Radiologic Placement of Side-hole Catheter with Tip Fixation for Hepatic Arterial Infusion Chemotherapy

Toshihiro Tanaka, MD, Yasuaki Arai, MD, Yoshitaka Inaba, MD, Kiyoshi Matsueda, MD, Takeshi Aramaki, MD, Yoshito Takeuchi, MD, and Kimihiko Kichikawa, MD

PURPOSE: To investigate the technical outcome of radiologic catheter placement with use of a side-hole catheter with distal fixation for hepatic arterial infusion chemotherapy.

MATERIALS AND METHODS: Between January 1993 and September 1999, 426 patients were referred to our department to undergo intraarterial infusion chemotherapy for unresectable malignant liver tumors. A subclavian artery was exposed under local anesthesia and a catheter was inserted. After inserting the tip of the side-hole catheter into the gastroduodenal artery, splenic artery, or peripheral branch of the hepatic artery, the catheter tip was fixed to the vessel with use of coils and a mixture of n-butyl cyanoacrylate (NBCA) and iodized oil. The proximal end of the catheter was connected to an implanted port, and the port system was embedded subcutaneously.

RESULTS: Placement was successful in 425 of 426 patients (99.8%) in a mean time of 76 minutes. Catheter dislodgement was noted in 12 patients (2.8%). Cumulative patency rates of the hepatic artery calculated according to the Kaplan-Meier method for the entire group were 91.0%, 81.4%, and 58.1% at 6 months and 1 and 2 years, respectively. Complications related to catheter placement were observed in nine cases and included dysfunction of the implanted system (n = 3), significant bleeding around the implanted port (n = 2), improper infusion of NBCA and iodized oil (n = 2), and cerebral infarction (n = 2).

CONCLUSION: Radiologic catheter placement via a subclavian artery with side-hole catheter placement with distal fixation for hepatic arterial infusion chemotherapy is a highly successful procedure with a reduced risk of catheter dislodgment and arterial occlusion.

Index terms: Chemotherapeutic infusion • Hepatic arteries, chemotherapeutic infusion

J Vasc Interv Radiol 2003; 14:63–68

Abbreviation: NBa = n-butyl cyanoacrylate

ALTHOUGH the impact on survival is still controversial, hepatic arterial infusion chemotherapy is a frequently employed option for the management of unresectable liver malignancies (1–7). In 1982, Arai et al (8) first reported a radiologic method of placing an indwelling catheter system via a subclavian artery for hepatic arterial infusion chemotherapy. In this method, the catheter tip is simply inserted into the common or proper hepatic artery. Thereafter, this method became widely used in Japan and European countries (9–12); however, frequent dislodgement of the catheter tip and hepatic arterial occlusion were noted as major limitations of this original technique (9,10,13,14). Since 1992, to overcome these drawbacks, we have used a modified version of the procedure in which we fix the catheter tip to a vessel with use of embolizing coils and/or liquid glue and infuse anticancer agents through a side hole of the catheter (16,17). The purpose of this paper is to describe the technical outcome of radiologic catheter placement by this method.

MATERIALS AND METHODS

Patients

Between January 1993 and September 1999, radiologic catheter placement with use of a side-hole catheter with the distal fixation method was performed in 426 consecutive patients who had unresectable liver malignancies. There were 210 men and 216 women ranging in age from 29 to 87
years (mean, 59 y). Four hundred four patients had liver metastases from colorectal cancer (n = 169), breast cancer (n = 103), gastric cancer (n = 66), pancreatic cancer (n = 13), esophageal cancer (n = 10), lung cancer (n = 8), gallbladder cancer (n = 8), uterine cancer (n = 7), bile duct cancer (n = 4), duodenal cancer (n = 2), epipharyngeal cancer (n = 2), ovarian cancer (n = 2), and other cancers (n = 10). The remaining 22 patients had primary liver cancers including hepatocellular carcinoma (n = 13) and cholangiocellular carcinoma (n = 9). In all patients, the liver lesions were judged by physicians or surgeons to be unresectable and to be the factor limiting survival.

Consequently, all patients were referred to receive radiologic catheter placement for hepatic arterial infusion chemotherapy in our department. Before the procedure, informed consent was obtained from all patients in writing. Institutional review board approval was obtained for this study.

Techniques

All procedures were performed in angiographic suites by interventional radiologists. Before catheter placement, all patients underwent angiography for arterial road mapping and, if necessary, arterial redistribution to convert multiple hepatic arteries into a single arterial supply and prevent extrahepatic drug distribution (17–19). Catheter placement was typically performed on a different day. Under local anesthesia, a skin incision approximately 4 cm in length was made at the left chest wall below the left clavicle and the left subclavian artery was surgically exposed. Then, a branch of the left subclavian artery, commonly the thoracic–acromial artery, was exposed, ligated, and cut distally. A 5-F, 25-cm-long angiographic sheath (Terumo, Tokyo, Japan) was introduced via the branch. When an appropriate arterial branch for sheath insertion was not found, the sheath was introduced directly via the subclavian artery. When surgical access to the left subclavian artery was difficult because of previous treatment in this region, the right subclavian artery was accessed by the same method. Through the angiographic sheath, a 5-F angiographic catheter was inserted into the gastroduodenal artery, and the angiographic catheter was then replaced by a less-thrombogenic indwelling catheter (Anthorn PU; Toray, Tokyo, Japan) with use of a 0.018-inch guide wire (20). This catheter was made of polyurethane and its surface was coated with heparin. The outer diameter of the sheath was 5 F and the tip was tapered to 2.7 F, and the inner diameter of the tip was adjusted to accommodate a 0.018-inch guide wire. The tapered tip was 20 cm in length. Before insertion of the indwelling catheter, a tip of the catheter was cut to adjust the length of the tapered portion to the length of the gastroduodenal artery and a side hole was manually made on the catheter. The position of the side hole was adjusted to the common hepatic artery when the catheter tip was placed in the deep portion of the gastroduodenal artery. The diameter of the side hole was large enough for a 3-F microcatheter (Tracker-18 infusion catheter; Target Therapeutics, Fremont, CA) to pass.

After the insertion of the indwelling catheter into the gastroduodenal artery, a 3-F microcatheter was coaxially inserted into the indwelling catheter and advanced into the gastroduodenal artery through the side hole. Embolizing metallic coils (Complex helical; Target Therapeutics; Tornado; Cook, Bloomington, IN; Vortex; Target Therapeutics; Trufill; Cordis, Miami Lakes, FL) were inserted into the gastroduodenal artery through the microcatheter to occlude the gastroduodenal artery and fix the indwelling catheter tip to the gastroduodenal artery. For this purpose, a mixture (1:1.5) of n-buty 1 cyanacrylate (NBCA; Histoacryl; Braun, Melsungen, Germany), which is a liquid acrylic surgical adhesive, and iodized oil (Lipiodol ultrafluide; Laboratoire Guerbet, Roissy, France) was commonly used along with metallic coils (21,22).

When the diameter of the common hepatic artery was smaller than 3 mm, to prevent common hepatic arterial occlusion, we placed a side-hole catheter into the splenic artery, with the side hole located in the celiac axis, and embolized the proximal portion of the splenic artery with use of the same technique. In such cases, the gastroduodenal artery, right gastric artery, and, if necessary, left gastric artery or dorsal pancreatic artery were embolized to prevent extrahepatic drug distribution. When the hepatic artery was large enough and there was no appropriate gastroduodenal artery into which to insert the catheter tip because of previous surgery, a side-hole catheter was inserted into the peripheral branch of the hepatic artery—usually a segmental branch—and the catheter tip was fixed with use of NBCA and iodized oil with the side hole positioned in the proper hepatic artery.

After it was confirmed that the contrast medium injected from the catheter hub was flowing out from the side hole and distributed into the liver (Fig 1), the sheath was removed and the proximal portion of the indwelling catheter was fixed by ligation to a branch of the subclavian artery or sutured with subcutaneous soft tissue. Finally, the proximal end of the catheter was cut and connected with an implanted port and then the whole system was embedded under the skin (Fig 2). All patients were given antibiotics (cefoxolin sodium) for 2 days after the procedure, but anticoagulant therapy was not administered in any cases.

Hepatic arterial infusion chemotherapy with use of this system was started a few days after the procedure, depending on the clinical circumstances. The infusion protocols were decided for each malignancy by our oncologists. Commonly, 1,000 mg/m² 5-fluorouracil was administered by continuous 5-hour infusion once a week repeatedly in patients with liver metastases from colorectal cancer, and 330 mg/m² 5-Fu (every week), 2.7 mg/m² mitomycin-C (every 2 weeks), and 30 mg/m² epirubicin (every 4 weeks) were injected as boluses in patients with liver metastases from gastric, breast, or pancreatic cancer (23–25). Similar regimens were used in the remaining patients. After the administration of chemotherapeutic agents, the implanted port and indwelling catheter system were flushed and filled with 2 mL of heparin solution (1,000 IU/mL). During the interval of chemotherapy, 5 mL of saline solution and 2 mL of heparin were infused every 2 weeks by the same method to prevent system occlusion. Abdominal radiographs were taken within 1 week after the procedure to check for dislodgement of the catheter tip. Digital subtraction angiography and computed tomography were per-
formed during injection of contrast medium through the implanted port–catheter system within 1 week after the procedure and every 3 months to confirm that the catheter and hepatic artery were patent and the entire liver was perfused adequately. They were also performed whenever the patients reported any symptoms that might be related to hepatic arterial infusion chemotherapy. We observed all patients in this study until the end of hepatic arterial infusion chemotherapy.

**Evaluation**

The outcome was evaluated by the success rate of arterial access, time required for the catheter placement procedure from skin incision to closure, success rate of placement of the catheter–port system, incidence of catheter dislodgement, cumulative patency rate of the hepatic artery, and complications observed in catheter placement procedures and during the follow-up period of 3–1,241 days (mean ± SD, 234 d ± 214). We categorized minor and major complications according to SCVIR reporting standards (26). Minor complications necessitated no therapy or resulted in cure in less than 24 hours by drug administration for symptom(s). Major complications required therapy for more than 24 hours or were more severe or irreversible conditions. The cumulative patency rate of the hepatic artery was calculated with the Kaplan-Meier method.

**RESULTS**

Arterial access was successfully achieved in all patients. The total time required for the procedure ranged from 27 to 200 minutes (75.9 min ± 41.2). Access to the subclavian artery was achieved by surgical exposure in 407 patients and by percutaneous puncture in 19. The indwelling catheter was inserted from a branch of the subclavian artery in 324 patients and directly from the subclavian artery in 102. In nine patients, access was created from the right subclavian artery or its branch because either the patient had undergone previous radiation therapy for breast cancer or there was vascular damage caused by previous procedures at other hospitals.

Placement of the catheter–port system succeeded in 425 of 426 patients (99.8%). In the one failed case, which involved liver metastases from breast cancer, NBCA and iodized oil injected to fix the indwelling catheter tip to the proximal portion of the splenic artery perfused into the common hepatic artery and occluded it. No abnormal data were observed in this patient’s liver function tests and no adverse effects occurred as sequelae of this event, but the procedure had to be stopped. The patient was treated with systemic chemotherapy, but died 3 months after the procedure because of uncontrolled liver metastases and disseminated disease. The tip of the catheter was fixed to the gastroduodenal artery or its branches in 294 patients, the splenic artery in 94, and a peripheral branch of the hepatic artery in 38. Fixation of the catheter tip to the vessel was performed with the combination of coils and NBCA/iodized oil in 343 patients, coils alone in 29, and the mixture of NBCA and iodized oil alone in 54.

Dislodgment of an indwelling catheter from which the injected contrast medium did not distribute to the entire liver or distributed to extrahepatic organs occurred in 12 patients (2.8%) 1–385 days (82.5 d ± 121.1) after placement. To fix the catheter in place, the combination of coils and NBCA/iodized oil was used in nine patients, coils alone were used in two, and the mixture of NBCA and iodized oil alone was used in one. Five of these 12 catheters were found within 1 week after the procedure. The tip of the catheter moved toward the periphery of the artery in which it was placed in six patients. All cases were corrected radiologically by either hooking the catheter with use of an angiographic catheter inserted from the femoral artery (n = 2) or pulling the catheter itself out after exposing the implanted port site (n = 4). The indwelling catheter was inadvertently withdrawn from the placed position in the other six patients. In two of them, the whole system fixed with NBCA and iodized oil was replaced with a new one. At removal of the indwelling catheter inserted from the left subclavian artery, we pulled the catheter out from the femoral artery with use of a snare after exposing and cutting the implanted port because NBCA or thrombi clinging to the tip of it could flow into the
left vertebral artery when the catheter was pulled out from the left subclavian artery. In one patient, after the proximal portion of the placed catheter was exposed, a 3-F microcatheter (Tracker-18; Target Therapeutics) was inserted into the appropriate position through it and was then connected directly to the implanted port with use of a connecting device. In another patient, the proximal portion of the catheter was similarly exposed and the placed catheter was successfully advanced to the appropriate position with use of a 0.035-inch hydrophilic guide wire (Radifocus M; Terumo). The remaining two patients refused further treatment, so correction of the position was not performed and regional chemotherapy was abandoned.

Cumulative patency rates of the hepatic artery calculated for patients with successfully placed catheter–port systems were 91.0% (95% CI, 87.3–94.7), 81.4% (73.7–89.0), and 58.1% (38.4–77.8) at 6 months, 1 year, and 2 years, respectively. Hepatic arterial infusion chemotherapy was performed 3–102 times (mean, 35) in 425 of 426 patients.

In the procedure itself for catheter placement, there were no major complications except for the one case mentioned in whom the procedure was stopped because of the perfusion of NBCA and iodized oil into the common hepatic artery. In the follow-up period, procedure-related major complications were found in nine of 426 patients (2.1%). Significant bleeding around the implanted port occurred in two patients. One required extraction of the implanted system because of infection around the port 3 weeks after the procedure but, after treatment of the infection, this patient underwent catheter placement again via the left inferior epigastric artery. In another case, a hematoma around the port occurred 3 days after the procedure as a result of incomplete ligation of the branch of the left subclavian artery, but was controlled by repeat ligation of the branch under exposure. Dysfunction of the implanted system occurred in three patients at 2.5, 4, and 14 months after the procedure as a result of kinking of the catheter near the connection of the indwelling catheter and port. In these patients, the implanted system was exposed again and the proximal portion of the catheter was cut off and reconnected to the port. Improper infusion of NBCA and iodized oil occurred in two patients, including the case previously described. In the other patient, although NBCA and iodized oil injected to fix the indwelling catheter tip to the gastroduodenal artery perfused into the proper hepatic artery and occluded it, we recanalized it by placing a balloon-expandable stent (Palmaz-Schatz; Cordis), which was 5 mm in diameter and 15 mm in length. The patient’s liver function tests revealed no change after the event and the hepatic artery was patent 16 months after stent placement (27). Cerebral infarction occurred in two patients after catheter placement. It developed in one patient in the left thalamus 16 months after the procedure and in the other in the left cerebellar hemisphere 7 months after the procedure. The catheter was inserted from the left subclavian artery in both. After the patients were treated conservatively and recovered without sequelae, hepatic arterial infusion chemotherapy was resumed within a few weeks. No hepatic or splenic infarction was observed in any of the cases.

**DISCUSSION**

Although it remains controversial whether hepatic arterial infusion chemotherapy significantly prolongs the survival of patients with unresectable liver malignancy compared with systemic chemotherapy (1–7), this therapy has been widely adopted, with many reports describing promising results (1–7,23–25). Many papers have also described surgical procedures by laparotomy and radiologic procedures for this therapy, with the surgical procedures used more commonly in most centers (5,6,28). One reason for this is that complications such as catheter dislodgement or hepatic arterial occlusion are more frequently associated with radiologic procedures than with surgical ones (28). These problems are
thought to be related to the absence of fixation of the indwelling catheter tip to the vessel when simple radiologic catheter placement in the hepatic artery is employed, in contrast to the surgical procedure in which the catheter tip is fixed to the gastroduodenal artery by ligation (16,17).

According to previous reports of radiologic catheter placement, catheter dislodgment occurs in 6.1%–41.3% of procedures (9,10,13,14,29,30). In this study, we experienced only a 2.8% incidence of catheter dislodgment, with this better result probably attributable to improved stability of the catheter tip achieved by fixation to vessels with coils and/or glue. In the five cases in which catheter dislodgment was noted within 1 week after the procedure, we suspected that it was caused by incomplete fixation of the catheter, which might have been prevented with use of additional coils or NBCA and iodized oil. However, further fixation might increase the risk of the other procedure-related complications; we experienced inadvertent infusion of NBCA and iodized oil into the proper hepatic artery (27). There were seven cases of catheter dislodgment much later, in each of which the liver tumors showed a marked response to hepatic arterial infusion chemotherapy and the size of the liver reduced significantly. This was the likely cause of these late catheter dislodgements.

Hepatic arterial occlusion is another problem to be overcome in patients treated with hepatic arterial infusion chemotherapy (9–11,13,14). The hepatic artery is more likely to occlude when the catheter tip is inside the proximal hepatic artery and anticaner agents are infused from the end hole of the catheter because the catheter tip mechanically stimulates the inner lumen of the hepatic artery and most anticaner agents are toxic to the endothelium of the artery (16). In this study, we achieved an 81.4% cumulative patency rate in the hepatic artery 1 year after the procedure, which was similar to the results reported by Seki et al (10) with use of a similar technique. These results were much better than those of the first study by Arai et al (15), which had been performed radiologically but without fixation of the catheter tip. This system made it possible to administer infusion chemotherapy 35 times on average, which might be a sufficient number to control life-threatening liver malignancies in most cases (1–7,12,23–25).

Cerebral infarction, which is the most undesirable complication, was noted in 0.5% of patients after catheter placement in this study. Although it was undeniable that the infarction was caused by the catheter across the left vertebral artery origin, the real relation of cause and effect was not evident in this study.

This study was not a comparative study with a surgical procedure performed under general anesthesia and with laparotomy. However, our results demonstrated that radiologic catheter placement of a side-hole catheter with distal fixation is highly successful and safe under local anesthesia without laparotomy. Our high technical success rate and acceptable time requirement for the procedure suggest that this technique can replace the surgical one by virtue of its reliability and low invasiveness (30,31).

In summary, we modified the technique of radiologic placement of a catheter and port system for hepatic arterial infusion chemotherapy by fixing the catheter tip to the vessel and infusing anticaner agents from the side hole of the catheter. We conclude that this technique is a safe and not unduly time-consuming method that obviates surgical laparotomy and represents a significant therapeutic advance in the medical oncology field for patients with liver malignancies.

References