The Value of Portal Vein Pulsatility on Duplex Sonograms as a Sign of Portal Hypertension in Children with Liver Disease

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OBJECTIVE. The purpose of this study was to determine the significance of portal vein pulsatility on duplex Doppler waveforms in children with end-stage hepatic failure undergoing liver transplantation.

SUBJECTS AND METHODS. Thirty-eight children with end-stage hepatic decompensation were examined with color-assisted spectral Doppler waveform analysis of the hepatic artery and the portal vein. Correlation was made with age, duration of illness, clinical and pathologic diagnosis, and presence of portal hypertension. Findings were compared with those for six patients with acute viral hepatitis and 12 healthy control subjects.

RESULTS. Portal vein pulsatility was noted in all 36 patients in whom portal vein flow was detected by Doppler imaging. The majority of these (34) had clinical or sonographic evidence of portal hypertension. In two patients, no portal vein flow was identified in the liver hilum; both had a large portosystemic shunt through collaterals or surgical graft. Significantly increased pulsatility of the hepatic artery waveform (resistive index [RI] = 0.89 ± 0.15, $p < .0001$) was seen in patients with end-stage liver disease. In contrast, no portal vein pulsatility and normal hepatic artery pulsatility (RI = 0.60 ± 0.11) was noted in all patients with acute hepatitis and control subjects.

CONCLUSION. Portal vein waveform pulsatility is 94% sensitive and 90% specific for portal hypertension in end-stage liver disease.

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The role of Doppler sonography in the examination of patients with chronic liver disease who are candidates for liver transplantation has been well described [1, 2]. For assessment of hepatic vascular size, patency, and flow direction, Doppler sonography has in most instances replaced angiography. One of the most important complications of chronic liver disease is portal hypertension and its sequelae, such as variceal hemorrhage and hepatic encephalopathy, which have a substantial impact on the optimal timing of the transplantation and the surgical technique of the vascular anastomosis. The presence of portal hypertension is generally inferred from indirect signs, such as venous collaterals in the abdominal wall, gastroesophageal varices as shown by upper gastrointestinal radiography or endoscopy, ascites, and splenomegaly. Ability to measure portal venous pressure preoperatively in a noninvasive manner would be desirable, but currently no such test is available. Sonographic indicators of portal hypertension are enlarged caliber of portal vein, lack of respiratory variation of portal venous flow [3], presence of collaterals such as paraumbilical veins [2, 4], reversal of flow in the portal vein, and decrease in antegrade flow volume in the portal vein [5, 6].

In our population of children with chronic liver disease and portal hypertension, referred for sonographic evaluation of the liver before transplantation, we noticed strikingly pulsatile waveforms in the portal vein. We therefore embarked on a prospective study to determine the significance of portal vein pulsatility in patients with chronic liver disease who are awaiting transplantation.

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Subjects and Methods

In all patients referred for preoperative evaluation with color Doppler sonography for possible liver transplantation since early 1990, we prospectively evaluated portal venous and hepatic arterial perfusion with color and duplex spectral Doppler sonography. To date, we have done 45 studies in 38 patients 1 month to 17 years old (mean age, 3.3 years), 18 boys and 20 girls, with end-stage liver disease. Liver biopsy results were available for all 38 patients in the study group, 32 of whom underwent liver transplantation during the study; the remaining six either died, were lost to follow-up, or are awaiting transplantation.

Thirty-six patients had chronic liver disease. The causes included failure of the Kasai procedure for biliary atresia (n = 23), Budd-Chiari syndrome (n = 1), Alagille syndrome with biliary hypoplasia (n = 2), chronic active autoimmune hepatitis (n = 1), neonatal hepatitis with cirrhosis (n = 1), and hemochromatosis (n = 1). Seven patients were classified as having cryptogenic cirrhosis, as no underlying cause could be determined with extensive studies before and after transplantation (serology, biopsy, and pathologic examination of resected liver specimen including viral immunohistochemistry). Two patients were evaluated for possible transplantation on an emergent basis with subacute hepatic failure and no evidence of viral infection. Pathologic examination of the resected liver showed submassive liver cell necrosis, regeneration, and active hepatitis.

Findings were compared with those obtained in a consecutive series of six patients 3 to 11 years old (mean age, 6.7 years), 4 boys and 2 girls, with acute viral hepatitis diagnosed during the study period, all of whom had a complete recovery. Findings were also compared with those obtained in a randomly selected control group of 12 patients 2 months to 14 years old (mean age, 4.2 years), 5 boys and 7 girls, with no clinical and laboratory evidence of liver disease, referred for renal sonography.

We studied all patients and control subjects with the same commercially available color Doppler scanner (Ultramark 9, Advanced Technology Laboratories, Bothell, WA). The standard imaging protocol included real-time evaluation of the liver for size, contour, and internal architecture; presence of ascites; and splenomegaly. Color and duplex Doppler imaging was performed with a low-frequency (3-MHz) phased array transducer in order to optimize the return of Doppler signals from deeper lying tissues. With color Doppler sonography, patency and flow direction in the main portal vein, its left and right intrahepatic branches, and the hepatic artery were evaluated. A subjective assessment of the relative flow rates through the portal vein and the hepatic artery was attempted by comparing their calibers in the liver hilum and the degree of visualization of their intrahepatic branches. This assessment was facilitated by reviewing a cine-loop recording of real-time color flow images at a reduced frame rate, and color hues displayed within the hepatic artery and portal vein were compared with each other on frames acquired at different times within the cardiac cycle. The entire upper abdomen was screened for the presence of portal venous collaterals. Specifically, the presence of collaterals in the gallbladder wall, around the falciform ligament (paraumbilical veins), between splenic vein and left renal vein, and in the region of the lesser omentum and gastric wall was ascertained whenever technically possible.

Subsequently, we did a duplex Doppler examination with spectral waveform analysis in the main portal vein in the liver hilum and the hepatic artery, using angle correction and adaptation of the sample size to vessel diameter. Duplex Doppler parameters were optimized by using maximal gain without background noise, lowest pulse repetition frequency without aliasing, a sweep speed of 4 sec, and by keeping the wall filter as low as possible (50 Hz). Portal venous waveform pulsatility was defined as visible variations of flow velocity that could be related to the cardiac cycle and was differentiated from the normal respiratory variations by observing the patient's respirations and cardiac activity and relating these to the waveforms obtained. By opening the sample volume to include both portal vein and hepatic artery in the liver hilum, flow signals could be recorded from both vessels simultaneously, allowing study of the temporal relationship between both waveforms.

We recorded the following sonographic parameters: resistive indexes (RI) for the portal vein and hepatic artery, defined as $RI = [V_{max} - V_{min}] / V_{max}$ (V_{max} and V_{min} are maximum and minimum flow rates recorded during one cardiac cycle), calculated as the mean of at least three measurements; the relationship between the dip in the portal vein waveform and arterial systole; and the direction of flow in the main portal vein (hepatopetal, bidirectional, hepatofugal).

In three patients, visceral angiography was done with selective injections in the celiac axis and superior mesenteric artery and delayed filming for visualization of the portal vein. The indications for angiography were no visualization of portal venous flow in the liver hilum on routine preoperative color Doppler sonography in two patients and a history of variceal hemorrhage in one.

Charts were reviewed retrospectively for duration of illness; clinical signs of portal hypertension, such as the presence of venous collaterals in the abdominal wall, gastroesophageal varices or hypertensive gastropathy on endoscopy, and a history of upper gastrointestinal hemorrhage; findings at resection of the native liver (patency of portal vein, presence of collaterals); and findings on pathologic examination of liver biopsy specimens and the resected liver specimen. Right-sided heart failure was excluded at the time of the sonographic study in all patients by physical exam and chest radiography (absence of cardiomegaly, central venous distention and pleural effusions).

Portal hypertension was defined as the presence of two or more of the above-mentioned clinical or sonographic signs (ascites, splenomegaly, collaterals, flow reversal in main portal vein). Portal hypertension was present in 36 of the 38 patients with end-stage liver disease. One patient without portal hypertension was a young infant with Alagille syndrome and biliary hypoplasia with no cirrhosis on biopsy, and one patient had subacute hepatic necrosis with no fibrosis on biopsy. The other child with subacute hepatic necrosis had portal hypertension (ascites, splenomegaly, hepatofugal flow in the portal vein) and extensive regeneration with fibrosis on biopsy. None of the patients with acute viral hepatitis and none of the control subjects had clinical or sonographic evidence of portal hypertension.

Statistical analysis of differences in mean RI between groups was performed using a nonparametric analysis of variance procedure (Kruskal-Wallis method) for the portal vein data and a one-way analysis of variance procedure (Bonferroni method) for the hepatic artery data.

Results

Pulsatility was seen in the portal venous waveform of all 34 patients with chronic liver disease in whom we could show flow of the main portal vein by Doppler imaging (Table 1, Figs. 1 and 2) and in the two patients with subacute liver necrosis. Flow direction in the main portal vein was hepatopetal in 23 patients, hepatofugal in 11, and bidirectional in two. One patient who was examined twice with four months' interval initially had pulsatile hepatopetal and subsequently had hepatofugal flow in the portal vein. In contrast, all patients with acute viral hepatitis

TABLE 1: Findings of Doppler Sonography of Portal Vein and Hepatic Artery in Patients with End-Stage Liver Disease, Compared with Acute Viral Hepatitis and Normal Controls

Group	Number of Patients	Portal Vein RI	Flow Direction				Hepatic Artery RI
			Petal	Fugal	Bidir.	Occl.	
End-stage liver disease							
With PHT	36	0.60 ± 0.33[a, b] (0.23–1.50)	21	11	2	2	0.89 ± 0.15[a, c] (0.62–1.25)
Without PHT	2	0.35 ± 0.04[b] (0.33–0.37)	2				0.81 ± 0.15[c] (0.70–0.92)
Acute viral hepatitis	6	0.00 ± 0.00[a, d]	6				0.60 ± 0.11[a, d] (0.50–0.70)
Controls	12	0.00 ± 0.00[a, d]	12				0.61 ± 0.11[a, d] (0.50–0.70)

Notes.—RI = resistive index, PHT = portal hypertension. Flow direction in the portal vein is indicated as hepatopetal, hepatofugal, bidirectional, or occluded (no flow indentified); values for RI are indicated as mean plus or minus one standard deviation, and range (between parentheses). Differences of mean RI between labeled groups: [a]statistically significant, $p < .0001$; [b]not significant, $p = .12$; [c]not significant, $p = .46$; [d] not significant, $p = 1$.

and all control subjects had continuous, nonpulsatile hepatopetal flow in the portal vein, modulated only by respiration.

In two patients with chronic liver disease, no portal vein was seen in the liver hilum, and both had large portosystemic shunts. In one, patency of a small portal vein was subsequently shown by angiography, but the majority of portal venous blood was diverted from the liver through a large collateral vessel. In the other patient, a splenorenal shunt had been created surgically, and no angiographic study of portal vein patency was performed.

Hepatic arterial signals in patients with chronic liver disease indicated high peripheral resistance, with a mean RI of 0.89, significantly increased ($p < .0001$) compared with patients with acute viral hepatitis and healthy controls. In 31% of patients with end-stage liver disease, end-diastolic flow was zero (RI = 1, Fig. 1D) or reversed (RI > 1, Fig. 2D). Arterial systole coincided with a dip in the portal venous waveform in all patients with hepatopetal flow in the portal vein (Fig. 1E), whereas in patients with hepatofugal flow in the portal vein, a peak in the portal venous waveform occurred at peak systole (Fig. 1F).

Table 1 summarizes our findings of Doppler sonography of the portal vein and the hepatic artery with respect to the presence or absence of portal hypertension. The sensitivity of Doppler studies to detect portal hypertension was 94% in the general population and 100% in those with identifiable portal venous flow in the liver hilum. The specificity of Doppler studies to predict portal hypertension, as defined by our criteria, was 90%. However, the waveforms of the two patients with portal vein pulsatility who had no portal hypertension were less pulsatile than were those of patients with portal hypertension, as indicated by a lower RI (0.35 versus 0.60, $p = .12$). These two false-positive results were obtained in a young infant with neonatal hepatitis and no cirrhosis on biopsy and in a child with subacute liver necrosis without regeneration or fibrosis. We found no correlation between the resistive index of the hepatic artery or portal vein and the age of the child, duration of illness, clinical and pathologic diagnosis, number of indicators of portal hypertension, or final outcome.

On color flow images, the hepatic artery subjectively appeared increased in caliber, with high peak systolic flow rates and enhanced visualization of peripheral branches, and the portal vein was relatively small and difficult to identify (Figs. 1A and 2A). Qualitative assessment of flow direction and magnitude in the portal vein and hepatic artery on real-time color flow images recorded in cine-loop and reviewed at a reduced frame rate demonstrated pulsatility in portal venous flow when comparing color hues displayed within the vessels at frames acquired at peak-systole with diastolic frames (Figs. 1A, 1B, 2A, and 2B). However, spectral Doppler analysis was required in all cases to confirm the real-time findings and to provide a more quantitative assessment of temporal flow relationships.

Discussion

Portal blood flow is influenced by numerous factors such as feeding or fasting state, autonomous innervation, intestinal hormones, medications, systemic hemodynamics (cardiac output, circulating blood volume, systemic arterial and venous blood pressure, body position), and the presence of portosystemic collateral vessels [5, 7, 8]. Under normal circumstances, approximately three quarters of liver perfusion is supplied by the portal vein [9], which predominantly supplies the hepatic sinusoids, whereas the connective tissues and biliary ducts of the portal triads are perfused predominantly by the hepatic artery. It is believed that an increase in connective tissue (fibrosis) originating from the portal triads,

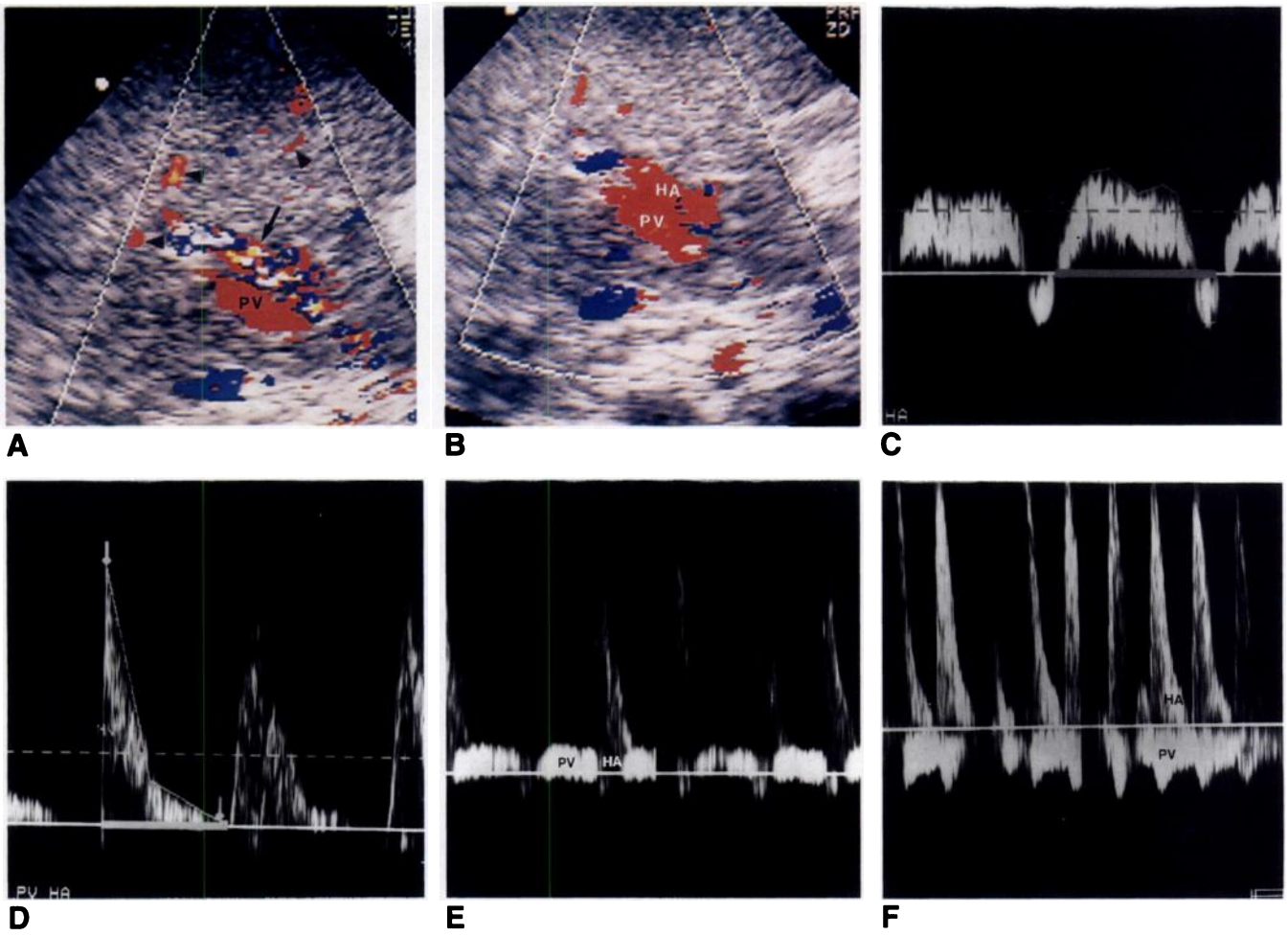

Fig. 1.—7-month-old boy with biliary atresia who underwent a Kasai procedure and had end-stage hepatic decompensation, splenomegaly, and venous collaterals in abdominal wall. Micronodular cirrhosis was found at liver transplantation.

***A* and *B*, Oblique color Doppler sonograms through liver hilum show small, hyperechoic liver. Systolic frame (*A*) shows large caliber of hepatic artery (*arrow*) with increased visualization of peripheral branches (*arrowheads*), high flow rate as evidenced by color aliasing (white, yellow, and blue) within vessel, and hepatopetal (red) flow in portal vein (PV). Diastolic frame (*B*) shows decrease in flow in hepatic artery (HA), increase in PV flow (note orange pixels centrally in vessel), as compared with *A*.**

***C* and *D*, Spectral waveform analysis of PV (*C*, with systolic flow reversal; resistive index (RI) = 1.5) and HA (*D*, with high-resistance waveform, absence of end-diastolic flow; RI = 1.0).**

***E* and *F*, Simultaneous recording of HA and PV by opening sample volume to encompass both. *E*, (same patient as in *A–D*): Dip in PV waveform coincides with HA systole. *F*, (different patient): Pulsatile hepatofugal flow in PV with peak coinciding with HA systole.**

relative to the functional hepatocytic parenchyma, is the cause of the increase of arterial relative to portal venous flow that is observed in cirrhosis. Progressive fibrosis leads to an increase in peripheral resistance in the arterial microvascular bed and also to loss of compliance of the liver parenchyma to accommodate pressure variations within the confined space of the liver capsule, as are brought about by the increased pulsatile arterial inflow. Therefore, early in the pathogenesis of portal hypertension, portal venous inflow is impeded during peak arterial systole. It appears likely that the development of bidirectional and hepatofugal blood flow in the portal vein indicates successive degrees of increased portal venous pressure, but this is also modified by the development of collaterals shunting blood away from the liver, which may actually decrease portal pressure [2]. In addition, as part of the cirrhotic process, arterioportal venous fistulas may have developed at the microscopic level, which would modulate flow in the portal vein more directly.

The results of our study indicate that a pulsatile waveform is present in the portal vein in the majority of children with end-stage liver disease who have portal hypertension (sensitivity 94%). False-negative results were found when no portal venous flow could be identified in the liver hilum, due to thrombosis or large portosystemic shunts in combination with a small-caliber portal vein with slow flow that is below the detection threshold of the equipment. In the absence of portal hypertension in acute viral hepatitis and healthy controls, portal venous flow is generally continuous, with only respiratory variations (specificity 90%). As we studied most children during the terminal phase of their liver disease, we

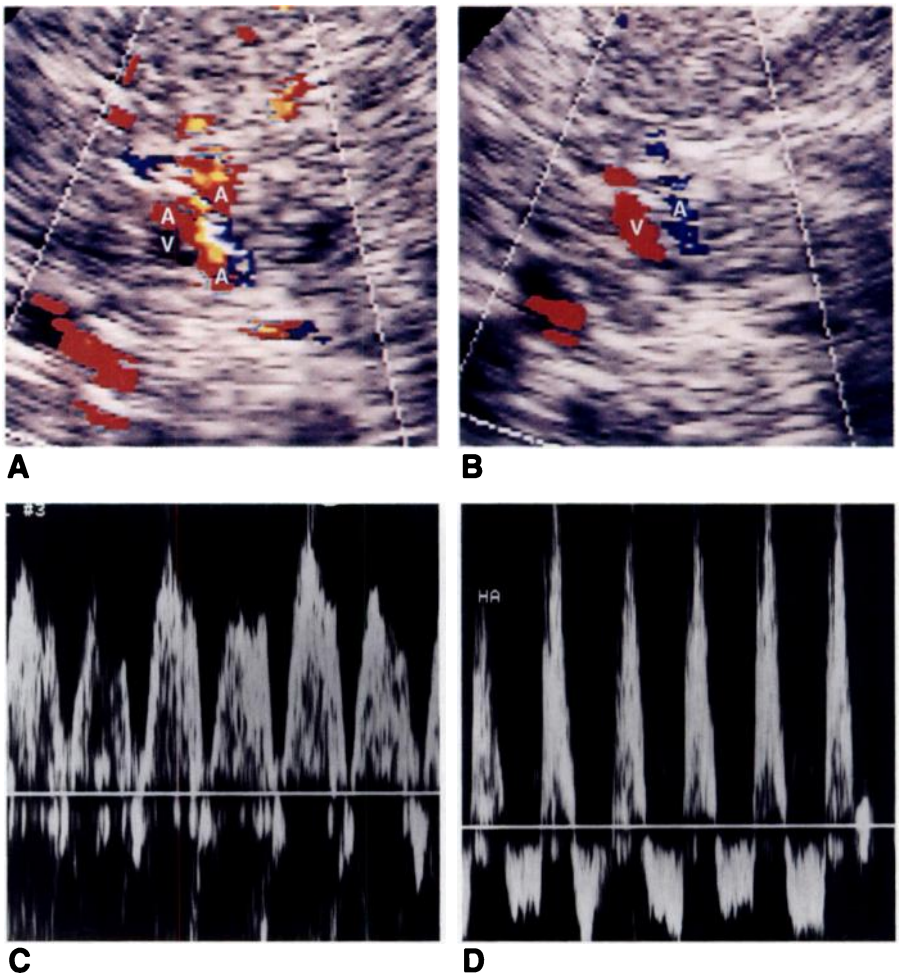

Fig. 2.—9-month-old girl with biliary cirrhosis and severe portal hypertension. Liver transplantation was successful.

***A*, Peak-systolic sonogram shows enlarged hepatic artery (A) with increased visualization of peripheral branches, no color flow is seen in portal vein (V).**

***B*, Diastolic sonogram shows hepatopetal (red) flow in portal vein (V), reversal of flow (blue) in hepatic artery (A).**

***C*, Spectral waveform of portal vein shows strikingly pulsatile waveform with peak-systolic flow reversal (resistive index [RI] > 1).**

***D*, Spectral waveform of hepatic artery shows high resistance with diastolic flow reversal (RI = 1.25).**

do not know whether portal vein pulsatility is to be considered an early sign of portal hypertension, before splenomegaly, ascites, and the formation of collaterals occur. Portal vein pulsatility as indicated by RI was less in two patients with end-stage liver disease who did not yet conform with our criteria for portal hypertension, compared with the mean RI of the group with portal hypertension. However, this difference did not reach statistical significance due to the small number of patients involved. To corroborate our impression that the degree of pulsatility may correlate with the severity of portal hypertension, a prospective, longitudinal study of infants with biliary atresia, the most frequent disorder requiring transplantation in children, will be required, in conjunction with animal studies [10]. We did not find a direct correlation between the degree of pulsatility and the number of indicators of portal hypertension; however, the severity of portal hypertension would be better assessed by direct, invasive measurements of portal venous pressure at surgery before resection of the native liver, and these were not part of our study design.

Bias may have been introduced into this study, as the examiners were not blinded to the clinical diagnosis, and our definition of portal hypertension included sonographic criteria such as portosystemic collateral vessels and flow reversal in the portal vein. However, an independent, noninvasive criterion to identify portal hypertension is currently not available [11], precluding the performance of a study that is more controlled and is blinded and randomized.

Pulsatility of Doppler flow signals in the portal vein has been described in patients with tricuspid regurgitation [12], a finding that has been explained by retrograde transmission of exaggerated hepatic venous pressure variations through the sinusoids to the portal venous system. An alternative explanation of this phenomenon may be that venous congestion of the hepatic parenchyma within the limited space provided by the liver capsule leads to the above-described competition between portal venous and hepatic arterial inflow during peak systole. Portal vein pulsatility in patients with Budd-Chiari syndrome and subacute liver necrosis with extensive parenchymal swelling may be explained on similar grounds. In this study, we did not attempt to systematically evaluate the possible role of passive venous congestion and tricuspid regurgitation on portal venous waveforms, but we believe these factors did not influence our results substantially, as none of our patients had clinical signs of right-sided heart failure at the time of examination.

In normal healthy adult volunteers, modulation of portal vein flow by cardiac activity has been described [13, 14], but we did not see this finding in our control population of children without liver disease. A possible explanation is that in some older individuals even without clinical signs of central venous congestion or parenchymal liver disease, the compliance of the hepatic parenchyma to accommodate arterial pressure variations within the capsule is less than that in healthy children.

We conclude that portal venous pulsatility is a sensitive and specific sign of portal hypertension in children with end-stage liver disease. This finding may aid in the management of this group of patients, specifically in decisions about what is the correct timing of temporary palliation of portal hypertension and finally liver transplantation.

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REFERENCES

1. Longley DG, Skolnick ML, Zajko AB, Bron KM. Duplex Doppler sonography in the evaluation of adult patients before and after liver transplantation. *AJR* **1988**;151:687–696
2. Patriquin H, Lafortune M, Burns PN, Dauzat M. Duplex Doppler examination in portal hypertension: technique and anatomy. *AJR* **1987**;149:71–76
3. Bolondi L, Gandolfi L, Arienti V, et al. Ultrasonography in the diagnosis of portal hypertension: diminished response of portal vessels to respiration. *Radiology* **1982**;142:167–172
4. Lombardi G, Salmi A, Polotti R, Tarantola P, Paterlini A, Inzoli MR. Is it possible to recognize portal hypertension with continuous-wave Doppler ultrasonography? *J Clin Ultrasound* **1987**;15:121–125
5. Ohnishi K, Saito M, Nakayama T, et al. Portal venous hemodynamics in chronic liver disease: effects of posture change and exercise. *Radiology* **1985**;155:757–761
6. Foster GS, Rapoport MI, Sankary HN, Brown E, Foster P. Quantitative Doppler flowmetry of the portal vein in hepatic allografts: initial results in animal and human subjects. *Eur Radiol* **1992**;2:346–349
7. Okazaki K, Miyazaki M, Onishi S, Ito K. Effects of food intake and various extrinsic hormones on portal blood flow in patients with liver cirrhosis demonstrated by pulsed Doppler with the Octoson. *Scand J Gastroenterol* **1986**;21:1029–1038
8. Sabbá C, Ferraioli G, Genecin P, et al. Evaluation of postprandial hyperemia in superior mesenteric artery and portal vein in healthy and cirrhotic humans: an operator-blind echo-Doppler study. *Hepatology* **1991**;13:714–718
9. Bombelli L, Genitoni V, Biasi S, Materazzo C, Bonfanti G. Liver hemodynamic flow balance by image-directed Doppler ultrasound evaluation in normal subjects. *J Clin Ultrasound* **1991**;19:257–262
10. Schenck E, Nelson JA, Starr FL, Coldwell D. Animal model of portal hypertension with observations regarding the relationship between portal flow and pressure. *Invest Radiol* **1993**;28:442–445
11. Fukui H, Kashiwagi T, Kasahara A, et al. Evaluation of effective portal venous flow in chronic liver diseases using echo-Doppler flowmetry combined with per jejunal portal scintigraphy. *J Nucl Med* **1993**;34:1103–1108
12. Duerinckx AJ, Grant EG, Perrella RR, Szeto A, Tessler FN. Pulsatile portal vein in cases of congestive heart failure: correlation of duplex Doppler findings with right atrial pressures. *Radiology* **1990**;176:655–658
13. Abu-Yousef MM. Normal and respiratory variations of the hepatic and portal venous duplex Doppler waveforms with simultaneous electrocardiographic correlation. *J Ultrasound Med* **1992**;11:263–268
14. Wachsberg RH, Needleman L, Wilson DJ. Portal venous pulsatility in the absence of cardiac disease (abstr). *Radiology* **1992**;185(P):318