

## 《原 著》

# Radionuclide Study on Hepatic Blood Flow in Schistosomiasis Japonica

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**Abstract** Schistosomiasis Japonica is a regional disease found in elderly people who were living in once-endemic areas in Japan. Yamanashi was one of these areas until 1970, since when no newly infected patients were reported. The disease is characteristic of developing irreversible interstitial fibrosis of the liver, where parasites migrate and lay eggs. Portal hypertension, esophageal varices and hepatocellular carcinomas are the common features of the results. In order to estimate patient's hepatic blood flow, radionuclide angiography of the liver with the use of 10–15 millicuries of Tc-99m phytate were performed prior to the conventional multiview imaging. Twenty-two patients with schistosomiasis and twelve adults without evidence of liver disease were studied. A time-activity curve of the right lobe of the liver was generated by a computer, and the ratio of arterial blood flow to portal blood flow was calculated. As a result, a good correlation was found between the arterial to portal blood flow ratio and the grade of hepatic fibrosis verified by laparoscopic biopsy. The development of esophageal varices were likely to correlate well with the blood flow ratio rather than scores on the conventional static liver and spleen scintigram. The study was useful for evaluating patient's clinical stages and prognosis.

## Introduction

Schistosomiasis Japonica is a regional disease found in elderly people who were living in once-endemic areas in Japan. Yamanashi was one of these areas until 1970, since when no newly infected patients were reported<sup>1)</sup>. The disease is known to be still endemic in several areas of Southeast Asia<sup>2)</sup>. Interstitial fibrosis, induced by the immunological process against the schistosome's eggs, becomes irreversible and often produces portal hypertension. It is still important therefore, even in no-more endemic areas, to keep those patients under medical surveillance.

Purpose of this study is to evaluate the hemodynamics of the liver in patients with schistosomiasis Japonica using a non-invasive radionuclide

angiography, and to use the test for estimating their clinical stages and prognosis.

## Material and Method

Twenty two patients with schistosomiasis Japonica and twelve controls were studied. Liver biopsies were performed on these twenty two patients under laparoscopic procedure. By these specimens the grade of interstitial fibrosis was evaluated; mild, moderate and marked liver fibrosis. They also had fiberoptic endoscopies to detect esophageal varices which were often the causes of death from massive bleedings.

Ten to 15 mCi of Tc-99m phytate were rapidly injected into patient's antecubital vein so that the radionuclide bolus could reach the abdominal aorta. The head of a gamma camera faced the patient's upper abdomen, and digital data of sequential organ images were stored into a data processing system at 1 second intervals for 60 seconds right after the radionuclide appeared in the lungs.

Time-activity curves on the abdominal aorta, liver and kidney were generated afterwards using ROI techniques. Aortic time-activity curve was used for the assessment of adequacy of bolus injection. If the time to reach peak from the half-

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受付: 60年10月18日

最終稿受付: 61年5月12日

別刷請求先: 千葉市亥鼻 1-8-1 (☎ 280)

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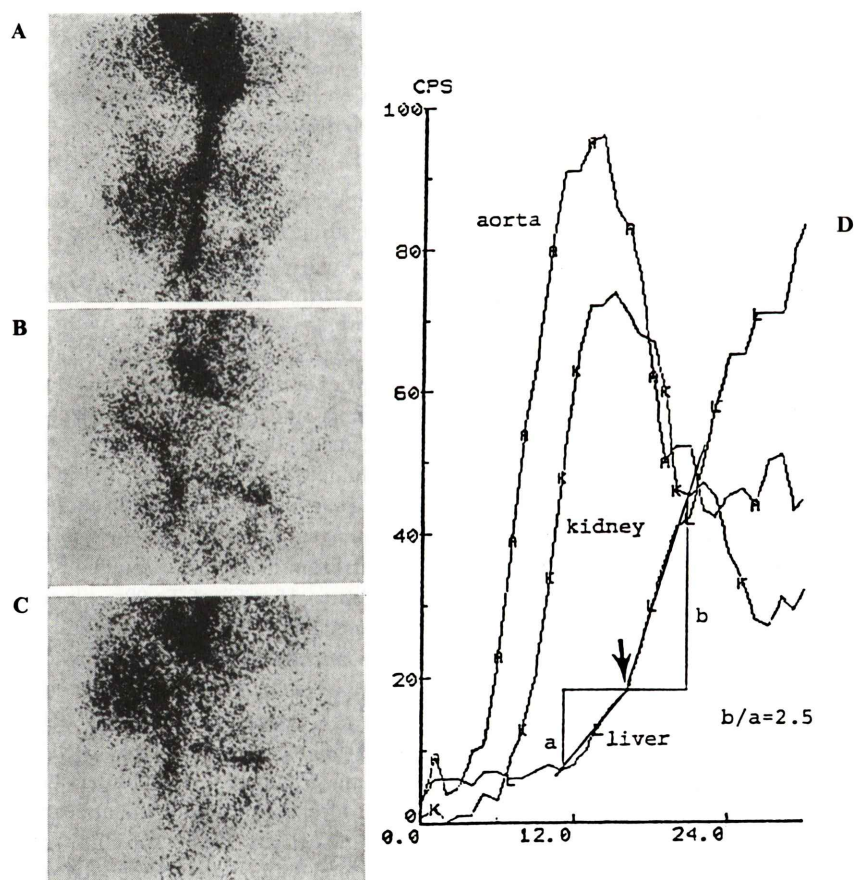
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maximum point on the ascent of the curve was greater than 8 seconds, the study was discarded. A rising slope of a hepatic time-activity curve is composed of an arterial phase and a portal phase. A point at the end of arterial phase and the beginning of portal phase is usually observable as a bending portion of the curve, shown in Fig. 1. When the point is not readily recognized, a peak time of a right renal time-activity curve was used to identify the transitional portion of a hepatic curve. The reason is, according to Sarper et al.<sup>5)</sup>, the peak of the renal curve is coincidental with the transitional portion of the hepatic curve in many cases. The ratio of the portal slope (b) to the arterial slope (a) was calculated, and b/a value was used as the hepatic blood flow ratio.

Conventional multiview liver images were also obtained and carefully interpreted. Liver images of schistosomiasis Japonica were quite similar to those of liver cirrhosis. The characteristic findings are (1) the atrophy of the right lobe, (2) enlargement of the left lobe, (3) splenomegaly and (4) increased bone marrow accumulation of radio-nuclide. Each findings were scored 1 to 3 points. By adding scores of these findings of conventional liver and spleen scintigrams, all livers were divided into four classes; normal, mildly impaired, moderately impaired and severely impaired.

### Representative Cases

**Case 1** The patient is 54-year-old female. She had been proved to have schistosoma's eggs in her liver



**Fig. 1** Selected images from radionuclide angiography (A, B, C) and time-activity curves of aorta, kidney, and liver (D). Transition point of a liver curve was shown by an arrow.

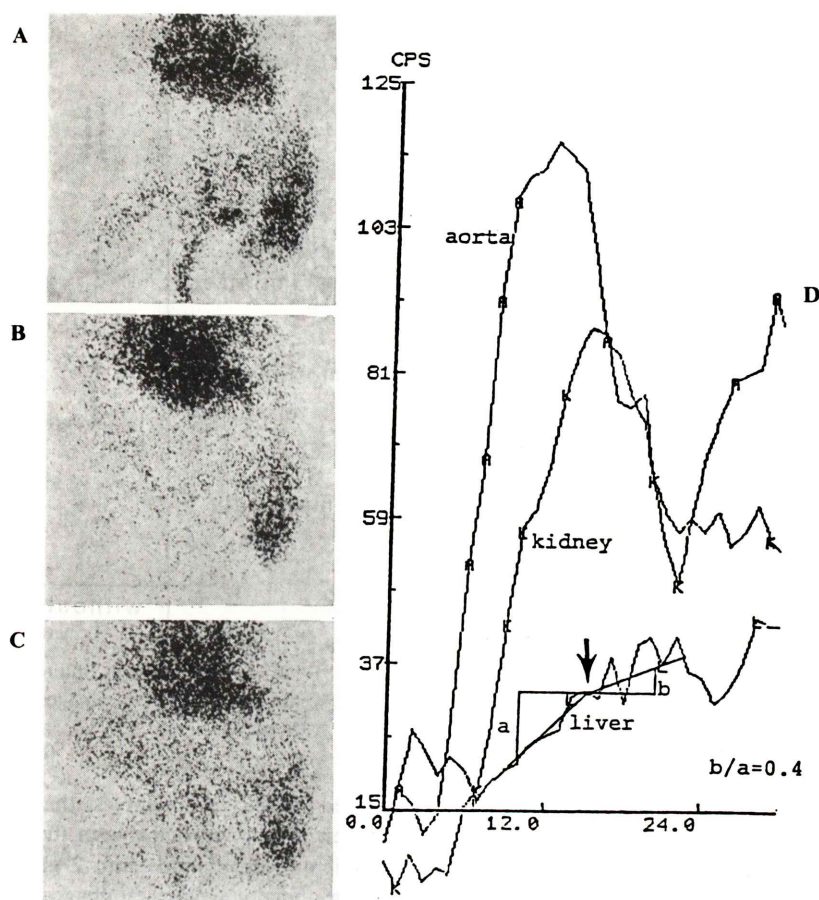


Fig. 2 Case 2. Selected images (A, B, C) and time-activity curves (D).

tissue, but the interstitial fibrosis was mild. Images recorded in 2 seconds for each frame showed rather good accumulation of the radiopharmaceutical in the liver. Selected images from radionuclid angiography (Fig. 1) showed the peak radioactivity in the right kidney, the portal inflow to the liver (10 seconds later) and good accumulation of radioactivity in the liver (20 seconds later). Time-activity curves on the aorta, kidney and liver of this patient are shown in Fig. 1. Aortic curve suggests the bolus injection was good enough for analysis. Transition point of a liver curve was evident as shown by an arrow. Portal to arterial flow ratio, namely  $b/a$  was 2.5 in this case.

**Case 2** The patient is 54-year-old male. He displayed marked periportal fibrosis in his biopsied specimen. The liver blood flow was rather poor in

comparison with the previous patient. The liver image was very faint in photos selected in the same manner. Time-activity curve of the liver was rather horizontal and  $b/a$  value was 0.4 (Fig. 2).

### Results

Relation between  $b/a$  value and the grade of interstitial fibrosis is shown in Fig. 3. The mean value  $\pm$  standard deviation of  $b/a$  values of each group of normal, mild fibrosis, moderate fibrosis and marked fibrosis, were  $2.8 \pm 1.2$ ,  $2.3 \pm 0.9$ ,  $1.5 \pm 0.7$ , and  $0.5 \pm 0.4$  respectively. There is no definite cut-off value which separate abnormal from normal individuals. But, it could be said that the heavier the interstitial fibrosis observed, the less the  $b/a$  value obtained. While normal controls gave  $b/a$  values more than 1.6, patients with

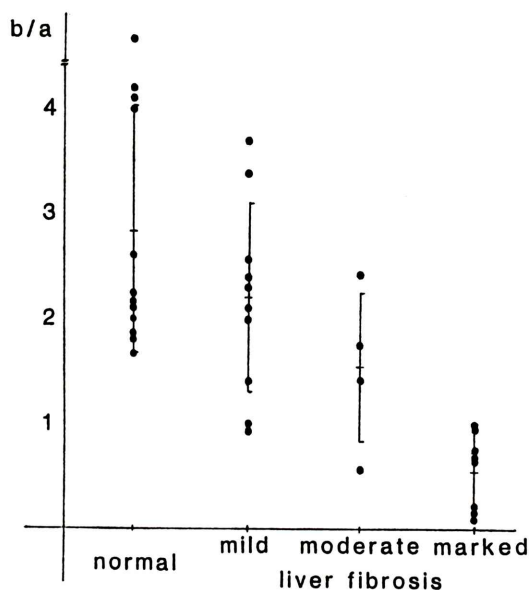


Fig. 3 Relationship between b/a values and the grade of interstitial fibrosis.

normal :  $m=2.8$   $SD=1.2$   
 mild fibrosis :  $m=2.3$   $SD=0.90$   
 moderate fibrosis :  $m=1.5$   $SD=0.70$   
 marked fibrosis :  $m=0.53$   $SD=0.43$

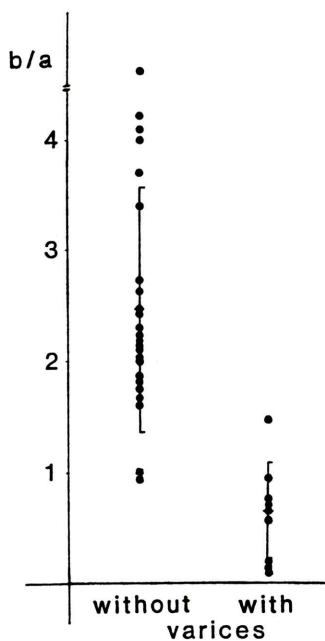


Fig. 4 Relationship between b/a values and esophageal varices.

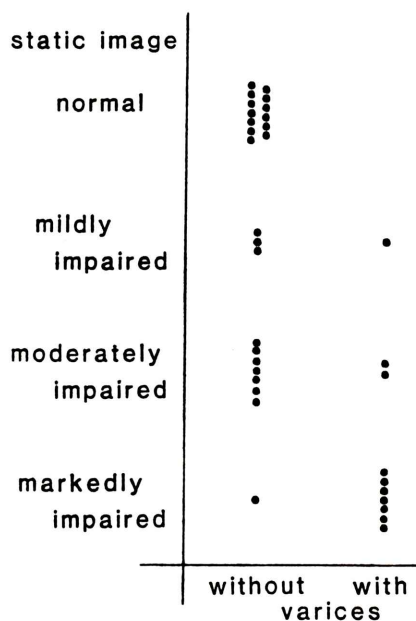


Fig. 5 Relationship between finding-scores in conventional liver-spleen images and esophageal varices.

marked fibrosis gave them less than 1.0. Statistical difference was evident between these two groups.

Patients were divided into 2 groups who were having and not having esophageal varices by the fiber-optic endoscopies. Their b/a values were fairly well separated from each other as shown in Fig. 4. While patients not having esophageal varices gave b/a values more than 1.0, most of patients with varices gave them less than 1.0. There was statistically significant difference between values of these 2 groups. The result suggests that when b/a value is less than 1.0, the probability that the patient has esophageal varix is high. On the other hand, there was no good separation between 2 groups when we applied the scores of findings in the conventional liver and spleen scintigrams (Fig. 5). Using only static liver and spleen images, it is not possible to predict whether patients have or have not esophageal varices.

#### Discussion

Schistosomiasis Japonica is characteristic in developing irreversible interstitial(periportal)fibrosis of the liver, where parasites migrate and lay

their eggs. Glisson's sheath is invaded by eggs of schistosoma around the portal vein. Portal hypertension, esophageal varices and possibly hepatocellular carcinomas are the common features of prognosis<sup>2,6,7</sup>. Therefore, to study the patients once infected is still of importance to evaluate their clinical stages and to predict their prognosis.

There are papers on the techniques of evaluating the hepatic blood flow by analyzing time-activity curves of the liver after intravenous rapid injection of radionuclides<sup>5,8-10</sup>. Among these methods our analyzing technique, the one dealt with the ratio of slopes of arterial to portal phase, namely b/a value, is similar to those of Sarper et al.<sup>5</sup> and Boyd et al.<sup>8</sup> In our preliminary studies, This method showed better reproducibility than the technique proposed by Biersach et al.<sup>10</sup>, which applied the ratio of integrated area of arterial phases to that of portal phase.

The good correlation between b/a values and the grade of interstitial fibrosis of the liver was obtained. The result supports the concept that the portal perfusion decreases with the severeness of periportal fibrosis of the liver. The blood flow ratio, b/a value, also proved to be able to reflect the probability of having esophageal varices more than the conventional static liver and spleen images.

Iio et al. studied on the schistosomiasis patients with the conventional liver and spleen scintigrams<sup>3,4</sup>, and their results showed that the small liver size and splenomegaly were the most prominent sign in the severely damaged schistosomiasis liver. They also suggested that the fibrotic change in the liver in female patients produced splenomegaly with high incidence of esophageal varices<sup>4</sup>. The b/a value described in this paper could also give an

careful tool to this kind of study.

In patients with schistosomiasis Japonica, the radionuclide angiography with quantitative evaluation of hepatic blood flow was valuable test for estimating their clinical stages and prognosis.

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## 要 旨

## 肝 RI アンジオグラフィーを用いた慢性日本住血吸虫症肝の血流動態解析

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日本住血吸虫症の感染後数か月から数年して生じる肝の線維化は不可逆的な変化であり肝癌や門脈圧亢進症の発生母地となるため、本疾患における肝の病態解析やいったん罹患した者の管理はなお重要な問題である。今回われわれは慢性日本住血吸虫症患者22例、正常者12例を対象とし肝の血流動態解析を行った。 $^{99m}\text{Tc}$ -フチン酸10~15 mCiを急速静注し肝に関心領域をおいた時間放射能曲線を解析することにより肝動脈の門脈に対する血

流比 (b/a 値)の算出した。病理所見上肝の線維化が強いほど b/a 値は低下する傾向にあり、食道静脈瘤の有無に関しては従来の肝シンチグラム静態像による評価よりも優れた相関を示した。慢性日本住血吸虫症の重症度判定、予後の評価に b/a 値は有用な指標である。

**Key words:** Schistosomiasis Japonica, Hepatic blood flow, Liver scintigram, Radionuclide angiography, Esophageal varices.