Does the right inferior phrenic artery have a supplying role in liver cirrhosis without hepatocellular carcinoma? A 64-slice CT study

Nilgün Işıksalan Özbülbül, Mehmet Yurdakul, Muharrem Tola

PURPOSE
To investigate whether the right inferior phrenic artery (RIPA) has a role in supplying the liver in cirrhotic patients without hepatocellular carcinoma (HCC) using 64-slice computed tomography (CT).

MATERIALS AND METHODS
Fifty-eight consecutive cirrhotic patients were categorized into two groups in regard to the absence (group 1, n=33) or presence of portal vein thrombosis (group 2, n=25). In addition, 35 patients without liver disease were included as a control group (group 0). The diameters of the RIPA and left inferior phrenic artery (LIPA) were measured in the ascending portion of these vessels using arterial-phase CT images. The discrepancy between the diameters of the RIPA and LIPA were calculated. The diameters of the RIPA and LIPA and the discrepancy between the diameters of the RIPA and LIPA were then compared.

RESULTS
The characteristics of all RIPA and LIPA were visualized. The diameter of the LIPA among the three groups was not significantly different ($P = 0.363$). The mean diameters of the LIPA were 1.8±0.19, 1.8±0.22, and 1.7±0.38 mm for groups 0, 1, and 2, respectively. The diameter of the RIPA was significantly greater (2.1±0.54 mm) in groups 1 and 2 (1.9±0.19 mm) than in group 0 (1.8±0.18 mm). There was significantly difference between groups 0 and 2 ($P = 0.003$), and groups 1 and 2 ($P = 0.01$) with regard to the discrepancy of the diameters of RIPA and LIPA.

CONCLUSION
The RIPA may contribute to the blood supply of the liver in cirrhotic patients, especially those with portal venous thrombosis.

Key words: • liver • tomography, X-ray computed • cirrhosis • inferior phrenic artery

From the Department of Radiology (N.I.Ö. ✉ *nilgunisiksalan@ yahoo.com*), Türkiye Yüksek İhtisas Hospital, Ankara, Turkey.

The right inferior phrenic artery (RIPA) is the most common extrahepatic collateral vessel that supplies peripherally-located hepatocellular carcinoma (HCC), even when the hepatic artery is patent (1–5). However, the RIPA is one of the extrahepatic arteries that provides blood supply to the liver in hepatic arterial ligation or occlusion (2, 4). In cirrhotic patients without HCC, there is a restriction of liver blood supply. Moreover, portal venous thrombosis (PVT), which is often encountered in these patients, aggravates the restriction of liver blood supply that already exists (6, 7). However, to our knowledge, the role of the RIPA on cirrhotic livers without HCC is still unexplored. Therefore, we investigated whether the RIPA has a role in supplying the liver in cirrhotic patients without HCC using 64-slice computed tomography (CT).

Materials and methods

An institutional review board approved this study and determined that informed consent was not required. Between January and December 2009, we prospectively evaluated patients who underwent triphasic liver computed tomography (CT) using a 64-slice CT scanner (Aquillion 64; Toshiba Medical Systems, Tokyo, Japan) to evaluate the liver in patients with cirrhosis. The scanning protocol consists of an initial, unenhanced study to identify liver location with 5 mm collimation. Contrast material was then intravenously injected (110 mL nonionic contrast material, with 350 mgI/mL at a rate of 5 mL/s) through a 18 G cannula placed into the right median antecubital vein using a double-head power injector, followed by an injection of 40 mL of normal saline at 5 mL/s. Arterial-phase imaging was initiated within 5 s after enhancement of the descending aorta to 150 HU, as measured by a bolus-tracking technique (SureStart, Toshiba Medical Systems) with 0.5 mm collimation. This was followed by portal (65 s delay) and equilibrium phase (120 s delay) imaging. CT scans were performed at 120 kV, 180–340 mAs, and 0.5 mm collimation. Acquired images were transferred to a workstation (Vitrea, version 3.2, Vital Images, Minneapolis, USA).

A total of 58 patients with liver cirrhosis (29 men, 29 women; mean age, 51.44±11.62 years; age range, 31–81 years) were enrolled in the study. None of the patients included in the study had clinically or laboratory documented benign/malignant or metastatic hepatic neoplasm, such as HCC, at the time of the CT scan. Also, no patients showed signs of hepatic vascular disease on the CT scan. None of the patients had a history of pleural or diaphragmatic disease. The diagnosis of cirrhosis was made by histopathologic examination in 22 (37.9%) patients. In the remaining 62.1% cases, the diagnosis was made by ultrasonography (US), upper endoscopic findings, and laboratory abnormalities. The cause of the cirrhosis was viral hepatitis in 43 patients, cryptogenic in 10 patients, primary

biliary cirrhosis in 1 patient, Wilson disease in one patient, and alcohol use in three patients. Eighteen patients had Child-Pugh class A, and 24 patients had Child-Pugh class B. Finally, 16 patients had Child-Pugh class C.

All patients were divided into two groups with regard to the presence or absence of PVT according to the CT findings. The presence of PVT was noted if complete thrombosis of the portal vein was identified on the portal phase of the axial CT images. The partial and/or acute portal vein thrombus was excluded.

Additionally, the control group (group 0) was added. The control group consisted of 35 patients (21 men and 14 women; age range, 20–77 years; mean age, 52.6±14.8 years) who underwent abdominal CT scans for indications other than liver disease and did not have benign or malign neoplasm or hepatic vascular disease.

The RIPA and left IPA (LIPA) were recognized by following the possible origin sites on the arterial phase axial CT maximum intensity projection images in all patients. The origin and the type of origin of the RIPA and LIPA were recorded. The measurements of vessel lumens were performed with electronic calipers within the ascending portion by an experienced abdominal radiologist on the MIP images, which were magnified three times.

Statistical analysis

Statistical analyses were performed with commercially available statistical software (SPSS, version 11.5 for Windows; SPSS Inc., Chicago, USA). Quantitative variables were expressed as mean values and standard deviations. The difference between the three groups with regard to age was investigated using a one-way variance analysis (ANOVA). The difference among the three groups with regard to sex was investigated using a chi-square test. The discrepancy between the diameters of the RIPA and LIPA was calculated in all patients. The difference in the diameter of the RIPA across the three groups was assessed using the Kruskal-Wallis test because of the inhomogeneity of variance. We also investigated whether the differences in the diameter of the RIPA and LIPA changed across the three groups when using multiple comparison tests. Statistical significance was set at $P < 0.05$.

Results

In this study, the origins of all IPAs were clearly visualized. The RIPA and LIPA origins are summarized in Table 1. There were no significant differences across the three groups with regard to age and sex ($P = 0.56$, and $P = 0.69$, respectively).

The characteristics of the groups were shown in Table 2. There was significant difference between the three groups with regard to the diameter of the RIPA ($P = 0.013$). Further, there was significant difference between groups 0 and 1 ($P = 0.032$) and groups 0 and 2 ($P = 0.005$) in regard to the diameter of the RIPA (Fig. 1a). There was no significance difference observed between groups 1 and 2 in regard to the diameter of the RIPA ($P = 0.397$). There was no difference across the three groups in regard to the diameter of the LIPA ($P = 0.363$) (Fig. 1b). We found significant differences across the three groups in regard to the discrepancy between diameters of the RIPA versus the LIPA ($P = 0.007$) (Fig 1c, Fig. 2). There were significant differences between groups 0 and 2 ($P = 0.003$) and groups 1 and 2 ($P = 0.010$) in regard to the diameters of the RIPA and LIPA. There were no significance differences observed between groups 0 and 1 in regard to the discrepancy between the diameters of the RIPA versus the LIPA ($P = 0.664$).

Discussion

The liver is a highly vascularized organ and receives 25% of all cardiac output (8). Also, it has a dual blood supply comprised of the portal vein (80%) and hepatic artery (20%) (9, 10). There is some communication between the portal vein and the hepatic artery, including trans-sinusoidal, transvasal, and transplexal routes (8, 10, 11). If portal

Table 1. Origin sites and types of different groups of patients

| Type of origin	Origin	Group 0 (n)	Group 1 (n)	Group 2 (n)
Common trunk of the RIPA and LIPA	Aorta	9	5	2
	Celiac artery	7	4	7
Separate origination of the RIPA	Aorta	5	11	8
	Celiac artery	10	11	5
	Right RA	3	2	3
Separate origination of the LIPA	Aorta	4	10	7
	Celiac artery	14	13	7
	RIPA	0	1	2

RIPA, right inferior phrenic artery; LIPA, left inferior phrenic artery; RA, renal artery.

Table 2. Characteristics of the groups

	Group 0 (n=35)	Group 1 (n=33)	Group 2 (n=25)	P
Age	52.6	52.9	49.9	0.557
Sex				
Female (n)	14	16	13	0.690
Male (n)	21	17	12	
Diameter of RIPA (mm)	1.83±0.17	1.95±0.19	2.2±0.54	0.013
Diameter of LIPA (mm)	1.71±0.19	1.82±0.22	1.81±0.39	0.363
Discrepancy of RIPA and LIPA (mm)	0.11±0.16	0.13±0.13	0.36±0.38	0.007

Data expressed as mean±standard deviation (SD).
RIPA, right inferior phrenic artery; LIPA, left inferior phrenic artery.

a

b

c
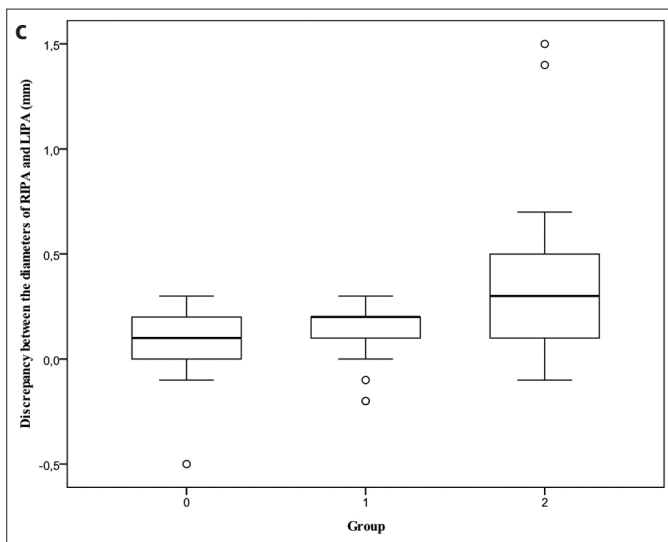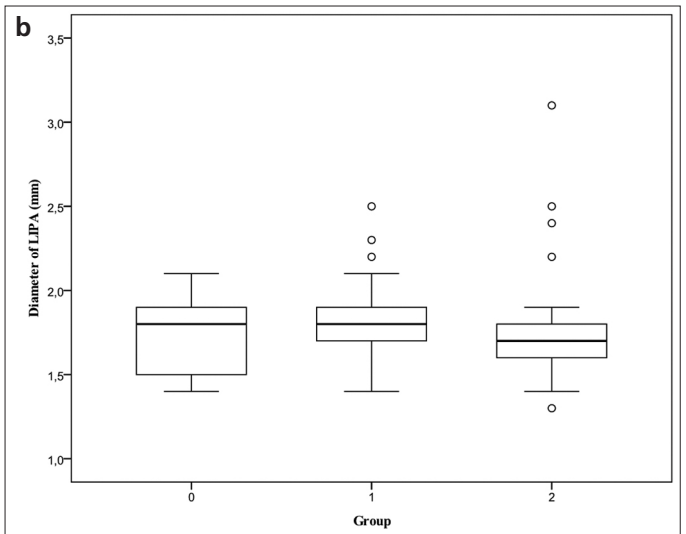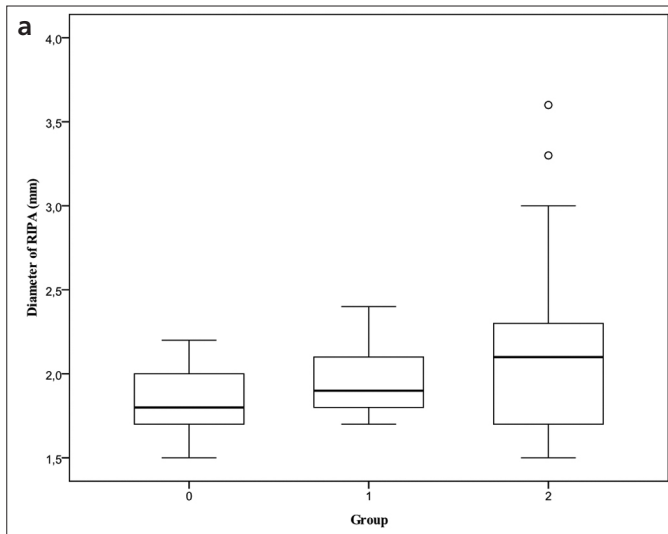
Figure 1. a–c. Box plots for the diameter of the RIPA **(a)**, the LIPA **(b)**, and the discrepancy between the diameters of the RIPA and LIPA **(c)** among the three groups. RIPA, right inferior phrenic artery; LIPA, left inferior phrenic artery. ○ shows the extremes of the data.
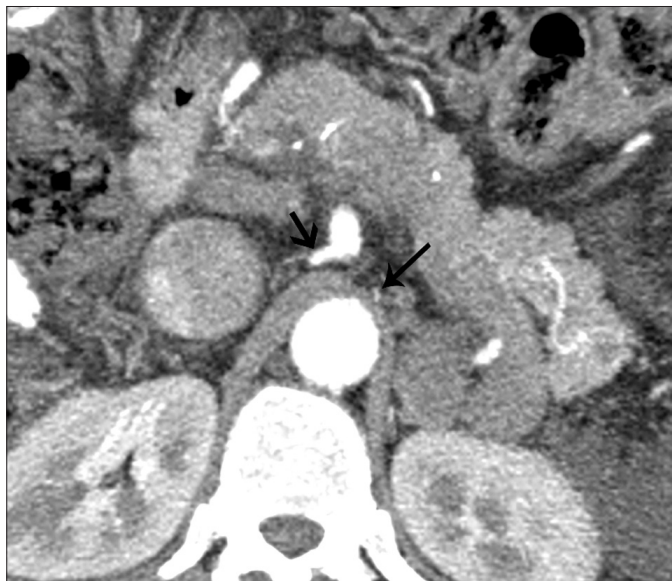
Figure 2. A 55-year-old man with cryptogenic cirrhosis and portal vein thrombosis. Arterial phase MDCT scan with thin-slab maximum-intensity projection on the axial plane at the level of the celiac artery show that the discrepancy of the diameters between the RIPA (2.9 mm) and LIPA (1.4 mm). RIPA *(thick arrow)* originates from the celiac trunk, and the LIPA *(thin arrow)* originates from the aorta (not shown). RIPA, right inferior phrenic artery; LIPA, left inferior phrenic artery.

blood flow is decreased, the hepatic artery blood flow increases to preserve the total hepatic blood flow. However, Ternberg and Butcher showed that the portal vein flow declined when the hepatic artery flow decreased (12, 13).

The portal venous stasis occurs in cirrhosis. The decreased and reversed portal flow due to liver architectural derangement is the most important mechanism associated with non-malignant PVT. Thrombotic tendency is based on endothelial injury due to elevated portal pressure, coagulation abnormalities, and increased intrahepatic resistance to portal flow (14–16).

In response to PVT, portoportal and portosystemic collateral veins develop within a few days to compensate for the decreased portal blood flow (6, 7). The portal cavernoma is a typical feature of chronic PVT, which consists of a network of collateral vessel around the portal vein. The central portion of the liver is preserved via collateral blood flow. However, collateral blood flow is insufficient to preserve the blood flow to the subcapsular regions of the liver (15).

In this study, we compared two groups of patients who did and did not have PVT to clarify the role of the RIPA on the blood supply to the liver using 64-slice CT scans. Thinner collimation with multidetector-row (MDCT) provided detailed and multiplanar images about small vessels. Inferior phrenic arteries (IPAs) were clearly visualized in

patients with and without liver disease using MDCT (17).

IPAs are paired small vessels that supply most of the diaphragm, including the area in contact with the bare area of the liver, and the anastomose with its adjacent arteries, including the internal mammary, intercostal, and adrenal arteries (1–4, 18). The RIPA has branches to the esophagus, stomach, and retroperitoneum. The anterior branch of the LIPA supplies the dome of the left diaphragm and esophagogastric junction. The RIPA and LIPA are usually thought to be symmetrical in size without pathologic conditions (2). However, our results did not support these findings; we found RIPA predominance in the control group.

Dynamic CT imaging has been used to demonstrate the presence of parasitic arteries supplying HCCs from the RIPA via measurement of this vessel lumen (4). In this study, since we aimed to investigate whether the RIPA supplies blood to the liver in cirrhosis using MDCT, we used the diameter of the RIPA and the discrepancy between the diameters of the RIPA and LIPA to analyze the RIPA's relationship with blood supply to the liver.

In patients with HCC, extrahepatic collateral arteries develop without occlusion of the hepatic arteries. The RIPA can become a parasitic artery if the HCC is peripherally located in the liver. It is important to recognize that these extrahepatic collaterals are important for effective transarterial catheter chemoembolization. Gokan et al. (2) suggested that significant asymmetric dilatation of RIPA is a predictor of parasitic supply. They found in their study that the mean diameter of the RIPA was 3.3 mm (range, 2.0–4.8 mm) in patients with HCC. In our study, we found that the mean diameter of RIPA was 2.2 mm (range, 1.5–3.6 mm) and 1.9 mm (range, 1.7–2.4 mm) in cirrhotic patients with and without PVT, respectively. Since MDCT and laboratory findings did not reveal HCC in our patients with cirrhosis, a documented hepatic/celiac artery, hepatic venous occlusion, or significant stenosis, there was no reason to significantly dilate the RIPA in group 2. We speculate that the RIPA may have a supplying role for the liver in cirrhosis, but this function becomes more prominent in cirrhosis with PVT. However, the RIPA could not be dilated in cirrhotic patients with PVT as much as in patients with supplying HCC.

We found no differences in the diameters of the LIPA across the three groups. We also found a discrepancy between the diameter of the RIPA and LIPA (with the diameter of the RIPA being greater) in cirrhotic patients with PVT. This finding supports our hypothesis. We thus maintain that impairment of the blood supply to the liver due to stasis or reversed portal flow is aggravated by PVT and that RIPA provides blood supply to the liver at this stage. We assume that the RIPA may have a supplying role in cirrhotic patients with PVT.

However, this study is limited insofar as we could not confirm our results with conventional angiography since further angiographic study was not necessary for our population.

In conclusion, the RIPA may contribute to supplying blood to the liver in cirrhotic patients, especially those with PVT.

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