

Elastography for Measuring Liver Fibrosis

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Fibrosis is the end result of many pathological processes that involve liver. It is the consequence, and in itself a perpetuator, of ongoing liver damage due to any aetiology. Monitoring the progression of hepatic fibrosis in patients with chronic liver disease (CLD) is imperative for early detection and control of complications. Approximately 20 to 40% of patients with CLD will develop significant liver fibrosis. The scoring of fibrosis is according to METAVIR scoring system for fibrosis, with histological classification showing stage two fibrosis (F2), 10% will progress to cirrhosis and 1% to 5% will develop hepatocellular carcinoma (HCC) within two to three decades^{1,2}. The diagnosis of liver fibrosis stage is also important for evaluating the severity and extent of autoimmune/cholestatic liver diseases^{3,4} and for reinforcing interventions in patients with Non Alcoholic Fatty Liver Disease (NAFLD) and Alcoholic Liver Disease (ALD). Extent of liver fibrosis is also important to determine whether anti-viral therapy should be given in individuals with chronic viral hepatitis and for dietary and behavioral interventions in subjects with metabolic syndrome. The measurement of fibrosis is also important considering the prevalence of hepatitis B and/or C, and metabolic syndrome in the Pakistani population¹⁻⁴.

Liver biopsy has traditionally been considered the gold standard to stage liver fibrosis. But it is an invasive and costly procedure, besides being associated with post-procedure complications of pain

and discomfort in 30%, haemorrhage in 0.3% and a mortality of 0.01% of the cases⁵. Patients may refuse liver biopsy especially in those cases where a repeat biopsy is required, because of the perceived risks and previous experience. Liver biopsy typically samples only 1/50,000 of liver and is subject to sampling error and inter observer variability in a significant number of biopsies⁶. As, liver biopsy is a procedure with some degree of morbidity and mortality and not an easily acceptable procedure for the patients and their attendants despite counseling, hence increasing demand for a non-invasive and reliable test for assessing liver fibrosis are being considered.

To meet with this demand, a number of non invasive tools for liver fibrosis estimation have been developed. Fibrosis can be measured noninvasively based either on a biological approach which refers to evaluation with serum biomarkers in consideration with clinical parameters, or on a physical approach of directly measuring liver stiffness which is the principal behind imaging based elastography. The most validated serum biomarkers include Fibrotest (combining gammaglutamyltranspeptidase, total bilirubin, α -2-macroglobulin, apolipoprotein A1, haptoglobin, age and gender) and aspartateaminotransferase-to-platelet ratio index (APRI). These, however, are not liver specific and cannot differentiate between the stages of fibrosis at any given point. The fibrosis score panels based on combinations of several blood tests also have limited accuracy in differentiating moderate and severe fibrosis and are not widely available⁷⁻⁹.

Imaging based stiffness measurement employs either ultrasound or Magnetic Resonance Imaging (MRI). Ultrasound-based techniques include tran-

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sient elastography (TE) and acoustic radiation force impulse imaging (ARFI). Elastography is based on a simple physical principal of strain and stress measurement. Fibrosed tissue has less elasticity than the normal tissues and allows faster propagation of strain or shear wave measurable in KPascals (KPa) providing an ultrasound or MR-based surrogate measure of liver fibrosis by quantifying stiffness. The ultrasound based TE is easier, economical and now increasingly available even in Pakistan. It is referred to as (TE), Fibroscan™ (after the first commercial instrument employing strain wave elastography) or LSM (liver stiffness measurement). The results are easily measurable and comparable over successive follow up examinations. Most of the equipment available in Pakistan is the shear wave technology based, which the radiologist find easier to use as it gives a background gray scale image of rather good resolution and one can readily exclude mass lesions, and fat or secondary deposits, as well as surrounding free fluid. The University of Pavia, Italy, has been the pioneer in the field of liver ultrasound shear wave elastography (SWE); most of their work has been based on studying patients with chronic hepatitis C (CHC)⁷. In CHC patients, elastography has been found to be accurate in discriminating between the various stages of fibrosis (METAVIR stages F0-F4) with cut off values defining the progressive stages of fibrosis and ultimately cirrhosis. However, the performance of elastography in patients with CLD of causes other than CHC, has not been evaluated as extensively. Only a few reports are available in patients with chronic hepatitis B (CHB) and with steatosis. The few studies that have been performed in patients with other aetiologies of CLD have used the reference ranges obtained from CHC studies. The performance of strain wave and shear wave elastography has been compared in many studies and declared as equivalent with a difference of a few units defining each fibrosis stage^{9,10}.

Noninvasive methods for liver fibrosis diagnosis are gaining more credibility across guidelines and experts recommendations, particularly in chronic viral hepatitis¹⁰. However there are a number of fac-

tors that affect the accuracy of these measurements. These include obesity i.e. patient's body mass index (BMI), respiratory status, necrosis and inflammatory score/ grade, coexistent cholestasis, and congestion due to right heart disease and all those diseases that may affect liver texture including the quite common hepatic steatosis. Again it is likely to be affected by operator skill. This is important in Pakistan where both gastroenterologists and radiologists with varying degree of expertise are doing TE. The presence of ascites and previously unsuspected mass lesions in liver as well as deranged LFTs, markedly skew the measurements, which requires careful interpretation and clinical correlation. TE has high performance for the diagnosis of cirrhosis, but is moderately accurate for diagnosing mild to moderate liver fibrosis and may not be interpretable in about 20% of cases⁸. The accuracy of ARPI is similar if not superior to TE for the diagnosis of liver fibrosis⁹.

Magnetic resonance elastography (MRE), an MRI-based technique, is an accurate predictor of liver fibrosis, studies have shown that MRE is more accurate than serum fibrosis markers¹¹. In one study, MRE was shown to be even more accurate than both TE and APRI. Although biopsy remains the primary diagnostic tool for almost one half of respondents, non invasive methods, particularly Fibroscan/ elastography, have significantly reduced the need for liver biopsy in many parts of the world.

Finally, there is a big need for clinical guidelines and policy to implement the currently noninvasive tools to assess liver fibrosis in local scenario.

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Editors Note

Sina Aziz

In March issue of 2016, articles have been published on a fast track system. Most articles were processed and published in less than a month. This was done, as in the last review of the Annals of Abbasi Shaheed Hospital and Karachi Medical and Dental College by the competent authorities such as Higher Education Commission (HEC) and Pakistan Medical and Dental Council (PMDC) it was requested that Annals of Abbasi Shaheed Hospital and Karachi Medical and Dental College should be quarterly.

The usual payment was taken from authors (as per routine). No extra cost was taken. The Editor acknowledges the effort put in by the team (authors, peer reviewers and editorial board) for helping in making Annals of Abbasi Shaheed Hospital and Karachi Medical and Dental College quarterly.

The Editor congratulates the authors, peer reviewers, editorial board member (within and outside KM&DC) and International Advisors for recognition of Abbasi Shaheed Hospital and Karachi Medical and Dental College by Higher Education Commission (HEC) and Master list of Thomson Reuters (ESCI).

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