Optimal Contrast Medium Protocol in Computed Tomography during Arterial Portography for Detection of Hepatoma

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Due to the high sensitivity of computed tomography during arterial portography (CTAP), it has become an important method used in the preoperative planning for the treatment of patients with primary or secondary malignant neoplasms of the liver. According to different reports, various doses of contrast material and rates of injection have been used over the past several years. For setting a rational routine protocol, we carried out this study to evaluate the optimal concentration of contrast media used in CTAP for detection of hepatic tumors. The overall sensitivities of tumor detection were 91%, 92% and 93% among three groups using 300 mgI/ml, 225 mgI/ml, and 150 mgI/ml, respectively. There were no statistically significant differences in the tumor detection rate among the groups. However, lesions were better demarcated from the liver parenchyma in 300 mgI/ml and 225 mgI/ml groups than 150 mgI/ml group. There was also more homogeneity of portal perfusion in the 225 mgI/ml groups than the 300mgI/ml group.

According to our study results, 80 ml of diluted contrast medium with the concentration of 225 mgI/ml injected at a rate of 2 ml/sec was satisfactory for the detection of hepatic tumors using CTAP. In conclusion, CTAP can be done confidently using slower injection rates and smaller amounts of contrast medium with intermediate concentrations for detection of hepatomas than the protocols reported in the literature.

Key words: Computed tomography, portography; Contrast media; Hepatoma

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Various amounts and concentrations of contrast materials with different injection rates were applied [7-18]. Almost all of the data were gathered in western countries. For setting a rational protocol suitable for routine applications in our patients, we carried out this study to evaluate the optimal concentration of contrast media used in CTAP for detection of hepatic tumors.

**MATERIALS AND METHODS**

From August 1997 through July 1999, 120 patients (83 men and 37 women; range of age, 26 to 85 years; mean age, 58 years) with proved hepatocellular carcinoma and varying degrees of cirrhosis of the liver were enrolled in this study. All CT studies were performed using a spiral CT scanner (CTi, GE Medical System, Milwaukee, Wis USA). All CTAP tests were done within 30 minutes after regular celiac and hepatic angiographies. After the tip of a 5-F RC-1 visceral angiographic catheter was placed at the orifice of the superior mesenteric artery, the patients were transferred immediately to the CT suite. All spiral CTAP tests were performed with 5-mm collimation, 2.5-mm/sec table speed 1:2 pitches, 1 second exposure, 120 kVp and 260 mAs and cranio-caudal table incrementation. One breath-hold spiral acquisition was obtained during each pass through the liver. Data acquisition was started at 30 seconds after initiation of contrast injection through the catheter. Nonionic iodinated contrast medium (Ultravist 300, Schering AG, Germany) was used in all patients. The patients were randomly divided into three groups. The groups received 80 ml of contrast media at different concentrations i.e. 300 mgI/ml, 225 mgI/ml and 150 mgI/ml. The contrast media with concentrations of 225 mgI/ml and 150 mgI/ml were diluted using sterile water from 300 mgI/ml. They were injected into the superior mesenteric arteries at a rate of 2 ml/sec through the catheter using the automated power injector. Patients were instructed to hold their breath during the scan to eliminate motion artifact. Contiguous 5-mm-thick axial sections were reconstructed from the volumetric data.

All CTAP test results were reviewed retrospectively by two of the authors (J.C.M. & K.C.H.), who are experienced in gastrointestinal radiology, without knowing the results of sonography or regular CT. Both readers scored the number of lesions sequentially side by side, and consensus was obtained on same occasions. Three grades of tumor demarcation (most clearly visible, clearly visible and faintly visible) between the lesions and the liver parenchyma were evaluated for all tumors.

Twenty-eight solitary tumors in 28 patients were proven using results of pathological examinations of surgical specimens. Sixty-four tumors in 33 patients were proven histologically using results of needle core biopsies. In the patients with more than one lesion in this group, all lesions which appeared similar to the tumors that underwent biopsies were considered to be HCC. The diagnosis of HCC for the other 59 patients with 93 tumors without direct histological proof were based on an increased level of serum a-fetoprotein, typical biphasic CT appearances and angiographic findings, follow up CT scans with changes in size of the tumors and positive response with reduction of the serum-a-fetoprotein level after transcatheter arterial chemoembolization (TACE) or percutaneous ethanol injection (PEI), and/or an unfavorable clinical course [19-21].

Those pseudolesions found on CTAP were excluded after correlation with findings on ultrasound, biphasic CT, angiograms, post-TAE CT and follow-up imaging at 6 months after initial discovery [21].

The readers’ scores for each image set were collected for statistical analysis for comparison of the detectability of the tumors using the Chi-squared test. A P value of less than 0.05 was considered a statistically significant difference.

### Table 1. Grading of Tumor Demarcation in CTAP with Contrast Media of Different Concentrations

<table>
<thead>
<tr>
<th>Concentrations of contrast media</th>
<th>300 mgI/ml</th>
<th>225 mgI/ml</th>
<th>150 mgI/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grading of tumor demarcation**</td>
<td>+++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td><strong>Grading of tumor demarcation</strong></td>
<td>40 (59%)</td>
<td>34 (54%)</td>
<td>29 (41%)</td>
</tr>
<tr>
<td><strong>Grading of tumor demarcation</strong></td>
<td>18 (26%)</td>
<td>16 (25%)</td>
<td>30 (43%)</td>
</tr>
<tr>
<td><strong>Grading of tumor demarcation</strong></td>
<td>4 (6%)</td>
<td>8 (13%)</td>
<td>6 (9%)</td>
</tr>
<tr>
<td><strong>Grading of tumor demarcation</strong></td>
<td>6 (9%)</td>
<td>5 (8%)</td>
<td>5 (7%)</td>
</tr>
</tbody>
</table>

*+++ = most clearly visible; ++ = clearly visible; + = faintly visible; - = not visible.

The number within the ( ) were percentage of tumor detectability in each group.

CTAP: computed tomography during arterial portography.
RESULTS

A total of 62, 58 and 65 focal hepatic tumors were detected in each of the 40-patient groups using contrast media with concentrations of 300 mgI/ml, 225 mgI/ml, and 150 mgI/ml, respectively. The mean diameters of neoplastic nodules were 5.8 cm (range, 0.5-13.0 cm), 4.5 cm (range, 1.0-10.0 cm), and 3.8 cm (range, 1.0-8.0 cm) in three groups, respectively. Multifocal tumors were found in five, six and eight patients of each group, respectively.

In the grading of tumor visibility among the groups (Table 1), 40 (59%) were clearly visible in 300 mgI/ml group, 18 (26%) and four (6%) tumors were clearly visible and faintly visible, respectively. For the patients in the group using 225 mgI/ml of contrast medium, 34 (54%), 16 (25%), eight (13%) were found in each of the tumor visibility grades, respectively. In the patients in the group using 150 mgI/ml of contrast medium, 29 (41%), 30 (43%), six (9%) tumors of the three tumor grades were found, respectively (Fig. 1).

The overall sensitivities of tumor detection were 91%, 92% and 93% in three groups, respectively (Table 2). There were no statistically significant differences in the sensitivity of

Table 2. The Sensitivity in Detection of Tumors between CTAP with Contrast Media of Different Concentrations

<table>
<thead>
<tr>
<th>Concentrations of contrast media</th>
<th>True positive</th>
<th>False negative</th>
<th>True negative</th>
<th>False positive</th>
<th>Sensitivity*</th>
<th>P value**</th>
</tr>
</thead>
<tbody>
<tr>
<td>300 mgI/ml</td>
<td>62</td>
<td>6</td>
<td>0</td>
<td>2</td>
<td>91%</td>
<td>P &gt; 0.9</td>
</tr>
<tr>
<td>225 mgI/ml</td>
<td>58</td>
<td>5</td>
<td>0</td>
<td>2</td>
<td>92%</td>
<td></td>
</tr>
<tr>
<td>150 mgI/ml</td>
<td>65</td>
<td>5</td>
<td>0</td>
<td>4</td>
<td>93%</td>
<td></td>
</tr>
</tbody>
</table>

* Because of the lack of histologic proof for each tumorous nodule, the sensitivity data obtained can only be used as a relative indicator of the difference in tumorous detection between each group using contrast media of different concentrations.

** Analysed with chi-squared test.
tumorous detection among the groups (Fig. 1). However, lesions were most clearly demarcated from the liver parenchyma for patients in the 300 mgI/ml and 225 mgI/ml groups than in the 150 mgI/ml group. There was more homogeneity of portal perfusion in the 225 mgI/ml group than in the 300 mgI/ml group (Fig. 2).

There were six (9%), five (8%) and five (7%) tumors missing from the three respective groups. The were not included either due to obvious hepatofugal flow or the lesions were located within regions which lacked portal perfusion due to obstruction of the portal vein. The latter conditions resulted either from compression by the main neoplastic mass or portal venous thrombosis due to direct invasion of the main lesion. The diameters of these obscured tumors were ranged from 2.3 to 5.5 cm (mean, 3.5 cm).

**DISCUSSION**

For liver tumor imaging, CTAP has been found to be the most sensitive preoperative imaging study for focal liver lesions, although it lacks specificity. The reported sensitivity of CTAP was 81% to 91% in series which correlated with surgical findings [1, 2]. This was even more significant for lesions larger than 1.5 to 2.0 cm [1, 22-24]. CTAP is based on portal enhancement of the liver using infusion of contrast material through the superior mesenteric artery. More than 70% of the blood supply of the liver is from the portal vein; less than 30% originates from the hepatic artery. In contrast, hepatic tumors are predominantly supplied by arterial blood. Because all the injected contrast medium is delivered to the liver from the portal vein essentially, the enhancement of the disease-free liver is high. Hepatic tumors generally do not have a portal venous blood supply, and they are detected as areas of low attenuation compared with a healthy enhanced liver. The lesion-to-liver attenuation difference is thus maximized on CTAP compared with CT obtained using intravenous administration of contrast medium [22].

Over the past several years, a number of researchers have reported their extensive experiences with spiral CTAP in the literature, and overall, the results have been extremely favorable [7-18]. However, many protocols for contrast material injection and timing of the spiral CTAP study following the injection have been proposed [6]. Various amounts and concentrations of contrast materials, and different injection rates were applied in the studies [7-18]. All of the researchers obtained rates of high detection in spite of the use of different protocol. They generally used relatively high injection rates of 3-5 ml/sec and large amounts of contrast material which ranged from 120 to 200 ml of 300 mgI/ml in concentration.

Eighty milliliters of contrast media in different concentrations i.e. either 300 mgI/ml, 225 mgI/ml or 150 mgI/ml was injected in each group in our study. We used the injection rate of 2 ml/sec in all cases routinely in our study. Data acquisition was started at 30 seconds after initiation of contrast injection through the catheter. Therefore, 60 ml of contrast media would have been delivered into the superior mesenteric venous-portal system at the start of scanning. An additional 20 ml of contrast medium would play the role of a maintenance dose over the course of the scanning. Though we used a slower injection rate and smaller amount of contrast medium in compared with other

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**Figure 2.** In spite of well demonstration of the perfusion defect representing a hepatic tumor (arrow), perfusion without homogeneity of portal flow (arrowhead) is prominent in certain cases using contrast media of higher concentration, i.e. 300 mgI/ml. a. 46-year-old female patient, b. 43-year-old male patient.
authors, we obtained comparable detection rates of 91-93% despite using contrast medium of different concentrations.

The grading of tumor visibility was influenced by different contrast media concentrations. The percentages of the most clearly visible tumors were relatively higher in the groups using contrast media of higher concentrations, i.e. 59% in the 300 mgI/ml group, 54% in the 225 mgI/ml group, versus 41% in the 150 mgI/ml group (Fig. 1). In the 300 mgI/ml group, there were fewer tumors (6%) faintly visible in comparison with 13% and 9% of the other two groups, respectively.

On the other hand, despite better demonstration of the perfusion defect representing hepatic tumors in patients using contrast media of 300 mgI/ml in concentrations, perfusion inhomogeneity of portal flow was prominent in some of them. Such appearances might reduce the rate of detectability in the study (Fig. 2).

However, in spite of the different percentages the grading of the tumor demarcations from the liver parenchyma, the total detection rates were not much different among the three groups. There were no statistically significant differences (P>0.9) in the sensitivity of lesion detection among these groups using contrast medium of varying optimal concentrations.

Theoretically, in patients with portal hypertension, the delivery of contrast medium to the liver from the portal vein may diminish and substantially decrease hepatic enhancement [15,18]. However, we found that the tumors missed on spiral CTAP were only seen in patients with extremely severe liver cirrhosis with obvious hepatofugal portal flow. In addition, we found areas with complete lack of portal flow due to portal venous occlusion by the larger tumors.

Our study showed that 80 ml of diluted contrast medium at the concentration of 225 mgI/ml can be injected at a rate of 2 ml/sec to obtain satisfactory results on CTAP for detection of hepatic tumors. In conclusion, a CTAP can be performed confidently with slower injection rate and smaller amounts of contrast medium at intermediate concentrations for detection of hepatomas than the protocols reported in the literature.

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利用動脈化門靜脈攝影－CT偵查肝癌時的適當造影劑劑量

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國泰綜合醫院 放射線科

電腦斷層動脈化門靜脈攝影（CTAP）的高敏感度，使它自從被引用之後，就成為對原發性或繼發性惡性肝臟腫瘤作手術前治療計劃的重要評估方法。在過去數年間的多篇報告中，各自採用不同的造影劑劑量和注射速率。本研究的主要目的在評估CTAP中最適當造影劑用法，以設定探查肝臟腫瘤的合理例行CTAP步驟。在使用濃度分別為300 mgI/ml、225 mgI/ml及150 mgI/ml的三組患者中，對腫瘤的整體偵查敏感度分別為91%、92%及93%。對這三組患者的腫瘤
偵查敏感度的差異，在統計學上並沒有意義。然而，在300 mgI/ml及225 mgI/ml兩組患者的腫
瘤與肝臟實質之間的分界，比150 mgI/ml組更為明顯：而225 mgI/ml組的門靜脈灌流不均勻度
又比300 mgI/ml組要少。利用80 ml從300 mgI/ml濃度稀釋的225 mgI/ml造影劑，以2 ml/sec
的速率注射，就能獲得可偵查肝臟腫瘤的理想CTAP。因此，本研究認為可比大多數文獻採用較
少量的中濃度造影劑，並且以較低速率注射，就能得到可靠的CTAP。

關鍵詞：電腦斷層攝影，門靜脈攝影，造影劑，肝癌