—**Original**—

Effect of Prostaglandin E_1 on Contrast Enhanced CT of the Liver: Statistical Analysis During Arterial Portography

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Abstract

Purpose: To determine the diagnostic effect of prostaglandin E_1 on contrast enhancement quality of CT during arterial portography (CTAP).

Materials and Methods: Our patients population included 30 patients (11 women, 19 men; age range, 41～81 years) with liver tumors (23 hepatocellular carcinoma and 7 metastatic liver tumor) who had undergone angiography. We divided the 30 patients, who had undertaken CTAP twice, into two groups at random (group A; n＝15, group B; n＝15). In group A, first CTAP was performed without prostaglandin E_1. Approximately 5 minutes later, a second CTAP was again initiated 30 seconds after injection of prostaglandin E_1 under the same conditions. In group B, prostaglandin E_1 was injected before the first CTAP only. We measured the mean CT numbers and standard deviation (SD) numbers of anterior, posterior, medial and lateral segments in the liver at the same section of the CTAP using the same size and location of the regions of interest, and these values with and without prostaglandin E_1 were compared.

Results: 1) CT numbers: The CT numbers were significantly increased in the medial segment after the injection of prostaglandin E_1 ($p<0.05$) in all cases of both groups. On the other hand, they were clearly decreased in the posterior segment after the injection of prostaglandin E_1 ($p<0.05$) in both groups. There were no statistical differences in the CT numbers in the anterior and lateral segments in all patients. In addition, the CT numbers of anterior and posterior segments showed high attenuation compared with the medial and lateral segments in group A without prostaglandin E_1. 2) SD numbers: The SD numbers, which are an index of the homogeneous enhancement, were significantly decreased in the posterior, medial and lateral segments after the injection of prostaglandin E_1 ($p<0.01$, $p<0.05$, $p<0.01$, respectively) in both groups. There were no significant differences in the SD numbers in the anterior segment regardless of the injection of prostaglandin E_1 in all cases.

Conclusion: CTAP with injection of prostaglandin E_1 makes contrast enhancement of liver parenchyma more homogeneously than the conventional procedure, and it may be a useful technique for the detection of liver tumors. (J Nippon Med Sch 2003; 70: 307–312)

Key words: liver, neoplasm, CT, portography

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Introduction

In the past several years, noninvasive techniques, such as dynamic computed tomography (CT), multidetector-row CT or magnetic resonance imaging with intravenous injection of contrast materials, have found widespread acceptance as the main methods of diagnosing liver masses[1-3]. Surgical treatment of liver neoplasms is dependent on reliable radiologic assessment of the liver to identify lesions and determine resectability. In spite of the usefulness of those noninvasive techniques, CT during arterial portography (CTAP) has become a key technique for work-up of patients being examined for partial hepatectomy[4-7]. CTAP examination is hampered, however, by pseudolesions i.e. the artifacts produced by differential enhancement of the liver. Most of these pseudolesions can be differentiated comparatively easily from tumorous lesions not only by their location but also by their shape, which is typically described as wedge-shaped or serpiginous[8-11]. In some patients, however, they are round and difficult to be differentiated from tumors[12].

CTAP performed after the injection of contrast material into the splenic artery provides greater enhancement of the liver with fewer perfusion abnormalities than that performed after the injection into the superior mesenteric artery (SMA) because of the greater blood flow through the splenic artery in comparison with that through the SMA[13]. On the other hand, the increase of portal blood flow and pressure after the injection of vasodilators, such as prostaglandin E_1, via the SMA would influence the blood perfusion in the liver parenchyma. The purpose of this study was to determine the diagnostic quality of CTAP with the injection of prostaglandin E_1 using statistical analysis.

Materials and Methods

Our patient population included 30 patients (eleven women, 19 men; age range, 41～81 years) with liver tumor (23 hepatocellular carcinoma and 7 metastatic liver tumor) who had undergone angiography for diagnosis, transcatheter arterial infusion therapy, and/or transcatheter arterial embolization therapy if surgical resection was impossible, when the patients had multiple tumors. Tumors were diagnosed with histopathologic examination in most cases. Twenty-three patients with hepatocellular carcinoma had cirrhosis of the liver. The primary sites of the metastatic liver tumors were the colon (n=2), the stomach (n=3), and the breast (n=2).

Spiral volumetric CT (Hitachi Radix Prima; Hitachi Medical Systems, Tokyo, Japan) was performed during arteriography and/or arterial portography before and after the injection of prostaglandin E_1 via the SMA. After the puncture of the bilateral femoral arteries, 5-F catheters were introduced into the SMA for CTAP, and the proper hepatic artery (n=18), the common hepatic artery (n=12) for CT arteriography. CTAP and CT arteriography were performed to detect the number of liver tumors.

For CTAP, a total volume of 80 m*l* of diluted nonionic contrast material (100 milligrams of iodine per milliliter diluted with physiologic saline) was injected into the SMA at a rate of 3.0 m*l*/sec with a power injector. Total hepatic spiral volumetric scan was started 25 seconds after the onset of injection. The CT table was moved at a rate of 7 mm/sec.

We divided the 30 patients, who had undergone CTAP twice, into two groups at random (group A; n=15, group B; n=15). In group A, first CTAP was performed without prostaglandin E_1. Approximately 5 minutes later, second CTAP was again initiated 30 seconds after the injection of prostaglandin E_1 (5 μg, LipoPGE$_1$, Mitsubishi Pharma Corporation) under the same conditions. In group B, first CTAP was performed with prostaglandin E_1. Approximately 5 minutes later, second CTAP was performed again without prostaglandin E_1. The degree of enhancement of the liver parenchyma with and without prostaglandin E_1 was compared. For each patient, we measured the CT numbers (Hounsfield Unit, H.U.) and the standard deviation (SD) numbers in the anterior, posterior, medial and the lateral segments in the liver at the same section of the CTAP using the same size and location of the regions of interest (ROI), and these values with and without prostaglandin E_1 were compared.

Table 1 Statistical Analysis during Arterial Portography

CT numbers

Segment	Group	Mean (H.U.)		p
		PGE_1 (+)	PGE_1 (−)	
Anterior	total	120.80	123.12	0.103＞0.05
	A	124.12	124.29	0.477＞0.05
	B	117.48	121.96	0.026＜0.05
Posterior	total	123.36	126.41	0.046＜0.05
	A	127.61	130.95	0.146＞0.05
	B	119.11	121.86	0.079＞0.05
Medial	total	117.45	116.14	0.030＜0.05
	A	118.01	109.53	0.011＜0.05
	B	116.89	122.74	0.048＜0.05
Lateral	total	114.11	112.60	0.153＞0.05
	A	117.52	111.36	0.058＞0.05
	B	110.70	113.85	0.167＞0.05

SD numbers

Segment	Group	Mean		p
		PGE_1 (+)	PGE_1 (−)	
Anterior	total	9.77	9.96	0.289＞0.05
	A	9.59	10.17	0.097＞0.05
	B	9.96	9.74	0.320＞0.05
Posterior	total	9.71	10.55	0.004＜0.05
	A	9.54	10.56	0.010＜0.05
	B	9.87	10.54	0.012＜0.05
Medial	total	9.52	10.33	0.025＜0.05
	A	8.93	9.79	0.091＞0.05
	B	10.12	10.86	0.087＞0.05
Lateral	total	9.22	9.99	0.001＜0.05
	A	8.59	9.31	0.009＜0.05
	B	9.84	10.68	0.010＜0.05

The CTAP images were assessed by three radiologists (Y.A., S.M., H.H.) who were blinded to all clinical data. All data were analyzed with paired Student t-test, and a value of $p<0.05$ was considered significant.

Results (Table 1)

Regarding the CT numbers, the CT numbers of the right hepatic lobe (anterior and posterior segments) showed high attenuation compared with the left lobe (medial and lateral segments) in group A without prostaglandin E_1.

Segmental analyses were as followed ;

1) Anterior segment

The CT numbers were significantly decreased ($p=0.026$) in cases with the injection of prostaglandin E_1 in group B. However, there was no significant difference of changes in group A and in all patients of both groups.

2) Posterior segment

The CT numbers were significantly decreased ($p=0.046$) in cases with the injection of prostaglandin E_1 in all patients. But, there was no significant difference of changes in each of group A and group B.

3) Medial segment

The CT numbers were significantly increased in cases with the injection of prostaglandin E_1 in both groups ($p=0.030$) and in group A ($p=0.011$). On the other hand, they were significantly decreased in cases with the injection of prostaglandin E_1 in group B ($p=0.048$).

4) Lateral segment

There was no significant difference of the degree of the mean enhancement in the liver regardless of the injection of prostaglandin E_1 in all groups.

The SD number is an index of the degree of homogeneous contrast enhancement. The more the SD numbers decrease, it means that the more the liver is homogeneously enhanced. Regarding SD numbers, the following observations were made;

1) Anterior segment

No significant difference in the SD numbers was observed in all groups regardless of the injection of prostaglandin E_1.

2) Posterior segment

The SD numbers were significantly decreased in cases with the injection of prostaglandin E_1 in all groups ($p<0.05$) (**Fig. 1, 2**).

3) Medial segment

The SD numbers were significantly decreased in cases with the injection of prostaglandin E_1 in all patients of both groups ($p=0.025$) (**Fig. 3**). However, there was no significant difference in SD numbers in either of group A or B.

4) Lateral segment

The SD numbers were significantly decreased in cases with the injection of prostaglandin E_1 in all groups ($p<0.05$) (**Fig. 1, 2**).

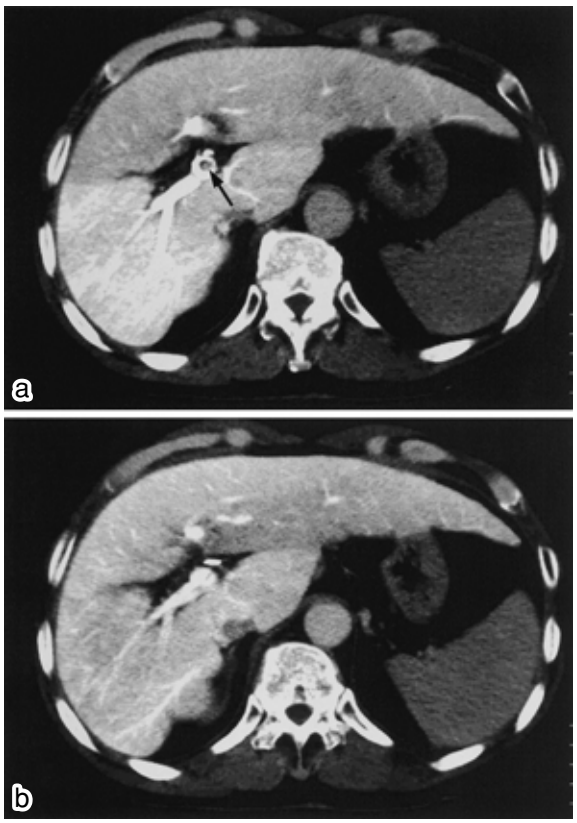

Fig. 1 CTAP without (a) and with (b) injection of prostaglandin E_1 in a 47-year-man with hepatocellular carcinoma. (a) CTAP shows the higher enhanced parenchyma in the right lobe compared with that in the left lobe and a low density area in portal vein which is caused by the laminar blood flow volume from splenic vein. (b) On the other hand, the differences of contrast enhancement between the right and the left lobes are improved on CTAP with injection of prostaglandin E_1. And the low density area in the portal vein is almost diminished.

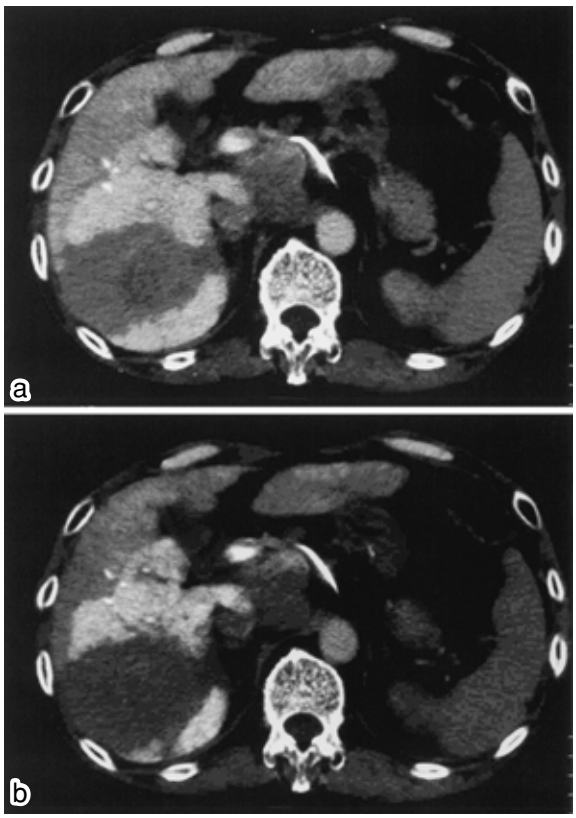

Fig. 2 CTAP with (a) and without (b) injection of prostaglandin E_1 in a 71-year-man with hepatocellular carcinoma. (a) CTAP with injection of prostaglandin E_1 shows the homogeneously enhanced parenchyma in the left lobe, and the perfusion defect in the right lobe due to hepatocellular carcinoma and portal venous tumor thrombus. (b) On the other hand, CTAP without injection of prostaglandin E_1 shows the unhomogeneously enhanced parenchyma in the left lobe, and the wide perfusion defect in the right lobe compared to that with injection of prostaglandin E_1.

Discussions

CTAP has been shown to be the most sensitive technique for identifying hepatic lesions and determining the number and location of these lesions[4–7,14]. Unfortunately, however, CTAP results are often difficult to interpret because of the high occurrence rate of non-tumor-related perfusion defects, which may mimic malignancy[15]. Many reviews have examined various facets of the CTAP technique with emphasis on increased differentiation of parenchyma from lesion[16] and evaluation of the optimal scanning window before equilibration[17].

Two major factors were considered to be the causes of non-tumor-related perfusion defects in CTAP examination. One is that there are variations in portal flow, which were included non-portal venous system originated from the pancreaticoduodenal and gastric regions. The other is that the admixture of opacified and unopacified blood from the splenic and superior mesenteric veins in the portal vein, which is called the laminar blood flow volume, may have an effect on the perfusion abnormalities. In our study, the CT numbers of the

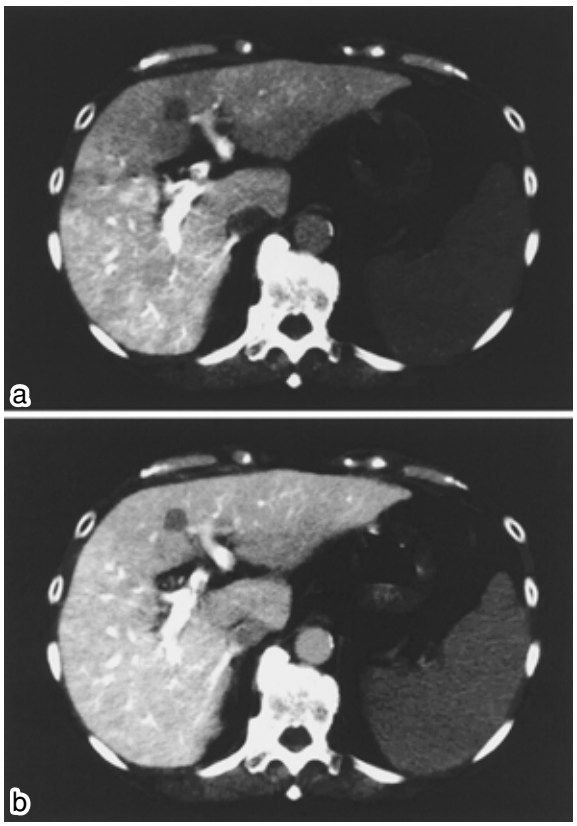

Fig. 3 CTAP without (a) and with (b) injection of prostaglandin E_1 in a 58-year-woman with hepatocellular carcinoma. (a) CTAP without injection of prostaglandin E_1 shows the unhomogeneously enhanced parenchyma in the left lobe, and a small perfusion defect in the medial segment. (b) CTAP with injection of prostaglandin E_1 shows the homogeneously enhanced parenchyma in the left lobe, and the margin of the small perfusion defect in the medial segment is clearly demonstrated compared with that of CTAP without injection of prostaglandin E_1.

hepatic right lobe (anterior and posterior segments) showed high attenuation compared with the left lobe (medial and lateral segments). These data reflect the physiological circulation of the portal system. To resolve these problems, some researchers tried to perform CTAP with injecting contrast material via the splenic artery, not via the SMA because there is no variation in the splenic arterial flow[13,18]. On the other hand, a number of more recent studies have used intra-arterial injection of papaverine to increase portal blood flow via the superior mesenteric vein[16]. In these reports, however, CTAP with and without vasodilating agent was not performed in the same patient, that is, it was not performed under the same conditions. Moreover, these authors' viewpoint was on the degree of contrast enhancement, not on the degree of parenchymal homogeneity in which we were especially interested.

In our present study, SD, that was an index of the degree of homogeneous contrast enhancement, was significantly decreased in the posterior, medial and lateral segments in cases with the injection of prostaglandin E_1. These results suggested that CTAP with the injection of prostaglandin E_1 could decrease the laminar blood flow volume. The reason it was unable to find an advantage in the anterior segment with the injection of prostaglandin E_1 could be thought that the anterior segmental branch of the portal vein is straightly running through compared to other segmental branches, and that this anatomical situation allows large volume of blood flow and decreases the laminar blood flow volume in the anterior segment of the liver.

In conclusion, CTAP with the injection of prostaglandin E_1 makes contrast enhancement of liver parenchyma more homogeneously, and it may be a useful technique for the detection of liver tumors.

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