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Salvage high-dose-rate brachytherapy for esophageal cancer in previously irradiated patients: A retrospective analysis

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ABSTRACT

PURPOSE: To evaluate outcomes after exclusive salvage high-dose-rate (HDR) intraluminal esophageal brachytherapy given to previously irradiated patients with recurrent esophageal cancer.
METHODS AND MATERIALS: We reviewed medical records of 30 patients who were treated by salvage HDR brachytherapy for local esophageal cancer. Brachytherapy delivered four to six fractions of 5–7 Gy at 5 mm from the applicator surface and 20 mm above and below the macroscopic tumor volume.
RESULTS: Eighty percentage of patients received treatment as initially planned. Complete response rate, evaluated 1 month after brachytherapy by endoscopy and biopsy, was 53%. Squamous histology and complete endoscopic tumor response at 1 month were significantly associated with better local tumor control. Median local progression-free survival was 9.8 months. Overall survival was 31.5% and 17.5% at 1 and 2 years, respectively. On univariate analysis, preserved performance status and limited weight loss (<10%) before salvage brachytherapy were associated with better overall survival. Severe toxicity (Grade ≥3) occurred in 7 patients (23%).
CONCLUSIONS: Although esophageal cancer in previously irradiated patients is associated with poor outcomes, HDR brachytherapy may be a valuable salvage treatment for inoperable patients with locally limited esophageal cancer, particularly in the subset of patients with preserved performance status and limited weight loss (≤10%) before salvage brachytherapy.

Keywords: Esophageal; Cancer; Salvage; Brachytherapy; High-dose rate

Introduction

Esophageal cancer is the eighth most common cancer worldwide, with an estimated 482,300 new cases each year; it is also the sixth most common cause of death from cancer, with an estimated 406,800 deaths/yr. In Europe, the incidence of esophageal cancer and mortality rate was 51/100,000 and 44/100,000, respectively (1). Incidences of adenocarcinoma of the esophagus have been increasing in western countries because of increased body weight and the prevalence of obesity, whereas the occurrence of squamous cell carcinoma of the esophagus has been decreasing because of long-term reductions in tobacco use and alcohol consumption.

Treatment options for advanced esophageal cancer are exclusive chemoradiotherapy or a trimodality therapy combining chemoradiotherapy followed by surgery. Unfortunately, a significant proportion of patients develop a local relapse or persistent disease after chemoradiotherapy. A local relapse or persistent disease is associated with a poor prognosis. Relapses are difficult to treat; salvage surgery can provide a higher survival rate compared with no surgery but is associated with serious postoperative morbidity and mortality (2–4). The use of a palliative expandable esophageal stent or photodynamic

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therapy is also treatment options (5). In some cases, persistent disease or a relapse seem to be limited to the wall of the esophagus and may then be accessible to esophageal brachytherapy if the patient is unfit for salvage surgery.

High-dose-rate (HDR) brachytherapy is a technique which delivers HDR radiation, often >12 Gy/h, to the tumor, temporarily using the catheters placed in or adjacent to the tumor. ^{192}Ir is a commonly used isotope in HDR brachytherapy. Radiation dose is delivered to the tumor based on the predefined dwell time and dwell locations in the catheters, which are removed after the completion of the radiation delivery (6).

Definitive HDR brachytherapy can be performed either as a monotherapy or as a boost treatment after external beam radiotherapy. HDR intraluminal esophageal brachytherapy (HDR-IEBT) offers a highly conformal treatment with the possibility of delivering a relatively high radiation dose to the tumor volume while also delivering a relatively low dose to the surrounding normal tissues, particularly the lung, the spinal cord, and the adjacent normal esophageal mucosa.

Historically, esophageal brachytherapy has been previously delivered at a low-dose rate but is now usually delivered at a HDR using a miniaturized high-activity iridium source, offering more convenient utilization.

The aims of this retrospective study are to evaluate the efficacy and tolerance of salvage HDR-IEBT for esophageal cancer given to inoperable patients who had been previously treated by radiation therapy.

Methods and materials

Patients

Between January 1991 and October 2013, we identified, in our institution, 36 patients previously irradiated by external beam radiotherapy who had been treated by HDR-IEBT for recurrent or new primary esophageal cancer. Among these 36 patients, 6 patients were excluded from our study: 4 patients who had been previously treated with external beam radiotherapy for head-and-neck cancer and 2 patients for Hodgkin lymphoma. Finally, we analyzed, in the present study, 30 patients treated by HDR-IEBT who had recurrent esophageal cancer after radiotherapy or chemoradiotherapy. Patients were recommended salvage brachytherapy because they were medically inoperable. Among these 36 patients, 30 patients had recurrent esophageal cancer after radiotherapy or chemoradiotherapy; 6 patients were excluded from our study: 4 patients who had been previously treated with external beam radiotherapy for head-and-neck cancer and 2 patients for Hodgkin lymphoma.

Previous treatment before salvage brachytherapy consisted of external beam radiation therapy alone in 8 patients (26.5%), chemoradiotherapy in 20 patients (67%), or surgery followed by adjuvant radiotherapy in 2 patients (6.5%) (Table 1).

The mean total dose previously delivered to the esophageal tumor/involved lymph nodes and uninvolved

Table 1
Patient characteristics

Characteristics	*n* (%)
Number of patients (*N*)	30
Gender	
Male	25 (83.5)
Female	5 (16.5)
Age (yr)	
Mean	65
Range	46–87
Tumor histology	
Squamous cell carcinoma	26 (86.5)
Adenocarcinoma	4 (13.5)
PS status	
0	18 (60.5)
1	8 (26.5)
2	2 (6.5)
NA	2 (6.5)
Tumor location	
Upper third	5 (16.5)
Middle third	16 (53.5)
Lower third	9 (30)
Tumor length (cm)	
≤2	16 (53.5)
>2	14 (46.5)
N stage	
N0	27 (90)
N1	3 (10)
Tumor length (cm) and nodal status	
≤2 and N0	15 (50)
>2 or N1	15 (50)
Weight loss (%)	
<5	14 (47)
5–10	8 (26.5)
>10	3 (10)
NA	5 (16.5)
Previous treatment	
Radiotherapy	8 (26)
Chemoradiotherapy	20 (66.5)
Surgery and radiotherapy	2 (6.5)
Brachytherapy regimen (fraction size, fraction number)	
5 Gy, 1 fraction	2 (7)
5 Gy, 2 fractions	5 (17)
5 Gy, 3 fractions	3 (10)
5 Gy, 4 fractions	3 (10)
5 Gy, 5 fractions	4 (13)
5 Gy, 6 fractions	5 (17)
6 Gy, 3 fractions	1 (3)
6 Gy, 4 fractions	2 (7)
6 Gy, 5 fractions	1 (3)
7 Gy, 3 fractions	1 (3)
7 Gy, 4 fractions	3 (10)
Tumor response after brachytherapy	
CR	16 (53.5)
No CR	11 (36.5)
NA	3 (10)

PS = performance status; NA = not available; CR = complete response.