ASSESSMENT OF AQUAPORINS FUNCTION IN STAGES OF CLINICAL LIVER FIBROSIS USING MULTI-B DWI

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Introduction:

Liver fibrosis, induced by chronic liver diseases, could be reversible in a certain circumstance. So an early detection of liver fibrosis takes a key role in prevention of cirrhosis and even liver cancer. There are many AQPs have been found in liver tissues, including AQP0/1/3/4/7/8/9/11[1]. Recent studies show that AQPs may be involved in bile secretion, gluconeogenesis and other physiological activities[2]. Besides, AQP-1 enhances osmotic water permeability and FGF-induced dynamic membrane blebbing in LEC and thereby drives invasion and pathologic angiogenesis during cirrhosis[3]. However, all of these are preliminary studies. Diffusion weighted (DW) MRI techniques, based on the Brownian motions of water molecules between tissues and cells, is considered an effective, molecular level evaluation method of liver fibrosis. However, the discovery of the aquaporin family of water channels brought a novel understanding of the transport mechanism of water molecules across cell membranes[4]. It is thought that DWI include three parts: perfusion in capillary, free diffusion in intercellular space, and the active transport by AQPs. Wlile the third part is what we focus on. In our previous study, we found that the liver fibrosis stages are positively correlated with the AQP1 expression in animal fibrosis model[5]. Based on our pre-clinical research results, we have the clinical study of AQP function in liver fibrosis.

Purpose:

To investigate the value of aquaporins function in diagnosis of early liver fibrosis in patients by using multiple b-value(multi-b) diffusion weighted magnetic resonancce imaging(MR-DWI).

Materials and Methods:

A total of 6 volunteers,16 patients who had chronic HBV or HCV hepatitis and underwent liver biopsy were enrolled in this study. The study were approved by the Medical Ethics Committee of the hospital, all volunteer and patients signed an informed consent before MRI scanning. Besides the conventional T1WI and T2WI performed, a multi-b DWI was carried out with 18 b values selected from 0 to 4500 s/mm2. A newly developed tri-exponential model equipped at an Advantage Workstation (GE, Mikauwee) was applied for the DW images post-processing (the thresholds that separated the low-b, middle-b and high-b domains were defined as 200 s/mm2 and 1700 s/mm2). We got the standard ADC values, low-b ADC values, middle-b ADC values and high-b ADC values. The biopsy tissue samples were collected for the routine HE staining, Sirius red staining and AQP1immunohistochemistry to determine the stage of liver fibrosis and the AQP1 expression level.SPSS17.0 software was applied for statistical analysis, with $p<0.05$ considered statistically significant.

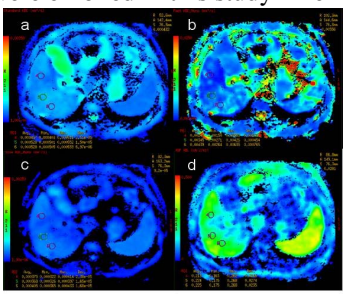

Fig. 1 ADC mappings obtained by the tri-exponential model. a:standard ADC value, b: low-b ADC values c: mid-b ADC values, d: high-b ADC values .

Results:

The AQP1 expression in the liver endothelial of liver fibrosis increased comparing with F0.There was statistical difference between F0 and F4 in each ADC values. While there was statistical difference between F0 and F1 at both low-b values and high-b values.

Discussion:

The "standard" ADC value obtained by conventional method and low-b, mid-b and high-b ADC value mesured by tri-exponential model all can distinguish normal from cirrhosis of the liver tissue. However, the "standard" ADC value can be hardly used to grade early liver fibrosis. While difference can be found between F0 and F1 at both low-b values and high-b values. Limitations of the study: there are many types AQPs with liver cell membranes, . We just observe the expression of AQP1 on pathology.

Conclusion:

The multi-b DW MRI technique, especially at low b and high b values, was capable to detect the F1 stage liver fibrosis, thus a promising tool to realize an early clinical diagnosis of liver fibrosis.

References:

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