Does Barrett's esophagus respond to chemoradiation therapy for adenocarcinoma of the esophagus?

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Background: Adenocarcinoma of the esophagus is frequently associated with Barrett's esophagus (BE). The response of esophageal adenocarcinoma to chemoradiation therapy is well described; however, the effect of chemoradiation on tumor-associated BE has not been specifically reported.

Objective: To determine the response of tumor-associated BE to chemoradiation therapy.

Design: Retrospective cohort study.

Setting: A single National Cancer Institute Comprehensive Cancer Care Center experience.

Patients: The study cohort consisted of 43 patients with stage I to IVA esophageal adenocarcinoma associated with BE who received either neoadjuvant or definitive chemoradiation therapy and underwent either esophagectomy or surveillance at our institution.

Main Outcome Measurement: The presence and extent of BE after chemoradiation therapy of esophageal adenocarcinoma associated with endoscopically documented pretreatment BE.

Results: BE persisted after chemoradiation therapy in 93% (40/43) of cases (95% CI, 83%-99%). Twenty-seven patients received neoadjuvant chemoradiation therapy before esophagectomy. Persistent BE was detected in all 27 surgical specimens (100%). In 59% (16/27) of the cases, there was complete pathologic tumor response. Sixteen patients received definitive chemoradiation therapy. Persistent pretreatment BE was identified in 88% (14/16) by surveillance endoscopy (95% CI, 60%-98%). The mean length of BE before and after chemoradiation was 6.6 cm and 5.8 cm, respectively ($P = .38$).

Limitations: Retrospective design, small sample size, and single-site data collection.

Conclusions: Chemoradiation therapy of esophageal adenocarcinoma does not eliminate tumor-associated BE, nor does it affect the length of the BE segment. (Gastrointest Endosc 2010;71:235-40.)

The incidence of esophageal adenocarcinoma is increasing by 4% to 10% per year and is increasing at a more rapid rate than any other malignant neoplasm in the United States and Western Europe.[1-4] Barrett's esophagus (BE) is the major risk factor for the development of esophageal adenocarcinoma[5,6] and is frequently found in association with all stages of esophageal adenocarcinoma. Theisen et al[7] reported that BE existed in 75% of patients with esophageal adenocarcinoma and that chemoradiation-induced tumor regression ''unmasked'' BE in an additional 22% as determined by restaging after therapy. Theisen et al did not comment on the response of BE to chemoradiation therapy in the 75% of patients with tumor-associated pretreatment BE.

The majority of symptomatic esophageal cancer patients present with locoregional disease corresponding to American Joint Committee on Cancer (AJCC) stages II and III. Neoadjuvant chemoradiation therapy followed by esophagectomy (trimodality therapy) is the preferred approach for stage II and III esophageal cancer[8] and can achieve 5-year survival rates of 33% to 39%.[9-11]

Abbreviations: AJCC, American Joint Committee on Cancer; BE, Barrett's esophagus; cCR, complete clinical response; cPR, complete pathological response; IQR, interquartile range; PDT, photodynamic therapy.

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Nonetheless, an increasing number of patients receive definitive chemoradiation therapy because of medical comorbidities that preclude surgery and because many patients refuse to undergo esophagectomy. Definitive chemoradiation therapy can achieve 5-year survival rates of 25% to 30% in stage II and III esophageal cancer.[12,13]

The response of tumor-associated BE to chemoradiation therapy for esophageal adenocarcinoma has not been specifically reported. There is an informal awareness among esophageal surgeons that neoadjuvant chemoradiation therapy does not produce regression of BE by the time esophagectomy is performed, and, therefore, esophageal surgeons typically adjust their resections to achieve a BE-free proximal margin. Medical and radiation oncologists who manage patients receiving definitive chemoradiation are less aware of this phenomenon. Because of the paucity of published information on the response of pretreatment tumor-associated BE to chemoradiation therapy for esophageal adenocarcinoma, we conducted a retrospective cohort study to determine the effect of chemoradiation therapy on pretreatment BE.

Capsule Summary

What is already known on this topic

- Barrett's esophagus (BE) is frequently found with all stages of esophageal adenocarcinoma.

What this study adds to our knowledge

- In a retrospective cohort study of 43 patients with esophageal adenocarcinoma associated with BE who received either neoadjuvant or definitive chemoradiation therapy, BE persisted in 93%.
- The mean length of BE before and after chemoradiation was unchanged.

METHODS

The study was approved by both the Moffitt Cancer Center Scientific Review Committee and the University of South Florida Biomedical Institutional Review Board. We reviewed the medical records of 137 patients referred for chemoradiation as treatment for esophageal adenocarcinoma between January 1, 2000, and January 1, 2009, at the Moffitt Cancer Center. A total of 94 patients were excluded (Fig. 1). Forty-one patients were excluded because they did not have BE associated with their adenocarcinoma pretreatment. The absence of BE was confirmed both endoscopically and histologically through review of pretreatment staging endoscopy and surgical pathology reports. Nineteen patients deferred surveillance endoscopy after chemoradiation and were therefore excluded. Eleven patients underwent primary esophagectomy for clinical stage I cancer after consultation with medical, radiation, and surgical oncology. Surveillance endoscopy was not performed in a total of 23 patients who received palliative chemoradiation for stage IVB esophageal adenocarcinoma. Our population cohort was therefore composed of 43 patients with clinical stage I to IVA esophageal adenocarcinoma associated with BE receiving treatment with curative intent.

All patients underwent pretreatment clinical staging including EUS at our institution. All patients had either esophagectomy in conjunction with trimodality therapy or at least one surveillance endoscopy after definitive chemoradiation therapy. Esophagectomy was performed within 6 to 8 weeks after neoadjuvant chemoradiation therapy. Staging endoscopy and related pathology reports were reviewed to obtain a pretreatment description of the BE segment as well as the tumor histology and stage.

Oncology treatment records were reviewed to determine dose and duration of chemotherapeutic regimens. Radiation oncology treatment records and films were reviewed to obtain radiation technique and the size of the treatment field. Two radiation oncologists reviewed the actual treatment simulation and port films to determine the anatomic extent of irradiated esophageal tissue. A reference system was created by marking the carina on each film and designating this point as equivalent to 25 cm from the incisors. By using the scale on the films, the superior and inferior treatment margins as equivalent to the distance from the incisors were then measured and noted. This allowed data to be collected from each case verifying the extent of actual tissue within the irradiated field.

Esophagectomy pathology reports were reviewed in patients receiving trimodality therapy to determine whether BE was present in resection specimens and to assess the completeness of resection with respect to BE persisting after neoadjuvant chemoradiation therapy. Surveillance endoscopy and coinciding mucosal biopsy pathology reports were used to assess the effect of definitive chemoradiation therapy on pretreatment BE. BE was defined as columnar-lined epithelium in the tubular esophagus visible above the gastroesophageal junction in association with histologic evidence of specialized intestinal metaplasia.[14] The BE segment length was measured as the maximum length of contiguous columnar epithelium. Because the intent of surveillance endoscopy was detection of residual tumor, as many as 6 biopsy specimens were obtained from the area of the previous or persistent tumor and adjacent mucosa and not necessarily throughout the length of visible BE.

In consultation with the Moffitt Cancer Center Biomedical Statistics Group, the R statistical package, version 2.6.0 (www.r-project.org) was used to generate descriptive statistics and confidence intervals and to compare pre- and posttreatment mean lengths of BE by using a 2-tailed paired t test. Statistical significance was defined as $P < .05$.