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Computerized analysis of enhancement kinetics for preoperative lymph node staging in rectal cancer using dynamic contrast-enhanced magnetic resonance imaging

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ABSTRACT

For this feasibility study, dynamic contrast-enhanced magnetic resonance imaging (dceMRI) was performed preoperatively in 9 patients with histologically proven rectal carcinoma. A total of 41 lymph nodes detected were matched to histopathology. Their contrast enhancement patterns were evaluated using computer-aided analysis and categorized in persistent, plateau, and washout curve type. Highest diagnostic accuracy for detecting malignancy was observed, when less than 31.8% of the voxels within a lymph node demonstrated a washout curve (sensitivity/specificity of 81.8%/89.7%; area under the curve, AUC=0.87). In comparison, conventional size measurements revealed lower AUC of 0.81 (sensitivity/specificity of 75%/72.4%). We conclude that dceMRI might be of diagnostic value for preoperative lymph node staging.

1. Introduction

Colorectal cancer is the third most frequent malignancy in Western countries and is associated with a high rate of morbidity and mortality [1]. Although implementation of total mesorectal excision (TME) reduced rates of local recurrence and functional problems, rectal cancer patients still have worse prognosis compared to colon cancer patients due to the anatomical conditions of the pelvis [2,3]. Determination of the preoperative tumor stage has wide-ranging consequences for the recommended therapeutic regime in rectal cancer without suspected distant organ metastasis. Most crucial factors are the invasion depth (T category) and whether tumor cells have already spread to locoregional lymph nodes or not (N category). Local recurrence rates can be decreased by administration of neoadjuvant chemoradiation to nodal positive patients, while primary resection of tumors with limited expansion may lead to lower postoperative morbidity without reducing oncological results [2,4–6]. Thus exact presurgical determination of the lymph node status is essential. Magnetic resonance imaging (MRI) is a promising modality in the staging of rectal cancer [7–13]. However, existing magnetic resonance (MR) criteria for nodal involvement are not standardized and are varying from institute to institute with reported accuracies ranging from 43% to 85% [9,10]. Measurement of lymph node size with application of different cut-off values is the most common technique for evaluation of lymph node status. Diffusion-weighted imaging (DWI) as a further method has been proposed [14,15], but apparent diffusion coefficient values between benign and malignant lymph nodes seem to overlap significantly, in particular, in small nodes [14].

In recent years, dynamic contrast-enhanced magnetic resonance imaging (dceMRI) gained increasing attention in differentiating pathologies due to different temporal patterns of contrast enhancement [16–20]. However, to the best of our knowledge, an assessment of lymph nodes using dceMRI and computerized postprocessing has not been performed yet.

The purpose of the current study was to evaluate if dceMRI of mesorectal lymph nodes in patients with rectal cancer is feasible and whether it can reliably identify metastatic involved lymph nodes. Contrast enhancement kinetics of lymph nodes were evaluated by calculating time–contrast intensity curves (TIC) voxelwise using computer-aided evaluation.

2. Materials and methods

2.1. Patients

The study was approved by the local ethics committee of our institution and informed consent was obtained from each patient. A total of 9 patients (4 females, 5 males, median age of 65 years,

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standard deviation (S.D.)±7.3) with histologically proven primary rectal adenocarcinoma scheduled for surgical resection with TEM were enrolled in the study (Table 1). They underwent routine MRI with additional dynamic sequences prior to operation. Exclusion criteria were previous surgery of the pelvis, neoadjuvant chemotherapy, a history of previous malignancies, and general contraindications for MRI.

2.2. MRI

MRI was performed in a 1.5-T system (Magnetom Avanto, Siemens Medical Systems, Erlangen, Germany) using a wrap-around pelvic phased array surface coil with the patient in supine position. The imaging protocol included T2-weighted TSE images in sagittal view [3 mm slice thickness, field of view (FOV)=300 mm, time of echo (TE)=95 ms, time of repetition (TR)=4500 ms], transversal view (5 mm slice thickness, FOV=250 mm, TE=104 ms, TR=5880 ms), and a diffusion-weighted sequence in transversal view (fast SE single shot echo planar imaging with fat suppression and free breathing, FOV=300 mm, TE=76 ms, TR=3700 ms; *b*-values: 50, 300, and 600 s/mm^2). Additionally, a high-resolution T2-weighted TSE sequence with a small FOV and a slice thickness of 3 mm perpendicular to the longitudinal axis of the tumor was performed (FOV=180 mm; TE=93 ms; TR=4850 ms). For the dynamic study, a multislice T1-weighted three-dimensional gradient echo sequence (VIBE, TR=9.98 ms, TE 4.76 ms, FOV=300 mm, flip angle=80°, slice thickness=3.0 mm, FOV=350 mm, axial orientation) was obtained before and 60 s after i.v. bolus injection of 0.1 mmol/kg bodyweight of gadopentetate dimeglumine (Gd-DTPA, Magnevist, Bayer HealthCare, Leverkusen, Germany) as an automated injector bolus followed by 20 ml of a saline solution, both with a flow rate of 2.5 ml/s. The duration of the VIBE sequence was 60 s. Dynamic serial scanning was continued with the same sequence parameters for a total of 6 min. During the MR examination, we applied a spasmolytic agent iv (butylscopolamine) for reducing movement artifacts.

2.3. Nodal comparison

TME according to established quality criteria [3,4] was performed within 10 days after MR examination. For better anatomical reproducibility, each surgical specimen was fixed in a buffered formalin–saline solution for 48 h without cutting open. For pathological examination, the specimen was sectioned transversely from the distal to the proximal aspect at 5 mm intervals. The tissue slices were laid out and numbered sequentially. Each tissue slice was than matched to the corresponding MR image. Consecutively, each slice was carefully evaluated for mesorectal lymph nodes by an experienced pathologist. Each lymph node found was matched to the corresponding node visible on the MR images. Only nodes, which could be unambiguously correlated to the MR images, were included in the study.

Table 1
Patient details including age, sex, TNM stage, tumor grade, and number of identified lymph nodes on MRI that could be correlated with histopathology (LN=lymph nodes)

No.	Age	Sex	TNM stage	Tumor grade	Correlated LN
1	70	male	pT4bN1aM0	G3	9
2	72	female	pT3N1aM0	G2	6
3	65	female	pT2pN0M0	G1	1
4	59	male	pT3aN2bM0	G2	4
5	52	male	pT3N2aM0	G3	5
6	71	male	pT2N1aM0	G2	4
7	73	male	pT3N0M0	G2	9
8	62	female	pT3N1bM0	G3	2
9	59	female	pT3N0M0	G2	1

2.4. Image analysis

All MR images were postprocessed using the Syngo BreVis computer-aided evaluation software (Siemens, Erlangen, Germany) (Fig. 1). Data were recorded by an experienced radiologist, who was trained in the computer-aided program. Lymph node size was measured at the shortest diameter. The radiologist was unaware of the histopathological diagnosis. The program incorporates the precontrast and postcontrast T1 MR gradient echo VIBE series and calculates time–intensity curves (TIC) from signal intensities at different times for each voxel of the whole image. If the voxel value between the precontrast and the first postcontrast series increases by a determined threshold of 50%, the voxel is shown in color on the MR image, i.e., all voxels exceeding this threshold will be color-coded within the image (Fig. 1B). The color depends on the enhancement type in the delayed phase: If the signal intensity on the last contrast-enhanced series (6 min after contrast medium application) decreases by more than 10% compared with the immediate postcontrast series, the TIC is defined as washout enhancement pattern [16] (Fig. 2). A voxel value increase by more than 10% is defined as persistent (continuous) enhancement pattern. If a voxel value does not change in either direction by more than 10%, TIC is defined as plateau. The total color-coded area (TCCA) within a user-specified volume of interest, which was manually drawn around the lymph nodes, is calculated automatically. The percentual distribution of the different TIC patterns within the TCCA is summarized in a profile map (Fig. 1C).

2.5. Statistical analysis

To test for significance between size measurements and enhancement patterns in benign and malignant lymph nodes, we used Mann–Whitney *U* test with $P<.05$ indicating significance. Statistical analysis was performed with MedCalc Version 10 (Mariakerke, Belgium).

3. Results

3.1. Size

In 9 patients, a total of 41 mesorectal lymph nodes were identified on the MR images (Table 1). Size of the lymph nodes varied between 3 and 16 mm with a mean of 7.5 mm (S.D.±3.2 mm). Of the 41 lymph nodes, 12 proved to be malignant at histopathology, and 29 lymph nodes were free of tumor cells. Mean size of positive lymph nodes was 9.2 mm (range, 5–16 mm), while that of negative nodes was 5.4 mm (range, 3–11 mm) ($P<.05$). The receiver operator characteristic (ROC) curve is depicted in Fig. 3. Highest sensitivity and specificity (75% and 72.4%, respectively) for differentiating malignant from benign lymph nodes was reached at a cut-off value of 6 mm (area under the curve, AUC=0.81).

3.2. Enhancement characteristics

Mean percentual distribution of TIC in all lymph nodes demonstrated washout enhancement curve in 48.1% of the voxels, plateau curve in 15.6%, and persistent curve in 35.9%.

Mean percentual distribution of TIC in lymph nodes with pathological evidence of tumor cell infiltrates showed washout enhancement curve in 17.7% of the voxels, plateau curve in 14.6%, and persistent curve type in 66.7% (Table 2). In comparison, mean percentual distribution in negative lymph nodes demonstrated washout curve type in 60.8% of the voxels ($P<.05$), plateau curve type in 16.4% ($P=.76$), and persistent curve type in 22.6% ($P<.05$). ROC curves are depicted in Fig. 3. Highest diagnostic accuracy for diagnosing malignancy was observed, when less than 31.8% of the voxels within a lymph node demonstrated a washout curve type (corresponding sensitivity/specificity of 81.8%/89.7%; AUC=0.87).