TABLE 2. Mean scores for prognostic indices (range 0–2 [11] in 17 biopsies of 22 grafts with resistant rejection

	Mean score (±SD)	
	1982–83: (10)	1983–84: (+ cyclosporine [7])
Arteries		
Mononuclear infiltrate	1.6±0.7	1.4±0.8
Medial necrosis	0.4±0.7	0.3±0.5
Glomeruli		
Thrombosis	0.2±0.5	0
Endothelial swelling	1.1±0.6	0.9±0.7
Interstitial hemorrhage	0.7±0.3	0.8
Tubules:necrosis	0.1	0

infiltrate, and there was no difference between the prognostic scores (Table 2).

These findings suggest that acute vascular rejection not controlled by conventional immunosuppression may respond, in some cadaver graft recipients, to introduction of cyclosporine. Vascular rejection has not previously been shown to improve with cyclosporine used as a secondary immunosuppressant. Other studies supporting its efficacy have shown variable benefit, without assessment of graft histology (*9, 10, 12, 13*). This suggests that some of the advantages of cyclosporine may be achieved by those preferring to use azathioprine and prednisolone as initial immunosuppression. Cyclosporine may complement the role of conventional therapy for treatment of acute vascular rejection.

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DOPPLER ULTRASOUND AS A SCREEN FOR HEPATIC ARTERY THROMBOSIS AFTER LIVER TRANSPLANTATION

Doppler ultrasound combined with real-time ultrasound allows evaluation of both the hepatic artery and hepatic parenchyma after liver transplantation. Hepatic artery thrombosis following liver transplantation is a devastating event that may require emergency retransplantation. Unfortunately, clinical signs are often nonspecific. Results of angiographic evaluation for clinically suspected hepatic artery thrombosis have been normal in 76% of patients at our institution.

In a prospective study utilizing pulsed Doppler and real-time ultrasound, 29 transplant patients were examined. Six transplants had no hepatic artery Doppler pulse. All six had abnormal angiograms: four had hepatic artery thrombosis, one had a significant anastomotic stenosis, and one had slow flow with biopsy-proved ischemia. Of 23 patients with a Doppler pulse, two had surgically proved hepatic artery thrombosis. However, both had a focal abscess in the liver by real-time ultrasound. There were no cases of hepatic artery thrombosis in 21 patients with both a normal Doppler hepatic artery pulse and normal liver parenchyma.

Our data demonstrate that a combination of hepatic artery Doppler ultrasound and anatomical imaging of the liver currently is the optimal screening test for selecting which patients need hepatic angiography following liver transplantation.

Doppler ultrasound (pulsed Doppler imaging combined with real-time ultrasound) is an exciting new radiographic imaging modality available to physicians involved in liver and renal transplantation (*1–3*). This duplex imaging device detects blood flow via the Doppler shift from a single selected vessel localized by real-time ultrasound. Thus, noninvasive detection of arterial and venous blood flow to and from the allograft organ is now possible.

Hepatic artery thrombosis following liver transplantation usually occurs within the first three postoperative months and is a devastating event that, in the majority of patients, requires

TABLE 1. Comparison of Doppler and real-time ultrasound (RTU) findings with the incidence of hepatic artery thrombosis after liver transplantation

Ultrasound findings	Number of transplants	Hepatic artery thrombosis
Normal Doppler, normal RTU	21	None[c]
Normal Doppler, abnormal RTU[a]	2	2
Abnormal Doppler,[b] normal RTU	3	1[d]
Abnormal Doppler,[b] abnormal RTU[a]	3	3

[a] Abnormal RTU = focal hepatic abscess or infarct.
[b] Abnormal Doppler = absent hepatic artery flow.
[c] Three by angiography, eighteen by clinical follow-up.
[d] In the other two patients, both had patent but abnormal hepatic arteries. In one, a severe anastomotic stenosis was present, and the other showed markedly reduced flow with biopsy-proved ischemia.

immediate therapeutic intervention. The patient may develop fever and elevated liver enzymes, especially serum transaminases. If hepatic infarction develops, infection often supervenes. Finally, toxic septicemia results from septic hepatic gangrene (*4, 5*). Emergency hepatic retransplantation is the patient's only hope for survival (*6*).

Angiography, an invasive examination, has been the definitive procedure to evaluate patency of the hepatic artery following liver transplantation (*7*). On the basis of clinical criteria alone, one cannot effectively predict which transplant patient needs an arteriogram.

From January 1981 to October 1984, prior to the availability of Doppler ultrasound, 33 angiographic studies (18 children, 15 adults) were performed at the University Health Center of Pittsburgh for the clinical suspicion of hepatic artery thrombosis after liver transplantation. Of these, 61% (11/18) of the children and 93% (14/15) of the adults had patent hepatic arteries.

Currently, we use three noninvasive imaging modalities to evaluate the liver after transplantation: computed tomography (CT),* real-time ultrasound, and Doppler ultrasound. CT and real-time ultrasound are useful for evaluating the liver parenchyma to detect focal areas of infarction and/or abscess. However, only Doppler ultrasound can detect flow within the allograft hepatic artery.

The purpose of this communication is to demonstrate the immense value of noninvasive imaging as a screen for angiography in liver transplant patients with suspected hepatic artery thrombosis. In our institution, the allograft liver parenchyma is imaged with real-time ultrasound when the patency of hepatic artery is evaluated with pulsed Doppler ultrasound. If ultrasonic visualization of the liver parenchyma is unsatisfactory or equivocal then CT of the liver may be performed without and with intravenous contrast material.

During the 51 month period 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 patients received three transplants each. There were 150 male and 180 female patients with an age range from 4 months to 57 years.

During this time 42 angiographic studies (25 in children, 17 in adults) were performed for evaluation of hepatic artery patency after liver transplantation. This includes the initial 33 patients evaluated prior to Doppler and 9 additional patients studied since Doppler ultrasound became available. In all cases, angiography was performed within the first two months following liver transplantation.

* Abbreviation used: CT, computed tomography.

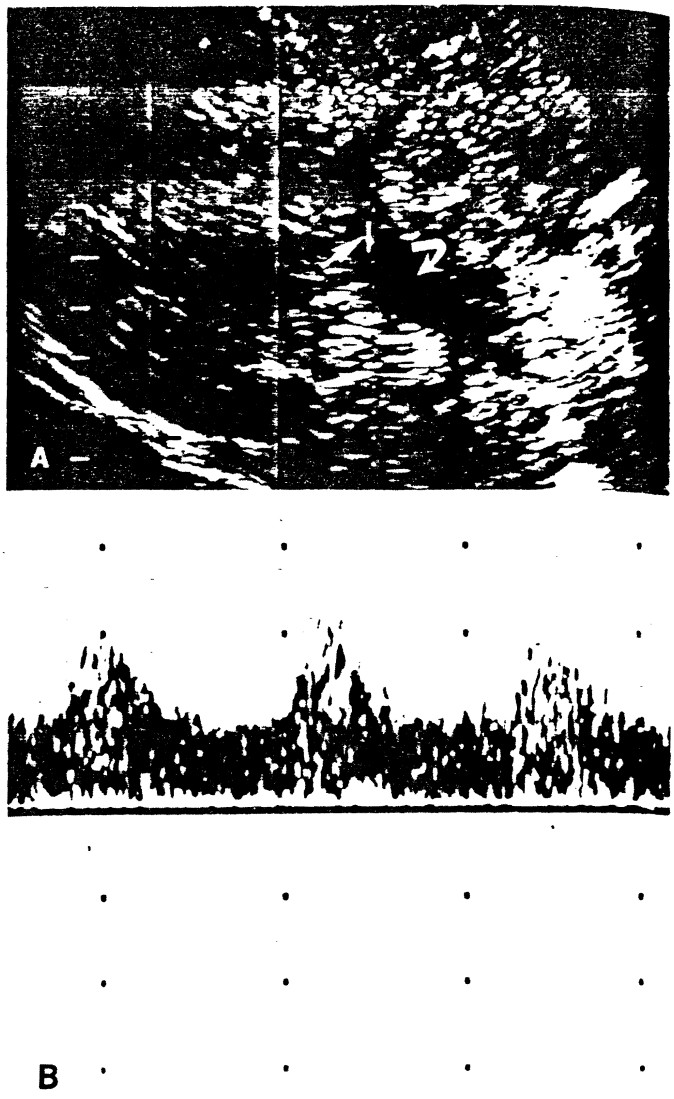

FIGURE 1. Normal Doppler ultrasound findings. (A) position of cursor line through hepatic artery (straight arrow) on sagittal view for Doppler waveform shown in (B). Portal vein (curved arrow); (B) normal Doppler hepatic artery waveform.

Between October 1984 and April 1985, pulsed Doppler and real-time ultrasound examinations have been performed on 29 liver transplants to evaluate hepatic artery patency and the liver parenchyma. Eighteen have been followed clinically without angiography. Nine transplants underwent angiography and two had emergency surgery without angiography.

Doppler and real-time ultrasound imaging were performed on 29 transplanted livers. A comparison of the Doppler and real-time ultrasound findings with the incidence of hepatic artery thrombosis is shown in Table 1. In 23 transplants, Doppler ultrasound demonstrated arterial flow to the liver (Fig. 1). Three patients underwent angiography that demonstrated patent hepatic arteries in each case. In twenty transplants, angiography was not performed, based on the normal Doppler study. In two of the twenty transplants, a focal abscess was identified in the liver by real-time ultrasound. Because of

clinical deterioration, both patients required emergency retransplantation. Both had hepatic artery thrombosis. Of the remaining eighteen, none have developed hepatic artery thrombosis. Four have required retransplantation for reasons other than hepatic artery thrombosis. Two patients died, one of graft failure and one of cardiac arrest.

In six transplants, no evidence of hepatic arterial flow was identified in the liver hilum by Doppler imaging. 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 while a small infarct was seen on ultrasound. In the fifth transplant, a severe stenosis was found at the hepatic artery anastomosis. In the sixth transplant, the hepatic arterial tree was narrowed with markedly reduced washout of contrast within the liver, suggesting slow flow. Liver biopsy showed changes consistent with ischemia.

Hepatic artery thrombosis following liver transplantation should be suspected if there is a focal hepatic abscess/infarct, or if there is absence of blood flow by Doppler examination in the hepatic artery within the porta hepatis. In the six transplants with absent Doppler findings of hepatic artery flow, all had abnormal angiograms. Of 14 patients with focal alterations (abscess/infarct) in the liver by CT and/or ultrasound from 1982 to 1985, 86% (12/14) have had hepatic artery thrombosis (*3*).

Doppler ultrasound imaging of the hepatic artery is the only currently available noninvasive method for detecting hepatic artery thrombosis before infarction occurs. In one patient, a single day of fever prompted a Doppler ultrasound examination that detected no evidence of arterial flow; angiography revealed hepatic artery occlusion. The patient was retransplanted the same day. Pathology of the liver revealed no evidence of hepatic infarction, even though hepatic artery thrombosis was present.

Doppler ultrasound imaging of the hepatic artery, together with real-time ultrasound examination of liver parenchyma, should be the initial test in patients suspected of having hepatic artery thrombosis after liver transplantation. CT may give complimentary information in difficult or equivocal cases. In experienced hands, Doppler confirmation of hepatic arterial flow with normal liver parenchyma on real-time ultrasound obviates angiography. Absence of hepatic artery flow in the porta hepatis by Doppler imaging or the presence of a focal hepatic abscess or infarct by real-time ultrasound or CT warrants immediate angiography.

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CYCLOSPORINE-ASSOCIATED MICROANGIOPATHY IN RENAL TRANSPLANTATION: A SEVERE BUT POTENTIALLY REVERSIBLE FORM OF EARLY GRAFT INJURY

Cyclosporine (CsA)* is a fungal metabolite that has been shown to have immunosuppressive properties, presumably through modulation of T lymphocyte activity (*1–3*). These properties have made CsA a clinically useful drug in suppressing rejection of transplanted bone marrow (*4*), kidney (*5–7*), liver (*7, 8*), and heart/lung (*9*). However, several important side-effects of CsA such as renal toxicity (*10*), hepatic injury (*10–12*), and hypertension (*13, 14*) have been found to interfere with the drug's usefulness. One complication that has been well documented in bone marrow transplant recipients given CsA is a condition similar to hemolytic-uremic syndrome (HUS), manifested by azotemia, anemia with red blood cell fragmentation, hypertension, thrombocytopenia, and glomerular capillary thromboses (*15–17*). This complication of CsA has not yet been reported as arising de novo in renal transplant recipients, perhaps because of the clinical and histopathological similarities to acute humoral-vascular rejection. We here describe a case of thrombotic microangiopathy and glomerulopathy in a renal allograft associated with CsA use, with rapid resolution upon withdrawal of the drug. This is a particularly important

* Abbreviations used: CsA, Cyclosporine; DVAH, Durham Veterans' Administration Hospital; HUS, hemolytic-uremic syndrome; PRA, percentage of panel-reactive antibody.