

Hepascore – A New Liver Function Test

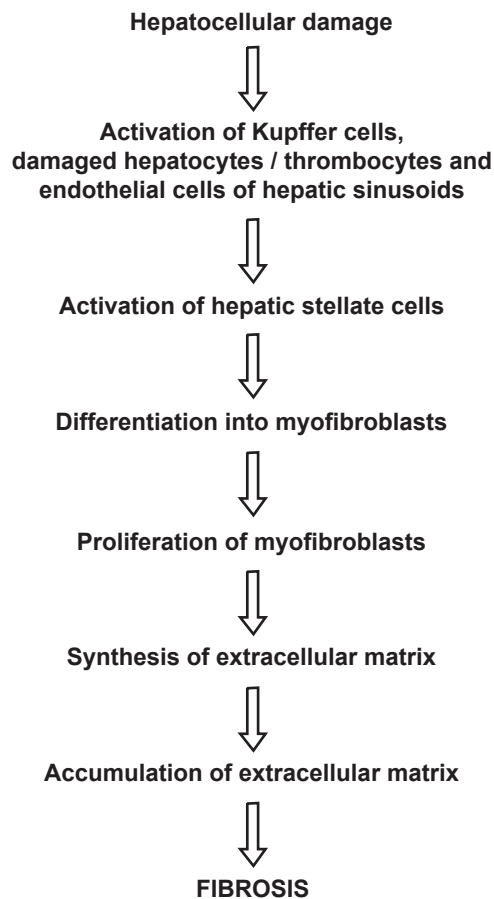
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INTRODUCTION

Hepascore is a new liver function test derived from a panel of four serum analytes which is capable of accurately predicting the extent of liver fibrosis (scarring) in a wide variety of liver diseases (1). It is a non-invasive method for assessment of liver fibrosis or cirrhosis in

HEPATIC FIBROSIS

Hepatic fibrosis is a gradual process of increased production and decreased degradation of extracellular matrix materials.



Hepatic fibrosis is an important consequence of a wide variety of chronic inflammatory disorders affecting the liver. Hepatic fibrosis is the basis for the development of portal hypertension, complications of chronic liver diseases i.e., esophageal varices and/or ascites, and liver failure. Progressive liver fibrosis develops over a number of years and the leading causes are hepatitis viruses, particularly hepatitis B and C, alcoholic and non-alcoholic fatty liver disease, hepatic immune diseases and drug-induced liver damage [3].

adults, developed by Australian investigators. High diagnostic performance was reported for both significant fibrosis and cirrhosis (2).

Assessment of the degree of liver fibrosis (i.e., staging) is done for various reasons: (i) To determine the prognosis of chronic liver disease (ii) To select patients for specific treatment (iii) To monitor the success of treatment.

Liver fibrosis is the main determinant of hepatitis C virus related morbidity and mortality. Furthermore, the stage of fibrosis is prognostic and provides information on the likelihood of disease progression and response to treatment.

Moreover, decision on whether patients need endoscopic screening for esophageal varices and ultrasound and serum α -fetoprotein screening for the development of liver cancer relies on the ability to accurately diagnose cirrhosis [4].

IS LIVER BIOPSY AN ADEQUATE REFERENCE TEST?

Until now the invasive needle biopsy of the liver is considered the "gold standard" for diagnosis of hepatic fibrosis and cirrhosis, which has several limitations [5].

Shortcomings of histological staging:

1. In liver biopsy specimens of inadequate size, stage is likely to be underscored in chronic viral hepatitis.
2. Due to subjective scoring there are chances of interobserver variation.
3. Lack of standardization of the fibrosis scores.
4. It is an expensive procedure.
5. It necessitates admission to a day ward.

Risk of complications of liver biopsy:

1. Pain
2. Bleeding
3. Biliary peritonitis
4. Pneumothorax
5. Death
6. Contraindicated in a number of patients with blood clotting disorders, such as coagulopathy, thrombocytopenia and ascites.

HEPASCORE (A COMPOSITE FIBROSIS PANEL)

The difficulties associated with liver biopsy have led to interest in the development of non-invasive testing such as hepascore to de-

termine the degree of hepatic fibrosis.

The knowledge of alterations in blood levels of various biomarkers reflecting the progressive degrees of fibrosis, and ultimately cirrhosis has led to the development of predictive models based on clinically determined algorithms that utilize selected markers. One such model is hepascore, based on the measurement of serum bilirubin, gamma glutamyltransferase, α_2 – macroglobulin and hyaluronic acid levels along with age and sex [6].

Hepascore requires serum from a small fasting blood sample (5-10ml) which should be protected from light. The diagnostic panel used to calculate hepascore comprises the results of four analyses and the age and sex of the patient. This data is inserted into an equation and the hepascore is easily calculated and presented as a number between 0.00 and 1.00. In patients with hepatitis C, the best diagnostic information is given by a central cut off point for the detection of significant liver fibrosis and a higher cut off point for cirrhosis.

A hepascore value ≥ 0.50 indicates significant liver fibrosis, whereas if the result is <0.50 significant fibrosis is absent. If the value is ≥ 0.84 , cirrhosis of the liver is likely present and if the value is <0.84 cirrhosis is absent(7).

Fibrosis is then scored on the 5 – point METAVIR scale as follows :

F0 - no fibrosis

F1 - portal fibrosis alone

F2 - portal fibrosis with rare septae

F3 - portal fibrosis with many septae

F4 - cirrhosis

“Significant fibrosis” corresponds to stages F2, F3 and F4.

“Advanced fibrosis” corresponds to stages F3 and F4 (8).

In an internal validation using paired liver biopsy and serum samples from patients with HCV infection, the optimum cut off was 0.55. Based on data from entire population; a score of ≥ 0.55 was 83% sensitive, and 65% specific for the presence of hepatic fibrosis METAVIR score $\geq F2$ (9).

FUTURE IMPLICATIONS OF HEPASCORE

1. Hepascore has been shown to be as accurate as liver biopsy in patients with hepatitis C virus infection.
2. The development of hepascore and its application to patients with hepatitis C infection.
3. Hepascore is applicable to the assessment of fibrosis in alcoholic and non-alcoholic fatty liver disease.
4. Hepascore will allow more frequent monitoring to detect progression of liver disease and also response to therapy.

CONCLUSION

The main advantages of non-invasive fibrosis tests like hepascore are the absence of risks and the potential to reflect the status of the entire liver.

Thus, hepascore represents a new class of liver function tests which gives information on fibrosis previously unavailable from se-

rum tests. It is a significant advance in the case of patients with liver disease and it replaces liver biopsy, a more expensive and potentially dangerous test. Moreover, hepascore makes monitoring at regular intervals possible, whereas repeated liver biopsies are fraught with difficulty and therefore, seldom performed.

LIMITATIONS

Most important limitation is lack of discrimination at intermediate stages of fibrosis. Besides, liver biopsy may still be needed to rule out concomitant pathologies known to influence response to anti-viral treatment [10].

Future practice guidelines must be addressed for the role of non-invasive tests in assessing the stage of fibrosis [11].

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