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Title: Non-invasive evaluation of liver stiffness after splenectomy on CCl₄-induced liver fibrosis in rabbits

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1 What did this study explore?

This study was to explore the diagnostic accuracy of liver stiffness measurement (LSM) by ElastPQ in liver fibrosis models, and to assay the longitudinal changes of liver stiffness by ElastPQ after splenectomy at different fibrosis stages.

2 How did the authors perform all experiments?

Wang MJ designed the research; Wang MJ, Wang H, and Ling WW performed the research, including animal modeling, Ultrasound-based examinations, serum parameters test, splenectomy and liver histological assessment.

3 How did the authors process all experimental data?

The quadratic-weighted κ coefficient of Cohen was used to assess the agreement between the two doctors who analyzed the histological sections, while the ICC (interclass correlation coefficient) was used to assess the agreement between the two examiners who performed the liver stiffness measurement via ElastPQ.

The median of LSM obtained by both operators for each rabbit form ElastPQ was calculated and for further analyses. Because the LSM values were not normally distributed, the Kruskal-Wallis nonparametric analysis of variance test was used to compare these values with the categories of the consensus fibrosis stage. Correlations between the LSM and the histologic fibrosis stage were further analyzed by using Spearman correlation coefficients. The diagnostic performance of ElastPQ and serum fibrosis markers including type IV collagen, and hyaluronic acid was assessed by using receiver operating characteristics curves (ROC). The optimal cutoff values for the prediction of different fibrosis stages were chosen to maximize the sum of sensitivity and specificity, and the corresponding positive predictive values (PPV), negative predictive values (NPV) were computed. AUC (area under ROC) values for the different diagnostic criteria for the same data were compared using the nonparametric DeLong test.

Quantitative data were presented as mean \pm SD (standard deviation) or median (quartile), while categorical data were expressed as number of cases with/without percentage. Statistical analyses also included nonparametric Mann-Whitney U test, and Student's t test.

All of the statistical analyses were performed using SPSS 19.0 (SPSS, Chicago, IL, USA) for windows, and with significance set at P value < 0.05 .

4 How did the authors deal with the pre-study hypothesis?

Splenectomy is one of surgical interventions for liver cirrhotic patients with hypersplenism. Previous studies indicated the improvement of liver function after splenectomy; however, whether the fibrosis stage will be improved following splenectomy is not well determined. We hypothesized that splenectomy could alleviate liver fibrosis, which can be detected by non-invasive method (ElastPQ).

5 What are the novel findings of this study?

ElastPQ is an available, convenient, objective and non-invasive technique for

the assessment of liver stiffness on CCl₄-induced liver fibrosis in rabbits, which pave the way for its clinical application. And liver stiffness measurement by ElastPQ could be useful for dynamic monitoring the changes of liver stiffness in rabbit models, or even patients after splenectomy.

Sincerely,

A handwritten signature in black ink, appearing to be 'Bing Peng', written over a horizontal line.

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