Original Article The Eurasian Journal of Medicine EAJM 2010; 42: 57-60

Diffusion-Weighted Magnetic Resonance Imaging in Evaluation of Gastric Cancer

Mide Kanserinin Değerlendirilmesinde Diffüzyon Ağırlıklı Manyetik Rezonans Görüntülemenin Yeri

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Abstract

Objective: To investigate the role of diffusion-weighted magnetic resonance imaging (DW-MRI) in the diagnosis of gastric tumors and discuss the diagnostic importance and potential use of apparent diffusion coefficient (ADC) measurements.

Materials and Methods: Beginning in March 2009, DW-MRI was added to the routine abdominal and pelvic MR examination for all patients imaged at our institution. A total of 21 patients (12 men and 9 women; mean age 55±6.3SD, range: 39-74 years) with known gastric malignancy were referred to our MR unit. All MRI examinations were performed using a 1.5-T MRI scanner (Magnetom Avanto, Siemens Healthcare). The evaluation of the DW-MRI examinations was made by radiologists' consensus. Changes in the signal intensity of the lesions were determined by their appearance in images at b=50, 400, and 800 s/mm^2 and in ADC maps. Results were compared with histopathological findings.

Results: All of the gastric tumors in this study showed high signal intensity in DW-MRI and low signal intensity in ADC maps. Mean ADC values for gastric tumor and normal gastric wall were 0.892±0.23 SD mm^2/s and 1.453±0.35 SD mm2/s respectively. The mean ADC values of gastric tumors were significantly lower than that of the normal gastric wall.

Conclusion: DW-MRI and ADC values together can successfully differentiate gastric tumors from normal gastric wall.

Key Words: ADC map, Diffusion Weighted Magnetic Resonance, Gastric Cancer

Özet

Amaç: Mide tümörlerinin tanısında diffüzyon ağırlıklı manyetik rezonans görüntülemenin (DA-MRG) rolünü araştırmak ve rölatif diffüzyon katsayısı (ADC) ölçümünün potansiyel kullanımını ve tanısal önemini tartışmak.

Gereç ve Yöntem: 2009 yılı Mart ayından başlayarak tüm hastaların, merkezimizde rutin olarak çekilen pelvik ve batın MRG tetkiklerine DA-MRG eklendi. Bu tarih aralığında bilinen mide kanserli 21 hasta (12 erkek ve 9 kadın; ortalama yaş: 55±6.3SD, aralık: 39-74 yıl) merkezimize yönlendirildi. Tüm MRG çekimleri 1.5 Tesla MRG tarayıcısı ile gerçekleştirildi (Magnetom Avanto, Siemens Sağlık Hizmetleri). DA-MRG ile elde edilen görüntüler iki radyoloğun ortak kararı ile değerlendirildi. Lezyonların sinyal intensitelerindeki değişikliklerine b= 50, 400, 800 s/mm^2 görüntüleri ve ADC haritaları değerlendirilerek karar verildi. Elde edilen değerler histopatolojik sonuçlar ile karşılaştırıldı.

Bulgular: Çalışmamızda tüm tümörlerde DA-MRG de sinyal intensitesinde artış ve ADC haritalarda sinyal intensitesinde azalma tespit edildi. Sırasıyla mide tümör dokusu ve normal mide duvarından elde edilen ortalama ADC değerleri 0.892±0.23 SD mm^2/s ve 1.453±0.35 SD mm^2/s olarak ölçüldü. Mide tümör dokusundan elde edilen ADC değerleri, normal mide duvarından elde edilen değerlerden anlamlı olarak daha düşüktü.

Sonuç: DA-MRG ile birlikte ADC ölçümü mide kanseri ile normal mide duvarının ayırt edilmesinde başarı ile kullanılabilmektedir.

Anahtar Kelimeler: ADC haritası, Diffüzyon ağırlıklı manyetik rezonans görüntüleme, Mide kanseri

Introduction

Gastric cancer is the second leading cause of cancer death worldwide, although there is considerable geographical variation. These cancers usually show metastatic spread at the time they are identified [1].

In patients affected by gastric carcinoma, early detection of the disease is the principal parameter in planning treatment and is a determinant of prognosis. Therefore, accurate preoperative diagnosis is vital in determining the most suitable therapy and avoiding inappropriate attempts at curative surgery.

There are many imaging modalities used to evaluate this malignancy. These techniques include ultrasonography (US), computed tomography (CT), positron emission tomography (PET) and magnetic resonance imaging (MRI). US is noninvasive, nonionizing, readily available, and lower in cost than the other methods. However, it is recognized as an operator-dependent technique. Indeed, the role of US is primarily in detecting hepatic metastases. CT is undoubtedly the most-used imaging modality in the evaluation of gastric tumors. It is non-invasive, but carries the risk of radiation. In addition, CT has been the primary tool in determining both the presence of recurrent tumors and their response to chemotherapy; however, its use is limited, particularly in the diagnosis of lymph node metastasis, peritoneal metastasis, and small hematogenous metastasis [2, 3]. PET has been recognized as a useful diagnostic technique in clinical oncology [4], but experience with its use in evaluating stomach cancer is limited.

Undoubtedly MR imaging has a potential role in evaluating gastric cancer. MRI is a noninvasive diagnostic modality and holds

Received: April 21, 2010 / **Accepted:** May 24, 2010

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doi:10.5152/eajm.2010.18

great potential for abdominal imaging. It does not entail ionizing radiation. In addition, it allows global, multiplanar depictions of the anatomy of the abdominal and pelvic cavities.

Diffusion-weighted imaging (DWI) of the abdomen and pelvis, which has been widely used for diagnostic purposes, provides a new contrast mechanism to evaluate patients with abdominal pathologies in solid abdominal and pelvic organs. In DW-MRI, we can track cellular characteristics of the tissue owing to visualization and measurement of the diffusivity of water molecules in the human body. Thus, it may be used for tumor detection and characterization throughout the body. For example, tumors with a high cellular density have a relatively high intracellular/extracellular space volume ratio, and consequently a relatively impeded diffusion. Current articles show that adding DW imaging to routine MRI examinations increases diagnostic accuracy [5-8].

In this study we aim to evaluate the potential use of DW-MRI in the evaluation of gastric cancer and discuss the diagnostic importance of ADC measurement.

Materials and Methods

Patients

Our retrospective study received institutional review board approval, and all of the patients provided informed consent. Beginning in March 2009, DW-MRI was added to the routine abdominal and pelvic MR examination for all patients imaged at our institution with known gastric malignancy. There were 21 patients (12 men and 9 women; mean age 55 ± 6.3SD, range: 39-74 years) referred to our MR unit.

MR Protocol

All MRI examinations were performed using a 1.5-T MRI scanner (Magnetom Avanto, Siemens Healthcare) with an 18-channel body coil and high performance gradients (maximum gradient, 45 mT/m; maximum slew rate, 200 T/m/s). Before DW-MRI, the subjects underwent a free-breathing axial and coronal turbo spin-echo T1-weighted sequence (TR, 536 ms; TE, 11 ms; FA, 150°), and an axial and coronal fat saturated turbo spin-echo T2-weighted sequence (TR, 5030 ms; TE, 101 ms; FA, 150°). Contrast-enhanced images were acquired with a fat suppressed gadolinium enhanced axial and coronal spoiled gradient-echo T1-weighted sequence (TR, 536 ms; TE, 11 ms; FA, 150°) with intravenous administration of a single dose (0.1 mmol/kg) of Meglumin gadoterat (Dotarem; Guerbet Group, France). DWI consisted of an axial diffusion weighted single-shot spin-echo echoplanar sequence with a chemical shift selective fat-suppression technique (TR/TE, 4900/93) with the following parameters: matrix, 192 × 192; number of slices, 30; slice thickness, 6 mm; interslice gap, 35%; FOV, 45 cm; averages, 5; acquisition time, approximately 3 minutes; PAT factor, 2; PAT mode, parallel imaging with modified sensitivity encoding. DW-MRI was performed with b factors of 50, 400 and 800 s/mm^2.

Image Review

The evaluation of the DW-MRI examinations was made by three radiologists' consensus. The MR images were transferred to a work station (Leonardo console, software version 2.0; Siemens AG Medical Solutions, Germany) for evaluation.

To calculate and analyze the ADC maps, the ADC values were measured from the most hypointense region of the tumor tissue by placing a circular region of interest (ROI) around the area. The mean area of this ROI was 53 mm^2. Changes in the signal intensity of the lesions were determined by their appearance in the b= 50, 400, and 800 s/mm^2 images and the ADC maps. The gastric tumors were hyperintense in the b= 50, 400, and 800 s/mm^2 images and hypointense in the ADC map compared with the normal gastric wall.

Laparoscopic Exploration and Histopathological Evaluation

Laparoscopic explorations were performed in all patients within two weeks of the preoperative MRI examination. Procedures were performed by two oncologic surgeons with more than 10 years of experience.

Results

The distribution of ADC values is shown in Figure 1. We found that all lesions showed increased signal intensity in DW-MRI and decreased signal intensity in the ADC maps (Figure 2A-C). Mean ADC values were 0.892 ± 0.23 SD mm^2/s and 1.453 ± 0.35 SD mm^2/s in the gastric tumor and normal gastric wall respectively (Table 1). The mean ADC values of gastric tumors were significantly lower than those found in the normal gastric wall ($p < 0.05$). In a ROC curve analysis, the cut-off value of ADC to differentiate gastric carcinoma from normal gastric wall was found to be 0.982 mm^2/s with a sensitivity of 87% and a specificity of 100% (Figure 3).

All of the histopathologic specimens were evaluated and confirmed as adenocarcinoma.

Discussion

Gastric cancer is an important public health problem worldwide with a generally poor prognosis. It usually shows metastatic spread at the time of diagnosis [1]. There are many imaging modalities used to evaluate this malignancy. These techniques include US, CT, PET and MRI. MR imaging has a critical role in the screening of this cancer group. It is a noninvasive diagnostic modality and holds great potential for abdominal imaging. MR imaging does not entail ionizing radiation or require an intravascular contrast medium.

Diffusion-weighted (DW) imaging has recently become available for abdominal imaging and is useful in the detection of malignant hepatic, renal, prostatic, colonic and uterine cervical tumors [9].

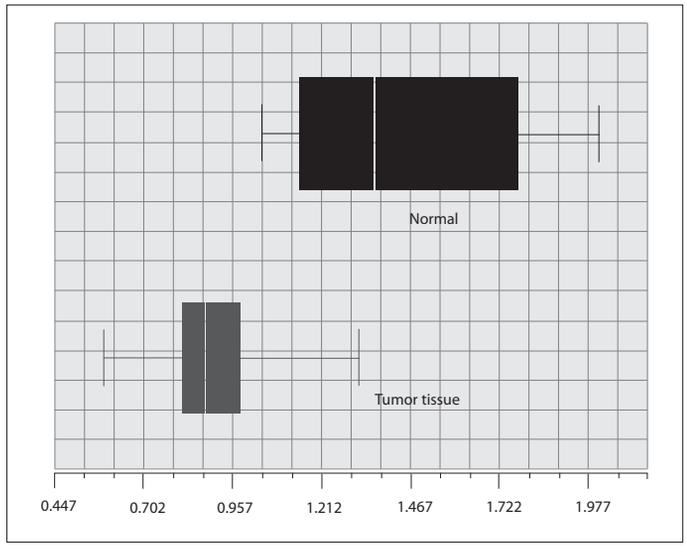

Figure 1. *Boxplots of ADC values for normal gastric wall ('normal') and tumor tissue ('tumor tissue') calculated from the ADC map.*

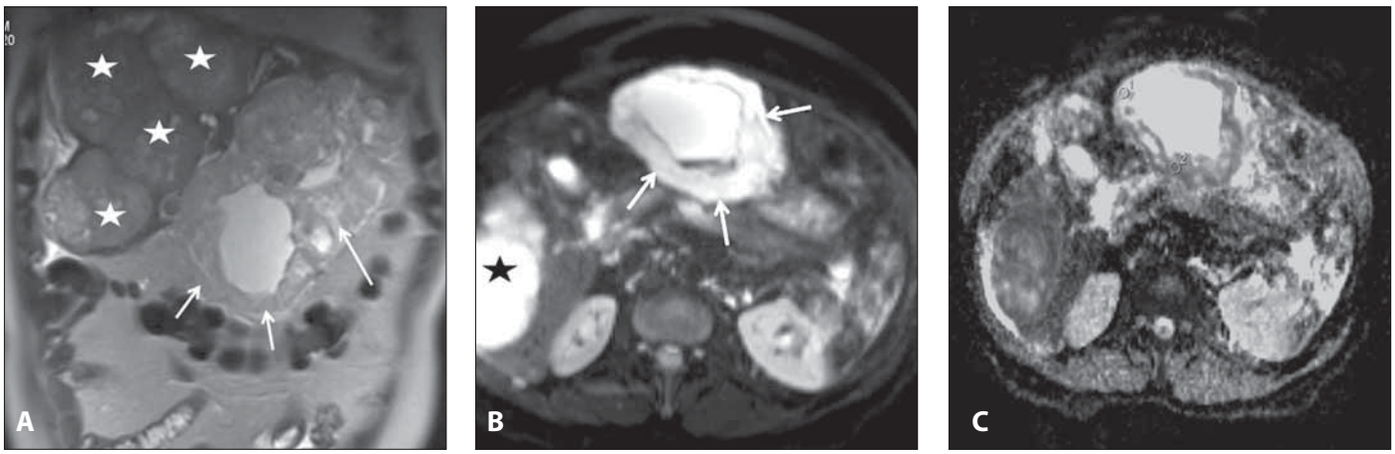

Figure 2. A) *Coronal T2 weighted MR images show diffuse wall-thickening of the stomach (arrows). Note the multiple metastatic foci in the liver (stars),* ***B)*** *Axial DW-MR image with a b value of 50 mm²/s shows diffuse wall-thickening of the stomach (arrows) and metastasis in the liver segment 6 (star),* ***C)*** *In axial ADC map images, the calculated ADC value from tumor tissue is lower than in the normal gastric wall.*

Table 1. ADC values for normal gastric wall and tumor tissue with DWI

Calculated ADC values (x10-3 mm²/ s)				
	Mean± SD	Min	Max	Wilcoxon test P value
Tumor tissue	0.892±0.23	0.579	1.320	0.003
Normal gastric wall	1.453±0.35	1.042	2.005	0.012
(SD) Standard deviation, (min) minimum, (max) maximum, (P value) significance of difference between (ADC) values for normal gastric wall and tumor tissue				

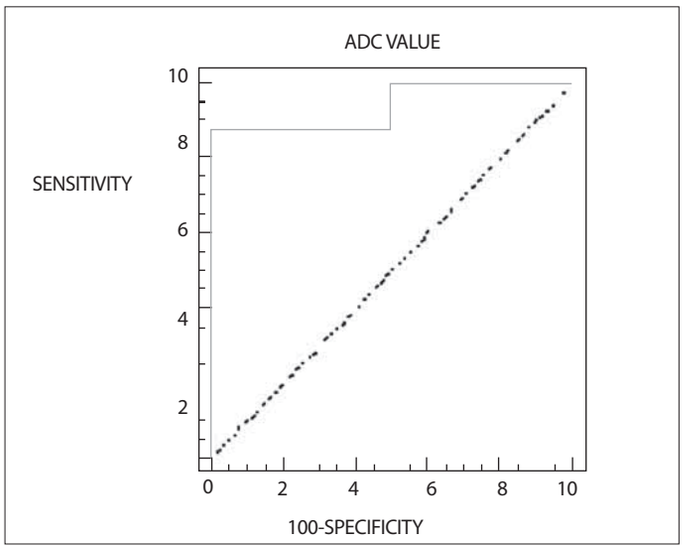

Figure 3. *ROC curve for differentiating normal gastric wall and tumor tissue from the ADC map.*

The DW-MRI technique extracts information from the diffusion of water molecules, which mainly reflects the degree of cellularity of the tissue. The degree of restriction to water diffusion in biologic tissue is inversely correlated with the tissue cellularity and the integrity of cell membranes. The motion of water molecules is more restricted in tissues with a high cellular density associated with numerous intact cell membranes. For example, tumors with a high cellular density have a relatively higher intracellular/extracellular space volume ratio and consequently a relatively impeded diffusion. An impeded diffusion has been reported for most malignant tumors [10, 11]. On the other hand, a loss of cell membrane integrity in necrotic tumors (i.e., an increase in the diffusing of water molecules from the intracellular to extracellular spaces) and a decrease in tumor cellularity (i.e., a decrease in the intracellular/extracellular space volume ratio) due to necrosis and/or apoptotic processes may result in increased diffusivity. In addition, intratumoral edema and cystic tumor components also increase diffusivity because of increased water content [10, 11].

Gastric tumor tissue shows restricted diffusion on DW images due to increased cellularity. Thus, we added DW imaging to the routine MRI examination of gastric tumors. DW-MRI can be performed using breath-hold, free breathing, or respiratory/cardiac–triggered techniques as dictated by specific anatomic locations. Scanning parameters should be prescribed to allow accurate and reproducible ADC quantification, and the chosen parameters should ideally be achievable across MR platforms to allow the meaningful comparison of results. However, peristaltic movement artifacts of the intra-abdominal hollow organs and T2 shine-through effects of fluids in the gastrointestinal system make it difficult to perform DW-MRI in the abdomen. With the use of advanced fast imaging sequences in MRI such as echo-planar imaging (EPI), these artifacts are largely eliminated, allowing DW-MRI to be used in the evaluation of abdominal organs [12-16].

By performing DW-MRI using different b values, quantitative analysis is possible. This analysis is usually performed by the calculation of ADC values within a region of interest (ROI).

DW-MRI has been reported to be useful in the characterization and diagnosis of tumors as malignant tumors show more restriction in diffusion and lower ADC values compared with benign ones. In these studies, ADC values were calculated, and differences in these ADC values were stated to be useful in the differential diagnosis of lesions, with significantly decreased values in the case of malignancy [17]. In another study, it was found that DW-MRI could describe high-

grade gastric cancer by means of increased signal in DW-MRI and decreased signal in ADC maps [18]. Moreover, diffusion-weighted MRI has also been investigated as a biomarker in the response to treatment of hepatocellular carcinoma [19], cerebral glioma [20] and soft tissue sarcoma [21]. These studies have found that individuals who respond to treatment show a significant rise in the ADC values after therapy.

DW-MRI can also be used to predict the response of a tumor to chemotherapy and radiation treatment in cancer patients. Studies in rectal carcinoma [22] and colorectal hepatic metastases [23] have shown that cellular tumors with low baseline pretreatment ADC values respond better to chemotherapy or radiation treatment than tumors that exhibit high pretreatment ADC values.

In our study, we find that gastric cancer tissue has a high intensity in DWI images due to the restriction of diffusion. We presume that increased cellularity of the tumor causes the restricted diffusion of water molecules. We also found that tumors have lower ADC values and that there is a significant difference in ADC values between tumor tissue and normal gastric wall.

Our study has some limitations. First, the patient population was relatively small. Our results will need to be confirmed with a larger prospective study. Second, all patients had the diagnosis of gastric adenocarcinoma. Further studies that evaluate gastric tumors such as lymphomas or stromal tumors are required. Third, there was a lack of enteric contrast material, which plays an important role in detecting lesions in hollow organs. We believe that with technical improvements, some of these disadvantages may be overcome. Limitations of DWI include its poor anatomic localization and relatively poor spatial resolution. In addition, anatomic distortion increases with the use of high b values.

DW-MRI is an attractive, noninvasive, quantitative and useful technique for assessing gastric tumors. ADC maps can successfully differentiate between tumor tissue and a normal gastric wall. We expect that ADC values will be used to monitor and predict the treatment response of gastric cancer in the near future.

Conflict of interest statement: The authors declare that they have no conflict of interest to the publication of this article.

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