Evaluation of Portosystemic Collaterals by SPECT Imaging After Endoscopic Variceal Sclerotherapy: Usefulness for Predicting Recurrence

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Bleeding from esophageal varices is a major cause of morbidity and mortality in cirrhotic patients. Identification of patients at high risk for bleeding is particularly important. The aim of this study was to determine whether detection of portosystemic collaterals by SPECT could predict the outcome of endoscopic injection sclerotherapy of esophageal varices and be useful for selecting appropriate therapy. **Methods:** Sixty-two patients with liver cirrhosis who were considered at high risk of bleeding were treated with endoscopic injection sclerotherapy. Endoscopy was performed every 3 mo after therapy or until bleeding occurred. Before and within 2 wk after therapy, tomographic images of intra-abdominal blood pool were constructed by SPECT. **Results:** Before therapy, the following portosystemic collateral routes were observed: coronary veins in 53 (85.5%) of 62 patients, short gastric veins in 8 patients (12.9%), splenorenal shunts in 10 patients (16.1%), and paraumbilical veins in 6 patients (9.7%). Patients positive for imaging of coronary veins were divided into 3 groups on the basis of changes in images after therapy: complete responders (n = 17), whose coronary vein images disappeared completely; partial responders (n = 18), whose images became smaller; and nonresponders (n = 18), whose images did not change significantly before or after therapy. The rates of recurrence after endoscopic injection sclerotherapy until 6 mo in complete responders (4/17, 23.5%) and partial responders (7/18, 38.9%) were significantly less ($P < 0.05$) than that in nonresponders (11/13, 84.6%). The rate of recurrence of esophageal varices until 6 mo in nonresponders treated with additional submucosal injection sclerotherapy (1/5, 20.0%) was significantly less ($P < 0.05$) than that in nonresponders without additional submucosal injection sclerotherapy (11/13, 84.6%). **Conclusion:** Abdominal blood-pool SPECT, a noninvasive method, is useful for evaluating the therapeutic effectiveness of endoscopic sclerotherapy, for predicting the recurrence of varices, and for selecting appropriate management after sclerotherapy.

Key Words: esophageal varices; sclerotherapy; SPECT; portal circulation

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Bleeding from esophageal varices is a major problem in portal hypertensive cirrhosis and is associated with a high risk of death (*1,2*). For this reason, several treatments aimed at preventing variceal bleeding and rebleeding after treatment have been tested in randomized controlled trials (*3*). Endoscopic injection sclerotherapy (EIS) is one of the most widely used treatments for esophageal varices. However, EIS is not fully satisfactory because the average rate of recurrence of varices on long-term follow-up is about 60% (*4*). Therefore, identification of patients at high risk of bleeding after EIS would permit careful follow-up and early treatment and eliminate unnecessary investigation of low-risk patients. These considerations emphasize the need for simple, accurate, and reproducible indicators of risk of recurrence. Although several factors, such as the variceal size, red color sign on varices, and portal pressure gradient, play important roles in variceal bleeding (*3*), they are not useful in predicting the recurrence of varices after treatment because varices have been eliminated by EIS. Collaterals of the portal venous system function as feeders of varices or drainage routes of varices (or both), so the changes of flow in these collaterals before or after EIS may influence recurrence of varices. Takase et al. (*5*) studied the portosystemic collaterals in patients who underwent EIS therapy by percutaneous transhepatic portography (PTP) and found that embolization of both esophageal varices and their feeders was required to lower the recurrence rate after EIS. Dilawari et al. (*6*) reported that splenorenal shunts protected patients from recurrence of varices as shown by splenoportography. PTP, splenoportography, and scintiphotosplenoportography (SSP) (*7*) are available to reveal the existence of portosystemic collaterals, but these techniques are rather invasive and are not available for poor-risk patients. In contrast, we found that SPECT is useful for noninvasive identification of portosystemic collaterals in patients with liver cirrhosis (*8*). We believed that we could detect the changes of flow in these collaterals with SPECT and that the changes of the collaterals on SPECT images might predict the recurrence of varices.

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The aim of this study was to determine whether SPECT is useful for predicting the outcome of sclerotherapy and for selecting appropriate therapy.

MATERIALS AND METHODS

Patients

The study population included 62 patients with liver cirrhosis, all of whom were treated at Osaka Kosei-nenkin Hospital. Of these patients, 12 had hepatocellular carcinoma without portal thrombus. Clinical data for these patients are shown in Table 1. The severity of liver dysfunction was classified according to Pugh's modification of the Child's grading system (*9*). Criteria for entry into this study were performance of SPECT before and after sclerotherapy, esophageal varices caused by liver cirrhosis, and high risk of esophageal bleeding (blue varices of the F2 or F3 form with the positive red color sign) (*10*) at the initial endoscopic evaluation. Written informed consent was obtained from all patients.

Study Design

Sclerotherapy was performed by injecting 5% ethanolamine oleate or 1% aethoxysclerol into all esophageal varices up to a total dose of 10–30 mL. Sclerotherapy was performed cyclically with an average interval of 1 wk until varices were of the F1 or F0 form and the red color sign disappeared. After sclerotherapy, endoscopic follow-up studies were performed at 3-mo intervals or until bleeding occurred. In 5 randomly selected patients with the reappearance of varices, SPECT was performed at the time of recurrence.

Before and within 2 wk (7–14 d) after the last EIS, the portal circulation was studied by abdominal blood-pool SPECT with 740 MBq intravenously injected ^{99m}Tc-human serum albumin-diethylenetriamine pentaacetic acid (HSA-D; Nihon Medi-Physics Co., Ltd., Nishinomiya, Japan). An effervescent agent was given orally before the study to distend the stomach. SPECT data were obtained with a single-head rotating γ camera equipped with a high-resolution, low-energy, parallel-hole collimator. For each patient, 64 views were obtained over 360° of elliptic rotation at 30 s/view, and each view was stored in computer memory as a 64 × 64 matrix. The thickness of each pixel was 5.5 mm. Before reconstruction, projection image sets were filtered using 2-dimensional digital filters—low-pass and Wiener filters. Attenuation was corrected using Sorenson's method. Thereafter the data were reconstructed using the filtered backprojection method with a Shepp-Logan filter and a thickness of 1 pixel. SPECT was performed using a previously reported method (*8*). Recognition of the portal venous system was easier on coronal views because of their resemblance to conventional angiograms. SPECT images also consistently revealed the abdominal aorta, inferior vena cava, spleen, kidney, and heart, aiding us in identification of the coronary vein, short gastric vein, paraumbilical vein, and splenorenal shunt (*8*). We measured changes of collaterals on the pre- and post-EIS treatment images on a slice on which the portal vein or the spleen (or both) appeared similar on the pre- and post-EIS treatment images. Two physicians reviewed all SPECT images twice for changes on the pre- and post-EIS treatment images.

TABLE 1
Clinical Data for 62 Patients Undergoing EIS

Characteristic	Clinical data
Gender (male:female)	38:24
Age (y)	40–76 (53.1)*
Child's grade	
A	28
B	30
C	4
Cause of cirrhosis	
Alcohol	2
Primary biliary cirrhosis	2
Hepatitis B virus	10
Hepatitis C virus	45
Unknown or obscure	3

*Mean age in parentheses.

Patients were assigned to 3 groups according to the effects of EIS: complete responders (CRs), patients whose coronary vein disappeared completely on SPECT images; partial responders (PRs), patients whose coronary vein was reduced in size but was still visualized on SPECT images; and nonresponders (NRs), patients whose coronary vein did not change significantly on SPECT images before or after therapy. We defined recurrence of varices as reappearance of the red color sign on varices or bleeding from varices. Recurrence rates were compared among these groups.

Five NRs were treated with additional injection of the sclerosant into the submucosa around the esophageal varices, because it was expected that patients with remaining feeders of esophageal varices after endoscopic intravariceal injection sclerotherapy would have a high rate of recurrence of varices (*5*).

Statistical Analysis

Statistical analysis was performed by the χ^2 test. All probability values were 2-tailed, and $P < 0.05$ was considered significant.

RESULTS

Portosystemic collateral vessels, such as coronary veins, short gastric veins, splenorenal shunts, and paraumbilical veins, become dilated in portal hypertension (Fig. 1). Before EIS, SPECT revealed the following portosystemic collaterals (Table 2). Of 62 patients studied, coronary veins were detected in 53 (85.5%), short gastric veins in 8 (12.9%), splenorenal shunts in 10 (16.1%), and paraumbilical veins in 6 patients (9.7%). Because the coronary vein is considered a main portosystemic collateral, patients with positive coronary vein images were assigned to 3 groups according to the changes on images after therapy. Of the 53 patients with positive coronary vein images, 17 (32.1%) were assigned to the CR group, 18 (34.0%) to the PR group, and 18 (34.0%) to the NR group. Furthermore, after EIS, the splenorenal shunt increased in size in 3 patients (1 CR, 1 PR, and 1 patient with a negative coronary vein image before EIS), and the paraumbilical vein increased in size in 1 CR.

Angiography was performed in 5 patients with hepatocellular carcinoma within 1 mo before sclerotherapy. Coronary veins were detected with superior mesenteric artery portography, and the flows were hepatofugal in all 5 patients whose coronary veins were detected on SPECT images. The paraumbilical vein was detected with superior mesenteric artery portography in a patient whose paraumbilical vein

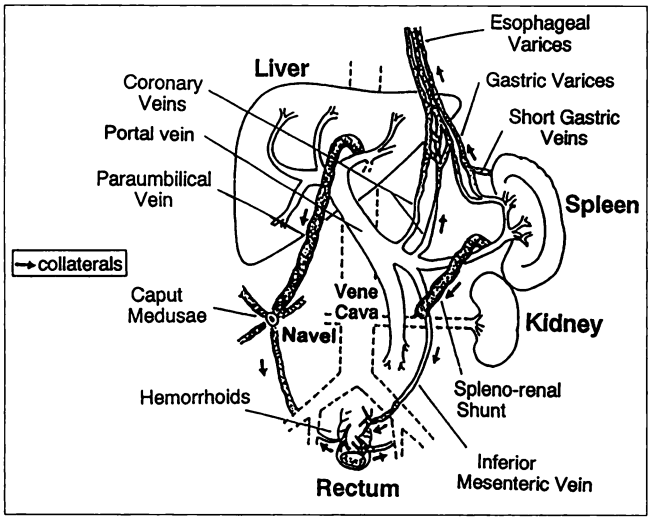

FIGURE 1. Portosystemic collaterals in portal hypertension.

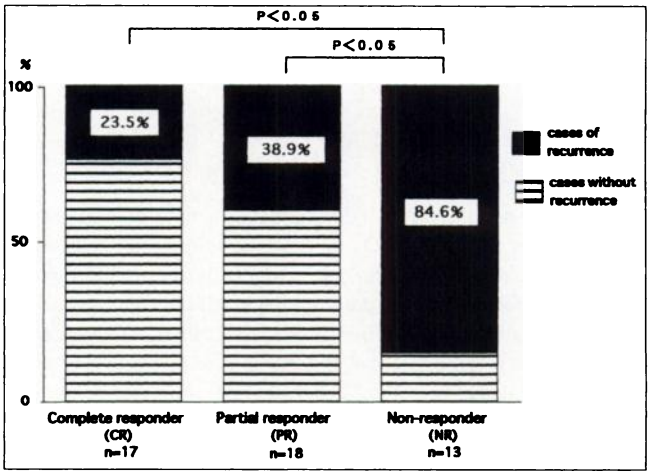

FIGURE 2. Rates of recurrence of esophageal varices after EIS.

was detected on the SPECT image. Because of the small number of patients who were positive for short gastric veins on the SPECT images, the relationship between the clinical outcome of EIS and changes in the short gastric vein could not be investigated.

Figure 2 shows changes in the coronary vein on SPECT images by endoscopic intravariceal injection sclerotherapy and the clinical outcomes of esophageal varices after therapy. Recurrence of esophageal varices until 6 mo was observed in only 4 patients (23.5%) in the CR group, 7 (38.9%) in the PR group, and 11 (84.6%) of 13 patients in the NR group without additional submucosal injection sclerotherapy. The rates of recurrence in the CR and PR groups were significantly less than that in the NR group ($P < 0.05$). Through 1 y, the rate of recurrence in the CR group (6/17, 35.3%) was significantly less than that in the NR group (11/13, 84.6%) ($P < 0.05$). The rate of recurrence in the PR group (9/18, 50.0%) through 1 y was less than that in the NR group, but not significantly.

TABLE 2
Frequency of Portal Collaterals Before and After EIS

Coronary veins	Short gastric veins	Splenorenal shunt	Para-umbilical veins	No. of patients Before EIS	No. of patients After EIS
+				38	27
+	+			4	3
+		+		6	3
+			+	5	2
	+			3	4
	+		+	1	1
		+		4	7
			+	0	3
				1*	12*
			Total	62	62

*No collaterals.

Recurrence of esophageal varices was observed endoscopically by 6 mo in 1 (20.0%) of 5 patients whose coronary vein SPECT images did not change significantly before or after endoscopic intravariceal injection sclerotherapy and who were treated with additional submucosal injection sclerotherapy. The rate of recurrence in these patients was significantly less than that in the NR group without additional submucosal injection sclerotherapy (11/13, 84.6%) ($P < 0.05$). Of the 22 patients with positive coronary vein images with recurrence during the 6-mo follow-up period after endoscopic intravariceal injection sclerotherapy, bleeding was observed in 1 patient in the CR group and in 2 patients in the NR group.

In 4 patients in whom the image size of the paraumbilical vein or splenorenal shunts increased after EIS, recurrence of esophageal varices was not observed during the study period. In 5 patients with recurrence of esophageal varices, SPECT was performed at the time of recurrence. Reappearance or increase in size of the coronary veins was observed in 2 patients, and increase in size of the short gastric veins was also observed in 2 patients.

CASE PRESENTATION

Case 1 was a 58-y-old man. Before EIS, he was positive for the coronary vein on a SPECT image. After EIS, the coronary vein disappeared (CR group), and varices did not reappear during the study period (Fig. 3).

Case 2 was a 56-y-old man. Before EIS, he was positive for the coronary vein on a SPECT image. There was no change before or after EIS (NR group), and the varices reappeared at 6-mo follow-up after endoscopy (Fig. 4).

Case 3 was a 67-y-old woman. Before EIS, she was positive for the coronary vein on a SPECT image. After EIS, the coronary vein disappeared (CR group), but the varices reappeared at 6-mo follow-up after endoscopy. Reappearance of the coronary veins was also observed on the image (Fig. 5).

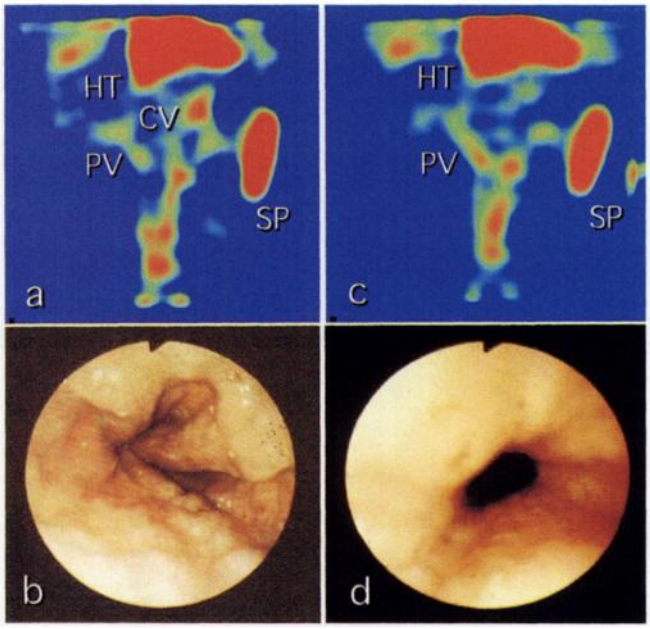

FIGURE 3. SPECT and endoscopic findings for esophagus of 58-y-old man (case 1). Before EIS, coronary vein was detected (A) (HT = heart, SP = spleen, PV = portal vein, CV = coronary vein), and blue F2 varices with positive red color sign were observed (B). Coronary vein disappeared after EIS (CR group) (C), and varices did not reappear during study period (D).

DISCUSSION

In an earlier study (*8*), we found that imaging of the intra-abdominal vascular blood pool by SPECT could be performed very safely and noninvasively and was useful for identifying portosystemic collaterals in patients with portal hypertension. In particular, reconstruction of the coronal planes provided images similar to angiograms and made recognition of blood vessels easy.

This study confirmed the previous results and, in addition, showed that SPECT images of the abdominal blood pool after EIS were quite useful in predicting the outcome of therapy after EIS. The main blood-flow supply to the esophageal varices, such as the coronary veins or the paraesophageal veins, will play important roles in the recurrence of esophageal varices after EIS (*5,11,12*). Takase et al. (*5*) also reported in their study using PTP that the embolization of feeders of esophageal varices (portosystemic collaterals) was required to lower the recurrence rate after EIS. Our findings agree with theirs, showing that the presence of coronary veins after EIS was a factor that was significantly related to the reappearance of varices. The important conclusion to be drawn from this study is that, because SPECT is noninvasive, it can be used for poor-risk or outpatient clinic patients and can be safely performed repeatedly. Because patients whose varices are at high risk of bleeding often have decompensated cirrhosis, a noninvasive modality such as SPECT is quite useful for them clinically. Although PTP, splenoportography, and SSP (*7*) can be used to reveal portosystemic collaterals, they cannot be used for patients with ascites or with the tendency to hemorrhage. For patients who do not have positive coronary veins on SPECT images before EIS, this method cannot be used to predict recurrence.

In this study, we confirmed that additional submucosal injection sclerotherapy after intravariceal injection sclerotherapy was effective in lowering the rate of recurrence of varices in the NR group. Kitano et al. (*13*) reported that injection of sclerosant into the submucosa around the varices was effective in preventing the recurrence of esophageal varices after intravariceal injection sclerotherapy. However, this method required a longer entrance time (over 2 or 3 wk) than did intravariceal injection therapy and had side effects (for example, stricture of the esophagus and hematoma). Therefore, we believe this method should be used for patients with high risk of recurrence, such as NRs whose coronary vein SPECT images did not change significantly before or after intravariceal injection sclerotherapy. Thus, SPECT should be useful for selecting appropriate therapy for esophageal varices.

In this study, because of the small number of patients who were positive for short gastric veins on SPECT images, the relationship between the clinical outcome of EIS and changes in the short gastric veins could not be investigated. The short gastric vein was near the spleen on SPECT images, and these images sometimes overlapped each other. Therefore, SPECT might underestimate the frequency of the short gastric vein. Indeed, Takase et al. (*5*) reported that, using PTP, short gastric veins were observed in 11 (62%) of

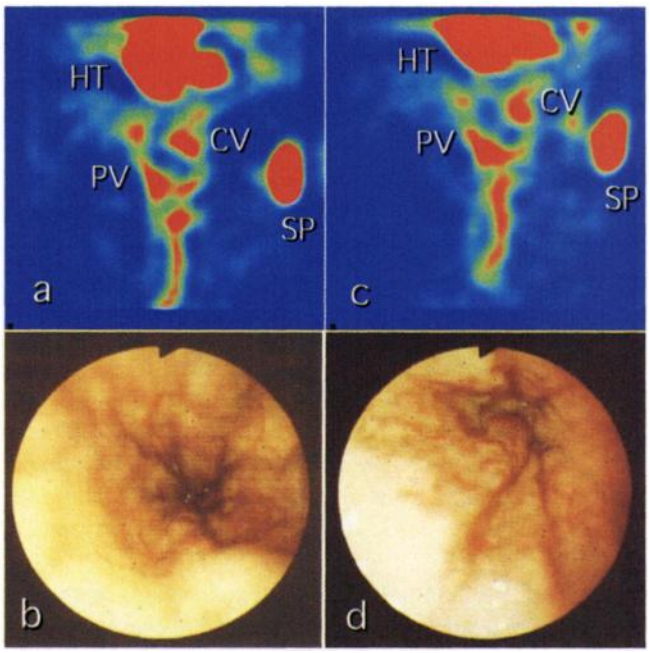

FIGURE 4. SPECT and endoscopic findings for esophagus of 56-y-old man (case 2). Before EIS, coronary vein was detected (A) (HT = heart, SP = spleen, PV = portal vein, CV = coronary vein), and blue F2 varices with positive red color sign were observed (B). Coronary vein did not change before or after therapy (NR group) (C), and varices reappeared at 6-mo follow-up after endoscopy (D).

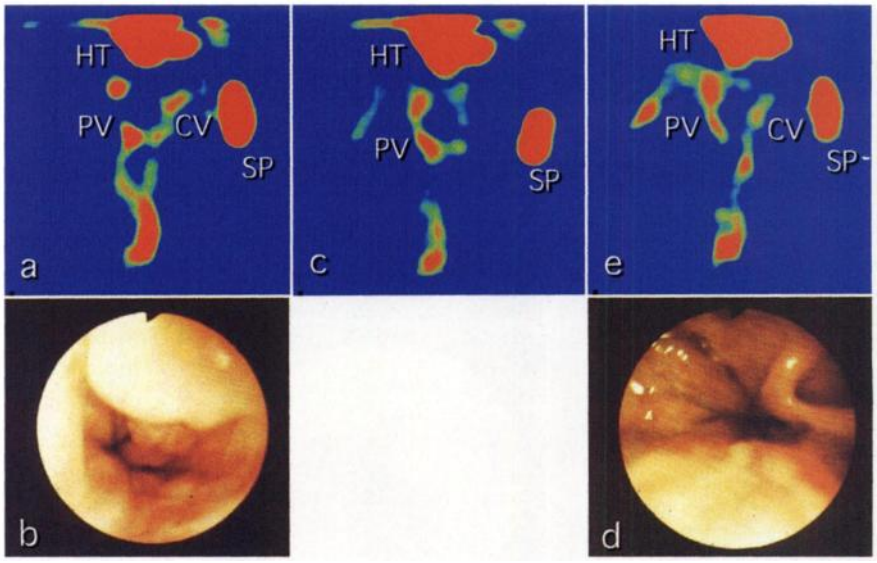

FIGURE 5. SPECT and endoscopic findings for esophagus of 67-y-old woman (case 3). Before EIS, coronary vein was detected (A) (HT = heart, SP = spleen, PV = portal vein, CV = coronary vein), and blue F2 varices with positive red color sign (B) were observed. (C) Coronary vein disappeared after EIS (CR group). However, varices reappeared at 6-mo follow-up after endoscopy (D), and reappearance of image of coronary vein was observed (E).

26 patients with esophageal varices. However, they also reported in the same study that the main feeders to the varices were coronary veins or a conflux of coronary veins and short gastric veins and that there were no patients with varices who had a short gastric vein alone as a feeding vein to varices. Therefore, coronary veins were considered more important as feeding veins to varices than were short gastric veins. The finding that 4 (80%) of 5 randomly selected patients, for whom SPECT was performed at the time of recurrence, had reappearance or increase in size of coronary or short gastric veins suggested that follow-up with SPECT after EIS might aid in detection of the recurrence of varices.

One of the interesting findings in this study was that, in 4 patients in whom spleno-renal shunt or paraumbilical vein increased in size after EIS, variceal recurrence was not observed during the study period. These findings suggested that an increase in these collaterals might act as a drainage route that could contribute in part to the decrease in portal hypertension.

Modalities other than EIS, such as pharmacologic therapy (β-blockers and agents with nitrovasodilating properties), endoscopic variceal ligation, and transjugular intrahepatic portosystemic shunt (*3,14–17*), aimed at preventing variceal bleeding have also been widely used. Whether abdominal blood-pool SPECT can predict the recurrence or bleeding of varices after these treatments has not been determined.

CONCLUSION

Abdominal blood-pool SPECT, a noninvasive method, is useful for evaluating the therapeutic effectiveness of sclerotherapy, for predicting the recurrence of varices, and for selecting appropriate therapy.

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