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Hepatectomy simulation discrepancy between radionuclide receptor imaging and CT volumetry: influence of decreased unilateral portal venous flow

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Background: Regional dysfunction demonstrated by Tc-99m-diethylenetriamine-penta-acetic acid-galactosyl human serum albumin (GSA) scintigraphy due to regional decrease in the portal venous flow has previously been reported. In this study, we call attention to the significance of unilateral portal venous flow decrease for preoperative hepatectomy simulation, and evaluate the hepatectomy simulation discrepancy between Tc-99m-GSA single-photon emission computed tomography (SPECT) and CT volumetry. ***Methods:*** Twenty-four hepatectomy candidates underwent preoperative hepatectomy simulation by both Tc-99m-GSA SPECT and CT volumetry. Both anatomical and functional resection ratios were calculated by means of CT volumetry and Tc-99m-GSA SPECT, respectively. The differences and ratios between anatomical and functional resection ratios were calculated in all patients, and compared in patients with and without unilateral portal venous flow decrease. ***Results:*** Anatomical resection ratios were 28.0 ± 11.7 (mean ± standard deviation) in patients with unilateral portal venous flow decrease, and 42.1 ± 15.7 in patients without unilateral portal venous flow decrease ($p = 0.0127$). Functional resection ratios were 14.7 ± 12.8 in patients with unilateral portal venous flow decrease and 40.5 ± 14.6 in patients without ($p = 0.0004$). The differences between anatomical and functional resection ratios were 13.0 ± 7.9 in patients with unilateral portal venous flow decrease and 5.6 ± 3.1 in patients without ($p = 0.0099$). The ratios between anatomical and functional resection ratios were 0.48 ± 0.29 in patients with unilateral portal venous flow decrease and 0.86 ± 0.10 in patients without ($p = 0.0018$). In 12 of the 13 patients with unilateral portal venous flow decrease, anatomical resection ratios were found to be larger than functional resection ratios, whereas this happened in only 6 of 11 patients without unilateral portal venous flow decrease ($p = 0.0063$). ***Conclusion:*** Unilateral portal venous flow decrease is suspected to be a major factor in the discrepancy between hepatectomy simulations with radionuclide receptor imaging and CT volumetry.

Key words: ^{99m}Tc-GSA, receptor imaging, CT volumetry, hepatectomy simulation, portal venous flow

INTRODUCTION

Tc-99m-diethylenetriamine-penta-acetic acid-galactosyl human serum albumin (GSA) is an analog ligand to asialoglycoprotein receptor, which exists on the surface of hepatocytes, and is used for radionuclide receptor imaging of the liver. It accumulates exclusively in normally-functioning hepatocytes.[1,2] Regional hepatic dysfunction demonstrated by Tc-99m-GSA scintigraphy due to regional decrease in the portal venous flow has been previously reported.[3–6] Thus, for example, in cases with hilar cholangiocarcinomas, functional differences between right and left lobes due to unilateral portal venous flow decrease might have an influence in planning interventional procedures such as percutaneous drainage.[7] This phenomenon may also have a bearing on surgical procedures such as hepatectomy and preoperative

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evaluation of hepatic functional reserve. In preoperative evaluation, it is important to estimate exact postoperative residual liver function for selection of hepatectomy candidates. With decrease in unilateral portal venous flow, hepatic function may become predominant in the contralateral lobe, and the influence of hepatectomy on function in the residual liver may differ from cases lacking unilateral portal venous flow decrease. Such hepatic functional inhomogeneities in themselves were, however, only recently reported, and are not well covered in the literature. Single-photon emission computed tomography (SPECT) after administration of Tc-99m-GSA, and CT volumetry have been used, especially for preoperative evaluation,[8–11] evaluation of percutaneous transhepatic portal embolization,[12,13] and for selection of candidates for preoperative transarterial chemoembolization,[14] etc. Tc-99m-GSA SPECT may reflect regional functional distribution of the liver, whereas CT volumetry may not, because it merely calculates the anatomical volume of the liver. In this study, we call attention to the significance of unilateral portal venous flow decrease for preoperative hepatectomy simulation and evaluate the hepatectomy simulation discrepancies between Tc-99m-GSA SPECT and CT volumetry in terms of the influence of unilateral portal venous flow decrease.

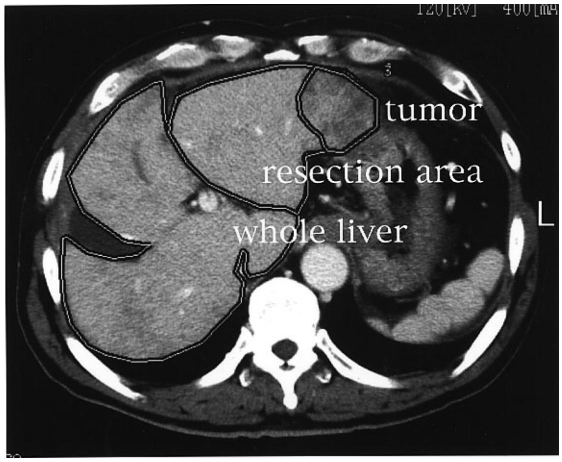


Fig. 1 Hepatectomy simulation by CT volumetry. Scheduled resection lines and liver surfaces were traced in all sections.

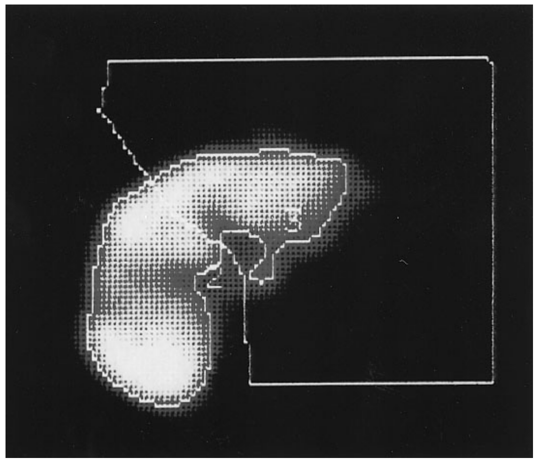


Fig. 2 Hepatectomy simulation by Tc-99m-GSA. Scheduled resection lines were traced on all transaxial SPECT images. Counts of whole liver (whole of the figure) and areas of resection (surrounded area) in all sections of SPECT were added up respectively.

MATERIALS AND METHODS

Study Population

Twenty-four hepatectomy candidates with various hepatic masses who underwent preoperative hepatectomy simulation by both Tc-99m-GSA SPECT and CT volumetry were the subject of this study. They were 16 men and 8 women, aged 44–86 years old (mean: 63 years). Unilateral portal venous flow decrease, due to hepatic masses, was seen in 13 patients, but not in the other 11 patients. Unilateral portal venous flow decrease was regarded as existing when unilateral portal venous stenosis or occlusion was clearly seen on contrast-enhanced CT or angiograms. The hepatic masses were cholangiocarcinoma in 10 patients, hepatocellular carcinoma in 8 patients, hepatic metastasis in 5 patients, and hepatic abscess in 1 patient. Scheduled hepatectomy simulation was for left lobectomy in 12 patients, left and caudate lobectomy in 3 patients, extended left lateral segmentectomy in 2 patients, left trisegmentectomy in 2 patients, and right lobectomy in 5.

In the 13 patients with unilateral portal venous flow decrease, hepatic masses were cholangiocarcinoma in 9 patients, hepatocellular carcinoma in 3 patients, and hepatic abscess in 1. Scheduled hepatectomy simulation was for left lobectomy in 8 patients, left and caudate lobectomy in 2 patients, left trisegmentectomy in 1 patient, and right lobectomy in 2.

In the 11 patients with no unilateral portal venous flow decrease, the hepatic masses were hepatocellular carcinoma in 5 patients, hepatic metastasis in 5 patients, and cholangiocarcinoma in 1. Scheduled hepatectomy simulation was for left lobectomy in 4 patients, extended left lateral segmentectomy in 2 patients, left trisegmentectomy in 1 patient, left and caudate lobectomy in 1 patient, and right lobectomy in 3. The intervals between Tc-99m-GSA SPECT and CT volumetry varied from 0 to 29 days.

CT Volumetry Simulation

CT scans were performed with a HiSpeed Advantage helical scanner (General Electric Medical System, Milwaukee, Wis). Scanning was done with 7 or 10 mm collimation at table speeds of 7 or 10 mm/sec, respectively. 100 m*l* of 300 mgI/m*l* non-ionic contrast material was intravenously administered at a rate of 3 m*l*/sec by means of a power injector (Autoenhance A50;

Table 1 Calculated parameters in 13 patients with unilateral portal venous flow decrease

Patient No. Sex/Age (y)	Lesion type	Scheduled surgery	Anatomical resection ratio (%)	Functional resection ratio (%)	Differences	Ratios	Bias
1. M/46	HCC	Left lobectomy	19.7	2.8	16.9	0.14	Anatomical
2. M/66	CC	Right lobectomy	33.0	25.3	7.7	0.76	Anatomical
3. M/63	Abscess	Left lobectomy	28.9	24.0	4.9	0.83	Anatomical
4. M/61	CC	Left lobectomy	27.0	9.1	17.9	0.33	Anatomical
5. M/78	CC	Left and caudate lobectomy	33.6	5.7	27.9	0.17	Anatomical
6. F/61	CC	Left lobectomy	14.3	6.3	8.0	0.44	Anatomical
7. M/86	CC	Left lobectomy	29.4	11.9	17.5	0.40	Anatomical
8. F/65	CC	Left and caudate lobectomy	10.5	2.0	8.5	0.19	Anatomical
9. M/62	HCC	Right lobectomy	41.0	20.5	20.5	0.50	Anatomical
10. M/50	HCC	Left trisegmentectomy	56.0	47.6	8.4	0.85	Anatomical
11. F/68	CC	Left lobectomy	21.0	21.2	0.2	0.99	Functional
12. M/70	CC	Left lobectomy	23.1	5.5	17.6	0.24	Anatomical
13. F/66	CC	Left lobectomy	26.4	9.3	17.1	0.35	Anatomical
			28.0 ± 11.7	14.7 ± 12.8	13.0 ± 7.9	0.48 ± 0.29	(Mean ± SD)

CC: chloangiocarcinoma, HCC: hepatocellular carcinoma

Table 2 Calculated parameters in 11 patients without unilateral portal venous flow decrease

Patient No. Sex/Age (y)	Lesion type	Scheduled surgery	Anatomical resection ratio (%)	Functional resection ratio (%)	Differences	Ratios	Bias
1. M/44	Metastasis	Left lobectomy	39.7	34.5	5.2	0.87	Anatomical
2. F/71	CC	Left and caudate lobectomy	31.9	33.2	1.3	0.96	Functional
3. M/50	HCC	Left lobectomy	34.4	29.4	5.0	0.85	Anatomical
4. F/68	Metastasis	Extended left lateral segmentectomy	37.0	39.0	2.0	0.95	Functional
5. M/75	HCC	Extended left lateral segmentectomy	37.0	34.7	2.3	0.94	Anatomical
6. F/58	Metastasis	Left trisegmentectomy	72.0	64.9	7.1	0.90	Anatomical
7. M/71	HCC	Right lobectomy	42.0	48.0	6.0	0.88	Functional
8. M/59	HCC	Right lobectomy	63.0	54.4	8.6	0.86	Anatomical
9. F/58	Metastasis	Right lobectomy	56.0	61.1	5.1	0.92	Functional
10. M/58	Metastasis	Left lobectomy	17.0	24.6	7.6	0.69	Functional
11. M/62	HCC	Left lobectomy	33.0	21.4	11.6	0.65	Anatomical
			42.1 ± 15.7	40.5 ± 14.6	5.6 ± 3.1	0.86 ± 0.10	(Mean ± SD)

CC: cholangiocarcinoma HCC: hepatocellular carcinoma

Nemotokyorindo, Tokyo, Japan). Triphasic whole liver helical CT scans were performed with the patient's breath held each time. Scans were done at 30, 70 and 180 seconds after the initiation of administration of the contrast material. Because most anatomical landmarks for hepatectomy simulation are blood vessels, the second (portal venous) phase, in which vessels are most clearly demonstrated, was used for hepatectomy simulation in most cases. In all other cases, precontrast scans were used. For hepatectomy simulation, scheduled resection lines and liver surfaces were traced carefully on all CT sections, referring to various anatomical landmarks (Fig. 1), e.g. the right hepatic vein, middle hepatic vein, umbilical portion of the left portal vein, and gallbladder fossa of the liver. Areas of the whole liver, areas of resection, and areas of tumors were added up in all CT sections respectively, and each volume was calculated. Anatomical resection ratio was calculated with the following formula:

$$\text{Anatomical resection ratio (\%)} = \frac{\text{resection volume} - \text{tumor volume}}{\text{total liver volume} - \text{tumor volume}} \times 100$$

Tc-99m-GSA SPECT Simulation

The patients were examined in the supine position with a dual-head rotating gamma camera interfaced to a mini-

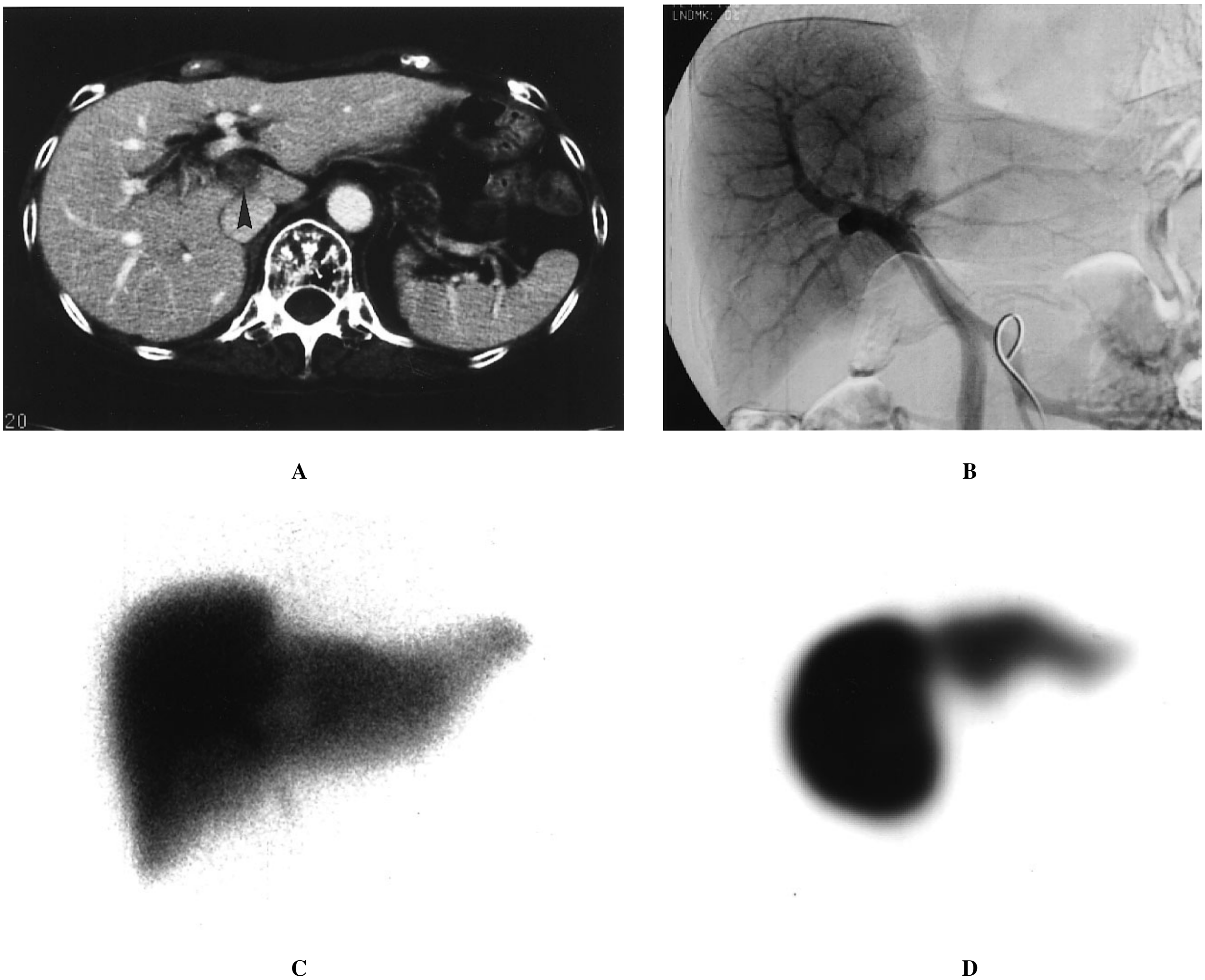


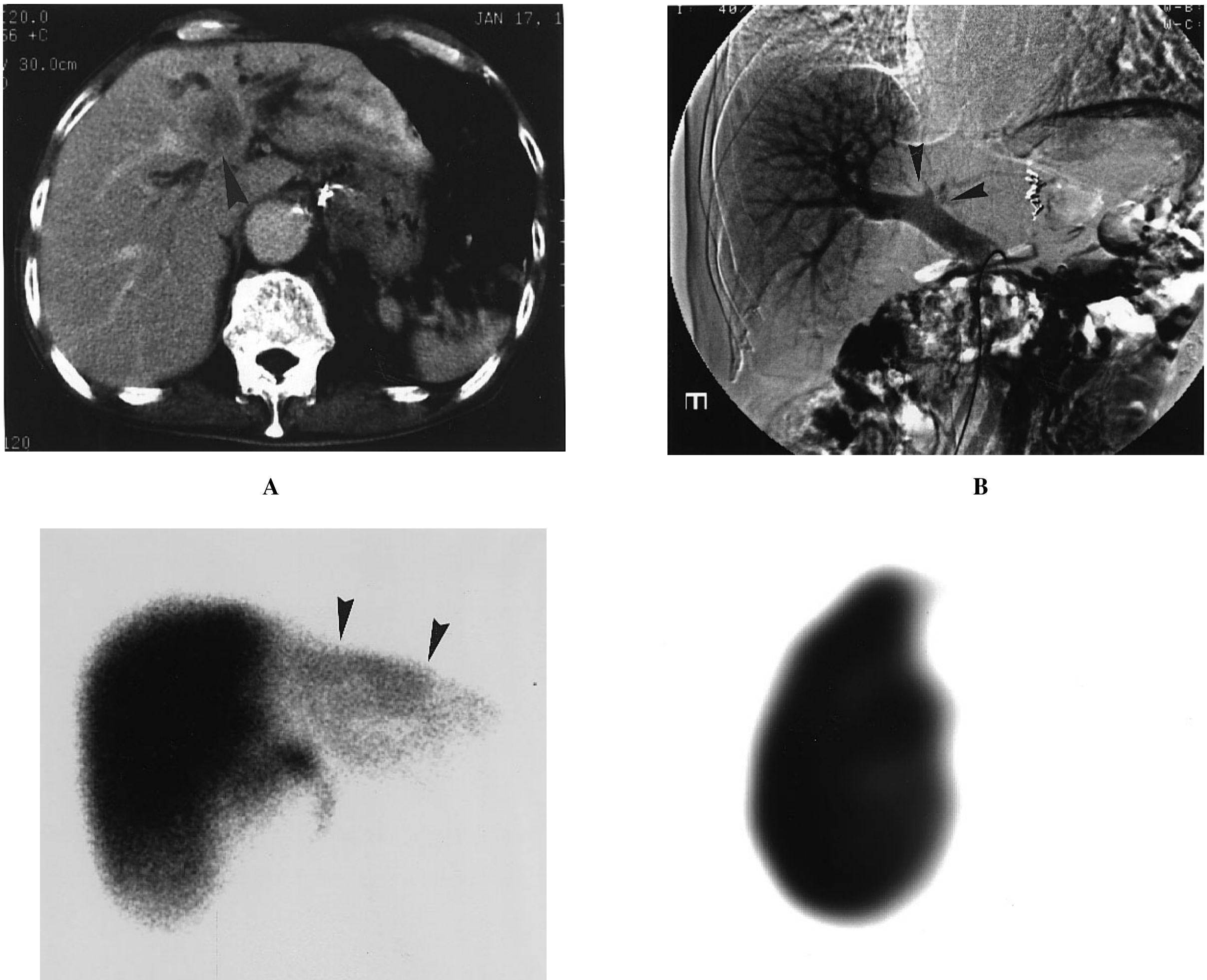
Fig. 3 A representative case of no unilateral portal venous flow decrease. On contrast-enhanced CT, a relatively small cholangiocarcinoma was seen in the caudate lobe (*arrowhead*) (A). On portogram via the superior mesenteric artery, there was no portal venous stenosis or occlusion (B). On Tc-99m-GSA planar image (C) and SPECT (D), there was no significant laterality in accumulation. Left and caudate lobe resection was scheduled for surgery in this patient and simulation was performed. Anatomical resection ratio was 31.9%, and functional resection ratio was 33.2%. The difference was 1.3 and the ratio was 0.96.

computer (GCA7200A/DI; Toshiba, Tokyo, Japan). A parallel-hole, low-energy, high-resolution collimator was used. Immediately after intravenous administration of 185 MBq of Tc-99m-GSA (Nihon Mediphysics, Nishinomiya, Japan), dynamic images were acquired in 15-sec frames for 30 min. Next, SPECT was performed by the acquisition of 60 projectional images over 360° in a 128 × 128 matrix. The data were obtained in from 35 to 47 min and reconstructed for transaxial sections 6.9 mm thick. Hepatectomy simulation by Tc-99m-GSA SPECT was performed by means of transaxial SPECT images. Scheduled resection lines were carefully traced on each section referring to those defined on CT sections. Counts of region of interest placed on whole liver and areas of resection in all transaxial sections of SPECT were each added up (Fig. 2). The addition was performed automatically with exclusive software (Simulation for Hepatectomy; Toshiba, Tokyo, Japan). Functional resection ratio was calculated with the following formula:

$$\text{Functional resection ratio (\%)} = \frac{\text{resection volume counts}}{\text{total liver volume counts}} \times 100$$

Data Analysis

Both anatomical and functional resection ratios were calculated for all patients, and the mean and standard deviations of these were calculated in patients with and



A B

C D

Fig. 4 A representative case having unilateral portal venous flow decrease (reprinted with permission, see reference 7). On contrast-enhanced CT, a cholangiocarcinoma was seen in the medial segment of the liver (*arrowhead*) (A). Severe stenosis of the left portal vein was seen on portogram (*arrowheads*) (B). Tc-99m-GSA accumulation was obviously decreased in the left hepatic lobe (*arrowheads*) (C, D). Left lobe and medial segment resection was scheduled for surgery in this patient. The two calculated resection ratios were severely discrepant. Anatomical resection ratio was 33.6%, and functional resection ratio was 5.7%. The difference here was 27.9 and the ratio was 0.17.

without unilateral portal venous flow decrease, respectively. The differences and ratios between anatomical and functional resection ratios were calculated in all patients. The ratios between anatomical and functional resection ratios were calculated by dividing the smaller ratio (anatomical or functional) by the larger ratio. They were also compared in patients with and without unilateral portal venous flow decrease, respectively. Furthermore, whether the resection ratio was larger or smaller than the others was recorded for each patient, and the number of each type of patient was counted and a comparison was made between patients with and without unilateral portal venous flow decrease. To compare differences and ratios between anatomical and functional resection ratios in patients with and without unilateral portal venous flow decrease, Mann-Whitney's-U test was used. To compare the number of patients in which one resection ratio was larger or smaller than the others, the chi-square test was used. Differences were considered statistically significant when the p value was < 0.05.

RESULTS

Tables 1 and 2 show calculated parameters in patients with and without unilateral portal venous flow decrease, respectively. Anatomical resection ratios were 28.0 ± 11.7 (mean ± standard deviation) in Table 1 patients, and 42.1 ± 15.7 in Table 2 patients. The latter were significantly larger than the former ($p = 0.0127$). Functional resection ratios were 14.7 ± 12.8 in Table 1 patients, and 40.5 ± 14.6

in Table 2 patients. Again the latter were significantly larger than the former ($p = 0.0004$). The differences between anatomical and functional resection ratios were 13.0 ± 7.9 in patients with unilateral portal venous flow decrease and 5.6 ± 3.1 in patients without. The former were significantly larger than the latter ($p = 0.0099$). The ratios between anatomical and functional resection ratios were 0.48 ± 0.29 in patients with unilateral portal venous flow decrease and 0.86 ± 0.10 in patients without, with the latter being significantly larger than the former ($p = 0.0018$). In 12 of the 13 patients with unilateral portal venous flow decrease, anatomical resection ratios were found to be larger than functional resection ratios. Also in 6 of 11 patients without unilateral portal venous flow decrease, anatomical resection ratios were found out to be larger than functional resection ratios. It became clear that in patients with unilateral portal venous flow decrease, anatomical resection ratios were more frequently found to be larger than functional resection ratios ($p = 0.0063$).

DISCUSSION

Evaluation of postoperative hepatic functional reserve is one of the most important preoperative studies for hepatectomy candidates. Estimation of resection volumes and hepatic remnant function must be done preoperatively in order to avoid life-threatening postoperative hepatic failure. In this study, we compared two radiological methods which calculate anatomical resection ratios and functional resection ratios respectively, with respect to the presence or absence of unilateral portal venous flow decrease. The two evaluation methods studied are relatively common, and thought to be performed widely.[8–15] Although Tc-99m-GSA, a radiopharmaceutical used in Japan and some other countries, is not used worldwide, it should be possible to apply this concept of preoperative radionuclide evaluation to any other radiopharmaceutical which is oriented to hepatocytes. In western countries, there are some reports on Tc-99m-galactosylneoglycoalbumin, which is also a radiopharmaceutical oriented to hepatocytes.[16,17]

In this study, anatomical resection ratios were significantly larger in patients with no unilateral portal venous flow decrease than in those having such decrease. Because resection volumes and sizes of hepatic lobes differ from patient to patient, this result is not in itself significant. Left lobe resection was, however, relatively frequent in this study both in patients with and without unilateral portal venous flow decrease. If the resection lobes or segments and their volumes can be thought to be fairly similar in the two groups in this study, then hepatic volume reduction might occur because of ipsilateral portal venous flow decrease. Functional resection ratios in patients lacking unilateral portal venous flow decrease were significantly larger than in patients with the decrease. Resection volumes and sizes of hepatic lobes likewise differed from patient to patient and even though this result may not be in itself significant. It does suggest that hepatic volume reduction or Tc-99m-GSA accumulation decrease in ipsilateral lobes might occur because of unilateral portal venous flow decrease.

Clinically significant are differences between anatomical and functional resection ratios, and they were significantly larger in patients with unilateral portal venous flow decrease than in patients without it. Likewise, the ratio between anatomical and functional resection ratio was significantly smaller in patients with a unilateral portal venous flow decrease. Moreover, in patients with a unilateral portal venous flow decrease, anatomical resection ratios were more frequently found to be larger than functional resection ratios. In these patients, the functional resection ratio obtained with Tc-99m-GSA is smaller, and the anatomical resection ratio obtained by CT volumetry is found to be larger. Mitsumori et al. previously reported the relative usefulness of simulation by means of Tc-99m-GSA.[8] They compared preoperative simulation by Tc-99m-GSA and by CT volumetry in candidates for hepatectomy, and reported that predicted postoperative clearance rates of indocyanine green obtained by simulation with Tc-99m-GSA correlated better with the actual postoperative clearance rates than those obtained with CT volumetry. They speculated that the difference might result from liver parenchymal damage around the tumor caused by mechanical compression and secondary parenchymal damage from compression of the vessels and bile ducts by the tumor. Moreover, the results of Hwang et al. and Kwon et al. also support the usefulness of Tc-99m-GSA.[9,10] In this study, unilateral portal venous flow decrease was suspected of being a major factor in the discrepancy between hepatectomy simulations with radionuclide receptor imaging and CT volumetry. Because Tc-99m-GSA accumulates normally-functioning hepatocytes, segments or lobes with decreased Tc-99m-GSA accumulation are considered to be hypofunctioning. In patients whose whole liver function is considered homogeneous, simulation by CT volumetry may be more satisfactory than by Tc-99m-GSA because it has better spacial resolution and also depicts anatomical landmarks more clearly, but it seems generally difficult to be always assured of the strict homogeneity of the whole liver function.[4] In patients with ipsilateral portal vein stenosis or occlusion, hepatectomy simulation by CT volumetry may overestimate the resection volume because it calculates lobes which have become hypofunctioning due to ispilateral portal venous flow decrease, as well as normally-functioning contralateral lobes. Although this phenomenon on CT volumetry may be a bias which helps to avoid postoperative complications such as hepatic failure, it is also possible that it might restrict the number of patients with hepatectomy indication and decrease the number of surgical candidates. Surgical indication should be carefully evaluated, especially in patients with unilateral portal flow decrease, and wider experience of this type of case should be gleaned.

CONCLUSION

In patients with unilateral portal venous flow decrease, a significant discrepancy may occur between hepatectomy simulations with radionuclide receptor imaging and CT volumetry. Attention must be called to this phenomenon in preoperative evaluation.

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