Hepatic Artery Thrombosis after Liver Transplantation:
Radiologic Evaluation

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Hepatic artery thrombosis after liver transplantation is a devastating event requiring emergency retransplantation in most patients. Early clinical signs are often nonspecific. Before duplex sonography (combined real-time and pulsed Doppler) capability was acquired in October 1984, 76% of all transplants in this institution referred for angiography with a clinical suspicion of hepatic artery thrombosis had patent arteries. In an effort to reduce the number of negative angiograms, CT, real-time sonography, and pulsed Doppler have been evaluated as screening examinations to determine which patients need angiography. Of 14 patients with focal inhomogeneity of the liver architecture detected by CT and/or real-time sonography, 12 (86%) had hepatic artery thrombosis, one had slow arterial flow with hepatic necrosis, and one had a biloma with a patent hepatic artery. In 29 patients undergoing duplex sonography of the hepatic artery, six (21%) had absence of a Doppler arterial pulse. All six had abnormal angiograms: Four had thrombosis, one had a significant stenosis, and one had slow flow with biopsy-proven ischemia. Of 23 patients with a Doppler pulse, two had hepatic artery thrombosis at surgery. However, real-time sonography demonstrated focal inhomogeneity in the liver in both cases. Our data demonstrate that pulsed Doppler of the hepatic artery combined with real-time sonography of the liver parenchyma currently is the optimal screening test for selecting patients who require hepatic angiography after liver transplantation. A diagnostic algorithm is provided.

Hepatic artery thrombosis after liver transplantation is a devastating event that requires immediate therapeutic intervention in most patients. The typical course is hepatic infarction followed by septic hepatic gangrene and septicemia. Emergency hepatic retransplantation is these patients' only hope for survival [1].

In 1969, Starzl [2] described two cases of fatal hepatic artery thrombosis that were not initially recognized on the basis of clinical findings or laboratory studies. He concluded, "It is likely that aortography will prove to be the only really decisive way of consistently establishing the diagnosis while there is still time to attempt repair, providing the procedure is done at the first suspicion of a vascular accident." Since then, angiography has been the definitive procedure for evaluation of the hepatic artery after liver transplantation.

From January 1981 to October 1984, before availability of duplex sonography (combined real-time and pulsed Doppler), 33 angiographic studies (18 children and 15 adults) were performed at the University Health Center of Pittsburgh for the clinical suspicion of hepatic artery thrombosis after liver transplantation. Of these, 11 (61%) of 18 children and 14 (93%) of 15 adults had patent hepatic arteries. It is clear that clinical criteria alone led us to perform an undesirably large number of normal arteriograms.

We now use three noninvasive imaging techniques to evaluate the liver after transplantation: computed tomography (CT), real-time sonography, and Doppler. We have undertaken a review to determine if these imaging methods can be used to select patients with suspected hepatic artery thrombosis who require angiography.

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Subjects and Methods

During 51 months from January 1981 to April 1985, 330 patients (147 children, 183 adults) received 435 orthotopic liver transplants at the University Health Center of Pittsburgh. Seventy-seven patients received two transplants each and 14 received three transplants each. There were 150 male and 180 female patients aged 4 months to 57 years.

TABLE 1: **Comparison of Angiography (Pre-Doppler) with Results of Computed Tomography and Real-Time Sonography**

Hepatic Artery at Angiography	Computed Tomography		Real-Time Sonography	
	Abnormal*	Normal	Abnormal*	Normal
Patent ($n = 12$)	1/7†	6/7	1/8†	7/8
Occluded ($n = 7$)	5/5	...	4/5	1/5‡
Slow Flow ($n = 1$)§	1	...	...	1

* Focal area of inhomogenerty in liver (see figs. 1 and 2).
† Same patient with biloma in liver.
‡ One study performed 3 days before angiogram, ?interval occlusion.
§ Decreased perfusion confirmed by radionuclide hepatic flow study; patient required retransplantation because of hepatic necrosis.

During this time, 42 angiographic studies (25 children and 17 adults) were performed for evaluation of hepatic artery patency. This includes the initial 33 patients evaluated up to October 1984 (pre-Doppler) and nine additional patients studied since duplex sonography became available. In all cases, angiography was done in the first 2 months after liver transplantation.

Pre-Doppler

Of 15 adult transplant patients with angiograms, five had CT only, one had real-time sonography only, and two had both CT and sonography within a few days of the angiogram. Of 18 pediatric transplant patients with angiograms, one had CT only, six had real-time sonography only, and five had both examinations within a few days of the angiogram. All CT scans were obtained on either a GE 8800 or 9800 scanner at 120 kVp and 4.8-sec (8800) or 3.0-sec (9800) scan times. The entire liver was scanned at 10- or 15-mm intervals at a slice thickness of 10 mm; when clinically permissible, a rapid intravenous drip of iodinated contrast medium was used; in children, the amount was adjusted to weight (maximum, 3 ml/kg). Real-time sonographic evaluation was performed on an Advanced

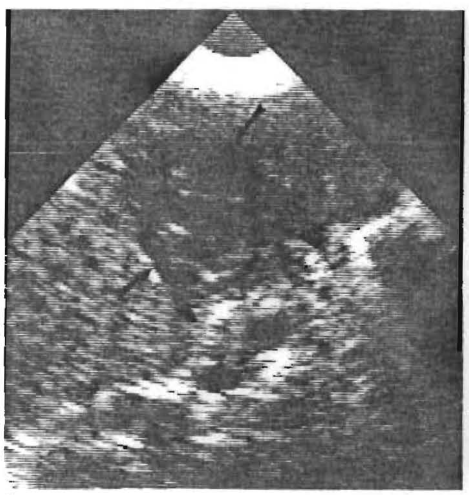
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Fig. 1.—Focal area of hepatic parenchymal inhomogeneity (*arrows*) on sonogram of 3-year-old girl with hepatic artery thrombosis. At retransplantation, pathology revealed infected infarct.

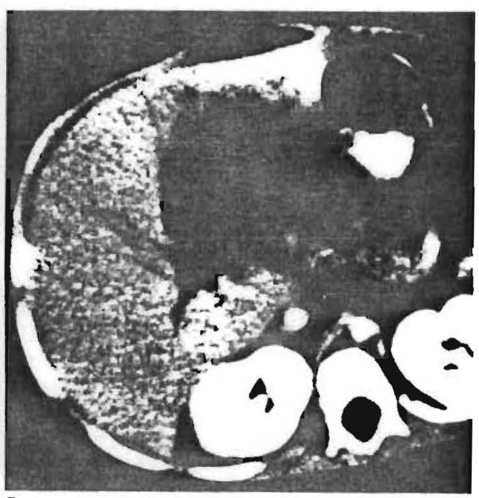
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Fig. 2.—Large area of abnormal liver parenchyma on CT scan of 2-year-old girl with hepatic artery thrombosis. At retransplantation, pathology revealed infected infarct.

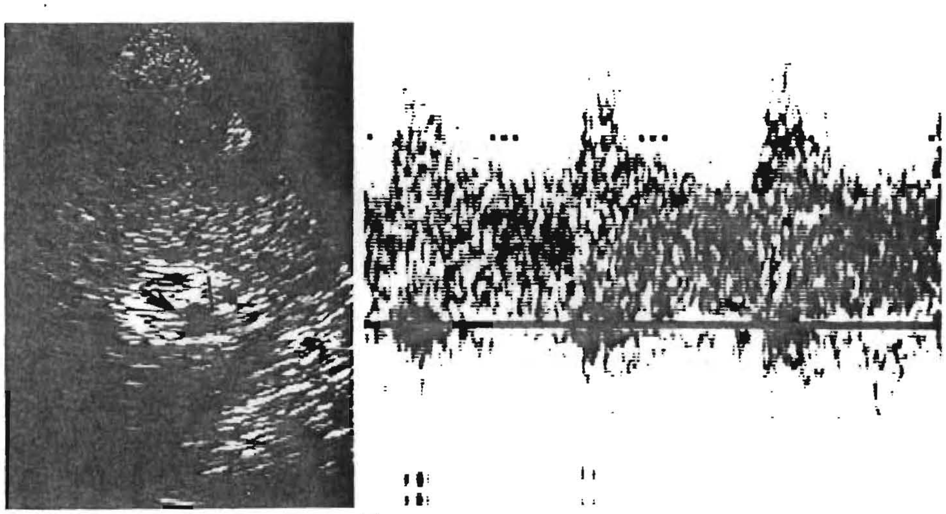
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Fig. 3.—Normal Doppler. **A**, Position of cursor line through hepatic artery (*curved arrow*) on sagittal view for Doppler waveform shown in **B**. Portal vein (*straight arrow*). **B**, Normal Doppler artery waveform.

TABLE 2: **Comparison of Pulsed Doppler and Real-Time Sonography as Individual Imaging Tests and as a Combined Test to Screen for Hepatic Artery Abnormalities after Liver Transplantation**

	Pulsed Doppler Sonography of Hepatic Artery Alone	Real-Time Sonography of Liver Parenchyma Alone	Pulsed Doppler & Real-time Sonography Combined
No. of patients	29	29	29
True positive	6*	5†	8‡
True negative	21§	21‖	21¶
False positive	0	0	0
False negative	2	3	0
Sensitivity (%)	75	62.5	100
Significance (p)**			<0.00001

* No flow in hepatic artery.
† Focal inhomogeneity in liver.
‡ Either no flow in hepatic artery or focal inhomogeneity in liver.
§ Normal hepatic artery flow.
‖ Normal liver parenchyma.
¶ Normal hepatic artery flow and normal liver parenchyma.
** Computed by Fisher exact test.

Technology Laboratories MK 300 scanner and Hewlett Packard mechanical and phased-array scanners.

Post-Doppler

Since October 1984, pulsed Doppler study of the hepatic artery combined with real-time sonography of the liver parenchyma has been performed on 29 liver transplant patients. Eighteen have been followed clinically without angiography. Nine transplant patients underwent angiography, and two had emergency surgery without angiography. Duplex examinations were performed on Hewlett Packard mechanical and phased-array scanners incorporating pulsed Doppler capabilities.

Results

CT and Real-Time Sonography (Pre-Doppler)

The combined results for adults and children, comparing angiography with CT and real-time sonography, are shown in table 1. Of the five adult transplant patients having only CT, two had focal low-density lesions in the liver. One had hepatic artery thrombosis by angiography. A donor liver was not available for retransplantation. The patient died, and hepatic infarction was present at autopsy. The second had a patent hepatic artery; however, the intrahepatic arteries were narrowed and there was decreased perfusion by angiography. Decreased perfusion was also noted by a radionuclide hepatic flow study. Retransplantation was performed, and pathologic evaluation revealed diffuse coagulation necrosis.

In all six adult transplant patients with normal CT and/or sonography of the liver, the hepatic artery was patent by angiography. One patient had a mild anastomotic stenosis.

Of the 12 children with CT and/or sonography, seven had focal hepatic masses (figs. 1 and 2), and one of the seven had a thrombosed arterial graft detected by real-time sonography. Six of the seven had hepatic artery occlusion by angiography. In one transplant patient with a CT scan showing a focal mass, the hepatic artery was patent. The fluid collection was a biloma that was successfully drained percutaneously. In each of the five children with normal CT and/or sonography of the liver, the hepatic artery was patent by angiography.

In an 11-month-old transplant patient with an occluded hepatic artery, sonography demonstrated a focal area of inhomogeneity in the liver. A donor liver was not available for retransplantation. However, liver function gradually improved. Follow-up angiography 6 weeks later showed arterial collaterals that reconstituted the intrahepatic arterial tree. CT of the liver was normal. Ensuing bile duct stricture was treated by percutaneous balloon dilatation; liver function was normal at 20 months after thrombosis of the hepatic artery.

Pulsed Doppler and Real-Time Sonography

Pulsed Doppler of the hepatic artery combined with real-time sonography of the liver parenchyma was performed on 29 transplanted livers. Of 21 cases with both normal Doppler and real-time sonographic studies, there were no cases of hepatic artery thrombosis. The value of using both tests to screen for hepatic artery abnormalities after liver transplantation is shown in table 2.

In 23 transplant patients, duplex sonography demonstrated arterial flow to the liver (fig. 3). Three had angiography, which demonstrated patent hepatic arteries in each case. In 20, angiography was not performed because of the normal Doppler study. In two of these 20, a focal abscess was identified in the liver by real-time sonography. Because of clinical deterioration, both patients required emergency retransplantation. Both had hepatic artery thrombosis. Of the remaining 18, none has developed hepatic artery thrombosis. Four have required retransplantation for reasons other than hepatic artery thrombosis. Two patients died, one from graft failure and one from cardiac arrest.

In six transplant patients, no evidence of hepatic arterial flow was identified in the liver hilum by pulsed Doppler. Angiography was abnormal in all six cases. Four had hepatic artery thrombosis. In one of the four, angiography also revealed arterial collaterals to the transplanted liver (fig. 4), but a small infarct was seen on sonography. In the fifth case, a severe stenosis was found at the hepatic artery anastomosis. In the sixth, the hepatic arterial tree was narrowed with markedly reduced washout of contrast material within the liver, suggesting slow flow. Liver biopsy showed changes consistent with ischemia.

Discussion

Crucial Role of Hepatic Artery

Hepatic artery thrombosis, a complication that usually occurs within 2 months after liver transplantation, is a major cause for retransplantation [1, 3]. This catastrophic event may result in hepatic gangrene and death unless prompt retransplantation is performed.

The consequences of hepatic arterial thrombosis in liver transplant patients are much more severe than in non-liver-

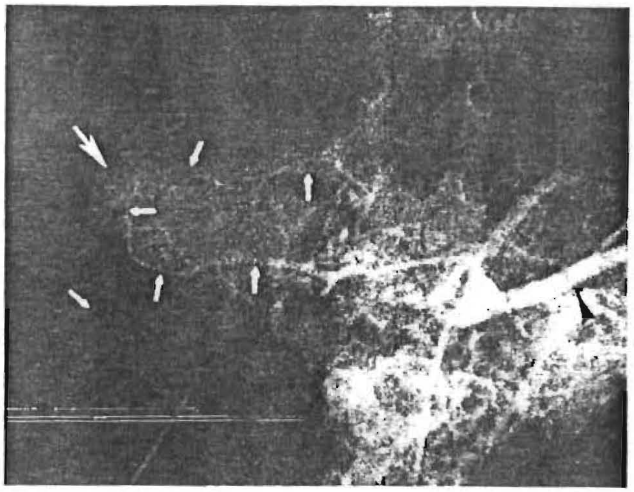

Fig. 4.—Collateral development after hepatic artery thrombosis. Late arterial film from celiac arteriogram 3 weeks after liver transplantation shows occlusion of common hepatic artery at its origin and reconstitution of intrahepatic branch arteries (*small white arrows*). Splenic artery (*large arrowhead*); left gastric artery (*small arrowhead*); portal vein (*large white arrow*).

transplant patients because, with proximal hepatic artery occlusion in a nontransplant liver, collateral arterial supply develops rapidly and prevents hepatic ischemia and infarction [4–10]. Because of the rapidity with which collateral circulation develops, liver survival probably is not solely attributable to a patent portal venous system [11, 12].

When complete dearterialization of a nontransplant liver is accomplished by embolization, septic hepatic infarction will occur [12]. In orthotopic liver transplantation, all potential collaterals have been severed. Hepatic artery occlusion after transplantation completely dearterializes the liver, and hepatic infarction is expected. A massively necrotic liver often becomes infected with Gram-negative enteric organisms in an immunosuppressed patient [13]. After hepatic artery thrombosis is diagnosed, emergency retransplantation is performed as soon as a donor liver is available.

Most transplant patients with hepatic artery thrombosis for whom a donor liver was not immediately available have died. However, four patients did survive with angiographically documented hepatic artery occlusion after transplantation. Massive hepatic infarction did not occur. Two of the four have angiographic documentation of extrahepatic arterial collaterals supplying the transplanted liver (fig. 4). Presumably the other two patients have developed collaterals. How such arterial collaterals develop communications to the transplanted liver remains unclear.

Imaging Approach

Ideally, noninvasive imaging should be able to suggest hepatic artery occlusion before the stage of hepatic gangrene. CT and real-time sonography may document focal hepatic infarction, prompting emergency angiography. Of patients with focal alterations in the liver by CT or real-time sonography, 86% (12 of 14) will have hepatic artery thrombosis. However, at this stage the patient often already has clinical toxic septicemia with marked elevations in serum transaminases.

Consequently, noninvasive evaluation of hepatic artery blood flow is needed to detect occlusion of the hepatic artery before infarction occurs. Early in our experience (1981–1983), radionuclide hepatic flow studies were occasionally done. Unfortunately, because of the difficulty in unequivocally distinguishing the hepatic artery phase from the portal vein phase, this test was not considered reliable to screen for hepatic artery occlusion. Future advances in radionuclide imaging may surmount this problem.

Intravenous digital subtraction angiography (DSA) has been used on occasion when the femoral artery could not be catheterized. As a screening test, it is too costly and lengthy; it also requires suspension of body motion, which is impossible for many sick patients. The test is also invasive, since a catheter should be placed into the right atrium for an optimal study [14]. As a definitive test, it lacks the absolute conclusiveness needed in transplants with suspected hepatic artery abnormalities. Overlying mesenteric and renal vessels could be mistaken for the vascular homografts occasionally used in transplantation. Furthermore, in patients with direct hepatic artery-hepatic artery reconstruction, the vascular anastomosis may be difficult to adequately demonstrate, occasionally requiring several views. If intravenous DSA is nondiagnostic, conventional angiography would be required for a definitive diagnosis. Contrast medium limitations could easily be exceeded, especially in children.

Dynamic intravenous CT scanning of the hepatic artery is not used as a screening test in our institution. CT is costly and motion dependent; emergency scheduling is difficult. Also, we doubt that an intravenous bolus of contrast material from a peripheral vein could adequately demonstrate the hepatic artery in most patients. Failure to image the hepatic artery on CT would necessitate angiographic evaluation, which could result in contrast medium limitations being exceeded.

Visual detection of hepatic artery pulsation with real-time sonography is feasible in children but generally not in adults. In small children, a 5-MHz transducer penetrates adequately, but in adults a lower-resolution 3-MHz transducer often is needed. Using the higher-resolution transducer, our experience in children has shown that unequivocal intrinsic pulsation of the hepatic artery equates with patency. There are two important cautions: (1) Inexperienced examiners may mistake transmitted pulsation from the aorta for intrinsic pulsation, and (2) the surgeon must inform the radiologist of unusual anastomoses, such as those involving iliac and aortic grafts, and the locations of such grafts [15], as they are exceedingly difficult to see with real-time sonography.

In our opinion, pulsed Doppler of the hepatic artery is very useful for detecting hepatic artery thrombosis before infarction occurs. In one patient, 1 day of fever prompted a Doppler study that detected no evidence of arterial flow. Angiography revealed hepatic artery occlusion, and the patient underwent retransplantation the same day. Pathology of the liver revealed no evidence of hepatic infarction, although hepatic artery thrombosis was present.

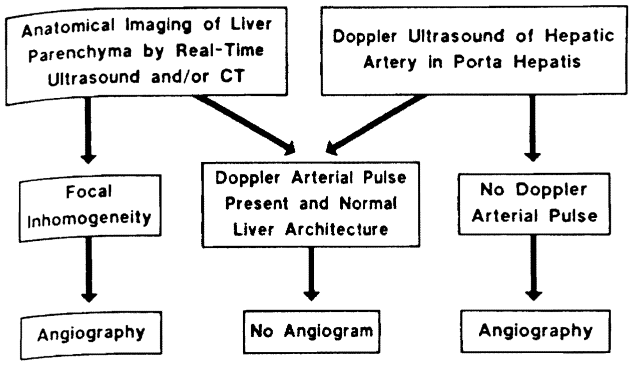

Fig. 5.—Diagnostic algorithm for radiologic evaluation of patient with suspected hepatic artery thrombosis after liver transplantation.

In two patients, the Doppler study was interpreted as demonstrating patent hepatic arteries when occlusions existed. In one, a technical error was made. In the second case, the examiner was inexperienced; Doppler skills require a significant learning period. We believe that a postoperative baseline Doppler study, combined with detailed examination of the liver architecture using real-time sonography, would be useful.

Failure to detect hepatic artery blood flow with Doppler is reliable evidence of a hepatic artery abnormality and warrants angiographic evaluation. In all six patients in whom the sonographer was confident of the absence of Doppler blood flow from a discrete hepatic artery within the porta hepatis, angiograms also were abnormal. Four had hepatic artery thrombosis; three also had focal areas of inhomogeneity in the liver by sonography. One patient with hepatic artery thrombosis had arterial collaterals keeping the liver alive (fig. 4). Of the two transplant patients without Doppler arterial flow who had angiographically patent hepatic arteries, one had a severe stenosis at the hepatic artery anastomosis and the other had markedly reduced washout of contrast material suggesting slow flow. Liver biopsy showed evidence of ischemic damage.

In summary, we believe that pulsed Doppler of the hepatic artery combined with real-time sonography of the liver parenchyma should be the initial imaging test in patients suspected of hepatic artery thrombosis after liver transplantation. CT may give complementary information in difficult or equivocal cases. In experienced hands, Doppler confirmation of hepatic arterial flow with normal liver architecture on real-time sonography obviates angiography. Absence of hepatic artery flow in the porta hepatis by Doppler or the presence of a focal area of hepatic inhomogeneity by real-time sonography or CT warrants immediate angiography (fig. 5).

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