Value of Doppler ultrasonography in the depiction of changes in hepatic hemodynamics due to primary liver tumours

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Abstract

Background. Ultrasound (US) is the imaging method most frequently used for the detection and diagnosis of hepatocellular carcinoma (HCC). The ability to resolve hepatic arterial and portal venous components of blood flow on a global and regional basis constitutes the primary goal of liver perfusion imaging.

Aim. The purpose of our study was to estimate alterations in the hepatic blood flow in large hepatocellular carcinomas occurring in liver cirrhosis, in comparison with liver cirrhosis.

Methodology. By using the color Doppler velocity profile technique, portal vein and hepatic artery hemodynamic status was assessed in 42 patients with hepatocellular carcinoma. 20 patients with liver cirrhosis were taken as control.

Results. Portal vein average velocity was 8.33 cm/sec ± 2.31 in patients with HCC vs 15.80 cm/sec ± 2.31 in cirrhotic patients without HCC (p=0.72). Portal vein flux was significantly lower in patients with HCC (209 mL/mm ± 83.08 vs. 649 mL/min ± 83.08 in cirrhotic patients; p=0.02). The hepatic arterial blood flow was increased in patients with hepatocellular carcinoma as compared to the cirrhotic patients (P < 0.001). The ratio of hepatic arterial flow to portal vein flow was 1.239 ± 0.246 in patients with hepatocellular carcinoma, which is twice the basic control value (0.66 ± 0.259 l/min).

Conclusions. These results suggest that in hepatocellular carcinomas there is a decreased portal vein blood flow, accompanied by an increased hepatic arterial blood flow. In the case of a hypo-echoic or hyperechoic, mass in the cirrhotic liver, increased blood flow in the hepatic artery, and decreased portal venous flow, a malignant liver tumor is virtually certain.

Key-words: Hepatocellular carcinoma, Doppler ultrasonography, hepatic hemodynamic

Introduction

Hepatocellular carcinoma is one of the five most common cancers worldwide, with a particularly high prevalence in Asian countries due to endemic hepatitis B virus infection [1]. Lately, the incidence of HCC is also rising in Western countries as a result of increasing hepatitis C virus infection. More than 80% of patients with HCC have associated cirrhosis and impaired liver function, making treatment of HCC more difficult than many other cancers [1].

Primary liver tumours grow in an uncontrolled fashion with the propensity to spread into the surrounding tissues. These critical features are closely dependent from the tumour vascular network [2]. As passive diffusion alone would limit the passage of nutrients and the removal of waste products to a few millimetres of tissue, the development of neoformed vessels is essential for the tumour growth. Unlike the dual supply of the normal hepatic parenchyma provided by vessels arising from the systemic arterial circulation and the portal venous circulation, an advanced HCC is abundantly supplied by systemic arteries alone. This abundancy facilitates the angiographic diagnosis of malignancy and differentiates non-neoplastic or preneoplastic conditions, such as liver cirrhosis, hepatocellular adenoma, focal nodular hyperplasia and adenomatous hyperplasia.

The purpose of our study was to estimate alterations in the hepatic blood flow in large hepatocellular carcinomas occurring in liver cirrhosis, in comparison with liver cirrhosis.
Materials and methods

Between January 2007 and March 2008, 42 cirrhotic patients (30 men and 12 women; mean age 62 ±8.8 years) with evidence of hepatic focal lesions attending our inpatient liver unit and 20 cirrhotic patients (15 men and 5 women; mean age 60 ±7.8 years) without hepatic focal lesions were enrolled. Informed consent was obtained from each patient. Imaging and Doppler signals were performed with General Electric Duplex US Logiq 7 scanner using 3.5-5 Hz convex and phased-array transducers. Patients were studied after overnight fasting, in supine position, and during suspended respiration. By using the color Doppler velocity profile technique, portal vein and hepatic artery hemodynamic status was assessed in the study and control groups. The following Doppler parameters were assessed: (1) pattern of Doppler frequency spectrum, i.e., arterial or venous; (2) resistance index (RI) calculated according to the formula: RI (systolic peak frequency_end-diastolic frequency)/peak systolic frequency; (3) pulsatility index (PI) calculated according to the formula (systolic peak frequency - end-diastolic frequency)/ mean frequency.

Blood Tests. Routine liver biochemistry and alpha-fetoprotein (AFP) were performed. AFP was determined by radioimmunoassay.

Statistical Analysis. Data are expressed as mean±SD. Differences between groups were analyzed using two tailed Student t test for unpaired observations. The value P<0.05 was considered statistically significant.

Results

Mean volume of nodules was 119.74±15.2 mm, with a mean maximal diameter of 51.23±29.79mm. 12 of the 42 nodules were isoechic, 16 were hypoechoic and 14 were hyperechic.

Mean AFP in patients with HCC was 22 ±28 (range 2-110). In cirrhotic patients AFP mean serum level was 8.3 ± 6.2 (range 3-20) (Table 1).

Table 1. Characteristic features in the study and control groups (media±SD)

<table>
<thead>
<tr>
<th></th>
<th>HCC</th>
<th>Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nr patients</td>
<td>42</td>
<td>20</td>
</tr>
<tr>
<td>Men/Women</td>
<td>30/12</td>
<td>15/5</td>
</tr>
<tr>
<td>Age</td>
<td>62 ±8.8</td>
<td>60 ±7.8</td>
</tr>
<tr>
<td>BMI</td>
<td>34.8±8.9</td>
<td>30.7±6.06</td>
</tr>
<tr>
<td>Diabetes mellitus 2</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>AFP</td>
<td>22 ±28</td>
<td>8.3 ± 6.2</td>
</tr>
</tbody>
</table>

Portal vein average velocity was 8.33 cm/sec ± 2.31 in patients with HCC vs. 15.80 cm/sec ± 2.31 in cirrhotic patients without HCC (p=0.72). Portal vein flux was significantly lower in patients with HCC (209 mL/ mm ± 83.08 vs. 649 mL/min ±83.08 in cirrhotic patients; p = 0.02).

The hepatic arterial blood flow was increased in patients with hepatocellular carcinoma as compared to the cirrhotic patients. Spectral analysis of the signal indicated that the mean peak RI and PI were significantly lower in cirrhotic patients than in HCC liver (0.82 ±0.09 and 1.56 ± 0.2 in HCC and 0.62 ±0.08 and 0.82 ±0.08 in cirrhotic patients , respectively, p=0.002 and 0.0001) (Table 2).

Owing to the opposite changes in the afferent circulation, the total hepatic blood flow did not change significantly. The ratio of hepatic arterial flow to portal vein flow was 1.239 +/- 0.246 in patients with hepatocellular carcinoma, which is twice the basic control value (0.66 +/- 0.259 l/min).

Table 2. Characteristic features of the spectral analysis of the hepatic artery signal in the study and control groups (mean±SD)

<table>
<thead>
<tr>
<th>Group</th>
<th>RI</th>
<th>SDV</th>
<th>PI</th>
<th>SDV</th>
<th>Mean velocity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis</td>
<td>0.82</td>
<td>0.09</td>
<td>0.62</td>
<td>0.08</td>
<td>26.98</td>
</tr>
<tr>
<td>HCC</td>
<td>1.56</td>
<td>0.2</td>
<td>0.82</td>
<td>0.08</td>
<td>30.83</td>
</tr>
<tr>
<td>p</td>
<td>0.002</td>
<td></td>
<td>0.0001</td>
<td></td>
<td>0.065</td>
</tr>
</tbody>
</table>

Discussion

Cirrhosis of the liver is not a vascular disease but the effects on the liver architecture result in severe disease often accompanied by hepatic vascular changes [3]. Portal hypertension is one of the most frequently seen sequelae of liver cirrhosis. It results in the formation of porto-systemic collateral channels which may lead to varices and hemorrhage. Primary liver cancer is also strongly associated with liver cirrhosis [1]. Recent reports have stressed the importance of the role of color and power Doppler sonography in the diagnosis of HCC in comparison with other liver tumors, such as metastases, hemangioma, and focal nodular hyperplasia [4,5] in particular when color-filled pattern [6] or intra- and peritumoral flow signal are analyzed [7]. Ultrasound (US) is an accessible, non-invasive and relatively inexpensive technique, ideal for longitudinal, in vivo, investigations involving a large number of subjects [8]. Using the presently available US instruments, the Doppler signal can be represented by different sophisticated modalities, including duplex, colour and power Doppler. Doppler US is able to detect tumour neovascularity and the model of the tumour vascularization (fig 1 and 2). This is important because there is a strong correlation between the index of flow resistance and histological features of aggressiveness [9].
Fig. 1. A Grey scale: tumoural mass, encephaloid, homogeneous, hyperechoic, developed on a liver with inhomogeneous structure and irregular contour; **B and C** - Tumoural angioarchitectural model: increased, anarchical vascularisation, originated from a lot of vascular pedicles (Colour Doppler and Power Doppler, respectively).

Fig. 2. A Grey scale: Liver hyperechoic tumoural mass in segment 6, well-delimited from the liver parenchima through a transonic halo; **B and C** – Tumoural vascularisation is predominantly peripheral, with an anarchical disposition, originated from a lot of vascular pedicles (Colour Doppler and B-flow, respectively).
In our study portal vein flux was significantly lower in patients with HCC and the hepatic arterial blood flow was increased in patients with hepatocellular carcinoma as compared to the cirrhotic patients. Owing to the opposite changes in the afferent circulation, the total hepatic blood flow did not change significantly. Most likely haemodynamic abnormalities associated with hepatocellular carcinoma can be explained by the alterations of portal venous flow caused by compression, infiltration, tumor invasion or associated thrombosis of the branches of the portal vein.

Also, in our study, the ratio of hepatic arterial flow to portal vein flow was twice the basic control value in patients with hepatocellular carcinoma. The pronounced increase in the ratio of hepatic arterial flow may be attributed to the decrease in portal venous flow caused by the primary hepatocellular carcinoma. This phenomenon might be useful for Doppler US diagnosis, e.g. in case of hypoechoic or hyperechoic mass in the liver and of decreased portal vein flow, and of increased hepatic artery flow, a malignant tumor may be suspected.

HCC nodules have characteristic ultrasound patterns which help in differential diagnosis. Doppler ultrasound provides functional as well as anatomical information about blood flow in the liver and is especially useful in detecting HCC and the abnormal blood vessel architecture which surrounds a tumor [8,9].

US imaging allows the location of the sample volume into the vessel in duplex Doppler, to obtain the Doppler frequency spectral trace, which reflects the velocity distribution of blood cells across the diameter of the vessel over successive cardiac cycles [9]. The parameters peak frequency, spectral broadening and resistive index (RI) derived from the spectral analysis provide information on blood flow velocity, turbulence and vascular impedance, respectively, and may be useful to characterize flow patterns observed in the different tumours (fig 3). Colour Doppler displays a map of vascular spaces in a selected portion of the real-time US scan, with the advantage of rapidly assessing the presence and direction of blood flow and the spatial distribution of vessels, the latter being helpful in the mapping of tumoural angioarchitecture [10,11,12]. Power Doppler displays the integrated amplitude of the Doppler signal, and it is inherently more sensitive than conventional colour Doppler in displaying presence of flow in very small vessels [13,14], increasing the depiction of both benign and malignant liver lesions vascularization [15,16,17,18]. The relative limitation of power Doppler is that it does not provide any information regarding flow direction, velocity and turbulence [19]. Despite the advancement of technology, there are some limits on the performance of Doppler US, particularly in the evaluation of deeply located lesions, such as tumours of the posterior segments of the liver, of low velocity flows and of very small vessels (as it occurs in tumoural vasculature) [20,21].

![Fig. 3. Spectral Doppler signal - Hepatic artery flux in a cirrhotic liver with HCC](image)

In our study the most striking circulatory alterations were as follows: the significant increase of hepatic artery flow, and the significant decrease of portal vein flow. The decrease of the venous flow can be attributed to the HCC. A limit of our study is the lack of a healthy control group in order to delineate the circulatory alterations due to cirrhosis and to tumoral transformation of the liver.

In conclusion our results indicate that in hepatocellular carcinomas there is a decreased portal vein blood flow, accompanied by an increased hepatic arterial blood flow. In the case of a hypoechoic or hyperechoic mass in the liver, increased blood flow in the hepatic artery, and decreased portal venous flow, a malignant liver tumor is virtually certain.

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**References:**


