

Evaluation of Hepatic Metabolite Changes for Differentiation Between Non-Alcoholic Steatohepatitis and Simple Hepatic Steatosis Using Long Echo-Time Proton Magnetic Resonance Spectroscopy

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Abstract : Purpose: To assess the changes of hepatic metabolite for differentiation between non-alcoholic steatohepatitis (NASH) and simple steatosis on proton magnetic resonance spectroscopy (1H-MRS) in both humans and animal model. Methods: The local institutional review board approved this study and subjects gave written informed consent. 1H-MRS measurements were performed on a localized voxel of the liver using a point-resolved spectroscopy (PRESS) sequence and hepatic metabolites of alanine (Ala), lactate/triglyceride (Lac/TG), and TG were analyzed in NASH, simple steatosis and control groups. The group difference was tested with the ANOVA and Tukey's post-hoc tests, and diagnostic accuracy was tested by calculating the area under the receiver operating characteristics (ROC) curve. The associations between metabolic concentration and pathologic grades or non-alcoholic fatty liver disease (NAFLD) activity scores were assessed by the Pearson's correlation. Results: Patient with NASH showed the elevated Ala ($p < 0.001$), Lac/TG ($p < 0.001$), TG ($p < 0.05$) concentration when compared with patients who had simple steatosis and healthy controls. The NASH patients were higher levels in Ala (mean \pm SEM, 52.5 ± 8.3 vs 2.0 ± 0.9 ; $p < 0.001$), Lac/TG (824.0 ± 168.2 vs 394.1 ± 89.8 ; $p < 0.05$) than simple steatosis. The area under the ROC curve to distinguish NASH from simple steatosis was 1.00 (95% confidence interval; 1.00, 1.00) with Ala and 0.782 (95% confidence interval; 0.61, 0.96) with Lac/TG. The Ala and Lac/TG levels were well correlated with steatosis grade, lobular inflammation, and NAFLD activity scores. The metabolic changes in human were reproducible to a mice model induced by streptozotocin injection and a high-fat diet. Conclusion: 1H-MRS would be useful for differentiation of patients with NASH and simple hepatic steatosis.

Keywords : non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, 1H MR spectroscopy, hepatic metabolites

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