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Clinical impact of tumor volume reduction in rectal cancer following preoperative chemoradiation

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KEYWORDS
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Tumor volume reduction ratio;
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Disease-free survival

Abstract
Purpose: The purpose of this study was to correlate tumor volumetric analysis obtained using magnetic resonance (MR) imaging with disease-free survival in patients with advanced rectal cancer who underwent preoperative chemoradiotherapy (CRT).
Patients and methods: Institutional review board approval was obtained and patient informed consent was waived. This study included 74 patients (47 men, 27 women; mean age, 64 years ± 10 [SD] years) who underwent preoperative CRT and subsequent rectal surgery between January 2007 and December 2010. Two radiologists who were blinded to the clinical outcome measured tumor volume separately on two sets of MR images obtained before and after CRT. Patients were classified into two groups according to the episode of recurrence and recorded disease-free survival. To assess factors relevant to disease-free survival, univariate and multivariate Cox regression analysis were performed for tumor volume reduction ratio, circumferential resection margin, tumor regression grade, and pathologic staging.

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Results: Tumor volume reduction ratio ($P = 0.009$), circumferential resection margin ($P = 0.008$) and tumor regression grade ($P = 0.002$) were significantly associated with disease-free survival. At multivariate analysis, tumor volume reduction ratio was the single variable that was associated with disease-free survival ($P = 0.003$). Tumor volume reduction ratio was also a reliable parameter with an excellent interobserver correlation between two readers for pre-CRT volume (ICC = 0.939; 95%CI: 0.885—0.979; $P < 0.001$) and post-CRT volume (ICC = 0.889; 95%CI: 0.845—0.934; $P < 0.001$).
Conclusions: MR volumetric measurement of rectal cancer helps predict disease-free survival in patients with rectal cancer who underwent preoperative CRT.

Chemoradiotherapy (CRT) before total mesorectal excision has been used for appropriate treatment of locally advanced rectal cancer due to its usefulness in anal sphincter preservation and reduced local recurrence [1—3]. Magnetic resonance (MR) imaging provides crucial information with respect to clinical prognosis as well as preoperative assessment [4,5], despite their uncertainties as a parameter to evaluate tumor response in rectal cancer after CRT. Post-CRT tumor pathologic staging is an important prognostic factor in rectal cancer after neoadjuvant CRT. However, estimations of restaging on post-CRT MR imaging are considered unsatisfactory due to low accuracy [6—13]. Many pathologic factors including post-CRT pathologic staging, tumor cellular differentiation, biological features have been studied to predict outcomes [14—21]. However, these parameters are obtained only after surgery and pathologic examination. More accurate tumor response assessments and reliable imaging parameters are required prior to surgery to evaluate clinical prognosis that could help clinicians determine an optimal treatment plan. Tumor volume reduction on MR imaging after neoadjuvant CRT has been previously studied [22—27]. Tumor volume reduction ratio (TVRR) also revealed a high correlation with pathologic parameters such as tumor regression grade (TRG) and pathologic staging, which are acknowledged prognostic factors for rectal cancer [23,24,26,27]. Prior studies reported a good correlation between these pathologic parameters and disease-free survival (DFS) [15—19]. However, few recent studies have evaluated the direct relationship between tumor volume reduction and clinical outcomes such as tumor recurrence and DFS [23,25].

The purpose of this study was to correlate tumor volumetric analysis obtained using MR imaging with DFS in patients with advanced rectal cancer who underwent preoperative chemoradiation therapy.

Patients and methods

Patients

This study received study-specific institutional review board approval with a waiver of informed consent. We reviewed our electronic medical record databases from January 2007 to December 2010 for patients who satisfied the following inclusion criteria:

- the patient had histopathologically confirmed rectal adenocarcinoma;
- the patient received neoadjuvant CRT;
- the patient had surgery at our institution;
- the patient underwent pre-CRT and post-CRT rectal MR imaging;
- the patient had non-metastatic disease at initial state.

We selected 78 consecutive patients for our study. A total of 74 patients (47 men, 27 women) with a mean age of 64 ± 10 (SD) years; range, 37-84 years) were ultimately enrolled in our retrospective study after 4 patients were excluded due to severe MR metallic artifacts ($n = 2$) and immediate follow-up loss after surgery ($n = 2$).

MR imaging technique

MR imaging studies were performed using a 1.5 T (Achieva®, Phillips, Best, The Netherlands) or a 3 T (Verio®, Siemens Healthcare, Erlangen, Germany) MR unit with a six-channel phased array surface coil. Before MR scanning, approximately 50-100 mL of sonography transmission gel was administered for adequate rectal luminal distention and to help delineate small rectal tumors. MR images were obtained using the following sequences. First, sagittal images were obtained with a T2-weighted fast spin-echo sequence. A plane perpendicular to the long axis of the rectal cancer was selected for axial scanning. Oblique axial diffusion-weighted echo planar images were acquired using the three b factors of 0, 500, and 1000 s/mm^2 in a 3-T system and the two b factors of 0 and 1000 s/mm^2 in an 1.5-T system. Gadolinium-chelate enhanced fat-suppressed T1-weighted sequences in the transverse and sagittal plane were obtained after an intravenous bolus injection of 0.1 mmol/kg of Gadobutrol (Gadovist®, Schering, Berlin, Germany) at a rate of 3 mL/s, followed by a 25 mL of saline flush. Table 1 summarizes the detail imaging parameters.

MR volume measurement and image interpretation

Two radiologists with an experience of 11- and 2-years in abdominal imaging independently measured tumor volume

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