Doppler ultrasonography of hepatic artery in malignant liver tumors

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SUMMARY
Hepatic artery is dominant compared to portal vein in liver tumor vascularization. Malignant tumors have uncontrolled growth and spread onto neighboring tissues through a tumor vascular network. Based on this we discussed the use arterial flow parameters including systolic and diastolic speed, Doppler perfusion index, and resistance index for early detection of liver metastasis. We also discussed possibility to make differential diagnosis from other disease such as arterial stenosis, liver cirrhosis, steatosis using these parameters in better diagnosis confirmation.

Key words: Liver Neoplasms; Ultrasonography, Doppler; Ultrasonography, Doppler, Color; Hepatic Artery; Doppler Effect; Liver Diseases

INTRODUCTION
Doppler ultrasonography enables non-invasive hemodynamic investigation of portal circulation. Doppler examination offers significant information on arterial flow velocity waveforms in splanchnic arteries (hepatic artery) of the abdominal organs. Normal arterial flow of these arteries is anterograde both in systole and diastole (biphasic flow), which indicates small flow resistance (Figure 1).

Vascularization and liver tumor hemodynamics
Hepatic artery is dominant compared to portal vein in liver tumor vascularization. Malignant tumors have uncontrolled growth and spread onto neighboring tissues through a tumor vascular network (1). Tumor vessels are complex and chaotic, with dual origin: liver vascular network (peripheral vessels with radial branches on the edge of the tumor) and newly formed (central) vessels, as the angiogenic response to stimuli (peptides, cytokines) from tumor cells (2-4). These vessels have a special architecture: they are primitive, with thin incomplete endothelium and weak or absent muscular layer. Some studies have estimated the thickness and distribution of vessels within the tumors. The future lays in further development of color Doppler ultrasonography, particularly the development of 3D, harmonic ultrasound and application of contrasting agents. Power color and Doppler sonography are used for the research of hepatic arterial perfusion in tumor tissues (Figure 2a,b,c).
Doppler Index

Doppler indices are calculated from the Doppler spectrum and enable indirect examination of vascular resistance in blood vessels with pulsatile flow. Physical principles of Doppler technique: the probe emits beams of ultrasonic, which reflect against the moving particles, i.e. erythrocytes in the blood vessel (Figure 3). The beams then return into the probe, resulting in a change of frequency $\Delta f$ of the ultrasound wave (Doppler effect). The Doppler signal is transformed into a spectrum which can be analyzed (systolic, diastolic, average flow velocity, volume flow, direction of blood flow, resistance index RI and pulsatile index PI).

The resistance index (RI) of the hepatic artery is an indicator of altered arterial flow (Figure 4).

Many authors consider systolic velocity in the hepatic artery to be the most suitable parameter for hepatic artery perfusion research (16). In hepatic artery stenosis, there are high systolic velocities (> 2m/sec) and a post-stenotic tardus-parvus wave with a drop of the resistance index (< 0.55). The mechanisms that cause changes in the Doppler indices of the hepatic artery, are mostly related to changes in liver structure, as well as dilation/constriction of liver arteries, through inflammatory and tumor-based substances.

The presence of micro-metastasis in liver is connected to changes in liver circulation, although current visualization methods are unable to detect them due to limited resolution and weak contrasting substances (17). Because of structural and hemodynamic alterations in metastasis (i.e. increased vasoconstriction), the arterial resistance is changed, along with the decline of the hepatic artery RI. Such a finding could indicate an existence of liver metastasis, invisible to ultrasound. According to Leen et al., the value of RI can be compared to the values of CEA.

In primary liver tumors, blood vessels have abnormally high systole velocities of the flow, which distinguishes them from metastasis. Within tumors, there are also A-V shunts (between neighboring arteries and veins), which is why there are high diastolic velocities with a decrease in the resistance index (Figure 5) (18,19). There are relatively few reports on this issue.

Hypervascular liver metastases derive from kidney cancer, melanoma and certain endocrine tumors, with rapid, frequently turbulent flows (19).

Liver metastases are vascularized from branches of the hepatic artery, which shows an increased flow, with a subsequent decrease in flow in the portal vein, due to the influence of humoral factors on the splanchic vascular resistance (6). The researches by Leen et al. in 1996 represent a new approach in detecting colorectal liver metastases, using the color Doppler technology. These authors were the first to introduce the hemodynamic index (Doppler perfusion index), as a relation between the arterial and portal vein flow, and was later experimentally used on animals by other authors (20), who have demonstrated that DPI changes appear in the early phase of metastasis development.

DPI measures the relation between the hepatic arterial flow, on one hand, and the overall liver flow, on the other, and seems to be more accurate than other indices in the hepatic hemodynamic study (21,22). Doppler perfusion index

Figure 3. The Doppler effect principle

Figure 4. Calculation of RI of the hepatic artery

RI = (S - D) ÷ S; S - systolic velocity in the artery; D - end-diastolic velocity

Figure 5. Color Doppler ultrasonography of liver tumor: high diastolic velocity and low resistance index (RI)
(DPI) is a liver oxygenation index, where the arterial component is relevant in relation to the overall liver perfusion (6,12).

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\text{DPI} = \frac{FV_{ha}}{FV_{ha} + FV_{pv}}
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In case of liver tumor, DPI is increased (6). It reflects changes in blood flow in chronic liver diseases (12), as well as in liver tumor (6), chronic hepatitis C (23), liver steatosis (21) and alcoholic liver damage (24), although some of the reports are not conclusive (25).

There are a relatively small number of studies regarding DPI in chronic liver diseases, particularly because the determination of this index demands great experience from an ultrasonographer, which makes routine investigation and reproducibility difficult (6,12,26). Fowler et al. in 1998 were researching DPI among healthy volunteers and determined an average value of 0.25, whereas higher DPI values point out to liver disease. According to Walsh et al. (12), the average DPI among the group of patients with liver cirrhosis (HCV +) is 0.27, in comparison to the 0.17 average in the healthy control group.

The increase in DPI is a result of a violated vascular network in liver cirrhosis, as well as focal lesions (hemangioma and metastasis) with a relative increase in arterial flow (25,27-33). Leen et al. introduced a contrasting agent in DPI investigation and found heightened DPI values of 0.33 in liver hemangioma and 0.59 in liver metastasis. Afterwards, in 2002, Leen et al. published a duplex Doppler perfusion index study after intra-arterial Angiotsensin II application (the connection of the flow with the renin-angiotensin system) to define the Doppler perfusion index, and found increased values of DPI among patients with occult changes in liver parenchyma. Afterwards, in 2002, Leen et al. introduced a contrasting agent in DPI investigation and found heightened values of 0.33 in liver hemangioma and 0.59 in liver metastasis.


Conflict of interest
We declare no conflicts of interest.

REFERENCES
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