Pharmacokinetic Analysis of Dynamic Contrast-Enhanced Magnetic Resonance Imaging for Distinguishing Hepatocellular Carcinoma From Cholangiocarcinoma in Pre–Liver Transplantation Evaluation

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ABSTRACT

Objective. Liver transplantation for intrahepatic cholangiocarcinoma is notorious for rapid recurrence with poor survival rate postoperatively and has therefore been discontinued in most centers. The purpose of this study is to distinguish hepatocellular carcinoma (HCC) from cholangiocarcinoma in pretransplantation imaging evaluation by dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI).

Materials and Methods. From January 2014 to September 2015, 19 patients were included in the study, with a mean age of 62.8 years. All subjects underwent pretransplantation DCE-MRI and surgical excision or core biopsy. The DCE-MRI parameters were measured using the Tofts model 1999. Statistical analysis included nonparametric tests and area under the curve for the receiver operating characteristic.

Results. Fourteen HCCs and 5 cholangiocarcinomas were diagnosed by surgical pathology. The mean size of tumor was 6.4 cm (range, 1.5 cm to 13.7 cm). All DCE-MRI parameters were calculated as the ratio between the tumor and normal liver parenchyma and K^{trans} (1/min) was used as a distinguishing parameter between the two tumors. K^{trans} was higher in the cholangiocarcinoma group (1.89 ± 1.13) than in the HCC group (0.46 ± 0.35). Univariate analysis revealed that K^{trans} has a high significant difference ($P = .001$). The optimal K^{trans} value cutoffs were 1 or more (area under the curve = 0.971) for detection of HCCs or cholangiocarcinomas.

Conclusion. The analysis of DCE-MRI with the kinetic model (Tofts, 1999) presents a new and practical approach indiscrimination of HCC from cholangiocarcinoma for pretransplantation imaging evaluation.

CHOLANGIOCARCINOMA is the second most common primary liver tumor worldwide after hepatocellular carcinoma (HCC) [1]. Historically, liver transplantation for cholangiocarcinoma has been associated with rapid recurrence of disease and poor survival rates [2]. Therefore, to be able to differentiate HCC from cholangiocarcinoma in pre–liver transplantation evaluation would be very important.

Liver tumors can be diagnosed with ultrasound, computed tomography (CT), and magnetic resonance

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imaging (MRI). Although CT and positron-emission tomography – CT [3] studies are good modalities for liver tumor differential diagnosis, radiation burden is of practical concern. An MRI can provide more information than a CT, has excellent contrast between liver parenchyma and tumor, and is without radiation burden [4].

Dynamic contrast-enhanced MRI (DCE-MRI) [5] is a functional image that uses turbo gradient sequence to calculate hemodynamic and perfusion parameters [6,7]. This technique is widely used in cancer diagnosis and follow-up, which can provide information about tumor angiogenesis, distinguish benign from malignant tumors, and monitor treatment response [8,9]. Therefore, the aim of this study is to develop a more reliable method for the diagnosis and differentiation of the two most common primary liver tumors, HCC and cholangiocarcinoma, by analyzing the correlation of DCE-MRI parameters and histopathology, which becomes valuable in pretransplantation evaluation.

MATERIALS AND METHODS

Patients

This study protocol was approved by the Institutional Review Board for Human Studies in this institution. Written informed consent was obtained from all patients. From January 2014 to September 2015, a total of 19 liver transplant recipients (15 male and 4 female) who underwent DCE-MRI of the liver for pretransplantation evaluation and surgical excision or core biopsy were included in this study.

Acquisition Technique

All the DCE-MRI was performed using a 1.5-T scanner (Discovery 450; GE Healthcare, Milwaukee, Wisconsin, United States). A 12-channel body array coil was used for signal reception. Gadolinium (0.5 mm/mL, Magnevist, Bayer AG, Germany) was used as the contrast agent, with a contrast dose of 0.2 mL/kg, injected at a rate of 2 mL/s using an MR-compatible power injector (Optistar MR Injector, Mallinckrodt, St Louis, Mo, United States). DCE-MRI was performed with acquisition of oblique coronal sections with a non–breath-holding technique. Acquisition of T1WI was done with use of Tracks the Ach scanning (K-space sampling) technique in the shortened scan time and variable flip angle sequence (thickness/gap 5 mm/0 mm, TR 3.6 ms, TE 1.3 ms, flip angle 15, number of excitations 1.0, field of view [FOV] = 350 × 350 mm, matrix size = 512 × 512, frequency 320, phase 224, total scan phase 48, per phase 26 images). All patients were asked to breathe slowly and smoothly during imaging.

Imaging Analysis

Post-processing analysis of all DCE-MRI data was performed using commercial software tool (MIStar; Apollo Medical Imaging, Melbourne, Australia) for image segmentation and registration. Regions of interest were manually drawn and set in two areas, one in the tumor and the other in the normal liver tissue, avoiding major blood vessels and the hilar area and not too close to the right and left margins of the liver. The DCE-MRI parameters were measured and analyzed with the Kinetic Model (Tofts 1999) [22]. Analysis of parameters was done using MIStar 3.2 63 workstation. All imaging was performed by the same technician (C.C. Lin with 6 years of experience in MRI examination) to reduce possible technical errors.

Pathology

Tumor pathology was obtained before liver transplantation. Most of the recipients (n = 15) underwent surgical resection for biopsy, whereas 4 patients received core needle biopsy. Pathologic analysis included the histologic grade, pathologic grade, necro-inflammatory activity, fibrosis score (maximum of 6), and histologic type. Two experienced hepatopathologists (more than 10 years in practice) gave the pathologic diagnosis.

Statistical Analysis

To determine the accuracy of results from DCE-MRI using K^{trans} maps, the pathologic results were used as the gold standard. The parameters were calculated as the ratio between liver tumor and normal liver parenchyma. Data were expressed as means and standard deviations. All values were expressed as mean ± SD or median, as appropriate. The Mann-Whitney U test was used to determine the possible relationship between pathology and individual parameters. The optimal cut-off value was determined by using receiver operating characteristic curve analysis. A P value of $< .05$ was considered significant data and analysis was performed using statistics computer software SPSS 17.0 (IBM, Chicago, Illinois, United States).

RESULTS

Based on the histopathology results, 19 subjects were divided into two groups: Group A with HCC (n = 14) and group B with cholangiocarcinoma (n = 5). The mean size of tumor for all was 6.4 cm (range, 1.5 cm to 10 cm). Univariate analysis revealed that K^{trans} (1/min) had a high significant difference ($P = .001$) between groups A and B (Fig 1). The K^{trans} (1/min) was higher in group B (1.89 ± 1.13) than in group A (0.46 ± 0.35). When K^{trans} (1/min) is 1 or greater, high sensitivity (100%) and high specificity (92.9%) were obtained for the diagnosis of intrahepatic cholangiocarcinoma (area under the curve [AUC] = 0.971). For the rest of the parameters {volume of extravascular extracellular space per unit volume of tissue (EES); rate constant between EES and blood plasma (kep); total blood plasma volume (Vp); the AUC from the baseline time point up to 90 s post bolus arrival within the tumor (iAuc90-BN)}, analysis showed no significant difference between the two groups.

DISCUSSION

Living-donor liver transplantation has become a widely accepted modality in treating HCC combined with end-stage liver disease. Invasive biopsy is the gold standard for tumor diagnosis but with associated morbidity and mortality, as well as with an important risk of tumor tract seeding after liver transplantation. Cholangiocarcinoma is the second most common primary liver tumor worldwide, after HCC [1]. Liver transplantation for intrahepatic cholangiocarcinoma is fraught with rapid recurrence and thus has been abandoned by most centers [2]. Many noninvasive methods are adopted during evaluation of the liver recipient for preoperative characterization of the liver tumor.