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Mean ADC values discriminate rectal mucinous carcinoma from rectal nonmucinous adenocarcinoma

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Background/aim: This study aimed to differentiate rectal mucinous carcinoma (MC) from nonmucinous rectal adenocarcinoma (AC) using mean apparent diffusion coefficient (mADC) values obtained with diffusion-weighted imaging.

Materials and methods: Sixty-two pathologically confirmed rectal AC (n = 44) and MC (n = 18) patients were included in this study. The two groups underwent pelvic MRI to determine the local staging baseline for rectal tumors. Once the region of interest (ROI) was determined, a border was drawn around each hyperintense tumor (b = 1000 s/mm^2 images). Following a repeat of this procedure for each patient, the ROIs were recorded to apparent diffusion coefficient (ADC) maps, and mADC values were measured. The mADC was determined per slice, followed by a calculation of whole tumor volume ADC mean using the individual mADC values. The Mann–Whitney test was performed to compare mADCs for the two groups. A receiver operating characteristic (ROC) curve was generated to determine the differentiating capacity of ADCs from MC to AC.

Results: The mADC was higher in MC (1.631 ± 0.375 × 10^{-3} mm^2/s) (range: 0.95–2.36 × 10^{-3} mm^2/s) than in AC (0.921 ± 0.157 × 10^{-3} mm^2/s) (range: 0.6–1.48 × 10^{-3} mm^2/s) (P < 0.001). mADCs were effective in distinguishing MC from AC (area under the ROC curve, 0.972 (95% CI : 0.928–1.00)). A threshold of 1.27 × 10^{-3} mm^2/s was set that corresponded with high sensitivity (94.4%) and specificity (97.7%). Twelve MCs (67%) were predominantly hypointense, and 6 MCs (33%) were seen as mixed signal intensity lesions. Forty ACs (91%) were observed as hyperintense lesions, and 4 ACs (9%) had mixed signal intensity. There was a significant difference in the signal intensities between MC and AC (c^2 = 54.7, P < 0.001).

Conclusion: MCs and ACs show different diffusion characteristics, which can be distinguished with high sensitivity and specificity and can help to improve prognostic treatment options.

Key words: Rectal cancer, adenocarcinoma, mucinous adenocarcinoma, diffusion-weighted imaging, apparent diffusion coefficient

1. Introduction

Colorectal carcinoma is a major cause of cancer-related mortality. Rectal cancer comprises approximately one-third of the cases of colorectal cancer. Adenocarcinomas comprise 96% of colorectal cancers (1). Mucinous adenocarcinoma (MC) is a specific rectal cancer subtype, encompassing 10.0% of all cases, and it is associated with a poorer prognosis than nonmucinous adenocarcinoma (AC) (2,3). Tumors are defined as MC when a minimum of 50.0% mucin-to-tumor volume is determined (4). Interestingly, MCs have limited response to oncological treatments (5,6). Therefore, it is important to differentiate MC from AC.

Diffusion-weighted imaging (DWI) is a version of MRI based on fluid dynamics and the molecular mechanics of water mobility (7). The signal intensity increases when water mobility is restricted, such as in cases of dense cellularity lesions and poor interstitium (8). The apparent diffusion coefficient (ADC) is used to quantitate diffusivity based on the fluid restrictions described above compared to the surrounding tissues. The measurable data obtained by DWI can clarify the nature of the lesions in various parts of the body (9).

Our goal was to investigate the usefulness of ADC values in order to distinguish MC from AC.

2. Materials and methods

2.1. Patients

This was a retrospective study. We subjected 64 patients diagnosed with rectal carcinoma to pelvic MRI to determine the local staging baseline for rectal tumors. The patients were included in the study based on histopathologically

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(biopsy) proven rectal ACs and MCs. The exclusion criterion was low MRI quality and data from two patients could not be used due to artifacts. Therefore, the patient cohort included 62 patients. Forty-four of these patients were AC patients (24 males and 20 females; age range 41–80 years [mean: 60 years of age]), and 18 (11 males and 7 females; age range 19–74 years [mean: 53 years of age]) were MC patients. The institutional ethics committee approved this retrospective study, and informed written consent was obtained from each patient before imaging.

2.2. MR techniques

The patient cohort was subjected to a preexamination food fast (5–6 h) to reduce bowel peristalsis. Therefore, the administration of an antiperistaltic agent, rectal cleansing, and/or an enema was not necessary.

A 3.0-T MRI system (MAGNETOM Verio, Siemens, Erlangen, Germany) was used to screen patients for rectal tumors based on previously described parameters. Briefly, the maximum gradient of 45 mT/m and a slew rate of 200 mT/m per second in all three directions were used, and MR and DW images were acquired during the same procedure. All pulse sequence parameters (other than those of DWI used in this study) are listed in the Table. DW images were collected using a single-shot multislice echoplanar imaging sequence with the following parameters: repetition time/echo time, 6800/75 ms; EPI factor, 78; field of view, 360 × 271 mm; matrix size, 130 × 104; slice thickness, 5 mm; distance factor, 20%; averages, 4.0; reduction factor, 2.0; and receiver bandwidth, 2402 Hz/Px. The acquisition time for the DWI was 265 s.

2.3. Image interpretation: ADC measurement

The maps for the ADC were designed using a monoexponential decay model with all 3 b-values included (Siemens, Germany). Regions of interest (ROIs) of the tumor were traced on the DW images with b = 1000 s/mm^2. Once the ROI was determined, a border was drawn around each hyperintense tumor (b = 1000 s/mm^2 images). Following a repeat of this procedure for each patient, the ROIs were recorded to ADC maps and mean ADC (mADC) values were measured. The mADC was determined per slice, followed by a calculation of the whole tumor volume ADC mean using the individual mADC values.

2.4. Statistical analysis

Compliance with the normal distribution of data in the two groups was examined by Shapiro–Wilk test. The data were not distributed normally. The Mann–Whitney test was used to compare mADCs for the two groups. The ROC curve was generated to show the ability of ADCs to distinguish MC from AC. $P < 0.05$ was considered statistically significant. All statistical analyses were performed using SPPS 15.0. (SPSS Inc., Chicago, IL, USA).

Table. Pulse sequence parameters.

Parameter	Sagittal T2-weighted TSE	Axial T2-weighted TSE	Oblique axial T2-weighted TSE (high resolution)	Oblique coronal T2-weighted TSE (high resolution)	T1-weighted fat suppressed contrast-enhanced
Matrix size	384 × 307	320 × 240	320 × 240	320 × 240	320 × 240
Slice thickness (mm)	3.50	5.00	3.00	3.00	3.50
Distance factor	15.0%	20.0%	16.0%	16.0%	14.0%
Repetition time (ms)	4500.0	5450.0	5460.0	5180.0	495.0
Echo time (ms)	104.0	93.0	58.0	58.0	12.0
Flip angle (degree)	120.0	150.0	145.0	135.0	140.0
Reduction factor	2.0	2.0	2.0	2.0	2.0
Averages	2.0	3.0	4.0	4.0	2.0
FoV (mm)	220 × 220	220 × 220	180 × 180	180 × 180	200 × 200
Orientation	Sagittal	Axial	Oblique axial	Oblique coronal	Oblique axial
Band width (Hz/Px)	250.0	260.0	260.0	260.0	260.0
Acquisition time (min and s)	4 min, 5 s	2 min, 18 s	4 min, 54s	6 min	3 min, 17 s

FoV: Field of view; TSE: turbo spin echo.

3. Results

The thickness of the tumor was between 1.5 and 2.7 cm for ACs (mean: 1.8 cm) and 1.4 and 3 cm for MCs (mean: 2.2 cm). The mADC value was higher for MC (1.631 ± 0.375 × 10^{-3} mm^2/s) (range: 0.95 ± 2.36 × 10^{-3} mm^2/s) than for AC (0.921 ± 0.157 × 10^{-3} mm^2/s) (range: 0.6–1.48 × 10^{-3} mm^2/s) ($P < 0.001$). An example of our cases is presented in Figure 1. Mean ADCs were effective for distinguishing MC from AC (area under the ROC curve, 0.972 (95% CI: 0.928–1.00)) (Figure 2). A threshold of 1.27 × 10^{-3} mm^2/s was used due to the high sensitivity (94.4%) and specificity (97.7%) of distinction. Twelve MCs (67%) were predominantly hypointense, and 6 MCs (33%) were seen as mixed signal intensity lesions. Forty ACs (91%) were seen as hyperintense lesions and 4 ACs (9%) had mixed signal intensity. There was a significant difference in proportions in signal intensities between MC and AC ($P < 0.001$).

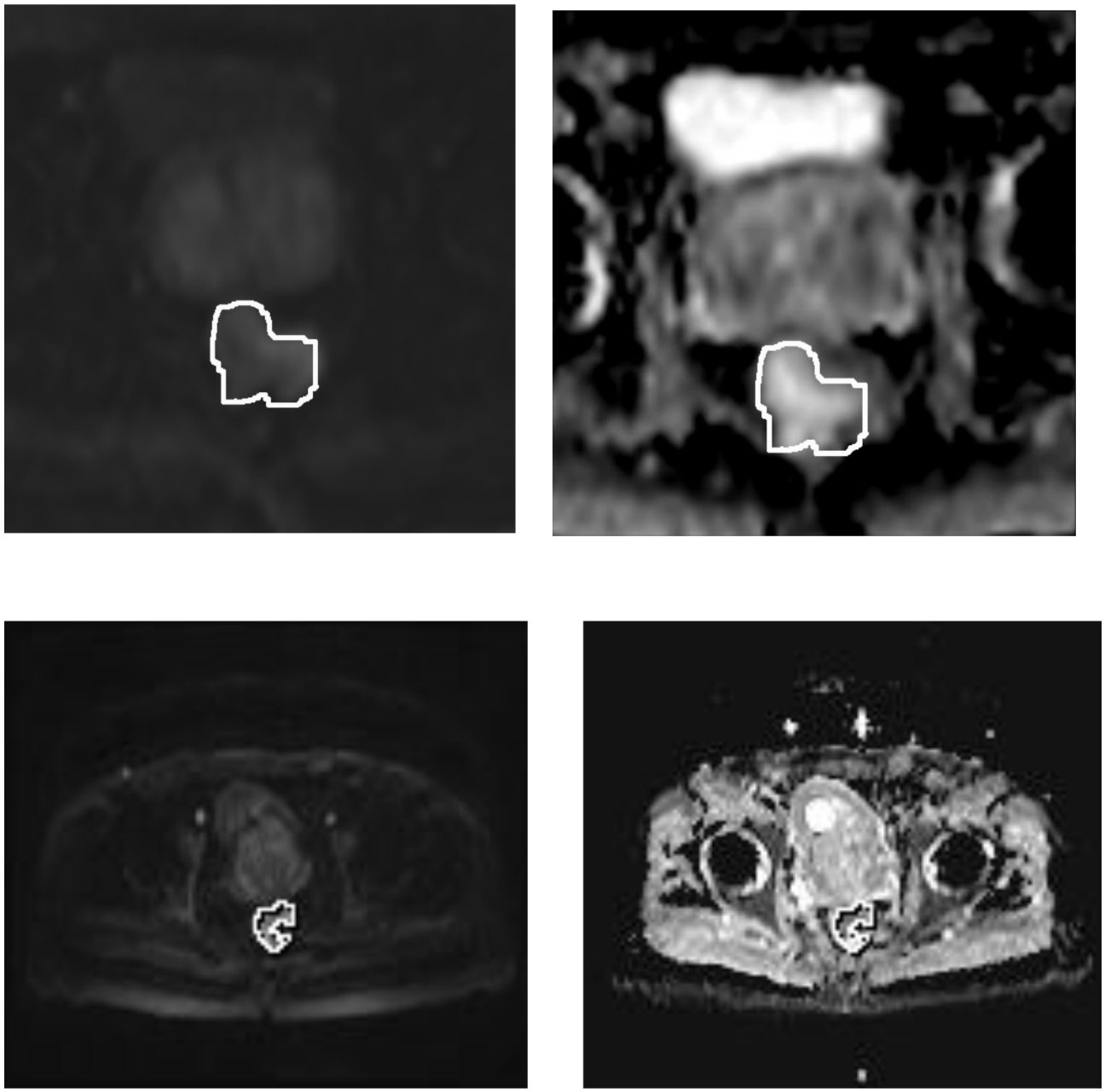

Figure 1. a) DW image (b = 1000 s/mm^2) shows rectal MC in a 58-year-old male. A representative ROI manual trace is seen in the DW image. b) ADC map shows the copied representative ROI manual trace for calculating tumor mADC values. c) DW image (b = 1000 s/mm^2) shows rectal AC in a 60-year-old male. A representative ROI manual trace is seen in the DW image. d) ADC map shows the copied representative ROI manual trace for calculating tumor mADC values.

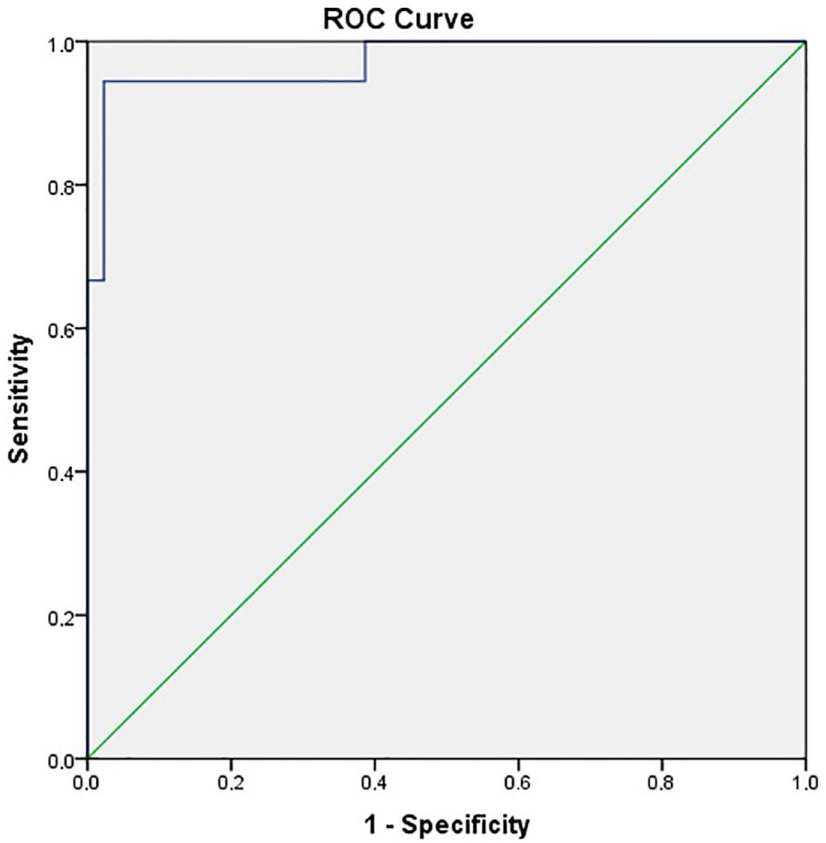

Figure 2. A representative ROC curve. A threshold of 1.27×10^{-3} mm^2/s was used to determine high sensitivity (94.4%) and specificity (97.7%).

4. Discussion

Mucin-producing tumors have been described in several different regions of the body, including the pancreas, breasts, and ovaries, and they are more aggressive than ACs (10,11). An analysis of colon and rectum MCs demonstrated poorer prognosis compared to ACs (12). Hyngstrom et al. demonstrated that rectum mucinous tumors have worse survival outcomes (2). The surgical treatment for MCs is different from that of ACs (13). Therefore, it is important to differentiate MCs from ACs before surgery.

Mucinous carcinomas have a high content of mucin and low cellular density. Although they are malignant, they have increased ADC value with unrestricted diffusion (14). We attempted to evaluate this form in rectal carcinomas.

In most studies, ADC measurements were performed by a variety of methods for ROI placement. Interestingly, some reports included the volume of the whole tumor (15–20), whereas others used a single tumor slice for their analysis (21,22) or small tumor samples (23). Consequently, it is still unclear whether the entire tumor or a representative section is enough for ADC measurements or not. In our study, however, we used the whole tumor volume, selected and drew an ROI and border, and determined the signal intensity using b1000 images. Then we obtained the mADC for each slice and generated the mADC for the whole tumor volume, which is different from the single-slice method (24).

Malignant lesions are determined through signal intensities, which are typically high (associated with a high b value) and calculated by DWI. Multiple reports have shown a negative association with ADC and tumor cellularity (25). Interestingly, rectal MC has a higher ADC value than AC due to reduced cellularity (26). In our study, twelve MCs (67%) were predominantly hypointense, and 6 MCs (33%) were seen as mixed signal intensity lesions. Forty ACs (91%) were seen as hyperintense lesions; 4 ACs (9%) had mixed signal intensity. There was a significant difference in proportions in signal intensities between MC and AC ($P < 0.001$).

We showed that the mADC value was significantly higher in MCs ($1.631 \pm 0.375 \times 10^{-3}$ mm^2/s) (range: $0.95 \pm 2.36 \times 10^{-3}$ mm^2/s) than in ACs ($0.921 \pm 0.157 \times 10^{-3}$ mm^2/s) (range: $0.6–1.48 \times 10^{-3}$ mm^2/s) ($P < 0.001$). Furthermore, our study showed that a threshold of 1.27×10^{-3} mm^2/s was the precise value to produce high sensitivity (94.4%) and

specificity (97.7 %) of distinction. Nasu et al. used a cut-off of 1×10^{-3} mm^2/s to diagnose MC if the tumors with mean ADCs of this value or more were diagnosed as MC (26). Sensitivity and specificity were 93% and 94%, respectively. The authors used two different b values (0 and 1500 s/mm^2) for DWI, whereas we obtained DW images with 3 different b values (50, 400, and 1000 s/mm^2), which we used routinely in our department for abdominal imaging at 3.0 T.

The results demonstrated that mucinous tumors were more common in younger patients (27–29). It is believed that the genetic make-up of the tumors may be responsible for and reflect their aggressive nature. Another explanation may be that early tumors do not present symptoms like those of more locally advanced tumors due to their localization (i.e. the bowel wall). For example, mucinous tumors are more frequently observed at the advanced stage (30). Wu et al. compared mucinous and nonmucinous tumors within a cut-off of 39 years. They found that mucinous tumors were more frequent in patients younger than 39 years (31). Another study showed an average age at presentation (54.2 ± 16.25 years) that was statistically less than that of AC patients (mean age at presentation: 58.73 ± 13.62 years) (32). Dozois et al. demonstrated that MC patients had an average age at presentation of 42.2 years (33). Interestingly, rectal cancers were more frequent under the age of 50. In our study, the mean age for MC patients was 53 years, which was less than that of patients with AC.

Our study has certain limitations. We assessed a small number of mucinous carcinoma patients, and the ROIs were obtained by a single person. Further studies would benefit from multiple people calculating these measurements. Several factors, such as ROI shape, partial volume effects, and MRI equipment affect ADC measurements (34,35). Another weak point of our study was that the mean age among the groups was heterogeneous.

MCs and ACs show different diffusion characteristics that can be distinguished with high sensitivity and specificity and can help to improve prognostic treatment options.

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