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The usefulness of diffusion-weighted imaging in the characterization of liver lesions in patients with cirrhosis

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AIM: To evaluate if diffusion-weighted imaging (DWI) is useful in characterizing liver lesions in patients with cirrhosis.

MATERIALS AND METHODS: A retrospective review revealed 37 patients with cirrhosis who had 41 histologically proven hepatocellular carcinoma (HCC) lesions. Another 20 patents with cirrhosis had 29 solid nodules that remained stable for at least 12 months and were deemed to be benign hepatic nodules (BHN). Of the HCC lesions, 14 were well-differentiated (WD HCC), 20 were moderately differentiated, and seven were poorly differentiated histology. For all lesions, two reviewers analysed signal characteristics and made apparent diffusion coefficient value (ADC) measurements.

RESULTS: Visual analysis of DWI was useful in that no HCC was hypointense and no BHN was hyperintense to liver. Visual analysis of DWI was not useful in separating WD HCC from higher grades. There was substantial overlap in ADC values of the HCC and BHN. Among HCC lesions, ADC values of more than 0.99×10^{-3} mm^2/s had sensitivity and specificity of 85% and 86% for reviewer 1, and 63% and 64% for reviewer 2 in diagnosing WD HCC.

CONCLUSIONS: ADC measurements of BHN were higher than that of HCC, and the ADC values of WD HCC were higher than that of more aggressive grades of HCC. However, quantitative measurements may not help in determining the histological grade of individual cases of HCC.

Introduction

Sonography, computed tomography (CT), and magnetic resonance imaging (MRI) are the investigative tools utilized in screening for liver tumours in cirrhotic patients. On MRI, T2-weighted signal intensity and enhancement patterns on multiphasic contrast-enhanced series have been used to differentiate benign from malignant lesions in cirrhotic patients. Hypervascularity on the arterial phase, washout on the venous phase, and the presence of a peripheral capsule on delayed phases have been shown to signify hepatocellular cancer (HCC).[1–3] Nevertheless, there remain many cases where imaging tests cannot easily differentiate benign and malignant lesions.[4,5]

The number and size of HCC lesions, and not the histological grading, are used in the Milan criteria for determining eligibility for liver transplantation.[6] Several papers suggest that the histological grade of HCC, in addition to the tumour size, predicts the outcome after surgical resection,[7–9] transplantation,[10,11] and radiofrequency ablation.[12,13] Identifying the biology of HCC may not only help with estimating prognosis but may also affect

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management decisions. For instance, consideration may be given to excluding patients with poorly differentiated HCC from orthotopic transplantation,[14] and include for transplantation those patients with tumours larger than 5 cm with a well-differentiated histology.[15] A study using positron-emission tomography (PET) found that 2-[18F]-fluoro-2-deoxy-D-glucose (FDG) uptake tended to correlate with tumour grade and 2-year recurrence-free survival.[16] As MRI is used often for the diagnosis of HCC, it would be useful to determine whether MRI techniques may also help determine the grade of the tumour. The aim of the present study was to determine not only the usefulness of DWI in differentiating benign and malignant lesions in cirrhotic patients, but also whether DWI may be useful in subtyping malignant lesions according to histology.

Materials and methods

Patients

This retrospective Health Insurance Portability and Accountability ACT (HIPAA)-compliant study reviewed the MRI database between January 2007 and March 2009 for cirrhotic patients who underwent DWI. Institutional review board permission for retrospective analysis of radiology and clinical databases, with waiver of informed consent, had been obtained. A total of 260 patients were identified. Patients that excluded from the analysis were those with masses that did not have surgical histopathology or core biopsy results ($n = 51$); those with only cysts or haemangiomas or lesions less than 1 cm ($n = 36$); those with benign-appearing solid lesions that did not have 12 months' follow-up ($n = 29$); and those without any mass lesions ($n = 87$). Stability over a 12-month follow-up period was deemed to indicate benignity as several studies have indicated that the median tumour doubling time of HCC was less than 6 months.[17–20] Patients who had histopathological proof of the grade of HCC were included, regardless of the contrast-enhanced appearances of the tumour. A minimum lesion size of 1 cm was required for enrolment as, from the authors' prior experience, lesions smaller than this size were difficult to visualize on DWI.

Following these exclusions, 57 patients were enrolled in the study. In total, there were 41 males and 16 females. The mean age was 55 years (range 24–74 years). Thirty-seven patients had core biopsy ($n = 5$) or explantation/resection ($n = 32$) proof of the histological grade of the HCC. In the HCC group, there were 30 males and seven females. These patients had 41 HCC lesions (all with histopathological proof). Four patients had two HCC lesions, with grade of histology determined on explant. There were 14 well-differentiated HCC, 20 moderately differentiated HCC, and seven poorly differentiated HCC. Another 20 patients had solid nodules that were stable for at least 12 months' follow-up. In this group, there were 11 males and nine females. There were 29 lesions that were stable for 12 months and deemed to be benign hepatic nodules (BHN). Two patients had three nodules, and five patients had two nodules. The mean ages of the HCC and BHN groups were 57 and 51 years ($p > 0.05$), respectively.

MRI examinations

MRI examinations were performed in a supine position using a 1.5 T MRI system (Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany) and a body phased-array coil. The standard imaging protocol consisted of pre-contrast T1- and T2-weighted images, and post-gadolinium three-dimensional T1-weighted gradient-echo sequences (Table 1). Gadobenate dimeglumine (MultiHance, Bracco Diagnostics, Princeton, NJ, USA) was intravenously injected at a rate of 2 ml/s using a power injector (Medrad Spectris Solaris, Medrad Inc, Indianola, PA, USA) followed by a 20 ml saline flush. The dose of gadolinium was 0.1 mmol/kg of body weight.

Prior to the administration of gadolinium, a single-shot echoplanar DWI sequence was acquired according to parameters given in Table 1. The acquisition was carried out during free-breathing, without electrocardiography (ECG) or respiratory gating, using b-values of 0 or 50, 400 or 500, and 800 s/mm^2. From the authors' prior experience, a b-value of 800 s/mm^2 gave images with adequate signal-to-noise ratios and without artefacts. Parallel imaging technique, i.e., generalized autocalibrating partially parallel acquisition (GRAPPA) was used with an acceleration factor of 2. Apparent diffusion coefficients (ADC) maps were calculated mono-exponentially with all b-value sequences using the imaging software (Syngo vB15 or vB13, Siemens Medical Solutions).

Image analysis

Two reviewers independently analysed the images, blinded to the histology or radiological follow-up. The reviewers were abdominal radiologists with 5 years (A.P.) and 12 years (K.S.) of experience in reading MRI. At least one region-of-interest (ROI) was placed in the lesions on the

Table 1
Magnetic resonance imaging parameters.

Sequence	TR/TE (ms)	Flip angle (degrees)	ST/SG (mm)	NEX	RBW (Hz/pixel)	Matrix
T1-weighted 2D gradient echo	123/2.2 (OP), 4.93 (IP)	70	7.0/0.7	1	445	256 × 135
Diffusion-weighted imaging[a]	1500/71	90	6.0/7.8	4	1735	192 × 115
3D fat-suppressed gradient echo[b]	4.98/2.27	12	3.0/0.0	1	300	256 × 144

TR, repetition time; TE, echo time; IP, in-phase; OP, opposed phase; ST, section thickness; SG, intersection gap; NEX, number of excitations.
[a] Three b-values used for diffusion-weighted images were 0 or 50, 400 or 500, and 800 s/mm^2.
[b] Sequence used for intravenous contrast medium.