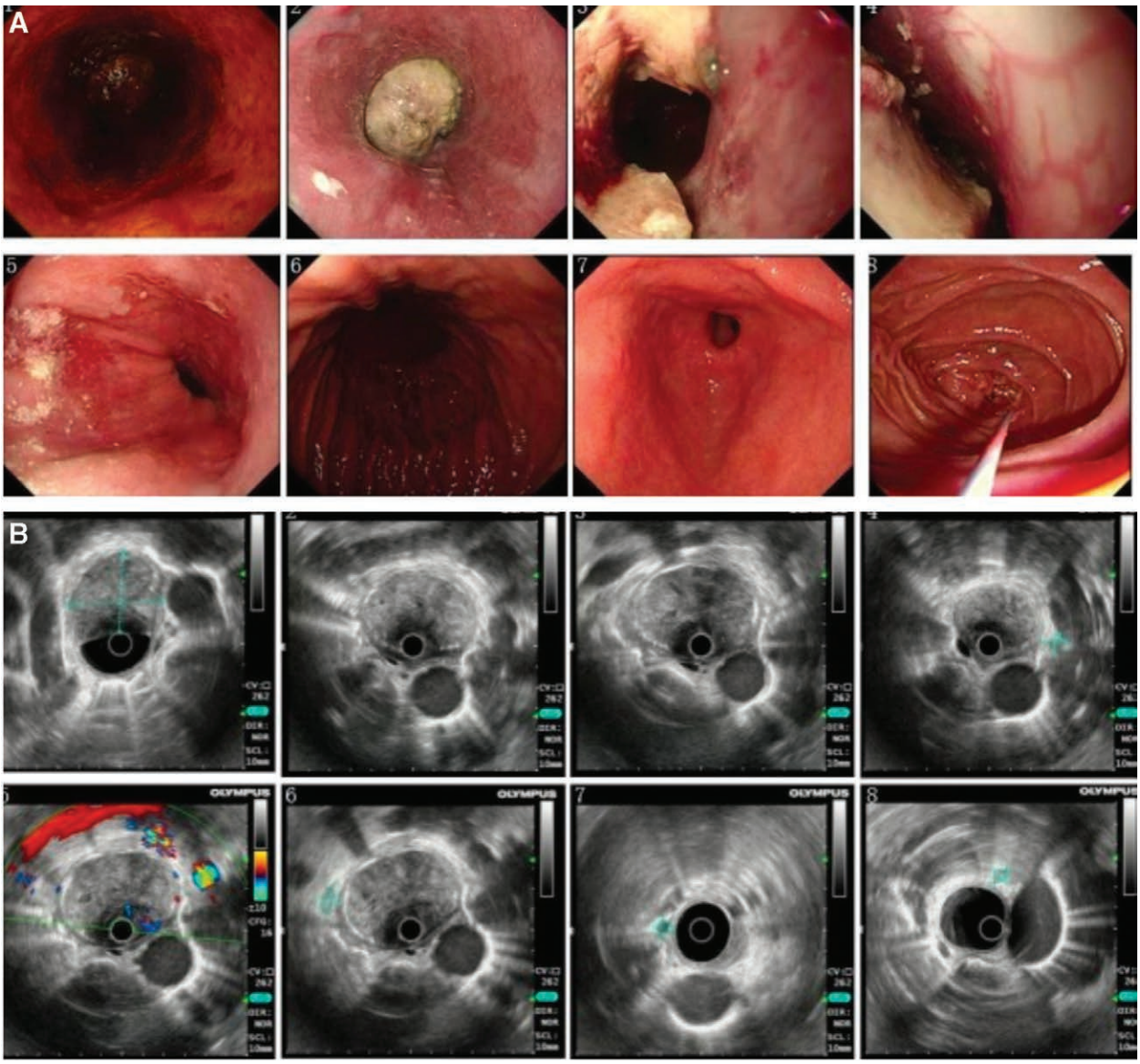

Figure 2. Endoscopic appearance of the esophageal tumor. (A) Esophagoscopy reveals a huge mass with an irregular surface occupying the esophageal lumen of the thoracic esophagus. (B) Esophageal ultrasonography reveals that the lesions are mainly located in the mucosal layer and submucosa, some layers are closely related to the muscularis propria and the boundary is unclear, the adventitia is intact, and the lymph nodes beside the esophagus are observed.

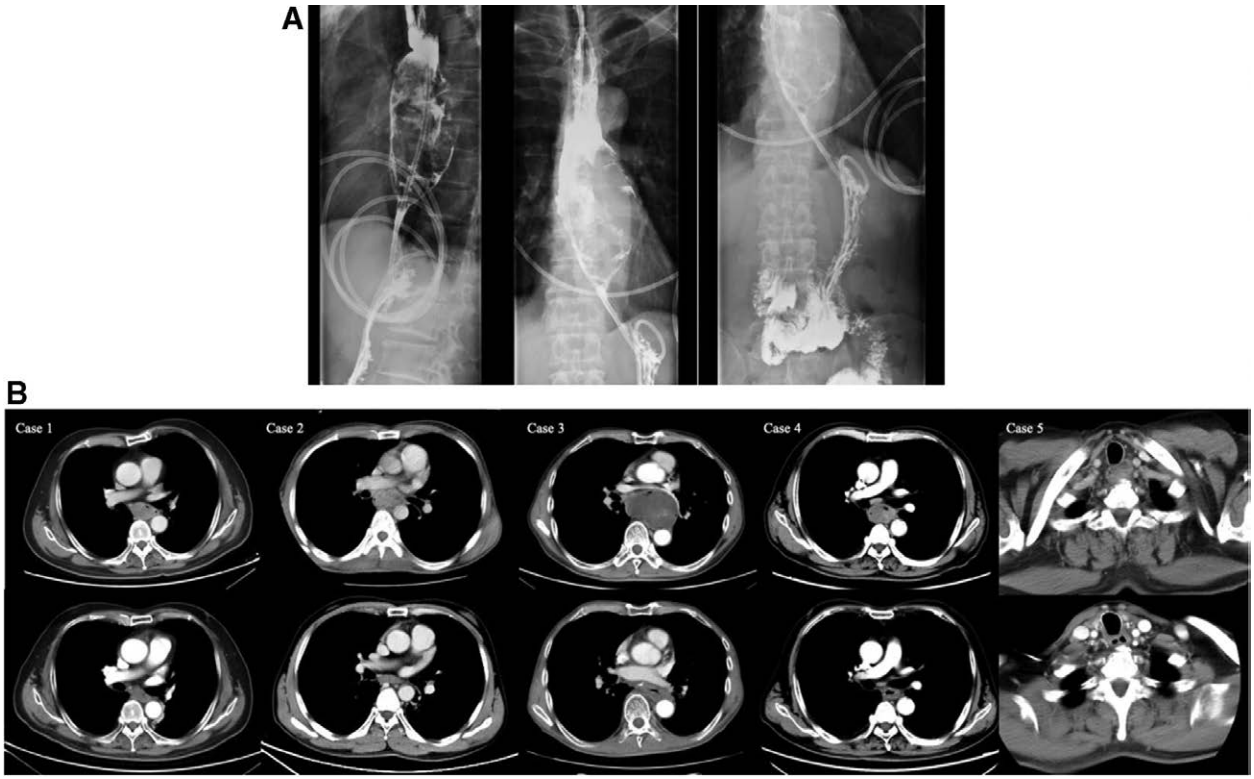

Figure 3. Radiographic assessment of the tumor by esophagus barium meal and computed tomography (CT). (A) Esophagography shows that the middle and lower part of the esophagus is obviously expanded and the mucosal folds is interrupted. The irregular filling defects and irregular niches can be seen. The barium flow is narrowly passed through the tube. (B) The CT scan demonstrates irregular thickening of the esophageal wall and narrowing of the lumen of the thoracic esophagus in the 5 patients received curative or neoadjuvant radiotherapy, and relatively apparent relief after radiation treatment or chemoradiotherapy 1 to 3 mo later.

shown in Figure S1, Supplemental Digital Content, http://links.lww.com/MD/H667, the most common clinical symptom was difficulty swallowing (72.7%). Except for the depth of infiltration and lymph node involvement, the main clinical characteristics of the two groups were similar.

3.2. Treatments and efficacy evaluation

In the curative/neoadjuvant RT group, 3 patients received curative RT alone or CRT for locally advanced disease or concurrent secondary primary tumors. One patient received concurrent paclitaxel combined with cisplatin, while the other patients received RT alone. After curative RT, all patients had reached partial remission in the post-treatment evaluation 1 to 3 months later. The patients in the adjuvant group underwent thoracoscopic radical esophagectomy with regional lymph node dissection following neoadjuvant CRT. One patient received concurrent S-1, whereas the other received RT alone. The postoperative pathological results showed that both patients underwent R0 resection, one of which had mild to moderate pathological response with Mandard TRG Grade 4 and decreased stage from clinical (c) stage III to yield-pathological (yp) stage II. The other patient, who was too weak to receive current CRT, had partial remission at 1 month after RT alone, but surgery was postponed because of epidemic coronaviruses. During the watch and wait period, the patient developed local recurrence after 4 months, received salvage chemotherapy based on etoposide combined with cisplatin, and underwent surgery 2 months later. The postoperative pathological results showed a mild pathological response with Mandard TRG Grade 4, but ypN0 (1 lymph node with severe pathological response).

3.3. Toxicities and survival outcomes

The side effects of RT alone and CRT mainly presented as grade 1 acute radiation esophagitis and myelosuppression, and grade 3 toxicity was only observed in 1 patient who received curative concurrent RT and intravenous chemotherapy. The symptoms were mostly relieved after treatment and the entire cohort completed the entire RT/CRT treatment course.

All patients were monitored afterwards. After a median follow-up of 43.1 months (IQR, 14.6–41.1), the median time of OS and PFS were 40.2 months (95% confidence interval [CI], 13.1–67.3 months) and 19.0 months (95% CI, 13.9 months—24.1 months) for the entire cohort, 30.9 months (95% CI, 3.4–58.3 months) and 16.1 months (95% CI, 12.2–20.1 months) for adjuvant RT group. In the curative/neoadjuvant RT group, the median OS and PFS were not reached. Only 1 patient developed multiple failures during the study period, including local recurrence, regional recurrence, and oligo-bone metastasis, and received salvage CRT and immunotherapy but died from multiple distant metastases. One patient died of concurrent liver cancer with ECS under well-controlled conditions. The remaining 3 patients remained disease-free, as shown in Table 3.

Figure 4A–B shows that OS (hazard ratio [HR] 1.24, 95% CI, 0.23–6.79; $P = .805$) and PFS (HR 0.59, 95% CI, 0.12–2.89; $P = .519$) did not differ significantly between the 2 groups. When considering the literature view data in the final analysis, OS was also not different between the 2 groups, with the median survival time not reached and 40.1 months compared with the adjuvant RT group (HR 0.84, 95% CI, 0.25–2.81; $P = .779$). PFS showed slight trend but not significant benefit in neoadjuvant/curative group, with the median PFS time of 36.0 months and 16.1 months compared with adjuvant RT group (HR, 0.68, 95% CI, 0.26–1.76; $P = .425$), as shown in Figure 4C–D.

Table 2

Characteristics of the esophageal carcinomsarcoma patients received neoadjuvant/definitive and adjuvant radiation treatment

Variables	N (%)	Curative/neoadjuvant RT group (N = 15) (%)	Adjuvant RT group (N = 10), (%)	*P* value
Age (yrs, range)	63 (39–89)	64 (49–89)	54 (39–66)	.046
Sex				.125
Male	21 (84.0)	11 (73.3)	10 (100.0)	
Female	4 (16.0)	4 (26.7)	0 (0.0)	
Location of esophagus				.605
Cervix	2 (8.0)	3 (13.3)	0(0.0)	
Upper third	6 (24.0)	4 (26.7)	2 (20.0)	
Middle third	11 (44.0)	5 (33.3)	6 (60.0)	
Lower third	6 (24.0)	4 (26.7)	2 (20.0)	
Depth of infiltration				.036
Submucosa layer	5 (20.0)	4 (26.7)	1 (10.0)	
Muscularis propria layer	6 (24.0)	6 (40.0)	0 (0.0)	
Fibrous membrane	12 (48.0)	4 (26.7)	8 (80.0)	
Peripheral structure	2 (8.0)	1 (6.7)	1 (10.0)	
Lymph node involvement				.023
N0	7 (28.0)	6 (40.0)	1 (10.0)	
N1	12 (48.0)	8 (53.3)	4 (40.0)	
N2-3	6 (24.0)	1 (6.7)	5 (50.0)	
Stage				.129
I–II	10 (41.7)	8 (57.1)	2 (20.0)	
III–IV	14 (58.3)	6 (42.9)	8 (80.0)	
Treatments				-
Surgery + adjuvant RT/CRT	10 (66.7)	-	-	
Neoadjuvant RT/CRT + surgery	9 (13.3)	-	-	
Curative CRT/RT alone	6 (20.0)	-	-	

CRT = chemoradiotherapy, N = number, RT = radiation treatment.

Table 3

Clinical, demographic presenting features and clinical outcomes of the patients received curative/neoadjuvant radiotherapy

Case	Overview	Endoscopic findings	Biopsy pathological diagnosis	Clinical stage	Treatments	Regimens	Pathological stage	Side-effects	PFS (m)	OS
1	70 YO, M	Ulcerating	Spindle cell carcinoma	III (cT3N1M0)	CCRT + surgery	S-1 + 44.94 Gy	II (pT2N0M0)	Grade 1	37.4	37.4 mo alive
2	49 YO, M	Protruding	Carcinomsarcoma	IVB (cT4N1M1b)	CCRT	TP + 59.92 Gy	-	Grade 3	19.0	33.4 mo alive
3	55 YO, M	Protruding	Carcinomsarcoma	IVB (cT3N1M1b)	RT alone	59.68 Gy	-	Grade 1	4.9	12.0 mo dead
4	63 YO, M	Protruding	Spindle cell carcinoma	III (cT3N2M0)	RT alone	59.92 Gy	-	Grade 1	6.3	6.3 mo dead
5	62 YO, M	Protruding	Spindle cell carcinoma	I (cT1N1M0)	RT + savlage CT + surgery	47.08 Gy + EP	II (pT3N0M0)	None	22.7	22.7 mo alive

CCRT = concurrent chemoradiotherapy, CT = chemotherapy, EP = etoposide + cisplatin, M = male, mo = months, OS = overall survival, PFS = progression-free survival, PR = partial response, RT = radiotherapy, S-1 = tegafur, TP = paclitaxel liposome + nedaplatin, YO = years old.

4. Discussion

The results showed that intensity-modulated RT or CRT with neoadjuvant or curative intent might be effective for downstaging primary tumors in advanced ECS patients with acceptable treatment-relative toxicity.

ECS, also known as spindle cell carcinoma (SpCC) (WHO classification 2000),[10] is a rare type of neoplasm. It is composed of neoplastic squamous and sarcomatous spindle cells. In histological studies, the 2 components are mixed and often dominated by sarcomatoid components. Enrile et al proposed that sarcomatoid spindle cells are produced in response to cancer,[11] Iwaya et al assumed that 2 separate stem cells are transformed independently or simultaneously into malignant cells to form a separate tumor,[12] and Taniyama et al revealed that the individual components are derived from a single common progenitor cell.[13] Ota et al postulated that these components originated from a single clone of granulocyte colony-stimulating factor (G-CSF), which was detected in both squamous cell carcinoma cells and sarcoma cells.[14] The current concept refers to earlier reports that carcinosarcoma could arise from cells of epithelial origin. Chino et al[15] found that the general type of ECS is related to the main components of the tumor. When the sarcoma component is the main component, it presents as polypoid type, and when it is dominated by carcinomatous components, it is mostly ulcerative.

Clinically, the ECS is characterized by rapid growth.[16] Akagi et al[17] reported that the doubling time of ECS is approximately half that of esophageal carcinoma. However, lesions typically demonstrate a polypoid growth pattern that spreads superficially.[18] Because of intraluminal growth, patients with ECS manifest symptoms of dysphagia relatively early,[19] and the prognosis of ECS appears to be better than that of other esophageal malignancies.[7,20,21]

A standard curative local treatment for ECS, except for surgery, has not been established because of the small number of reports. However, RT is also an option for patients with unresectable tumors or those who cannot tolerate surgery.

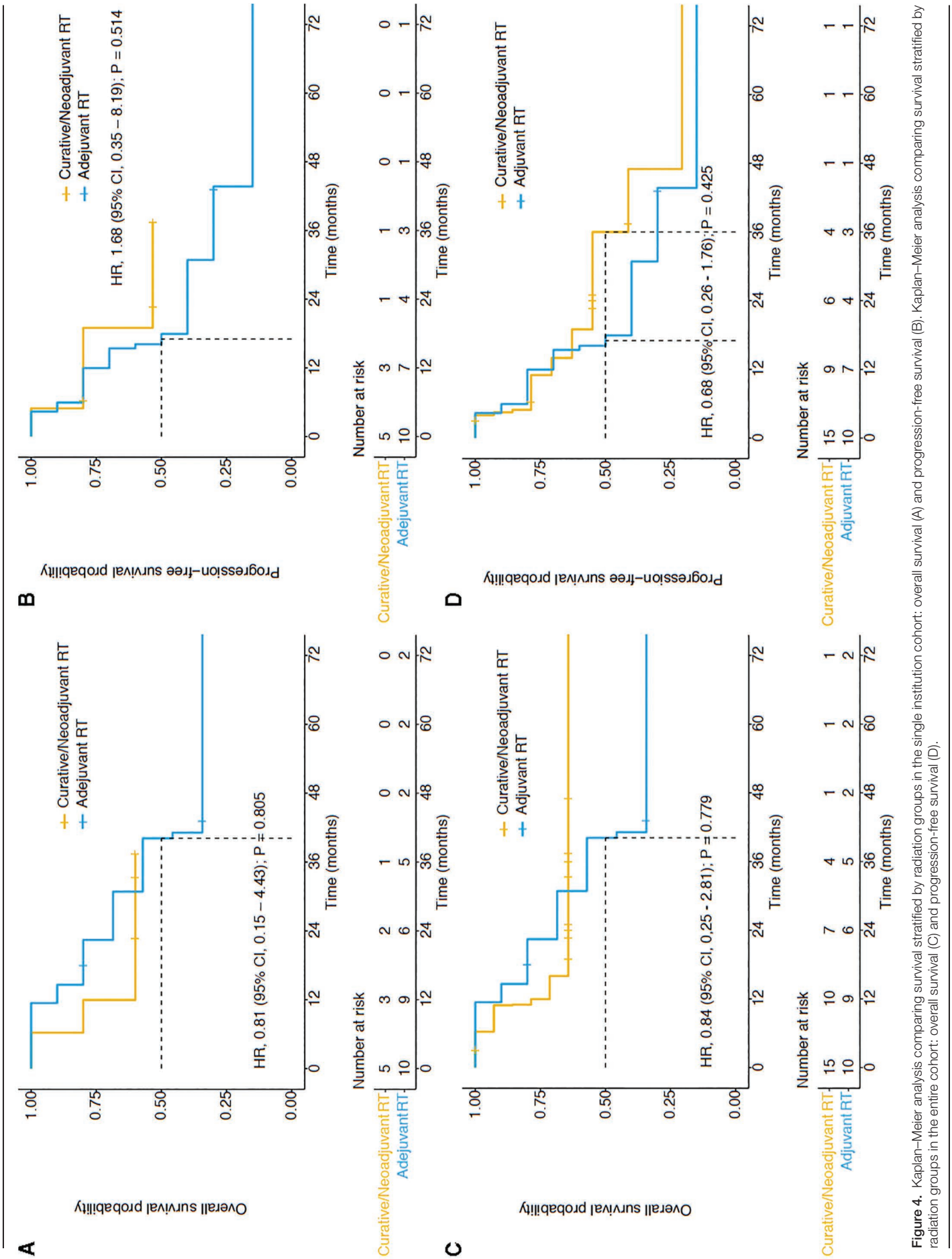

Figure 4. Kaplan–Meier analysis comparing survival stratified by radiation groups in the single institution cohort: overall survival (A) and progression-free survival (B). Kaplan–Meier analysis comparing survival stratified by radiation groups in the entire cohort: overall survival (C) and progression-free survival (D).

The clinical outcomes of RT alone and CRT have mostly been reported with postoperative or palliative tent.[22–24] Several studies listed in Table 1 have reported RT alone and CRT to be effective against esophageal carcinoma, which might be useful for reducing the tumor volume in esophageal carcinosarcoma; however, it is unknown whether it can cure the malignancy. Several studies have reported that CRT or RT alone with 40 Gy is effective against ECS along with surgery.[25] Appropriate RT prescriptions were inconsistent for treatments with curative intent. Kimura et al[26] reported that palliative radiotherapy alone (45 Gy/15 f) achieved complete pathological response (pCR) in an 89 years old patient with a tumor diameter (T2N0M0) of 80 mm. However, the results of the study by Hameed et al showed a progressive disease response after 110 Gy RT with concurrent DDP.[27] This may be explained by improvements in RT technology. Patients develop severe complications after high-dose two-dimensional or three-dimensional conformal radiotherapy. Currently, however, IMRT not only effectively protects organs at risk,[28] but also improves survival outcomes.[29] From the most common point of view, 50 Gy was mostly used in western countries,[30] while 60 Gy was still the curative RT prescription for unresectable or inoperable ECS in Asian,[31] similar to common EC. Our results showed that RT and CRT were relatively sensitive and effective for ECS treatment. OS and PFS did not differ significantly between the curative/neoadjuvant and adjuvant groups and were similar to those in previous reports.[22]

A platinum-based chemotherapy regimen was used according to previous experience of treating EC.[32] In most reported cases, a combination of 5-FU and DDP (FP) was utilized as the conventional chemotherapeutic component, such as ESCC, and patients could benefit from preoperative therapy.[33] For patients who did not tolerate the prolonged hospitalization needed for fractionated delivery of intravenous 5-FU, the drug was replaced with S-1, an oral derivative of tegafur, which is known to be active against the squamous carcinoma component. Concurrent RT with S-1 has been proven to be effective and tolerable in patients with EC.[34,35] Moreover, docetaxel-based chemotherapy targeting sarcomatous components is currently used in several areas, such as bone, soft tissue, and gynecological sarcomas, and has shown favorable response rates.[36,37] Thus, chemotherapy that is effective for both carcinomatous[38] and sarcomatous components may be a rational option for preoperative chemotherapy in patients with ECS. Several studies have shown that chemotherapy regimens including paclitaxel, such as docetaxel, cisplatin, and 5-fluorouracil (DCF),[20,21] have good efficacy for preoperative chemotherapy.

Although our study showed promising results with RT treatment in patients with locally advanced ECS, some limitations should be addressed. This was a retrospective study with a small database that had inherent biases despite our effort to narrow down the inclusion criteria and consider the data of the literature review. Further research with a larger sample size is needed to validate this reliability.

These findings suggest that preoperative intensity-modulated RT or CRT may be effective in downstaging the primary tumor in patients with advanced ECS. This may provide patients who cannot undergo surgical resection with adequate local control and longer survival. Treatment-related toxicity was acceptable.

5. Conclusion

These findings suggest that preoperative intensity modulated RT or CRT may be effective for downstaging the primary tumor in patients with advanced ECS. It may provide patients who cannot undergo surgical resection with adequate local control and probably longer survival. The treatment-relative toxicity was acceptable.

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