Accuracy of magnetic resonance imaging in predicting dentate line invasion in low rectal cancer

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The Ethics Committee of our institution approved this retrospective study (Approval No. 2219) and waived the requirement to obtain informed consent. Information about this study is presented on our institutional home page. All participants were given the opportunity to opt out of this study.

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Abstract

Purpose

To retrospectively assess the accuracy of magnetic resonance imaging (MRI) in predicting dentate line invasion in low rectal cancer.

Materials and methods

Eighty-one patients with primary rectal cancer were assessed by dynamic contrast-enhanced MRI. The location of the dentate line was assessed on MRI in 27 patients with upper-mid rectal cancer. Two observers independently evaluated the distance between the distal tumor edge and the MRI-defined dentate line in 54 patients with low rectal cancer, and the imaging and histological findings were compared.

Results

The MRI-defined dentate line was 24.0 ± 3.8 mm above the anal verge in patients with upper-mid rectal cancer. The dentate line invasion status agreed with the histological findings in 49/54 (91%) patients (κ = 0.72 [95% CI 0.50–0.95]) for observer 1, and in 51/54 (94%) patients (κ = 0.83 [0.65–1.00]) for observer 2 in patients with low rectal cancer. Interobserver agreement was good (κ = 0.83 [0.65–1.00]). The MRI-derived distance between the distal tumor edge and the dentate line had significant correlation with the histological distance (r = 0.86 for reader 1, 0.75 for observer 2).

Conclusion

MRI demonstrates high accuracy in predicting dentate line invasion in low rectal cancer.

Keywords:

Anal canal; Dentate line; Magnetic resonance imaging; Rectal cancer; Rectum

Introduction

Along with advances in preoperative staging, surgical treatment, and neoadjuvant therapy, sphincter-preserving resection for low rectal cancer has been performed extensively in recent years instead of abdominoperineal resection [1-3]. The most limiting factor of sphincter-preserving surgery is the lower edge of the tumor, and the optimal landmark is probably the dentate line [4-6]. In particular, intersphincteric resection with coloanal anastomosis has been adopted as the ultimate sphincter-preserving procedure; the resection line for this surgery varies depending on the distance of the tumor from the dentate line [7,8].

The dentate line is the most significant anatomical landmark of the anal canal. The anatomical anal canal begins cranially at the dentate line, which is the fusion point of the endodermal and ectodermal contributions to the hindgut, and ends caudally at the anal verge. In contrast, the surgical anal canal is defined as the portion of the terminal intestine extending from the level where the rectum passes through the pelvic visceral aperture (the anorectal ring) to the anal verge. The anal canal above the dentate line is lined mostly by columnar or transitional epithelium, whereas the anal canal below the dentate line is covered by squamous epithelium [9]. In addition, the dentate line is an important surgical landmark for differentiating the vasculature, nerve supply, and lymphatic drainage [9].

Many studies have reported the accuracy of magnetic resonance imaging (MRI) in staging for local extension of rectal cancer [2,10]. However, to the best of our knowledge, no report has defined the dentate line on MRI or assessed the accuracy of MRI for predicting dentate line invasion and for measuring the distance between the tumor margin and the dentate line in low rectal cancer. The aim of our study was to assess the accuracy of preoperative MRI for predicting dentate line invasion and for measuring the distance between the tumor and the dentate line.

Materials and methods

Patients

This retrospective study was approved by the local Institutional Review Board (Approval No. 2219) and the requirement for informed patient consent was waived. Tumors with the distal edge within 6 cm from the anal verge were defined as low rectal cancer [11]. From the institutional radiology databases, we

identified 128 consecutive patients with adenocarcinoma of the low rectum and upper-mid rectum who were treated at our institution between February 2010 and March 2019, and who met the following inclusion criteria: (a) dynamic contrast-enhanced MRI was performed before surgery, and (b) surgery was performed at our institution within 3 months of MRI. We excluded 47 patients who had previously undergone chemotherapy/radiotherapy for rectal cancer or whose MR images were technically inadequate in terms of contrast medium bolus, scan range, or motion artifact. Overall, our MRI data set included 81 patients with low rectal cancer or upper-mid rectal cancer.

Magnetic resonance imaging

All MRI examinations were performed with a 1.5-T MRI (MAGNETOM Avanto, Siemens, Forchheim, Germany) and 3.0-T MRI (MAGNETOM Verio, MAGNETOM Skyra, Siemens). No bowel preparation was given. Patients were injected intravenously with 20 mg of scopolamine butylbromide to reduce colonic motility. Routine pelvic MRI and dynamic contrast-enhanced MRI (DCE-MRI) were acquired. DCE-MRI was obtained with the following parameters: injection speed 2 ml/s; dose 0.1 mmol/kg; and scan timing (first, second, and third phases) 30, 90, and 180 s. Subsequent analysis was performed on the 30- and 90-s postcontrast images. The details of the sequences are shown in Electronic Supplementary Material (Supplementary Table 1).

Image interpretation

Evaluation of the MRI-defined dentate line

We performed an initial analysis to evaluate the dentate line on MRI in 27 patients (mean age, 65.4 years; range, 43–79 years) with upper-mid rectal cancer. We found that radiological appearance of the lumen of the anal canal differs based on its location on cross-sectional dynamic contrast-enhanced MRI (Fig. 1). In approximate terms, in the upper third, the luminal surface is covered by tall mucosa (Fig. 1-b) and then becomes irregular and covered by flattened mucosa (Fig. 1-c); in the middle and lower thirds, the luminal surface is smooth and covered by flattened mucosa (Fig. 1-d). The morphological appearances of the MR images in Fig. 1-b, c, and d are consistent with the colorectal region, transition zone, and squamous zone, respectively [12,13]. Therefore, we defined the dentate line on cross-sectional dynamic contrast-enhanced MRI as the superior border of the smooth anal canal lumen covered by flattened mucosa. Figure 2 shows

the various enhancement patterns of the anal canal mucosa below the MRI-defined dentate line on axial contrast-enhanced fat-saturated T1-weighted imaging.

A single radiologist with 8 years of experience in reading pelvic MRI investigated the location of the dentate line on MRI and measured the length of the anatomical anal canal (from the dentate line to the anal verge) on MRI. The length of the anatomical anal canal was measured by assessing the position of the dentate line on an axial contrast-enhanced fat-saturated T1-weighted image, and then measuring the shortest distance from this line to the anal verge on a sagittal image (Fig. 1).

Measurement of the distance between the distal tumor edge and the dentate line

Based on the above measurement results, dentate line invasion was evaluated and the distance between the tumor margin and the dentate line was measured in 54 patients with low rectal cancer (mean age, 67.7 years; range, 42–87 years). The characteristics of the low rectal cancer patients are listed in Table 1. The median time from MRI to surgery was 31 days (range, 2–71 days). The MR images were retrospectively and independently reviewed by two radiologists (more than 20 and 6 years of experience in pelvic MR image interpretation, respectively) who were aware that the patients had rectal cancer. The radiologists were blinded to the clinical information and the pathological findings. For prediction of the distance between the distal margin of the tumor and the dentate line, the observers located the MRI-defined dentate line on axial contrast-enhanced fat-saturated T1-weighted images, and then measured the shortest distance from the distal margin of the tumor to the dentate line on the sagittal or coronal images. When the tumor invaded the MRI-defined dentate line, a distance of 0 mm was recorded.

Pathological interpretation

An experienced pathologist with 10 years of experience in pathologic diagnosis for rectal cancer evaluated the pathologic status of dentate line invasion. The distance between the distal edge of the tumor and the dentate line was assessed macroscopically, and the shortest distance between the tumor and the dentate line was measured. If it was difficult to measure the distance because the tumor was close to or involved the dentate line, the distance was assessed microscopically (Fig. 3). A distance of 0 mm was recorded if the tumor invaded the squamous epithelium, which covers the surface below the dentate line.

Statistical analysis

The histological distance to the dentate line was taken as the gold standard against which the MRI findings were compared. Agreement between the MRI findings and histological invasion status, and that between observers were measured with the κ statistic [2, 14]. With regard to dentate line invasion, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were also assessed. In all patients who underwent abdominoperitoneal resection, Pearson's correlation analysis was performed on the MRI-determined and histologically determined distance between the tumor and the dentate line. Scatterplots of the MRI and histological distances were analyzed using the linear regression method with 95% confidence interval [2,15]. A p-value < 0.05 was considered statistically significant. Statistical analysis was performed using MedCalc Statistical Software version 18.5 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2018).

Results

Determination of the baseline MRI-defined dentate line

The MRI-defined dentate line was located 24.0 ± 3.8 mm (standard deviation) above the anal verge. The distance from the MRI-defined dentate line to the anal verge was significantly shorter in females than in males (21.6 vs. 25.6 mm, $p = 0.0055$).

Accuracy of predicting dentate line invasion on preoperative MRI

For observer 1, the MRI dentate line invasion status agreed with the histological findings in 49/54 patients (91%; κ = 0.72 [95% CI 0.50–0.95]). The sensitivity, specificity, PPV, and NPV for the prediction of dentate line invasion were 82%, 93%, 75%, and 95%. For observer 2, the MRI dentate line invasion status agreed with the histological findings in 51/54 patients (94%; κ = 0.83 [95% CI 0.65–1.00]). The sensitivity, specificity, PPV, and NPV for the prediction of dentate line invasion were 83%, 97%, 91%, and 95%, respectively. Interobserver agreement was good (κ = 0.83 [95% CI 0.65–1.00]). The mean histological distance between the tumor and the dentate line was 11.4 mm (range, 0–35 mm). The mean radiological distance between the tumor and the dentate line as measured on dynamic contrast-enhanced T1-weighted MRI was 7.3 mm for observer 1 (range, 0–23.5 mm) and 5.7 mm for observer 2 (range, 0–23.5 mm). Figures

4,5 and 6 show the MRI appearances of three of these cases. Histologic slices were obtained at the anal canal for the correlation between the dentate line and the MRI-defined dentate line (Fig. 6). Figure 7 shows scatterplots of the radiologically determined distance between the tumor and the dentate line against the histologically determined distance for both observers. The least squares regression equation was y = 1.130 + 1.343x for observer 1, and y = 3.245 + 1.355x for observer 2. Pearson's correlation analysis showed a statistically significant correlation between the MRI-predicted and histological distances (observer 1: correlation coefficient r = 0.86, $p < 0.0001$; observer 2: r = 0.75, $p < 0.0001$).

Discussion

To the best of our knowledge, this is the first study to define the dentate line on MRI and to assess the accuracy of MRI for predicting dentate line invasion and for measuring the distance between the tumor margin and the dentate line in low rectal cancer. In the present study, MRI showed high accuracy for predicting dentate line invasion, which is important for the colorectal specialist when considering the feasibility of sphincter preservation and appropriate choice of procedure. Furthermore, we are convinced that the present results are useful for the evaluation of diseases of the anal canal such as anal canal cancer, anal fistula, and hemorrhoids, in which the relationship to the dentate line is important [16].

An awareness of a few subtle but critical features of anorectal anatomy lays the foundation for the development of rectal cancer management [17]. We found that the radiological appearance of the lumen of the anal canal differs according to the location on cross-sectional dynamic contrast-enhanced MRI. We speculate that these differences in appearance are due to anatomical differences between the glandular columnar epithelium with microvilli in the upper surgical anal canal and the stratified squamous epithelium in the lower surgical anal canal [12,13], and also to physiological differences. The resting tone is higher in the lower anal canal than in the upper anal canal due to myogenic factors and tonic sympathetic excitation [18,19]. As an additional finding of dynamic contrast-enhanced MRI, the luminal surface below the MRI-defined dentate line was better depicted in the arterial phase than in the delayed phase. The sphincter muscle, venous plexus, and mucosal epithelium all show enhancement in the delayed phase, thus decreasing the contrast between these tissues [20,21]. With experience, we found that dynamic contrast-enhanced MRI was better able to differentiate the epithelium of the anal canal morphologically. Unfortunately, the

transition zone was not always depicted clearly on contrast-enhanced MRI. We speculate that the anal valves and sinuses of this zone are particularly prominent in children but become less pronounced with age [22].

In the present study, the MRI-defined dentate line was located 24.3 mm above the anal verge, and the distance between the line and the anal verge was significantly shorter in females than in males. These results are similar to those assessed by proctoscope in previous studies; in men, the average length was 2.2 cm, whereas in women the average length was 2.0 cm [23].

Low rectal cancers have a high risk of local recurrence and poor outcome compared with lesions located in the middle and upper rectum because of the geometric constraint of the bony pelvis, which impedes surgical access to the distal rectum and visualization of correct dissection planes [17]. Low rectal cancer with dentate line invasion is associated with inguinal and femoral nodal metastases [9]. Accurate preoperative evaluation of the distal margin is therefore essential in planning the clinical management of low rectal cancer, and the optimal landmark is probably the dentate line [4-6]. Currently, the distance between the distal margin of the rectal cancer and the dentate line is assessed by barium enema or endoscopy; most commonly the latter. These approach results in better identification of the surface of the anal canal above the dentate line, but assessment of the submucosal space and sphincter muscle is difficult. In particular, intramural distal spread of low rectal cancer, which is reportedly observed in ~10% of cases of advanced rectal cancer and is regarded as the major source of local recurrence, is difficult to assess endoscopically [6]. In contrast, technical advances in MRI have resulted in dramatic improvements in spatial resolution and MRI has been shown to satisfactorily depict the normal gastrointestinal structures, with good differentiation between mucosa, submucosa, and muscle [16,20,24]. In the present study, MRI predicted dentate line invasion accurately, and the radiologically determined distance between the tumor and the dentate line as measured on dynamic contrast-enhanced MRI had a positive correlation with the histologically determined distance. Therefore, MRI is a valid method for describing the spatial relationship between the distal tumor edge of low rectal cancer and the dentate line including the intramural space.

In our study, the mean distance between the tumor and the MRI-defined dentate line was 4.9 mm shorter

than the histologically determined distance. The possible causes of this discrepancy may be due to difficulty in interpreting the transition zone and to overestimation of lesion size due to desmoplastic reaction and inflammation around the tumor, which can show enhancement after the administration of gadolinium-based contrast agent [25]. More importantly, the histological distance could be affected by the force used to extend the resected rectal specimen by pinning during macroscopic measurement; in contrast, the radiological distance is determined in the physiological condition, in which the basal tone of the anal canal can withstand opening pressure, thought to have a role in the continence mechanism [18,19].

Our study had some important limitations. First, precise matching between histology and MRI for the identification of the dentate line was insufficient in this study. Thus, this limits the consistency between the dentate line and the MRI-defined dentate line. Second, diagnostic bias was possibly introduced by using sagittal and coronal contrast-enhanced T1-weighted images to interpret the distance between the tumor margin, whereas axial contrast-enhanced T1-weighted images were used to assess the dentate line. However, multi-planar reconstruction images are assessed in standard radiology practice and surgical planning. Third, because the structure of anal canal is very detailed, the MRI appearances are subtle. The dentate line is formed by the anal columns. Therefore, we must pay close attention to the morphological appearances of the transition and squamous zones on MRI, particularly around the middle third of the surgical anal canal [26]. Fourth, because the MR images were reviewed retrospectively, the imaging techniques were not standardized. In particular, we assessed the accuracy of preoperative MRI for predicting dentate line invasion using 1.5T and 3.0T systems. Differences in technical parameters between the two systems may have caused variation in image quality.

In conclusion, MRI demonstrates high accuracy in predicting dentate line invasion in low rectal cancer, and can assist in deciding the extent of surgery and the need for preoperative chemoradiotherapy in patients with low rectal cancer.

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Tables and Figure Legends:

Table 1. Clinical and histopathological characteristics of patients with low rectal cancer

Characteristics	No. Value
Gender	
Male	27 (50)
Female	27 (50)
Tumor size (cm)	
0-5	42 (78)
5.1-10.0	12 (22)
Tumor differentiation	
Well or moderate	49 (91)
Poor	5 (9)
Surgical procedures	
Abdominoperitoneal resection	27 (50)
Low anterior resection	21 (38)
Intersphincteric resection	3 (6)
Other procedures	3 (6)

[a] Data are numbers of patients with percentages in parentheses.

Figure legends

Fig. 1 Dynamic contrast-enhanced fat-saturated T1-weighted MR images of the normal anal canal in the arterial phase in a 78-year-old male. (a) Three-dimensional morphological volume-rendered image of anal canal mucosal enhancement. (b–d) Axial images at the corresponding levels marked on (a) demonstrate strong mucosal enhancement and show morphological differences of the luminal surface of the anal canal according to location. Note mucosal alignment along the long axis (between b and d) that is consistent with that of the anal columns. The dashed line is the distance between the MRI-defined dentate line and the anal verge.

Fig. 2 Schematic drawings and corresponding axial dynamic contrast-enhanced MR images show various enhancement patterns of anal canal mucosa below the MRI-defined dentate line. White area = anal canal mucosa

Fig. 3 Photograph of a histology slide showing low rectal cancer. We measured the distance between the distal tumor edge and the dentate line (dashed line)

Fig. 4 Images of a 74-year-old man with low rectal cancer (small arrow) in whom the histologically determined distance between the tumor and the dentate line was 20 mm. (a) Sagittal dynamic contrast-enhanced T1-weighted image. The distance between the distal tumor edge and the MRI-defined dentate line is 18 mm (dashed line). (b) Double-contrast barium enema, lateral view.

Fig. 5 Images of a 73-year-old man with low rectal cancer in whom the histologically determined distance between the tumor and the dentate line was 4 mm. (a) Coronal dynamic contrast-enhanced T1-weighted image. The distance between the tumor and the MRI-defined dentate line was assessed as 0 mm, for both observers. (b) Double-contrast barium enema, posterior–anterior view.

Fig. 6 Images of a 67-year-old man with low rectal cancer and intersphincteric fistula in whom the enteric entry point of the fistula was on the dentate line. (a) Coronal dynamic contrast-enhanced MR image shows a left-sided intersphincteric fistula. Note the entry site in the middle third of the surgical anal canal

(arrowhead). (b,c) Axial images at the corresponding levels marked on (a) demonstrate irregular anal canal lumen covered by flattened mucosa (b) and the superior border of the smooth anal canal lumen covered by flattened mucosa (c). Note that the MRI-defined dentate line and the entry point of the fistula (arrowhead) are therefore located on the same level. (d) Corresponding macroscopic section shows the enteric entry point of intersphincteric fistula (arrowhead) on the dentate line.

Fig. 7 Scatterplot showing the distance between the distal tumor edge and the dentate line as determined from histology specimens compared with the distance between the distal tumor edge and the dentate line as determined by MRI ($r = 0.86$, $y = 1.130 + 1.343x$ for reader 1; and $r = 0.75$, $y = 3.245 + 1.355x$ for observer 2)