

Comparison of efficacy and safety of low-dose-rate vs. high-dose-rate intraluminal brachytherapy boost in patients with superficial esophageal cancer

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ABSTRACT

PURPOSE: To compare the efficacy and the incidence of complications of high-dose-rate (HDR) and low-dose-rate (LDR) intraluminal brachytherapy (IBT) boost after external beam radiation therapy in patients with superficial esophageal cancer.

METHODS AND MATERIALS: Fifty-four consecutive patients with Stage I thoracic esophageal squamous cell carcinoma who were treated with definitive radiotherapy using IBT between 1991 and 2007 were studied retrospectively. LDR-IBT and HDR-IBT were performed for 19 and 35 patients, respectively. After external beam radiation therapy of 56–60 Gy with a conventional fractionation, LDR-IBT (5 Gy × 2) or HDR-IBT (3 Gy × 3) was given within 2 weeks. The median follow-up was 47 months (7–151 months).

RESULTS: Overall, the 5-year overall survival, cause-specific survival (CSS), and locoregional control (LRC) rates were 61%, 86%, and 79%, respectively. The 5-year overall survival, CCS, and LRC rates did not differ significantly between the LDR-IBT and HDR-IBT groups (68% vs. 58% ($p = 0.50$), 83% vs. 85% ($p = 0.63$), and 84% vs. 75% ($p = 0.42$), respectively). Salvage treatment was given in 8 locally recurrent patients, and 6 patients were rescued. The Grade ≥ 2 late morbidities of esophagus and heart/lung were observed in 5 patients (4 in the LDR-IBT group and 1 in the HDR-IBT group) and 2 patients (one from each group), respectively.

CONCLUSIONS: In view of the safety profile and effectiveness, our results encourage the continued adoption of HDR-IBT as radiation boost in medically inoperable or elderly superficial esophageal cancer patients undergoing definitive radiotherapy. © 2012 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Keywords: Superficial esophageal cancer; Intraluminal brachytherapy; Dose rate

Introduction

With the advancement of endoscopic techniques, such as application of iodine dye, magnifying endoscopy, and narrow-band imaging, increasing number of esophageal cancer patients are detected at an early stage in recent years in Japan (1), where up to 30% of all esophageal cancers are superficial cancers (2, 3). Although the standard treatment for both early-stage esophageal cancer and advanced disease is a definitive esophagectomy with lymph node dissection (4–7), a significant portion of the patients are not able to receive surgery because of other confounding factors, such as the advanced age and coexisting medical

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There are no actual or potential conflicts of interest.

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issues. For medically inoperable superficial esophageal cancer (SEC) patients, external beam radiation therapy (EBRT) with or without concurrent chemotherapy is another treatment option. We have previously reported the efficacy of intraluminal brachytherapy (IBT) for SEC patients and have shown that EBRT combined with IBT yields an excellent local control and survival, even for medically inoperable patients (8–10).

Although low-dose-rate (LDR) brachytherapy is considered to produce less adverse effects on normal tissue while delivering adequate dose to the target, high-dose-rate (HDR) brachytherapy has many advantages. These include the ability to create a favorable dose distribution using well-optimized treatment planning, shorter treatment time per session, and avoidance of radiation exposure to medical personnel. For the treatment of cervical cancer, an intense effort has been made to compare the results of the LDR and HDR intracavitary brachytherapy, and most reports have concluded that the intracavitary brachytherapy using two different dose rates can yield almost equal clinical results with similar incidence of complications (11). On the other hand, few reports have focused on the difference in dose rate in the brachytherapy of esophageal cancer, although IBT has been used as a boost therapy for SEC patients (8–10, 12–21). A previous report has compared the effectiveness of LDR-IBT and HDR-IBT for the improvement of dysphagia in patients with advanced esophageal cancer and has concluded that these two methods are equally effective (22). However, the comparison of efficacy and incidence of late complications in the curative treatment using uniform protocols has been lacking.

In our previous report that showed the usefulness of IBT combined with EBRT for SEC, the effect of dose rate was not studied in patients treated with brachytherapy (10). Hence, in this report, the clinical efficacy and the incidence of complications after definitive radiotherapy (RT) using IBT for SEC patients were analyzed with special regard to the dose rate of brachytherapy.

Methods and materials

Patients

The characteristics of patients in this study are summarized in Table 1. This study retrospectively evaluated 54 consecutive patients with thoracic esophageal cancer classified as Stage I (T1N0M0) according to 2002 Union for International Cancer Control criteria (23) who were treated with combination therapy of EBRT and IBT between 1991 and 2007 at either Gunma University Hospital or Gunma Prefectural Cancer Center. The median age of the patients was 70 years (range, 49–86 years). Nineteen patients were treated with LDR-IBT using cesium-137 source, and 35 patients were treated with HDR-IBT using iridium-192 source. The tumors were located at the upper thoracic, middle

Table 1
Characteristics of patients

Patient characteristics	Total	Number of patients in IBT groups, n (%)		p-Value
		LDR IBT	HDR IBT	
Gender				
Male	44	14 (74)	30 (86)	0.47
Female	10	5 (26)	5 (14)	
Age				
<70	23	7 (37)	16 (46)	0.53
≥70	31	12 (63)	19 (54)	
Performance status				
0	22	7 (37)	15 (43)	0.67
1–2	32	12 (63)	20 (57)	
Location				
Upper thoracic	11	3 (16)	8 (23)	0.54
Middle thoracic	33	11 (58)	22 (63)	
Lower thoracic	10	5 (26)	5 (14)	
Tumor length (cm)				
≤5	39	14 (74)	25 (71)	0.86
>5	15	5 (26)	10 (29)	
T classification				
T1a	8	2 (11)	6 (17)	0.80
T1b	46	17 (89)	29 (83)	
Total dose (Gy)	67.8 ± 2.1	67.6 ± 3.7	67.9 ± 1.8	0.77
Reason for RT				
Medically inoperable	42	12 (63)	30 (86)	0.12
Refusal of surgery	12	7 (36)	5 (14)	

IBT = intraluminal brachytherapy; LDR = low-dose-rate; HDR = high-dose-rate; RT = radiotherapy.

thoracic, and lower thoracic esophagus in 11, 33, and 10 patients, respectively. Pathology examination of biopsy samples obtained with endoscopy proved that all patients had primary squamous cell carcinoma of the esophagus. These patients received curative RT because either they were evaluated to be medically inoperable for reasons such as advanced age or existing complications ($n = 42$) or refused surgical treatment ($n = 12$). Thus, more than 75% of patients in this study were unsuitable for curative surgery. Patients who received HDR-IBT were more likely to be medically inoperable compared with LDR-IBT (Table 1). Staging evaluation was performed by using chest X-ray, ultrasound, esophagography, endoscopic ultrasound, and CT.

External beam radiation therapy

The RT treatment policy for the present study was previously described in detail (8, 9). In brief, two to four surgical clips were placed at the tumor edges while the patient underwent endoscopy before the initial treatment planning to identify the tumor location on treatment planning. A total dose of 40–46 Gy by using a 10-MV photon beam with anteroposterior-opposed fields was delivered, and then additional irradiation was delivered using either bilateral oblique portals or more than three beam ports with shrinking fields to avoid irradiating to the spinal cord.

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