Sensitivity of Superselective Arteriography for Small Hepatocellular Carcinoma Compared with Proximal Arteriography and Computed Tomography During Superselective Arteriography

Kenichi Takayasu, Tetsuo Maeda and Ryoko Iwata

Department of Diagnostic Radiology, National Cancer Center Hospital, Tokyo, Japan

Received January 11, 2002; accepted March 28, 2002

Purpose: To obtain successful arterial chemoembolization for hepatocellular carcinoma (HCC), we evaluated the sensitivity of proximal arteriography, superselective (subsegmental or more distal branch) arteriography and computed tomography (CT) during superselective arteriography and assessed the method for the injection of contrast medium.

Methods: Thirty-two patients with 38 HCCs (≤5 cm) with a mean diameter of 2.2 cm underwent digital subtraction arteriography of proximal and superselective arteriography. In addition, they also had helical CT during superselective arteriography. The contrast medium was injected with a mechanical injector (n = 6 lesions) or by hand (n = 32) for superselective arteriography and CT during superselective arteriography. The amount of contrast medium used for superselective arteriography and CT during superselective arteriography with the mechanical injector was 3.5 times and 9 times that with manual injection, respectively.

Results: Overall, 31 lesions (81.6%) were detected by proximal arteriography, 25 (65.8%) by superselective arteriography and 35 (92.1%) by CT during superselective arteriography. CT during superselective arteriography was significantly superior to superselective arteriography (P = 0.005). In both studies, manual injection of contrast medium had a significantly higher sensitivity than mechanical injection (P = 0.013).

Conclusion: To detect small HCC, CT during superselective arteriography showed significantly higher sensitivity than superselective arteriography. Manual injection of contrast medium was significantly superior to mechanical injection. Therefore, manual injection CT during superselective arteriography is recommended for accurately targeted, transarterial chemoembolization therapy.

Key words: small hepatocellular carcinoma – computed tomography during superselective hepatic arteriography – superselective arteriography

INTRODUCTION

Hepatocellular carcinoma (HCC), which is one of the most lethal malignancies, is prevalent in areas such as Africa and Southeast Asia (1). Although surgery and percutaneous ablation such as ethanol injection and radiofrequency give good survival rates, transarterial oily chemoembolization (TOCE) remains the indispensable treatment because most patients are in advanced stages and/or have poor liver function (2), although some studies showed no benefit of chemoembolization for advanced HCC compared with supportive therapy (3,4). Approximately half of HCC patients underwent TOCE as the initial treatment in Japan (2). For ideal TOCE, superselective catheterization of the subsegmental or more peripheral feeding artery is required to maximize the efficacy of TOCE and to minimize unnecessary injury to non-cancerous hepatic parenchyma (5–7). With the recent introduction of the unified helical computed tomography (CT) and angiography system, more accurate and more objective TOCE for the targeted lesion (targeted TOCE) has become possible with a lower local recurrence and good survival rates (7).

Nevertheless, we found in routine studies that some lesions detected by proximal arteriography could not be demonstrated...
Figure 1. Case 1. A 60-year-old man with a solitary hepatocellular carcinoma in segment 8. (a) Arteriogram through the right hepatic artery replaced from the superior mesenteric artery showing a hypervascular lesion (arrow). (b) Subsegmental arteriography (left anterior oblique position) with manual injection of the contrast medium did not show tumor staining. (c) CT during subsegmental arteriography of (b) demonstrating a high attenuated mass (arrowheads). Arrow indicates the right hepatic vein.

Figure 2. Case 2. A 66-year-old man with a 2.5 cm hepatocellular carcinoma in segment 3. (a) Common hepatic arteriography disclosing a hypervascular lesion (arrowheads). The entire tumor was well enhanced by contrast CT before angiography (not shown). (b) The tip of a microcatheter (arrowhead) was advanced close to the lesion and the arteriogram was made 20 s after the beginning of injection of 10 ml of contrast medium at a rate of 0.7 ml/s using a mechanical injector. A hypovascular tumor (thin arrow) with small lateral staining (thick arrow) was contrasted by the hypervascular non-cancerous portion. A curved arrow indicates the left hepatic vein. (c) CT during superselective arteriography of (b), in which 12 ml of diluted contrast medium (1:3 ratio) were injected with a mechanical injector at a rate of 0.7 ml/s. Most of the lesion was seen as low attenuated areas (arrow) compared with the surrounding parenchyma. The left hepatic veins are also recognized (arrowheads), suggesting that excessive contrast medium predominantly entered the non-cancerous parenchyma rather than targeted lesion.
by superselective arteriography, which causes some apprehension that the catheterized artery might be inadequate for targeted TOCE. Consequently, CT during superselective arteriography (combination study of helical CT and superselective arteriography) became necessary to ensure that the targeted lesion is actually enhanced. In this study, we evaluated the sensitivities of proximal arteriography, superselective arteriography and CT during superselective arteriography for small HCC. For the last two studies, two different methods of injection of contrast medium, manual and mechanical injection, were compared and their sensitivity to detect small HCC was evaluated.

PATIENTS AND METHODS

Between April 1996 and June 1999, a total of 544 consecutive patients with HCC underwent TOCE. Of these, 32 patients who satisfied the following criteria were retrospectively analyzed; there was one main lesion (≤5 cm) associated with no more than two lesions (≤3 cm) and the proximal and superselective (subsegmental or more distal) arteriography followed by CT during superselective arteriography were performed before targeted TOCE.

The study population consisted of 22 men and 10 women with an average age of 65.1 years (range, 49–81 years). Thirty-two patients had a total of 38 HCC lesions; 26 had one lesion and six had two lesions. The mean tumor diameter was 2.2 cm (range, 0.7–4.5 cm). Five patients were positive for the hepatitis B surface antigen (HBsAg) and 27 were positive for the hepatitis C virus antibody (anti-HCV, second-generation test). Of these, two patients were positive and three were negative for both HBsAg and anti-HCV. The alpha-fetoprotein (AFP) level at angiography ranged from 3.5 to 19,930 ng/ml (average, 1118 ng/ml). The degree of hepatic dysfunction using Child’s classification (8) was A in 18, B in 11 and C in three patients. The diagnosis of HCC was made histopathologically in eight of 32 patients who underwent targeted TOCE followed by wedge hepatic resection and made clinically in the remaining 24 patients using various imaging techniques such as triple phase helical CT, ultrasonography, MR imaging, intraoperative ultrasonography and laboratory data. The non-cancerous hepatic portion of the resected specimens was cirrhosis in two and chronic hepatitis in six patients.

The study was performed as the following order: CT during arterial portography (CTAP) (9) followed by proximal arteriography, CT during proximal arteriography, superselective arteriography and CT during superselective arteriography. For arteriography, Ioversol (Optiray, 350 mg I/ml, Yamanouchi, Tokyo, Japan) was used, and for the combination study of CT and arteriography, contrast medium diluted with saline (1:3) was used. Digital subtraction angiography was performed with three films per second for 6 s and one for 12 s. Beam collimation and image reconstruction were 7 mm and the table incrementation rate was 7 mm (pitch, 1:1).

CTAP was begun 20 s after the injection of 90 ml of contrast medium at a rate of 3 ml/s using a unified helical CT and angiography system (Interventional-CT, Toshiba, Tokyo, Japan) (7). Proximal arteriography was performed at the celiac artery in 12, at the common hepatic in 16, at the proper hepatic in one and at a replaced right hepatic in three patients. The dose of contrast medium used for the proximal arteriography ranged from 12 to 25 ml (average, 17.5 ml) depending on the site of the artery for angiography and the injection rate ranged from 2.4 to 5 ml. Subsequently, CT during proximal arteriography started 10 s after the beginning of the injection of 10–23 ml of contrast medium at a rate of 1.4–3 ml/s.

Using a 2.3-French microcatheter (Rapid Transit TM 2, 100 cm long, Cordis Endovascular System, Miami, FL), superselective catheterization was performed; the injection site was a subsegmental branch for 34 lesions and more distal for four lesions. For superselective arteriography, the contrast medium was injected with a mechanical injector (Mark V Plus, Medrad, Pittsburgh, PA) for six lesions using a mean dosage of 8.5 ml (range, 6–10 ml) at an average rate of 0.82 ml/s (range, 0.6–1.0 ml/s) for the initial 6 months of this study and with manual injection for 32 lesions using a mean dosage of 2.4 ml (range, 2–3 ml) for the last 2.5 years. The injection of contrast medium was performed carefully by hand so as not to cause regurgitation. The contrast medium used with the mechanical injector was 3.5 times that with manual injection.

Subsequently, CT during superselective arteriography was performed for six lesions with a mechanical injector with an average dose of 20.6 ml (range, 12–27 ml) at an average rate of 0.72 ml/s (range, 0.6–0.8 ml/s) and for 32 lesions by manual injection with a mean amount of 2.3 ml (range, 1.8–2.9 ml) at about the same injection rate as that in subsegmental arteriography and CT was started 5–8 s after the start of contrast injection. The dose of contrast medium used with mechanical injection was nine times that with manual injection.

The arteriography findings for the lesions were rated as hypervascular, isovascular (not detected) or hypovascular compared with the surrounding hepatic parenchyma. The CT findings during arteriography were rated similarly as high, iso or low attenuation.

These findings were independently reviewed by two experienced radiologists (K.T. and T.M.) and the consensus was obtained by discussion with a third radiologist in case of discrepancy. For statistical analyses, the chi-squared test was used [P < 0.05 (two-tailed test) was considered significant].

RESULTS

All 38 HCCs were detected by both CTAP and CT during proximal arteriography. The attenuation of the lesions on CT during proximal arteriography was high in 37 and low in one. Proximal arteriography detected 31 lesions (81.6%) as a hypervascular one (Figs. 1a and 2a) (Table 1). On superselective arteriography, 25 lesions (65.8%) were detected; 24 lesions were hypervascular, 13 isovascular (not detected) (Fig. 1b) and one hypovascular (Table 1). CT during superselective arteriography detected 35 lesions (92.1%), with high attenuation in 32 lesions (Fig. 1c) and low attenuation in three. A significant dif-


Table 1. Sensitivity of proximal arteriography, superselective arteriography and CT during superselective arteriography with mechanical and manual injection for 38 small hepatocellular carcinomas

<table>
<thead>
<tr>
<th>Examination method</th>
<th>Mechanical</th>
<th>Manual</th>
<th>Overall $^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal arteriography</td>
<td>31/38 (81.6)</td>
<td>Not done</td>
<td>31/38 (81.6)</td>
</tr>
<tr>
<td>Superselective arteriography</td>
<td>4/6 (66.7)$^{****}$</td>
<td>24/32 (75.0)$^{***}$</td>
<td>25/38 (65.8)$^*$</td>
</tr>
<tr>
<td>CT during superselective arteriography</td>
<td>31/32 (96.9)$^{****}$</td>
<td>35/38 (92.1)$^*$</td>
<td></td>
</tr>
</tbody>
</table>

$^a$Values in parentheses: percentage of lesions. Statistical significance: * and ***, there was a significant difference between superselective arteriography and CT during superselective arteriography overall ($P = 0.005$) and with manual injection ($P = 0.013$); *** and ****, a significant difference was recognized between mechanical and manual injection on superselective arteriography ($P = 0.006$) and CT during superselective arteriography ($P = 0.012$).

1One lesion was predominantly hypovascular.
2One lesion was low attenuated.
3Two lesions were low attenuated.
4Three lesions were low attenuated.

Differences were recognized between superselective arteriography and CT during superselective arteriography ($P = 0.005$) and was not between proximal arteriography and superselective one ($P = 0.118$).

For six lesions in which the mechanical injector was used for superselective arteriography, the sensitivity was 16.7% (Table 1); five were isovascular (not detected) and one was predominantly hypovascular (Fig. 2b). In contrast, CT during superselective arteriography detected four lesions (66.7%), with high attenuation in three lesions and low attenuation in one (Fig. 2c). However, there was no significant difference between these two studies.

For 32 lesions in which superselective arteriography was carried out with manual injection, 24 lesions (75.0%) were demonstrated as hypervascular (Table 1). CT during superselective arteriography detected 31 lesions (96.9%); 29 lesions were highly attenuated and two were low attenuated. There was a significant difference in detection rate between the two studies ($P = 0.013$).

The sensitivities were significantly different between mechanical and manual injection in superselective arteriography ($P = 0.006$) and CT during superselective arteriography ($P = 0.012$).

**DISCUSSION**

Superselective catheterization of the subsegmental or more peripheral feeding artery is important for successfully targeted TOCE; it reduces the incidence of local recurrence after TOCE and gives a good survival rate (5–7). The development of the microcatheter and the introduction of a unified helical CT and angiography system have allowed superselective catheterization of a subsegmental or more distal artery with greater certainty and ease (7). Before we started CT during superselective arteriography with a unified helical CT and angiography system, it was thought that superselective arteriography was more sensitive than proximal arteriography in detecting a small HCC.

However, this study revealed that the sensitivity of superselective arteriography (65.8%) was considerably lower than that of proximal arteriography (81.6%). Moreover, superselective arteriography was significantly inferior to CT during superselective arteriography for the detection of HCC overall ($P = 0.005$) and with manual injection ($P = 0.013$).

Regarding the injection method, mechanical injection showed a significantly lower sensitivity than manual injection in both superselective arteriography ($P = 0.006$) and CT during superselective arteriography ($P = 0.012$). To our knowledge, this work is the first to show that superselective (subsegmental or more distal) arteriography tends to be inferior to proximal arteriography. The mechanical injector was not useful for detecting small HCC in superselective arteriography compared with manual injection.

A possible reason for superselective arteriography being inferior to proximal arteriography for detecting lesions is as follows. A hypervascular HCC has rich feeding arteries compared with non-cancerous parenchyma (10,11), but once excessive contrast medium has been injected into the subsegmental or a more distal artery through a microcatheter, the feeding artery does not respond to pressurized injection and the injected contrast medium might flow mainly into the non-cancerous parenchyma rather than HCC itself, because tumor vessels do not respond to the excessive volume of injected contrast medium, unlike non-cancerous parenchyma vessels. Consequently, a poor or no contrast image is produced against the surrounding hepatic parenchyma, resulting in low sensitivity of superselective arteriography. In particular, it frequently occurred when a mechanical injector was used, where the amount of contrast medium injected was 3.5 times that with manual injection on superselective arteriography and nine times that with CT during arteriography. The characteristic findings in which the lesion was demonstrated to be a low attenuated one in CT during superselective arteriography (Fig. 2e) could be explained by this mechanism, although hypothetical.

Another possible reason for the higher sensitivity of CT during superselective arteriography than superselective arteri-
ography is the higher contrast resolution in CT compared with angiography.

Based on these results, we recommend CT during superselective arteriography using a small dose of contrast medium injected manually before TOCE for HCC, if the tumor stain could not be confirmed by superselective arteriography. If a unified machine of CT and angiography is not available, slow manual injection of contrast medium is to be preferred for subsegmental arteriography.

References


