Etiology and Functional Status of Liver Cirrhosis by 31P MR Spectroscopy

M. Dezortova[1], P. Taimr[2], J. Spicak[2], M. Hajek[1]

[1]MR-Unit, ZRIR, Institute for Clinical and Experimental Medicine, Prague, Czech Republic, [2]Dept. Hepatogastroenterology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic

Introduction:

Liver cirrhosis is the final stage of various diseases. Regardless of etiology (i.e. viral, alcoholic, autoimmune, metabolic and others) liver injury leads to accumulation of fibrosis septa and nodular regeneration of parenchyma. Information about liver derangement is indispensable and usually needs to be verified by the means of liver biopsy. This examination is invasive, uncomfortable for the patient and not without serious complications. So, an effort has been made to obtain information about the degree of liver injury non-invasively.

Additional important information is the degree of functional limitation of the liver. In clinical settings, this is usually described by Child-Pugh score (CPS), which is calculated from clinical and laboratory tests. As clinicians need to find out the specific etiological diagnosis and disease which caused the liver cirrhosis, all possible additional information is valuable in clinical practice. Imaging examinations which are capable of improving the diagnostic process are very helpful and sought-after.

The aim of the study was to assess the functional status and etiology of liver cirrhosis by quantitative ^{31}P MR spectroscopy.

Methods:

Subjects: A group of 80 patients (49.7±11.5 years) with liver cirrhosis of different etiology (alcoholic cirrhosis in 33 cases, viral hepatitis B or C in 22 cases, cholestatic liver disease in 16 cases, and other etiology in 9 cases) was examined. Results were compared to those of a group of 11 healthy volunteers (40.5±10.9 years). All controls and patients underwent standard clinical biochemical testing before the MR examination which was performed early morning after an overnight fast (at least 8 hours of fasting). A Child-Pugh score (CPS - by standard scoring system)[1] was obtained for all patients (mean CPS = 9.3). Controls and patients were informed about the protocol of the examination in accordance with rules approved by the ethical committee.

MR examination: MR examination was performed on a whole-body MR imager Siemens Vision 1.5T with a dual ^{1}H/^{31}P surface coil. The subjects were examined in the prone position with the liver centered on the surface coil. No tremor because of encephalopathy that could influence the quality of MR examination was observed. Basic MR images in all orientations were obtained for the localization of volumes of interest (VOI) (see Figure 1). ^{31}P MR spectra were measured using a standard two-dimensional chemical shift imaging (CSI) technique in the transversal plane with these parameters: TR/TE = 323/2.3 ms, matrix 16x16, FOV = 480 mm, flip angle = 90º, slice thickness = 4 cm, voxel volumes were 3x3x4 cm^3, 12 acquisitions, total time 16 min.

Spectra evaluation: The position of the VOI for spectroscopic evaluation was chosen in the CSI matrix in the area of the liver where no large intrahepatic blood vessels were visible. We found that a VOI of 36 ml was large enough to neglect structural heterogeneities. Spectra were evaluated manually using standard Siemens Numaris software. Signal intensities of PME, Pi, PDE and βATP were used for the calculation of absolute molar concentrations. The methodology of the absolute quantification using the CSI sequence was published previously[2]. Statistical analysis was done by standard u-, t- and F-tests.

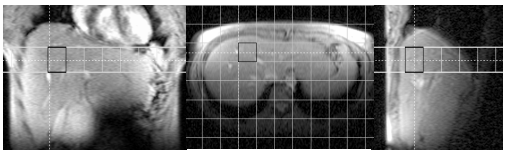

Figure 1. VOI position for MR spectra evaluation

Results:

The spectroscopic data of all patients independent of etiology and controls together with Child-Pugh score are summarized in Table 1.

The relationship between calculated molar concentrations and selected etiologies of liver cirrhosis is summarized in Table 2.

Table 1. Degree of liver injury in MR spectroscopic data

	N	**PME** [mM]	**Pi** [mM]	**PDE** [mM]	**ATP** [mM]
Controls	11	3.09 (1.45)	1.63 (0.55)	10.83 (2.68)	3.72 (0.99)
All patients	80	3.53 (1.45)	1.33 (0.61)	7.16 (2.88)$^{\#}$	2.95 (0.84)*
CPS-A	18	3.64 (1.68)	1.37 (0.56)	9.16 (2.32)	3.24 (0.85)
CPS-B	25	3.60 (1.31)	1.31 (0.57)	7.31 (2.62)$^{\#,\S}$	2.93 (0.78)*
CPS-C	37	3.44 (1.46)	1.33 (0.66)	6.07 (2.80)$^{\#,+}$	2.83 (0.87)*

$^{*}p<0.01$, $^{\#}p<0.001$ from controls; $^{\S}p<0.05$, $^{+}p<0.001$ from CPS-A

Table 2. Different etiologies in MR spectroscopic data

	N	**CPS A:B:C**	**PME [mM]**	**Pi [mM]**	**PDE [mM]**	**ATP [mM]**
Controls	11	-	3.09(1.45)	1.63(0.55)	10.83(2.68)	3.72(0.99)
Alcohol	33	5:6:22	3.48(1.53)	1.19(0.39)$^{\#,\S}$	6.52(2.29)$^{\#,+}$	2.86(0.80)*
Viral	22	7:8:7	3.64(1.55)	1.57(0.77)§	6.47(3.13)$^{\#,+}$	2.84(0.92)*
Cholestatic	16	2:10:4	3.59(1.31)	1.43(0.63)	9.36(2.70)	3.27(0.90)

$^{*}p<0.01$, $^{\#}p<0.001$ from controls; $^{+}p<0.001$ from cholestatic group;
$^{\S}p<0.01$ between alcohol and viral etiological groups

Discussion/Conclusion:

Diagnosis of liver cirrhosis is mainly based on invasive methods such as liver biopsy, various radiological examinations and other clinical tests. The functional severity of liver disease is insufficiently described by the Child-Pugh score or the MELD system. On the other hand, signals from ^{31}P MR spectroscopy reflect intracellular and membrane metabolism in vivo non-invasively. Up till now, there have been only a limited number of studies concerning human liver diseases. The authors have mostly described the increased ratio PME/PDE or PME/ATP in patients classified according to Child's grading system[3-5]. ^{31}P MRS data correlated well with the histological grade and stage.

Contrary to previous studies, where only relative signal ratios were used, we calculated absolute concentrations of the metabolites[2]. We believe that relative quantification using only signal intensity ratios cannot fully describe metabolic changes and absolute quantification should be taken into account even if a number of correction factors must be calculated.

Our data suggest that the concentration of PME in patients, which mainly represents the intermediates on the pathway of phospholipid biosynthesis, is the same as in the controls whereas the most important changes can be found in a decrease of PDE which is considered to be a marker of membrane phospholipids and catabolic processes. We may speculate that decreased concentration of PDE in liver cirrhosis correlates with a decreased number of active hepatocytes. In this way, the decrease of ATP and Pi concentrations may correspond to altered energy turnover.

According to differences in ^{31}P MR spectra of patients to controls, we can distinguish alcoholic, viral and cholestatic etiologies of liver cirrhosis. Patients with alcoholic and viral etiology differed in PDE ($p<0.001$) and ATP ($p<0.01$) from the control group. Contrary to viral etiology, patients with alcoholic etiology also differed in Pi ($p<0.001$) from controls. No significant changes were found in patients with cholestatic disease from controls, nevertheless, this group differed from both alcoholic and viral groups ($p<0.001$) in PDE. We suppose that it reflects different pathophysiological mechanisms in various liver diseases.

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