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Hepatic fibrosis imaging: Trends and feasibility

Saba Sohail

EDITORIAL

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Hepatic fibrosis is the end result scarring of extensive damage to the parenchymal structure with collagen fibers proliferation. The key event is the local inflammation induced by a myriad causes but most commonly by the damage induced by chronic viral hepatitis though hepatic steatosis and concomitant HIV infection is being increasingly recognized both as a cause and companion finding.[1,2] On the one hand, inflammatory reaction triggers the hepatic stellate cells to deposit fibrous material at the site of injury. On the other hand, intracellular oxidative stress causes mitochondrial and endoplasmic reticulum dysfunction with resultant production of the biochemical mediators of injury.[3] Alpha 2(1) collagen expression in cultured liver cells has been shown to act as a profibrogenic cytokine by altering collagen gene expression.[4] Regardless of the cause, the end result of fibrosis is increased liver stiffness and scarring with continued structural changes leading to cirrhosis and even hepatocellular carcinoma. Evaluation of fibrosis, therefore, remains an important issue in the management of any chronic liver disease particularly with reference to hepatitis and hepatic steatosis.

There are many direct and indirect methods for this evaluation ranging from biopsy - the gold standard - to radiological imaging modalities to indirect biochemical indices. Biopsy is an invasive method associated with definite complications and sampling error is argued as a limitation.[5] Non-invasive diagnosis is ideally desired. Many combinations and models have been developed to achieve this aim. The most popular has been AST - to - platelet - ratio index (APRI) with specificity ranging from 67-97% and NPV of about 80% which mainly serves to exclude marked fibrosis.[6] Another combined index is FIB4 which combines platelet count, AST and ALT levels with age, and a value of 1.45 or greater predicts significant fibrosis.[7] Other routine indices such as Forn's index (using age, gamma glutamyl transpeptidase, total serum cholesterol and platelets) and non-routine measurements of extracellular matrix remodelling markers, Hyaluronic acid and Methacetin breath tests and even mathematical models have been utilized in the non-invasive evaluation of fibrosis and shown to be expensive and not markedly superior over each other.[8,9] Fibroscore is another development in this regard as reported by Ashraf *et al.* in the current issue.

The available local literature is increasingly brimming with initially biopsy-based and now clinico-biochemical-based parameters and models. Notable is the paucity of local reports on hepatic fibrosis and steatosis imaging. Radiology has the advantage of non-invasive imaging of the liver and biliary tract and its related vasculature in the context of fibrosis and the subsequent complications. The spectrum includes gray scale and Doppler ultrasound as the basic modality supplemented by transient elastography (TE), CT scanning, MRI including MR Elastography (MRE), single positron emission tomography (SPECT) and even dual energy X-ray absorptiometry (DEXA) scanning.

Fibrosis is associated with scarring and increasing liver stiffness so that the liver surface becomes rough and finally irregular with blunting of the inferior edge. It was initially believed that fibrosis cannot be detected or evaluated with ultrasound.[10] This view has been questioned time and again with reports of accurate grading with simultaneous use of multiple-frequency probes and a combination of gray scale and Doppler parameters which serve to improve the accuracy of sonographic diagnosis and grading of fibrosis quite comparable to histopathology.[11,12] However, the concept remains debatable with conflicting reports pouring in and, therefore, research vistas remain open.

The same morphological change i.e. increasing liver stiffness can also be evaluated with TE, MRE and DEXA. TE introduced under the brand name of '*Fibroscan*' caught on the fancy of clinicians in the belief that it may provide a reliable alternative to biopsy for the evaluation of fibrosis. It measures liver stiffness in units termed kPa and the stiffness itself is displayed as a spectrum of blue to green colour superimposed over the gray scale ultrasound image. However, with increased experience, its limitations have been recognized as an inability to differentiate between the cause of stiffness with steatosis, fibrosis and deposition disorders such as amyloidosis giving nearly the same results and obesity being a considerable technical limitation.[13-15] In Pakistan, very few centres have the equipment; the clinical utility is under establishment and yet to gain the clinician's confidence. Cost and limited experience are very important considerations in its widespread

Department of Radiology, Dow Medical College and Civil Hospital, Karachi.

Correspondence: *Dr. Saba Sohail, Department of Radiology, Dow Medical College and Civil Hospital, Karachi.*
E-mail: saba.sohail@aku.edu

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acceptability and evidence-based reports are certainly needed on this aspect from the centres that are actually using the modality.

MRI uses many diffusion based chemical shift and elastography techniques for evaluation of fibrosis. MRE also measures hepatic stiffness measurements in kPa with steatohepatitis without fibrosis having greater stiffness (mean of 3.24 kPa) than simple steatosis (mean kPa of 2.51) and lower than fibrosis (mean 4.16 kPa).[16] MRE is reported to have an even greater ability than DWI to distinguish between the stages of fibrosis.[17] At present, the use of the various MR techniques is limited by restricted availability of the equipment and the high cost of the technique.

Perfusions changes on CT scanning and mean contrast time perfusing through the liver is said to have the potential of discriminating between the various stages of fibrosis.[18] The accuracy is yet to be proved with gold standard.

To sum-up imaging hepatic fibrosis remains an under-utilized and overlooked possibility in the current local clinical settings. This might be due to the fact that the cost-effective modality (ultrasound) has high operator dependability making its results as subjective. While the more objective techniques are either very costly or unavailable; this limits their feasibility. Still, the trends in fibrosis evaluation are undergoing a change and a shift to imaging from biochemistry and histopathology needs to be worked upon based on local evidence.

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