Master's Thesis of June Suh

Diagnostic Performance of Dedicated High-resolution Rectal CT for Rectal Cancer Staging:

Comparative Results with High-Resolution MRI

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Graduate School of College of Medicine
Seoul National University
Radiology Major

June Suh

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Se Hyung Kim

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Graduate School of College of Medicine
Seoul National University
Radiology Major

June Suh

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June Suh
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Abstract

Objectives: To compare the diagnostic performance of high-resolution CT in preoperative rectal cancer staging to conventional CT, with high-resolution MRI results as gold standard.

Methods: Fifty-one patients who underwent both CT and MRI with rectum distension for preoperative rectal cancer staging were enrolled. High-resolution CT images were obtained with a quadrupled matrix size and oblique multiplanar reconstruction. Two radiologists compared the diagnostic performance of T staging, extramural depth of invasion (EMD), ≤T2/≥T3, extramural venous invasion (EMVI), mesorectal LN metastasis between conventional and high-resolution CT, considering MRI results as gold standard. Results were compared using the Chi-square test, Fisher's exact test, linear weighted kappa, ROC analysis, and Pearson's correlation coefficients.

Results: Compared to conventional CT, high-resolution rectal CT showed higher accuracy in T staging (reviewer 1, 82.4% vs. 76.5% [P=0.463]; reviewer 2, 82.4% vs. 62.7% [P=0.027]) and better correlation to MRI results (weighted kappa; reviewer 1, 0.89 vs. 0.83; reviewer 2, 0.82 vs. 0.64 [Ps<0.001]). In categorizing ≤T2/≥T3, high-resolution CT showed better correlation with MRI than conventional CT (weighted kappa; reviewer 1, 0.87 vs. 0.78; reviewer 2, 0.74 vs. 0.57). Reviewer 2 yielded better correlation to MRI in high-resolution CT than conventional CT in EMD (Pearson's coefficient; 0.97 vs 0.91) and EMVI (weighted kappa; 0.78 vs 0.47), while the difference was minimal in reviewer 1. Accuracy of mesorectal LN metastasis did not significantly differ between both CT modalities.

Conclusion: High-resolution rectal CT showed better performance in the T staging of rectal cancers than conventional CT, considering high-resolution MRI as gold standard.

Keyword : Rectal cancer, High-resolution Computed Tomography
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Chapter 1. Introduction

1.1. Study Background

Colorectal cancer is the fourth most frequently diagnosed cancer in the world, with rectal cancer contributing to one-third of all cases [1, 2]. Accurate clinical staging is critical for determining individualized optimal treatment strategies since local staging information is used to stratify patients who would benefit from neoadjuvant therapy and to predict the extent of surgery [3, 4]. Rectal MRI plays an essential role in preoperative imaging of rectal cancer, as it provides accurate images of the depth of tumor penetration; thereby, facilitating the prediction of circumferential resection margin (CRM) by clearly depicting the mesorectal fascia (MRF) [5-8]. Recently, standardized report forms have been developed in rectal MRI to systematically evaluate essential imaging features that guide optimal patient management, including tumor location, extramural depth (EMD) of tumor invasion, presence of extramural venous invasion (EMVI), and mesorectal/extra-mesorectal lymph node (LN) spread [9, 10].

Contrast-enhanced CT is a widely available modality for rectal cancer patients. However, CT is not currently recommended as an initial modality for local staging of rectal cancer, as it has shown limited accuracy in determining the depth of local invasion [5, 6] and lower sensitivity in predicting the CRM status and LN involvement than MRI [6, 11]. These limitations may be attributed to its low soft-tissue contrast and low spatial resolution, which obscures the rectal wall layers and makes delineating the MRF difficult [6]. Recently, an ultra-high-resolution CT has been introduced to improve spatial resolution in clinical lung imaging, with larger matrix sizes in the x and y axes (1024×1024 and 2048×2048), compared to the conventional 512×512 matrices [12, 13]. High-resolution CT has been reported to provide anatomical details with doubled or quadrupled precision compared to

conventional CT [12, 13]. Furthermore, the application of rectal distension prior to MRI examination has been introduced as a safe and effective tool for better tumor visualization [14–16]. A recent study has adopted the use of sonographic gel for rectal distension before CT examination, showing better results in T staging compared with CT without rectal distension [17]. In addition, compared to rectal MRI, which provides oblique coronal and axial MR images perpendicular to the rectal curve, CT images are routinely reconstructed in orthogonal coronal and axial planes. Therefore, an exact measurement of extramural tumor depth or distance from the tumor to the MRF cannot be performed using these orthogonally reconstructed CT images. Therefore, we hypothesized that a dedicated high-resolution rectal CT that applies higher spatial resolution (1024×1024 matrix), rectal distention using sonographic gel, and oblique axial and coronal reconstruction may improve the diagnostic performance of CT for rectal cancer staging. However, to the best of our knowledge, no studies have addressed this issue.

1.2. Purpose of Research

Therefore, this study aimed to compare the diagnostic performance of high-resolution CT to conventional CT images in preoperative rectal cancer staging using high-resolution rectal MRI results as the gold standard.

Chapter 2. Materials and Methods

This study was approved by the institutional review board of our institution, and the requirement for informed consent was waived due to the retrospective nature of this study.

2.1. Patient Selection

Between November 2019 and March 2021, 97 patients with pathologically proven rectal adenocarcinomas who underwent both CT using high-resolution mode and high-resolution rectal MRI for preoperative rectal cancer staging were included in our study. The exclusion criteria were as follows: (1) > 1-month time interval between CT and MRI (n=5), (2) pathologies other than adenocarcinomas such as neuroendocrine tumor or lymphoma (n=36), and (3) rectal distension or high-resolution image reconstruction not performed on dedicated rectal CT (n=5). Finally, 51 patients were enrolled in the study. Twenty-seven patients received neoadjuvant concurrent chemoradiotherapy, while 24 patients received upfront curative-intent surgery.

2.2. CT techniques

All patients underwent rectal distension before CT examination. They were asked to lie in the right lateral decubitus position with their knees crouched, and approximately 100-150mL of sonographic gel was gently administered through the anus using an enema syringe [17]. After rectal distention, MDCT examination was performed in the supine position with one of the three 128 detector-row CT scanners using high-resolution mode (Ingenuity Elite, Philips [n=49]; IQon, Philips [n=1]; and Brilliance iCT, Philips [n=1]). CT images were obtained using the following acquisition parameters: detector configuration, 0.625 mm; helical pitch, 0.80–1.22; rotation time, 0.5–0.83 s; tube voltage, 100–120 kV; tube current, 100–250 mAs; and slice thickness, 2 mm. CT

images were reconstructed at 2-mm intervals. Portal phase contrast-enhanced CT images were acquired after intravenous administration of an iodinated contrast agent at a concentration of 370 mg·L/mL at a dose of 1.5 mL/kg body weight and a rate of 3–5 mL/s f or 30 s using an automatic power injector. For the portal phase scan, a fixed delay of 70 s was used. For all CT phases, scanning was performed from the dome of the liver to the upper thigh, sufficiently covering the anal verge.

CT images were reconstructed from the raw data according to two different protocols: conventional CT and high-resolution rectal CT. Conventional CT images were reconstructed with a reconstruction matrix of 512×512 pixels and a field-of-view (FOV) of 280×280mm^2–400×400mm^2 in orthogonal axial, coronal, and sagittal planes. In-plane resolution of these conventional CT images ranges 0.55×0.55mm^2–0.84×0.84mm^2 according to patients' body size. For high-resolution dedicated rectal CT images, images were reconstructed with a higher reconstruction matrix of 1024×1024 pixels and a narrower FOV of 123×123mm^2–235×235mm^2, with an in-plane resolution ranging from 0.12×0.12mm^2–0.23×0.23mm^2. Furthermore, axial and coronal images for high-resolution CT were reconstructed perpendicular or parallel to the long axis of the rectal lumen, analogous to the multiplanar acquisition of rectal MRI.

2.3. MRI techniques

All rectal MRI images were obtained using a 3-T MRI scanner (Ingenia CX, Philips) using a standard imaging protocol [15]. Patients underwent bowel preparation with a bisacodyl suppository (Dulcolax, Boehringer Ingelheim) 1 h before image acquisition. Twenty milligrams of scopolamine butylbromide (Buscopan, Boehringer Ingelheim) was then intravenously injected 30 min before scanning to minimize bowel peristalsis unless contraindicated. Moreover, approximately 150 mL of a sonographic gel was inserted through the anus just before the MRI examination [15]. Acquisition

parameters were as follows: repetition time, 3500 ms; echo time, 100 ms; slice thickness, 3 mm; flip angle, 90°; FOV, 240×240 mm^2; and matrix, 480×400. T2-weighted fast-spin echo sequences with multiplanar images (orthogonal sagittal in addition to oblique axial and oblique coronal images perpendicular or parallel to the long axis of the rectum, respectively) were obtained.

2.4. Image analysis

Conventional CT, high-resolution dedicated rectal CT, and high-resolution MRI images were independently evaluated by two abdominal radiologists with 13 and 8 years of experience in abdominal imaging, respectively. The following items were analyzed: T staging, EMD of tumor invasion, the presence of EMVI, and the presence of mesorectal LN metastasis. For T staging, reviewers were asked to report their confidence level in classifying the tumor stage into either ≤T2 or ≥T3, and ≤T3b or ≥T3c, respectively, on a 5-point scale: 1, definitely ≤T2/≤T3b; 2, probably ≤T2/≤T3b; 3, possibly ≥T3/≥T3c; 4, probably ≥T3/≥T3c; 5, definitely ≥T3/≥T3c. A score of ≥3 was chosen as the cutoff point for defining ≥T3 or ≥T3c. T staging was categorized into T0, T1, T2, T3, T4a, and T4b according to the International Union against Cancer/ the American Joint Committee on Cancer staging system. T3 stage was subdivided into T3a (<1 mm), T3b (1–5 mm), T3c (> 5–15 mm), and T3d (>15 mm) based on the EMD of tumor invasion. Radiologists also graded the presence of EMVI on a 5-point scale: 1, definitely EMVI negative; 2, probably EMVI negative; 3, possibly EMVI positive; 4, probably EMVI positive; 5, definitely EMVI positive. A score of ≥3 was chosen as the cutoff point for defining the presence of EMVI.

2.5. Pathologic analysis

Histopathologic diagnosis, histological grade, pathologic T and N stages, EMD, and the presence of EMVI were analyzed by a board-

certified gastrointestinal pathologist with 5-year of experience.

2.6. Statistical analysis

For all 51 patients, diagnostic performance regarding T staging, EMD, and mesorectal LN metastasis were compared between conventional CT and high-resolution dedicated rectal CT with high-resolution MRI as the gold standard using the chi-square test, Pearson's correlation test, and Fisher's exact test, respectively. Inter-modality agreement between CT and MRI was tested in terms of T staging (T1–T4b) and the presence of EMVI (on a 5-point scale) using linear weighted kappa statistics. The decision criteria for weighted kappa values were as follows: 0–0.20, slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial; and 0.81–1 as almost perfect agreement [16].

Diagnostic performance in differentiating ≤T2 vs. ≥T3, ≤T3b vs. ≥T3c, and the presence of EMVI were compared between conventional CT and high-resolution rectal CT using a ROC curve analysis with high-resolution MRI results as the gold standard.

For a subset of 24 patients who underwent surgery without CCRT, concordance rates of conventional CT, high-resolution rectal CT, and high-resolution MRI with histopathologic results were evaluated regarding T stage, the presence of mesorectal LN metastasis, and EMVI. P values were calculated between CT (conventional or high-resolution CT) and high-resolution MRI using Fisher's exact test. The EMD of tumor invasion was compared with the pathologic results using Spearman's correlation test.

All statistical analyses were performed using SPSS version 26 for Windows (SPSS Inc.) and MedCalc statistical software (version 19.6; MedCalc Software). Statistical significance was set at $P < 0.05$.

Chapter 3. Results

3.1. Patients

Patients' demographics and clinical information are described in Table 1. Of the 51 patients enrolled in our study, 35 were men and 16 were women, and mean age was 62.1 (30-88) years. Mean interval between CT and MRI was 3.1 (0-15) days. Regarding tumor location, 8 (15.6%) were in the upper rectum, 26 (50.1%) in the mid rectum, and 17 (33.3%) in the lower rectum.

24 patients received one of the following upfront curative-intent surgery: low anterior resection (n=19), transanal excision (n=2), ultralow anterior resection (n=1), abdominoperineal resection (n=1), and intersphincteric resection (n=1). Location of tumor was classified as the following: 6 (25.0%) in the upper rectum, 15 (62.5%) in the mid rectum, and 3 (12.5%) in the lower rectum. Distribution of pathologic T stage and N stage are provided in Table 1.

3.2. Results for all 51 patients with MRI as the gold standard

For T staging, high-resolution CT provided better accuracy than conventional CT in both reviewers (82.4% vs. 76.5% for reviewer 1 [P=0.463] and 82.4% vs. 62.7% for reviewer 2 [P=0.027]), and the difference was statistically significant in reviewer 2 (Table 2). On weighted kappa statistics, high-resolution rectal CT showed almost perfect agreement with high-resolution MRI in both reviewers (weighted kappa value: 0.89 for reviewer 1 and 0.82 for reviewer 2), whereas substantial agreement was shown between conventional CT and rectal MRI in reviewer 2 (weighted kappa value: 0.83, reviewer 1 and 0.64 for reviewer 2, respectively) (Table 2). Weighted kappa values were significantly higher on high-resolution CT by both reviewers (P<0.001).

For differentiating ≤T2 and ≥T3, high-resolution CT showed

better agreement with high-resolution MRI compared to conventional CT in both reviewers (weighted kappa values: 0.87 vs 0.78 for reviewer 1 and 0.74 vs 0.57 for reviewer 2) (Table 3). On ROC analysis, AUC values were higher in high-resolution CT compared to conventional CT in both reviewers (0.89 vs 0.79 for reviewer 1 [P=0.057] and 0.94 vs 0.90 for reviewer 2 [P=0.041]). The difference was statistically significant according to reviewer 2 (P=0.041) (Table 3). In terms of differentiation between ≤T3b and ≥T3c, compared to conventional CT, high-resolution CT provided better agreement (weighted kappa value: 0.78, vs. 0.62) with rectal MRI and a significantly higher AUC value (0.97 vs 0.85, P=0.030) in reviewer 2 (Table 3). However, similar agreement and insignificantly higher AUC were noted on high-resolution CT in reviewer 1.

For the measurement of EMD of tumor invasion, high-resolution CT showed slightly better agreement with rectal MRI compared to conventional CT in both reviewers (Pearson's correlation coefficient: 0.98 vs 0.97 for reviewer 1 and 0.97 vs 0.91 for reviewer 2).

For the determination of EMVI, high-resolution rectal CT provided better agreement with high-resolution MRI compared to conventional CT in both reviewers (weighted kappa values: 0.88 vs. 0.85 for reviewer 1 and 0.78 vs. 0.47 for reviewer 2) (Table 3). On ROC analysis, the AUC value of high-resolution rectal CT was higher in reviewer 2 (1.0 vs 0.79, P=0.008), with a statistical difference (Table 3).

In terms of estimating mesorectal LN metastasis, high-resolution rectal CT provided a higher concordance rate with rectal MRI compared to conventional CT in both reviewers (98.0% vs. 96.1% for reviewer 1 [P=1.0] and 98.0% vs. 88.2% for reviewer 2 [P=0.109]); however, the difference was not statistically significant.

3.3. Results for 24 patients with pathology as gold standard

In a subset of 24 patients who underwent upfront surgery without neoadjuvant CCRT, the final pathologic T stages consisted of pT1 in four patients, pT2 in six, pT3a in one, pT3b in eight, pT3c in four, and pT3d in one patient. Pathologic N stage was diagnosed as pN0 in 15 patients, pN1 in six, and pN2 in three patients (Table 1).

Regarding T staging, concordance rates of conventional CT and high-resolution CT to pathologic results were lower than those of high-resolution MRI for both reviewers (reviewer 1: 58.3% [14/24] for conventional CT, 58.3% [14/24] for high-resolution CT, 75.0% [18/24] for rectal MRI; reviewer 2: 33.3% [8/24], 37.5% [9/24], 45.8% [11/24]). However, there was no statistical difference between MRI and both conventional and high-resolution CT (P=0.778, P=0.778, reviewer 1, P=0.560, and P=0.784 for reviewer 2) (Table 4). Regarding the added value of high-resolution CT in T staging, reviewer 2 accurately categorized T staging in one more patient on high-resolution CT (9/24) compared to conventional CT (8/24). Cross-tables between conventional CT, high-resolution CT, high-resolution MRI and pathologic results are provided in Supplementary Material (Table E1).

When EMD measurements were compared with pathologic results, Spearman's correlation coefficients were identical among the three imaging modalities in reviewer 1, while high-resolution CT showed the best correlation among the three modalities in reviewer 2 (reviewer 1: 0.90 for conventional CT, 0.90 for high-resolution CT, and 0.90 for rectal MRI [all P<0.001]; reviewer 2: 0.45 [P=0.039], 0.57 [P=0.015], 0.47 [P=0.010]) (Table 4).

In terms of mesorectal LN evaluation, there were no significant differences among the three modalities by either reviewer (Table 4). The concordance rates of EMVI between imaging and pathologic results were identical among the three modalities in reviewer 1 (87.5% [21/24]), while reviewer 2 showed slightly better accuracy

with high-resolution CT (87.5%, 21/24) and high-resolution MRI (87.5%, 21/24) compared to conventional CT (79.2%, 19/24) (Table 4). When concordance rates of two CT modalities were compared to those of high-resolution MRI, there was no statistical difference in evaluating mesorectal LN (P=1.0 for conventional CT and P=1.0 for high-resolution CT in reviewer 1; P=1.0 and P=1.0 in reviewer 2) and EMVI (P=1.0 and P=1.0 in reviewer 1; P=0.701 and P=1.0 in reviewer 2) (Table 4).

Chapter 4. Discussion

In our study, a dedicated, high-resolution rectal CT showed a better diagnostic performance in terms of T staging of advanced rectal cancer compared to conventional CT with a better correlation with high-resolution MRI interpretations. Although current National Comprehensive Cancer Network (NCCN) guidelines recommend dedicated rectal MRI as the primary modality for rectal cancer staging [5], its high cost, low availability and patient contraindications are considerable hurdles to its use in routine clinical practice. As our results indicate that the diagnostic accuracy of local T staging can be significantly enhanced using high-resolution reconstruction methods without further radiation exposure, we believe that a dedicated high-resolution rectal CT can be a reliable alternative modality in institutions where MRI is not available or in patients who are contraindicated for MRI.

We believe that such improved performance may be attributed to several technological advancements that we have implemented to enhance the spatial resolution of CT. By virtue of combining a quadrupled matrix size (1024×1024) and a narrower FOV setting (123×123–235×235mm^2), we were able to achieve a marked improvement in in-plane resolution (0.12×0.12–0.23×0.23mm^2) compared to that of conventional CT (0.55×0.55–0.84×0.84mm^2). Moreover, oblique multiplanar reconstruction (MPR) images, which were referred to as the centerline of the rectal lumen, may be responsible for the better diagnostic performance of dedicated rectal CT compared to conventional orthogonally reconstructed CT. Although the current National Comprehensive Cancer Network guidelines do not recommend CT as a modality for local staging [5], a number of studies involving recent advances in MDCT and MPR have suggested that CT may be reliable for local T staging of advanced rectal cancers [18, 19]. Additionally, we believe that the application of ultrasound gel to distend the rectal lumen may play a positive role in improving the performance of CT. Several recent

publications have proved this method to be cheap, non-invasive, and effective for rectal cancer staging [14, 15, 17]. As our study has shown encouraging results in improving the accuracy of T staging, combining recent technical advances such as high in-plane spatial resolution and oblique MPR may increase the feasibility of CT as a primary modality for rectal cancer staging.

In terms of differentiating ≤T2 and ≥T3, high-resolution CT also showed superior performance to conventional CT when a 5-point confidence score was used. Similar results were shown in the dichotomized results with marginal statistical significance. These results imply that high-resolution CT may influence the reader's conspicuity in delineating the outer rectal wall and determining the presence of perirectal tumor infiltration. Considering that current clinical guidelines recommend neoadjuvant CCRT for advanced rectal cancers with ≥cT3 or N+ [5], an exact differentiation between ≤T2 and ≥T3 becomes critical and may alter patients' management plans. In this regard, a better performance of high-resolution rectal CT for differentiation between ≤T2 and ≥T3 could correctly induce an exact clinical decision. A similar trend was observed for the differentiation between ≤T3b and ≥T3c in our study. In one of the two reviewers, high-resolution CT provided a significantly enhanced diagnostic performance in determining ≤T3b from ≥T3c using both a 5-point confidence scale and a dichotomized method. We believe that this result could also have an important clinical impact on patients' care, as rectal cancers with ≥T3c have a drastically lower survival rate than those with ≤T3b [17, 18].

We also found that high-resolution CT showed a slight improvement in quantitative EMD measurement, with a slightly better agreement with high-resolution MRI, compared to conventional CT in both reviewers. This result might be noteworthy as the sub-categorization of the clinical T3 stage based on EMD measurement serves as a direct prognostic indicator for patient survival [20]. We speculate that a marked improvement in in-plane resolution and oblique coronal or axial reconstruction along or

perpendicular to the rectum centerline may be responsible for such better results in high-resolution rectal CT.

As expected, high-resolution rectal CT did not show significantly better performance for N staging than conventional CT. Furthermore, there are no established CT criteria other than size to predict metastatic LNs. However, considering that morphologic criteria such as irregular border and heterogeneous signal intensity of LNs on rectal MRI indicate metastatic LNs and showed an improved diagnostic accuracy for determining LN metastasis [21], similar attempts using high-resolution CT such as border characteristics and enhancement patterns may be a future topic of research in high-resolution rectal CT.

In our study, a dedicated high-resolution rectal CT also provided better results for determining EMVI with statistical significance in one of the two reviewers. We believe that this result deserves special consideration as radiologically detected EMVI is a well-known prognostic factor related to disease-free and overall survival [22]. Considering that low kVp CT can enhance iodine contrast agents within the vessels, a low-kVp dedicated rectal CT may further improve the diagnostic accuracy for determining EMVI. Thus, future research using low-kVp CT with or without deep learning-based iterative reconstruction is strongly recommended.

In the current study, there was a considerable discrepancy between the two reviewers' diagnostic performances of both conventional and high-resolution CT. With high-resolution CT, reviewer 2 showed a significantly improved accuracy in T staging (82.4% vs. 62.7%) and more dramatically improved accuracy compared to reviewer 1's results (82.4% vs 76.5%). Furthermore, reviewer 2 showed improved conspicuity and accuracy in differentiating ≤T3b from ≥T3c as well as in determining the presence of EMVI. However, reviewer 1 did not show any significantly improved results for those items. We believe that this discrepancy between the reviewers might be related to the different level of experience. Indeed, because reviewer 1 has a longer experience in abdominal imaging (more specifically, rectal cancer

imaging) than reviewer 2, the benefit of high-resolution CT imaging may have been underestimated. Considering that diagnostic performance of high-resolution dedicated rectal CT can be more dramatically improved in less experienced reviewers, we believe that our results can provide a promising result for less experienced or novice radiologists who have a lower level of experience in rectum-dedicated imaging.

We acknowledge several limitations of our study. First, our study population was small, and there might have been selection bias due to strict inclusion criteria. In this study, we included only patients who had undergone both preoperative rectal CT and MRI; therefore, many patients, particularly those with early-stage cancers who did not undergo preoperative MRI, were excluded. Second, a comparison between imaging (CT or MRI) and histopathology was not performed in all patients. Instead, CT images were compared with rectal MRI. We believe that such a study design comparing CT with MRI was inevitable as a large number of patients with locally advanced stage (≥T3) cancers underwent neoadjuvant CCRT, making it impossible to compare imaging with pathologic results. Third, as we recruited two expert abdominal radiologists for image review, the added value of high-resolution CT over conventional CT may have been underestimated. Therefore, further studies recruiting more radiologists, including less experienced or novice radiologists, may help generalize our results. Finally, although we obtained oblique MPR images that were parallel or perpendicular to the long axis of the rectum for high-resolution rectal CT, we did not consider the curved nature of the rectum. To circumvent this limitation, a curved MPR regarding the actual centerline of the curved rectum is required.

In conclusion, compared to conventional CT, a dedicated high-resolution rectal CT with quadrupled matrix size, oblique MPR, and rectal distension with ultrasound gel showed better diagnostic performance for determining T staging, EMD measurement, and EMVI in advanced rectal cancer using high-resolution MRI as the gold standard.

Tables

Table 1. Patients' Demographics and Clinical Information

		All patients (n=51)	Patients with surgery without CCRT (n=24)
M:F		35:16	18:6
Mean age (years, range)		62.1 (30 – 88)	63.0 (34 – 88)
Mean interval between CT and MRI (days, range)		3.1 (0 – 15)	1.9 (0 – 7)
Location of tumor	Upper rectum	8 (15.6%)	6 (25.0%)
	Mid rectum	26 (50.1%)	15 (62.5%)
	Lower rectum	17 (33.3%)	3 (12.5%)
Operation method			Low anterior resection (n=19) Transanal excision (n=2) Ultralow anterior resection (n=1) Abdominoperineal resection (n=1) Intersphincteric resection (n=1)
Pathologic T stage			pT1 (n=4) pT2 (n=6) pT3a (n=1) pT3b (n=8) pT3c (n=4) pT3d (n=1)
Pathologic N stage			pN0 (n=15) pN1 (n=6) pN2 (n=3)

Table 2. Comparative Results between Conventional CT and High-resolution Rectal CT for T Staging with MRI as Gold Standard in All 51 Patients

			High-resolution MRI																	P value
			T1	T2	T3a	T3b	T3c	T3d	T4a	T4b			T1	T2	T3a	T3b	T3c	T3d	T4a	T4b	
Reviewer 1	Conventional CT	T1	**3**	0	0	0	0	0	0	0	High-resolution CT	T1	**3**	0	0	0	0	0	0	0	
		T2	1	**5**	1	0	0	0	0	0		T2	1	**8**	1	0	0	0	0	0	
		T3a	0	3	**1**	0	0	0	0	0		T3a	0	2	**2**	0	0	0	0	0	
		T3b	0	3	2	**11**	0	0	0	0		T3b	0	1	1	**11**	1	0	0	0	
		T3c	0	0	0	1	**14**	0	0	0		T3c	0	0	0	1	**13**	0	0	0	
		T3d	0	0	0	0	1	**3**	0	0		T3d	0	0	0	0	1	**3**	0	0	
		T4a	0	0	0	0	0	0	**0**	0		T4a	0	0	0	0	0	0	**0**	0	
		T4b	0	0	0	0	0	0	0	**2**		T4b	0	0	0	0	0	0	0	**2**	
	Accuracy*		76.5% (39/51)										82.4% (42/51)								0.463
	Kw†		0.83										0.89								*<0.001*
			T1	T2	T3a	T3b	T3c	T3d	T4a	T4b			T1	T2	T3a	T3b	T3c	T3d	T4a	T4b	
Reviewer 2	Conventional CT	T1	**0**	0	0	0	0	0	0	0	High-resolution CT	T1	**0**	0	0	0	0	0	0	0	
		T2	1	**6**	1	3	0	0	0	0		T2	1	**6**	0	0	0	0	0	0	
		T3a	0	1	**0**	0	0	0	0	0		T3a	0	0	**1**	1	0	0	0	0	
		T3b	0	0	2	**9**	0	0	0	0		T3b	0	1	2	**19**	1	0	0	0	
		T3c	0	0	0	7	**11**	0	0	0		T3c	0	0	0	1	**10**	0	0	0	
		T3d	0	0	0	0	0	**4**	0	0		T3d	0	0	0	0	0	**4**	0	0	
		T4a	0	0	0	0	0	0	**0**	0		T4a	0	0	0	0	0	0	**0**	0	
		T4b	0	0	0	2	2	0	0	**2**		T4b	0	0	0	0	2	0	0	**2**	
	Accuracy*		62.7% (32/51)										82.4% (42/51)								*0.027*
	Kw†		0.64										0.82								*<0.001*

* Accuracy was compared using the Chi-square test. † The weighted kappa values were calculated using weighted kappa statistics. Numbers in **bold** indicate concordant results between the two modalities. P values in ***bold and italic*** indicate statistically significant results.

Table 3. Comparative Results between Conventional CT and High-resolution Rectal CT for T Staging and EMVI with MRI as Gold Standard in All 51 Patients

		Reviewer 1			Reviewer 2		
		Conventional CT	High-resolution CT	P value	Conventional CT	High-resolution CT	P value
≤T2 vs ≥T3	Kw*	0.78	0.87		0.57	0.74	
	AUC+	0.79	0.89	0.057	0.90	0.94	***0.041***
≤T3b vs ≥T3c	Kw*	0.94	0.94		0.62	0.78	
	AUC+	0.98	0.96	0.320	0.85	0.97	***0.030***
EMVI	Kw*	0.85	0.88		0.47	0.78	
	AUC+	1.0	1.0	1.0	0.79	1.0	***0.008***

* The weighted kappa values were calculated using weighted kappa statistics. † Area under the curve values were obtained using a receiver operating characteristic curve analysis. P values in ***bold and italic*** indicate statistically significant results. AUC=area under the receiver operating characteristics curve, EMVI=extramural venous invasion.

Table 4. Comparative Results of Conventional CT, High-resolution Rectal CT, and MRI with Pathologic Results as Gold Standard in 24 Patients

		Reviewer 1			Reviewer 2		
		Conventional CT	High-resolution CT	High-resolution MRI	Conventional CT	High-resolution CT	High-resolution MRI
T staging	Concordance rate*	58.3% (14/24)	58.3% (14/24)	75.0% (18/24)	33.3% (8/24)	37.5% (9/24)	45.8% (11/24)
	P value†	0.778	0.778		0.560	0.784	
EMD‡		0.90 (P<0.001)	0.90 (P<0.001)	0.90 (P<0.001)	0.45 (P=0.039)	0.57 (P=0.015)	0.47 (P=0.010)
Mesorectal LN metastasis	Concordance rate*	75.0% (18/24)	79.2% (19/24)	79.2% (19/24)	62.5% (15/24)	58.3% (14/24)	58.3% (14/24)
	P value†	1.0	1.0		1.0	1.0	
EMVI	Concordance rate*	87.5% (21/24)	87.5% (21/24)	87.5% (21/24)	79.2% (19/24)	87.5% (21/24)	87.5% (21/24)
	P value†	1.0	1.0		0.701	1.0	

* Concordance rates were determined between imaging (CT or MRI) and pathologic results. † P values were calculated between CT (conventional or high-resolution CT) and high-resolution MRI using the Fisher's exact test. ‡ For EMD, values were Spearman's correlation coefficients between imaging and pathologic results. EMD=extramural depth of tumor invasion, LN=lymph node, EMVI=extramural venous invasion.

Figures and Legends

Figure 1. A 37-year old man with rectal cancer. **A.** Conventional coronal CT shows a focal enhancing wall thickening (arrow) at the upper rectum. Note a clear and smooth outer margin of the lesion. Two radiologists staged this lesion as T2 on conventional CT. **B.** On high-resolution coronal rectal CT reconstructed along the perpendicular plane to the center of the rectum, there is a contour bulging of the tumor (arrow). Two radiologists measured the extramural depth of the tumor as 4.3 mm and staged this lesion as T3b. **C.** On high-resolution coronal rectal MRI, an exophytic tumor bulging (arrow) is noted. Two radiologists measured the extramural depth of the tumor as 4.5 mm and staged this lesion as T3b. The patient has undergone laparoscopic low anterior resection. **D.** On microscopic histologic specimen (hematoxylin & eosin stain, original magnification 5X), a 2.7 cm ulcerofungating moderately-differentiated adenocarcinoma (arrows) is demonstrated. The pathologist measures the extramural depth of the tumor as 4.0 mm and finally stages this lesion as pT3b.

Figure 1 (A-D).

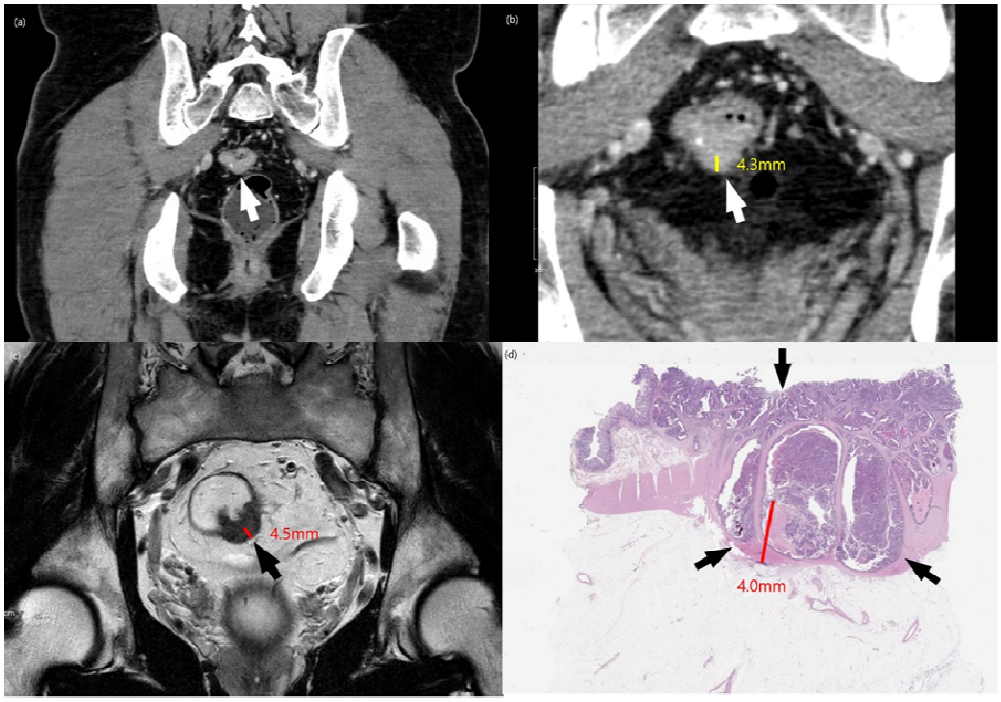


Figure 2. A 74-year old woman with rectal cancer. **A.** Conventional axial CT shows a focal enhancing wall thickening (arrow) from 4 o' clock to 7 o' clock of the rectum. Note subtle perirectal infiltration (arrowheads) around the lesion. Two radiologists stage this lesion as T3a or T3b on conventional CT. **B.** On high-resolution axial rectal CT reconstructed along the perpendicular plane to the center of the rectum, the outer margin of the tumor appears to be clear (arrowheads). Moreover, the two radiologists stage this lesion as T2. **C.** On high-resolution axial rectal MRI, the tumor (arrow) is confined to the intramural portion of the rectum, showing the clear outer margin of the rectum (arrowheads). Two radiologists also stage this lesion as T2.

Figure 2 (A-C).

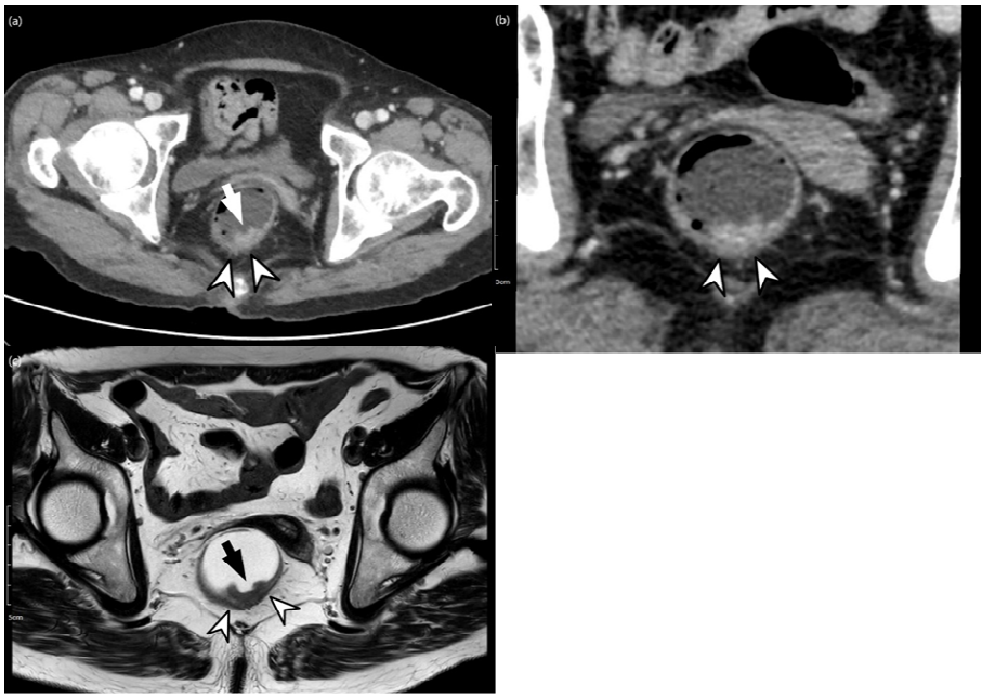


Figure 3. A 64-year old woman with rectal cancer. **A.** Conventional coronal CT shows an ulceroinfiltrative wall thickening (arrow) at the rectum. There are suspicious peritumoral spiculations. Two radiologists score 3 (possibly present) for extramural venous invasion (EMVI) on conventional CT. **B.** On high-resolution coronal rectal CT reconstructed along the perpendicular plane to the center of the rectum, a curvilinear tumor density (arrowheads) is demonstrated around the tumor (arrow). Therefore, the confidence score for EMVI is upgraded to 4 (probably present) by two radiologists on high-resolution CT. **C.** High-resolution coronal rectal MRI also clearly depicts a curvilinear tumor signal (arrowheads) extended from the main tumor (arrow). Two radiologists score 4 or 5 (definitely present) for EMVI on high-resolution rectal MRI. The patient has received neoadjuvant chemoradiation therapy and has undergone subsequent laparoscopic abdominoperineal resection. **D.** On microscopic histologic specimen (hematoxylin & eosin stain, original magnification 5x), a 6 cm moderately-differentiated adenocarcinoma (arrows) is diagnosed with a stage of ypT3bN0. EMVI is reported to be present (arrowheads).

Figure 3 (A–D).

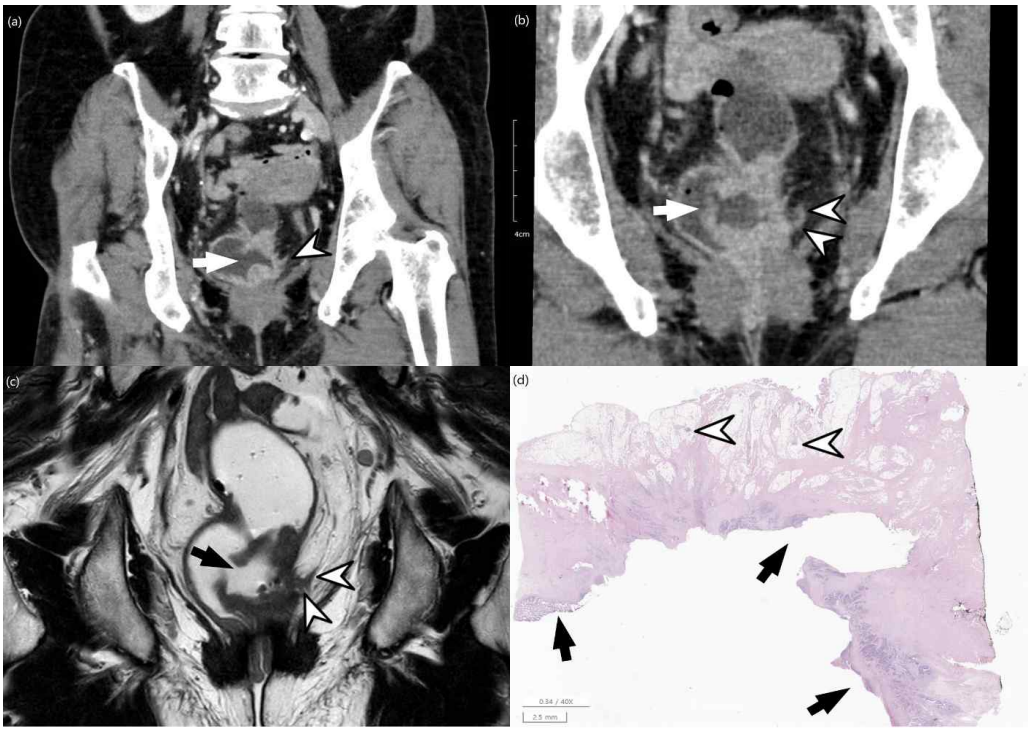
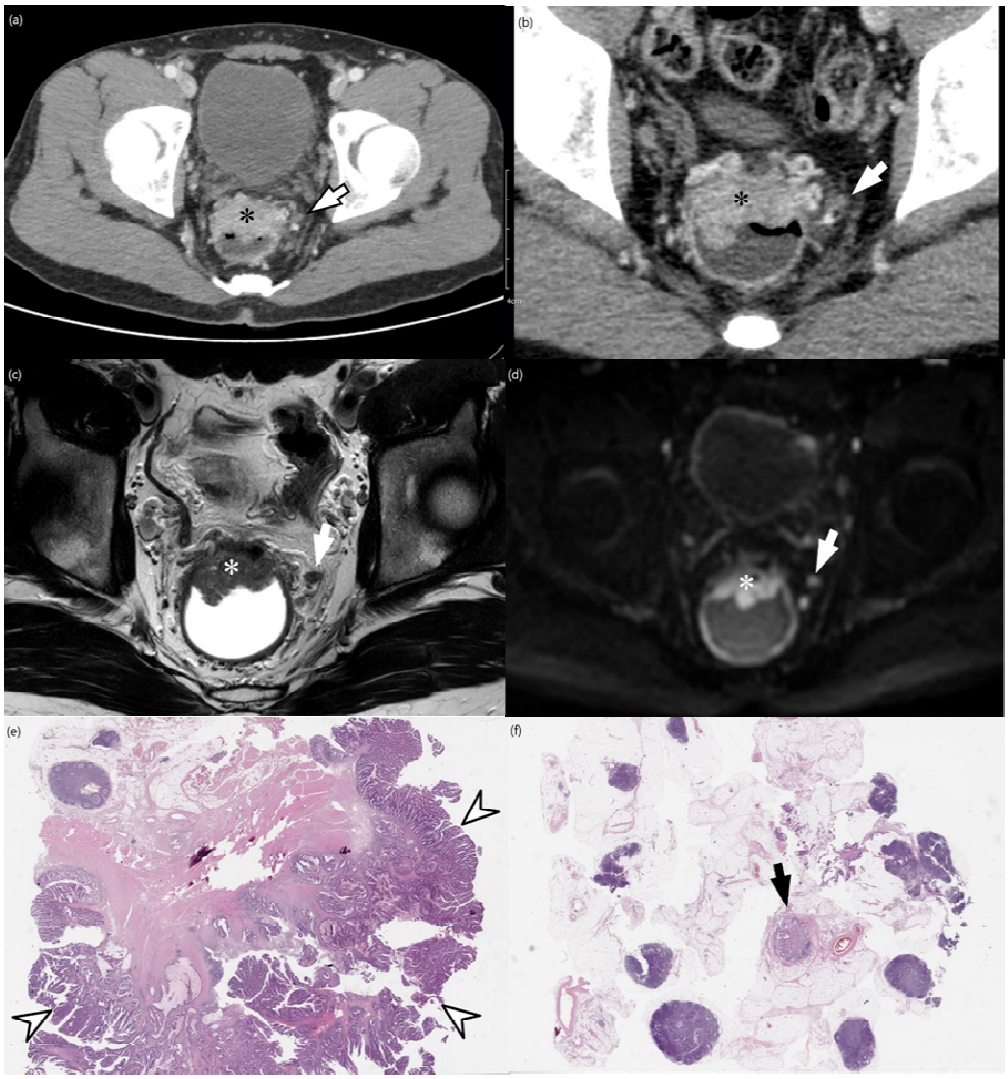


Figure 4. A 40-year old man with rectal cancer. **A.** Conventional axial CT shows an enhancing wall thickening (*) at the rectum. A small suspicious ovoid lymph node (LN, arrow) is found at the perirectal area. **B.** On high-resolution axial rectal CT, an enhancing rectal wall thickening (*) and a suspicious ovoid perirectal LN are well demonstrated. Two radiologists mark this lesion as a metastatic perirectal LN on both conventional and high-resolution CT images. **C.** On a T2-weighted axial image of high-resolution rectal MRI, a polypoid rectal mass (*), as well as a perirectal LN (arrow), are depicted. Note the subtle spiculated margin of the LN (arrow), which strongly suggests the malignant nature of the LN. **D.** An axial diffusion-weighted MRI (b=1000) shows marked diffusion restriction on both primary rectal tumor (*) and perirectal LN (arrow). Laparoscopic low anterior resection with total mesorectal excision is performed. **E.** On microscopic histologic specimen (hematoxylin & eosin stain, original magnification 5x), a 5 cm moderately-differentiated adenocarcinoma (arrowheads) is diagnosed. F. Among 25 harvested LNs, there is one metastatic perirectal LN (arrow). The final pathologic staging is pT2N1a.

Figure 4 (A-F).



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Supplementary Material

Table E1. Comparative Results among Conventional CT, High-resolution Rectal CT, and Rectal MRI for T Staging with Pathologic Results as Gold Standard in 24 Patients

		Pathologic Results																					
Reviewer 1			T1	T2	T3a	T3b	T3c	T3d			T1	T2	T3a	T3b	T3c	T3d			T1	T2	T3a	T3b	T3c	T3d
	Conventional CT	T1	**3**	0	0	0	0	0	High-resolution CT	T1	**3**	0	0	0	0	0	High-resolution MRI	T1	**4**	0	0	0	0	0
		T2	1	**3**	0	1	0	0		T2	1	**3**	0	1	0	0		T2	0	**6**	0	0	0	0
		T3a	0	2	**0**	0	0	0		T3a	0	2	**0**	0	0	0		T3a	0	0	**1**	1	0	0
		T3b	0	1	1	**4**	1	0		T3b	0	1	1	**4**	1	0		T3b	0	0	0	**4**	1	0
		T3c	0	0	0	3	**3**	0		T3c	0	0	0	3	**3**	0		T3c	0	0	0	3	**3**	1
		T3d	0	0	0	0	0	**1**		T3d	0	0	0	0	0	**1**		T3d	0	0	0	0	0	**0**
	Accuracy*	58.3% (14/24) (P=0.382)							Accuracy*	58.3% (14/24) (P=0.382)							Accuracy*	75.0% (18/24) (P=0.382)						
	Kw†	0.70 (P<0.001)							Kw†	0.70 (P<0.001)							Kw†	0.85 (P<0.001)						
Reviewer 2			T1	T2	T3a	T3b	T3c	T3d			T1	T2	T3a	T3b	T3c	T3d			T1	T2	T3a	T3b	T3c	T3d
	Conventional CT	T1	**0**	0	0	0	0	0	High-resolution CT	T1	**0**	0	0	0	0	0	High-resolution MRI	T1	**1**	0	0	0	0	0
		T2	2	**2**	0	2	2	0		T2	2	**2**	0	0	2	0		T2	1	**3**	0	0	2	0
		T3a	0	1	**0**	0	0	0		T3a	0	0	**0**	1	0	0		T3a	0	1	**0**	1	0	0
		T3b	1	2	0	**4**	1	0		T3b	1	3	1	**5**	1	0		T3b	1	1	1	**5**	1	0
		T3c	0	1	1	2	**1**	0		T3c	0	1	0	2	**1**	0		T3c	0	1	0	2	**1**	1
		T3d	0	0	0	0	0	**1**		T3d	0	0	0	0	0	**1**		T3d	0	0	0	0	0	**1**
		T4b	1	0	0	0	0	0		T4b	1	0	0	0	0	0		T4b	1	0	0	0	0	0
	Accuracy*	33.3% (8/24) (P=0.664)							Accuracy*	37.5% (9/24) (P=0.664)							Accuracy*	45.8% (11/24) (P=0.664)						
	Kw†	0.15 (P=0.25)							Kw†	0.20 (P=0.10)							Kw†	0.32 (P=0.01)						

* Accuracy was compared using the Chi-square test. † The weighted kappa values were calculated using weighted kappa statistics. Numbers in **bold** indicate concordant results between imaging and pathologic results.

국문초록

직장암 병기 설정에서 직장 전용 고해상도 전산화단층촬영기법의 진단능 평가: 직장 자기공명영상 결과와의 비교

목적: 직장암의 수술 전 병기 설정에서 고식적 CT와 비교하여 고해상도 CT (high-resolution CT)가 보다 나은 진단능을 보이는지, 고해상도 MRI 결과를 기준으로 하여 비교하고자 한다.

대상과 방법: 대상 환자는 51명으로, 수술 전 직장암의 병기 설정을 목적으로 CT와 MRI를 모두 촬영하였으며 검사 전 초음파 젤을 이용하여 직장을 팽창시킨 상태로 촬영하였다. 고해상도 CT 영상은 고식적 CT와 비교하여 4배 크기의 매트릭스와 사위 삼차원 다평면재구성 (oblique multiplanar reconstruction) 방법을 적용하여 재구성하였다. 두 명의 영상의학과 전문의가 각 환자의 고해상도 CT 및 고식적 CT 영상에서 T 병기, 직장외 침윤깊이 (EMD), ≤T2/≥T3 여부, 직장외 정맥침범 (EMVI), 직장간막 림프절 침범 여부를 분석하여 MRI 분석 결과를 기준으로 하여 서로 비교하였다. 통계분석으로 카이제곱 검정, 피셔의 정확검정, 선형 가중카파 분석, 수신자조작특성곡선 분석, 피어슨의 상관계수 검정을 사용하였다.

결과: 직장암의 T 병기 설정에서 고식적 CT와 비교하여 고해상도 CT에서 보다 높은 정확도를 보였으며 (판독자 1, 82.4% 대 76.5% [P=0.463]; 판독자 2, 82.4% 대 62.7% [P=0.027]), 가중카파 분석에서도 MRI와 보다 일치하는 결과를 보였다 (판독자 1, 0.89 대 0.83; 판독자 2, 0.82 대 0.64 [각각 P<0.001]). ≤T2/≥T3 여부를 구분하는 데 있어 고해상도 CT가 고식적 CT에 비해서 MRI와 보다 일치하는 결과를 보였다 (가중카파 계수: 판독자 1, 0.87 대 0.78; 판독자 2, 0.74 대 0.57). 판독자 2에서는 고해상도 CT가 고식적 CT보다 직장외 침윤깊이 (EMD) (피어슨 상관계수 0.97 대 0.91) 및 직장외 정맥침범

(EMVI) (가중카파 0.78 대 0.47) 평가에서 MRI와 보다 유사한 결과를 보였으나, 판독자 1에서 이러한 차이는 거의 없었다. 직장간막 림프절 침범은 두 CT 사이에서 정확도에 차이가 없었다.

결론: 고해상도 MRI 결과를 기준으로 비교하였을 때 고해상도 CT는 고식적 CT에 비하여 직장암의 T 병기 설정에서 우수한 결과를 보였다.

주요어: 직장암, 병기설정, 고해상도 전산화단층촬영

학 번: 2020-24185