

Clinical usefulness of per-rectal portal scintigraphy by Tc-99m pertechnetate in evaluation of the severity of portal hypertension in cirrhotic patients

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ABSTRACT

Introduction: Variceal haemorrhage is a potentially life-threatening complication in cirrhotic patients. Identification of patients at high risk for bleeding is particularly important. The aim of this study was to determine the clinical usefulness of per-rectal portal scintigraphy (PPS) in the evaluation of the severity of portal hypertension in cirrhotic patients, in terms of correlation between cirrhosis and the parameters of hepatic functional reserve, and identifying the difference of the portal shunt index (PSI) of the bleeding oesophageal variceal (BEV) patients and non-BEV patients.

Methods: Portal circulations in 67 patients with cirrhosis and oesophageal varices were evaluated by Tc-99m pertechnetate PPS. Tc-99m pertechnetate (550 MBq) was instilled into the upper rectum, and dynamic images of upper abdomen were taken. Radioactivity curves for the liver and the heart were generated sequentially. Through the analysis of these curves, the PSI was determined.

Results: The results, expressed as PSI, were: 11.4 +/- 98.4 percent (mean 66.8) in all 67 cirrhotic patients, 56.4 +/- 27.1 percent in cirrhotic patients without history of BEV, and 74.9 +/- 13.6 percent in cirrhotic patients with history of BEV. The PSI was significantly lower in cirrhotic patients without BEV than those with BEV (p-value equals 0.001). The PSI calculated with this method was correlated with the serum albumin, the serum bilirubin, the

prothrombin time, and the Child-Turcotte-Pugh score.

Conclusion: Tc-99m pertechnetate PPS has clinical usefulness as a noninvasive method of choice for quantitatively evaluating the severity of portal hypertension in cirrhotic patients.

Keywords: liver cirrhosis, oesophageal varices, per-rectal portal scintigraphy, portal hypertension, porto-systemic shunt index

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INTRODUCTION

Survival of cirrhotic patients depends on preventing both hepatocellular dysfunction and portal circulation disturbances. The main complications related to porto-systemic shunt include gastrointestinal bleeding from ruptured varices, ascites, and hepatic encephalopathy. Among those complications, the bleeding from oesophageal varices is a potentially life-threatening complication of cirrhosis and portal hypertension. Bleeding from oesophageal varices is a major cause of morbidity and mortality in cirrhotic patients. Almost 90% of patients with cirrhosis develop varices, and approximately 30% of these varices bleed.⁽¹⁾ The first episode of variceal haemorrhage is estimated to carry a mortality rate of 30%–50%.⁽²⁾ Identification of patients at high risk of bleeding is particularly important. Therefore, detection of portal hypertension in patients with cirrhosis must be done for the purpose to prevent the occurrence of variceal bleeding. The diagnosis of portal hypertension requires the measurement of hepatic venous pressure by a direct method, such as umbilical vein or portal vein catheterisation, or transhepatic puncture of portal vein, or by indirect methods, such as hepatic vein catheterisation or hepatic venous pressure gradient (HVPG). These

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techniques are highly invasive for the patients and inconvenient for clinical follow-up.

Many less invasive methods, including clinical, biochemical, and histological criteria, have been used for assessing the severity of the disease and prognosis in cirrhotic patients. Each investigation has its advantages. The Child-Turcotte-Pugh (CTP) score,⁽³⁾ which is obtained from clinical and laboratory data, is widely applied as prognostic markers in clinical practice due to their simplicity for use.^(4,5) The CTP score has been proven to reflect the hepatocellular impairment and portal circulation disturbance, and is a good indicator for assessing the severity of cirrhosis; however, this score can be used for predicting only preoperative risk,⁽³⁾ and may not be a suitable parameter for evaluating whether medical treatment or surgical treatment is likely to be beneficial.

Since its introduction as a relatively non-invasive method for evaluating portal circulation in 1988,⁽⁶⁾ numerous large studies have suggested that per-rectal portal scintigraphy (PPS) with Tc-99m pertechnetate is a useful, sensitive and non-invasive procedure for early detection and quantitation of the porto-systemic shunts secondary to cirrhosis.⁽⁷⁻¹⁴⁾ The aim of this study was to determine the clinical usefulness of PPS in the evaluation of the severity of portal hypertension in cirrhotic patients, in terms of correlation between cirrhosis and parameters of hepatic functional reserve, and identifying the difference of the portal shunt index (PSI) of the bleeding oesophageal varices (BEV) group and non-BEV group of patients.

METHODS

The study was carried out using retrospective cases referred to the Division of Nuclear Medicine, Department of Radiology, Faculty of Medicine, Chiang Mai University, Thailand between January 1997 and December 2000. This included a total of 67 patients with a diagnosis of cirrhosis and oesophageal varices. Each patient underwent a full clinical examination, biochemical analysis, upper gastrointestinal tract endoscopy for detection of oesophageal varices, abdominal ultrasonography for detection of ascites and PPS. History of upper gastrointestinal bleeding was also recorded. The criterion for the diagnosis of variceal haemorrhage was haematemesis or melaena without other potential sources of blood loss. The study group consisted of 60 men (89.6%) and seven women (10.4%). The mean age of the subject was 48.99 years (ranging 23–98 years). The severity of liver dysfunction was classified according to a CTP grading system into three classes: A (score 5–6), B (score 7–9), and C (score 10–15). 36 patients had an episode of variceal haemorrhage before the PPS investigation.

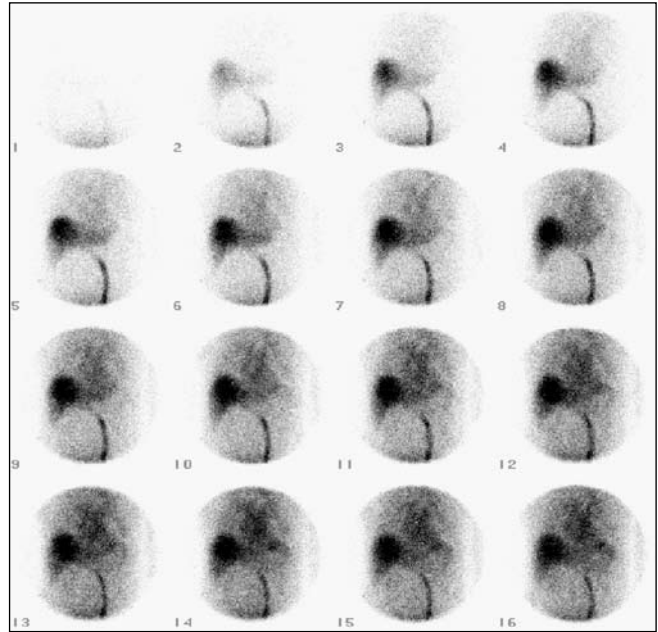


Fig. 1 Scintigraphic uptake activity is present in the liver before the heart.

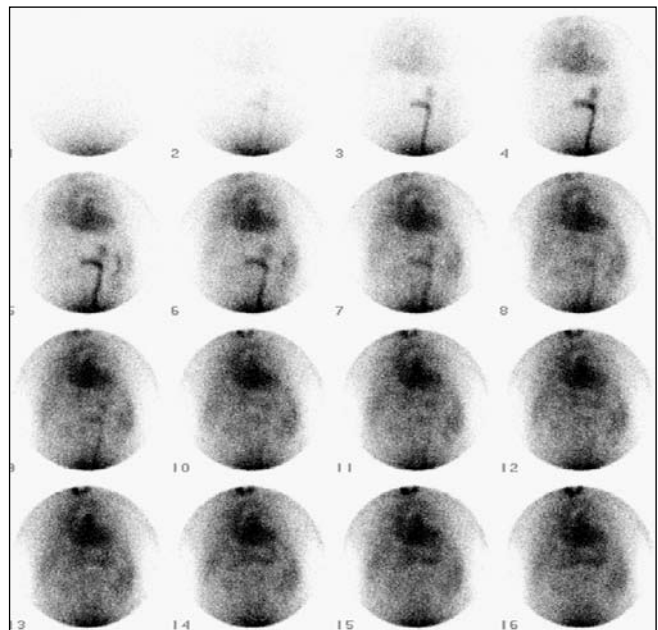


Fig. 2 Scintigraphic uptake activity is present in the heart before the liver.

In this study, PPS was performed according to the protocol of Shiomi et al,⁽⁶⁾ with slight modifications. The patients were to fast for a 12-hour period before the study. A laxative was given the day before the study to reduce the faecal content in the upper rectal region. 550 MBq of Tc-99m pertechnetate in 2.0 ml saline was prepared in a syringe. The subject was positioned in the right lateral recumbency and a soft polyethylene tube (Ne'luton catheter, French 18), fitted

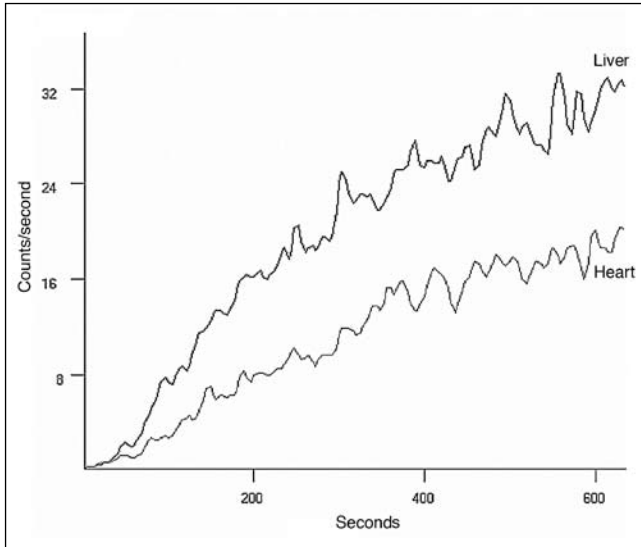


Fig. 3 Time-activity curve shows rising activity in the liver before that of the heart.

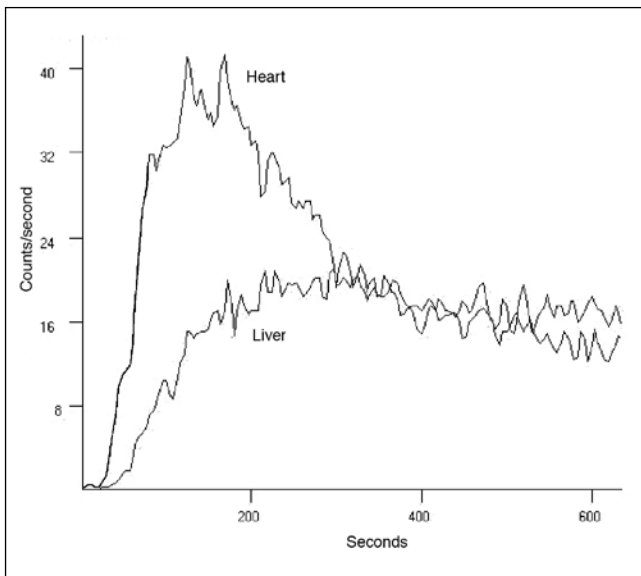


Fig. 4 Time-activity curve shows rising activity in the heart before that of the liver.

with a three-way stopcock, was inserted 20 cm up into the rectum. The tip of the catheter was located in the upper rectal region. The radiopharmaceutical was administered through the catheter and flushed with 15 ml room air.

Five minutes after instillation, the catheter was removed and the acquisition was started. The radiopharmaceutical injected into the upper rectum was absorbed quickly by the rectal mucosa. A dynamic scintigraphy of 4-second images was acquired over a 640-second period by using a LFOV single-head

gamma camera (Elsint's SP4 APEX) equipped with low-energy-multipurpose, parallel-hole collimator. The matrix size was 128 × 128. The detector of the camera was positioned over the patient's abdomen in a fashion to encompass the heart and the liver in the field of view. The summed-up scintigraphic images were analysed, and the time-activity curves were then generated for quantitative assessment of the portosystemic shunt. The dynamic images were categorised into two groups: (1) in a normal study, activity was identified in the liver before the heart (Fig. 1); (2) in a positive study, activity was identified in the heart, before it was redistributed in the abdominal organs, particularly the liver (Fig. 2). The data from the dynamic studies were used for generating the time-activity curves. There were two obvious patterns seen in the curves: pattern I showing rising activity of the liver before that of the heart (Fig. 3), and pattern II displaying rising of heart activity before that of the liver (Fig. 4).

The PSI was calculated according to the method of Shiomi et al.⁽⁶⁾ Through the analysis of time-activity curves, the PSI was determined by calculating the ratio of counts in the liver to counts in the heart integrated for 24 seconds immediately after the appearance of the liver or heart time-activity curve, using the following equations. Equations (1) and (2) were used to calculate the PSI for patients with pattern I and II curves, respectively.

$$\text{PSI} = \frac{\sum_0^{(n+24)/4} X_i(\text{H})}{\sum_0^{(n+24)/4} X_i(\text{L}) + \sum_0^{(n+24)/4} X_i(\text{H})} \times 100(\%) \quad (1)$$

$$\text{PSI} = \frac{\sum_0^{(n'+24)/4} X_i(\text{H})}{\sum_0^{(n'+24)/4} X_i(\text{L}) + \sum_0^{(n'+24)/4} X_i(\text{H})} \times 100(\%) \quad (2)$$

where:

n: the time at which the radionuclide appeared in the area of the liver

n': the time at which the radionuclide appeared in the area of the heart

X_i(L): the count per 4 sec over the area of the liver

X_i(H): the count per 4 sec over the area of the heart

All data were analysed using the Statistical Package for Social Sciences version 12.0 (SPSS Inc, Chicago, IL, USA). The results of the statistical analysis were expressed as mean values (± standard deviation [SD]). Quantitative variables were compared

Table I. Baseline characteristics of 67 patients with cirrhosis.

Characteristics	Clinical data (%)
Gender (M:F)	60(89.6):7(10.4)
Age (years)	
Minimum	23
Maximum	98
Mean \pm SD	49.0 \pm 12.8
CTP classification	
A	18 (26.9)
B	28 (41.8)
C	21 (31.3)
History of BEV	
Absent	31 (46.3)
Present	36 (53.7)
Serum albumin	
Minimum	1.1
Maximum	4.5
Mean \pm SD	2.8 \pm 0.7
Serum bilirubin (mg/dL)	
Minimum	0.22
Maximum	31.79
Mean \pm SD	4.0 \pm 5.1
CTP score (g/dL)	
Minimum	5
Maximum	15
Mean \pm SD	8.4 \pm 2.4
PSI (%)	
Minimum	11.4
Maximum	98.4
Mean \pm SD	66.3 \pm 22.8

by *t*-test. The correlation between continuous variables was evaluated by Spearman's correlation. A *p*-value of less than or equal to 0.05 was considered to be statistically significant.

RESULTS

The patient baseline characteristics are shown in Table I. The results, expressed in PSI, were: 56.4% \pm 27.1% in cirrhotic patients without BEV, and 74.9% \pm 13.6% in cirrhotic patients with BEV, whereas the mean CTP scores in cirrhotic patients without BEV

and with BEV were 31 \pm 2.47 and 36 \pm 2.38, respectively. The PSI was significantly lower in cirrhotic patients without BEV than those with BEV (*p* = 0.001). The CTP score was not different in cirrhotic patients without BEV than those with BEV (*p* = 0.929). The mean of the PSI were 73.76% \pm 18.44% in cirrhotic patients with ascites and 60.64% \pm 24.36% in cirrhotic patients without ascites; this difference was not significant (*p* = 0.18). According to the CTP classification; the mean PSI in class A, B and C cirrhotic patients were 52.6%, 64.4% and 80.6%, respectively (Table II). The study revealed a significant difference in the mean PSI between class B and class C (*p* = 0.002), but found no difference in the mean PSI between class A and class B (*p* = 0.089). The correlation of the PSI with parameters for hepatic functional reserve was found. Correlation was significant between the PSI and the serum albumin level (*r* = -0.310, *p* < 0.05), the serum bilirubin level (*r* = 0.359, *p* < 0.01), the prothrombin time (*r* = 0.256, *p* < 0.05), and the CTP score (*r* = 0.452, *p* < 0.01).

DISCUSSION

Portal hypertension can lead to severe outcomes in patients with cirrhosis, including bleeding of oesophagogastric varices. Varices are common in patients with cirrhosis; however, only in a third of patients will bleeding occur.⁽¹⁾ The goal of management is to prevent variceal bleeding. Identification of patients at high risk of BEV would permit early treatment, careful follow-up, and eliminate unnecessary investigation of low-risk patients. Portal hypertension can be evaluated invasively by HVPG, which is a useful clinical marker of portal pressure. It has been shown to correlate well with portal pressure in both alcoholic cirrhosis and hepatitis C.^(15,16) HVPG is a rather invasive technique and is not available for all patients, especially patients with a low risk of BEV. Another relatively non-invasive way to evaluate the

Table II. Patient's characteristics according to the CTP classification.

	CTP classification		
	Class A	Class B	Class C
Age (years)	49	50	48
History of BEV (no. of cases)	10	13	13
Ascites (no. of cases)	2	13	14
Hepatic encephalopathy (no. of cases)	0	1	7
Mean serum albumin(g/dL)	3.67	2.73	2.29
Mean serum bilirubin (mg/dL)	1.65	2.35	8.18
Mean CTP score	6	8	11
Mean PSI (%)	52.6	64.4	80.6

changes in portal haemodynamics is by PPS. Since its introduction by Tonami et al in 1981,⁽¹⁷⁾ many tracers, such as thallium-201,^(17,18) sodium iodine-131,⁽¹⁹⁾ and I-123 iodoamphetamine,^(20,21) have been studied for the evaluation of portal circulation. The use of these radiopharmaceuticals is limited by the cost and allowable injected dose. In this study, we used Tc-99m pertechnetate because of its short half-life and low cost. Therefore, we could use enough dosage to show the portal circulation with a good image quality. Another merit of Tc-99m pertechnetate PPS is its simple usage and that it can be used for outpatients. Tc-99m pertechnetate PPS was introduced by Shiomi et al in 1988.⁽⁶⁾ After the tracer is instilled into the upper rectum, approximately 20% of the total radioactivity is absorbed into the venous system within five minutes, and then circulated throughout the body. In normal subjects, the radioactivity is absorbed into the portal circulation and rapidly transported to the liver. However, in patients with a portosystemic shunt, the radioactivity bypasses the liver and appears in the heart first, through the shunts and inferior vena cava. Therefore, the extent of portosystemic shunting can be reliably evaluated with the PSI.

Several studies have proven that PSI correlated strongly with portal pressure and the presence of oesophageal varices.^(6,10) Slightly or markedly abnormal PSIs were detected in cirrhotic patients.⁽⁶⁾ A PSI value of 10% or higher is considered to be abnormal,⁽⁶⁾ and a PSI of 30% or higher has an especially poor prognosis for chronic liver disease.⁽²²⁾ The presence of oesophageal varices could correctly be predicted when PSI value was greater than 30% (100% specificity, 56% sensitivity).⁽²³⁾ The PSI rose gradually with disease advancement, and rapidly when varices developed.⁽⁶⁾ The PSI obtained by PSS was significantly higher in the cirrhotic patients with complications (oesophageal varices, ascites, and hepatic encephalopathy).⁽⁶⁾ Therefore, PSS could be used for identifying the risk of developing oesophageal varices in cirrhotic patients. Shiomi et al demonstrated that the PSI was significantly higher in cirrhotic patients with oesophageal varices (22.0 ± 21.8) than in patients without oesophageal varices (70.3 ± 17.6).⁽⁶⁾ They also found that PPS can be useful for predicting the formation of oesophageal varices, in establishing prognosis and in predicting survival rates.⁽²²⁾

All 67 cirrhotic patients with oesophageal varices in this study had an abnormal PSI (range 11.4%–98.4%). Seven patients (10.5%) had PSI lower than 30%, five patients were classified with CTP class A and two patients with CTP class B. With the cut-off point of 30%, PSI identified 60 patients

(89.5%) with oesophageal varices. In this study, we performed PSS in cirrhotic patients who all had oesophageal varices. Our study had three major findings. First, there was a significant correlation between PSI and the parameters for hepatic functional reserve, even though the correlation was relatively poor. This is because the modifications of PPS in liver disease are due to portal hypertension, rather than to liver function impairment.⁽¹⁸⁾ Second, the PSI was higher for more severe disorders, in increasing order of severity: class A, B, and C. We found that PSI in this study was related to the severity of hepatocellular failure, as assessed by CTP classification. Third, mean values of PSI were higher in patients with BEV than in those without BEV. On the other hand, the CTP score did not show a significant difference in both groups. PSI should be useful for the observation and monitoring of cirrhotic patients with oesophageal varices during the course of treatment, because it is a simple and relatively non-invasive method, unlike hepatic venous catheterisation, which needs hospitalisation. The limitation of this study was that the sensitivity and specificity of PSI (greater than 30%) could not be calculated for detecting oesophageal varices as normal subjects were not included in this study.

In conclusion, this study demonstrated that the PPS using Tc-99m pertechnetate can provide the useful quantitative data to estimate the extent of the portosystemic shunt, and can be used by clinicians to identify cirrhotic patients at risk of developing BEVs. The PSI can be used by clinicians, for planning follow-up and evaluating the effectiveness of the medical treatment.

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