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Physics Contribution

A Contralateral Esophagus-Sparing Technique to Limit Severe Esophagitis Associated With Concurrent High-Dose Radiation and Chemotherapy in Patients With Thoracic Malignancies

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Summary

Severe esophagitis is a dose-limiting toxicity in patients receiving chemoradiation for lung cancer. We reviewed the dosimetry and esophageal toxicity outcome in patients treated with an innovative approach based on intensity modulated radiation therapy to spare the lateral or posterior side of the esophagus opposite the tumor from high-dose radiation. This contralateral esophagus-sparing technique was associated with a favorable esophageal toxicity profile and warrants prospective examination in a larger cohort

Purpose: Severe (Radiation Therapy Oncology Group [RTOG] grade 3 or greater) esophagitis generally occurs in 15% to 25% of non−small cell lung cancer (NSCLC) patients undergoing concurrent chemotherapy and radiation therapy (CCRT), which may result in treatment breaks that compromise local tumor control and pose a barrier to dose escalation. Here, we report a novel contralateral esophagus-sparing technique (CEST) that uses intensity modulated radiation therapy (IMRT) to reduce the incidence of severe esophagitis.

Methods and Materials: We reviewed consecutive patients with thoracic malignancies undergoing curative CCRT in whom CEST was used. The esophageal wall contralateral (CE) to the tumor was contoured as an avoidance structure, and IMRT was used to guide a rapid dose falloff gradient beyond the target volume in close proximity to the esophagus. Esophagitis was recorded based on the RTOG acute toxicity grading system.

Results: We identified 20 consecutive patients treated with CCRT of at least 63 Gy in whom there was gross tumor within 1 cm of the esophagus. The median radiation dose was 70.2 Gy (range, 63-72.15 Gy). In all patients, ≥99% of the planning and internal target volumes was covered by ≥90% and 100% of prescription dose, respectively. Strikingly, no patient experienced grade ≥3 esophagitis (95% confidence limits, 0%-16%) despite the high total doses delivered. The median maximum dose, V45, and V55 of the CE were 60.7 Gy, 2.1 cc, and 0.4 cc, respectively, indicating effective esophagus cross-section sparing by CEST.

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of patients with thoracic malignancies.

Conclusion: We report a simple yet effective method to avoid exposing the entire esophagus cross-section to high doses. By using proposed CE dose constraints of V45 <2.5 cc and V55 <0.5 cc, CEST may improve the esophagus toxicity profile in thoracic cancer patients receiving CCRT even at doses above the standard 60- to 63-Gy levels. Prospective testing of CEST is warranted.

Introduction

Acute esophagitis (AE) is a common toxicity in patients undergoing concurrent chemoradiation therapy (CCRT) for treatment of locally advanced lung cancer (1, 2). Symptoms of AE frequently develop after the third week of initiating radiation treatments (3) with severe (Radiation Therapy Oncology Group [RTOG] grade 3 or greater) AE reported in 15% to 25% of lung cancer patients receiving CCRT (4-6). In addition to symptom management, fluids, and nutritional support, patients with severe AE can require hospitalization and invasive diagnostic or surgical procedures (eg endoscopy, percutaneous gastrostomy tube placement). This often mandates radiation treatment breaks, which may compromise overall treatment efficacy (1, 2, 7). Furthermore, severe AE has been associated with an increased risk for the development of radiation-induced late esophageal toxicity, which is associated with poor quality of life in surviving patients (1-3, 8). This highlights the importance of devising new strategies to improve esophageal sparing and ultimately minimize the rates of severe AE in patients undergoing CCRT.

Intensity modulated radiation therapy (IMRT) has been developed as a strategy to improve dose conformality and spare nearby organs at risk (3, 7, 9, 10). However, the reported rates of AE remain undesirably high even in patients treated with IMRT. Jiang et al (3) reported toxicity outcomes in 165 inoperable non−small cell lung cancer (NSCLC) patients treated with definitive IMRT (median dose, 66 Gy), of whom 136 received concomitant chemotherapy. The incidences of Common Terminology Criteria for Adverse Events (CTCAE) grade 2 and 3 AE they encountered were 70% and 18%, respectively. On long-term follow-up, the development of AE was associated with late esophageal stricture in 15 patients (9%). In another report, IMRT was associated with 28% grade 3 AE (11). Similarly, Kwint et al (12) assessed the AE outcomes in 139 patients with inoperable NSCLC treated with IMRT and concomitant chemotherapy. With use of a hypofractionated regimen of 64 Gy in 24 fractions, 22% experienced grade 3 CTCAE toxicity. These results are similar to the esophageal toxicity outcomes observed in patients treated with CCRT using 3-dimensional conformal radiation therapy (3D-CRT) (1, 4, 5, 13). Therefore, it remains unclear how best to use IMRT for optimal esophageal sparing.

By contrast, the dosimetric benefits of IMRT have been exploited to show an improvement in the toxicity outcomes in patients with other types of cancer. Of significance, IMRT has become the modality of choice for treatment of localized prostate cancer, in part because of the improved rectal toxicity profile associated with IMRT compared with 3D-CRT (14-16). In addition to limiting the rectal volume receiving high dose, several groups have demonstrated that improved sparing of the posterior rectal wall with IMRT can lead to a further decrease in the rates of radiation-induced proctitis (17-21). Similarly, we applied this approach to spare the contralateral esophageal (CE) wall in patients with locally advanced lung cancer treated with CCRT, with the goal of decreasing the incidence and severity of AE. This study aims at describing the contralateral esophageal-sparing technique (CEST) and reviews the acute esophageal toxicity outcomes of consecutive patients treated using this technique.

Methods and Materials

Patients

We reviewed the radiation records of consecutive patients undergoing definitive thoracic CCRT for thoracic malignancies in the senior author's practice between January 1, 2013, and March 31, 2014. The study was approved by the Institutional Review Board. Eligible study participants included patients treated with IMRT and concurrent chemotherapy for gross tumor (primary or nodal) located within 1 cm of the esophagus. A minimum dose of 63 Gy was required for eligibility.

Simulation

All patients were simulated in treatment position using CT scanners capable of acquiring 4-dimensional (4D)-CT image datasets. The imaging sessions for each patient consisted of a free-breathing treatment planning CT image dataset and a 4D-CT image dataset consisting of 10 phase-resorted CT sets representative of a single respiratory cycle. Custom patient immobilization was required for all patients. The CT images were acquired with the application of intravenous contrast medium unless that was medically contraindicated. Oral contrast medium was not given.

Targets and organs at risk

Gross tumor volume (GTV) was defined as all known gross disease visible on the exhale phase of the 4D planning CT.