European Journal of Radiology 84 (2015) 1444–1451

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Intrahepatic and hilar mass-forming cholangiocarcinoma: Qualitative and quantitative evaluation with diffusion-weighted MR imaging

Hassan El Fattach[a], Anthony Dohan[a,b,c], Youcef Guerrache[a], Raphael Dautry[a,b], Mourad Boudiaf[a], Christine Hoeffel[d], Philippe Soyer[a,b,c,*]

[a] Department of Abdominal Imaging, Hôpital Lariboisière, Assistance Publique-Hôpitaux de Paris, 2 rue Ambroise Paré, 75010 Paris, France
[b] Université Paris-Diderot, Sorbonne Paris Cité, 10 Avenue de Verdun, 75010 Paris, France
[c] UMR INSERM 965-Paris 7 "Angiogenèse et recherche translationnelle", 2 rue Amboise Paré, 75010 Paris, France
[d] Department of Radiology, Hôpital Robert Debré, 11 Boulevard Pasteur, 51092 Reims Cedex, France

ARTICLE INFO

Article history:
Received 17 November 2014
Received in revised form 11 April 2015
Accepted 2 May 2015

Keywords:
Intrahepatic cholangiocarcinoma
Hilar cholangiocarcinoma
Diffusion-weighted magnetic resonance imaging
Normalized ADC
Malignant hepatic tumor
MR Imaging

ABSTRACT

Objective: To qualitatively and quantitatively analyze the presentation of intrahepatic and hilar mass-forming cholangiocarcinoma with diffusion-weighted magnetic resonance imaging (DW-MRI).
Materials and methods: Twenty-eight patients with histopathologically proven mass-forming cholangiocarcinoma (hilar, $n = 17$; intrahepatic, $n = 11$) underwent hepatic DW-MRI at 1.5-T using free-breathing acquisition and three *b*-values (0,400,800 s/mm^2). Cholangiocarcinomas were evaluated qualitatively using visual analysis of DW-MR images and quantitatively with conventional ADC and normalized ADC measurements using liver and spleen as reference organs.
Results: All cholangiocarcinomas (28/28; 100%) were visible on DW-MR images. DW-MRI yielded best conspicuity of cholangiocarcinomas than the other MRI sequences ($P < 0.001$). Seven cholangiocarcinomas (7/11; 64%) showed hypointense central area on DW-MR images. Conventional ADC value of cholangiocarcinomas (1.042×10^{-3} mm^2/s $\pm$ 0.221×10^{-3} mm^2/s; range: 0.616×10^{-3} mm^2/s to 2.050×10^{-3} mm^2/s) was significantly lower than that of apparently normal hepatic parenchyma (1.362×10^{-3} mm^2/s $\pm$ 0.187×10^{-3} mm^2/s) ($P < 0.0001$), although substantial overlap was found. No significant differences in ADC and normalized ADC values were found between intrahepatic and hilar cholangiocarcinomas. The use of normalized ADC using the liver as reference organ resulted in the most restricted distribution of ADC values of cholangiocarcinomas (variation coefficient = 16.6%).
Conclusion: There is a trend towards a common appearance of intrahepatic and hilar mass-forming cholangiocarcinomas on DW-MRI but variations may be observed. Familiarity with these variations may improve the diagnosis of mass-forming cholangiocarcinoma.

1. Introduction

Intrahepatic and hilar cholangiocarcinomas are malignant tumors that develop from the biliary tract [1,2]. Cholangiocarcinoma is the second most frequent primary malignant tumor of the liver after hepatocellular carcinoma, accounting for 5-30% of all primary hepatic malignant tumors [3]. Cholangiocarcinoma is now classified into intrahepatic (previously referred to peripheral) and extrahepatic, depending on the site of origin [1]. In this regard, intrahepatic cholangiocarcinoma originates from an interlobular biliary duct. Extrahepatic cholangiocarcinoma is further categorized into hilar cholangiocarcinoma (the so-called "Klatskin's tumor), which originates from a main (right or left) hepatic duct or from the bifurcation of the common hepatic duct and cholangiocarcinoma of the extrahepatic bile duct, which originates below the bifurcation [1,3]. Although classified as extrahepatic, hilar carcinoma can present as a mass-forming, exophytic hilar tumor similar to intrahepatic cholangiocarcinoma [3,4].

In order to better detect and characterize intrahepatic and hilar cholangiocarcinoma and discriminate between other hepatic tumors, several imaging techniques have been developed [5–7]

* Corresponding author at: Department of Abdominal Imaging, Hôpital Lariboisière, Assistance Publique-Hôpitaux de Paris, 2 rue Ambroise Paré, 75010 Paris, France. Tel.: +33 149 958 484; fax: +33 149 958 546.
E-mail addresses: hassangreenmed@gmail.com (H.E. Fattach), anthony.dohan@lrb.aphp.fr (A. Dohan), docyoucef05@yahoo.fr (Y. Guerrache), raphael.dautry@lrb.aphp.fr (R. Dautry), mourad.boudiaf@lrb.aphp.fr (M. Boudiaf), choeffel-fornes@chu-reims.fr (C. Hoeffel), philippe.soyer@lrb.aphp.fr (P. Soyer).

http://dx.doi.org/10.1016/j.ejrad.2015.05.003
0720-048X/

and more recently new imaging techniques have been tested [8–10]. In this regard, several researchers have suggested that diffusion-weighted (DW) MRI helps increase the sensitivity of MRI for cholangiocarcinoma detection and also discriminate between intrahepatic and hilar mass-forming cholangiocarcinomas and other malignant tumors [11,12].

Regarding focal liver lesions, analysis of DW-MR images can be made quantitatively (*i. e.*, with apparent diffusion coefficient (ADC) measurement) and qualitatively (*i. e.*, with visual analysis of DW-MR images) [13,14]. A variety of malignant hepatic tumors have been studied with DW-MRI. However, a few studies have placed a special focus on the appearance of intrahepatic and hilar cholangiocarcinomas on DW-MRI [9,10,12]. Of these, only one has specifically described qualitatively the variability of cholangiocarcinoma presentation on DW-MRI [12]. In addition, there are no studies in the literature that have comprehensively evaluated DW-MRI findings of mass-forming cholangiocarcinomas both quantitatively and qualitatively.

A major issue in DW-MRI of focal liver lesions is the variability in ADC values as reported among studies [15–17]. To reduce the possible influence of technical parameters on the calculated ADC value, researchers have advocated the use of a normalized ADC to improve lesion characterization with DW-MRI in several organs [18–22]. However, this relatively recent approach has not been applied to mass-forming cholangiocarcinoma yet.

The purpose of this retrospective study was twofold. First, we aimed to qualitatively and quantitatively analyze the DW-MRI features of intrahepatic and hilar mass-forming cholangiocarcinomas using high *b* values and report the variability in presentation of these tumors on this specific MRI sequence. Second, we wished to evaluate to what extent the use of a normalized ADC may influence the distribution of ADC values of intrahepatic and hilar cholangiocarcinoma by comparison with those obtained with a conventional ADC.

2. Materials and methods

2.1. Patients

From December 2010 through April 2014 inclusively, the MR imaging database of our Institution was retrospectively queried to identify all patients referred for MRI evaluation of suspected or confirmed intrahepatic or hilar mass-forming cholangiocarcinoma. This study was approved by our institutional review board and informed consent was waived.

The study coordinator initially identified 53 patients for whom clinical, histopathological and imaging data were analyzed to ascertain that they actually had intrahepatic or hilar mass-forming cholangiocarcinoma. Twenty-five patients were thus excluded from the study because the cholangiocarcinomas were infiltrating and not mass-forming ($n = 10$), the lesion seen at MRI corresponded to an alternate diagnosis ($n = 7$), the patients had actually cholangiocarcinoma of the main bile duct ($n = 4$) or no definite confirmation of the diagnosis of cholangiocarcinoma was available ($n = 4$) according to our reference standard.

The final cohort comprised 28 patients with intrahepatic or hilar mass-forming cholangiocarcinoma. There were 20 men and 8 women with a mean age of 65.5 years ± 14.5 (SD) [range: 24–90 years]. Eleven patients had intrahepatic cholangiocarcinoma and 17 had hilar cholangiocarcinoma. Cholangiocarcinoma was unifocal in all patients. No patients had underlying hepatic steatosis as evidenced by the absence of signal drop on unenhanced out-of-phase T1-weighted MR images [23] or pre-existing chronic diffuse liver disease as evidenced by the results of imaging or normal results of prior biological liver tests.

2.2. Reference standard

The standard of reference for ascertaining the diagnosis of cholangiocarcinoma was established by a radiologist who was not involved in the MR image analysis and ADC measurements and had full access to the patients files, including clinical files, pathology reports and complete imaging history. The diagnosis of cholangiocarcinoma was confirmed by the results of histopathological and immunohistochemical examination after surgical resection in 18 patients or percutaneous biopsy in 10 patients who had unresectable cholangiocarcinoma.

2.3. MR imaging

All patients underwent MRI examination of the abdomen using a 1.5-T system (Magnetom Avanto®, Siemens Healthcare, Erlangen, Germany, running software Syngo MR B17). The gradient strength of the magnet was 45-mT/m with a maximal gradient slope of 200 T/m/s. High-resolution free-breathing fat-suppressed T2-weighted turbo spin-echo (TSE; TR/TE = 3000/88 msec; matrix size = 230 × 384; section thickness = 7 mm; field of view = 340–360 mm) sequence with respiratory triggering using prospective acquisition correction (PACE) and fat-suppressed three-dimensional volumetric interpolated breath-hold gradient-echo (3D VIBE; TR/TE = 5.4/1.8 msec; flip angle = 10°; section thickness = 3 mm; matrix size = 166 × 320; field of view = 340–400 mm) sequence before and 30, 60, 120 s and 5 min after intravenous administration of a gadolinium-chelate (gadoterate meglumine, Dotarem®, Laboratoires Guerbet, Roissy-Charle de Gaulle, France) were obtained in all patients in addition to DW-MRI sequence using a protocol that was described in details elsewhere [24]. All MRI examinations were performed with a nine-channel anterior phased-array coil and a nine-channel posterior phased-array coil. Patients were imaged in supine position. No bowel preparation before MRI examination and no antispasmodic agents were used.

All DW-MRI examinations were obtained with a free-breathing acquisition before intravenous injection of gadolinium-chelate, with a fat-attenuated single-shot echo-planar DW technique in the axial plane using 3 diffusion *b* factors ($b = 0$, 400 and 800 s/mm^2) within the same acquisition as part of our routine protocol for patients with suspected biliary tumor. The single-shot echo-planar imaging readout was preceded by a diffusion-sensitizing block consisting of two 180° radiofrequency pulses and four motion probing gradient pulses. Parallel imaging with generalized autocalibrating partially parallel acquisition (GRAPPA) was used with an acceleration factor of 2. Fat attenuation was obtained with a frequency-selective fat saturation to reduce chemical shift artifacts. No cardiac gating was used. Parameters for DW-MR image acquisition were as follows: TR/TE = 3900/91 msec; echo spacing, 0.83 msec; reconstruction matrix size, 144 × 192; section thickness, 5 mm; intersection gap, 2 mm; voxel size, 2.1 mm × 2.0 mm × 5.0 mm; field of view, 340–400 mm; number of signal averages, four; receiver bandwidth, 1,302 Hz/pixel; 25 axial sections acquired; acquisition time, 120 s. Partially parallel imaging datasets were reconstructed using a GRAPPA-based algorithm.

2.4. MR image analysis

DW-MRI examinations were blindly analyzed using a commercially available workstation (MMWP with VB17 Syngo Software, Siemens Healthcare) by two radiologists working in consensus. For all readings, a consensus agreement was reached. For qualitative assessment, the three sets of DW-MR images were initially reviewed separately during three different reading sessions and a final review was made during which the three sets were analyzed