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Clinical Investigation: Gynecologic Cancer

Duodenal and Other Gastrointestinal Toxicity in Cervical and Endometrial Cancer Treated With Extended-Field Intensity Modulated Radiation Therapy to Paraaortic Lymph Nodes

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Summary

Patients were treated with extended-field (EF) intensity modulated radiation therapy (IMRT) to the paraaortic nodes. EF-IMRT is associated with low rates of gastrointestinal toxicities and no duodenal-specific toxicity. EF-IMRT allows sufficient dose sparing of the bowel to enable safe dose escalation to at least 65 Gy with concurrent chemotherapy.

Purpose: To characterize the rates of acute and late duodenal and other gastrointestinal (GI) toxicities among patients treated for cervical and endometrial cancers with extended-field intensity modulated radiation therapy (EF-IMRT) to the paraaortic nodes and to analyze dose-volume relationships of GI toxicities.

Methods and Materials: Fifty-three patients with endometrial or cervical cancer underwent EF-IMRT to the paraaortic nodes, of whom 46 met the inclusion criteria for GI toxicity and 45 for duodenal toxicity analysis. The median prescribed dose to the paraaortic nodes was 54 Gy (range, 41.4-65 Gy). The 4 duodenal segments, whole duodenum, small bowel loops, peritoneum, and peritoneum plus retroperitoneal segments of colon were contoured retrospectively, and dosimetric analysis was performed to identify dose-volume relationships to grade $\geq$3 acute ($<$90 day) and late ($\geq$90 day) GI toxicity.

Results: Only 3/46 patients (6.5%) experienced acute grade $\geq$3 GI toxicity and 3/46 patients (6.5%) experienced late grade $\geq$3 GI toxicity. The median dose administered to these 6 patients was 50.4 Gy. One of 12 patients who received 63 to 65 Gy at the level of the renal hilum experienced grade 3 GI toxicity. Dosimetric analysis of patients with and without toxicity revealed no differences between the mean absolute or fractional volumes at any 5-Gy interval between 5 Gy and the maximum dose. None of the patients experienced duodenal toxicity.

Conclusions: Treatment of paraaortic nodes with IMRT is associated with low rates of GI toxicities and no duodenal-specific toxicity, including patients treated with concurrent chemotherapy. This technique may allow sufficient dose sparing of the bowel to enable safe dose escalation to at least 65 Gy.

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Introduction

Intensity modulated radiation therapy (IMRT) uses multiple beams and controls the intensity from individual beam subsegments to produce conformal distributions with steep dose gradients. These advantages should improve the therapeutic ratio relative to conventional radiation therapy (RT) (1). RT for gynecologic malignancies may result in gastrointestinal (GI) toxicities (2-4); in cases with lymph node involvement, high doses may improve tumor control (5).

Several studies have assessed treatment of the whole pelvis using IMRT (IM-WPRT) and show <2% GI toxicity rates, but relatively few have addressed extended-field IMRT (EF-IMRT). Kidd et al demonstrated a 5.2% rate of grade ≥3 GI toxicity among cervical cancer patients receiving IMRT, of whom 13% had EF-IMRT, significantly lower than the 10.7% rate associated with conventional RT (6). Other EF-IMRT series have reported dosimetric improvements, including decreased volumes of small bowel, rectum, and bladder receiving the 45-Gy prescription dose relative to conventional EFRT plans (7) or with dose escalation to 59.4 Gy with adequate sparing of the stomach, liver, and colon (8). Dose sparing of the small intestine is limited by proximity to the paraaortic nodes; about 20% to 25% of small bowel received ≥45 Gy (8). A limit of the V25 of the small intestine to <50% has been demonstrated to be feasible (9). The average V50 and V60 of bowel may be less than 10% and 1%, respectively (10).

EF-IMRT series reporting clinical outcomes are limited. In 1 report, using at least 45 Gy to the paraaortic nodes, no patients experienced acute grade ≥3 GI toxicity (11). In a second study, EF-IMRT with dose escalation to 55 to 60 Gy administered to involved nodes along with concurrent cisplatin resulted in grade 3 acute and late GI toxicity rates of 2.8% and 5.6%, respectively (12). Our series uniquely divides the most sensitive structure, the duodenum, and reports detailed dose-volume data to each segment of the duodenum and bowel, and rates of associated duodenal and GI toxicities.

Methods and Materials

Patient population

The records of 53 patients treated at our institution from 2003 to 2011 for cervical or endometrial cancer for which EF-IMRT to the paraaortic nodes was prescribed were retrospectively reviewed with institutional review board approval and a waiver of consent. Treatment of primary or recurrent disease was included, as were all histologic subtypes. Twenty patients had treatment to 45 Gy, and 33 had a boost to the paraaortic nodes (range, 50-65 Gy). All patients received 1.8 Gy per daily fraction for the EF-IMRT. For the boost, after a mean of 25 fractions to 45 Gy, sequential dose escalation was performed in most cases, with 2 Gy per fraction to a maximum of 65 Gy when feasible, based on dose-volume histogram (DVH) constraints to the kidney (volume receiving more than 20 Gy <30%), small bowel (D5cc <55 Gy), and spinal cord (maximum dose <45 Gy). Fifty-one patients had chemotherapy, either concurrently (n=24), sequentially (n=25), or both (n=2).

Exclusions from the GI toxicity analysis included patients with stage IVB (n=5) or stage IVA (n=2) disease with bowel involvement. Therefore, 46 patients met the criteria for inclusion into the GI toxicity analysis. For the duodenal toxicity analysis, of the 53 eligible patients, 8 were excluded because they had fewer than 6 months of follow-up; thus, 45 patients were in this subgroup. This ensured minimum sufficient follow-up time based on the expected time course of late duodenal toxicities. Table 1 summarizes the patient, disease, and treatment characteristics of those included in each analysis.

Treatment planning: contouring and dose-volume histogram calculations

Planning computed tomography (CT) scans were performed 15 to 30 minutes after the administration of oral contrast medium. Patients were positioned supine on a carbon fiber board, using

Table 1 Patient, disease, and treatment characteristics

Patient characteristics	GI toxicity analysis		Duodenal toxicity analysis	
	No toxicity	Toxicity	No toxicity	Toxicity
Total	40	6	45	0
Median age (y) (range)	45 (38-83)	54 (38-82)	46 (38-82)	N/A
Primary cervical cancer	7	3	10	0
Recurrent cervical cancer	1	0	1	0
Primary endometrial cancer	17	2	21	0
Recurrent endometrial cancer	15	1	13	0
History of abdominal surgery	29	2	31	0
History of prior abdominal RT	6	0	3	0
EF-IMRT	7	2	9	0
EF-IMRT + conedown	24	3	25	0
WART + conedown	7	1	8	0
WPRT + conedown	2	0	3	0
Median dose to PAN (Gy) (range)	54 (45-65)	50.4 (41.4-65)	50.4 (41.4-65)	N/A
Intracavitary brachytherapy	27	5	33	0
Concurrent chemotherapy	18	3	19	0

Abbreviations: EF-IMRT = extended-field intensity modulated radiation therapy; GI = gastrointestinal; PAN = paraaortic nodes; RT = radiation therapy; WART = whole abdominal radiation therapy; WPRT = whole pelvis radiation therapy; N/A: not applicable.