Minimally Invasive Therapy. 2014;23:241–246

informa
healthcare

ORIGINAL ARTICLE

Comparison of Tc-99m GSA scintigraphy and CT volumetry for evaluation in portal vein embolization

YUMIKO KONO[1], SHUJI KARIYA[1], ATSUSHI KOMEMUSHI[1], MIYUKI NAKATANI[1], RIE YAGI YOSHIDA[1], SATOSHI SUZUKI[1], SUNG KIL HA-KAWA[1], KEITA UTSUNOMIYA[1], YASUHIRO UENO[1], SOHEI SATOI[2], MASAKI KAIBORI[2], MASANORI KON[2], NOBORU TANIGAWA[1]

[1]*Department of Radiology, Kansai Medical University, Osaka, Japan, and* [2]*Department of Surgery, Kansai Medical University, Osaka, Japan*

Abstract

Purpose: To determine the correlation of the rate of change of each future remnant liver (FRL) before and after portal vein embolization (PVE), by CT volumetry and Tc-99m galactosyl human serum albumin scintigraphy (GSA scintigraphy). ***Material and methods:*** From December 2007 to July 2012, ten patients underwent PVE before hepatic resection. CT volumetry and GSA scintigraphy were performed before and after PVE. The FRL was divided at Cantlie's line for CT volumetry, and volume change rates before and after PVE were calculated. The maximum removal rate (Rmax) was calculated using a radiopharmacokinetic model in GSA scintigraphy. The FRL Rmax change rates before and after PVE were calculated. The correlation between the volume change rates and the Rmax change rates was analyzed. ***Results:*** The FRL volume change rate was 1.28 ± 0.26 (mean ± SD); the FRL hypertrophied in all patients significantly ($p = 0.005$). The FRL Rmax change rate was 1.66 ± 0.75; excluding one patient, there was significant FRL Rmax increase ($p = 0.022$). Although both increased significantly, no correlation between the volume change rate and the Rmax change rate was observed. ***Conclusion:*** No correlation was observed between the FRL volume rate and the Rmax rate.

Key words: *PVE, CT volumetry, GSA scintigraphy, Rmax*

Introduction

Liver failure due to lack of remaining liver function is a serious complication after hepatic resection. Portal vein embolization (PVE) before hepatic resection has been used to prevent this complication. PVE was established by Kinoshita et al. in 1986 to increase the future remnant liver (FRL) before hepatic resection (1). However, the FRL does not always hypertrophy after PVE, and an error in assessment may lead to post-hepatic resection liver failure. CT volumetry for FRL volume change rates before and after PVE has been used for morphological assessment (2–5). Tc-99m galactosyl serum albumin scintigraphy (GSA scintigraphy), compared to CT volumetry for morphological assessment, is useful for functional assessment of the FRL before surgery (6,7). However, functional assessment by Tc-99m GSA scintigraphy of the FRL after PVE has seldom been reported. After PVE, there is rapid compensatory hypertrophy of the FRL, but the rapid volume increase of the hypertrophied FRL may not correlate with an increase in liver function. Therefore, in this study, CT volumetry and GSA scintigraphy were performed before and after PVE, change rates in the FRL were calculated, and the correlation between test findings was examined.

Material and methods

The study protocols for this retrospective analysis were approved by our institutional review board.

Correspondence: S. Kariya, Department of Radiology, Kansai Medical University, 2-5-1 Shinmachi, Hirakata-shi, Osaka, 573-1010, Japan. Fax: +81 72 804 2547. E-mail: kohnoy@hirakata.kmu.ac.jp

ISSN 1364-5706 print/ISSN 1365-2931 online
DOI: 10.3109/13645706.2014.897955

Table I. Patient characteristics.

				PVE	
Patient No.	Age (years)/Sex	Disease	Child-Pugh score	Embolized portal vein	Material
1	55/M	BDC	6	Right	NBCA + Iodized oil
2	57/M	BDC	5	Right	Gelatin sponges + Iodized oil
3	61/M	MT	5	Right	NBCA + Iodized oil
4	62/M	MT	5	Right	NBCA + Iodized oil
5	65/M	GBC	5	Right	NBCA + Iodized oil
6	65/M	BDC	6	Right	Gelatin sponges + Iodized oil
7	67/M	HCC	5	Right	NBCA + Iodized oil
8	70/F	MT	5	Right	NBCA + Iodized oil
9	71/M	BDC	5	Right	Gelatin sponges + Iodized oil
10	76/F	ML	5	Right	NBCA + Iodized oil
Mean ± SD	65 ± 7		5.3 ± 0.5		

PVE: portal vein embolization; BDC: bile duct carcinoma, MT: metastatic carcinoma, GBC: gallbladder carcinoma, HCC: hepatocellular carcinoma, ML: malignant lymphoma; NBCA: n-butyl-2-cyanoacrylate.

The requirement to obtain informed consent was waived. Data were gathered retrospectively by means of a review of clinical records, including images.

Patients

This study included ten patients (eight men, two women; mean age 65 years) who underwent PVE before hepatic resection between December 2007 and July 2012. All patients were Child-Pugh A (Table I).

PVE

All but one case underwent percutaneous transhepatic PVE under sonographic guidance; one case underwent two-step PVE due to concerns about the development of liver failure after PVE, and a second PVE was performed under laparotomy. Percutaneous transhepatic PVE was performed under sonographic guidance. The portal vein in the liver to be resected was punctured, and a catheter was inserted by the Seldinger technique. After portal vein imaging, the portal vein in the liver to be resected was embolized.

Table II. The future remnant liver volume and Rmax change rates before and after portal vein embolization and hepatic complications.

	CT volume (mL)			Rmax (mg/min)			
Patient No.	Before PVE	After PVE	Rate	Before PVE	After PVE	Rate	Hepatic complications
1	535.0	608.0	1.1	0.27	0.41	1.51	
2	529.6	620.0	1.2	0.26	0.34	1.28	Cholangitis after PVE
3	409.0	475.9	1.2	0.22	0.45	2.05	
4	405.1	445.1	1.1	0.24	0.46	1.93	
5	396.1	512.1	1.3	0.16	0.37	2.30	
6	517.5	586.6	1.1	0.21	0.24	1.13	Cholangitis after PVE
7	690.0	774.0	1.1	0.41	0.34	0.83	Liver cirrhosis
8	160.8	311.3	1.9	0.14	0.18	1.28	Insufficient embolization
9	229.8	303.0	1.3	0.19	0.63	3.29	
10	364.6	538.0	1.5	0.33	0.31	0.96	Insufficient embolization
Mean ± SD	423.8 ±154.5	517.4 ±154.5	1.28 ± 154.5	0.25 ± 0.08	0.38 ±0.13	1.7 ± 0.75	

PVE: portal vein embolization.

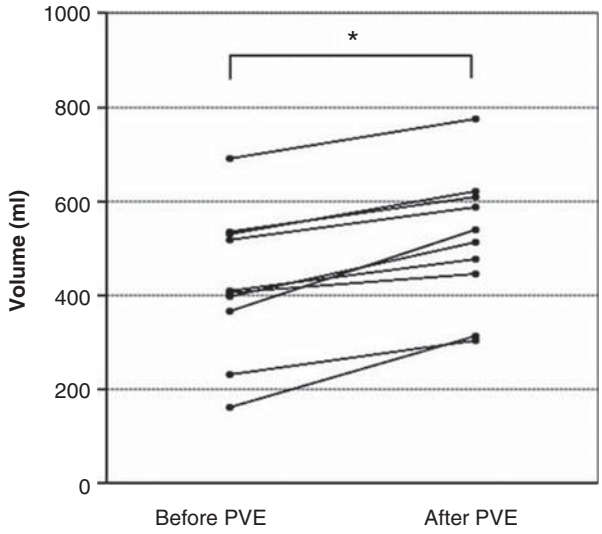

Figure 1. The future remnant liver volume after portal vein embolization. There is non-embolized lobe hypertrophy before and after PVE in all patients, and the volume has increased significantly ($p = 0.005$).

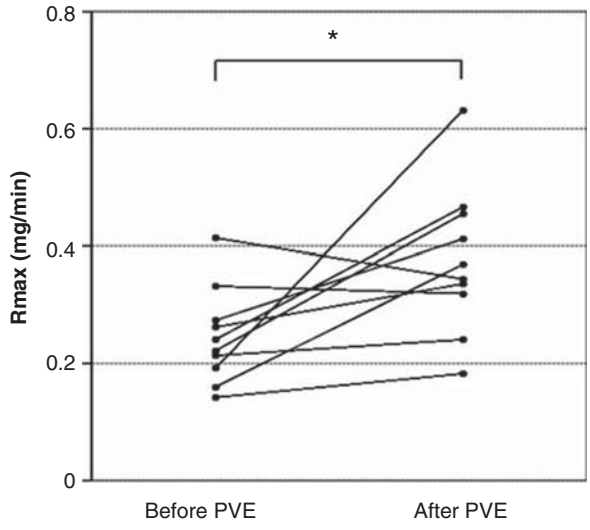

Figure 2. Rmax of future remnant liver after portal vein embolization. Rmax has increased significantly after PVE ($p = 0.022$), but the rate of increase varies among patients.

The embolic material used was a mixture of gelatin sponges and iodized oil (Lipiodol, Laboratoire Guerbet, Roissy, France), a mixture of n-butyl-2-cyanoacrylate (NBCA) (Histacryl-Blue; Braun, Melsungen, Germany) and iodized oil, or a combination of both. PVE was performed under laparotomy in order to approach the portal vein in an antegrade fashion through the venous circulation mesenteric vein; catheter manipulation, imaging, and the embolization methods were the same as for percutaneous transhepatic PVE.

CT volumetry

CT volumetry was performed before and 23 ± 3 days after PVE. The CT scanner was an Aquilion 64 (Toshiba Medical Systems, Tokyo, Japan) or Somatom Sensation 16 (Siemens AG, Erlangen, Germany). First, 100 mL of iopamidol (Bystage 370, Teva Pharma Japan Inc., Aichi, Japan) was injected intravenously at 3 mL/sec using a power injector, and then arterial phase imaging and portal venous phase imaging were performed. The delay time was 40 sec for arterial phase imaging and 90 sec for portal venous phase imaging. Imaging from the diaphragm to the inferior pole of the right kidney was performed under the following conditions: Collimation of 1.5 mm (Aquilion 64) or 1 mm (Somatom Sensation 16) and pitch of 0.844 (Aquilion 64) or 0.8–0.9 (Somatom Sensation 16). From the portal venous phase data, three dimensions volumes were constructed using VirtualPlace (AZE Ltd., Tokyo, Japan). The future remnant liver (FRL) was divided at Cantlie's line for volumetry, and volume change rates before and after PVE were calculated.

$$\text{Volume change rate} = \text{FRL volume after PVE} / \text{FRL volume before PVE}$$

GSA scintigraphy

GSA scintigraphy was performed before and 23 ± 4 days after PVE. First, 3 mg of Tc-99m GSA (185 MBq; Nihon Medi-Physics, Tokyo, Japan) were injected intravenously, followed by dynamic acquisition for 20 min at 30 sec/ flame using a gamma camera (E.CAM Signature, Toshiba, Tokyo, Japan). A high-resolution, parallel-hole collimator was used with the heart and liver as the center. Next, single-photon emission computed tomography (2 rotations/6 min) was performed. Image processing was done using a GMS-7700R (Toshiba Medical Systems). The maximum removal rate (GSA-Rmax) was calculated using a radiopharmacokinetic model (8). Rmax was calculated from SPECT imaging for each liver lobe divided at Cantlie's line. Then, the FRL Rmax change rates before and after PVE were calculated.

$$\text{Rmax change rate} = \text{FRL Rmax after PVE} / \text{FRL Rmax before PVE}$$

Comparison examination

The correlation between the calculated volume change rates and the Rmax change rates was analyzed.

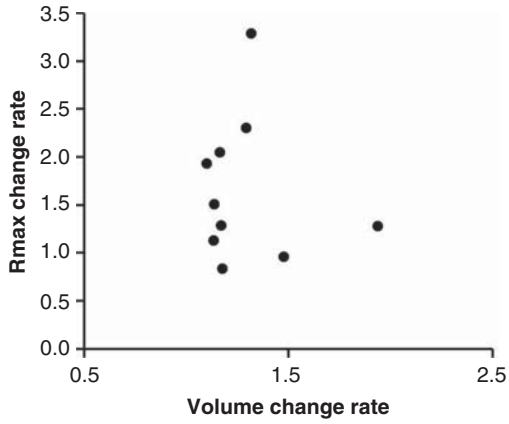

Figure 3. Correlation between CT volumetry and Tc-99m GSA scintigraphy in all patients. $p = 0.803$, r = 0.105.

Statistical methods

The Wilcoxon signed-rank test was used to analyze volume change rates and Rmax change rates before and after PVE. The correlation between volume change rates and Rmax change rates was examined by Spearman's rank correlation analysis. The level of statistical significance was $p < 0.05$.

Results

Table II and Figures 1 and 2 show the FRL changes before and after PVE. The FRL volume change rate from before to after PVE was 1.28 ± 0.26 (mean ± SD); the FRL hypertrophied in all patients, and the increase was significant ($p = 0.005$). The FRL Rmax change rate was 1.66 ± 0.75 (mean ± SD); in all but one patient, there was an FRL Rmax increase. Again, the increase was significant ($p = 0.022$). Although both increased significantly, no correlation between the volume change rate and the Rmax change rate was observed ($p = 0.803$, r = 0.105) (Figure 3).

Evaluation in the "GSA good response group," with higher than the median Rmax change rate on Tc-99m GSA scintigraphy showed a strong positive correlation between the FRL volume change rate and the Rmax change rate ($p = 0.037$, r = 0.826). However, evaluation in the "GSA poor response group", with lower than the median Rmax change rate showed no correlation ($p = 0.872$, r = 0.361) (Figure 4a and b).

Discussion

In the present study, most of the cases which became the adaptation of percutaneous transhepatic portal embolization (PTPE) involved mildly to moderately damaged liver instead of normal liver. It was predicted that more time would be needed to regenerate than normal. Thus, by agreement with the surgical department, four to six weeks after PTPE, just before the operation, is the more precise and reasonable period to evaluate future remnant liver function with the result of CT volumetry. Similar to the present study, other studies have reported that, before PVE for a right lobe resection, a 50% increase was seen in FRL volume on CT volumetry within six weeks after PVE (9). However, the increase was 28% in the present study, a value lower than in previous studies. The reason for this difference may be that CT volumetry in the present study was performed a mean of 22 days after PVE, earlier than in the other reports, so that the present evaluation may have occurred during the hypertrophy process.

In another report on Tc-99m GSA scintigraphy, the GSA index, calculated from the blood clearance index (HH15) and the receptor index (LHL15), was used to

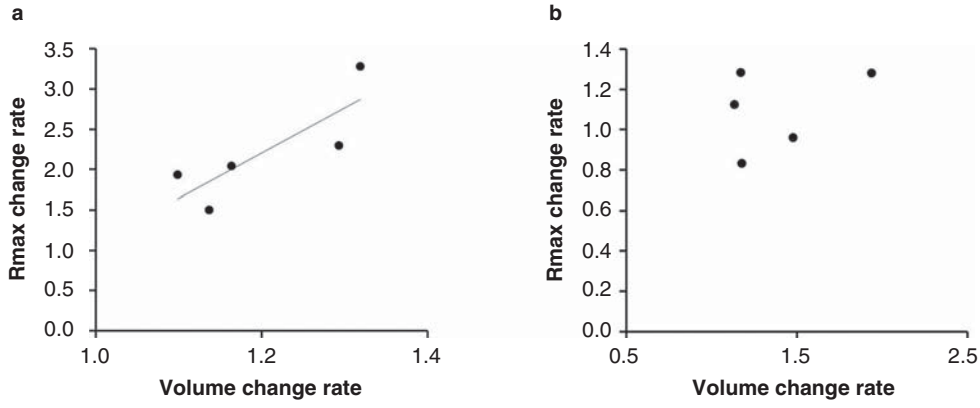

Figure 4. Correlation between CT volumetry and Tc-99m GSA scintigraphy in the GSA good response group and the GSA poor response group. (a) GSA good response group: $p = 0.037$, r = 0.826, (b) GSA poor response group: $p = 0.872$, r = 0.361.

evaluate FRL function. The FRL GSA index increased 30% on evaluation two weeks after PVE (10). Kawa et al. reported that Rmax was more useful than the GSA index to evaluate liver function (11). In the present study, Rmax was also used to evaluate FRL function.

The present study found no overall correlation between CT volumetry and Tc-99m GSA scintigraphy. The GSA poor response group, which we believe was the reason for this result, included one patient with cirrhosis in the background liver and two patients who had cholangitis after PVE. Tc-99m GSA scintigraphy, by assessing receptor density and distribution, can evaluate function in each hepatic lobe. Therefore, Tc-99m GSA scintigraphy also correlates with fibrosis in cirrhosis (12) and is useful to evaluate living donor liver transplantation in patients with cirrhosis and chronic inflammation (7). To evaluate functional reserve before a standard hepatectomy in which PVE is not performed, Tc-99m GSA scintigraphy is reported to be more useful than CT volumetry to predict postoperative liver failure (13). However, CT volumetry is used more often than Tc-99m GSA scintigraphy to evaluate FRL function after PVE.

Yokoyama et al. reported that, in compensatory hypertrophy of non-embolized lobes after PVE, mediators such as inflammatory cytokines, vasoregulators, growth factors, eicosanoids, and various hormones play a role in hepatocyte regeneration (14). Therefore, infection, bile duct obstruction, diabetes, or malnutrition can inhibit these mediators, thus reducing hepatocyte regeneration. In a study of liver specimens after resection, Matsui et al. reported that, because the stroma is increased in cirrhotic patients, hepatocyte volume more accurately reflects hepatic functional reserve than liver volume (15). However, according to Wakabayashi et al., liver volume and liver blood flow are not proportional to hepatocyte volume (16). Based on these reports, in patients with cirrhosis, because CT volumetric evaluation also includes enlarged extracellular components such as stroma and sinusoids, it may not accurately assess hepatocyte volume.

Hepatic resection has been increasing in minimally invasive surgery so that surgical indication is expanding (17). Accurate evaluation of liver function is more indispensable. In patients with liver disease such as cirrhosis or cholangitis, Tc-99m GSA scintigraphy should be used to evaluate liver function after PVE. In patients without such lesions, evaluation by CT volumetry may be acceptable. In addition, if portal vein embolization is insufficient, evaluation of liver function by Tc-99m GSA scintigraphy may be necessary.

The limitations of this study are its retrospective nature and small number of cases.

Conclusions

When all cases were included in the analysis, no correlation was observed between the FRL volume rate and the Rmax rate, but a highly positive correlation was observed between the FRL volume rate and the Rmax rate in the GSA good responder group.

Declaration of interest: The authors declare that they have no conflict of interest.

References

1. Kinoshita H, Sakai K, Hirohashi K, Igawa S, Yamasaki O, Kubo S. Preoperative portal vein embolization for hepatocellular carcinoma. World J Surg. 1986;10:803–8.
2. van Lienden KP, van den Esschert JW, de Graaf W, Bipat S, Lameris JS, van Gulik TM, et al. Portal vein embolization before liver resection: a systematic review. Cardiovasc Intervent Radiol. 2013;36:25–34.
3. Thakrar PD, Madoff DC. Preoperative portal vein embolization: an approach to improve the safety of major hepatic resection. Semin Roentgenol. 2011;46:142–53.
4. Madoff DC, Abdalla EK, Gupta S, Wu TT, Morris JS, Denys A, et al. Transhepatic ipsilateral right portal vein embolization extended to segment IV: improving hypertrophy and resection outcomes with spherical particles and coils. J Vasc Interv Radiol. 2005;16:215–25.
5. Simoneau E, Aljiffry M, Salman A, Abualhassan N, Cabrera T, Valenti D, et al. Portal vein embolization stimulates tumour growth in patients with colorectal cancer liver metastases. HPB (Oxford). 2012;14:461–8.
6. Ha-Kawa SK, Tanaka Y. A quantitative model of technetium-99m-DTPA-galactosyl-HAS for the assessment of hepatic blood flow and hepatic binding receptor. J Nucl Med. 1991;32:2233–40.
7. Kaibori M, Ha-Kawa SK, Maehara M, Ishizaki M, Matsui K, Sawada S, et al. Usefulness of Tc-99m-GSA scintigraphy for liver surgery. Ann Nucl Med. 2011;25:593–602.
8. Kwon AH, Ha-Kawa SK, Uetsuji S, Inoue T, Matsui Y, Kamiyama Y. Preoperative determination of the surgical procedure for hepatectomy using technetium-99m-galactosyl human serum albumin (99mTc GSA) liver scintigraphy. Hepatology. 1997;25:426–9.
9. Uhl M, Euringer W, Makowiec F, Adam U, Schneider A, Langer M. Portal vein embolization preparation for major hepatic resection: a new standard in liver surgery. Rofo. 2007;179:31–7.
10. Kubo S, Shiomi S, Tanaka H, Shuto T, Takemura S, Mikami S, et al. Evaluation of the effect of portal vein embolization on liver function by (99m)Tc-galactosyl human serum albumin scintigraphy. J Surg Res. 2002;107:113–18.
11. Ha-Kawa SK, Tanaka Y, Hasebe S, Kuniyasu Y, Koizumi K, Ishii Y, et al. Compartmental analysis of asialoglycoprotein receptor scintigraphy for quantitative measurement of liver function: a multicentre study. Eur J Nucl Med. 1997; 24:130–7.
12. Yoshida M, Shiraishi S, Sakaguchi F, Utsunomiya D, Tashiro K, Tomiguchi S, et al. A quantitative index measured on 99mTc GSA SPECT/CT 3D fused images to evaluate severe fibrosis in patients with chronic liver disease. Jpn J Radiol. 2012;30:435–41.

13. Yokota R, Ishizu H, Kondo Y, Okada K, Masuko H, Hata T, et al. Prediction of liver failure after right hepatectomy with 99mTc GSA SPECT scintigraphy. Jpn J Gastroenterol Surg. 2006;39:429–34.
14. Yokoyama Y, Nagino M, Nimura Y. Mechanisms of hepatic regeneration following portal vein embolization and partial hepatectomy: a review. World J Surg. 2007;31:367–74.
15. Matsui Y, Tu W, Kitade H, Nakagawa A, Kamiya T, Kwon AH, et al. Hepatocyte volume as an indicator of hepatic functional reserve in cirrhotic patients with liver tumours. J Gastroenterol Hepatol. 1996;11:540–5.
16. Wakabayashi H, Nishiyama Y, Ushiyama T, Maeba T, Maeta H. Evaluation of the effect of age on functioning hepatocyte mass and liver blood flow using liver scintigraphy in preoperative estimations for surgical patients: comparison with CT volumetry. J Surg Res. 2002;106: 246–53.
17. Cipriani F, Catena M, Ratti F, Paganelli M, Ferla F, Aldrighetti L. LESS technique for liver resection: the progress of the mini-invasive approach: a single-centre experience. Minim Invasive Ther Allied Technol. 2012; 21:55–8.