Letters

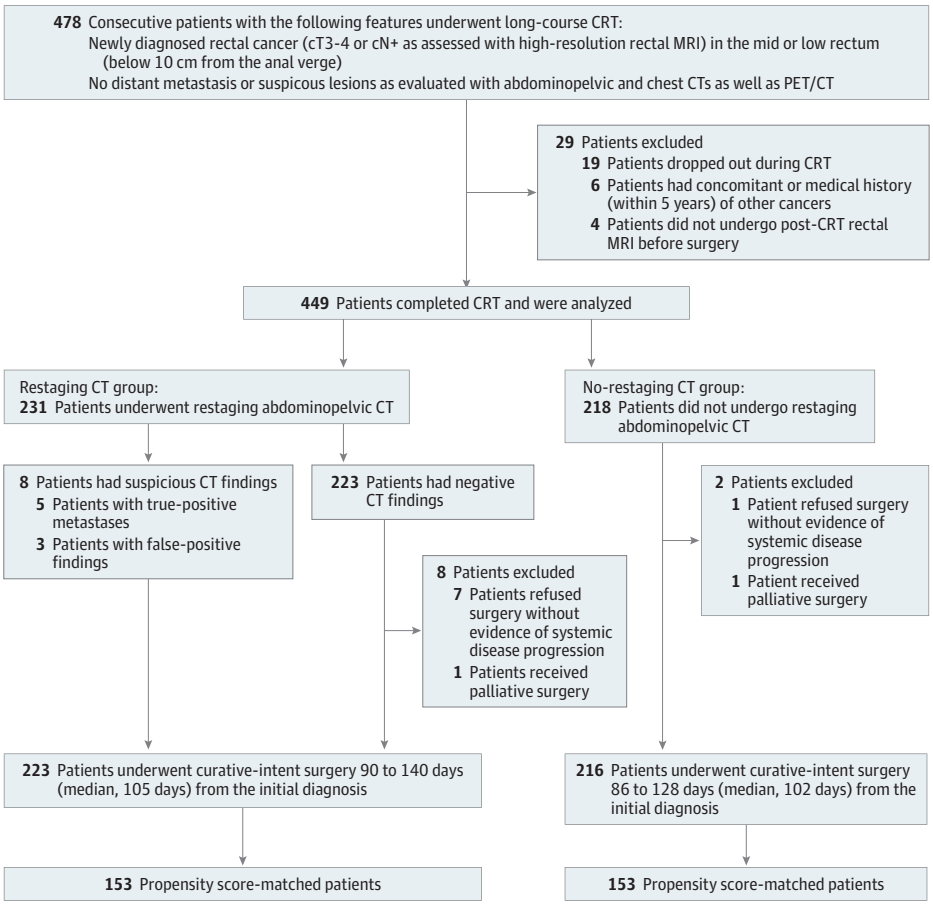
RESEARCH LETTER

Restaging Abdominopelvic Computed Tomography Before Surgery After Preoperative Chemoradiotherapy in Patients With Locally Advanced Rectal Cancer

Chemoradiotherapy (CRT) before surgery is a standard treatment for locally advanced cancer in the mid or low rectum. Long-course CRT delays surgery for several months, which may introduce a possibility, albeit small, for the tumor to make systemic progression or for occult metastasis to grow and manifest. Currently, there is no consensus regarding whether restaging abdominopelvic computed tomography (CT) is necessary before surgery after long-course CRT. Several studies have investigated this issue[1-5]; however, results were conflicting. Most of the studies were small.[1,2,4,5] None of them compared the oncologic outcomes between patients who received and those who did not receive (as controls) the restaging CT.[1-5] This study investigated restaging abdominopelvic CT performed before surgery after CRT in patients with locally advanced rectal cancer regarding its diagnostic yield and effect on postsurgical recurrence-free survival (RFS).

Methods | The institutional review board of Asan Medical Center approved this observational study and a waiver of written informed consent was included. Between 2011 and 2015, 449 eligible patients (294 [65%] men with a mean [SD] age of 62.5 [11.6] years and 155 [35%] women with a mean [SD] age of 61.8 [11.9] years) were included (**Figure**). Patients underwent long-course preoperative CRT over 5 to 6 weeks including either fluorouracil plus leucovorin or capecitabine (details are available elsewhere).[6] All patients were reexamined with high-resolution rectal magnetic resonance imaging (MRI) approximately 4 to 6 weeks after completing CRT, and 231 also underwent restaging contrast-enhanced abdominopelvic CT 77 to

Figure. Patient Flow Diagram



CRT indicates chemoradiotherapy; CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

Table. Comparison Between Patients Who Underwent and Did Not Undergo Restaging CT Among Those Undergoing Curative-intent Surgery After CRT, Before and After Applying Propensity Scores[a]

Characteristic	Before Propensity Score Matching					After Propensity Score Matching			
	Restaging CT Group (n = 223)	No-Restaging CT Group (n = 216)	Standardized Difference	*P* Value[b] Without Inverse Weighting	*P* Value[b,c] After Inverse Weighting	Restaging CT Group (n = 153)	No-Restaging CT Group (n = 153)	Standardized Difference	*P* Value[b]
Baseline									
Age, mean (SD), year	62.3 (11.4)	62.0 (11.6)	0.03	.74	.95	61.6 (11.9)	62.1 (11.7)	0.04	.73
Sex, No. (%)			0.12	.24	.93			0.03	.90
Female	82 (36.8)	67 (31.0)				50 (32.7)	48 (31.4)		
Male	141 (63.2)	149 (69.0)				103 (67.3)	105 (68.6)		
Pre-CRT cT on MRI, No. (%)			0.25	.04	.96			0.06	.86
T2	25 (11.2)	10 (4.6)				12 (7.8)	10 (6.5)		
T3	174 (78.0)	181 (83.8)				124 (81.0)	124 (81.0)		
T4	24 (10.8)	25 (11.6)				17 (11.1)	19 (12.4)		
Pre-CRT cN on MRI, No. (%)			0.07	.69	.89			0	.99
Negative	3 (1.3)	5 (2.3)				2 (1.3)	2 (1.3)		
Positive	220 (98.7)	211 (97.7)				151 (98.7)	151 (98.7)		
Pre-CRT EMVI on MRI, No. (%)			0	.99	.98			0	.99
Negative	196 (87.9)	190 (88.0)				134 (87.6)	134 (87.6)		
Positive	27 (12.1)	26 (12.0)				19 (12.4)	19 (12.4)		
Concurrent chemotherapy, No. (%)			0.65	<.001	.98			0.04	.82
Fluorouracil and leucovorin	93 (41.7)	156 (72.2)				90 (58.8)	93 (60.8)		
Capecitabine	130 (58.3)	60 (27.8)				63 (41.2)	60 (39.2)		
mrTRG, No. (%)			0.19	.43	.99			0.10	.95
Grade 1	39 (17.5)	27 (12.5)				22 (14.4)	23 (15.0)		
Grade 2	55 (24.7)	57 (26.4)				34 (22.2)	38 (24.8)		
Grade 3	76 (34.1)	88 (40.7)				51 (33.3)	50 (32.7)		
Grade 4	51 (22.9)	42 (19.4)				44 (28.8)	41 (26.8)		
Grade 5	2 (0.9)	2 (0.9)				2 (1.3)	1 (0.7)		
CEA change after CRT,[d] No. (%)			0.01	.99	.95			0.09	.62
No worsening	213 (95.5)	206 (95.4)				146 (95.4)	143 (93.5)		
Worsening	10 (4.5)	10 (4.6)				7 (4.6)	10 (6.5)		
Postsurgical outcome									
1-y RFS (95% CI), %	91.7 (87.1-94.7)	90.7 (85.9-93.9)				91.3 (85.5-94.8)	91.5 (85.8-95.0)		
2-y RFS (95% CI), %	79.7 (73.4-84.6)	86.1 (80.6-90.1)				81.8 (74.3-87.2)	87.2 (80.6-91.6)		

Abbreviations: CEA, carcinoembryonic antigen; CRT, chemoradiotherapy; CT, computed tomography; EMVI, extramural venous invasion; MRI, magnetic resonance imaging; mrTRG, MR tumor regression grade; RFS, recurrence-free survival.

[a] Data are shown as the number of patients with percentages in parentheses unless specified otherwise. Propensity scores were calculated by a binary logistic regression model to predict the probability of each patient undergoing restaging CT using all 8 baseline characteristics (age through CEA change after CRT). An adequate model was obtained (*P* = .14 by the Hosmer-Lemeshow goodness-of-fit test) despite the lopsided distribution of pre-CRT cN, and propensity scores with and without pre-CRT cN were similar (Bland-Altman limits of agreement of −0.02 to 0.02). Area under the curve was 0.68 (95% CI, 0.65-0.75).

[b] *P* values for group comparisons were obtained using the independent *t*-test, Mann-Whitney *U* test, or χ^2 test as appropriate according to data types.

[c] Standardized weights and a robust estimator were used for the propensity score-based inverse weighting.

[d] Worsening was defined as normal (≤3 ng/mL)-to-abnormal conversion or increase in the abnormal range after CRT compared with the pre-CRT state.

124 days (median, 94 days) from the initial staging evaluation. The use of restaging abdominopelvic CT was at the discretion of attending physicians and distributed throughout the study without a remarkable time-trend. The restaging CT results were recorded regarding any detection of abdominopelvic lesions to suggest metastasis, and their true identities were determined by correlating them with findings at surgery, pathologic analyses, and further tests. In patients who underwent curative-intent surgery for rectal cancer as well as metastasis (when present), the postsurgical cancer recurrences or patient deaths of all causes and the time elapsed until such events from surgery were recorded. Recurred tumors were confirmed by histologic analysis when feasible or with PET/CT. In addition, baseline patient characteristics (**Table**) were collected. Diagnostic yield of restaging abdominopelvic CT, ie, per-patient rate of true-positive CT detection of abdominopelvic metastasis, was determined. The RFS rates after curative-intent surgery were compared between restaging CT and no-

restaging CT groups using Cox regression analysis combined with multivariable adjustment and inverse probability weighting and matching using propensity score (PS). We included the baseline characteristics mentioned above (Table) as covariates. *P* values <.05 were considered statistically significant.

Results | The diagnostic yield of restaging abdominopelvic CT was 2.2% (5 of 231 patients; 95% CI, 0.8%-5.1%), all as hepatic metastases treated with curative resection. Restaging abdominopelvic CT yielded false-positive findings in 3 patients (1.3%; 95% CI, 0.3%-3.9%), causing unnecessary hepatic resection, radiofrequency ablation, and follow-up liver MRI. When patients who had pre-CRT extramural venous invasion, MR tumor regression grade 4 to 5, or worsening of carcinoembryonic antigen after CRT were considered, the yield was 5.1% (4 of 78; 95% CI, 1.6%-12.9%). The RFS was not significantly different between the restaging CT (followed postoperatively for 1-74 months) and no-restaging CT (followed postoperatively for 1-70 months; reference) groups: hazard ratios of 1.20 (95% CI, 0.78-1.84) for multivariable-adjusted regression, 1.14 (95% CI, 0.74-1.76) for PS-based inverse probability weighting, and 1.10 (95% CI, 0.68-1.77) for PS matching.

Discussion | Despite benefits in a small fraction of patients, performing restaging abdominopelvic CT routinely before surgery after CRT for locally advanced rectal cancer is not beneficial if a thorough initial staging evaluation excluded metastasis. It had low diagnostic yield, comparable risk of harm, and no apparent gains in postsurgical RFS (possibly harmful or, at most, modest beneficial effect). Further studies are needed to identify patients at high risk of developing metastasis during CRT for whom restaging abdominopelvic CT could be indicated. Nonrandomized observational design was a study limitation.

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