Correlation between the Severity of Hepatitis B Cirrhosis and CT Volumetry-Based Hepatic Segmental Anatomic Changes

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Objective: *To study the correlation between the changes of hepatic segmental volumes and the severity of hepatitis B cirrhosis, classified by Child-Pugh score.*

Material and Method: *The study cohort comprised viral hepatitis B cirrhotic patients with different severity (Child-Pugh score grade A to C) and control subjects who underwent hepatic computed tomographic (CT) scan between February 2006 and May 2012. The volumes of total liver (TLV), right lobe (RV), left medial segment (LMV), left lateral segment (LLV), and caudate lobe (CV) were measured and compared between the control group and Child-Pugh A, B, and C groups.*

Results: *Among 120 hepatitis B cirrhotic subjects, there were 85 males (70.8%) with the mean age of 59.2 years (range 36-86 years). Sixty-two subjects were Child-Pugh A, 39 were Child-Pugh B, and 19 were Child-Pugh C. Among 62 control subjects, there were 28 males (45.2%) with the mean age of 54.5 years (range 19-82 years). The TLV and RV were significantly decreased in Child-Pugh B and C subjects when compared with control subjects. LMV was significantly decreased in Child-Pugh A and continually decreased along with the severity of the disease. LLV was significantly increased in Child-Pugh A and B, but relative in Child-Pugh C subjects. CV was not significantly different in these four groups.*

Conclusion: *Hepatitis B cirrhotic patients had progressive hepatic atrophy, initially by left medial segment, followed by right lobe and the whole liver. Hypertrophy of left lateral segment was evident in early cirrhosis but not significantly shown in severe cirrhosis. Hypertrophy of caudate lobe was not evident in any degrees of hepatitis B cirrhosis.*

Keywords: *Hepatitis B virus, Cirrhosis, Child-Pugh score, Liver volume*

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Liver cirrhosis is an irreversible process of fibrotic replacement of normal liver tissue after chronic liver damages, which leads to progressive deterioration of liver function and eventually complications (ascites, spontaneous bacterial peritonitis, variceal bleeding, hepatorenal syndrome, hepatic encephalopathy, and hepatocellular carcinoma, etc.). Predisposing factors of liver cirrhosis include chronic alcoholism, hepatitis B and C viral infection, non-alcoholic steatohepatitis (NASH), autoimmune hepatitis, drug/toxic substances induced hepatitis, chronic biliary obstruction, chronic cardiac congestion, hemochromatosis/hemosiderosis, and Wilson's disease, etc. In some patients, no definite etiology can be determined (cryptogenic cirrhosis)[1].

The diagnosis of hepatic cirrhosis may rely on clinical presentations, physical examination, laboratory studies, and radiographic findings. In equivocal cases, liver biopsy may be considered although this will have a high impact on further treatment[1].

Radiographic studies (ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI)) play a major role in the diagnosis of liver cirrhosis and the detection of various complications (ascites, portal hypertension, hepatocellular carcinoma, etc.)[2]. Several imaging characteristics suggest liver cirrhosis. These include the classic signs of hepatic fibrosis (small-sized liver with nodular surface, widening hepatic fissures and coarse, lacelike enhancement of hepatic parenchyma), hepatic segmental anatomic changes (atrophic change, more specific at left medial segment and right lobe with compensatory hypertrophy of left lateral segment and caudate lobe), and the signs of portal hypertension (splenomegaly, abdominal varices, and ascites)[3,4].

The changes in hepatic segmental volume are different among the various etiologies of liver cirrhosis. For example, hypertrophy of left lateral segment was significantly found in hepatitis B cirrhosis, compared

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to hepatitis C and alcoholic causes[5]. On the other hand, hypertrophy of caudate lobe was typically associated with alcoholic cirrhosis, compared to viral induced hepatitis[5,6]. The severity of liver cirrhosis also influences the changes in hepatic segmental volume. Zhou et al[7] studied the CT appearances in Child-Pugh A to C viral-induced cirrhotic subjects and found that hypertrophy of left lateral segment was absolute in Child-Pugh A and B subjects, but was relative in Child-Pugh C subjects. Enlargement of caudate lobe was absolute in Child-Pugh A subjects, but was relative in Child-Pugh B and C subjects.

From previous studies, confounding factors influenced the hepatic segmental anatomic changes, either the etiologies or the severity of liver cirrhosis. To minimize the mentioned confounding factors, the present study was designed to observe the correlation between the hepatic segmental anatomic changes and the severity of the liver cirrhosis (classified by Child-Pugh score) by focusing only on hepatitis B cirrhotic patients.

Material and Method

Study designs and subjects

This was a retrospective, single-center study performed at a 3,000-bed university hospital in central Thailand. The present study was approved by the authors' Institutional Review Board with waiver of written informed consent. The study inclusion criteria were hepatitis B viral-induced cirrhotic patients who underwent contrast enhanced hepatic CT scan at the authors' institution between February 2006 and May 2012. The liver function tests, coagulograms, and physical examination within two months from the CT date were needed for calculation of the subjects' Child-Pugh scores. Eligible subjects with hepatic space occupying lesions greater than 2 cm in largest dimension, thrombosis in portal or hepatic venous system, or biliary obstruction were excluded from the study population because these would affect the hepatic segmental volume. The subjects with history of alcoholism or other causes of liver cirrhosis (e.g. hepatitis C viral infection) were also excluded from the subject group.

The study subjects were categorized by the severity of liver cirrhosis, using Child-Pugh score to be three groups: Child-Pugh A (least severe liver cirrhosis) with the score of 5 to 6 points, Child-Pugh B (moderately severe liver cirrhosis) with the score of 7 to 9 points, and Child-Pugh C (most severe liver cirrhosis) with the score of 10 to 15 points[8,9] (Table 1).

The inclusion criteria for control subjects were patients without history of any liver disease, jaundice or chronic alcohol assumption who underwent contrast enhanced hepatic CT scan at the authors' institution at the same period. The liver function tests within two months from the CT date were needed to confirm that the control subjects had no liver impairment. With the same reason, eligible control subjects with hepatic space occupying lesions greater than 2 cm, thrombosis in the portal or hepatic venous system, or biliary obstruction were excluded from the study.

CT techniques

The CT scans of the study participants (hepatitis B cirrhotic and control groups) were performed on two 64 detector helical CT scanners (LightSpeed VCT, GE Healthcare, United States; and SOMATOM Definition Dual Source, Siemens, Germany). All subjects were in supine position with a

Table 1. Child-Pugh classification

Clinical and lab criteria	Points		
	1	2	3
Encephalopathy	None	Mild to moderate (grade 1 or 2)	Severe (grade 3 or 4)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	<2	2-3	>3
Albumin (g/dL)	>3.5	2.8-3.5	<2.8
Prothrombin time			
Seconds prolonged	<4	4-6	>6
International normalized ratio	<1.7	1.7-2.3	>2.3

Child-Pugh Class obtained by adding score for each parameter (total points)
Class A = 5 to 6 points (least severe liver disease)
Class B = 7 to 9 points (moderately severe liver disease)
Class C = 10 to 15 points (most severe liver disease)

breath hold during the scan. The scan coverage included at least from liver dome to inferior tip of liver. The slice collimations were 1.25 mm (reconstructed at 7.0 mm), and 1.5 mm (reconstructed at 7.0 mm) for LightSpeed VCT, and SOMATOM Definition Dual Source, respectively. All subjects underwent precontrast and postcontrast studies, before and after a bolus intravenous injection of 80 to 100 ml of nonionic iodinated contrast agent and 20 ml of water via a power injector at a rate of 2 to 3 ml/second. A standard 80-second delay for portovenous phase was applied in all studies. Additional arterial phase at 35-second delay or extra 5-minute delay were obtained in some subjects in either hepatitis B cirrhotic group or control group.

Hepatic segmental volume measurement

After the guidance by an experienced abdominal radiologist (PA; with 18 years of experience), the liver volume measurement of each CT study was performed by one of the investigators (DW). The outline of total liver, right lobe, left medial segment, left lateral segment, and caudate lobe were drew by computer mouse on consecutive thick slices (7.0 mm) portovenous CT images on the GE workstation (HDAW01). The outline of each hepatic segment was based on Goldsmith and Woodburne classification[10] (Fig. 1). The right lobe and left medial segment were divided by an imaginary line between middle hepatic vein and gallbladder fossa. The left medial and left lateral segment were divided by an imaginary line between left hepatic vein and falciform ligament. The right and caudate lobes were divided by an imaginary line perpendicular to right portal vein bifurcation[11]. The left and caudate lobes were divided by an imaginary line between fissure for ligamentum venosum and right portal vein. The right lobe volume (RV), left medial segment volume (LMV), left lateral segment volume (LLV) and caudate lobe volume (CV) were computed by volume rendering software in milliliters (ml). The total liver volume (TLV) was calculated by the addition of RV, LMV, LLV, and CV. The repeated measurement was randomly performed in some subjects of either control or hepatitis B cirrhotic groups, showing the excellent agreement of intraclass correlation coefficient (ICC) with the lowest ICC of 0.88. The means of TLV, RV, LMV, LLV, and CV were compared between the control subjects (Group I) and Child-Pugh A, B, and C subjects (Group II-IV, respectively).

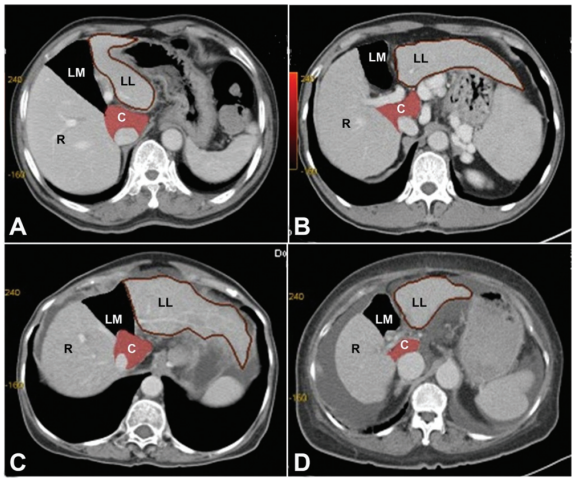

Fig. 1 The outlines of right lobe (R), left medial segment (LM), left lateral segment (LL), and caudate lobe (C) were based on the Goldsmith and Woodburne classification[10] in the control (1A), Child-Pugh A (1B), Child-Pugh B (1C) and Child-Pugh C (1D) subjects.

Statistical analysis

The hepatic segmental volumes were displayed as the means ± standard deviation (SD). The one-way analysis of variance (ANOVA) and Welch test were used to compare the quantitative variables between the four groups. Bonferroni and Games-Howell tests were used for post hoc multiple comparisons. A 2-sided *p*-value of less than 0.05 was considered as a statistical significance. All statistical data analyses were performed by using PASW statistic 18 (SPSS Inc., Chicago, Illinois, United States).

Results

Subjects

Based on the aforementioned inclusion and exclusion criteria, the authors recruited 120 hepatitis B cirrhotic patients and 62 control subjects. All 120 hepatitis B cirrhotic subjects were proved to be chronic carriers for viral hepatitis B by viral hepatitis profiles. The diagnosis of liver cirrhosis was together established by clinical evaluation, liver function tests, and radiographic findings. None of them underwent liver biopsy. These 120 subjects had been referred for hepatic CT scans for many reasons such as; elevation of serum alpha-fetoprotein level, evaluation the severity of liver cirrhosis and portal hypertension, suspected hepatic lesions from ultrasound, and routine imaging study before liver transplantation. They were 85 males and 35 females with the mean age of 59.2 years (range 36-86 years) (Table 2). Based on

Child-Pugh classification, 62 of 120 subjects were categorized in Child-Pugh class A, 39 subjects in Child-Pugh class B, and 19 subjects in Child-Pugh class C.

Sixty-two control subjects had been referred for hepatic CT scan during the same period for many reasons such as check-up, surveillance for liver metastasis, etc. They were 28 males and 34 females with the mean age of 54.5 years (range 19-82 years) (Table 2).

Hepatic segmental volume measurement

The hepatic segmental volume of both control and hepatitis B viral-induced cirrhotic subjects were shown in Table 3 and Fig. 2. The TLV and RV were significantly decreased size in cirrhotic patients, significantly in Child-Pugh B and C when compared to the control subjects (p-value <0.001). Decreased LMV was one of initial CT signs of liver cirrhosis, significantly found in Child-Pugh A (p-value <0.001), and continually found when the disease turned severe. Increased LLV was another initial CT sign of liver cirrhosis, significantly found in Child-Pugh A and B (p-value = 0.002), but not significantly found in Child-Pugh C subjects. Interestingly, CV showed no statistical difference between the control and any severity of hepatitis B cirrhotic groups (p-value = 0.587).

Discussion

The authors designed the present study to explore the correlation between the hepatic segmental anatomic changes and the severity of the liver cirrhosis by focusing on hepatitis B cirrhotic subjects. The results of the study may help predicting the severity of hepatitis B cirrhosis based on the CT findings.

The authors found that atrophic change of the left medial segment was significantly found in early hepatitis B cirrhosis (Child-Pugh A subjects) and continually found when the disease turned severe. This could be explained by the vascular restriction of left medial segment[12]. Left medial segment was the hepatic segment that received the least portal venous supply when compared to other hepatic segments. When the hepatic portal venous supply was decreased in cirrhotic patients, left medial segment was inevitably the first and the most influenced segment.

Hypertrophy of left lateral segment was another initial CT sign of hepatitis B cirrhosis found in the present study. This was significantly found in Child-Pugh A and B, but not in Child-Pugh C, when compared to the control group. These findings were well corresponded with the study by Zhou et al[7]. The hypertrophy of left lobe, esp. left lateral segment was explained by it received the hepatotrophic factors from pancreas via splenic vein more than right lobe[5,13].

Table 2. Demographic data of the control and Child-Pugh A to C hepatitis B cirrhotic groups

Groups	No. of subjects	Male	Female	Mean age ± SD (years)	Age range (years)
Control (Group I)	62	28 (45.2%)	34 (54.8%)	54.5±14.5	19-82
Cirrhosis	120	85 (70.8%)	35 (29.2%)	59.2±10.1	36-86
Child-Pugh A (Group II)	62	51 (82.3%)	11 (17.7%)	61.0±10.3	36-86
Child-Pugh B (Group III)	39	21 (53.8%)	18 (46.2%)	57.3±9.2	42-86
Child-Pugh C (Group IV)	19	13 (68.4%)	6 (31.6%)	57.4±9.8	39-76

Table 3. Comparison of hepatic segmental volume in the control and Child-Pugh A to C hepatitis B cirrhotic groups

Segmental volume (ml)	Control (Group I) n = 62	Child-Pugh A (Group II) n = 62	Child-Pugh B (Group III) n = 39	Child-Pugh C (Group IV) n = 19	p-value	Remarks
TLV	1,215.4±278.0	1,149.3±345.4	956.8±303.9	904.1±385.6	<0.001	I-III, I-IV, II-III, II-IV
RV	796.9±185.3	706.4±222.2	544.3±223.8	547.0±272.5	<0.001	I-III, I-IV, II-III, II-IV
LMV	185.0±54.1	134.6±72.1	107.4±46.4	96.4±63.5	<0.001	I-II, I-III, I-IV
LLV	196.7±74.0	274.3±125.1	270.5±159.7	230.6±120.5	0.002	II-I, III-I
CV	36.8±18.2	34.0±18.6	34.5±19.9	30.1±21.8	0.587	

TLV = total liver volume; RV = right lobe volume; LMV = left medial segment volume; LLV = left lateral segment volume; CV = caudate lobe volume

Values are presented as mean ± SD

Identify the pairs of which are significantly different (p-value <0.05) in hepatic segmental volume. The former number represents the group that is significantly larger to the latter number.

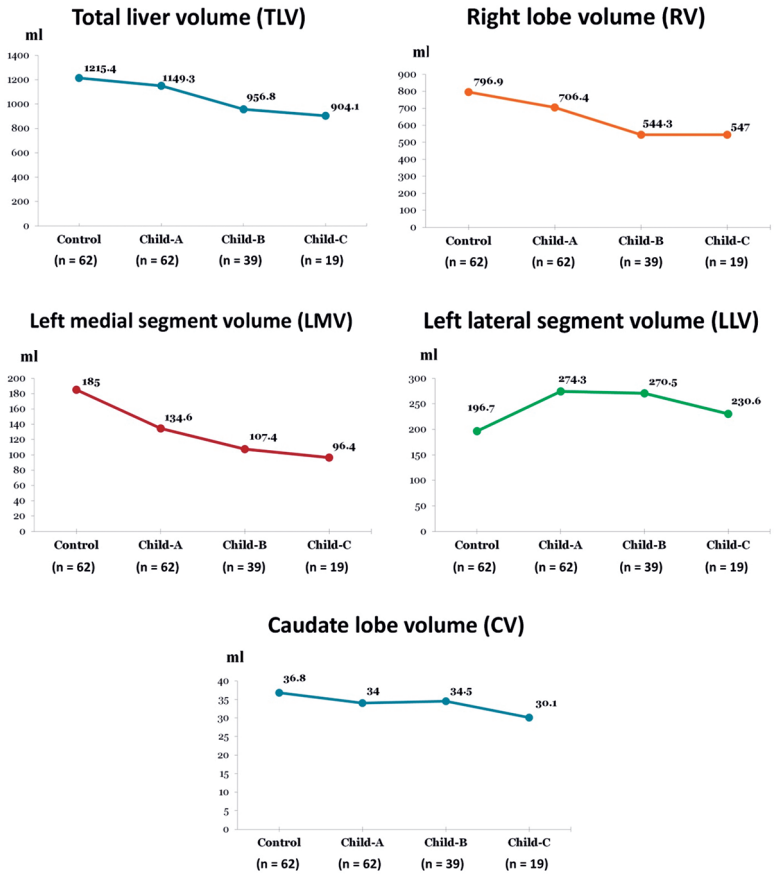

Fig. 2 Linear graphs display the total liver volume (TLV), right lobe volume (RV), left medial segment volume (LMV), left lateral segment volume (LLV) and caudate lobe volume (CV) in the control and Child-Pugh A to C hepatitis B cirrhotic groups.

Unfortunately, in Child-Pugh C, the whole liver was shrinkage and the left lateral segment could not further compensate. In the present study, the mean LLV in Child-Pugh C was relatively larger than the control group, but this did not reach the statistically significant level.

Atrophic change of right lobe in liver cirrhosis was believed due to it received the toxins via superior mesenteric blood flow more than the left lobe[5]. In the present study, atrophic change of right lobe was significantly found in moderate and severe degree hepatitis B cirrhotic subjects, not in the early cases. The TLV was also not significantly decreased in early liver cirrhotic subjects. This could be explained by the compensatory hypertrophy of left lateral segment in early cases, the TLV was therefore not strongly influenced.

In general, the compensatory hypertrophy of caudate lobe in liver cirrhosis was thought to be associated with the obstructed portal blood flow by fibrosis. The caudate lobe was probably supplied by the posterior right portal vein, which had the shorter intrahepatic course than other hepatic segments. This could prevent caudate lobe from atrophic change. Even more, it was enlarged to compensate the atrophic change of right lobe and left medial segment[7]. Interestingly, the present study showed no significant difference of the CV between the control and hepatitis B cirrhotic subjects. This result was well correlated with the studies by Kim et al[5] and Okazaki et al[6], which claimed that caudate lobe hypertrophy was more frequently found in alcoholic cirrhosis than viral induced cirrhosis.

As with all retrospective studies, the authors acknowledged several limitations. First, the sample size of the present study was small and included some selection biases. For example, the subjects in Child-Pugh B and C groups were relatively small when

compared to the control and Child-Pugh A groups. The majority of cirrhotic subjects were male, but the majority of control subjects were female. Second, the liver volume measurement was done by one observer. Although, the randomly repeated measurement showed the excellent agreement of ICC, another study with repeated measurement by another observer should be designed to get more accurate data.

In conclusion, hepatitis B cirrhosis showed segmental anatomical changes, initially by atrophic change of left medial segment, followed by atrophic change of right lobe and the whole liver. Hypertrophy of left lateral segment was evident in early cirrhosis but not significantly found in severe cirrhosis. Hypertrophy of caudate lobe was not evident in any severity of hepatitis B cirrhosis.

What is already known on this topic?

Previous studies showed that there were many confounding factors influenced the hepatic segmental anatomic changes in liver cirrhosis, either the etiologies of liver cirrhosis or the severity of liver cirrhosis.

What this study adds?

The present study was aimed to minimize the mentioned confounding factors, and focused only in hepatitis B cirrhotic group. The authors found that hypertrophy of caudate lobe was not evident in any severity of hepatitis B cirrhosis.

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Potential conflicts of interest

None.

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ความสัมพันธ์ระหว่างความรุนแรงของโรคตับแข็งจากไวรัสตับอักเสบบีและลักษณะการเปลี่ยนแปลงทางกายภาพของกลีบตับ

ปิยาภรณ์ อภิสารธนรักษ์, ดุลยพร วงศ์แสวง, กอบกุล เมืองสมบูรณ์

วัตถุประสงค์: เพื่อศึกษาความสัมพันธ์ระหว่างการเปลี่ยนแปลงปริมาตรของตับกลีบต่าง ๆ และความรุนแรงของโรคตับแข็งจากไวรัสตับอักเสบบี

วัสดุและวิธีการ: ผู้เข้าร่วมการศึกษาประกอบด้วยกลุ่มผู้ป่วยตับแข็งจากไวรัสตับอักเสบบี (ซึ่งมีความรุนแรงตั้งแต่ Child-Pugh A ถึง C) และกลุ่มควบคุม โดยผู้เข้าร่วมการศึกษาทั้งหมดได้รับการตรวจเอกซเรย์คอมพิวเตอร์ของตับในช่วงเดือนกุมภาพันธ์ พ.ศ. 2549 ถึง เดือนพฤษภาคม พ.ศ. 2555 โดยปริมาตรของตับทั้งหมด, ตับกลีบขวา, ตับกลีบซ้ายส่วนใกล้กลาง, ตับกลีบซ้ายส่วนริม และตับกลีบคอเดต ได้ถูกวัดและเปรียบเทียบในผู้ป่วยกลุ่มต่าง ๆ เพื่อหาความสัมพันธ์ระหว่างความรุนแรงของโรคตับแข็งจากไวรัสตับอักเสบบีและการเปลี่ยนแปลงปริมาตรของตับกลีบต่าง ๆ

ผลการศึกษา: มีผู้เข้าร่วมการศึกษาเป็นผู้ป่วยตับแข็งจากไวรัสตับอักเสบทั้งสิ้น 120 ราย (Child-Pugh A 62 ราย, Child-Pugh B 39 ราย, Child-Pugh C 19 ราย) และกลุ่มควบคุมจำนวน 62 ราย พบว่าปริมาตรของตับทั้งหมดและตับกลีบขวาจะมีขนาดลดลงกว่ากลุ่มควบคุมอย่างชัดเจนในผู้ป่วยกลุ่ม Child-Pugh B และ C ส่วนปริมาตรของตับกลีบซ้ายส่วนใกล้กลางจะมีขนาดลดลงอย่างชัดเจนตั้งแต่ Child-Pugh A และมีขนาดลดลงเรื่อย ๆ ตามความรุนแรงของโรค ส่วนปริมาตรของตับกลีบซ้ายส่วนริมจะเพิ่มขึ้นอย่างชัดเจนในกลุ่ม Child-Pugh A และ B แต่ไม่ชัดเจนในกลุ่ม Child-Pugh C ส่วนปริมาตรของตับกลีบคอเดตไม่พบความแตกต่างอย่างชัดเจนระหว่างกลุ่มผู้ป่วยความรุนแรงต่าง ๆ และกลุ่มควบคุม

สรุป: ผู้ป่วยตับแข็งจากไวรัสตับอักเสบบีจะมีปริมาตรตับลดลง โดยเริ่มจากตับกลีบซ้ายส่วนใกล้กลาง ตามด้วยตับกลีบขวา และตับทั้งหมด สำหรับตับกลีบซ้ายส่วนริมจะมีปริมาตรเพิ่มขึ้นในระยะแรกของโรค แต่ไม่พบลักษณะดังกล่าวในรายที่โรคมีความรุนแรง ส่วนตับกลีบคอเดตไม่พบความเปลี่ยนแปลงชัดเจนในผู้ป่วยตับแข็งจากไวรัสตับอักเสบบี