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Precision of the gallbladder ejection fraction obtained with Tc-99m-pyridoxyl-5-methyl-tryptophan (^{99m}Tc-PMT) hepatobiliary scintigraphy as compared with the contraction ratio in three-dimensional computed tomography

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The gallbladder ejection fraction (GBEF) obtained with Tc-99m-pyridoxyl-5-methyl-tryptophan (^{99m}Tc-PMT) hepatobiliary scintigraphy has been used as a parameter of gallbladder function. To determine the accuracy of GBEF, the relationship with the contraction ratio of the gallbladder (GBCR) obtained with three-dimensional helical computed tomography (3D-CT) was studied. *Patients and methods:* A normal volunteer, 8 patients suffering from cholecystolithiasis and a patient with gallbladder dyskinesia were examined. The percent initial dose (%ID) for the gallbladder and GBEF with hepatobiliary scintigraphy were used to compare the volume of the gallbladder and GBCR which was measured by 3D-CT. *Results:* The %ID of the gallbladder was correlated with the volume of the gallbladder by 3D-CT ($Y = 1.000X - 1.818$, r = 0.928). GBEF was correlated well with GBCR by 3D-CT ($Y = 0.916X + 6.296$, r = 0.975). *Conclusions:* The %ID of the gallbladder obtained with hepatobiliary scintigraphy may be a good indicator of the volume of the gallbladder. The accuracy of GBEF was confirmed by comparison with 3D-CT examination. GBEF is considered a useful parameter of pathophysiological gallbladder function.

Key words: gallbladder emptying, Tc-99m-pyridoxyl-5-methyl-tryptophan (^{99m}Tc-PMT) hepatobiliary scintigraphy, ejection fraction of the gallbladder, helical CT, three dimensional computed tomography

INTRODUCTION

IMAGES of the gallbladder obtained by hepatobiliary scintigraphy are non-geometrical but considered to be diagnostically important because they show serial changes in bile inflow and extraction.[1] In particular, the gallbladder ejection fraction (GBEF) obtained by hepatobiliary scintigraphy is widely used as a parameter of the physiological function of gallbladder emptying. Recently GBEF has become clinically valuable in the diagnosis and management of patients with various biliary diseases.[2] The accuracy of GBEF has been evaluated primarily by comparing it with the contraction ratio of the gallbladder volume (GBCR) measured by ultrasonography.[3] But we are apprehensive of the accuracy of GBCR obtained by this method,[4] and it is considered to lack reproducibility and objectivity. On the other hand, helical computed tomography (CT) allows imaging simultaneously with table transfer and is used for obtaining not only each slice image but also three-dimensional (3D)-CT images of various organs. Recently, 3D-CT of the gallbladder and bile duct has been performed and reported to be useful for the diagnosis of biliary tract diseases.[5] In addition, precise measurement of the gallbladder volume based on 3D-CT

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Fig. 1 ^{99m}Tc-PMT hepatobiliary scintigraphic images of a volunteer. The gallbladder was easily recognizable from 15 min after bolus injection of 185 MBq ^{99m}Tc-PMT. Radioactivities were well evacuated into the small intestine at 90 min (30 min after cerulein injection).

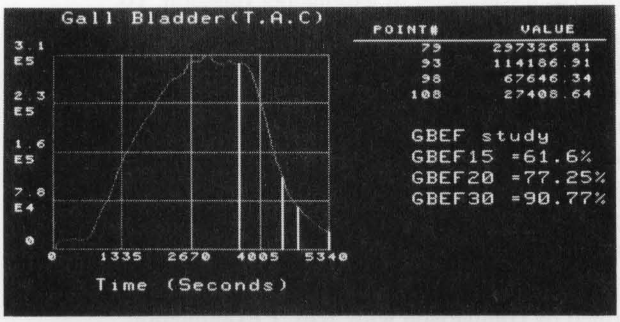

Fig. 2 The time activity curve of the gallbladder of a volunteer using ^{99m}Tc-PMT hepatobiliary scintigraphy reduced clearly after cerulein injection at 60 min. It was calculated that GBEF was 91%.

images has been reported.[6] To determine whether the radioactivity in the gallbladder on hepatobiliary scintigraphy reflects the gallbladder volume and to evaluate the degree of correlation between GBEF and GBCR, we compared the radioactivity or GBEF obtained by hepatobiliary scintigraphy with the changes in gallbladder volumes (i.e. before and after contraction), calculated on the basis of the 3D-CT images.

PATIENTS AND METHODS

Ten patients (3 males and 7 females) were examined: 1 normal volunteer, 8 patients with cholecystolithiasis, and 1 with gallbladder dyskinesia. They ranged in ages from 25 to 76 years (mean, 54.5 ± 17.5 years).

For hepatobiliary scintigraphy, Tc-99m-pyridoxyl-5-methyl-tryptophan (^{99m}Tc-PMT) (185 MBq) was injected as a bolus via the right cubital vein, and data were collected dynamically for 90 minutes with a Sophy gamma camera DHD (Sopha Medical, France). Sixty minutes after ^{99m}Tc-PMT injection, cerulein (0.4 μg/kg) as a cholecystokinetic agent was intramuscularly injected. Data were analyzed in a Sophy NXT computer (Sopha Medical, France). For the measurement of radioactivity in the gallbladder, Region of Interest (ROI) was established along the circumference of the gallbladder on a planar image, and the count in the ROI was measured from 59 to 60 minutes (GB60) and from 89 to 90 minutes (GB90) after ^{99m}Tc-PMT injection, i.e., from 29 to 30 minutes after the cerulein injection. Background correction, with the values in the tissue around the liver and the gallbladder, and decay correction were performed. The gallbladder percent initial dose (%ID) was obtained with the following formula:

$$\%ID = \{GB60 \text{ or } GB90/\text{initial injection dose}\} \times 100$$

GBEF was calculated as follows:

$$GBEF = \{(GB60 - GB90)/GB60\} \times 100\%$$

For CT examination, billiscopin DIC®, an intravenous contrast medium for the biliary tract, was drip infused at the rate of 100 m*l*/30 min. Sixty minutes after the initiation of the drip infusion, helical CT of the gallbladder was performed (3 mmTH, 3 mm/s, 1 mmRP) with a ProSeed Accell (Yokogawa Medical, Japan). Immediately after this helical CT, cerulein (0.4 μg/kg) was intramuscularly injected. After 30 minutes, helical CT of the gallbladder was performed again by a similar method. Processing of the helical CT images was performed with an Advantage Windows Workstation (GE Medical Systems, USA), and 3D-CT images of the gallbladder were produced by the surface rendering method, thereby calculating the gallbladder volume. For 3D-CT image construction, the threshold volume measurement (T_{VM}) was determined under the following conditions described by Shen et al.[6]:

$$(Ta - T_{VM})/(Ta - Tb) = 50\%$$

Ta: CT value in the gallbladder cavity (HU)
Tb: CT value around the gallbladder (HU)

GBCR was calculated on the basis of the gallbladder 3D-CT images with the following equation:

$$GBCR = \{(\text{GB volume at 60 min} - \text{GB volume at 90 min})/\text{GB volume at 60 min}\} \times 100\%$$

In statistical analysis, the Pearson's correlation test was used for between group comparisons, and probability values of $p < 0.05$ were considered to be significant.

CASES

In the normal volunteer, the gallbladder was adequately visualized within 60 minutes after ^{99m}Tc-PMT injection on planar scintigraphic images, and good contraction was

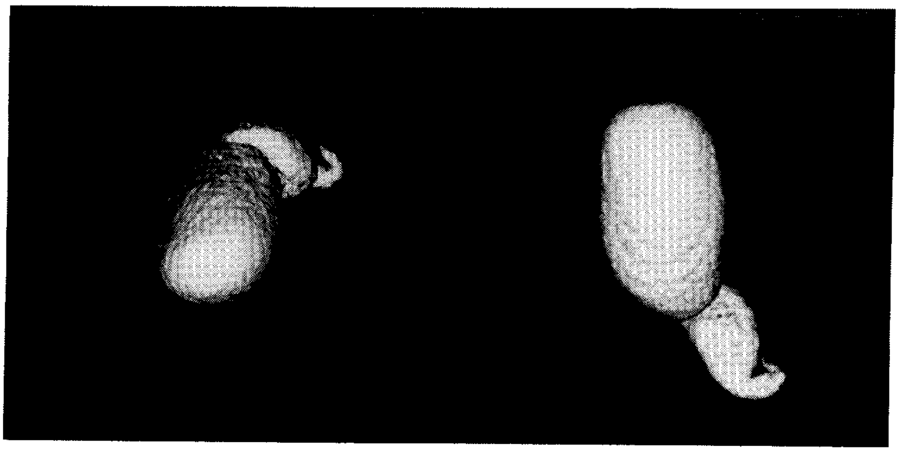

Fig. 3 The three-dimensional CT images of the gallbladder of a volunteer using the surface rendering method 60 min after the beginning of billiscopin DIC® drip intravenous infusion. The volume of the gallbladder was measured to be 31.4 m*l*.

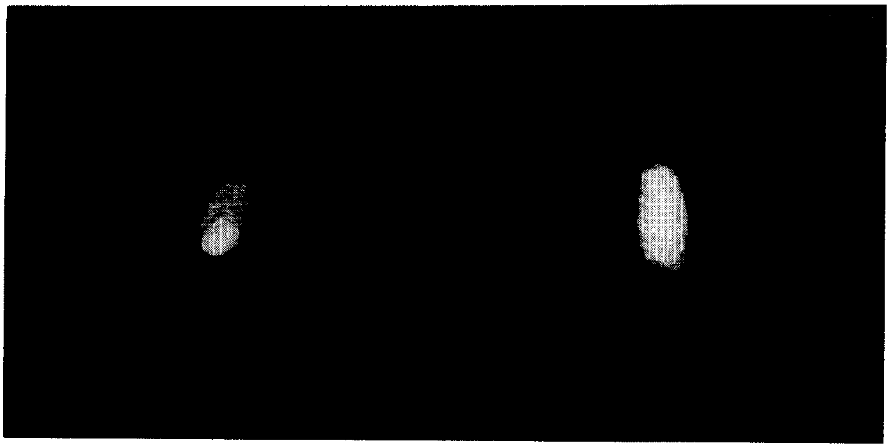

Fig. 4 The three-dimensional CT images of the gallbladder of a volunteer 30 min after cerulein injection. The volume of the gallbladder was measured to be 2.4 m*l*. It was calculated that GBCR was 92%.

observed 30 minutes after cerulein injection (Fig. 1). The initial dose of ^{99m}Tc-PMT was 1,001,999 counts per minute. Therefore, from the count at the time of establishment of ROI in the gallbladder with decay correction, the %ID at GB60 was 29.7, and that at GB90 was 2.7. The time activity curve for the gallbladder showed a good decrease after cerulein injection, and the GBEF was 91% (Fig. 2).

In this volunteer, clear gallbladder images were obtained by 3D-CT 60 minutes after the initiation of billiscopin DIC® infusion. The gallbladder volume calculated with an Advantage Windows Workstation was 31.4 m*l* (Fig. 3). Thirty minutes after cerulein injection, marked contraction was observed on gallbladder 3D-CT images, and the gallbladder volume was 2.4 m*l*. Therefore the GBCR obtained by 3D-CT was 92% (Fig. 4), which was almost same value as for the GBEF.

RESULTS

Evaluation of the %ID in the gallbladder at GB60 and that at GB90 obtained by hepatobiliary scintigraphy showed a good decrease in activity of in the volunteer and 3 patients with cholecystolithiasis, but a poor decrease was observed in the other 5 patients with cholecystolithiasis and the one with gallbladder dyskinesia.

Evaluation of the gallbladder volume at 60 min and that at 90 min obtained by 3D-CT showed a good decrease in the volunteer and the 3 patients with cholecystolithiasis as observed for the %ID, but a poor decrease was observed in the other 5 patients with cholecystolithiasis and the one with gallbladder dyskinesia (Table 1).

There was a good correlation between the gallbladder %ID obtained by scintigraphy and the gallbladder volume obtained by 3D-CT:

$$Y = 1.000X - 1.818 \ (r = 0.928, p < 0.0001) \text{ (Fig. 5)}.$$

Table 1 %ID of the gallbladder using hepatobiliary scintigraphy and the volume of the gallbladder using three-dimensional CT

No.	Sex	Age	Disease	GB %ID using hepatobiliary scintigraphy		GB volume using 3D-CT	
				GB60 (%)	GB90 (%)	GB60 (m*l*)	GB 90 (m*l*)
1	M	43	volunteer	29.7	2.7	31.4	2.4
2	F	66	cholecystolithiasis	36.4	0.9	29.3	0.4
3	F	76	cholecystolithiasis	26.8	2.3	20.5	1.9
4	M	72	cholecystolithiasis	31.2	9.1	35.2	11.1
5	F	59	cholecystolithiasis	27.2	18.6	28.4	19.3
6	F	65	cholecystolithiasis	14.0	11.6	16.5	16.1
7	F	25	cholecystolithiasis	14.9	12.1	17.1	17.6
8	M	33	cholecystolithiasis	5.6	5.0	17.0	16.3
9	F	42	cholecystolithiasis	1.1	1.2	1.7	1.7
10	F	64	GB dyskinesia	29.3	24.3	30.3	25.6

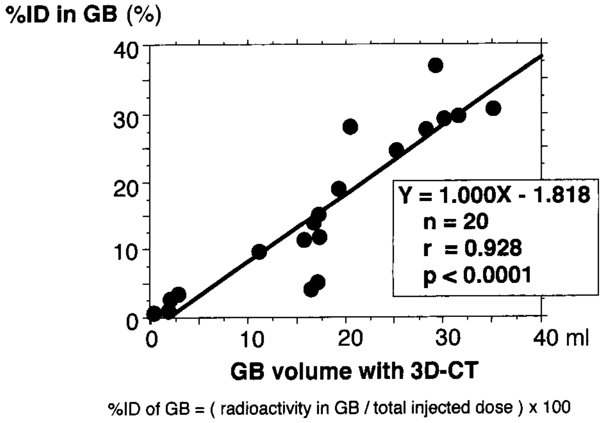

Fig. 5 Correlation between %ID of the gallbladder with hepatobiliary scintigraphy and the volume of the gallbladder with three-dimensional CT.

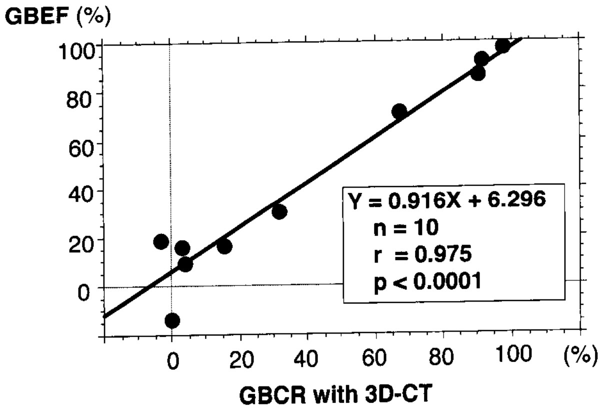

Fig. 6 Correlation between GBEF obtained by scintigraphy and GBCR obtained by three-dimensional CT.

A good correlation was also observed between GBEF obtained by scintigraphy and GBCR obtained by 3D-CT:

$Y = 0.916X + 6.296$ ($r = 0.975$, $p < 0.0001$) (Fig. 6).

DISCUSSION

The method of evaluating gallbladder contraction by hepatobiliary scintigraphy was reported by Englert et al.[7] in 1966. This method not only provides serial images over time in the biliary tract but also allows measurement of gallbladder contraction capacity with a cholecystokinetic agent.[2] In hepatobiliary scintigraphy, GBEF reflects changes in the functional bile volume excreted by gallbladder contraction.[1] GBEF, together with the half-emptying time,[8] is considered to be an important parameter of gallbladder contraction capacity. At present, GBEF is clinically used for evaluating chronic cholecystitis,[9] cystic duct syndrome,[10] choledocholithiasis,[11] and other biliary tract diseases.[12,13]

For the measurement of GBEF by hepatobiliary scintigraphy, cholecystokinin (CCK)[14] or CCK derivatives[15] are used as cholecystokinetic agents. Concerning the speed of infusion of the cholecystokinetic agent, slow infusion results in better gallbladder contraction and development of fewer side effects such as abdominal pain, nausea and vomiting than bolus injection or infusion. We therefore used intramuscular injection of cerulein, a CCK derivative. No side effects developed in any patient in this study. The data collection time after injection of a cholecystokinetic agent for the measurement of GBEF by scintigraphy is generally 30–60 minutes. Ziessmann et al.[14] reported a GBEF of 70 ± 22% 30 minutes after the initiation of slow injection of CCK. In this study, the GBEF was 50% or more in 4 patients (1 normal volunteer and 3 patients with cholecystolithiasis) but less than 50% in the other 6 patients (5 patients with cholecystolithiasis and 1 with gallbladder dyskinesia). These results were consistent with those obtained by 3D-CT.

As for the accuracy of GBEF obtained by hepatobiliary scintigraphy, Krishnamurthy et al.[1] reported a nearly 100% correlation when changes in the volume were between 0 and 50 m*l* in a phantom experiment. On the other hand, ultrasonography has been used mainly for clinical measurement of the gallbladder volume.[16,17] In general, the accuracy of GBEF obtained by clinical scintigraphy has been conventionally evaluated in association with changes in gallbladder volume measured by ultrasonography. Masclee et al.[3] reported a good correlation between GBCR calculated by ultrasonography and in a GBEF range of 20–50%, but overestimation (20–40%) by ultrasonographical GBCR in a GBEF range of 0–20%, and underestimation (45–60%) by ultrasonographical GBCR in a GBEF range of 55–80%. This difficulty in the measurement of the gallbladder volume by ultrasonography may be due to changes in the axis and shape during gallbladder contraction.[18] Helical CT, which allows continuous table transfer and imaging, has been applied to the construction on 3D-CT images. In biliary tract diseases, this method has been reported to be useful for evaluating the gallbladder morphology and the mode of union of the cystic duct[19] or for diagnosing the site of bile duct occlusion.[20] Recently, there have been studies on the calculation of the organ volume based on 3D-CT images, a liver volume measurement method[21] and a gallbladder volume measurement method.[6] In this study, the threshold value for gallbladder 3D-CT image contraction was determined by the method of Shen et al.[6] The intermediate value between the density in the gallbladder and that in the surrounding organ (liver in this study) was adopted. The gallbladder %ID obtained by scintigraphy correlated well with the gallbladder volume obtained by 3D-CT. Therefore, as Krishnamurthy et al.[1] demonstrated in a phantom study, the gallbladder %ID can be clinically applied as a parameter of the gallbladder volume.

GBEF obtained by hepatobiliary scintigraphy was also well correlated with GBCR measured by 3D-CT. In particular, GBEF : GBCR was nearly 1 : 1 in a wide GBEF range of 10–98%, confirming the high accuracy of GBEF. In some patients showing a GBEF of less than 10%, dissociation between GBEF and GBCR was observed. In these patients, the gallbladder was filled with stones. In principle, both GBEF of scintigraphical measurements and the gallbladder volume obtained by 3D-CT represent the gallbladder cavity excluding the area filled with stones. In the patient showing dissociation, refilling of contrast media in the gallbladder may have occurred early in addition to poor gallbladder contraction.

Concerning the reproducibility of GBEF by scintigraphy, Xynos et al.[22] evaluated normal subjects and patients after operations on the stomach and duodenum for 2–5 weeks, and reported good reproducibility despite various types of gallbladder emptying.

In conclusion, comparisons of the gallbladder volume on 3D-CT and data obtained by hepatobiliary scintigraphy show that it can be a parameter of the gallbladder volume, and the accuracy of GBEF is high. The measurement of GBEF by hepatobiliary scintigraphy can be readily performed without any side effects. Its application will be extended as a method of evaluating gallbladder function under physiological conditions.

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