Ultraselective Transcatheter Arterial Chemoembolization with a 2-F Tip Microcatheter for Small Hepatocellular Carcinomas: Relationship Between Local Tumor Recurrence and Visualization of the Portal Vein with Iodized Oil

Shiro Miyayama, MD, Osamu Matsui, MD, Masashi Yamashiro, MD, Yasuji Ryu, MD, Keiko Kaito, MD, Kumi Ozaki, MD, Taro Takeda, MD, Norihide Yoneda, MD, Kazuo Notsumata, MD, Daisyu Toya, MD, Nobuyoshi Tanaka, MD, and Takeshi Mitsui, MD

PURPOSE: To retrospectively evaluate the relationship between local tumor recurrence and iodized oil deposition in the portal vein by using ultraselective transcatheter arterial chemoembolization (TACE) for small hepatocellular carcinoma.

MATERIALS AND METHODS: One-hundred twenty-three tumors smaller than 5 cm in diameter (mean diameter, 1.9 cm; median diameter, 1.6 cm) were treated with TACE by using a 2-F tip microcatheter at a distal portion of the subsegmental artery of the liver. Portal vein visualization at spot radiography during TACE was divided into three grades, as follows: 0 = not visualized, 1 = limited near the tumor, and 2 = whole or extended to the embolized area. Local recurrence rates of each grade group were compared. The recurrent pattern was divided into intratumoral and peritumoral recurrence. Complications were also analyzed.

RESULTS: Of the 123 tumors, 53 (43.1%) were classified as grade 2, 52 (42.3%) were classified as grade 1, and 18 (14.6%) tumors were classified as grade 0. Overall local recurrence rates at 12, 24, and 36 months were 25.6%, 34.7%, and 34.7%, respectively. The local recurrence rates for the grades 2, 1, and 0 groups were 7.9%, 24.8%, and 85.7%, respectively, at 12 months and 17.7%, 38.9%, and 85.7% at 24 months. Recurrence rates in the grade 2 group were significantly lower than those in the grades 1 and 0 groups ($P = .0485$ and $P < .0001$, respectively). Intratumoral recurrence was observed in 21 tumors, most of which were in the grade 0 group. Peritumoral recurrence was noted in 16 tumors, most of which were in the grade 2 group. There were no major complications.

CONCLUSION: Ultraselective TACE was safe and effective in a significant number of tumors. In particular, local recurrence was significantly lower when a greater degree of portal vein visualization was demonstrated during TACE.

J Vasc Interv Radiol 2007; 18:365–376

Abbreviations: CTAP = CT during arterial portography, CTHA = CT during hepatic arteriography, HCC = hepatocellular carcinoma, PIVKA-II = protein induced in vitamin K absence II, TACE = transcatheter arterial chemoembolization

HEPATOCELLULAR carcinoma (HCC) is one of the most common malignant tumors in East Asia. The prognosis of patients with inoperable HCC has improved with advances in therapeutic options (eg, local ablation therapies) in addition to transcatheter arterial chemoembolization (TACE) (1–8). In general, it believed that radiofrequency ablation has a stronger therapeutic effect than TACE (6–8). Rossi et al (6) reported that the local recurrence rate of HCCs with diameters smaller than 3 cm treated with radiofrequency ablation was 0% at 1 year, 4% at 2 and 3 years, and 16% at 4 and 5 years. Conversely, we previously reported that

From the Departments of Diagnostic Radiology (S.M., M.Y., Y.R., K.K., K.O., T.T., N.Y.), Internal Medicine (K.N., D.T., N.T.), and Surgery (T.M.), Fukuiken Saiseikai Hospital, 7-1, Funabashi, Wadanaka-cho, Fukui 918-8503, Japan; and the Department of Radiology (O.M.), Kanazawa University, Graduate School of Medical Science, 13-1, Takara-machi, Kanazawa 920-8640, Japan. Received June 19, 2006; final revision received November 15, 2006; accepted December 3, 2006. **Address correspondence to** S.M.; E-mail: s-miyayama@fukui.saiseikai.or.jp

None of the authors have identified a conflict of interest.

DOI: 10.1016/j.jvir.2006.12.004

the local recurrence rate of HCCs smaller than 4 cm in diameter treated with subsegmental TACE was 18% at 1 year, 30% at 2 years, and 33% at 3 and 4 years (3). Tumors located near dangerous architectures, however, such as a main portal vein, inferior vena cava, gallbladder, or alimentary tract, are not usually candidates for radiofrequency ablation (8). In addition, in most patients with HCC initially treated by some therapeutic options other than TACE, TACE may be required during the subsequent course due to the high incidence of tumor recurrence. Therefore, TACE still plays an important part in the treatment of inoperable HCC, and the advancement of TACE technology remains crucial.

It has been reported that portal blood supply to tumors after TACE is one of the main causes of tumor recurrence (9,10). Several techniques to enhance the therapeutic effect of TACE have also been reported (11–13). We used a 2-F tip microcatheter for TACE of small HCCs and injected embolic materials into a limited area via a catheter navigated distally into the subsegmental artery to achieve the blockage of both arterial and portal blood flow by overflowed embolic materials into the portal vein. Herein, we analyze the preliminary results of our ultraselective TACE procedure with a 2-F tip microcatheter, especially with regard to the relationship between tumor recurrence and portal vein visualization during TACE.

MATERIALS AND METHODS

We performed a retrospective study to evaluate the therapeutic effects of ultraselective TACE by using a 2-F tip microcatheter, particularly with regard to the relationship between local tumor recurrence and visualization of the portal vein during TACE. Patients were included in the study if they (*a*) had fewer than three hypervascular tumors smaller than 5 cm in diameter; (*b*) had newly developed HCC without any previous treatment, including new HCC lesions in patients who had previously undergone treatment for HCC; (*c*) had HCC supplied by the hepatic artery and underwent TACE at the distal portion of the subsegmental artery; and (*d*) had tumors that were treated with TACE alone. Written informed consent was obtained from each patient before TACE. Institutional review board approval was not required at our institution for this type of study.

Patients

Between October 2002 and September 2004, 637 TACE procedures were performed with a 2-F tip microcatheter (Progreat α; Terumo, Tokyo, Japan) in 299 patients with HCC at our hospital. From these 299 patients, we selected 72 who met the aforementioned criteria. There were 43 men and 29 women with a mean age (±standard deviation) of 69.4 years ± 8.4 (range, 49–86 years). All patients had chronic hepatitis or liver cirrhosis, which was related to hepatitis C in 64 patients, hepatitis B in three patients, and alcohol abuse in one patient. The cause of chronic hepatitis or liver cirrhosis was unknown in four patients. In total, there were 123 tumors with a mean diameter of 1.9 cm ± 0.9 (range, 0.6–4.7 cm; median, 1.6 cm). Fifty-three tumors were initially revealed and 70 were newly developed during the follow-up period after HCC treatment. The diagnosis of HCC was made by means of imaging findings in addition to high serum levels of tumor markers (14). The imaging studies included dynamic computed tomography (CT) (n = 72), magnetic resonance (MR) imaging (n = 17), angiography (n = 72), CT during hepatic arteriography (CTHA) (n = 21), and CT during arterial portography (CTAP) (n = 72). The diagnosis of HCC was made by means of nodular staining at dynamic CT, dynamic MR imaging, angiography, or CTHA and nodular perfusion defects at CTAP in addition to low attenuation at delayed-phase CT and high signal intensity at T2-weight MR imaging (15). The serum α-fetoprotein level was elevated (>200 ng/mL [200 μg/L]) in 53 patients, the serum protein induced in vitamin K absence II (PIVKA-II) level was elevated (>40 μg/L) in 43 patients, and both were elevated in 24 patients.

TACE Procedure

After confirmation of the tumor stain at angiography, a 2-F tip microcatheter was inserted into the distal portion of the tumor-feeding subsegmental artery through a 4-F catheter placed in the celiac artery, superior mesenteric artery, or common hepatic artery. To navigate the microcatheter, a 0.016-inch guide wire (GT-wire; Terumo) was routinely used in all patients. When the selection of the feeding branch with the 0.016-inch guide wire was difficult, a 0.012-inch guide wire (GT-wire) was also used.

After the microcatheter was inserted into the target branch, 0.5 mL of 2% lidocaine (Xylocaine; Fujisawa, Osaka, Japan) was intraarterially injected to prevent pain and vasospasm. First, a mixture of 0.5–5 mL of iodized oil (Lipiodol; Andre Guerbet, Aulnay-sous-Bois, France), 10–20 mg of epirubicin (Farmorbicin; Kyowa Hakko, Tokyo, Japan), and 2–4 mg of mitomycin C (Mitomycin; Kyowa Hakko) was slowly injected through the catheter until the portal veins in the embolized area appeared. The total amount of iodized oil was determined on the basis of tumor size (almost equal to the diameter of the tumor, eg, 3 mL of iodized oil was used for a 3-cm tumor). Second, gelatin sponge particles (Gelfoam; Upjohn, Kalamazoo, Mich), which were cut into approximately 0.5-mm cubes and crushed into particles smaller than 0.2 mm by pumping with a three-way stopcock valve and two 2.5 mL syringes, were injected to completely obstruct the tumor-feeding branch. In patients with multiple tumors, all tumors were sequentially treated during one TACE session. A spot radiograph was obtained just after the TACE procedure for each tumor to evaluate the degree of portal vein visualization. The TACE procedure was terminated when the targeted tumor stain was not seen at angiography. If other feeding branches were demonstrated at angiography, TACE was also performed through these branches.

End Points of TACE

The end point of the TACE procedure was portal vein visualization in the entire embolized area and complete blockage of the tumor-feeding branch. Iodized oil injection was stopped when the portal vein extending to the embolized area appeared, and TACE was ended after the tumor-feeding branch had been completely obstructed with injection of the gelatin