Abdom Imaging 18:61–65 (1993)

Abdominal Imaging

Hepatic Arterial Resistive Indices: Correlation with the Severity of Cirrhosis

Venetia G. Vassiliades,[1] Todd D. Ostrow,[1] Judith L. Chezmar,[1] Gary L. Hertzler,[2] and Rendon C. Nelson[2]

Department of [1] Radiology and [2] Pathology, Emory University School of Medicine, Atlanta, Georgia, USA

Abstract. Forty-three patients who were scheduled to undergo a percutaneous liver biopsy were evaluated with Doppler sonography to determine the hepatic arterial resistive index (RI). The histologic specimens were graded by a pathologist regarding cirrhosis and inflammation. The specimens demonstrated no cirrhosis in 12 of 43 (28%) patients, early cirrhosis in 10 of 43 (23%), and established cirrhosis in 21 of 43 (49%). Analysis also revealed that inflammation was absent in three of 43 (7%) patients, minimal in seven of 43 (16%), mild in 17 of 43 (40%), moderate in 13 of 43 (30%), and severe in three of 43 (7%). Hepatic artery RIs (without correction for heart rate) ranged from 0.64 ± 0.06 in patients with early cirrhosis to 0.68 ± 0.09 in patients with severe inflammation. There was no significant correlation between the degree of cirrhosis and/or inflammation and hepatic artery RI (with or without correction for heart rate). We conclude that Doppler determination of hepatic artery RIs is not a reliable method of predicting the severity of hepatic cirrhosis and/or inflammation.

Key words: Liver, duplex sonography—Cirrhosis, diagnosis—Hepatic artery, resistive index.

Hepatic cirrhosis is a relatively common clinical entity worldwide and its incidence in Western countries is increasing. Although many of the clinical and radiological findings are classical, percutaneous biopsy is often necessary to establish the diagnosis and severity of cirrhosis. Imaging studies are therefore used to monitor progression and complications of the disease process, as well as to determine the feasibility of surgical intervention.

Duplex Doppler sonography has proved valuable in the evaluation of vascular flow in many parts of the body. Multiple studies have shown, in particular, its usefulness in the assessment of both native and transplanted abdominal organs [1–9]. Normally, the arterial inflow to these organs, whether native or transplanted, has low impedance with the Doppler tracing demonstrating flow throughout diastole. However, many pathologic entities, such as acute vascular rejection (AVR) in a renal allograft, increase vascular impedance resulting in a Doppler tracing with high velocity spikes during systole and diminished flow during diastole. Vascular impedance can be quantified by calculating the resistive index (RI). In a study examining duplex Doppler ultrasound of the porta hepatis, Alpern et al. reported that hepatic artery RI was specific for portal hypertension when greater than 0.78, but it was not sensitive [10]. We wondered if there was similar correlation between the degree of cirrhosis and/or inflammation and hepatic arterial RI.

The purpose of this study was to determine the ability of duplex Doppler sonography of the hepatic artery to predict noninvasively the severity of cirrhosis. Because hepatic inflammation often accompanies cirrhosis, we also were interested in determining any relationship between the degree of inflammation and the image findings.

Materials and Methods

In October 1989, we began routinely measuring hepatic arterial RI on all patients who presented for hepatic sonographic examination prior to percutaneous liver biopsy. Liver biopsy was deemed

Address offprint requests to: Rendon C. Nelson, M.D., Department of Radiology, Emory University Hospital, 1364 Clifton Road, N.E., Atlanta, GA 30322, USA

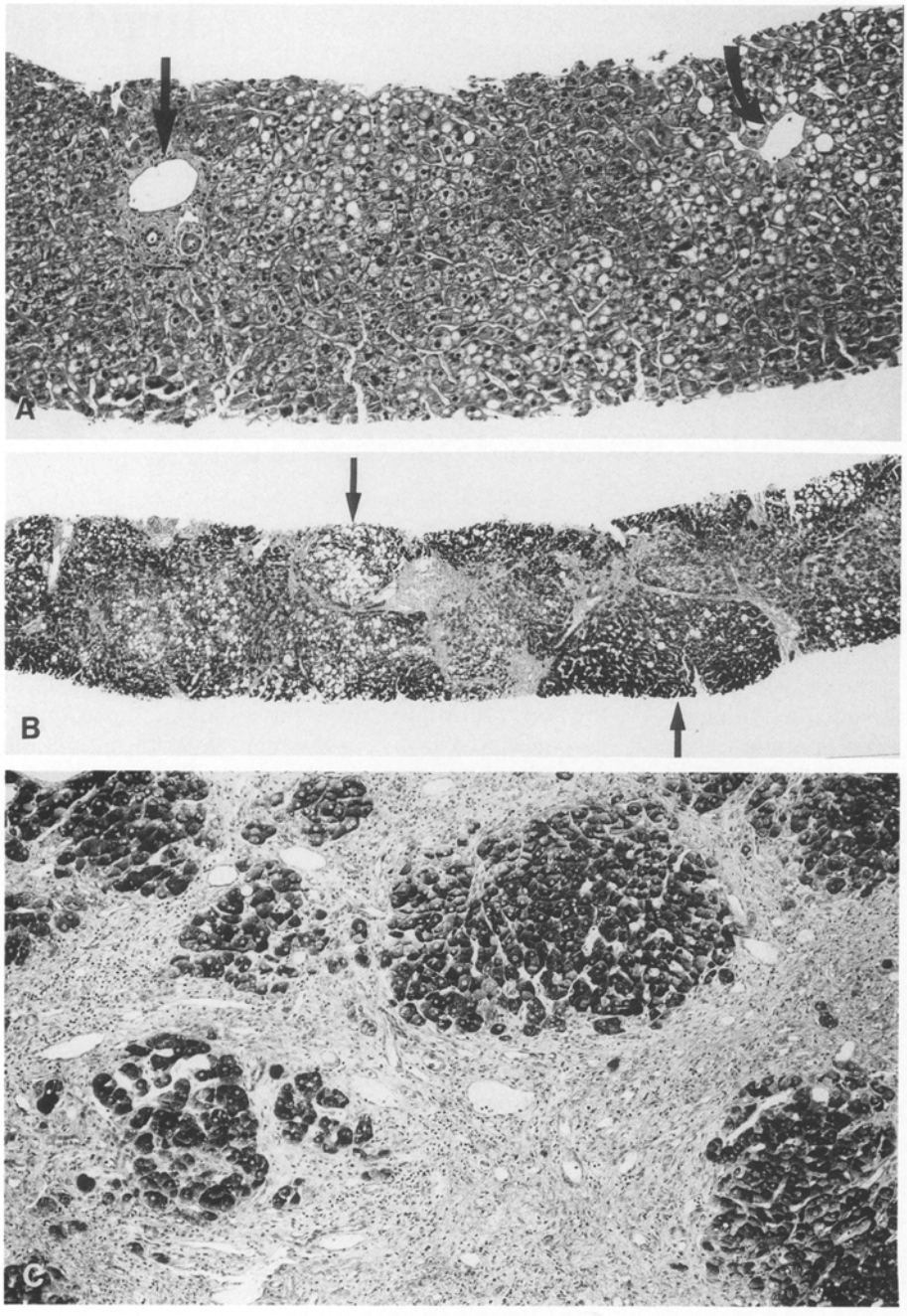

Fig. 1. A Normal hepatic architecture. Orderly hepatocytic plates lie between a normal portal tract (*straight arrow*) and a terminal hepatic vein (*curved arrow*) (hematoxylin & eosin; original magnification, ×100). **B** Early cirrhosis. Pale bands of bridging fibrosis surround regenerative nodules (*arrows*) while other areas remain architecturally intact (periodic acid-Schiff; original magnification, ×80). **C** Established cirrhosis. Small nodules of dark staining hepatocytes are ringed by broad fibrotic bands (periodic acid-Schiff; original magnification, ×100).

necessary in these patients because of abnormal historical, physical, or laboratory data indicating liver disease. By November 1990, 43 patients had undergone a prebiopsy hepatic sonogram, including hepatic arterial RI measurement. There were 23 men and 20 women ranging in age from 15–77 years (mean 47 years). The median time interval between the Doppler sonogram and percutaneous biopsy was 1 day, with a range of 0–64 days. In 21 of 43 (49%) patients, the biopsy was performed on the same day as the Doppler examination and in 35 of 43 (81%), it was performed within 3 days.

Duplex Doppler sonography was performed on an Acuson-128 computed sonography unit (Mountain View, CA, USA) using either a 2.5- or 3.5-MHz sector (phased-array) transducer. A high-pass filter setting of 125 Hz was used to minimize arterial wall motion. Three nonangle corrected Doppler tracings from the hepatic artery were obtained at the level of the porta hepatis as the vessel crosses the main portal vein anteriorly. A Doppler tracing could be obtained from this region even when the hepatic artery was not completely visualized. Because the hepatic artery was not routinely visualized for diameter determination, arterial flow measurements were not calculated. For each tracing, the transducer was positioned to optimize the Doppler measurement. The RI was calculated using the following formula:

Resistive index (RI) = (Peak systolic frequency shift − end-diastolic frequency shift)/Peak systolic frequency shift

Table 1. Comparison of hepatic artery RI with histology

	Cirrhosis		
	None (N = 12)	Early (N = 10)	Established (N = 21)
RI	0.66 ± 0.09	0.64 ± 0.06	0.67 ± 0.07
cRI	0.63 ± 0.07	0.62 ± 0.06	0.66 ± 0.08

	Inflammation				
	None (N = 3)	Minimal (N = 7)	Mild (N = 17)	Moderate (N = 13)	Severe (N = 3)
RI	0.65 ± 0.10	0.67 ± 0.06	0.66 ± 0.08	0.65 ± 0.07	0.68 ± 0.09
cRI	0.59 ± 0.10	0.64 ± 0.03	0.65 ± 0.09	0.64 ± 0.07	0.66 ± 0.06

	Score			
	0–1 (N = 9)	1.5–2 (N = 7)	2.5–3 (N = 20)	3.5–4 (N = 7)
RI	0.69 ± 0.08	0.60 ± 0.05	0.66 ± 0.08	0.65 ± 0.07
cRI	0.64 ± 0.08	0.60 ± 0.04	0.65 ± 0.09	0.64 ± 0.07

RI, resistive index; cRI corrected RI.

The mean RI was determined and adjusted for heart rate using the following formula [11]:

$$Corrected\ RI\ (cRI) = Observed\ RI - 0.0026\ (80 - heart\ rate)$$

Percutaneous liver biopsies were performed in the sonography department by a radiologist using an 18-gauge automated cutting needle (Biopty instrument, distributed by Bard Urological Division, Covington, GA, USA; manufactured by Radiplast, Uppsala, Sweden) or at the bedside by a gastroenterologist using a 14-gauge Tru-Cut needle (Baxter Healthcare Co., Malencia, CA, USA). A right lateral abdominal wall approach was used in all patients.

Histologic sections of liver needle biopsy specimens were examined by a single pathologist who was blinded to the imaging and laboratory findings. Specimens were categorized as showing no cirrhosis, early cirrhosis, or established cirrhosis (Fig. 1). In the absence of cirrhosis, biopsy tissue had maintained acinar architecture throughout. Early cirrhosis was characterized by bridging fibrosis and some regenerative nodules but preservation of acinar structures in portions of the specimen. Established cirrhosis was defined as complete alteration of normal architecture by bridging bands of mature collagen surrounding regenerative hepatocytic nodules. The degree of inflammation was also recorded semiquantitatively as absent, minimal, mild, moderate, or severe according to the density of leukocytic infiltration.

To assess the combined effect of cirrhosis and inflammation on imaging results, a scoring system was developed by assigning each grade of cirrhosis and each level of inflammation a numerical value ranging from 0–2 (0, 1, 2) for cirrhosis and from 0–2 (0, 0.5, 1, 1.5, 2) for inflammation. By adding these two numbers, the resultant score ranged from 0 (no cirrhosis, no inflammation) to 4 (established cirrhosis, severe inflammation).

The results from the liver biopsies were then compared with the Doppler arterial RI. One-way analysis of variance with the Turkey pairwise comparison were performed to determine significance.

Results

In all cases, the liver biopsy specimen was deemed adequate for evaluation. Histologic analysis revealed no evidence of cirrhosis in 12 of 43 (28%) patients, early cirrhosis in 10 of 43 (23%), and established cirrhosis in 21 of 43 (49%). Histologic analysis reported no inflammation in three of 43 (7%), minimal inflammation in seven of 43 (16%), mild inflammation in 17 of 43 (40%), moderate inflammation in 13 of 43 (30%), and severe inflammation in three of 43 (7%) patients (Fig. 1A–C). The mean RI determined for each of these histologic groups (cirrhosis and inflammation) is shown in Table 1. Statistical analysis revealed no correlation between the degree of cirrhosis and/or inflammation and hepatic artery RI (with or without correction for heart rate) ($p > 0.05$). Tabulation of the histologic scores showed a score of 0–1 in nine of 43 (21%) patients, 1.5–2 in seven of 43 (16%), 2.5–3 in 20 of 43 (47%), and 3.5–4 in seven of 43 (16%). There was no significant correlation between histologic score and RI ($p > 0.05$) (Figs. 2–4).

Discussion

Cirrhosis is conventionally defined as a diffuse hepatic process characterized by widespread fibrosis and nodular parenchyma [12]. These changes are felt by some to be due to abnormal reconstruction of

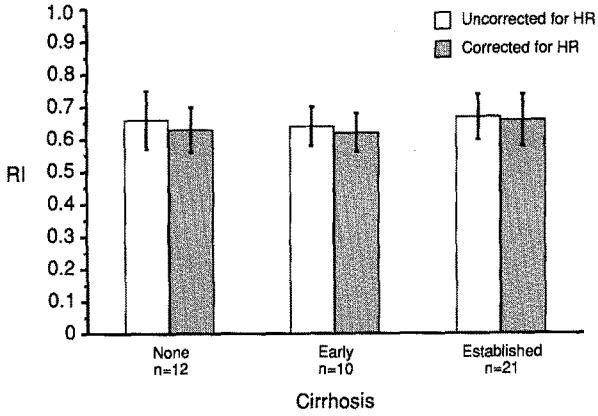

Fig. 2. Hepatic arterial RIs for each histologic grade of cirrhosis. The difference among the three groups was not statistically significant.

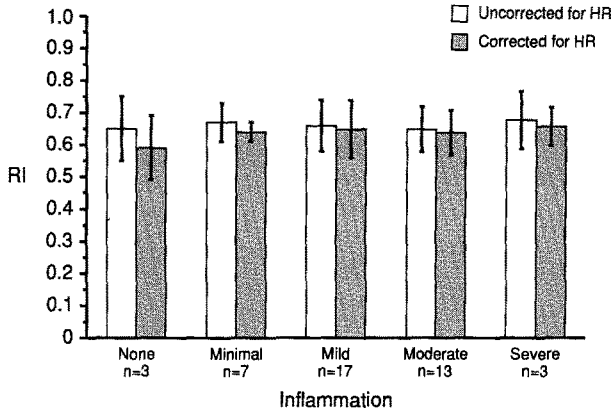

Fig. 3. Hepatic arterial RIs for each histologic level of inflammation. Patients with no inflammation (N = 3) show RI values which are slightly less than the other groups but the difference is not statistically significant.

preexisting lobular architecture [13]. As a result, there is often alteration in hepatic circulation. Furthermore, drainage from the liver may be impaired leading to portal hypertension. Several factors contribute to this outflow block including venous compression by regenerative nodules, perisinusoidal fibrosis, arteriovenous anastomoses, and portal tract scarring. Other hemodynamic changes include diversion of antegrade flow from the liver by portosystemic collaterals, diversion of hepatic parenchymal flow by anastomoses between hepatic artery and either portal venous branches or hepatic venous tributories, and decreased efficiency of the microcirculation [13]. Because of these numerous circulatory abnormalities we postulated that the peripheral vascular resistance of the liver may be affected in cirrhosis.

Inflammation is often found in cirrhosis and may be (a) a reaction to hepatocyte injury, (b) an immunologic process, and/or (c) stimulated by the offending agent [13]. The location of the inflammation determines its prognosis. For example, portal triad inflammation rarely progresses, whereas periportal inflammation may lead to necrosis. Because of the edema associated with inflammation, the peripheral vascular resistance might be expected to rise.

Previous work has shown that the RI can be used to estimate peripheral vascular resistance [2, 14]. Thus, we chose to compare the hepatic arterial RI as measured by Doppler sonography with the degree of cirrhosis and/or inflammation determined histologically. Although normal hepatic arterial RIs are low (<0.70) but not strictly defined, we hoped to detect a trend indicating elevated peripheral resistance with worsening cirrhosis and/or inflammation.

In renal transplants, previous investigators have demonstrated a correlation between high RIs in main and interlobar arteries and acute vascular rejection. This has been explained by an elevated peripheral vascular resistance [2, 14]. Other work has shown that the elevated RI, although indicative of pathology, is not specific for rejection and can be found in acute tubular necrosis, cyclosporine toxicity, and hydronephrosis [1, 3–5]. Even the weight of the transducer can affect the RI [14]. In liver transplants, attempts have also been made to correlate hepatic arterial RI with rejection, although both prospective and retrospective studies have shown no such correlation [6, 7]. One explanation is that hepatic transplant rejection is primarily a cell-mediated event as opposed to the acute vascular rejection often documented in renal allografts. Thus, although some evidence of vascular rejection can be found in the medium-sized hilar portal vessels, the peripheral portal branches are typically uninvolved.

In this study we were unable to demonstrate any correlation between the RI value and the degree of hepatic pathology. Specifically, there was no evidence of increasing peripheral vascular resistance (high RI) with worsening cirrhosis and/or inflammation. This may reflect the presence of abundant collateral channels which form in the septal tissue of cirrhotic livers. These channels are sinusoids which form out of necrotic hepatic tissue and communicate with the intrahepatic portal veins, hepatic arteries, and hepatic veins [13]. With time, the sinusoids dilate shunting blood from the afferent to the efferent system bypassing the capillary bed. In addition, pathologic studies of cirrhotic livers have revealed a striking proliferation of small arteries and an increase in peripheral arterial beds [13]. Thus, one might expect the peripheral resistance of the arterial system to actually be decreased and arterial inflow increased. Takahaski et al. studied the arterial circu-

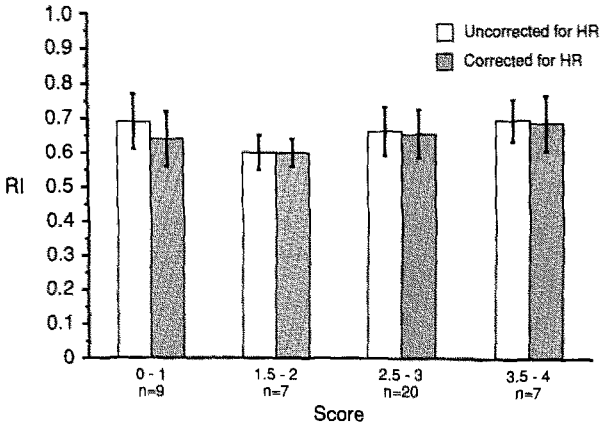

Fig. 4. Hepatic arterial RIs for patients grouped by score reflecting combined effect of cirrhosis and inflammation. The RI values for the patients with less disease (score 0–1) was not significantly different from those with severe disease (score 3.5–4).

lation in hepatic cirrhosis and demonstrated that the main arterial flow in cirrhotic livers was significantly greater than that in the normal liver [15]. It has also been demonstrated with sonography, that the diameter of the hepatic artery and its intrahepatic branches increase in the setting of cirrhosis [8, 9]. However, in our study, there was no evidence of either increased or decreased RI values with worsening cirrhosis and/or inflammation.

In conclusion, although hepatic Doppler sonography can provide qualitative information regarding hepatic cirrhosis and inflammation, the quantitative data derived from these studies does not aid in the prediction of disease severity. Perhaps with further refinement in abdominal Doppler imaging, these techniques will become more useful and accurate in the delivery of quantitative diagnostic information.

Acknowledgments. We thank Carol O'Connor for preparing the manuscript and Bobbie Hollis and Myra Taylor for technological assistance.

References

1. Drake DG, Day DL, Letourneau JG, et al. Dopper evaluation of renal transplants in children: a prospective analysis with histopathologic correlation. *AJR* 1990;154:785–787
2. Rifkin MD, Needleman L, Pasto ME, et al. Evaluation of renal transplant rejection by duplex Doppler examination: value of the resistive index. *AJR* 1987;148:759–762
3. Genkins SM, Sanfilippo FP, Carroll BA. Duplex Doppler sonography of renal transplants: lack of sensitivity and specificity in establishing pathologic diagnosis. *AJR* 1989;152:535–539
4. Allen KS, Jorkasky DK, Arger PH, et al. Renal allografts: prospective analysis of Doppler sonography. *Radiology* 1988;169:371–376
5. Platt JF, Rubin JM, Ellis JH, DiPietro M. Duplex Doppler US of the kidney: differentiation of obstructive from nonobstructive dilatation. *Radiology* 1989;171:515–517
6. Longley DG, Skolnick ML, Sheahan DG. Acute allograft rejection in liver transplant recipients: lack of correlation with loss of hepatic artery diastolic flow. *Radiology* 1988;169:417–420
7. Marder DM, DeMarino GB, Sumkin JH, Sheahan DG. Liver transplant rejection: value of the resistive index in Doppler US of hepatic arteries. *Radiology* 1989;173:127–129
8. Becker CD, Cooperberg PL. Sonography of the hepatic vascular system. *AJR* 1988;150:999–1005
9. Will UV, Teele RL. Hepatic arteries and the parallel-channel sign. *JCU* 1979;7:125–127
10. Alpern MB, Rubin JM, Williams DM, Capele P. Porta hepatis: duplex Doppler US with angiographic correlation. *Radiology* 1987;162:53–56
11. Mostbeck GH, Gossinger HD, Mallek R, Siostrzonek P, Schneider B, Tscholakoff D. Effect of heart rate on Doppler measurements of resistive index in renal arteries. *Radiology* 1990; 175:511–513
12. Anthony P, Ishak KG, Nayak NC, Poulsen HE, Scheuer PJ, Sobin LH. The morphology of cirrhosis. *J Clin Pathol* 1978;31:395–414
13. Popper H. Pathologic aspects of cirrhosis. *Am J Pathol* 1977;87:228–264
14. Pozniak MA, Kelcz F, Stratta RJ, Oberley TD. Extraneous factors affecting resistive index. *Invest Radiol* 1988;23:899–904
15. Takahashi T, Tezuka F. Hepatic arteries and arterial circulation in liver cirrhosis. *Tohoka J Exp Med* 1974;113:113–128

Received: February 11, 1992; accepted: April 2, 1992