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ORIGINAL ARTICLE

# Specific liver volume parameters in cirrhotic patients with peribiliary cysts

**Hsuen-En Hwang[a], Nai-Chi Chiu[a,b], Chien-An Liu[a,b], Yi-Hong Chou[a,b], Rheun-Chuan Lee[a,b,*]**

*[a]Department of Radiology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [b]Division of Radiology, School of Medicine, National Yang-Ming University, Taipei, Taiwan, ROC*

## Abstract

**Background:** The presence of peribiliary cysts and morphological changes in the volumes of lobes in the livers of patients with cirrhosis are both related to the alteration of portal flow. Our study explored the relationship between these two features in patients with cirrhosis.

**Methods:** We retrospectively selected 150 computed tomography (CT) images of cirrhotic livers and 105 CT images of healthy livers. The cirrhotic livers were further classified according to the presence of peribiliary cysts (peribiliary cysts group) or the absence of peribiliary cysts (control cirrhotic group). The characteristic features of liver cirrhosis, including modified caudate-right lobe ratio (mCR ratio), splenomegaly, ascites, and collateral shunts, were reviewed. Liver volume calculations included the sum of the left hepatic volume (LHV) and right hepatic volume (RHV; LHV + RHV) and the ratio of LHV to RHV (LHV/RHV).

**Results:** The two groups did not differ in the presence of splenomegaly, ascites, or collateral shunts. The control cirrhotic group exhibited a significantly higher mCR ratio and LHV/RHV ratio than the peribiliary cysts group did ($p < 0.001$). The healthy liver group exhibited a significantly higher LHV + RHV value than either the peribiliary cysts group or the control cirrhotic group did ($p < 0.001$). The peribiliary cysts group and the control cirrhotic group did not differ significantly for LHV + RHV ($p > 0.05$).

**Conclusion:** The control cirrhotic group exhibited a significantly higher mCR ratio and LHV/RHV ratio than the peribiliary cysts group did, but the two groups were similar for most measurements. Peribiliary cysts might result in reduction of portal flow, causing cirrhotic liver with peribiliary cysts with left-sided dominance not to demonstrate the typical morphological appearance of the common cirrhotic liver.

**Keywords:** Bile duct diseases; Hypertension, Portal; Liver cirrhosis

## 1. INTRODUCTION

Peribiliary cysts, first described in 1984 by Nakanuma et al,[1] typically involve the hepatic hilum and are distributed along portal tracts, with a prominent involvement of the left-sided intrahepatic ducts.[2,3] They represent cystic dilatation of the extramural glands and are believed to be caused by the obstruction of the neck of the periductal glands due to inflammation or deranged portal circulation.[4,5] This condition has close associations with cirrhosis, portal hypertension, and autosomal-dominant polycystic disease. Moreover, the lesions usually increase in size and number as cirrhosis and portal hypertension progress.[6,7]

In terms of cirrhosis, the characteristic imaging features include hypertrophy of the caudate lobe and the lateral segment of the left hepatic lobe, segmental atrophy affecting both the posterior segments (VI, VII) of the right lobe and the medial segment (IV) of the left lobe, and the presence of peribiliary cysts.[3,8–10] Because hypertrophy of the caudate lobe and atrophy of the right lobe are also believed to reflect changes in their portal supply, the purpose of our study was to evaluate the interaction and relationship between these two features, a point not addressed in other research.

*Address correspondence. Dr. Rheun-Chuan Lee, Department of Radiology, Taipei Veterans General Hospital, 201, Section 2, Shi-Pai Road, Taipei 112, Taiwan, ROC. E-mail address: rclee8888@gmail.com (R.-C. Lee).

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## 2. METHODS

### 2.1. Study population and study design

A retrospective observational study was performed for the period from January 1, 2014, to December 31, 2017, by reviewing 1771 abdominal computed tomography (CT) images that were Child-Pugh class C. The following exclusion criteria applied: (1) poor quality of images such that the hepatic volume could not be calculated accurately (13 patients); (2) receipt of cholecystectomy, hepatic segmentectomy, or hepatic lobectomy by the patient (84 patients); (3) the presence of portal venous thrombosis, hepatic artery thrombosis, hepatic vein thrombosis, or biliary dilatation (16 patients); (4) any anatomic variants of the portal vein exhibited by the patient (37 patients);[11] or (5) the presence of any space-occupying lesion that could interfere with volume interpretation of the liver, except for peribiliary cysts (1134 patients). A total of 337 patients met more than one of the exclusion criteria. After exclusions, the final study sample included 150 patients. In CT imaging, the peribiliary cysts appear as clusters of discrete cysts at the porta hepatis, as a string of cysts, or as a tubular structure parallel to the portal structures near the hepatic hilum, demonstrating water attenuation without any contrast enhancement or any communication to the biliary tracts. All images were from our hospital, and the hospital Institutional Review Board approved the study and waived the requirement for informed consent.

Two radiologists experienced in abdominal imaging carefully reviewed the images and reached a consensus interpretation that peribiliary cysts were present. The patient population was then divided into two groups: those with peribiliary cysts (Fig. 1), labelled the peribiliary cysts group, and those without peribiliary cysts (Fig. 2), labelled the control cirrhotic group. In addition, the CTs of 105 healthy adults <30 years of age who had received cross-sectional imaging as part of the evaluation process for liver donation in the same period were used for liver volume comparison.

### 2.2. Outcome measures

In addition to the presence of peribiliary cysts, the other parameters evaluated and interpreted in consensus included the presence or absence of ascites, the presence or absence of portosystemic collateral pathways, the modified caudate-right lobe ratio (mCR ratio),[10] and the presence or absence of splenomegaly (splenic index > 480).[12]

For volume calculation of the liver, Couinaud's classification[13] was used to define various segments of the liver. The software Myrian® XP Liver (Intrasense, Montpellier, France) was used for computer-assisted liver volume calculation. In addition, manual tracing of the liver boundary on each CT image was performed for a more precise calculation. The right hepatic volume (RHV; segments V, VI, VII, and VIII) and the left hepatic volume (LHV; segments II, III, and IV), along with the volumes of their respective segments, were measured and recorded (Fig. 3).

### 2.3. Statistical analysis

Statistical analysis was performed using Microsoft Excel 2010 (Microsoft Corp., Redmond, WA) and IBM SPSS 22 (IBM Corp., Armonk, NY). Differences between groups were assessed using the chi-squared test and the independent *t* test, as appropriate. Descriptive statistics, the Shapiro-Wilk test of normality, and Levene's test for equality of variances were also performed before analysis.

## 3. RESULTS

### 3.1. Description of the study population

In the peribiliary cysts group (n = 30), the average age was 60.4 ± 10.7 years; 12 patients had viral hepatitis, 13 had alcoholic hepatitis, 2 had viral hepatitis combined with alcoholic hepatitis, and 3 had cirrhosis resulting from other causes. In the control cirrhotic group (n = 120), the average age was 54.5 ± 8.9 years; 57 patients had viral hepatitis, 35 had alcoholic hepatitis, 11 had viral hepatitis combined with alcoholic hepatitis, and 17 had cirrhosis resulting from other causes. The characteristic features of liver cirrhosis are listed in Table 1. The chi-squared test revealed no statistically significant difference between the cirrhotic groups in prevalence of ascites, portosystemic collateral pathways, or splenomegaly.

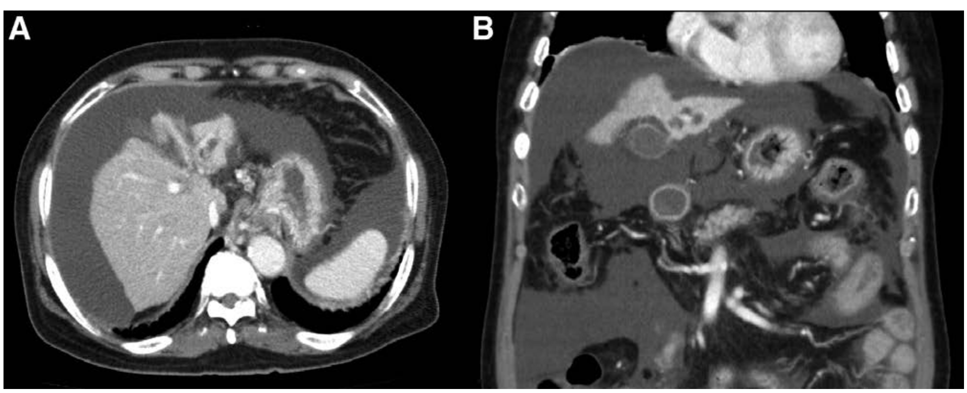


**Fig. 1** Peribiliary cysts in a 61-year-old male patient with a history of hepatitis B virus–related cirrhosis. Axial contrast–enhanced CT (A) and coronal contrast–enhanced CT (B) images show multiple cystic lesions with left-sided periportal distribution. CT = computed tomography.


**Fig. 2** A 62-year-old female patient with hepatitis B virus–related cirrhosis. (A) Axial contrast–enhanced CT and (B) coronal contrast–enhanced CT images reveal the characteristic features of splenomegaly, the presence of paraesophageal varices, and relatively greater hypertrophic change in the lateral segment. No peribiliary cysts were present. CT = computed tomography.

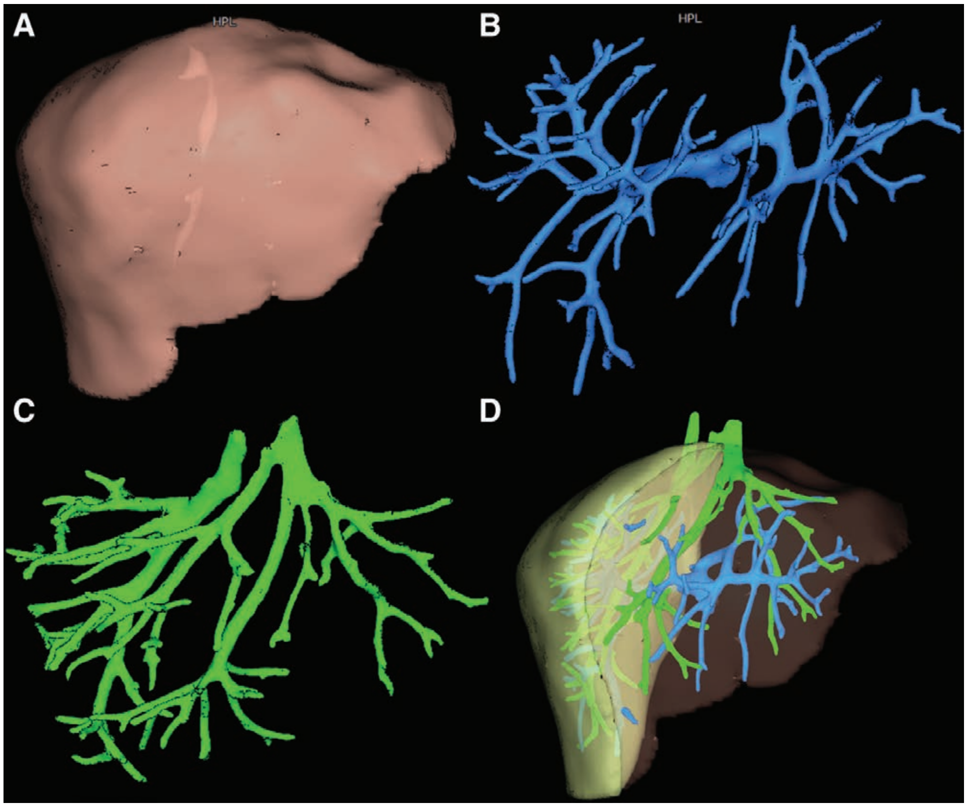


**Fig. 3** Volume calculation of the liver of a 24-year-old male with a healthy liver by Myrian® XP Liver. A, The whole liver is highlighted on the cross-sectional slices, which are then combined to form a 3D liver model. B and C, The volume of the portal veins, hepatic veins, and caudate lobe are then subtracted from the whole liver volume. D, The middle hepatic vein is used as a dividing line to calculate the volume of the right hepatic lobe and the left hepatic lobe. In this case, the volume of the left hepatic lobe is 463 $mm^3$ and that of the right hepatic lobe is 847 $mm^3$. 3D = three-dimensional.

**Table 1**

**Population features in patients with cirrhosis**

| | Peribiliary cysts group (n = 30) | Control cirrhotic group (n = 120) |
|---|---|---|
| **Demographics** | | |
| Sex (M:F) | 22:8 | 36:84 |
| Age (mean), y | 60.4 ± 10.7 | 54.5 ± 8.9 |
| Causes of cirrhosis | | |
| Viral hepatitis, % | 12 (40) | 57 (48) |
| Alcoholic hepatitis, % | 13 (43) | 35 (29) |
| Viral hepatitis with alcoholic hepatitis, % | 2 (7) | 11 (9) |
| Other causes, % | 3 (10) | 17 (14) |
| Characteristic features of liver cirrhosis | | |
| Modified caudate-right lobe ratio (mean ± SD) | 0.82 ± 0.23 | 1.12 ± 0.25 |
| Splenomegaly, % | 26 (86.7) | 109 (90.8) |
| Presence of ascites, % | 26 (86.7) | 107 (89.2) |
| Presence of portosystemic collateral pathways, % | 30 (100) | 117 (97.5) |

### 3.2. Statistical analysis of morphological changes in the liver

Normality analysis using the Shapiro-Wilk test were performed preliminarily, and the data from two outlier cases were identified and excluded from the peribiliary cysts group (Fig. 4). The two groups differed significantly in the mean value of the mCR ratio, with the control cirrhotic group exhibiting the greater value ($p < 0.001$; Fig. 5).

In terms of hepatic volume, 105 healthy livers were included in our comparison (Table 2). The sum of LHV + RHV in the healthy liver group was significantly larger than that in either the peribiliary cysts group or the control cirrhotic group (both $p < 0.001$), but the peribiliary cysts group and the control cirrhotic group did not exhibit significantly different values for LHV + RHV ($p = 0.642$). We divided LHV/RHV to identify any differences in morphological change between hepatic segments. The mean value of the LHV/RHV ratio in the control cirrhotic group was significantly larger than that in either the peribiliary cysts group or the healthy liver group (both $p < 0.001$). No significant differences in mean LHV/RHV ratio were observed between the peribiliary cysts group and the healthy liver group ($p = 0.784$) (Fig. 6).

## 4. DISCUSSION

CT imaging has become a valuable tool for evaluating the cirrhotic liver. Many imaging results have been reported, including morphological changes in the liver, irregular or nodular liver surface, blunt liver edges, liver parenchymal abnormalities, the presence of ascites, the presence of portosystemic shunts, increased diameter of the splenic and main portal veins, decreased diameter of the hepatic vein, and the presence of splenomegaly.[14]

Morphological change in the liver is one of the most characteristic features of cirrhosis. The causes of caudate lobe enlargement and right lobe atrophy are unclear but are believed to be associated with alterations in portal blood flow. The right lobe receives most of its blood from the superior mesenteric vein, whereas the left lobe and in most cases the caudate lobe receive most of their blood from the splenic vein. Absorbed toxins from the superior mesenteric vein and pancreatic hormones

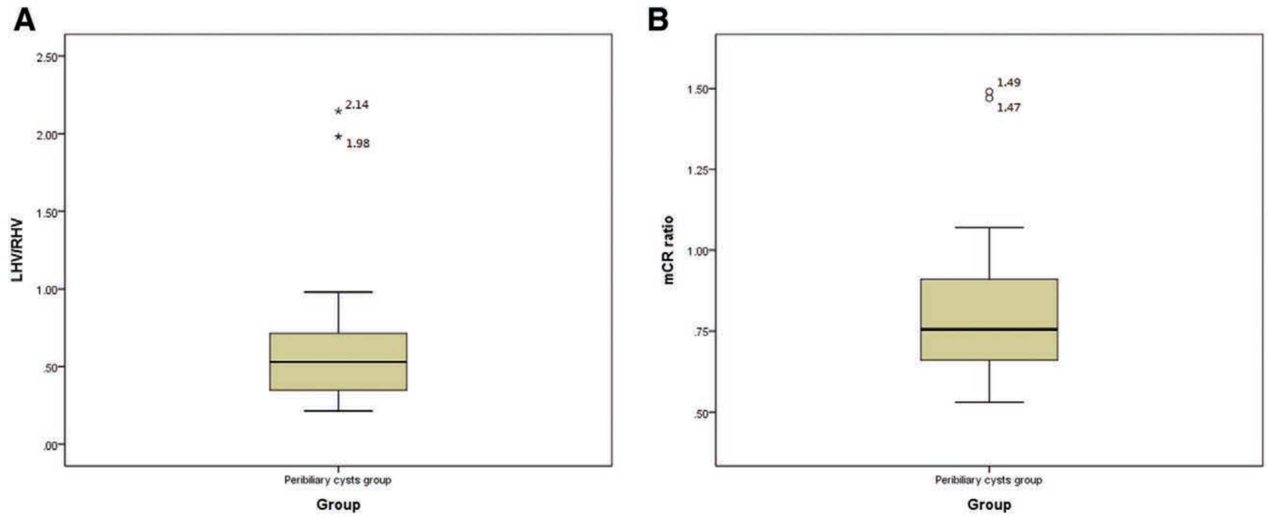


**Fig. 4** Box plots for the LHV/RHV (left) and mCR ratio (right) in the peribiliary cysts group; the rectangle reveals the lower and upper quartiles, and a horizontal line inside indicates the median value. The outlier is defined as the upper quartile ±3× the interquartile range. Two patients were therefore excluded from the peribiliary cysts group because of outlier data. LHV = left hepatic volume; mCR ratio = modified caudate-right lobe ratio; RHV = right hepatic volume.

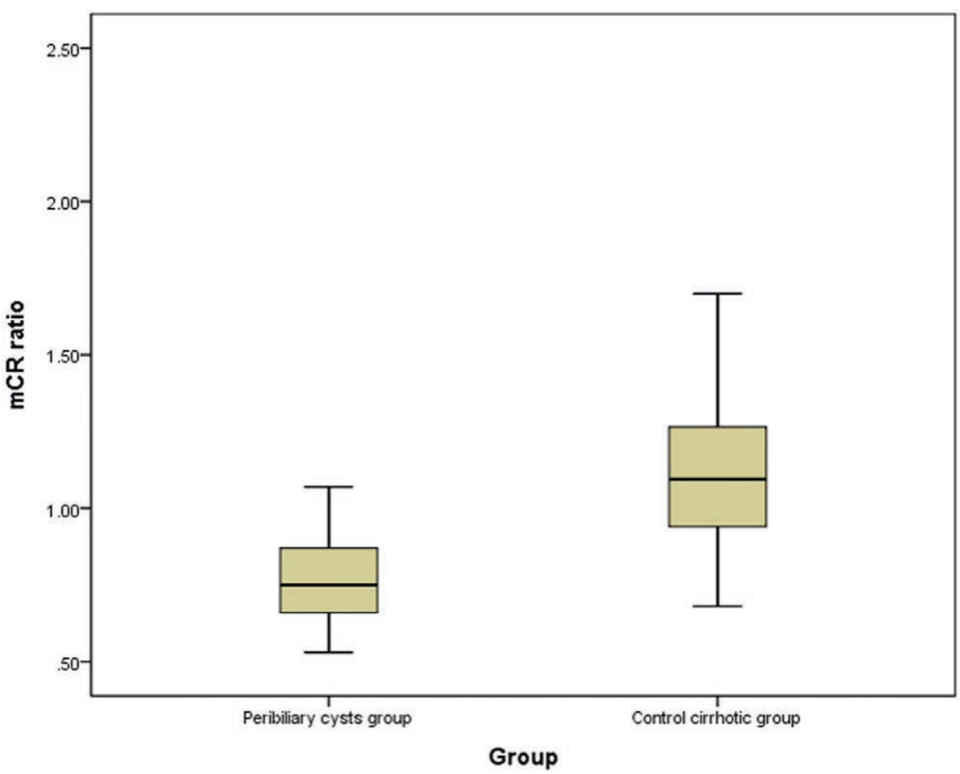


**Fig. 5** Box plots for the mCR ratio in the peribiliary cysts group and the control cirrhotic group. mCR ratio = modified caudate-right lobe ratio.

from the splenic vein may affect the volumetric changes in the hepatic lobes.[9,10,15]

A ratio of transverse caudate lobe width to right lobe width ≥0.65 constitutes a positive indicator for the diagnosis of cirrhosis.[8] Another mCR ratio, using the right portal vein instead of the main portal vein to set the lateral boundary, exhibited greater accuracy.[10] In our study, the mCR ratio differed significantly between the cirrhotic group and the peribiliary cysts group. An mCR ratio >0.90 was considered the threshold, with the best accuracy for the imaging diagnosis of cirrhosis achieved in the Awaya et al study series, in which the sensitivity was 77.4%. However, only 8 of 30 patients in the peribiliary cysts group had an mCR ratio >0.90, with a sensitivity of only 26.7%. By contrast, 103 of 120 patients in the control cirrhotic group exhibited an mCR ratio >0.90, with a sensitivity of 85.8%. Moreover, although both cirrhotic groups exhibited liver atrophy compared with the healthy liver group, the peribiliary cysts group demonstrated no characteristic morphological change in

**Table 2**

**Volume analysis between groups**

| | Peribiliary cysts group (n = 28) | Control cirrhotic group (n = 120) | Healthy liver group (n = 105) |
|---|---|---|---|
| LHV + RHV (mean ± SD) | 897.3 ± 246.5 $mm^3$ | 914.1 ± 270.4 $mm^3$ | 1182.3 ± 253.7 $mm^3$ |
| LHV/RHV (mean ± SD) | 0.63 ± 0.43 $mm^3$ | 1.11 ± 0.34 $mm^3$ | 0.51 ± 0.97 $mm^3$ |

LHV = left hepatic volume; RHV = right hepatic volume.

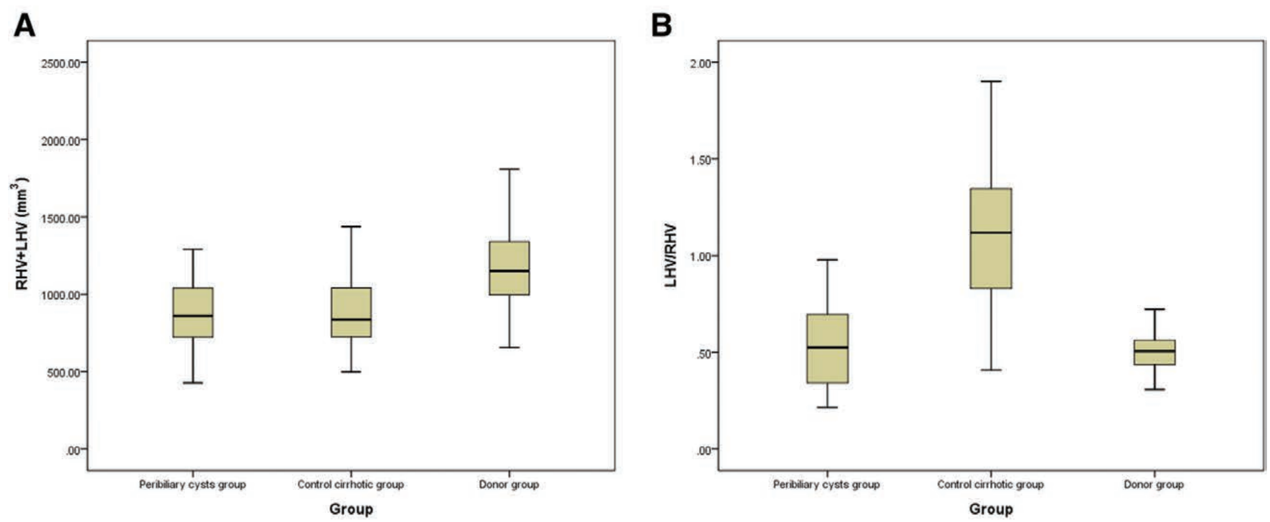


**Fig. 6** Box plots for the (A) LHV + RHV sum and (B) LHV/RHV ratio in the peribiliary cysts group, control cirrhotic group, and healthy liver group. LHV = left hepatic volume; RHV = right hepatic volume.

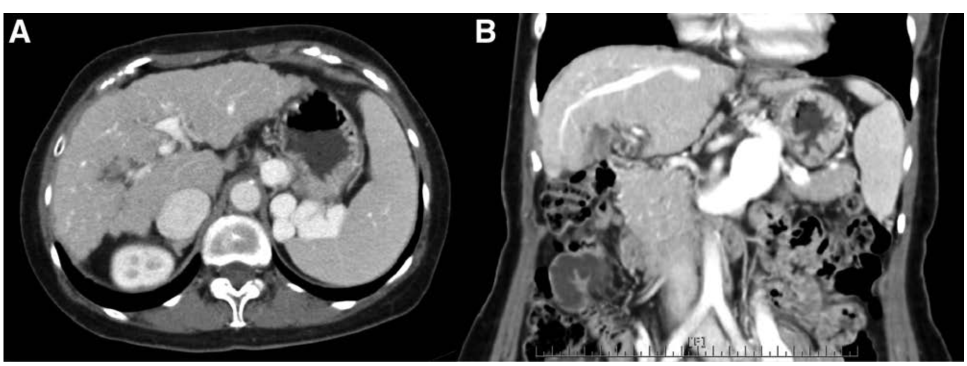


**Fig. 7** Peribiliary cysts in a 57-year-old female patient with a history of hepatitis C virus–related cirrhosis. (A) Axial contrast–enhanced CT and (B) coronal contrast–enhanced CT images show multiple cystic lesions with right-sided, rather than left-sided, periportal distribution. CT = computed tomography.

the form of a significantly decreased LHV/RHV compared with the control cirrhotic group.

Two patients in the peribiliary cysts group were outliers and were excluded from the data set before the independent *t* test was undertaken. Both patients exhibited elevated mCR ratios (1.47 and 1.49) and LHV/RHV ratios (1.98 and 2.15), skewing the range from a normal distribution in this group. Review of both patients' CT images identified right-side dominance of peribiliary cyst distribution (Fig. 7). In other words, these two patients exhibited the typical morphological change described in previous studies.

Peribiliary cysts are known to exert a considerable effect on the adjacent structures, such as the bile ducts, which may lead to acute cholangitis or obstructive jaundice.[5,16–18] We assumed that the presence of peribiliary cysts reduces portal venous flow, causing atrophic changes to the supplying hepatic lobe. This phenomenon was first described by Rous and Larimore[19] after they ligated portal vein branches and observed that the ligated lobe became atrophic. Other conditions such as portal vein thrombosis and tumor invasion have the same atrophic effect on the affected hepatic lobe.[20,21] Shibata et al[22] reported the relationship between refractory esophageal varices and peribiliary cysts and indicated that peribiliary cysts can easily compress the portal vein and that their presence may cause prehepatic portal hypertension. Our result, which indicated that peribiliary cysts might reduce the portal flow by external compression, is in agreement with this assumption. Therefore, the two excluded patients exhibiting peribiliary cysts with right-side dominance demonstrated typical morphological changes in the liver due to their uncompressed left portal vein. Moreover, because the caudate lobe is predominantly supplied by the left branches of the portal vein or by branches from the bifurcation of the portal vein, our result demonstrating a relatively low mCR ratio (0.82 ± 0.23) in the peribiliary cysts group compared with the control cirrhotic group (1.12 ± 0.25) could also be explained.

Our study had several limitations that merit attention. First, to evaluate the undisturbed relationship between peribiliary cysts and liver volume, we excluded the patients with vascular thrombosis, biliary obstruction, or space-occupying lesions other than peribiliary cysts. The study group therefore may not represent the cirrhotic population as a whole. Second, we did not quantify the portal flow by using ultrasound in this study, so no direct comparison is made between liver volume and portal flow. Third, the Child-Pugh scoring system and the CT findings, rather than liver biopsy, were used to select patients with cirrhosis patients and this might not have reflected the real extent of inflammation and fibrosis in the studied livers.[23–25] Fourth, the data for LHV + RHV in this study were not normalized based on body surface area and body weight.[26] Thus, a complete prospective study that includes body surface area or body weight, quantification of portal flow, longitudinal follow-up of liver volume, and the portosystemic collateral pathways would help to define the potential synergistic effect between peribiliary cysts and portal hypertension.

In conclusion, a reduction of portal flow, potentially caused by peribiliary cysts, might have caused cirrhotic liver with peribiliary cysts with left-sided dominance not to demonstrate the typical morphological appearance of the common cirrhotic liver.

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