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Original article

Relationship of Hepatic Functional Parameters with Changes of Functional Liver Volume using Technetium-99m Galactosyl Serum Albumin Scintigraphy in Patients undergoing Preoperative Portal Vein Embolization: A Follow-up Report

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Running title: Pre-PVE predictors of hepatic functional volume

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Gastrointestinal category

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ABSTRACT

Background. To identify predictors of changes in functional hepatic volumes after portal vein embolization (PVE) before hepatectomy, we examined the relationship between hepatic functional parameters and changes in functional volume of the embolized and non-embolized liver based on a previous volumetric analysis.

Patients and Methods. Subjects were 24 patients who underwent PVE, which was performed through the trans-ileocolic vein (n=4) or by percutaneous transhepatic puncture (n=20). The RI liver volume parameter was measured by liver scintigraphy with technetium-99m galactosyl human serum albumin (99mTc-GSA). CT volume parameter was also measured.

Results. Significant atrophy of the embolized liver and hypertrophy of the non-embolized liver (change of 72±108 cm$^3$ and 111±91 cm$^3$, respectively) (change of 7.8%) was observed after PVE. The change in these RI volume parameters (change of 173±175 cm$^3$ and 145±137 cm$^3$, respectively) (16.5%) was significantly greater than CT volume parameters (p<0.01). CT vol and RI vol in the embolized and non-embolized liver were well correlated (r=0.75 and 0.69, respectively). However, the correlation between CT and RI volume parameters in the embolized and non-embolized liver after PVE was very weak (r=0.17 and 0.03, respectively). Only alkaline phosphatase level correlated negatively with atrophic CT volume parameter of the embolized liver (r=-0.455, p<0.05). When compared with CT volume parameter, more parameters were significantly correlated with changes of RI volume parameter in the embolized liver: pre-PVE pressure; ICGR15; and serum levels of hyaluronate, total bilirubin, albumin, and alkaline phosphatase. Only platelet count was significantly correlated with hypertrophy of the non-embolized liver.
Conclusion. RI volume parameter might more accurately reflect functional changes in the embolized liver and non-embolized liver than CT volume parameter. Correlated parameters might allow us to predict the functional effect of PVE.

Key Words: Liver resection; portal vein embolization; functional liver volume; liver functional reserve; platelet count
INTRODUCTION

The risk of postoperative hepatic failure or related death in patients who undergo major hepatectomy has markedly decreased recently with adequate preoperative assessment of hepatic function, precise estimation of liver volume, and improvements in perioperative management [1, 2]. However, the risk of posthepatectomy hepatic failure after extensive resection for hilar bile duct carcinoma or liver malignancies with co-existing impaired liver function remains a problem [3, 4]. In patients undergoing right hepatectomy or more extensive liver resection, preoperative portal vein embolization (PVE), which allows a smaller hepatic resection and induces hypertrophy of the remnant liver, is a useful option. It can extend the operative indications and improve post-hepatectomy prognosis [5, 6]. The clinical significance of PVE has been well recognized, and it is often incorporated into the preoperative preparation for major hepatectomy [5-8].

When PVE is scheduled, it is worthwhile to predict the degree of hypertrophy of non-embolized liver. Better regeneration of non-embolized liver after PVE and hepatectomy may prevent post-hepatectomy complications. Predictors of changes in the embolized and non-embolized liver have been reported [9, 10]; however, these have not yet been widely clarified. Our previous examination of predictors of liver volume change after PVE found that alkaline phosphatase (ALP) level was negatively correlated with atrophy of the embolized lobe, and that platelet count was positively correlated with hypertrophy of the non-embolized lobe [11]. However, the clinical significance of these parameters was not obvious.

Liver volume is usually evaluated by computed tomography (CT); however, real functional liver volume may differ from morphological volume in the diseased liver, such
As in obstructive jaundice [12, 13]. Asialoglycoprotein receptors on hepatocytes reflect functional liver cells [14]. A reliable test assessing hepatic functional reserve, technetium-99m galactosyl human serum albumin (\(^{99m}\)Tc-GSA) scintigraphy, has been used in patients with liver disease and this type of scintigraphy reflects asialoglycoprotein receptors of living liver cells [15]. \(^{99m}\)Tc-GSA scintigraphy can provide useful information concerning functional liver volume in any part of the liver [16], and this is clinically useful to determine the appropriate hepatectomy. This examination reflects the effect of PVE better than CT volumetry [17]. We have hypothesized that the functional volume might more closely reflect a correlation with predictive parameters for PVE effect in comparison with morphological volume by CT. Therefore, we have continued to examine both morphological and functional hepatic volume before and after PVE to clarify our hypothesis in the present study, as a follow-up to our previous report [11].

In the present study, we examined the relationships between liver functional parameters and changes in functional liver volume using 99mTc-GSA scintigraphy of the embolized and non-embolized liver after PVE as a preliminary study. We hypothesized that there would be more parameters associated with functional volume than with morphological volume. We hope that identification of such parameters can help us improve the clinical strategy for patients undergoing major hepatectomy.
PATIENTS AND METHODS

Patients

Forty-four patients underwent PVE in the Division of Surgical Oncology, Department of Translational Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences (NUGSBS) between January 1995 and November 2009. Functional liver volume began to be examined in 24 patients (55%) in 1999, and these were the subjects of the present study. To examine the new factor of functional hepatic volume, data in 13 patients analyzed in the previous report [11] were included in the present analysis as a follow-up report. Participants were 15 men and 9 women with a mean age (±SD) of 63.7±12.3 years (range, 39-79 years). Liver diseases were hepatocellular carcinoma (n=5), intrahepatic cholangiocarcinoma (n=2), metastatic liver carcinoma (n=3), gallbladder carcinoma (n=4), and bile duct carcinoma (n=10). The background hepatic condition was normal liver function (n=12), chronic viral liver disease (n=5; caused by hepatitis B virus [n=3] or hepatitis C virus [n=2], including 2 with cirrhosis) and obstructive jaundice (n=7).

In our hospital, the volume of the liver to be resected is determined preoperatively based on the indocyanine green retention rate at 15 minutes (ICGR15) using Takasaki’s formula [18]. The estimated resected liver volume, excluding tumor volume (cm³), is measured by CT volumetry [12]. Essentially, in cases where the permitted resected volume of the liver is greater than the estimated resected volume of the liver, the planned hepatectomy is performed. In cases where the permitted resected volume is less than the estimated volume, or the estimated volume is over 65% in normal liver and over 50% in cirrhosis, preoperative PVE is selected [19]. Liver activity at 15 minutes (LHL15) in $^{99m}$Tc-GSA scintigraphy was performed pre-operatively with the ICGR15 [20].
Hemihepatectomy was performed in 9 patients and more extensive hepatectomy in 9 (including hepato-pancreato-duodenectomy in 3). Hepatectomy was abandoned during laparotomy in 6 patients because of advanced disease such as peritoneal carcinomatosis.

The study design was approved by the Ethics Review Board of our institution and written consent for PVE was obtained from each subject. The present analysis was a retrospective study. Data were retrieved from both anesthetic and patient charts plus the NUGSBS database, for the duration of the initial hospitalization following hepatectomy.

**Technique of portal vein embolization and evaluation**

The two approaches to the right portal vein were direct catheterization of the ileocolic vein (n=4) and percutaneous transhepatic puncture (n=20) [5, 7]. Between 1999 and 2007, substances used for embolization in our series included 1 g of absorbable gelatin sponge powder (Gelfoam®; Upjohn, Kalamazoo, MI) and 5,000 units (5 ml) of liquid thrombin (Sankyou Co., Tokyo, Japan) mixed in the contrast media, or iodized oil (Lipiodol; Savage Lab., Melville, NY) mixed with gelatin (Sponzel; Astellas Pharma, Inc., Tokyo, Japan). Since 2008, an liquid embolization material, 5% of ethanolamine oleate iopamiodole (EOI; Oldamin; Takeda Pharma, Osaka, Japan) was mainly used for embolization. Permanent embolization materials or coils were not used. Embolization was completed when the entire right portal vein was completely occluded. At 14 days after PVE, the hepatic volumes of the non-embolized lobe and embolized lobe (lobe to be resected) were reassessed by CT volumetry (CT vol) and $^{99m}$Tc-GSA scintigraphy (RI volume parameter) [21]. Scheduled hepatectomy was performed at 21-28 days after PVE.
Compared parameters

Clinicopathological parameters (age, gender, background liver disease), laboratory data (portal pressure; serum levels of hyaluronic acid (HA), bilirubin, alanine transaminase, total cholesterol, and albumin; prothrombin activity; platelet count; ICGR15, LHL15 on $^{99m}$Tc-GSA scintigraphy; and substance of embolization were examined and compared in relation to changes of hepatic volume (CT and RI volume parameters). Serum HA level was assayed using the sandwich binding protein assay by SRL, Inc. (Tokyo, Japan) and the manufacturer’s normal value of less than 50 ng/ml was used [22]. Portal pressure before and immediately after PVE was measured by cannulation of the portal trunk during PVE. A dose of 0.5 mg ICG/kg body weight was injected intravenously and the 15-minute retention rate was measure by a photopiece applied to the fingertip (Sumitomo Electric, Tokyo, Japan) without blood sampling.

Volumetric measurement by CT and $^{99m}$Tc-GSA liver scintigraphy

Morphological volume was measured using contrast computed tomography (CT volume parameter) [5, 12]. Serial axial scans were taken at 3 mm intervals by a 16-row multidetector CT scanner, and the hepatic volume of areas without tumors and large vessels in each liver region was 3-dimensionally measured using Workstation software (Ziostation version 1.1, Ziosoft Inc., Tokyo, Japan) as in Fig. 1a. Regarding $^{99m}$Tc-GSA liver scintigraphy, all patients received 3 mg (185 MBq) of $^{99m}$Tc-GSA (Nihon Medi-Physics, Nishinomiya, Japan) as a bolus dose into an antecubital vein. Images were obtained with a large field-of-view gamma camera (Picker PRISM-2000, Picker Prism International, Cleveland, OH) equipped with a high resolution, parallel-hole collimator centered on the liver and the precordium. Sequential abdominal digital images (128x128
matrixes) were acquired to an on-line nuclear data processor (Odyssey™ Series, Picker Prism International) at 30 sec/frame for the first 16 minutes after the injection. Hepatic single-photon emission CT (SPECT) images were acquired by axial or coronary imaging after the dynamic study (Fig. 1b) [23]. Each set of projection data was obtained in a 128x128 matrix, and 120 projections (3 degrees/step, 15 sec/projection) were acquired. A Butterworth filter was used as the pre-reconstruction filter, and final reconstruction was performed with a Ramp filter. Attenuation correction was performed with Chang’s method [24], and a value of 0.09 cm⁻¹ was used as the effective attenuation correction coefficient. Transaxial SPECT images were reconstructed with 3.91 mm-slice thickness. The border between the right and left lobe of the liver was manually determined through the gallbladder bed and inferior vena cava. A cut-off level was set at 40% of the maximum counts of the liver because the result closest to the actual volume was obtained in a phantom study (not yet published). The composite image of CT and ⁹⁹mTc-GSA was constructed by Ziostation.

**Statistical analysis**

All continuous data are expressed as mean ± SD. Data for different groups were compared using one-way analysis of variance (ANOVA). Chi-square test was used for comparison of categorical variables. Differences between groups were analyzed by Fisher’s exact test or Scheffe’s multiple comparison test. Correlations between two parameters were examined by calculating the Pearson’s correlation coefficient. The 95% confidence intervals for each correlation were calculated. A two-tailed P value < 0.05 was considered significant. StatView Software for Windows, version 5.0 (SAS Institute, Inc., Cary, NC) was used for all statistical analyses.
RESULTS

Results of PVE

No serious morbidity or mortality was recorded during the 3 weeks after PVE.

CT volume parameters

CT volume parameters estimated before surgery were as follows: total hepatic volume, 1080±240 cm$^3$ (range: 745-1582 cm$^3$); right hemi-liver volume, 714±200 cm$^3$ (range: 400-1095 cm$^3$); and left hemi-liver volume, 358±102 cm$^3$ (range: 176-609 cm$^3$). The proportion of the total liver occupied by the right hemi-liver estimated before surgery was 66±7% (range: 50-78%). Total hepatic volume after PVE (1093±227 cm$^3$) did not differ significantly from that before PVE (p=0.65). After PVE, the volumes of the embolized and non-embolized liver were 623±207 cm$^3$ (a decrease of 7.8%, $-72±108$ cm$^3$) and 470±130 cm$^3$ (an increase of 7.8%, $+111±91$ cm$^3$), respectively. Both the decrease in the volume of the embolized right liver and the increase in the volume of non-embolized left liver were significant (p<0.001).

RI volume parameters

RI volume parameters estimated before surgery were: total hepatic volume, 968±231 cm$^3$ (range: 804-1219 cm$^3$); right hemi-liver volume, 613±214 cm$^3$ (range: 132-1017 cm$^3$); and left hemi-liver volume, 355±124 cm$^3$ (range: 202-672 cm$^3$). RI volume parameters did not differ significantly from CT volume parameters. The proportion of the total liver occupied by the right hemi-liver estimated before surgery was 63±9% (range: 21-79%). Total hepatic volume after PVE (940±214 cm$^3$) did not differ significantly from that before PVE (p=0.78). After PVE, the volumes of the embolized and non-embolized liver were 440±205 cm$^3$ (a decrease of 16.5%, $-173±175$ cm$^3$) and 500±209 cm$^3$ (an increase of 16.5%, $+145±137$ cm$^3$), respectively. Both the decrease in the volume of the
embolized right liver and the increase in the volume of non-embolized left liver were significant (p<0.001).

**Comparison of CT and RI volume parameters**

Changes in volume parameters in the embolized and non-embolized liver were significantly higher for RI than for CT (p=0.003). Before PVE, a significant positive correlation between CT and RI volume parameters in the embolized and non-embolized liver was observed (r=0.75 and 0.69, respectively)(p<0.001) in the embolized and non-embolized liver. The 95% confidence intervals for each correlation was ranged between 0.499 and 0.886, and between 0.399 and 0.856, respectively. The correlation between CT and RI volume parameters was also significant in the embolized and non-embolized liver after PVE (r=0.69 and 0.51, respectively)(p=0.01). The 95% confidence intervals for each correlation was ranged between 0.397 and 0.855, and between 0.136 and 0.758, respectively. However, the correlation between changes in CT and RI volume parameters after PVE was not significant in either the embolized or non-embolized liver (r=-0.17 and -0.03, respectively)( p=0.36 and p=0.88, respectively). The 95% confidence intervals for each correlation was ranged between -0.537 and 0.250, and between -0.428 and 0.378, respectively.

**Parameters associated with changes in liver volume**

Tables 1-3 show the relationship between hepatic volume and various clinical and laboratory parameters. Gender, background liver disease, and embolization substance were not significantly related to changes in hepatic volumes after PVE, although changes of embolized liver volumes by CT and RI tended to be lower in cirrhosis than in other conditions. With respect to CT volume parameters, only ALP level was negatively
correlated with changes in the embolized (decreased) liver and only platelet count was associated with changes in the non-embolized (hypertrophic) liver (Table 2). On the other hand, with respect to RI volume, pre-PVE portal pressure; ICGR15; and serum levels of hyaluronic acid, total bilirubin, albumin, and ALP were significantly correlated with changes in the embolized liver, and platelet count was significantly correlated with increased volume of the non-embolized liver.
DISCUSSION

Following PVE, previous reports have shown that the morphological volumes of the embolized and non-embolized liver change dramatically and rapidly [9, 25, 26], and our present study confirmed similar results [21, 27]. PVE is an established strategy for major hepatectomy in patients with impaired liver function, hilar bile duct carcinoma, or hepatocellular carcinoma [3-11]. Atrophy of the embolized lobe and hypertrophy of the non-embolized lobe were also observed even in the impaired liver in the present study as well as our previous preliminary studies [21, 27]. Our present results showed that changes in hepatic volumes did not differ significantly between normal and impaired liver, although changes of liver volume tended to be lower in liver cirrhosis. Therefore, PVE can be applied for even patients with diseased liver as previously reported [26, 28].

Before performing PVE, surgeons would like to predict the extent of changes in the right and left lobes as a result of PVE. Based on our results and those of others, a 9-30% increase in the volume of the non-embolized lobe (estimated remnant liver) can be expected [6, 25, 26]. This supports the findings of Manizate et al., who emphasized the significance of PVE as a stress test of the liver’s regenerative capacity [30].

In patients who undergo PVE, background liver status varies, as in the present series, because PVE is often influenced by impaired liver function. In such heterogeneous subjects, we usually determine the indications for hepatectomy based on common criteria. Functional evaluation in each liver area is used to determine treatment. Embolization substances changed during the period of this study; however, complete embolization of the targeted portal vein was accomplished in the present series. In the present preliminary study, we focused on the changes of functional volume after PVE in comparison with morphological volume detected by CT. After PVE, the function of each liver cell may
deteriorate. Our previous study clarified a discrepancy between morphological volume and functional volume assessed by $^{99m}$Tc-GSA in cases with biliary obstruction [31]. The present results showed a significant difference between both volumes after PVE. We previously examined predictive factors for the degree of change of hepatic morphological volume after PVE [11]; however, few parameters were correlated with these morphological volumes. Based on the results using $^{99m}$Tc-GSA, we hypothesized that more correlated parameters could be clarified by conducting a comparison with functional liver volume because functional liver volume changed more dramatically than morphological liver volume, and because functional liver volume better reflects the extent of impairment caused by biliary obstruction or reduced hepatic perfusion. [7, 13, 21, 32, 33] As expected, more correlated preoperative parameters could be observed in the present study: pre-PVE portal pressure, serum hyaluronic acid level, ICGR15, total bilirubin, albumin level and ALP level were correlated with decreased liver volume, and bilirubin level and platelet count were correlated with hypertrophic liver volume. Portal hypertension reflects impairment of the liver secondary to chronic hepatitis, and it increases operative risk [34, 35]. In portal hypertension, there may already be impairment of the hepatocellular function or a decrease of functional liver cell mass resulting from chronic endothelial-cellular damage. Hence the atrophic response in liver with portal hypertension would be lower than in normal portal pressure [36]. After PVE, portal pressure dramatically increased in some cases and, therefore, we expected that increased portal pressure was correlated with changes of hepatic volumes after PVE. However, post-PVE pressure and increased portal pressure were not correlated with changes of functional volume in the present study. Jensen et al. reported that acute portal hypertension did not induce severe hypoxic damage in the functional part of the liver [37]
and, therefore, hepatic function could be preserved by an immediate increase of portal pressure from PVE. This increase of pressure may be correlated with the extent of the vascular bed in the embolized or remnant liver. With respect to PVE effect, pre-PVE portal pressure is thought to be a useful predictor.

Serum hyaluronic acid level correlates well with degree of fibrosis or impaired endothelial cell function in non-parenchymal liver cells [38, 39]. Our previous study showed that hyaluronic acid level was an independent predictive marker for postoperative complications such as uncontrolled ascites or hepatic failure [22]. This morbidity may be affected by potential liver function. Yachida et al. [39] also reported that hyaluronic acid level is a good predictor of amount of hypertrophy of the non-embolized lobe. Serum hyaluronic acid level also reflects endothelial cell damage of hepatic sinusoids by stress [40]. Therefore, sinusoidal damage from PVE may affect the decrease of liver volume in the embolized lobe.

ICGR15 and total bilirubin level are widely known functional parameters of the liver and are the most reliable tests to predict postoperative outcome [1, 4, 12, 18, 41]. In the present study, these parameters were correlated with the volume decrease in the embolized lobe.

As in our previous study concerning morphological liver volume [11], ALP level was negatively correlated with embolized liver volume. Increased ALP level might reflect tumor or hepatic damage due to tumor location [42, 43]. Furthermore, ALP is a prognostic marker of liver failure after hepatectomy [44]. Since hepatic tumors are predominantly located in the embolized lobe, hepatic cellular damage might be accelerated by portal embolization. However, recognition of this parameter as a specific predictor may be difficult because the mechanism is unknown.
In any case, the present results suggest that many sensitive markers could be useful to predict functional atrophy of the embolized liver.

We found fewer parameters related to increased volume in the non-embolized liver than to decreased volume in the embolized liver. This result could suggest that no dramatic alteration of liver function occurs by 2 weeks after PVE. Our previous report showed that hypertrophy of the remnant liver still progressed remarkably after hepatectomy in patients who underwent preoperative PVE [27]. Therefore, the regenerative capacity of the non-embolized liver should remain at this time after PVE. However, PVE may impede regeneration immediately after hepatectomy and thereby help overcome hepatic failure. The mechanism of hypertrophy of the left lobe might differ between PVE and hepatectomy [32]. Atrophy of the embolized lobe is thought to result from apoptosis [45], and because the hepatic parenchyma and its hepatic function remain after PVE, the extent of hypertrophy may be limited when compared with after hepatectomy. Unlike the non-embolized liver, the embolized liver may incur a great functional loss by embolization.

Platelet count also reflects the severity of liver injury in patients with chronic viral hepatitis [30]. Murata et al. reported that platelets promote liver regeneration in the early period in a murine model [46]. Furthermore, Alkozai et al. reported that a low platelet count immediately after partial hepatectomy was associated with delayed recovery of liver function [47]. Based on these results, platelet count appears to be a sensitive marker with respect to liver regeneration or functional recovery after liver stress or injury. Therefore, parameter alone would be useful to predict regeneration of the remnant liver after PVE.
Because PVE can also potentially induce adverse effects such as liver failure, thrombosis, intraabdominal bleeding, or cancer progression [48], the procedure should be avoided in patients who are predicted to have an inadequate effect. A predictive scoring system for changes in hepatic volume from PVE is desirable to evaluate the effect and to determine the indications of this procedure. To our knowledge, few previous studies have reported a systematic analysis using such predictors [17]. The present study is a preliminary trial, due to the small number of subjects and the heterogeneous patient background. Our next step is to attempt to design a scoring system in larger subject group, using the candidate parameters clarified in the present study. Furthermore, determining the relationship between prediction of PVE effect or measuring functional volume, and post-hepatectomy liver functions or outcomes will be necessary in order to clarify the clinical benefit of resectability.

In conclusion, we have reported the changes in hepatic volume measured by CT and RI with $^{99m}$Tc-GSA liver scintigraphy before and after portal vein embolization in patients scheduled for extensive hepatectomy. A correlation between CT and RI volume parameters was observed; however, this correlation decreased after PVE. Although few parameters were correlated with changes of CT volume after PVE, more parameters (portal pressure; ICGR15; serum levels of hyaluronate, bilirubin, albumin, and ALP; and platelet count) were significantly correlated with changes of RI volume. Based on the preliminary data in the present results, these parameters are useful predictors of functional PVE effect and a predictive scoring system should be established in future studies.
Figure legend

FIG 1. Three dimensional measurement of CT volume (a) and RI volume (b) in the right and left hemi-liver.

(a)
REFERENCES


### TABLE 1  Relationship between Changes in Hepatic Volume after Portal Vein Embolization and Clinicopathological Parameters

<table>
<thead>
<tr>
<th>Gender</th>
<th>Male (n=15)</th>
<th>Female (n=9)</th>
<th>Male (n=15)</th>
<th>Female (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Background liver</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (n=12)</td>
<td>62±124</td>
<td>96±82</td>
<td>191±130</td>
<td>116±94</td>
</tr>
<tr>
<td>Chronic viral hepatitis (n=3)</td>
<td>127±121</td>
<td>94±65</td>
<td>285±142</td>
<td>72±28</td>
</tr>
<tr>
<td>Cirrhosis (n=2)</td>
<td>7±4</td>
<td>106±2</td>
<td>36±33</td>
<td>60±90</td>
</tr>
<tr>
<td>Obstructive jaundice (n=7)</td>
<td>62±124</td>
<td>148±126</td>
<td>134±254</td>
<td>250±186</td>
</tr>
<tr>
<td>Embolization substance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sponge powder + thrombin (n=7)</td>
<td>64±109</td>
<td>114±60</td>
<td>202±186</td>
<td>86±52</td>
</tr>
<tr>
<td>Lipiodol + Sponzel (n=5)</td>
<td>67±45</td>
<td>99±154</td>
<td>50±242</td>
<td>187±135</td>
</tr>
<tr>
<td>EOI (n=12)</td>
<td>80±131</td>
<td>116±82</td>
<td>208±122</td>
<td>162±170</td>
</tr>
</tbody>
</table>

Data are mean±SD
**TABLE 2** Correlation between Parameters and Changes in CT Volume Parameter after Portal Vein Embolization

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Decrease in embolized liver volume (cm³)</th>
<th>95% Confidence intervals (upper/lower limit)</th>
<th>Increase in non-embolized liver volume (cm³)</th>
<th>95% Confidence intervals (upper/lower limit)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.152</td>
<td>-0.268/0.523</td>
<td>-0.079</td>
<td>-0.467/0.335</td>
</tr>
<tr>
<td>Pre-PVE portal pressure (mmHg)</td>
<td>0.112</td>
<td>-0.305/0.493</td>
<td>-0.026</td>
<td>-0.425/0.381</td>
</tr>
<tr>
<td>Post-PVE portal pressure (mmHg)</td>
<td>0.090</td>
<td>-0.325/0.476</td>
<td>-0.298</td>
<td>-0.626/0.112</td>
</tr>
<tr>
<td>Increase of portal pressure (mmHg)</td>
<td>0.011</td>
<td>-0.394/0.413</td>
<td>-0.373</td>
<td>-0.675/0.036</td>
</tr>
<tr>
<td>Hyaluronate (ng/ml)</td>
<td>0.044</td>
<td>-0.366/0.440</td>
<td>0.041</td>
<td>-0.368/0.437</td>
</tr>
<tr>
<td>ICGR15 (%)</td>
<td>0.118</td>
<td>-0.300/0.498</td>
<td>0.406</td>
<td>0.003/0.696</td>
</tr>
<tr>
<td>LHL15</td>
<td>-0.105</td>
<td>-0.488/0.312</td>
<td>-0.030</td>
<td>-0.428/0.378</td>
</tr>
<tr>
<td>Total bilirubin (mg/dl)</td>
<td>-0.114</td>
<td>-0.495/0.303</td>
<td>0.072</td>
<td>-0.341/0.462</td>
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<tr>
<td>Alanine aminotransferase (IU/l)</td>
<td>-0.123</td>
<td>-0.502/0.295</td>
<td>0.407</td>
<td>0.004/0.696</td>
</tr>
<tr>
<td>Prothrombin activity (%)</td>
<td>0.130</td>
<td>-0.289/0.507</td>
<td>0.048</td>
<td>-0.362/0.443</td>
</tr>
<tr>
<td>Platelet count (/mm³)</td>
<td>-0.121</td>
<td>-0.500/0.297</td>
<td>0.225</td>
<td>-0.196/0.576</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>-0.057</td>
<td>-0.450/0.355</td>
<td>0.360</td>
<td>-0.051/0.667</td>
</tr>
<tr>
<td>Alkaline phosphatase (IU/l)</td>
<td>-0.456*</td>
<td>-0.726/-0.064</td>
<td>0.290</td>
<td>-0.128/0.621</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>0.323</td>
<td>-0.092/0.643</td>
<td>0.393</td>
<td>-0.012/0.687</td>
</tr>
</tbody>
</table>

*: p<0.05

ICG: indocyanine green

LHL15: liver uptake ratio at 15 minutes by $^{99}$Tc-GSA liver scintigraphy
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Decrease in embolized liver (cm³)</th>
<th>95% Confidence intervals (upper/lower limit)</th>
<th>Increase in non-embolized liver (cm³)</th>
<th>95% Confidence intervals (upper/lower limit)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.190</td>
<td>-0.551/0.231</td>
<td>0.203</td>
<td>-0.218/0.561</td>
</tr>
<tr>
<td>Pre-PVE portal pressure (mmHg)</td>
<td>-0.488*</td>
<td>-0.745/-0.105</td>
<td>-0.002</td>
<td>-0.405/0.402</td>
</tr>
<tr>
<td>Post-PVE portal pressure (mmHg)</td>
<td>-0.231</td>
<td>-0.580/0.190</td>
<td>0.207</td>
<td>-0.214/0.563</td>
</tr>
<tr>
<td>Increase of portal pressure (mmHg)</td>
<td>0.105</td>
<td>-0.312/0.488</td>
<td>0.302</td>
<td>-0.115/0.629</td>
</tr>
<tr>
<td>Hyaluronate (ng/ml)</td>
<td>-0.494*</td>
<td>-0.748/-0.113</td>
<td>0.116</td>
<td>-0.302/0.496</td>
</tr>
<tr>
<td>ICGR15 (%)</td>
<td>-0.548*</td>
<td>-0.779/-0.186</td>
<td>-0.086</td>
<td>-0.473/0.329</td>
</tr>
<tr>
<td>LHL15</td>
<td>0.221</td>
<td>-0.200/0.573</td>
<td>0.286</td>
<td>-0.133/0.618</td>
</tr>
<tr>
<td>Total bilirubin (mg/dl)</td>
<td>-0.413*</td>
<td>-0.700/-0.012</td>
<td>0.227</td>
<td>-0.194/0.578</td>
</tr>
<tr>
<td>Alanine aminotransferase (IU/l)</td>
<td>0.175</td>
<td>-0.246/0.540</td>
<td>0.425*</td>
<td>0.026/0.707</td>
</tr>
<tr>
<td>Prothrombin activity (%)</td>
<td>0.043</td>
<td>-0.367/0.439</td>
<td>0.047</td>
<td>-0.363/0.442</td>
</tr>
<tr>
<td>Platelet count (/mm³)</td>
<td>-0.089</td>
<td>-0.475/0.326</td>
<td>0.546*</td>
<td>0.183/0.778</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>0.405*</td>
<td>0.002/0.695</td>
<td>-0.263</td>
<td>-0.602/0.157</td>
</tr>
<tr>
<td>Alkaline phosphatase (IU/l)</td>
<td>-0.455*</td>
<td>-0.725/-0.063</td>
<td>0.304</td>
<td>-0.113/0.630</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>0.222</td>
<td>-0.199/0.574</td>
<td>0.051</td>
<td>-0.360/0.445</td>
</tr>
</tbody>
</table>

*: p<0.05
ICG, LHL15; see in Table 2