Gastroenterologia Japonica
Vol. 19, No. 6

Printed in Japan

—Original Article—

QUANTITATIVE MEASUREMENT OF PORTAL BLOOD FLOW IN PATIENTS WITH CHRONIC LIVER DISEASE USING AN ULTRASONIC DUPLEX SYSTEM CONSISTING OF A PULSED DOPPLER FLOWMETER AND B-MODE ELECTROSCANNER

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Summary

Portal blood flow (PBF) can be measured quantitatively using a B-mode combined pulsed Doppler (BCD) system. This system combines a real time B-mode linear type electroscanner and a pulsed Doppler (D-mode) flowmeter. Since both modes are displayed in realtime, Dopper blood flow signals can be retrieved at will from any depth. The blood flow velocity determined by the Doppler spectrogram and the vascular cross-sectional area measured from the B-mode tomographic image enables the quantitative calculation of blood flow volume. Using this system, PBF was measured quantitatively in 88 healthy adults, 54 patients with chronic hepatitis, 65 with cirrhosis of the liver, 27 with primary hepatoma and 12 with idiopathic portal hypertension (IPH). Results of PBF volume measurement were as follows: 889 ± 284 ml/min (mean ± S.D.) for healthy adults, 851 ± 237 ml/min for patients with chronic hepatitis, 870 ± 289 ml/min for cirrhosis of the liver, 966 ± 375 ml/min for primary hepatoma and 1,047 ± 381 ml/min for IPH.

These preliminary results demonstrated that this ultrasonic Duplex system is clinically useful to determine the quantitative amount of PBF.

Received June 19, 1984. Accepted August 3, 1984.

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This paper was presented in part at the 69th meeting of the Radiological Society of North America.

Key Words: *Portal blood flow, Portal hypertension, Ultrasonic pulsed Doppler flowmeter, Ultrasonic duplex system.*

Introduction

The ultrasonic Doppler method was first clinically applied by Satomura et al. in 1955[1]. Since then the Doppler method has been widely used for blood flow measurements in various settings[2-5]. The recent development of the pulsed wave method added axial resolution to the Doppler technique and allowed the measurement of blood flow velocity at any given depth, promising much wider clinical applications[6,7]. Conversely, the tomographic technique by ultrasonic reflection method, the so-called B-mode scan method, has evolved from the contact compound method to gray-scale display and further to the mechanical scanning method and then to the electronic scanning method. With advancement in B-mode techniques, ultrasound imaging attained not only higher resolution, but also real time image display capability by the use of high frequency scanning. At the same time pulsed Doppler flowmetry, by virtue of frequency analysis, which incorporates Fast Fourier Transform (FFT), improved to the point where the entire process of emitting and receiving the ultrasound wave, frequency analysis and spectrum display can be performed in less than 20 msec. Thus, the Doppler-mode (D-mode) was able to attain real time capability through the above high speed arithmetic circuitry. By combination of these two modalities, using real time simultaneous display quantitative measurement of the blood flow of deep vessels became possible. This ultrasonic duplex system was developed to gather information from the cardiac cavity primarily in cases of valvular diseases. A real time sector-scanner was employed for B-mode display because the ultrasonic window is narrow in ultrasonic cardiography. The authors developed this system for the quantitative measurement of the portal venons system[8]. In the present study the results of measurement of the portal venous system in patients with chronic liver disease are described.

Materials and Methods

The principles of the newly developed ultrasonic B-mode Combined Doppler system (BCD System), TOSHIBA SAL-50A/SDL-01A (Toshiba Corp., Tokyo, Japan) are illustrated in **Fig. 1**. The Doppler flowmetric (D-mode) probe (a single-type probe) is mounted on the probe of the linear electroscanner at a fixed angle of 55°. Accordingly, the ultrasonic beam of the D-mode proceeds in the plane scanned by the B-mode at a fixed angle (**Fig. 2**). The B-mode electronic linear scanner has a frequency of 5 MHz, pulse repetition frequency of 4.39 kHz, axial resolution 1.0 mm, lateral resolution 1.5 mm, and effective scanning width of 5.5 cm. The Doppler-mode flowmeter has frequency of 2.27 MHz, pulse repetition frequency 4/6 kHz, and focal zone of 7 to 11 cm, at which the width of the beam is about 2 mm (−3 dB). The real time measurable depth under B mode monitoring is 3 to 12 cm. The D-mode utilizes a pulsed wave Doppler method. Desired sample points and sample volumes can be selected by a time-gate technique. Doppler shift spectrograms are displayed in real time. Maximum flow velocity (V_{Dmax}) at the central axis of a vessel is determined from this spectrum. Mean blood flow velocity (Vmean) was then calculated by the equation Vmean = 0.57 V_{Dmax} which had been determined, by the authors, from experimental measurements of bovine blood flow in silicon tubing, set up as a simulation model for in vivo blood flow. The coefficient 0.57 remained constant and was not

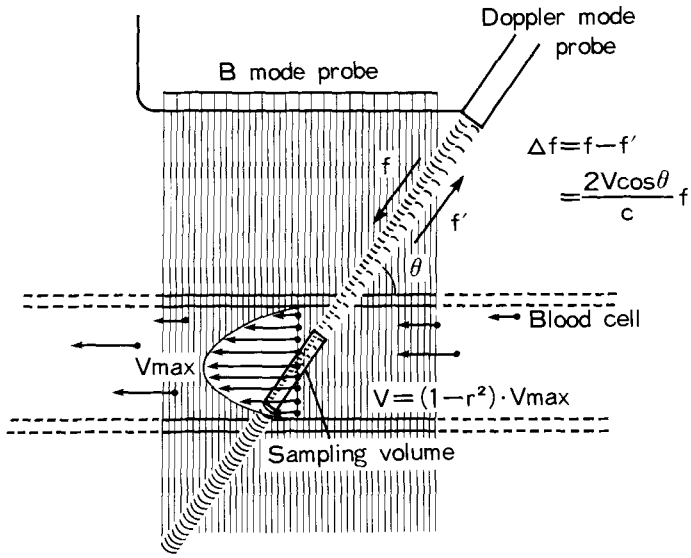

Fig. 1. Scheme of the B-mode combined Doppler system.
f: frequency of emitted ultrasonic wave, f′: frequency of received ultrasonic wave, Δf: Doppler shift frequency, C: velocity of the ultrasonic beam in the body (approximately 1,530 m/sec), θ: angle between the direction of the flow and the Doppler beam, V: velocity of blood flow, Vmax: maximum velocity at the center of the lumen, v: velocity of the flow at r, r: distance from the center of the vessel divided by the radius of the lumen. (0<r<1)

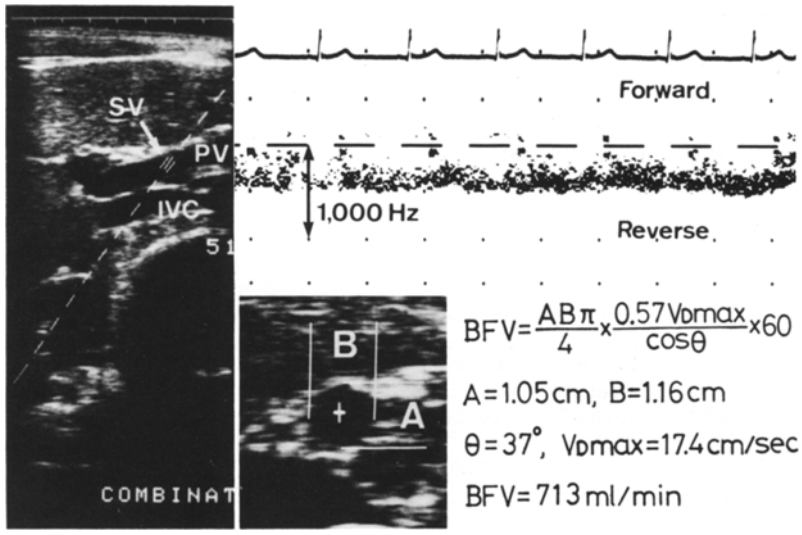

Fig. 2. B-mode scanning of the portal vein (left side), Doppler spectrogram (right upper side) and cross-sectional image of the portal vein (middle lower side) in a normal healthy adult.
PV: portal vein trunk, IVC: inferior vena cava, SV: sample volume, A: diameter between top and bottom, B: diameter between left and right, BFV: blood flow volume. In the spectrum recording, the broken line indicates zero-level. Signals above the broken line represent forward flow toward the Doppler probe and signals below the broken line represent receding flow from the probe. A Doppler shift of 1 kHz equals 34.4 cm/sec in velocity.

affected by the diameter of the tubing or hematocrit of the blood. Human studies were carried out in 246 subjects including 88 healthy adults, 54 patients with chronic hepatitis, 65 with cirrhosis of the liver, 12 with idiopathic portal hypertension (IPH) and 27 with primary hepatoma. Diagnoses were confirmed by liver biopsies and/or laparoscopy or angiography. Measurements were carried out with subjects fasting and resting in a 30 degree head-up position to avoid interference of the penetration of the ultrasound beam by bowel gas.

The portal vein was displayed first along the longitudinal axis by the B-mode scanner and the site for volume sampling was set at the mid-portion of the portal venous trunk. Doppler signals were recorded as well as the angle between the beam and the portal vein on the B-mode image.

To obtain the cross-sectional area of the vessel, another separate scanning at 90° to the longitudinal axis of the portal vein at the sample point, was performed immediately after flowmetry, and an enlarged image was photographed on a Polaroid printout. Major and minor axes were measured on the photograph and were aproximated to an ellipse to calculate the cross-sectional area of the vessel. Portal blood flow volume was obtained by the following equation;

$$PBF = \frac{AB\pi}{4} \times \frac{0.57}{\cos\theta} V_{Dmax} \times 60 \text{ (ml/min)}$$

(A: diameter between top and bottom, B: lateral diameter of the vessel, θ: angle between the D-mode ultrasonic beam and the vessel)

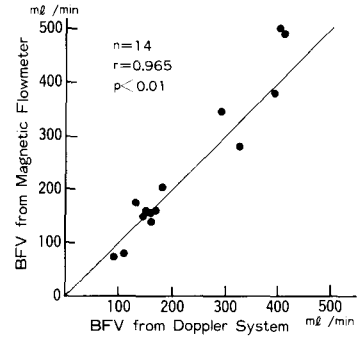

Fig. 3. Relationship between the electromagnetic flowmeter and B-mode combined Doppler system. (BFV: Blood flow volume.)

To investigate the capability of the duplex system in vivo, the simultaneous measurement of the blood flow in the canine inferior vena cava (IVC) was performed with an electromagnetic flowmeter (EMF) and with our BCD system. With this experiment excellent correlation between these two methods was confirmed, as shown in **Fig. 3.**

Table 1. Measurement of portal blood flow in chronic liver diseases

	Healthy adults (n=88)	Chronic hepatitis (n=54)	Cirrhosis (n=65)	Idiopathic portal hypertension (n=12)	Hepatoma (n=27)
Cross-sectional area (cm^2)	0.99±0.28	1.15±0.37*	1.49±0.49**	1.56±0.45**	1.53±0.60**
Mean velocity (cm/sec)	15.3±4.0	12.7±3.6**	9.7±2.6**	10.8±3.8**	10.9±3.9**
Blood flow volume (BFV) (ml/min)	889±284	851±237	870±289	1,047±381	966±375
BFV/Body weight (ml/min/kg)	16.3±5.0	15.4±4.5	15.1±4.8	21.2±7.8	18.2±8.5

*: $p<0.01$, **: $p<0.001$ versus healthy volunteer. (mean ± S.D.)

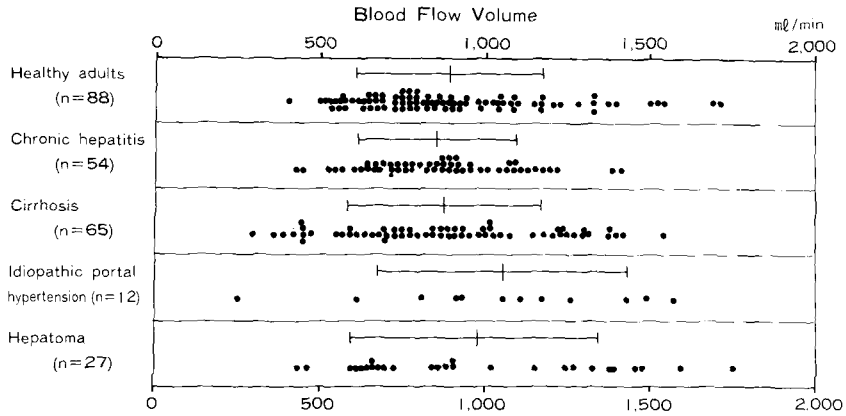

Fig. 4. Measurement of portal blood flow volume in chronic liver diseases.

Results

Results are summarized in **Table 1** and two typical cases are shown in **Figs. 5** and **6**. The cases summarized in this paper constituted approximately 90% of the total subjects ex-

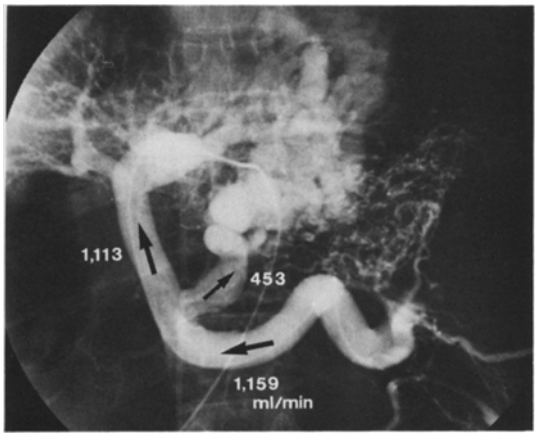

Fig. 5. Liver cirrhosis. The values of blood flow volume measured by B-mode combined Doppler flowmetry are superimposed on the respective vessels. Blood flow in the splenic vein is 1,159 ml/min, in the portal trunk 1,113 ml/min, and in the left gastric vein 453 ml/min in hepatofugal direction. Percutaneous transhepatic portography revealed a thick tortuous splenic vein and shunt formation from the left gastric vein to the esophageal varices. In this case, because of increased splenic blood flow, blood flow in the portal trunk appears to be maintained in spite of marked extrahepatic shunting pathway.

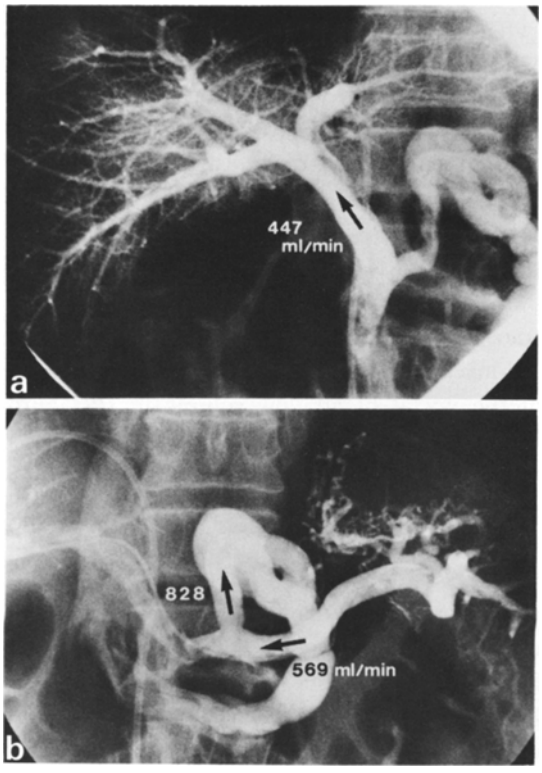

Fig. 6. Chronic hepatitis. Measurements of blood flow volume by BCD system are superimposed on PTP. (a: superior mesenteric venography, b: splenic venography) Due to a large amount of shunting from the splenic vein via the left gastric vein to the left renal vein, blood flow in the portal trunk is decreased.

amined. In the remaining 10% of subjects, the portal venous flow could not be measured mainly because of disturbance of ultrasonic transmission by intestinal gas. In healthy subjects, fairly good correlation of blood flow volume with body weight, height and body surface area were observed as follows; body weight/blood flow volume (BFV): $r=0.407$ ($p<0.01$), height/BFV: $r=0.567$ ($p<0.01$), body surface area/BFV: $r=0.437$ ($p<0.01$). Significant difference according to sex was observed in the cross-sectional area of the portal vein and the portal blood flow volume but this difference disappeared when the portal blood flow was expressed in terms of either body weight or body surface area. No difference was observed in blood flow velocity according to sex. In various chronic liver diseases common trends were seen: i.e. on average cross-sectional areas of the portal veins were significantly increased compared to healthy subjects. Conversely, the portal blood flow velocity was significantly decreased in liver diseases. If this phenomenon is viewed from the standpoint of blood flow volume however, only a mild and statistically unsignificant decrease was seen in chronic hepatitis and cirrhosis. Slight increases of the portal blood flow volume in IPH and hepatoma were also found (**Fig. 4**).

Discussion

The ultrasonic duplex system composed of a B-mode scanner and a pulsed Doppler flowmeter has been used mainly for the diagnosis of cardiac diseases. The portal vein is more convenient for quantitative measurements of blood flow compared to the heart and other major vessels, i.e., (1) flow velocity is relatively low in comparison to arteries, (2) in the portal vein flow is laminar, (3) phasic flow seen in arteries, the IVC and the renal vein is absent, (4) the cross-sectional area of the portal vein is large enough to be measured by B-mode ultrasonography. There are some problems which might cause possible inaccuracy in the quantitative measurement of the deep-seated blood vessels, i.e., (1) the blood flow velocity, (2) the cross-sectional area of the vessel and (3) the angle between the D-mode ultrasonic beam and the vessel. Among these factors, the measurement of mean flow velocity is most problematic. The present system measures the maximal flow velocity at the center of the longitudinal axis of the vessel and multiplies this value with a coefficient to obtain the mean flow velocity. This is practical and reproducible. For this premise it is critical to ascertain that the velocity vector profile does not change significantly depending on the case and/or pathophysiology. The authors' experience with several hundred measurements of PBF revealed no single case of turbulence in the blood flow through the portal vein in resting or fasting subjects. In all cases the spectrum of laminar flow was recorded. Turbulence was recorded only in occasional cases of post-prandial measurement and cases with indwelling portal catheters. This supports the idea of applying in vivo the $Vmean/V_{Dmax}$ ratio obtained from the experiment using bovine blood and silicon tubing which consisted of laminar flow. Also we obtained excellent correlation of result using the BCD system and an electromagnetic flowmeter (EMF) to simultaneously measure blood flow in the canine IVC which posesses the same characteristics and diameter as the human portal vein.

Portal blood flow in healthy adults was shown to be 889 ml/min (16.3 ml/min/kg BW) on an average. This value is comparable to previously reported values of human hepatic blood flow, two thirds of which is portal blood flow[9-12]. According to several reports on animal experiments performed by direct portal venous electromagnetic flowmetry gave the value in the range of 75 to 90 ml/min/100 g liver weight[13-16]. Assuming the liver weight to

be 2% of body weight[17-19], our results are in agreement with these reported values, supporting the viability of our method.

In portal hypertension, especially in cirrhosis of the liver, PBF of the portal vein trunk has been considered to be decreased. This notion has been based on intraoperative direct measurement by EMF[9,20]. Our data presented here, however, do not show any significantly decreased PBF in chronic liver diseases mainly consisting of cirrhosis of the liver. Furthermore, increased blood flow was documented in IPH and primary hepatoma.

Our results also showed a significantly increased cross-sectional area of the portal vein in chronic liver diseases, compared to healthy volunteers. Flow velocity was decreased significantly. This appears to reflect the presence of "congestion" in the portal venous system in patients with chronic liver diseases. However as mentioned above, congestion does not necessarily mean decreased blood flow volume. Conversely, formation of extra-hepatic shunting pathways are commonplace in portal hypertension, most of which are cases of cirrhosis of the liver[21]. The question arises as to why PBF volume in the portal vein trunk is maintained in spite of efflux from these shunting pathways? The probable answer may be splenomegaly, i.e.; in portal hypertension an enlarged spleen is the rule. Accordingly, as seen in the cases shown in **Figs. 5** and **6** splenic blood flow is increased considerably. Because of this large amount of splenic blood flow, the blood flow volume of the portal vein trunk is probably maintained in the face of extrahepatic shunting. In other words, in portal hypertension total influx to the portal venous system is increased, compared to normal subjects. In conclusion, in portal hypertension there exists a hyperdynamic state more prominent in the splenic circulation.

As mentioned above, the BCD system can measure the PBF quantitatively without any invasiveness. The system has several potential sources of errors, such as inaccuracy in the measurement of the angle between the blood vessel and the Doppler mode beam, the cross-sectional area of the blood vessels and the mean blood flow velocity. In order to avoid these errors, we have been using a method by which the maximum velocity is multiplying by a coefficient to obtain the mean flow velocity. However, this method was employed on the premise that the velocity profile of the portal vein is constant. We think that this method is also a source of error, because there are some variations in the velocity profile of the portal vein in each patient, especially in patients with portal hypertension who have congested portal venous flow.

Though there are some factors which may produce errors in measuring the portal blood flow as mentioned above, in clinical applications, the measurement of the portal blood flow with the ultrasonic duplex system is thought to be less than 20%. The usefulness of the ability to quantitatively measure the blood flow of deep vessels, especially portal blood flow under physiological conditions, is extensive, e.g. (1) to evaluate the functional hepatic reserve, (2) to evaluate the effects of foods and drugs, (3) to assist in decision making concerning major hepatectomies or (4) to quantitatively assess extrahepatic shunting pathways. We hope that clinical research concerning hepatic circulation may be significantly advanced by the addition of this new modality.

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