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Liver Hemodynamic Flow Balance by Image-Directed Doppler Ultrasound Evaluation in Normal Subjects

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Abstract: Image-directed Doppler ultrasonography of main hepatic vessels (hepatic artery, portal vein, hepatic veins, and inferior vena cava (IVC)] was performed in 22 healthy volunteers, 20 years to 65 years of age. For each vessel an estimate was made of the diameter, velocity time interval (VTI), volume blood flow in relation to heart rate (stroke volume in L/min/beat), and body size (blood flow index in L/min/m^2 body surface area). Moreover, a hemodynamic hepatic balance to define a range of values in normal population was described. **The summation of flow of hepatic veins and IVC flow, just over renal veins, (= IVC subhepatic flow) was significantly correlated with the IVC flow rate before entrance into the atrium** (R^2 = 0.90). Hepatic artery flux plus portal vein flux plus subhepatic vein flux was also related to IVC flux before right atrium entrance (R^2 = 0.92).

This study confirms the utility and efficiency of Doppler ultrasonography in understanding liver flow hemodynamic balance. **Indexing Words:** Hepatic flow balance · Pulsated Doppler · Flow analysis

Several invasive and complex techniques have been used to directly evaluate vessel patency.[1–5] Recently, image-directed Doppler ultrasonography has been employed to measure blood flow velocity, vascular cross-sectional area, and quantitative evaluation of intravascular flow.[4–8]

Portal vein flow, hepatic artery, and hepatic veins flow have been previously investigated both in healthy patients[3,9–13] and in patients with liver diseases,[11,14–25] but no data, to our knowledge, are available concerning hepatic input–output flow balance for the porta hepatis, inferior vena cava, and hepatic veins.

The purpose of this study is to define, in a noninvasive way, the range of normal values for the hepatic blood flow balance with the aim of evaluating if this method would be a valid instrument for the detection of hemodynamic abnormalities in hepatic surgery.

Our effort has concentrated on evaluating if cross-correlation of data acquired by noninvasive Doppler analysis would be useful in predicting reproducible values for hepatic blood flow despite the known problem of Doppler blood flow underestimation.

MATERIALS AND METHODS

Twenty-two adult healthy volunteers, 11 males and 11 females, from 20 years to 65 years of age (mean ± SD: 44.0 years ± 15.6 years), underwent Doppler examination of hepatic vessels.

All volunteers had routine physical examinations within normal limits, including no history of hypertension.

Doppler examinations were performed with an ATL Ultramark 8 scanner having a 3-MHz mechanical pulsed Doppler probe.

All subjects were in the supine position, breathing normally. Blood pressure values and the electrocardiogram (ECG) were monitored during the examination; heart rate ranged between 60 beats/min and 103 beats/min (mean ± SD: 76.1 beats/min ± 10.5 beats/min).

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Data on blood flow velocity and vessel diameters were recorded from (1) the inferior vena cava just before entering right atrium, (2) the inferior vena cava over renal veins, (3) the portal vein at the porta hepatis, (4) the right and left branches of the portal vein after its bifurcation at the hepatic hilus, (5) the common hepatic artery distal to the origin of the gastroduodenal artery, and (6) the hepatic veins 1 cm to 2 cm proximal to their entrance into inferior vena cava.

The maximal short axis diameter was measured in all vessels, except for inferior vena cava, where M-mode recordings from the vessel was attempted to obtain a mean diameter, averaging breathing fluctuations.

A cross-sectional area was calculated for every vessel using the equation for the area of a circle $[(D/2)^2 \times \pi]$. A sample volume was positioned lengthwise along the vessel course, and using the automatic computer angle correction, the blood velocity was determined. The size of sample volume was adjusted to be the same as that of the vessel so that an average of the velocity gradient was obtained.

The Doppler velocity profile was determined from the digitalized image and the velocity time integral (VTI) calculated for each heart beat; three consecutive waveforms were evaluated to obtain an estimate of the mean velocity.

Heart rate was calculated from the R-R interval of the ECG. Blood flow rate was calculated in every vessel in relation to the time domain (L/min) using the equation $F = V \times A$ (F is the blood flow rate, V is the mean velocity, and A is the vessel cross-sectional area).

Stroke volume in L/min/beat and blood flow rate index in L/min/m^2 were also calculated.

The sum of the blood flow rates in the right and left branch of portal veins was compared to that of common portal tract; the sum of the blood flow rates of the portal vein and hepatic artery was compared to the sum of the blood flow rates of the hepatic veins, and finally, the sum of the blood flow rates of the hepatic inferior vena cava and hepatic veins was compared with the blood flow rate of the inferior vena cava just before the atrium.

STATISTICAL ANALYSIS

The Student t test was used to compare the average vessel diameters, velocity time integrals, and blood flow rates in males and females. Sign tests were used to evaluate diameter and flux data. Regression analysis was used to compare measured and extrapolated blood flow rates and

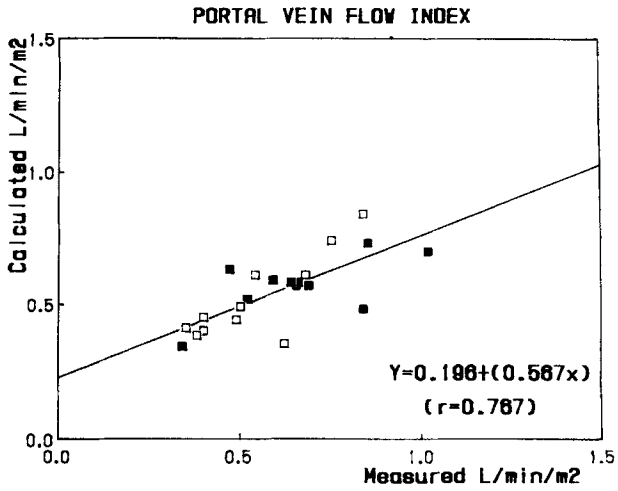

FIGURE 1. Regression analysis of flow index in portal branch veins versus common portal vein.

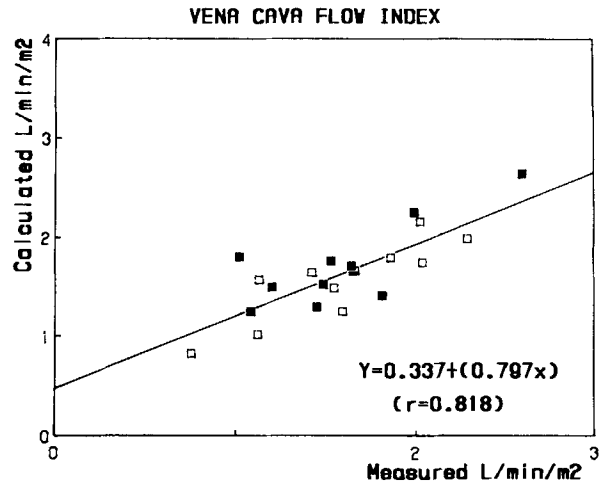

FIGURE 2. Regression analysis of flow index in portal vein, hepatic artery, and subhepatic vena cava vs inferior vena cava.

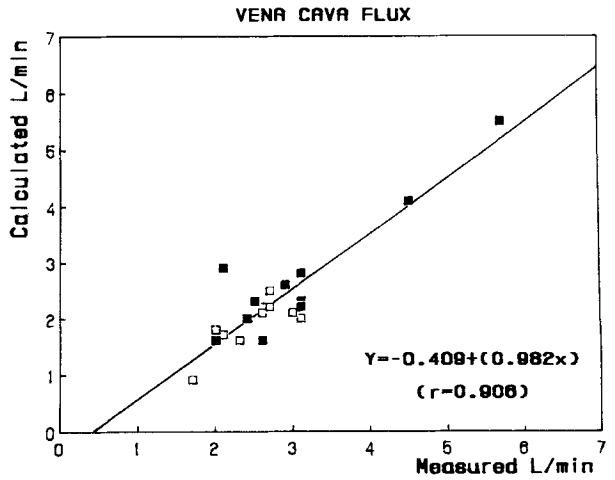

FIGURE 3. Regression analysis of flow rates in hepatic veins plus subhepatic vena cava vs inferior vena cava.

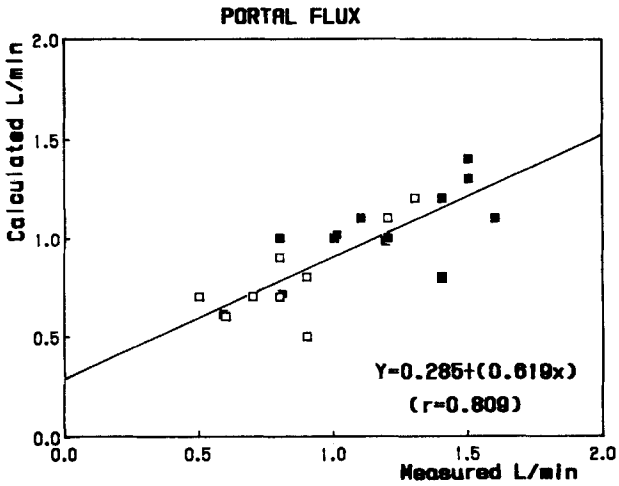

FIGURE 4. Regression analysis of flow rates in portal branch veins vs common portal vein (measured).

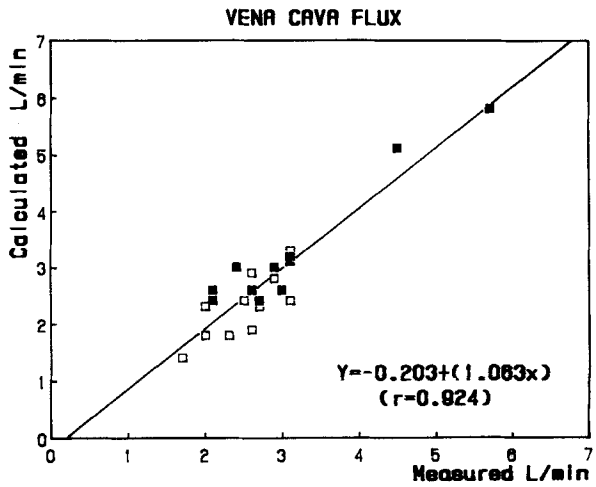

FIGURE 5. Regression analysis of flow rates in portal vein, hepatic artery, and subhepatic vena cava vs inferior vena cava.

blood flow indices (blood flow rate/m^2 body surface area) data (Figures 1–5).

Multiple regression analysis was carried out to evaluate the ability to predict blood flow rates in the most important hepatic vessels.

RESULTS

Satisfactory ultrasound images of the liver vascular tree were obtained in only 22 subjects; evaluation of 6 other adults was not possible because of difficulties in visualizing all hepatic vessels. Particular difficulty was encountered in obtaining an adequate approach to the hepatic veins in order to minimize the angle between the long axis of the vessels and the ultrasonic beam.

Diameter, VTI and blood flow rates for each vessel are given in Table 1. No significant differences were found between sex groups, although sign tests indicated increased values in the male group for the diameter and blood flow rate. The total flow rate (L/min) at the porta hepatis, both in males (3.24 ± 1.14) and in females (2.32 ± 0.56), was not significantly different from that of the vena cava before the atrium entrance (3.12 ± 1.08 and 2.49 ± 0.45, respectively).

Results of the regression analyses listed in Table 2 show a good correlation between expected blood flow values, obtained as sums of various components, and measured values.

A multiple regression analysis using the main vascular flow rates (Table 3) permits estimation

TABLE 1
Mean Values of Hepatic Diameter, Velocity Time Integral, and Flow Rate

	Males		Females		Total	
	Mean	SD	Mean	SD	Mean	SD
Diameter	cm		cm		cm	
Subhepatic vena cava	1.46	± 0.44	1.17	± 0.29	1.32	± 0.39
Portal vein	1.18	± 0.17	1.00	± 0.12	1.09	± 0.17
Hepatic artery	0.56	± 0.14	0.46	± 0.10	0.51	± 0.13
Inferior vena cava	2.07	± 0.34	1.72	± 0.31	1.09	± 0.36
Velocity time integral	m/min		m/min		m/min	
Subhepatic vena cava	0.14	± 0.06	0.16	± 0.05	0.15	± 0.05
Portal vein	0.17	± 0.06	0.14	± 0.03	0.15	± 0.05
Hepatic artery	0.19	± 0.08	0.21	± 0.11	0.20	± 0.09
Inferior vena cava	0.14	± 0.04	0.15	± 0.06	0.14	± 0.05
Flow rate	L/min		L/min		L/min	
Subhepatic vena cava	1.65	± 0.94	1.24	± 0.42	1.45	± 0.74
Portal vein	1.23	± 0.28	0.80	± 0.24	1.01	± 0.33
Hepatic artery	0.35	± 0.24	0.27	± 0.17	0.31	± 0.21
Hepatic veins (sum)	1.06	± 0.38	0.73	± 0.33	0.89	± 0.39
Total flow rate (sum)	3.24	± 1.14	2.32	± 0.56	2.78	± 0.99
Inferior vena cava	3.12	± 1.08	2.49	± 0.45	2.80	± 0.86

TABLE 2
Regression Analysis of Calculated vs Measured Parameters

	Intercept	Slope	R^2
Flow rate			
A	−0.203 ± 0.286	1.063 ± 0.097	0.924
B	−0.409 ± 0.300	0.982 ± 0.102	0.906
C	0.285 ± 0.107	0.619 ± 0.100	0.809
Flow index			
D	0.336 ± 0.205	0.797 ± 0.125	0.818
E	0.214 ± 0.206	0.710 ± 0.126	0.784
F	0.196 ± 0.066	0.567 ± 0.106	0.767

A: Regression of flow rates in the portal vein, hepatic artery, and subhepatic vena cava vs that in the inferior vena cava.

B: Regression of flow rates in the hepatic veins and subhepatic vena cava vs that in the inferior vena cava.

C: Regression of flow rates in the portal branch veins vs that in the common portal vein.

D: Regression of blood flow index in the portal vein, hepatic artery, and subhepatic vena cava vs that in the inferior vena cava.

E: Regression of blood flow index in the hepatic veins and subhepatic vena cava vs that in the inferior vena cava.

F: Regression of blood flow index in the portal branch veins vs that in the common portal vein.

of specific vessel blood flow rates from flow rates in other hepatic vessels in order to obtain flow rate information about vessels that are not readily accessible.

DISCUSSION

Quantitative hepatic hemodynamic assessment was accomplished, until a short time ago, by several techniques including electromagnetic flowmetry, radiocolloid clearance, and radiolabeled bile salt uptake by the liver.[13] These methods are complex, invasive, and often imprecise. Recently, real-time B-mode imaging and pulsed Doppler ultrasonography has been employed for portal hemodynamic evaluation.[13] This method, compared to angiography, appears to have the same accuracy in providing qualitative information about hepatic blood flow, particularly portal blood flow (vessel patency, stenosis, flow direction).[15] Although some authors[5,13] have used the pulsed-wave Doppler method for quantitative portal blood flow analysis, numerous investigators[8,10,23] have considered it inadequate due to technique-related errors. First of all, vessel area is calculated from its diameter assuming that the vessel is circular, which may not always be the case. Moreover, measurement of blood flow is dependent both on the incidence angle of insonation, which should range between 30° and 50°, and breathing changes.

Third, although intra-abdominal venous channel study is facilitated by comparison with the heart (physiologic laminar flux at relatively low velocity, no phasic changes in velocity except in the IVC), several drawbacks are reported: intra-abdominal vessels are rather small and the segment useful for investigation is relatively short.[8] Because of these disadvantages, the vessels under study must be recognized in a precise manner. Finally, the technique accuracy still depends, to a large degree, on the operator. However, this source of error can be minimized by applying a standardized method using the same ultrasonographer.

Our standard approach to each vessel in the normally breathing patient consisted in the use of the same scans to evaluate the vascular parameters and the time-averaged cross-sectional area in order to obtain a better assessment of volume blood flow.

TABLE 3
Flow Rate Multiple Regression Analysis

	Coefficient	SE	*t* Value	R^2
Vena cava flow rate				
Constant	1.140	0.550	2.071	0.893
Portal vein flow rate	0.740	0.223	3.316	
Hepatic artery flow rate	0.238	0.388	0.614	
Subhepatic vena cava flow rate	1.006	0.120	8.352	
Body surface area	−0.363	0.40	−0.898	
Subhepatic vena cava flow rate				
Constant	−1.270	0.454	−2.794	0.884
Inferior vena cava flow rate	0.799	0.095	8.352	
Portal vein flow rate	−0.548	0.218	−2.514	
Hepatic artery flow rate	−0.208	0.346	−6.602	
Body surface area	0.644	0.334	1.928	
Portal vein flow rate				
Constant	−0.440	0.510	−0.863	0.488
Inferior vena cava flow rate	0.530	0.159	3.316	
Subhepatic vena cava flow rate	−0.494	0.196	−2.514	
Hepatic artery flow rate	−0.106	0.331	−0.322	
Body surface area	0.419	0.335	1.253	

Nevertheless, there are no previous investigations, to our knowledge, reporting the hemodynamic balance of all the main hepatic vessels and the correlation among them.

In this study, ultrasonography is utilized as a quantitative noninvasive method to identify these correlations.

Our results (Tables 1 and 2) indicate that the quantitative assessment of liver vessels by image-directed Doppler ultrasonography is correct but not mathematically exact.

As a matter of fact, the sum of the portal vein flow rate at porta hepatis, the hepatic artery flow rate, and the inferior vena cava flow rate just over renal veins is well correlated to inferior vena cava flow rate recorded just before right atrium entrance ($R^2 = 0.924$), but it is not identical (Figure 5).

Moreover, a high correlation ($R^2 = 0.906$) was found, as expected, between the flow rates of hepatic veins and that of the inferior vena cava, recorded just over renal veins, and the flow rate of the IVC just before the atrium (Figure 3).

A good correlation ($R^2 = 0.809$) between the summation of the flow rates of the two branches of the portal vein with the flow rate of the common portal vein flux was also observed (Figure 4).

Regression analysis also demonstrated the influence of variable body surface area of various flow rates (Table 3).

Our work shows that vascular parameters of vessels that are difficult to study directly can be obtained from measurements made on vessels that are more accessible. If the portal trunk or the right and left portal branches are not visualized (10% of cases),[15] we could deduce, with good reliability, the blood flow rate ($R^2 = 0.809$) and the flow index ($R^2 = 0.767$) by regression analysis. Similarly, the common portal vein (PV) blood flow rate can be deduced by considering the difference between the sum of the blood flow rates of the common hepatic artery (HA), subhepatic vena cava (SVC), and that of the IVC at right atrium entrance (IVC) ($R^2 = 0.924$) [e.g., 3.12 L/min (IVC) − (0.35 L/min (HA) + 1.65 L/min (SVC) = 1.12 L/min (PV)]. The measured value for PV was 1.23 (Table 1).

In healthy adults the hepatic blood flow rate at the porta hepatis was 1.30 ± 0.42 L/min as reported by Doi,[19] about three fourths of which (1.01 L/min ± 0.33 L/min) supplied by the portal vein and 0.31 L/min ± 0.21 L/min by the hepatic artery. The hepatic arterial blood flow rate was 24% of the overall hepatic flow rate, in agreement with Schenk.[11]

The total flow rate for blood leaving the liver (hepatic veins) was 0.89 L/min ± 0.39 L/min.

The evident discrepancy between total hepatic inflow and outflow, equivalent to 0.4 L/min, can be explained by the small diameter of vessels with low velocity of flow or by the presence of he patic accessory veins (unsettled number for each subject) separately entering the inferior vena cava and not detectable with ultrasonography.[26]

A quantitative hemodynamic investigation of the liver under several pathologic circumstances could have important diagnostic and therapeutic implications. In particular, this technique could be useful for studies of hemodynamic changes in patients with chronic liver disease, in hepatic malignancies, and after intrarterial infusion of Mitomycin C microcapsules for hepatocellular carcinoma treatment. The diagnosis of hepatic vessels thrombosis and artero-portal shunts could also be facilitated by use of these techniques. They could be helpful, preoperatively, in selecting patients for surgical procedures (portocaval shunts, hepatectomy in cirrhosis) in order to avoid surgery in high-risk patients and to predict the results of therapy.

Recently, the image-directed Doppler ultrasonography has been employed in liver transplantations in order to analyze the basal hepatic hemodynamic state and to estimate, in the postsurgical phases, early blood flow balance modifications as a prognostic factor.[27–30]

Prospectively, we believe that the image-directed Doppler ultrasonography could become an essential method for evaluating liver perfusion in the place of invasive and more expensive procedures.

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