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Review

State-of-the-art imaging of liver fibrosis and cirrhosis: A comprehensive review of current applications and future perspectives

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Abstract

Objective: The purpose of this article is to provide a comprehensive overview of imaging findings in patients with hepatic fibrosis and cirrhosis; and to describe which radiological/clinical modality is best for staging hepatic fibrosis.
Conclusion: MR elastography (MRE) appears to be the most reliable method for grading liver fibrosis, although the CT fibrosis score derived from the combination of caudate-to-right-lobe ratio and the diameters of the liver veins significantly correlates with the stage of fibrosis.

Keywords: Hepatic fibrosis; Liver cirrhosis; Magnetic resonance elastography (MRE); CT fibrosis score; Fibroscan

Contents

1. Introduction

Hepatic cirrhosis is the pathological sequela of all chronic liver diseases [1]. The most common causes of hepatic cirrhosis are alcoholic fatty liver disease (AFLD), non-alcoholic fatty liver disease (NAFLD) and viral hepatitis [2]. Less frequent causes of cirrhosis are haemochromatosis, alpha1-antitrypsin deficiency, Wilson's disease, biliary cirrhosis and cardiac cirrhosis. Chronic inflammation leads to potentially reversible liver fibrosis and ends in irreversible cirrhosis with the cross-linking of collagen fibres and the formation of regenerative nodules. Pathologists routinely distinguish patterns of predominantly pericentral fibrosis (e.g., in AFLD/NAFLD fibrosis/cirrhosis) [3] from patterns of predominantly periportal fibrosis (e.g., in chronic viral hepatitis, autoimmune hepatitis or biliary disease-induced fibrosis/cirrhosis) [4]. The fibrotic stage is classified according to histological criteria using the METAVIR scoring system whereby stages F1–F4 predominantly assess periportal fibrosis [5] and stages B1–B4 predominantly assess pericentral

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fibrosis [6]. Because the two staging systems differ only in the fibrosis pattern (which depends on the aetiology of the fibrosis), the resultant data are comparable in terms of the severity of fibrosis (both stages 1 to 4). A liver with stage 4 fibrosis is equivalent to a cirrhotic liver.

All aetiologies of liver cirrhosis lead to the same process, namely macroscopic parenchymal changes and secondary changes due to portal hypertension. The difference in portal blood supply is thought to be responsible for the atrophy of the left lobe and hypertrophy of the right lobe: the right lobe is fed by the right portal vein which is haemodynamically supplied by the superior mesenteric vein, which drains the upper GI tract and contains higher concentrations of alcohol and toxins than the lower GI tract [7]. The inferior mesenteric vein with blood from the lower GI tract mainly supplies the left portal vein and the left and caudate lobes of the liver. A small cadaver study revealed that the right lobe was more fibrotic than the caudate lobe [8]. The disease process characterised by right lobe atrophy and left lobe hypertrophy is described by the modified caudate-to-right-lobe ratio described by Awaya et al. [9]. Later in the fibrosis/cirrhosis sequence, liver heterogeneity and a nodular surface associated with regeneration processes appear; these changes are more easily detectable radiologically following contrast administration [10–12]. This repair process results not only in the formation of regenerative nodules but also in the compression of the central liver veins. A right liver vein below 7 mm in diameter should raise suspicion for cirrhosis [13]. Indirect changes associated with portal hypertension occur relatively late in the development of cirrhosis and include dilation of the hepatic portal vein to a diameter greater than 14 mm, splenomegaly (>11 cm longitudinal axis distance), porto-systemic collateral vessels (recanalisation of the umbilical vein, gastro-spleno-renal collateral vessels, gastro-oesophageal varices and even rectal varices), ascites and thickening of the bowel walls [14–16]. Routine biochemical and haematological tests are unable to quantify liver fibrosis in approximately 50% of patients [17]. An early diagnosis of liver fibrosis can improve the benefit of early therapeutic interventions prior to the development of irreversible and potentially fatal complications such as loss of liver function, oesophageal variceal bleeding, hepatic encephalopathy and hepatocellular carcinoma [18]. Approximately 80% of all hepatocellular carcinomas (HCC) arise from an underlying cirrhotic liver [19].

2. Radiological examinations

2.1. Ultrasonography

The accuracy, sensitivity and specificity of regular B-mode sonography for diagnosing liver cirrhosis have been reported to be 64–79%, 52–69% and 74–89%, respectively [20–22]. An irregular or nodular surface and blunt edges or morphological changes in the liver are the most specific signs of cirrhosis on ultrasound (Figs. 1–4). Contrast-enhanced ultrasound with sulphur hexafluoride-filled micro-bubbles covered with a phospholipid shell may more easily detect HCC (+20%) than cirrhosis [23].

Considerable efforts have been devoted to detecting liver cirrhosis noninvasively. An inexpensive and simple approach is sonographic elastography [24], a noninvasive and reliable method of detecting liver cirrhosis. Two techniques for sonographic elastography have been described: transient elastography (Fibroscan) and acoustic radiation force impulse (ARFI) elastography. The area under the receiver operating characteristic (ROC) curve of Fibroscan and ARFI elastography ranges from 0.85 to 0.91 for cirrhosis (fibrosis stage 4) and severe fibrosis (fibrosis stage 3); for moderate fibrosis (fibrosis stages 1 and 2), Fibroscan produces significantly better results than ARFI elastography, with areas under the ROC curve of 0.88 and 0.81, respectively ($p = 0.008$). However, in 2–11% of cases, liver failure is not diagnosed with Fibroscan [25,26]. Another limitation of these techniques is that only a very small volume of the liver can be measured at one time and the accuracy of this measurement is very operator-dependent [27]. The usefulness of these techniques is also limited in obese patients and in patients with ascites, both of which are situations that often occur in patients with hepatic fibrosis [28]. In the case of obese patients, the area under the ROC curve for both Fibroscan and ARFI elastography drops to 0.63.

In conclusion, sonographic elastography is an inexpensive and accurate method of diagnosing hepatic cirrhosis. However, this approach is operator-dependent and of limited usefulness for detecting early pre-cirrhotic stages of liver fibrosis in cases of inhomogeneous fibrosis, in obese patients and in patients with ascites.

2.2. Computer-tomography (CT)

Abdominal CT scans are increasingly performed in routine clinical studies in hospitals and radiology institutes. A careful examination of the liver parenchyma and a thorough screening for fibrosis in CT scans is mandatory, particularly for patients with no suspected liver pathology. Numerous characteristic imaging findings associated with liver cirrhosis have been described; however, the diagnostic accuracy of CT scans remains disappointing. Imaging findings suggestive of liver cirrhosis include an irregular or nodular hepatic surface, a blunt liver edge, parenchymal abnormalities, morphological changes in the liver and manifestations of portal hypertension (Figs. 5–8). In a multicentre study conducted by Kudo et al., the diagnostic accuracy, sensitivity and specificity of CT for hepatic cirrhosis were 67–86%, 77–84% and 53–68%, respectively [20,29].

Harbin et al. developed a cirrhosis score for transverse imaging using the ratio of the width of the transverse caudate lobe to the width of the transverse right lobe. The sensitivity, specificity and accuracy of this score for detecting cirrhotic livers were 84%, 100% and 94%, respectively. A relative widening of the porta hepatis was sensitive but not specific for liver cirrhosis [8] (Fig. 5).

Few studies have investigated the accuracy of CT findings in pre-cirrhotic liver fibrosis. Measures such as the modified caudate-to-right-lobe ratio [9] and a decrease in the diameter of the liver vein [13] have been used to detect liver remodelling on MR images. The combination of both of these variables (i.e., the