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Efficiency of apparent diffusion coefficients in differentiation of colorectal tumor recurrences and posttherapeutical soft-tissue changes☆

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ABSTRACT

Objective: To evaluate effectiveness of apparent diffusion coefficient (ADC) values measured by diffusion-weighted magnetic resonance imaging (DW-MRI) in differentiation of colorectal tumor recurrences and posttherapeutical soft tissue changes.

Methods: For this prospective study, 30 patients (22 males, 8 females; age range 30–81 years; mean age 61 ± 12 years) who underwent surgery for colorectal tumors and had a mass detected by computed tomography (CT) and/or MRI during follow-up examinations were divided into 2 groups [17 patients (Group 1) with recurrence and 13 patients (Group 2) with benign fibrosis/granulation tissue]. Final diagnoses were based on histopathological examination in 14 patients and clinical follow-up at least 6 months in the remaining 16. In the latter, the diagnosis of recurrence was made in cases in which the lesion was larger on follow-up CT and MRI; recurrence was ruled out in cases of stable or shrinking lesions without any increase in tumor markers. DW-MRI was performed in the axial plane, for two different *b* values ($b = 0$ and 800 s/mm^2).

The mean apparent diffusion coefficient (ADC) values were measured by manual delineation of regions of interest on ADC maps.

Results: The median ADC values were 1.07×10^{-3} mm/s^2 (min: 0.82, max: 2.05) and 1.91×10^{-3} mm/s^2 (min: 1.51, max: 2.22) in Groups 1 and 2, respectively. A statistically significant difference was detected between the two groups ($P < 0.001$). When the threshold value used to determine whether the lesions recurred was 1.48×10^{-3} mm/s^2 based on ROC analysis, the sensitivity was 82% and the specificity was 100%. There were three patients with a false-negative diagnosis, and the primary histopathological diagnosis of all was mucinous adenocarcinoma.

Conclusions: Because recurrences in mucinous adenocarcinomas have high ADC values, they may show overlap with benign lesions. In the detection of the local recurrence of colorectal neoplasms, with the exception of mucinous adenocarcinomas, ADC measurements are reliable imaging techniques.

1. Introduction

The aim of follow-up evaluations in postoperative period for patients who previously underwent surgery for colorectal neoplasms is to determine the presence of local and distal recurrence [1]. Early detection of the presence of recurrence is important for the establishment of a new treatment protocol such as re-operation, radiotherapy (RT), or chemotherapy [2]. Because symptoms are not specific in these patients and physical examination may be limited, in addition to serum tumor markers and colonoscopy, computed tomography (CT) and/or magnetic resonance imaging (MRI) or positron emission tomography (PET)/CT may be used for the diagnosis of postoperative local recurrences of colorectal neoplasms. The most important challenge is the distinguishing local recurrence from changes such as the edema, granulation tissue, and fibrosis sequale of surgery or RT [3,4].

There are different opinions regarding which imaging techniques to use during routine follow-up. CT and MRI evaluations are performed by looking at the morphological features and contrast enhancement of the lesions. The ability to distinguish a tumor

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from fibrosis in T2-W images by the hyperintensity of the tumor makes MRI superior to CT. However, lesions that show high signal intensity in T2-W images do not always indicate a tumor. High signal intensity in T2-W images is related to the amount of protons in the lesion. Up until 1 year after surgery or 6 months after RT, high signal intensity can be observed without recurrence due to the high proton content as a result of inflammation and vasodilation [3,4]. In addition, the signal intensity of small recurrences present in dense fibrotic tissue that are not adequately vascularized cannot be detected due to fibrosis [3]. To overcome these problems, dynamic MRI evaluations were employed, and different sensitivities have been reported [3,5,6]. The requirement of more time for its analysis, and its limited value during the first 5 months after surgery prevents the widespread application of dynamic MRI [7]. Thus, trustworthy findings that lead to the diagnosis of recurrence in routine evaluations are needed.

Diffusion-weighted MRI (DW-MRI) is based on the principle of measuring the microscopic movements (diffusion) of water molecules in tissues. Signal changes occur based on the increased or limited diffusion movements of water molecules. Using this method, apparent diffusion coefficients (ADCs) can be calculated, and diffusion can be quantitatively measured. Malignant tumors are composed of tumor cells that are randomly organized and form a dense group. This structure prevents the free movement of water molecules and creates diffusion restriction. Studies show that malignant tumors have statistically significantly lower ADC values than benign tumors. This characteristic was first used in the differential diagnosis of intracranial masses, and it was later used in the evaluation of other organs and lesions [8–10]. In addition, it was shown that DW-MRI could be used in the initial detection of colorectal neoplasms [11,12].

DW-MRI was used in the detection of the recurrence of pelvic tumors and the soft tissue tumors of the extremities and was reported to be effective [1,13]. Although these studies did not specifically focus on colorectal neoplasms, its results are promising. To date, only one study in literature had reported the effectiveness of DW-MRI for determination of recurrence in post-operative period [14]. Nevertheless, ADC measurements were not performed in that study. The aim of the study was to evaluate the effectiveness of ADC values measured by DW-MRI in differentiation of colorectal tumor recurrences and posttherapeutical soft tissue changes.

2. Materials and methods

2.1. Patients

Our study group consisted of patients who were operated for colorectal tumor, followed clinically and had follow-up CT or MRI examination between June 2009 and May 2011. Our institutional approach for follow-up after primary surgery of colorectal cancer generally recommends clinical assessment every 3 months, including serum tumor markers carcinoembryonic antigen (CEA) and cancer antigen Ca 19.9; colonoscopy at 6–12 months, 2 years and 5 years after surgery. Contrast enhanced abdominal and pelvic CT or MRI is also recommended every 6–12 months for 2 years and then once a year for the following 5 years. CT and MRI examinations were performed earlier in some patients because they need re-staging after operation, experienced new symptoms or had abnormal physical examination or laboratory findings. Patients who had a detectable mass at the surgical and/or presacral regions or asymmetric thickening of colonic wall in follow-up examinations by CT and/or MRI during the postoperative period were included in the study. Asymetric wall thickening was defined as at least 5 mm thickening in bowel wall at the anastamosis region. Patients without any asymmetric wall thickening and detectable soft tissue mass at the surgical and/or presacral region were excluded. Patients were enrolled into the study according to the consensus of two radiologists who evaluated the first CT and/or MRI examination. Approval for this prospective study was obtained from our institutional ethics committee. Informed consent was obtained from all of the patients before additional DW-MRI examination.

Twenty-two males and eight females were included in the study. Their ages ranged from 30 to 81 with an average age of 61 ± 12 years. All patients underwent surgery for colorectal tumors. Twenty-eight patients had rectum and/or sigmoid colon neoplasms (23 rectum, 5 sigmoid colon), and two had descending colon neoplasms. Anastomoses were inside pelvis in all of the patients who were operated from primary sigmoid and descending colon tumor and in the field of routine imaging. Anterioposterior resection (APR) and low anterior resection (LAR) were performed in 20 and 8 patients, respectively. End to end anastomosis was performed in pelvis for 1 of 2 patients with descending colon tumor and total colectomy and ilioanal anastomosis due to familial adenomatosis for the remaining patients. Histopathological examination of the primary neoplasms revealed adenocarcinoma in 27 patients and mucinous adenocarcinoma in 3 patients. Sixteen patients had adjuvant chemotherapy, 12 had adjuvant chemotherapy and RT, and one had RT as an additional treatment. The median time between colorectal neoplasm operation and the detection mass on DW-MRI was 15 months (min: 1, max: 84) (Table 1). DW-MRI examination was performed before 6 months in 5 patients.

Final diagnoses were based on the histopathological findings for patients who underwent surgery and were biopsied. For patients who did not have histopathological examination, final diagnoses were based on clinical, laboratory and follow-up imaging findings. In followed-up patients, the diagnosis of recurrence was made in cases with larger lesions on follow-up CT and MRI. Recurrence was ruled out and the lesions were determined to be benign if the biopsy results of the cases who underwent colonoscopic investigation were negative, no increase in tumor markers were detected and the lesions were stable without any morphological change or shrinking on follow-up imaging for at least 6 months. Based on their final diagnoses, patients were segregated into two groups according to the presence of a recurrent colorectal neoplasm (Group 1) or its absence (Group 2).

2.2. Techniques

Examinations were conducted using a 1.5-T (Siemens Magnetom Symphony Quantum, Erlangen, Germany) MRI scanner using a phased-array body coil. The view of examination was determined according to the region containing suspicious lesion on the routine follow-up CT and MRI. Patients did not receive bowel preparation, spasmolytics and gel enema or air insufflation for rectal distention. The MRI analysis protocol was composed of axial T2-weighted (T2-W) TURBO spin echo and DW-MRI sequences. The T2-W sequence parameters were as follows: TR/TE/FA = 3200/138/160, 5-mm section thickness, 2-mm section interval, 134×256 matrix, and NEX = 1. Diffusion-weighted sequences were obtained in an axial plane in three directions (i.e., x, y, and z) to SSEP-SE T2 by applying diffusion-sensitive gradients with different b values (i.e., 0 and 800 s/mm^2). The technical parameters were as follows: TR/TE, 3400 ms/94 ms; section thickness, 5 mm; field of view (FOV), 400 mm; matrix, 128×128; bandwidth, 1346 Hz/pixel; NEX, 3; scan time, 76 s; and distance factor, 30%. Isotropic images were composed of images that eliminated signal differences based on direction, and they were generated by the instrument by taking the cube root of the product of the measured signal intensities in the x, y, and z directions. ADC maps of the isotropic images for the $b = 800$ s/mm^2 value were automatically generated by the