



Gastric cancer

Defining the target volume for post-operative radiotherapy after D2 dissection in gastric cancer by CT-based vessel-guided delineation



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ABSTRACT

Purpose: To determine the recurrent nodal gross tumor volume (rnGTV) based on CT-guided vascular structure to refine the clinical target volume (CTV) delineation in postoperative radiotherapy for advanced gastric cancer following radical gastrectomy with D2 dissection.

Materials and methods: We retrospectively reviewed follow-up images from 91 patients with their first regional recurrence after D2 dissection in stage III gastric cancer with N3 disease. We defined rnGTV as recurrent nodes shown in follow-up CT images, in which one diagnostic radiologist with specialty of gastrointestinal tract investigated. We drew rnGTVs at the equivalent location based on the same vessels of reference comparing CT images to recurrence CT images.

Results: We propose vessel-based locations of rnGTVs on CT images with axial and coronal views. We show different patterns of regional recurrence according to the location of primary gastric cancer using CT and digitally reconstructed radiograph (DRR) images. Frequently recurred sites, overlapped by more than five rnGTVs, are depicted in a DRR image.

Conclusions: This study suggests vessel-based delineations of rnGTVs on CT images depending on nodal recurrence sites from follow-up images after D2 lymphadenectomy. Our results could help reduce the inter-observer variation of CTV delineation after D2 dissection in gastric cancer.

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Gastric cancer is the most common cancer, and the third most common cause of cancer-related deaths, in Korea [1]. Post-operative chemotherapy as an adjuvant strategy has been adopted throughout Asia [2,3], whereas post-operative chemoradiotherapy (INT0116) and peri-operative chemotherapy (MAGIC study) are considered standard therapy in the West [4,5]. Despite surgical resection with curative intent, some studies have reported high locoregional as well as distant failure rates [6,7]. Due to high locoregional recurrence rates after curative surgery, postoperative radiotherapy (RT) has been considered an adjuvant treatment modality. The Intergroup trial 0116 (INT0116) demonstrated a significant survival benefit with chemoradiotherapy (CRT), but it has been criticized due to limited lymph node dissection (D0 or D1) [4]. Recently, a meta-analysis study also reported a favorable survival impact of RT for resectable gastric cancer [8]. The ARTIST trial, a

phase III clinical trial to investigate the role of postoperative CRT, showed that after curative en bloc resection with extensive (\geq D2) lymph node dissection, the addition of RT significantly prolonged disease-free survival in a subgroup of patients with pathologic lymph node metastasis at the time of surgery, but not in the overall group of patients [9]. However, until now, postoperative RT following D2 lymph node dissection has not been generally applied and tested in clinical trials in Korea and Japan.

In most studies of adjuvant RT, the target volume range for RT is extremely diverse. Postoperative RT volume based on patterns of failure after radical surgery has been defined as the primary tumor bed, resection margins, anastomosis site, duodenal stump, and regional lymph nodes [10,11]. If necessary, the remnant stomach in patients who underwent a subtotal gastrectomy has been often included. However, because a clinical target volume (CTV) has a wide range, the adjacent organs at risk, including the kidney, liver, small bowel, and spinal cord, remain the main limitations of abdominal RT. Furthermore, because the specific site of locoregional recurrence after curative surgery for advanced gastric cancer has not been established, the delineation CTV guideline could not be suggested based on the computed tomography (CT) images. A recent randomized prospective trial showed that intensity-modulated radiotherapy (IMRT) with chemotherapy was feasible for gastric

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cancer patients receiving D2 dissection [12]. This increased the necessity of evidence-based CTV definitions for IMRT.

In our previous study, we investigated patterns of regional recurrence after curative D2 resection for stage III (N3) gastric cancer. We demonstrated that the most prevalent nodal recurrence for advanced gastric cancer was in the nodal basin outside the D2 dissection field [13]. Using the data from 91 patients with regional failure from our previous study, we continued this study in an effort to propose the recurrent nodal gross tumor volume (rnGTV) based on the CT-guided vasculature to improve the CTV delineation in the postoperative RT of advanced gastric cancer after radical gastrectomy with D2 dissection.

Materials and methods

Patient, treatment, and tumor characteristics

We retrospectively reviewed a total of 91 patients with first regional recurrence in stage III gastric cancer with N3 disease, which had been reported in our previous study [13]. All patients underwent a curative gastrectomy with D2 lymph node dissection at a single institution between December 2004 and January 2008. In all patients, neither splenectomy nor pancreatectomy was performed. Patient, treatment, and tumor characteristics are listed in

Table 1. The median age was 57 years (range, 26–81 years), and 64 patients (70.3%) were male. Gastric adenocarcinoma of the tubular, mucinous type, and signet ring cell carcinoma were histologically proven in all patients. According to the American Joint Committee on Cancer (AJCC) staging system, five (5.5%), 21 (23.1%), and 65 patients (71.4%) were stages IIIA, IIIB, and IIIC, respectively. Subtotal gastrectomy was performed in 51 patients (56.0%) and total gastrectomy in 40 patients (44.0%). The median number of dissected and positive lymph nodes was 43 (range, 17–113) and 16 (range, 7–85), respectively. Eighty-six patients (94.5%) received adjuvant chemotherapy with various regimens. None of the patients underwent pre- or postoperative RT.

Follow-up and evaluation of recurrence

Patients were followed up in the Gastric Cancer Clinic at our institution every 3 months during the first 2 years and every 6 months during the next 3 years, following the completion of definitive treatment. A complete history and physical examination was performed at each visit. Regular follow-up evaluations consisted of endoscopy, CT scans of the chest and abdomen, and positron emission tomography (PET) or PET–CT. Generally, endoscopy and abdomen CT were performed every 6 months during the first 3 years and annually during the next 2 years. All available imaging

Table 1
Patient, treatment, and tumor characteristics.

| Characteristics | | No. patients (%) |
|-------------------------|-------------------------------------|------------------|
| Age (years) | Median | 57 |
| | Range | 26–81 |
| Sex | Male | 64 (70.3) |
| | Female | 27 (29.7) |
| ASA | Median | 1 |
| | Range | 1–7 |
| Location | Lower third | 41 (45.1) |
| | Middle third | 2 (25.3) |
| | Upper third | 10 (11.0) |
| Histology | More than two-thirds of the stomach | 17 (18.7) |
| | Tubular adenocarcinoma (PD) | 44 (48.4) |
| | Tubular adenocarcinoma (WD–MD) | 29 (31.9) |
| | Signet ring cell carcinoma | 13 (14.3) |
| Lymphovascular invasion | Mucinous adenocarcinoma | 5 (5.5) |
| | Yes | 74 (82.2) |
| | No | 8 (8.9) |
| Tumor size (cm) | Not reported | 8 (8.9) |
| | Median | 6.0 |
| Pathologic T stage | Range | 2.0–17.0 |
| | T2–3 | 20 (22.0) |
| Pathologic N stage | T4a | 69 (75.8) |
| | T4b | 2 (2.2) |
| | N3a | 45 (29.5) |
| Stage | N3b | 46 (50.5) |
| | IIIA | 5 (5.5) |
| | IIIB | 21 (23.1) |
| No. positive LNs | IIIC | 65 (71.4) |
| | Median | 16 |
| No. dissected LNs | Range | 7–85 |
| | Median | 43 |
| LN ratio | Range | 17–113 |
| | Median | 0.38 |
| Type of resection | Range | 0.10–0.93 |
| | Subtotal gastrectomy | 51 (56.0) |
| Lymphadenectomy | Total gastrectomy | 40 (44.0) |
| | D2 | 91 (100.0) |
| | Billroth-I | 17 (18.7) |
| | Billroth-II | 36 (39.6) |
| Type of reconstruction | Roux-en-Y | 36 (39.6) |
| | Others | 2 (2.2) |
| | Yes | 86 (94.5) |

Abbreviations: ASA = American Society of Anesthesiologists, PD = poorly differentiated, MD = moderately differentiated, WD = well differentiated, LNs = lymph nodes, Roux-en-Y = Roux-en-Y gastrojejunostomy.

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