

# Assessment of hepatic fibrosis in 2015, what should the clinicians know?

## Introduction

Liver fibrosis (LF) is the end result of different chronic inflammatory disorders of the liver. It can ultimately progress to liver cirrhosis with subsequent liability to develop portal hypertension, as cites, hepatocellular carcinoma (HCC) and liver failure. Assessment of liver fibrosis is of paramount importance in taking treatment decisions and for follow up of cirrhotic patients to guard against HCC. Liver biopsy is currently considered the standard reference for assessing liver fibrosis and cirrhosis. Recently; the discovery and validation of novel serum biomarkers and radiological methods to assess liver fibrosis has markedly decreased the need for liver biopsy.

## Biomarkers

Biomarkers are either direct or indirect depending upon whether they can reflect or not the pathogenesis of liver fibrosis. Direct markers which can reflect extracellular matrix deposition (e.g.; Procollagen I peptide, Procollagen III peptide, Type I collagen, Type IV collagen, chondrex (YKL-40), Laminin and Hyaluronic acid) or degradation, (e.g.; MMP-2, TIMP-1, -2) and some cytokine (e.g.; TGF-beta, TGF-alpha and PDGF) have been used widely to assess liver fibrosis with good reproducibility. Indirect markers (e.g.; AST, ALT, platelet count, coagulation profile, gamma-glutamyl transferase, total bilirubin, alpha-2-macroglobulin, and haptoglobin) although cannot reflect changes in extracellular matrix activity; they can reflect changes in liver function and are routinely used in clinical practice. Different panels combining biomarkers (direct; indirect or a combination of both) have been proposed and many of them were validated in the last decade. Examples of famous panels include AST to Platelet ratio index (APRI), FIB-4, FORNS which are non-patented and Fibro Test, ELF and Fibro Meters which are protected by patent and commercialized by biomedical companies. The discovery and validation of new biomarkers panels will continue until the perfect panel is reached.

## Radiological methods

Different array of radiological methods have been used to assess liver fibrosis recently. These methods include: vibration controlled transient elastography (VCTE), shear wave elastography (SWE), acoustic radiation force imaging (ARFI) and magnetic resonance elastography (MRE). Among all radiological methods; VCTE has been extensively validated and approved by food and drug administration (FDA) as a non-invasive tool for assessment of hepatic fibrosis in patients with liver disease. MRE is a promising tool however the cost

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and wide spread availability still limiting its use in clinical practice. Other emerging modalities including diffusion weighted magnetic resonance imaging and contrast enhancing ultrasound is still under investigations.

## Utility of non-invasive methods

Non-invasive methods to assess liver fibrosis have been used extensively in viral hepatitis however their use in alcoholic and non-alcoholic fatty liver disease is increasing. Non-invasive methods are useful in differentiating patients with cirrhosis (F4 METAVIR) or less precisely those with clinically significant fibrosis (F2 METAVIR). They can also predict complications of liver fibrosis and cirrhosis (e.g.; esophageal varices), monitor liver disease progression and response to therapy where liver biopsy cannot be repeated.

## Future of non-invasive diagnostics

It is expected that non-invasive methods either biomarkers or radiological methods will greatly replace liver biopsy for assessment of liver fibrosis especially in viral hepatitis; however liver biopsy will be still needed in other indications. Combining biomarkers and radiological methods increases their accuracy however validated algorithms are needed to establish this approach. More studies comparing non-invasive diagnostics with different liver related events are needed also exploring their role in post-transplant population is an area of future research.

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## Conflict of interest

Author declares that there is no conflict of interest.