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# Is this the end for liver biopsy?

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**TITLE** Serum markers detect the presence of liver fibrosis: a cohort study

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**LIST OF ABBREVIATIONS** Alanine aminotransferase (ALT), aspartate aminotransferase (AST)

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## SUMMARY

Liver biopsy is regarded by many as the gold standard by which the extent of liver fibrosis is identified and indeed quantified. Rosenberg[1] and colleagues report their work on non-invasive markers of fibrosis which may supersede the use of liver biopsy.

They examined nine surrogate markers of liver fibrosis which included collagen IV, matrix metalloproteinase 2, matrix metalloproteinase 9, tissue inhibitor of matrix metalloproteinase 1, tenascin, laminin and hyaluronic acid. Levels of these markers were then correlated with fibrosis seen on liver biopsy. In total 1,021 subjects were examined, and discriminate analysis was performed to identify an algorithm which best identified fibrosis as seen on biopsy.

The final algorithm incorporated Age, Hyaluronic Acid, amino-terminal propeptide of Collagen III and tissue inhibitor of matrix metalloproteinase 1. This detected fibrosis with a sensitivity of 90% whilst also accurately describing the absence of fibrosis (negative predictive value for significant fibrosis of 92%). The algorithm was particularly useful in alcoholic liver disease and non-alcoholic liver disease, and slightly less so in hepatitis C.

Notably, the algorithm was described as being as accurate as the assessment of blinded pathologists.

## OPINION

This algorithm is an improvement on those previously published although there are some limitations, namely its inability to discern intermediate grades of fibrosis between normal and severely fibrotic/cirrhotic liver. This may be of particular importance in conditions such as hepatitis C where decisions on treatment are potentially influenced by the amount of fibrosis present. Notably, it was in this patient group where the algorithm was least effective.

Furthermore, in such patients the liver biopsy also provides important information on the level of necro-inflammation which is not always predicted by serum ALT/AST. An editorial on this paper by Bissell[2] makes the interesting observation that, rather than looking for markers of fibrosis, we should be trying to identify markers which describe the balance of pro- and anti-fibrotic markers in the liver. This would provide important information on the direction in which fibrosis is heading (improving or worsening) in a given liver rather than information on the amount of fibrosis present.

Although liver biopsy is always referred to as the gold standard, it is important to be aware of its limitations. There are significant sampling issues with liver biopsy. A study in patients with hepatitis C demonstrated that if biopsies were taken from both the left and right lobe, in up to 25% of cases there was a difference of at least one fibrosis stage between the biopsies.[3] This is increased further when sub-optimal samples of tissue are obtained. A biopsy length of 2·5cm with at least 4 portal tracts has been described as standard for liver tissue.[4]

In addition there are well reported figures for mortality (0·13–0·33%) and morbidity such as pain (30%) and non-fatal bleeding (0·35–0·5%) associated with liver biopsy.[5] Of course these risks can be justified in cases where there is a genuine diagnostic dilemma, and ultimately the patient has the right to say no. However, with the emergence of increasingly accurate serum markers of fibrosis is it warranted to put a patient through a liver biopsy to measure the amount of fibrosis? I think not.

While there will always be a role for liver biopsy, I predict that this exciting new data will remove the need for liver biopsy in many patients.

## REFERENCES


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