Ultrasonography is not Reliable in Diagnosing Liver Cirrhosis in Clinical Practice

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ABSTRACT

Background: The diagnosis of liver cirrhosis is important in the evaluation and management of patients. Liver biopsy is the gold standard but it is invasive. Ultrasonography is a non-invasive and useful modality in assessing the liver for certain conditions but its sensitivity and specificity in diagnosing cirrhosis is unknown locally.

Aim: To assess the accuracy of ultrasonography in diagnosing compensated liver cirrhosis in daily clinical practice outside the context of clinical trials.

Methods: All the liver biopsies were identified from the Pathology Logbook retrospectively from January 1998 to March 2001. Only patients who had both liver biopsy and ultrasonography with no clinical evidence of cirrhosis were included. Patients with incomplete data, hepatoma or liver secondaries were excluded. Ultrasonographic diagnosis of cirrhosis was based on nodularity or irregularity of the liver surface, small liver size, coarse echotexture and increase attenuation by using the 3.5 to 5 MHz transducers.

Results: A total of 151 liver biopsies were performed during this period. Eighty-eight patients who had both ultrasound and liver biopsy were analysed. Seventeen patients had ultrasonographic diagnosis of cirrhosis but only six cases were proven by a liver biopsy. On the other hand, 10/16 cases of biopsy-proven cirrhosis were "missed" by ultrasound. Thus, the sensitivity of ultrasonography in diagnosing cirrhosis was 37.5% and the specificity was 84.7%. The positive and negative predictive values were 35.3% and 85.9% respectively.

Conclusion: Low frequency ultrasonography is not a sensitive test for the diagnosis of liver cirrhosis in daily clinical practice.

Keywords: cirrhosis, ultrasound, liver biopsy

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INTRODUCTION

Generally, liver cirrhosis is a pathological diagnosis. It is defined as a diffuse process characterised by fibrosis and alteration of normal liver architecture into abnormal nodules of liver cells surrounded by fibrosis[1]. The majority of cirrhotic patients are asymptomatic and some are diagnosed only during autopsy[2,3]. Liver biopsy is the gold standard for diagnosing this condition. However, there is a 10 to 20% false negative result[4,5]. It also carries with it some morbidity and mortality[6] depending on the coagulation profile, underlying diseases and experience of the operator. Other investigative modalities for the diagnosis of cirrhosis are clinical (stigmata of chronic liver disease, ascites, splenomegaly), biochemical (prolonged prothrombin time, hypoalbuminaemia ± elevated liver enzyme) and endoscopy (oesophageal/ gastric varices, portal gastropathy). Unfortunately all these modalities lack sensitivity and specificity and detect patients with cirrhosis at an advanced stage. Ultrasonography is a good alternative because it is non-invasive. However, it is operator dependent and has certain limitations. For instance, cirrhotic liver cannot be distinguished from fatty liver[7]. In recent years, reports on the usage of ultrasound on liver surface have been controversial[8-10]. The aim of our study was to assess the usefulness of ultrasound on liver surface and parenchymal in the diagnosis of liver cirrhosis in daily clinical practice outside the context of clinical trials.

METHODS

This is a retrospective study performed at the Universiti Kebangsaan Malaysia Hospital (National University Hospital Malaysia) from January 1998 to March 2001. All liver biopsies were identified from a logbook from the Pathology Department. All the patients who underwent liver biopsies were identified. The liver biopsy reports and the ultrasound findings were then correlated and analysed. Only those patients with both liver biopsy and ultrasound were included. Those with incomplete data (incomplete liver biopsy report or ultrasound report or missing files), insufficient liver tissue, hepatocellular carcinoma and liver metastasis

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Table I. Correlation of ultrasound and biopsy.

Ultrasonographic findings	Histology		Total
	cirrhosis	non-cirrhosis	
cirrhosis	6	11	17
non-cirrhosis	10	61	71
total	16	72	88

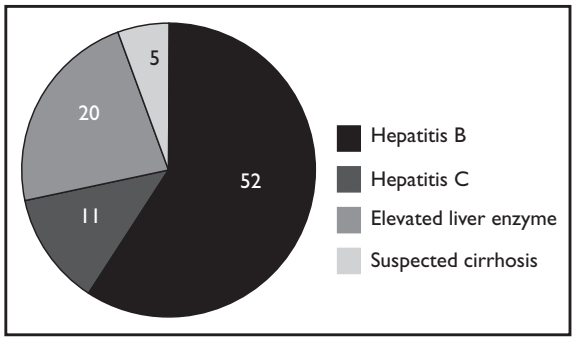
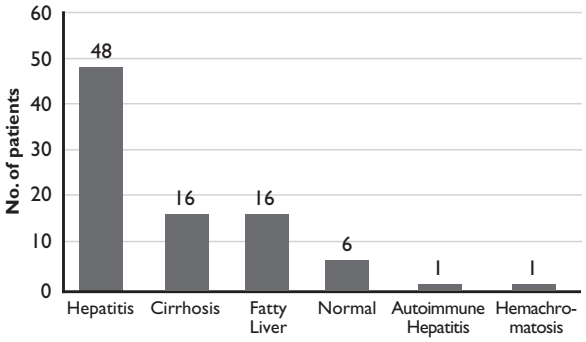


Fig. 1 Indications for liver biopsy (n=88).

Fig. 2 Histology of 88 cases.



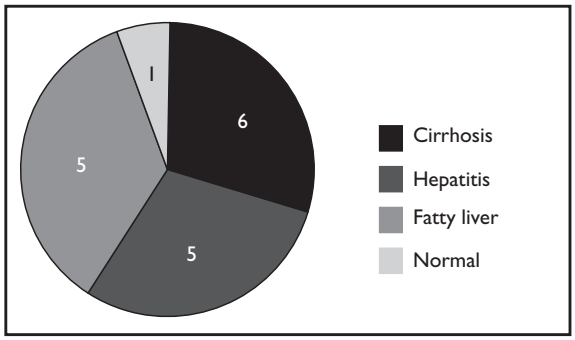


Fig.3 Histology of 17 cases of ultrasound diagnosis of "cirrhosis".

were excluded. Ultrasonographic examination of the liver was performed by trained and experienced radiologists using Aloka multiview SSD-2000 3.5 MHz to 5 MHz transducers. The diagnosis of liver cirrhosis was based on a few signs: nodularity/irregularity of liver surface, small liver size, echo coarseness or increased attenuation with/without splenomegaly and ascites. Histological diagnosis of liver cirrhosis was the presence of portal and lobular fibrosis with bridging fibrosis and fibrous band with regeneration nodules or Scheuer classification stage 4 for chronic hepatitis cases.

RESULTS

A total of 151 liver biopsies were performed during this study period. However, only 88 cases met the inclusion criteria. The mean age was 33 +/- 16 years (ranged three months to 68 years). There were 50 men and 38 women. Ethnic distribution was Chinese 45 (51.1%), Malay 36 (40.9%), Indian 4 (4.5%) and others 3 (3.5%). None of the patients had any evidence of liver cirrhosis clinically.

Of the 88 cases included, the indication for liver biopsy (Fig. 1) were Hepatitis B 52 cases (59.1%), persistently elevated liver enzymes 20 cases (22.7%), Hepatitis C 11 cases (12.5%) and suspected liver cirrhosis from ultrasound 5 cases (5.7%). Histologically, only 16 patients (18.2%) had proven cirrhosis; 48 (54.6%) hepatitis of various degrees, 16 (18.2%) fatty changes, 6 (6.8%) normal histology, one case (1.1%) each of autoimmune hepatitis and haemochromatosis (Fig. 2).

Of the 16 cases of biopsy proven cirrhosis, only 6 (37.5%) were diagnosed accurately by the ultrasound. The other 10 cases (62.5%) were misdiagnosed or reported as normal (Table I). On the other hand, 11/17 cases (64.7%) of cirrhosis reported by ultrasonography were proven wrong by liver biopsy (Table I). The histological diagnoses were 5 hepatitis (45.5%), 5 fatty livers (45.5%) and 1 normal histology (9%) (Fig. 3). Therefore the sensitivity of ultrasound in diagnosing liver cirrhosis in our study was 37.5% and specificity 84.7%. The positive and negative predictive values were 35.3% and 85.9% respectively.

DISCUSSION

The diagnosis of liver cirrhosis is important in the further management and monitoring of patients. Even though liver biopsy is considered the gold standard, it carries a false negative rate of 10% to 20%[4,5].

The accuracy of ultrasonography on liver surface had been controversial. In our study, the sensitivity and positive predictive value were only 37.5% and 35.5% respectively. Even though the sensitivity was higher than that of Ladenheim et al[10], it was relatively low compared to other studies where the sensitivity of as high as 91.1% was reported[7-9]. There are several reasons to account for this discrepancy. Firstly, high frequency (7.5 MHz) ultrasound probe, which was used by Ferral[9] and Simonovsky[11], had the advantage of detecting surface nodularity of the liver. Secondly, it was operator dependent. Di Lelio's[8] report was impressive because they were able to predict cirrhosis in 88% of patients with false positive and negative rate of 6% and 12% respectively by using a 5 MHz probe. This was probably because of the different techniques used in assessing the liver surface and the experience

of operator. Thirdly, laparoscopic biopsy was performed in Di Lelio[8] and Simonovsky's[11] studies as opposed to percutaneous liver biopsy performed in our study and Ladenheim et al[10]. This increased the sensitivity of a positive histology in the former two studies. Lastly, echo coarseness and increased attenuation, which is a subjective sign, was used in diagnosing cirrhosis in our study. This increased the false positivity rate to 64.7%. Fatty liver and hepatitis accounted for the majority (91%) of the cases wrongly diagnosed as cirrhosis by ultrasound. To differentiate between cirrhosis and fatty infiltration using ultrasound therefore is difficult, as has been suggested by Sanford et al[12] and Gosink et al[7].

Ultrasonography had been extensively studied in the last two decades but results were variable. Studies on the caudate to right lobe of liver ratio had a sensitivity ranging from 43%[13] to 84%[14] but specificity of 100% was reported. Hypertrophy of caudate lobe[15] also has high predictive value in the diagnosis of cirrhosis. However, this was not found in Di Lelio's study[8] where the majority of the patients had early cirrhosis. Decreased diameter of segment 4 (quadrate lobe) has also been recorded as an adjunctive sign of cirrhosis[16].

Gaiani et al[17] performed ultrasonography on 212 chronic liver disease patients without clinical signs of cirrhosis. Liver size, caudate/right lobe ratio, liver surface, echogenicity, portal vein diameter, portal vein mean flow velocity and spleen size were variables used in diagnosing cirrhosis. The diagnosis of cirrhosis was made in 47 patients by histology and 69 patients by ultrasound. In 37 patients, both histology and ultrasound diagnosis of cirrhosis was consistent. Liver surface nodularity and portal vein flow velocity were the two independent variables in diagnosing cirrhosis. They increased the sensitivity to 82.2%. In another study, Aube et al[18] found that among those with chronic liver disease, liver surface and liver length (at the level of right kidney) were the two variables that improved diagnostic accuracy to 85% and 82% respectively.

In an attempt to assess cirrhosis by hepatic vein enhancement following intravenous contrast, Albrecht et al[19] discovered that cirrhotic patients had a significantly much earlier and higher peak enhancement than non-cirrhotic patients and normal control.

The limitation of our study was the relative small number of patients diagnosed with liver cirrhosis. Nevertheless, we felt that a retrospective review like this will give us an insight into the usefulness of ultrasonography in the diagnosis of liver cirrhosis in our daily clinical practice outside the context of a clinical trial. Previous studies have demonstrated difficulties in differentiating fatty liver with cirrhosis even in trial settings[7,12].

In conclusion, low frequency ultrasound is not useful in the diagnosis of liver cirrhosis in daily clinical practice. However, the sensitivity can be improved if a high frequency probe is used and done by experienced and dedicated operators. Liver biopsy remains the gold standard especially when patients are clinically asymptomatic.

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