Doppler ultrasonography of hepatic artery in malignant liver tumors

Mirjana Perišić[1], Vladimir Jurišić[2], Mirko Kerkez[3]

Arch Oncol 2008;16(3-4):46-8.
UDC: 616.36-006:616-072
DOI: 10.2298/AOO0804046P

[1]Institute for Gastroenterology, Medical Faculty Belgrade, Serbia, [2]School of Medicine, Kragujevac, Serbia, [3]Institute for Abdominal Surgery, Belgrade, Serbia

Correspondence to:
Prof. Vladimir Jurišić,
Medical Faculty Kragujevac, P. Box 127,
34000 Kragujevac, Serbia

vdvd@mailcity.com

Received: 22.11.2008
Provisionally accepted: 25.11.2008
Accepted: 01.12.2008

© 2008, Oncology Institute of Vojvodina, Sremska Kamenica

SUMMARY

Hepatic artery is dominant compared to portal vein in liver tumor vascularization. Malignant tumors have uncontrolled growth and spread onto neighbouring tissues through a tumor vascular network. Based on this we discussed the use arterial flow parametrers 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 artery 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).

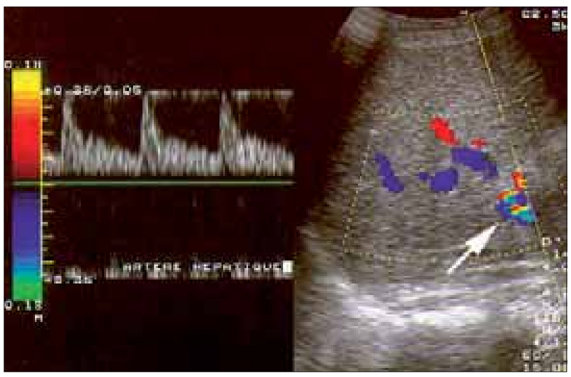
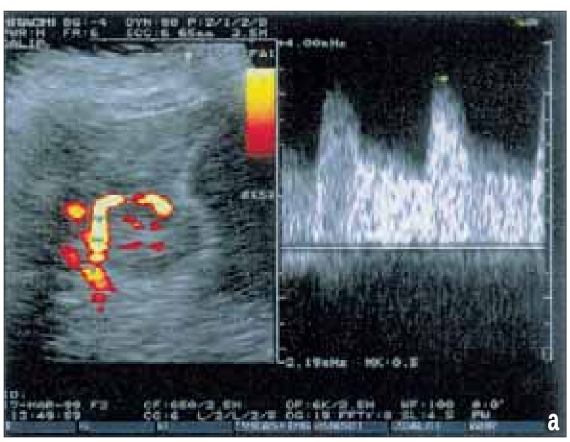
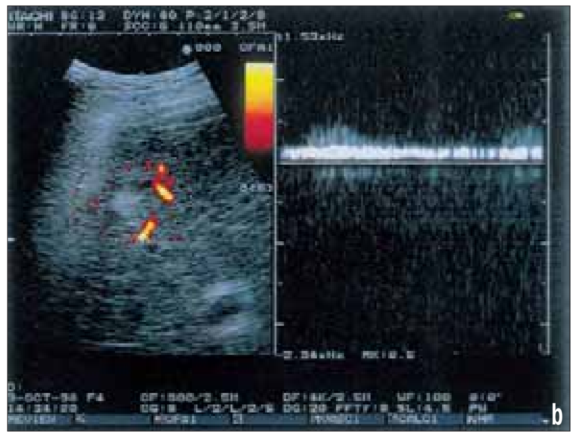


Figure1. Normal hepatic artery flow measured by Doppler ultrasonography

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





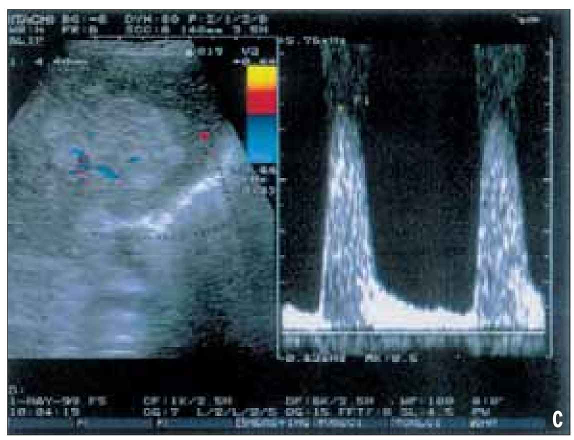


Figure 2. a) Power color and Doppler ultrasonography of nutritive artery around the liver node (focal nodular hyperplasia); b) Power color and Doppler ultrasonography of nutritive artery around the liver cirrhotic node; c) Doppler ultrasonography of nutritive artery around the tumor (hepatocellular carcinoma in the left liver lobe)

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 ultrasound, 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 Δf 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).

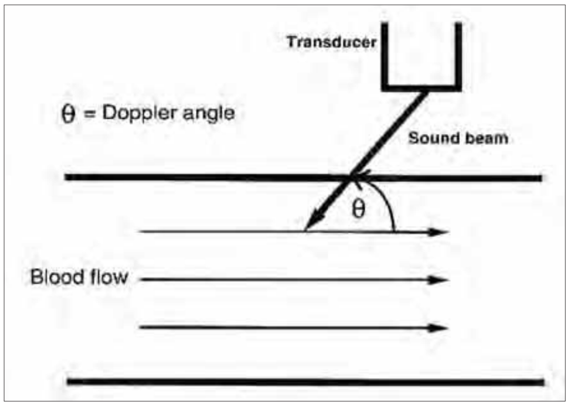


Figure 3. The Doppler effect principle

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

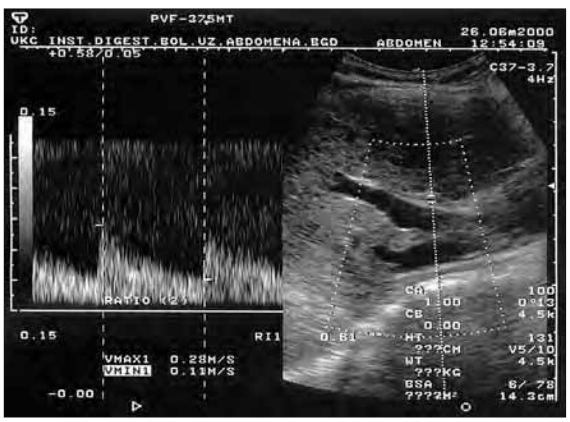


Figure 4. Calculation of RI of the hepatic artery
(RI = (S – D) ÷S; S - systolic velocity in the artery; D - end-diastolic velocity)

The hepatic arterial resistance index (RI) varies (0.55 - 0.81) with the digestion phases and depends on how old the liver is. In liver disease, Doppler indices are altered not only in the hepatic, but in the spleen artery, as well (6-8), due to their link within the portal system. The right hepatic artery is best seen through the right intercostal space and it is within it that measurements are made, because it reflects changes in vascularization better than the main hepatic artery.

The intensity of liver fibrosis changes the hemodynamics of the hepatic artery. Many studies have shown that changes in Doppler parameters of the hepatic artery depend on changes in the liver structure, as well as effects of various vasoactive substances (9-15).

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.

Figure 5. Color Doppler ultrasonography of liver tumor: high diastolic velocity and low resistance index (RI)

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 splanchnic 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

(DPI) is a liver oxygenation index, where the arterial component is relevant in relation to the overall liver perfusion (6,12).

$$\mathrm{DPI} = \frac{FVha}{FVha + FVpv}$$

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 ultrasonographist, 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). In as early as 1993. Leen et al. published a duplex Doppler liver perfusion study after intra-arterial Angiotensin 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.

Presented at 12th Studenica meeting “Advances in Clinical Oncology”, Studenica Monastery, Serbia, June 5-7, 2008.

Conflict of interest

We declare no conflicts of interest.

REFERENCES

1 Schor AM, Schor SI. Tumor angiogenesis. *J Pathol*. 1983;141:385-413.

2 Folkman J, Merler E, Abernathy C, Williams G. Isolation of a tumor factor responsible for angiogenesis. *J Exp Med.* 1971;33:275-88.

3 Folkman J. Tumor angiogenesis. *Adv Cancer Res*. 1985;48:2641-5.

4 Folkman J, Watson K, Ingber D, Hanahan D. Induction of angiogenesis during the transition from hyperplasia to neoplasia. *Nature*. 1989;339:58-61.

5 Gaiani S, Volpe I, Piscaglia F, Bolondi L. Vascularity of liver tumors and recent advances in Doppler ultrasound. *J Hepatol*. 2001;34:474-82.

6 Leen E, Goldberg JA, Robertson J, Angerson WJ, Sutherland GR, Cooke TG, et al. Image-directed Doppler ultrasonography: a novel technique for the diagnosis of colorectal liver metastases. *J Clin Ultrasound*. 1993;21(4):221-30.

7 Leen E, Angerson WG, Cooke TG, McArdle CS. Prognostic Power of Doppler Perfusion Index In Colorectal Cancer. Correlation with Survival. *Ann Surg*. 1996;223(2):199-203.

8 Leen E. The detection of occult liver metastases of colorectal carcinoma. *J Hepatobiliary Pancreat Surg*. 1999;6(1):7-15.

9 O’Donohue J, Ng C, Catnach S Farrant P, Williams R. Diagnostic value of Doppler assessment of the hepatic and portal vessels and ultrasound of the spleen in liver disease. *Eur J Gastroenterol Hepatol*. 2004;16:147-55.

10 Dietrich CF, Lee J-H, Gottschalk R, Herrmann G, Sarrazin C, Caspary WF, et al. Hepatic and portal vein flow pattern in correlation with intrahepatic fat deposition and liver histology in patients with chronic hepatitis C. *Am J Roentgenol*. 1998;171:437-43.

11 Iwao T, Toyonaga A, Oho K, Tayama C, Masumoto H, Sakai T, et al. Value of Doppler ultrasound parameters of portal vein and hepatic artery in the diagnosis of cirrhosis and portal hypertension. *Am J Gastroenterol*. 1997;92:1012–7.

12 Walsh KM, Leen E, Macsween RNM, Morris AJ. Hepatic Blood Flow Changes in Chronic Hepatitis C Measured by Duplex Doppler Color Sonography: Relationship to Histological Features. *J Digestive Diseases Sciences*. 1998;43(12):2584-90.

13 Haktanir A, Cihan BS, Celenk C, Cihan S. Value of Doppler sonography in assessing the progression of chronic viral hepatitis and in the diagnosis and grading of cirrhosis. *J Ultrasound Med*. 2005;24:311-21.

14 Piscaglia F, Gaiani S, Calderoni D, Donati G, Celli N, Gramantieri L, et al. Influence of liver fibrosis on hepatic artery Doppler resistance index in chronic hepatitis of viral origin. *Scand J Gastroenterol*. 2001;36:647-52.

15 Schneider AR, Teuber G, Kriener S, Caspary WF. Noninvasive assessment of liver steatosis, fibrosis and inflammation in chronic hepatitis C virus infection. *Liver Int.* 2005;25:1150-5.

16 Hübner GH, Steudel N, Kleber G, Behrmann C, Lotterer E, Fleig WE. Hepatic arterial blood flow velocities: assessment by transcutaneous and intravascular Doppler sonography. *J Hepatol*. 2000;32:893-9.

17 Kissel A, Rixe O, Methlin A, Nabet M, Tranquart F, Rubini B, et al. Quantification of hepatic arterial and portal venous flow using ultrasound contrast agents for early detection of liver metastases of colorectal cancers. *J Radiol*. 2001;82:1621-5.

18 Taylor KJW, Ramos I, Morse SS, Fortune K, Hammers L, Taylor CR. Focal liver masses: differential diagnosis with pulsed Doppler. *Radiology*. 1987;164:643-7.

19 Taylor KJW, Ramos I, Carter D, Morse SS; Snower D, Fortune K. Correlation of Doppler US tumor signals with neovascular morphological feature. *Radiology*. 1988;166:57-62.

20 Yarmenitis SD, Kalogeropoulou CP, Hatjikondi O, Ravazoula P, Petsas T, Siamblis D, et al. An experimental approach of the Doppler perfusion index of the liver in detecting occult hepatic metastases: histological findings related to the hemodynamic measurements in Wistar rats. *Eur Radiol*. 2000;10(3):417-24.

21 Kakkos SK, Yarmenitis SD, Tsamandas AC, Gogos CA, Kalfarentzos F. Fatty Liver in Obesity: Relation to Doppler Perfusion Index Measurement of the Liver. *Scandinavian J Gastroenterol.* 2000;35(9):976-80.

22 Stojačić-Đenić S, Jurišić V, Perišić M. Značaj ultrasonografskih ispitivanja hepatičke cirkulacije kod metastatskih promena u jetri. *Pons*. 2007;9:28-30.

23 Hirata M, Abkar SM, Horiike N, Onji M. Noninvasive diagnosis of the degree of hepatic fibrosis using ultrasonography in patients with chronic liver disease due to hepatitis C virus. *Eur J Clin Invest*. 2001;31:528-35.

24 Cosar S, Oktar SO, Cosar B, Yucel C, Ozdemir H. Doppler and gray scale ultrasound evaluation of morphological and hemodynamic changes in liver vasculature in alcoholic patients. *Eur J Radiol*. 2005;54:393-9.

25 Fowler RC, Harris K, Swift S, Ward M, Greenwood DC. Hepatic Doppler perfusion index: measurement in nine healthy volunteers. *Radiology*. 1998;209:867-71.

26 Bernatik T, Strobel D, Hahn EG, Becker D. Doppler measurements: a surrogate marker of liver fibrosis? *Eur J Gastroenterol Hepatol.* 2002;14:383-7.

27 Saftoiu A, Ciurea A, Tudorel A, Gorunescu FB. Hepatic arterial blood flow in large hepatocellular carcinoma with or without portal vein thrombosis: assessment by transcutaneous duplex Doppler sonography. *Eur J Gastroenterol Hepatol*. 2002;14(2):167-76.

28 Ramnarine KV, Leen E, Oppe K, Angerson WJ, McArdle CA. Contrast-enhanced Doppler perfusion index. *J Ultrasound Med*. 2002;21:1121-9.

29 Djenić SS, Sarenac-Kovac R, Kerkez M, Jurisić V. Doppler hemodynamic study in evaluation of liver metastases. *Acta Chir Iugosl*. 2007;54(2):9-12.

30 Perisic MD, Culafic DM, Kerkez M. Specificity of splenic blood flow in liver cirrhosis. *Rom J Intern Med*. 2005;43(1-2):141-51.

31 Culafic D, Perisic M, Vojinovic-Culafic V, Sagic D, Kerkez M. Spontaneous splenorenal shunt in a patient with liver cirrhosis and hypertrophic caudal lobe. *J Gastrointestin Liver Dis*. 2006;15(3):289-92.

32 Perisic M, Ilic-Mostic T, Stojkovic M, Culafic D, Sarenac R. Doppler hemodynamic study in portal hypertension and hepatic encephalopathy. *Hepatogastroenterology*. 2005;52(61):156-60.

33 Perisic M, Culafic D, Sagic D, Grbic R. Doppler-duplex ultrasonography in the diagnosis of cavernous portal vein. *Srp Arh Celok Lek*. 1998;126(9-10):368-73.