

Analysis of Clinical and Histopathological Changes That Influence Liver Stiffness measured by MR Elastography

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Purpose

MR Elastography (MRE) has been reported to be highly correlated with the substantial fibrosis stage. However, despite a high diagnostic accuracy, several studies reported incomplete concordance between MRE and liver fibrosis in patients with chronic liver diseases, owing to a substantial overlap between different fibrosis stages, especially in pre-cirrhotic changes of the liver. Recent data has been observed that lipid accumulation, acute liver inflammation or age may also produce higher liver stiffness (LS) and, therefore, resulting an overestimation of liver fibrosis stage. To our best of knowledge, those confounding factors are still not been elucidated clearly. The purpose of our study was to determine the influence of the histological or clinical parameters on LS measured by MRE in patients with chronic liver diseases.

Materials and Methods

From Jan. 2011 to Dec. 2013, total 354 patients with chronic liver diseases underwent MRE and histological examination during a 3-month interval. MRE was performed on a 1.5-T unit (Avanto, Siemens) with 16-channel phase-array coil, an acoustic driver system (Resoundant, Mayo Clinic). The mean LS was measured on the elastograms in kilopascals (kPa) (Fig.1). Clinical, laboratory data and histological parameters were recorded. The spleen volume was also measured at the continuous axial T1-weighted 3D GRE images using semiautomatic software on the workstation (GE Healthcare, Milwaukee, WI, USA). Relationships between LS and the confounding parameters were characterized using the Spearman correlation coefficients. The influence of the parameters on the LS was investigated through univariate- and multivariate standard regression.

Results

We found LS correlate with iron deposition ($r=0.122$, $p=0.024$), necroinflammatory activity ($r=0.389$, $p<0.001$) and a strong correlation with fibrosis ($r=0.777$, $p<0.001$). But, steatosis was not correlated with LS. The univariate regression analysis showed that age, etiology, fibrosis, activity, iron deposition, AST, ALT, total bilirubin and spleen size were positively correlated with LS. Platelet level was negatively correlated with LS. In multivariate regression analysis, there were three variables that independently correlated the LS: fibrosis stage ($p<0.01$), necroinflammatory activity ($p=0.03$), and spleen size ($p<0.01$) (Table 1). Those parameters together explained 58.7% of the variances of the LS ($R^2=0.587$, $p<0.0001$), with substantial liver fibrosis making the most unique contribution (26.0%).

Discussion

The results suggest that higher values of LS are obtained for patients with advanced fibrosis, increased necroinflammatory activity and increased spleen size. The stage of fibrosis is the single most important factor. Acute inflammation of the liver can also independently affect liver stiffness measured by MRE. Increased spleen size may positively correlate with liver stiffness because of portal hypertension.

Table 1. Influences of clinical, laboratory and histological parameters on liver stiffness measurement using MR Elastography

	Univariate	p	Multivariate	p	Unique contribution
Age (years)	0.041(0.029-0.054)	<0.01	-0.006(-0.002-0.008)	0.414	0.3%
Sex (male vs. female)	0.357(-0.077-0.79)	0.106	-	-	-
Etiology(viral vs. alcoholic)	1.005(0.656-1.354)	<0.01	-0.034(-0.353~0.284)	0.832	2.25%
Fibrosis	0.829 (0.729-0.928)	<0.01	0.707(0.545~0.868)	<0.01	26%
Activity (A0-A3)	0.691(463-0.919)	<0.01	0.261(-0.026~0.496)	0.03	2.2%
Fat (S0-S3)	0.052(-0.202-0.307)	0.687	-	-	-
Iron (Y vs. N)	0.952(0.125-1.779)	0.024	0.615(-0.053-1.284)	0.071	1.54%
AST(xULN)	0.469(0.318-0.619)	<0.01	0.307(-0.003~0.004)	0.648	2.7%
ALT(xULN)	0.265(0.115-0.414)	0.001	-0.355(-0.618~-0.092)	0.008	3.24%
Total Bilirubin	0.088(0.006-0.171)	0.035	0.025(-0.034-0.084)	0.405	0.3%
Platelet	-0.01(-0.012~-0.008)	<0.01	-0.001(-0.004~-0.002)	0.459	0.3%
Spleen Size	0.003(0.002-0.004)	<0.01	0.001(0.001~0.002)	<0.01	5.7%

Univariate and Multivariate analyses are expressed as unstandardized B coefficients with 95% confidence intervals.

Conclusions

The degree of liver fibrosis, necroinflammatory activity and spleen size independently and significantly exaggerated LS. The stage of fibrosis is the single most important factor.

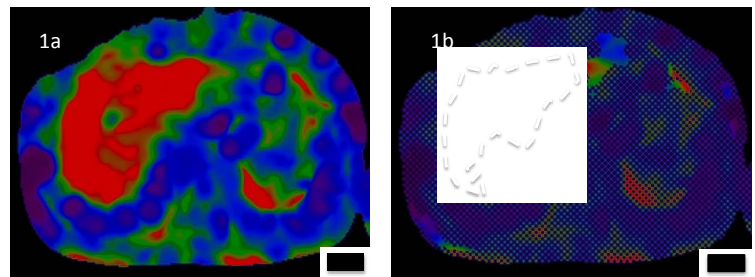


Figure 1. A 67-year-old male, a Hepatitis B carrier, underwent MRE. Active liver cirrhosis(F4) with necroinflammatory activity: A3 was confirmed. No fat or iron deposition. (1a): MR elastogram. (1b): confidence map. Liver stiffness was measured by place a region of interest (dotted line) as large as possible in the confidence area. The elastogram shows a mean stiffness value of 6.40 kPa.