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Clinical values for an index predicting postoperative residual liver function by pre-operative liver-scintigraphy in patients with liver disease

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Hepatic resection is essential in treating hepatocellular carcinoma. However, before an operation, it is difficult to predict the functional reserve in the remnant following massive resection. We devised an original method by which effective liver volume was measured by liver scintigraphy. In order to predict the residual liver function before hepatic resection in a preoperative radiocolloid study, we obtained a predictive index by combining the K values with effective liver volumes which seemed to have the estimated residual liver function. Twenty-one patients with liver or biliary tract disease were selected at random for the present study. We divided them into 3 groups in accordance with prognosis after hepatic resection. There were statistically significant difference between the deceased group who died from hepatic failure and the group who died from causes other than hepatic failure; and between the deceased group who died from hepatic failure and the living group in the preictive index ($p<0.01$). Our data suggest that if the predictive index is above 0.45, the probability of hepatic failure after hepatic resection is low. We concluded that our predictive index is useful to use in preoperative prediction of post-hepatectomic residual liver function.

Key words: predictive index, residual liver function, liver scintigraphy, liver volume, hepatocellular carcinoma

INTRODUCTION

HEPATOCELLULAR CARCINOMA (HCC) can only be completely cured by hepatic resection, but most patients with HCC have underlying cirrhosis. This often makes surgery impossible and limits the extent of surgical intervention.[1] Preoperative evaluation of patients with HCC involves two major considerations: First, whether the tumor is anatomically resectable or not. Second, whether patients can tolerate the removal of functioning liver tissue or not.

Based on the hypothesis that blood flow in the residual hepatic parenchyma is a determining factor in posthepatectomic liver function, liver perfusion before hepatic resection was estimated from the rate of clearance (K value) of intravenously injected radiocolloid.[2-7] As an accumulation of radiocolloid reflects the reticuloendothelial function, we expressed it in terms of effective residual liver or effective liver volume. There are several reports concerning volume estimation by means of liver scintigraphy.[8-11] We devised an original method in which effective liver volume was measured by scintigraphy. The estimated liver volume for the liver phantom was approximately equivalent to the real volume.[12] The effective volume estimated by radiocolloid correlated well with that measured by X-ray CT scan. In order to predict the residual liver function before hepatic resection, we have obtained a predictive index by combining the K value with effective liver volume which was estimated for residual liver function in a preoperative

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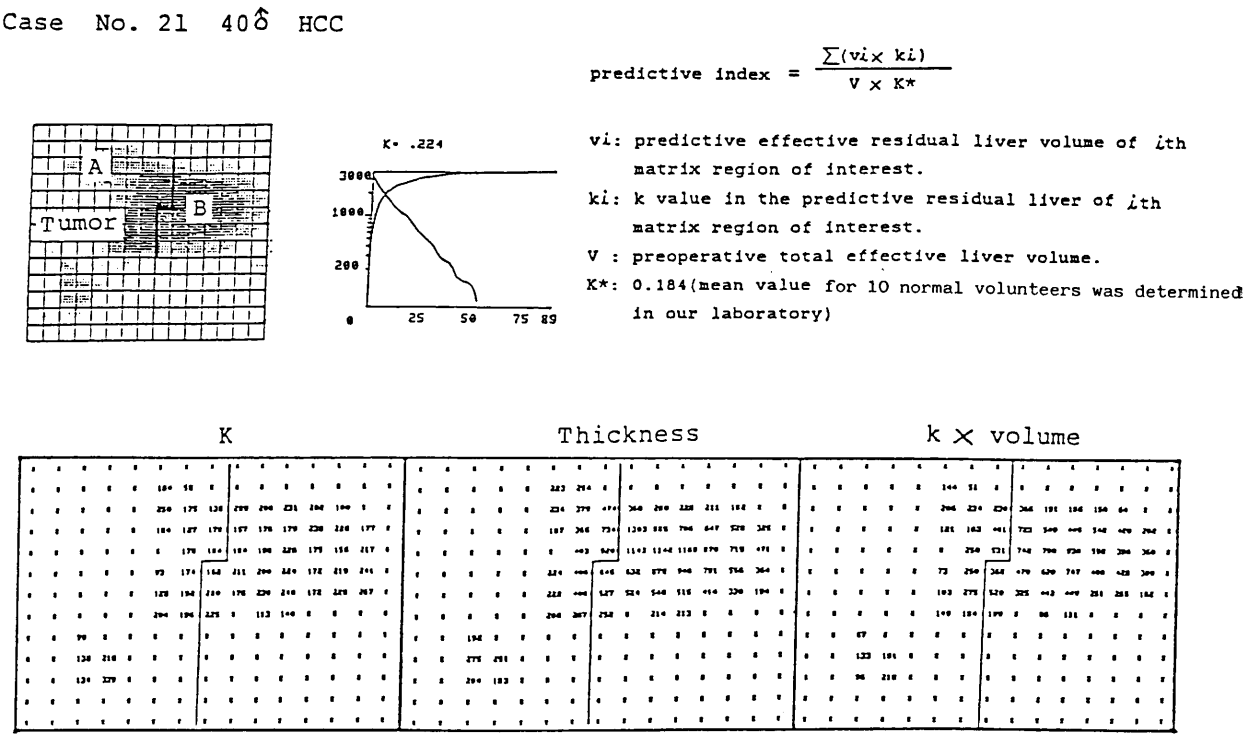

Fig. 1 a) Matrix ROI setting on digital liver scintigraphy with Au-198 colloid (upper left). b) Accumulation curve of Au-198 colloid in matrix ROI and K value (upper middle). c) Predictive index (upper right). d) K Value for each matrix ROI (lower left), liver thickness (lower middle) and product of the K value multiplied by the liver volume (lower right).

radiocolloid study.[12] The aim of the current study is to investigate retrospectively whether or not there is a correlation between the predictive index and postoperative patient prognosis.

SUBJECTS AND METHODS

Patients.

Twenty-one patients with liver or biliary tract disease treated between 1980 and 1982 were selected at random for the present study. The study group comprised 21 patients who underwent resection. Fifteen patients had HCC (12 patients with liver cirrhosis and 3 patients without liver cirrhosis). Three patients had hemangioma, one had a focal nodular hyperplasia, one had a liver abscess and one had a stone in the intrahepatic biliary tract. The patients' prognoses were evaluated on Oct, 1984. Before hepatic resection, all patients had had liver scintigraphy with Au-198 colloid and Tc-99m Sn-colloid to evaluate effective liver volume and hepatic perfusion.

Radionuclide techniques.

In the hepatic perfusion study, a scintillation camera equipped with a high energy collimator was positioned to view the entire liver and spleen from the anterior aspect. Au-198 colloid was obtained commercially as a sterile suspension stabilized with gelatin. The specific activity was about 1 mCi/m*l*. The particle size in a typical lot was on the average 30 mμ. Approximately 300 μCi (11.1 MBq) of Au-198 colloid was injected as a bolus through the antecubital vein. Data acquisition started simultaneously with the injection, and 120 frames were acquired at 20 sec per frame. Digital images recorded as on a 64×64 matrix were stored in an on-line computer system. Maximum liver thickness was estimated from the right lateral view of liver scintigraphy with Tc-99m Sn-colloid. Tc-99m-Sn colloid was used for measuring only the maximum liver thickness in this study.

The computer data were processed as follows: matrix ROI (region of interest) was set on the anterior digital liver image (Fig. 1). a) Au-198 accumulation curve was generated for each matrix of liver image. A typical accumulation curve obtained over each ROI matrix is shown in Fig. 1 (upper middle). From the curves we determined the time taken for half the radioactivity to disappear from the blood. This is the disappearance half time (T 1/2). The disappearance rate constant (K value=0.693/T 1/2) in each ROI was determined (Fig. 1. lower left). b) The depth under a mitrix ROI was calculated using the plateau value for the Au-198 accumulation curve and the energy absorption coefficient. On the assumption that the radiocolloid was homogenously

distributed in the liver, the scintigraphic liver volume was calculated as follows:

$$Ip=\int_0^W I_0\, e^{-\mu x}\, dx \qquad (1)$$

I_0: theoretical γ-ray intensity for unit depth

Ip: observed γ-ray intensity for W depth which is derived from the plateau level of the Au-198 colloid accumulation curve in each matrix.

μ: energy absorption coefficient (0.105, corresponding to water and 412 KeV of γ-ray energy)

$$Ip_0=\frac{I_0}{\mu}(1-e^{-\mu W_0}) \qquad (2)$$

W_0: maximum liver thickness from the right lateral view of liver scintigraphy with Tc-99m Sn-colloid

Ip_0: observed γ-ray intensity which is derived from the plateau level of the Au-198 colloid accumulation curve corresponding to maximum liver thickness.

The following equation is obtained,

$$W=\frac{1}{\mu}\,ln\left\{\frac{Ip_0}{Ip_0-Ip(1-e^{-\mu W_0})}\right\}$$

and the liver volume (V) is

$V=\Sigma(S\times Wi)$

S: area of matrix ROI

W: liver thickness of ith matrix region of interest

The estimated volume of the predicted effective residual liver, the total effective liver volume and disappearance rate constant in the predicted effective residual liver were evaluated. A predictive index was calculated with the following equation:

$$\text{predictive index}=\frac{\Sigma(Vi\times Ki)}{V\times K^*}$$

Vi: predictive effective residual liver volume of ith matrix region of interest.

Table 1 Demographic data on subjects

Patient No. (Partial resection)	Age	Sex	Diagnosis	Complication of liver cirrhosis	Prognosis	Cause of death	Predictive index
1	64	F	Hepatoma	Yes	Living		0.503
2	51	F	Hepatoma	No	+Survival time 9 months	Recurrence of hepatoma	0.538
3	63	M	Hepatoma	No	Living		0.452
4	47	M	Hemangioma	No	Living		0.806
5	60	F	Hepatoma	Yes	+Survival time 1 month	Respiratory failure	0.674
6	47	M	Hemangioma	No	Living		0.678
							0.609±0.121 (mean±SD)
(Resection of one seg.)							
7	63	M	Hepatoma	Yes	+Survival time 3 months	Hepatic failure	0.361
8	61	M	Hepatoma	Yes	Living		0.892
9	62	M	Hepatoma	Yes	+Survival time 8 months	Recurrence of hepatoma	0.953
10	54	M	Hepatoma	Yes	+Survival time 24 months	Recurrence of hepatoma	0.479
11	72	M	Hepatoma	Yes	Living		0.477
12	69	F	Hepatoma	Yes	+Survival time 6 months	Hepatic failure	0.384
13	73	F	Focal nodular hyperplasia	No	Living		0.420
14	50	M	Stone in intra hepatic biliary tract	No	Living		0.641
							0.576±0.216 (mean±SD)
(Resection of two seg.)							
15	44	M	Hepatoma	Yes	+Survival time 3 months	Hepatic failure	0.205
16	63	F	Liver abscess	Yes	Living		0.401
17	58	F	Hemangioma	No	Living		0.434
18	57	M	Hepatoma	Yes	+Survival time 38 days	Hepatic failure	0.324
19	48	M	Hepatoma	Yes	+Survival time 20 days	Hepatic failure	0.303
20	53	F	Hepatoma	Yes	+Survival time 25 days	Hepatic failure Renal failure	0.433
							0.350±0.082 (mean±SD)
(Resection of three seg.)							
21	40	M	Hepatoma	No	+Survival time 15 months	Brain hemorrhage	0.801

Ki: K value in the predictive residual liver of *i*th matrix region of interest.
V: preoperative total effective liver volume.
K:* 0.184 (mean value for 10 normal volunteers was determined in our laboratory)

To explain our method, case 21 is presented (Fig. 1). The upper left shows the matrix ROI set on the digital liver scintigraphic image. A is the predicted area of resection. B is the residual liver area. K value in the one ROI was calculated from the Au-198 colloid accumulation curve shown in the upper middle graph. K value is given for each ROI in the lower left chart. Liver thickness for each ROI is shown in the lower middle chart. Each matrix size consists of 9 pixels. Each pixel is 0.625 cm squared. Liver volume is the product of matrix size by thickness in each matrix. In order to obtain values of thickness in centimeter, numbers in the figure should be multiplied by ten to the minus second. The preoperative effective total liver volume was 943.5 cm^3, of which 246.8 cm^3 was resected and 696.7 cm^3 remained. From this data, we calculated the predictive index as follows; the product of the K value in the residual liver area multiplied by the volume of that area, divided by the product of the normal K value multiplied by the patient's preoperative liver volume. This calculation is shown in the top right hand part.

RESULT

The demographic data on these 21 patients are shown in Table 1. There was no operative death among the 21 patients who underwent hepatic resection. All who died from hepatic failure had liver cirrhosis. Of the 15 patients with HCC, one died of respiratory failure, 3 of hepatoma recurrence, and 6 of hepatic failure. Four of the 15 patients (26.7%) with HCC have survived for more than 2 years since hepatic resection. Three of these 4 patients had liver cirrhosis and one did not. Three patients with hemangioma, one with focal nodular hyperplasia, one with liver abscess and one with a stone in the intra hepatic biliary tract, have all survived for more than 2 years since hepatic resection. These patients did not have liver cirrhosis. We divided them into 3 groups in accordance with prognosis after hepatic resection, namely the living group, the group of those who died from hepatic failure and the group who died from causes other than hepatic failure. The predictive indices of the three groups were compared (Fig. 2). The mean values and standard deviations of the predictive indices were 0.335 ± 0.071, 0.692 ± 0.174 and 0.570 ± 0.165 in the hepatic failure, non-hepatic failure and living groups, respectively. The predictive index for the hepatic failure group was significantly different from that for the non-hepatic failure and living groups ($p<0.01$). Our data suggest that when our predictive index is above 0.45, there is a low probability of hepatic failure.

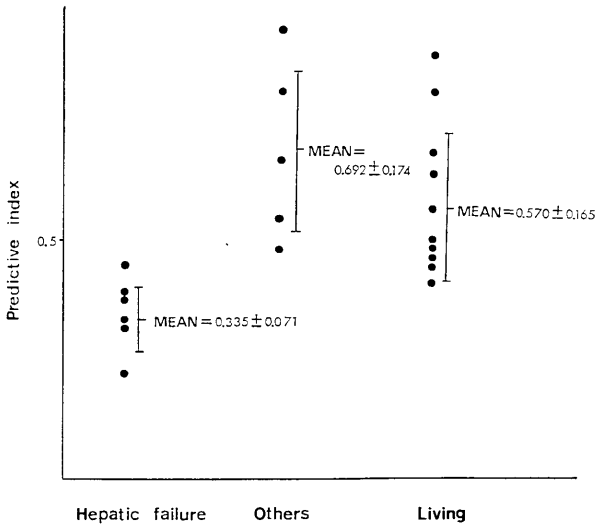

Fig. 2 Predictive value in each group. Coding as in Table 1.

DISCUSSION

Hepatic resection is essential in treating HCC. However, it is difficult to predict preoperatively the functional reserve in the liver remnant after massive resection.

Determination of the disappearance rate of radiocolloid has been proposed as a simple way to solve this problem. The disappearance rate was thought to be a measure of minimum hepatic blood flow.[2-6] The selection of an appropriate radiocolloid is one problem. It has been pointed out that the particle size of the radiocolloid should not only be uniform and suitable for measuring hepatic blood flow, but also that extrahepatic removal should be minimal.[6] Tc-99m sulfur colloid is eliminated from the blood stream more rapidly than Au-198 colloid.[6] The difference between the disappearance rate of Tc-99m sulfur colloid and that of Au-198 colloid can be explained by the greater accumulation of Tc-99m sulfur colloid in parts of the reticuloendothelial system other than the liver. As the bone marrow distribution of Au-198 colloid is minimal compared with other radiocolloids, we neglect the influence of its distribution. Tc-99m phytate forms colloid particles *in vivo* after intravenous injection. The properties of Tc-99m phytate *in vivo* which affect the hepatic blood flow measurement, i.e. the disappearance rate or tissue distribution are not always the same in different individuals.[5] Although Au-198 colloid is a nuclide of high energy and has a half life

of 2.7 days, Au-198 colloid seemed to be more sensitive and suitable for the measurement of hepatic blood flow by the clearance method than Tc-99m sulfur colloid or Tc-99m phytate.[5,6] Our previous animal experiments revealed that hepatic blood flows of normal adult mongrel dogs measured by Au-198 colloid, KICG and H_2 clearance methods significantly correlate with each other.[7,12]

Several authors reported on K value determination using liver accumulation curve analysis of Au-198 colloid (Dobson[2] 0.284, Veter[3] 0.236, Iio[4] 0.146). Using 10 normal volunteers, we adopted 0.184 as the normal K value. At present, Au-198 colloid is not available in Japan. We have examined the properties of Tc-99m Sn-colloid in a hepatic perfusion study and found that there were significant differences between the K values for normal volunteers and patients with liver cirrhosis. As a result, we conclude that Tc-99m Sn-colloid is also suitable for hepatic perfusion study.[13]

Several investigators have used liver scintigraphy to evaluate liver size and volume.[8–11] We devised a method of evaluating the effective liver volume using liver scintigraphy. Our predictive index combining the effective liver volume and the K value shows statistically significant differences between the group who died from hepatic failure and the group who died from causes other than hepatic failure; and between the group who died from hepatic failure and the living group. The data suggest that the probability of hepatic failure after hepatic resection is low in cases in which the predictive index is above 0.45.

There are many reports concerning SPECT volumetric measurement which provides a rapid and exact volume estimation.[14–15] A ring type detector and collimator based on the SPECT system have recently been developed.[15] If they are adapted for the clearance rate constant of radiocolloid and effective liver volume, this system would provide increased sensitivity and accuracy.

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