

## Original Article

# Hepatocellular Carcinoma with Blood Supply from Parasitized Omental Artery: Angiographic Appearance And Chemoembolization

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## ABSTRACT

**Objective:** To analyze angiographic appearance of hepatocellular carcinoma (HCC) with blood supply from parasitized omental artery (POA), and evaluate the technical feasibility, safety and therapeutic efficacy of chemoembolization via the POAs.

**Methods:** A total of 1,221 HCC patients who had undergone chemoembolization procedures were evaluated retrospectively. The evaluated indexes included the incidence rate of POAs, success rate of superselective catheterization, post-reaction after chemoembolization, and the cumulative survival rates.

**Results:** Totally 1,221 HCC patients had undergone 3,639 chemoembolization procedures, and 32 patients with POAs were enrolled, with 97 POAs found in 76 angiography procedures, giving an incidence rate of 2.09%. POA was observed mostly at the right lobe and left medial lobe except the segment II, and 62 POAs underwent superselective catheterization with microcatheter, giving a success rate of 63.9%. The angiographic appearance was: (1) hypertrophic POAs participating in tumor staining ( $n=28$ ); (2) stiff and distorted POA ( $n=11$ ), displaced due to tumor's oppression ( $n=8$ ); and (3) defective tumor staining close to either gastrocolic omentum distribution or liver capsule ( $n=7$ ). In 19 patients, chemoembolization via POAs was performed successfully (A group), while the remaining 13 patients failed (B group). Except 1 acute edema pancreatitis case, no serious complication was recorded. The cumulative survival rates of 6-, 12-, 18- and 24-month were 78.9%, 47.4%, 31.6% and 21.1% respectively for A group; correspondingly, 61.5%, 30.8%, 15.4% and 7.7% for B group, in which 2 patients died of ruptured HCC.

**Conclusion:** Chemoembolization with microcatheter via POAs is a relatively safe, feasible and valuable method.

**Key words:** Hepatocellular carcinoma; Omental artery; Angiography; Chemoembolization

## INTRODUCTION

Hepatocellular carcinoma (HCC) is one of the most common malignant tumors in China. Chemoembolization has become one of the most effective treatments for the inoperable HCC or postoperative recurrent HCC<sup>[1-4]</sup>, and the interventional therapeutic efficacy depends on adequate exposure and correct handling of HCC's intrahepatic and extrahepatic blood supplies.

Extrahepatic collateral or parasitized blood supplies can interfere effective treatment with chemoembo-

lization. Many studies<sup>[5-14]</sup> had reported chemoembolization through different extrahepatic blood supplies of HCC such as inferior phrenic artery, adrenal artery, internal mammary artery, intercostal artery, and renal capsular artery. Among them, omental artery (OA) is a rare one, which usually arises from right gastroepiploic artery (from gastroduodenal artery) or left gastroepiploic artery (from splenic artery near hilum of spleen), communicates with each other and forms the arch to supply the greater omentum.

Commonly, OA is only 2–3 mm in diameter, so it is not usually obvious during angiography, especially in healthy people. But when OA participates in both the tumor and peritoneal metastatic lesions, it can be easily recognized at digital subtraction angiography (DSA) and contrast abdominal computed tomography (CT) for its' significantly increased diameter<sup>[7]</sup>. Although a

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parasitized omental artery (POA) can supply HCC, due to the circuitous shape and anatomy of its origin, superselective catheterization and chemoembolization via the POA can be challenging, and has been infrequently performed.

In this article, we discussed and retrospectively analyzed the angiographic appearances of HCC with blood supply from POA, and evaluated its technical feasibility, safety, and efficacy of chemoembolization through POAs in HCC patients.

## MATERIALS AND METHODS

### Patients Population

The clinical and angiographic data of 1,221 patients with a diagnosis of HCC treated at Interventional Therapy Department of Peking University Cancer Hospital from January 1998 to February 2008 were retrospectively analyzed. HCC was diagnosed histopathologically or clinically in patients who had consistently increased (400 ng/ml) serum  $\alpha$ -fetoprotein (AFP) levels and space-occupying lesion(s) thought to be consistent with HCC on triple-phase CT.

Our retrospective study was approved by the local ethics committee and conducted according to the standards of the Declaration of Helsinki, and written informed consent was obtained from all patients before their chemoembolization treatment.

### Chemoembolization Procedure

For all patients, chemoembolization were undertaken at digital subtraction angiography machine (Multistar TOP, Siemens, Germany; Invova 4100IQ, GE, USA). Arteriography was routinely performed in patients before they underwent chemoembolization. After application of a local anesthetic agent, the Seldinger technique was used to access the femoral artery, and 5F Rösch hepatic, Cobra or Yashiro catheters (Terumo corporation, Tokyo, Japan) were utilized to perform angiography of the celiac axis, common hepatic artery, superior mesenteric artery and gastroduodenal artery to collect information about the number, type, and location of tumors and feeding arteries, as well as the presence of vascular anatomic variations. Portography through the superior mesenteric artery or spleen artery was also performed to evaluate the portal venous system.

The above vascular catheter was inserted into the proper hepatic artery, the left or right hepatic artery depending on where the target tumor was located. The chemotherapeutic regimens were perfused including combination of at least two of the following: fluorodeoxyuridine (FUDR) (500–750 mg, Haizheng Pharmaceutical Co., Ltd. Zhejiang, China), cisplatin (50 mg, Mayne, Melbourne, Australia), oxaliplatin (100 mg, Hengrui Pharmaceutical Co., Ltd. Jingsu, China),

mitomycin c (8–10 mg, Kyowa Hakko Kogyo, Tokyo, Japan), and hydroxycamptothecin (20 mg, Wanle Pharmaceutical Co., Ltd. Shenzhen, China). Embolization was performed via the proper hepatic artery, the left/right hepatic artery or segmental/subsegmental hepatic arteries under fluoroscopic control, and the embolization materials were iodized oil (lipiodol; Laboratoire Andre Guerbet, Aulnay-sous-Bois, France) and 2 mm × 2 mm × 1.5 mm spongostan particles (Absorbable gelatin sponge; Jin Ling Pharmaceutical Co., Ltd. Nanjing, China) or iodized oil only, which was mixed completely with epirubicin hydrochloride (20–40 mg, Haizheng Pharmaceutical Co., Ltd. Zhejiang, China) as an emulsion. A microcatheter (Progreat microcatheter system, 2.7F, Terumo Corporation, Tokyo, Japan) was used for superselective catheterization for the feeding arteries. If we failed to catheterize the tumor-feeding vessels or the tumor was large and supplied by multiple segmental hepatic arteries, chemoembolization was performed through the right or left hepatic artery. When an initial blockade of the hepatic artery was insufficient because of large tumor size or arteriovenous shunting, embolization was performed with gelatin sponge cubes.

After chemoembolization to the intrahepatic feeding arteries, the possibly existing extrahepatic feeding arteries (including POA) to the lesion were catheterized as selectively as possible by using the 2.7F microcatheter. Initially, 2–3 ml 2% lidocaine was given to relieve pain and avoid spasm, and then an appropriate amount of non-ionic contrast agent, an emulsion composed of epirubicin mixed with lipiodol oil was added with 2 ml syringe under fluoroscopy control. The procedures were performed by experienced physicians, including authors.

### Follow-up Care and Statistical Analysis

The characteristics of HCC patients with blood supply from POA were subsequently analyzed, and POA angiographic appearance was recorded and analyzed by two interventional radiologists (including authors). Patients underwent repeated chemoembolization cycles if the initial lesions were revascularized or new lesions were observed by enhanced CT or magnetic resonance imaging (MRI), and the time interval was 4–8 weeks. We gave up the chemoembolization if advanced liver disease (Child-Pugh class C) appeared. We defined technical success as successful catheterization into the tumor-feeding branch of POAs and delivery of chemoembolization using iodized oil and gelatin sponge particles, and the success rates of the superselective catheterizations were calculated. Complications related to POAs chemoembolization were retrospectively analyzed by laboratory tests and the CT findings, and the

postembolization complications, such as transient fever, abdominal pain, nausea and vomiting, were also evaluated and controlled with symptomatic treatments. The survival of HCC patients with blood supply from POA was followed up by telephone regularly. The 6-, 12-, 18-, and 24-month cumulative survival rates were calculated respectively with Kaplan-Meier method using SPSS software 17 version (SPSS Inc., Chicago, USA).

## RESULTS

### Characteristics of Patients with POAs

A total of 1,221 patients with the diagnosis of HCC received 3,639 chemoembolization procedures in all, for an average of 2.98 procedures per patient. POAs occurred in 32 HCC patients (29 males, 3 females) in 76 angiography procedures, and the incidence rate was 2.09% (76/3,639). The 32 enrolled patients (aged from 22 to 75 years old, median: 57 years), were diagnosed by pathological liver biopsy (19 patients), by postoperative pathological examination (2 patients), and by clinical manifestations, serum AFP, ultrasound (US), CT or MRI examination (11 patients) (according to American Association for the Study of Liver Diseases Hepatoma Study Guide)<sup>[15,16]</sup>. One patient received percutaneous microwave ablation after chemoembolization.

Nineteen HCC patients with successful superselective catheterization via the POA (A group) received chemoembolization, the remaining 13 patients failed (B group). Six patients were found the POA at the first angiographic procedure, and the other 26 patients were found the POA after 1–6 cycles of chemoembolization. Four patients underwent 2 or more repeated chemoembolization via POA.

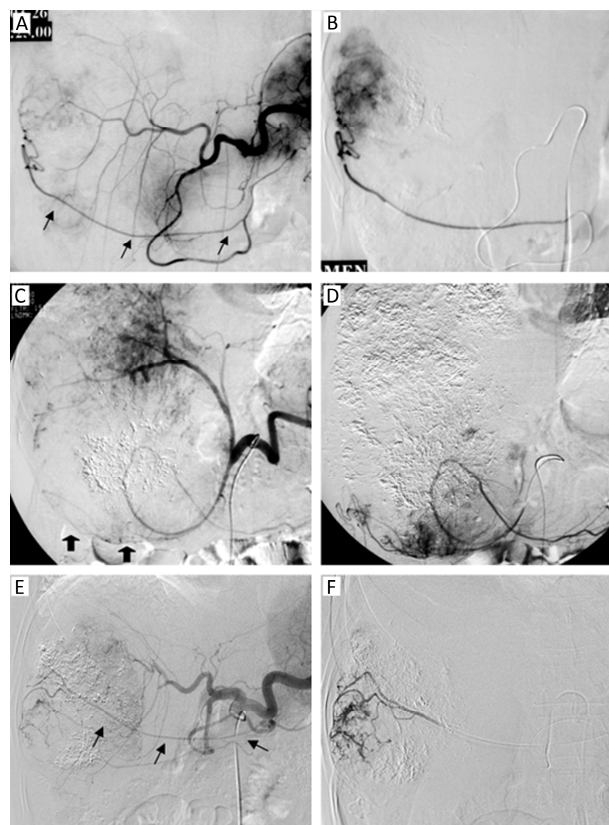
### POA Angiographic Appearance

The tumor with blood supply from POAs predominantly located in left medial lobe and right lobe (if a tumor occupied two or more segments, its location was assigned to the dominant segment, and for multinodular tumors, the location and size of tumors that were supplied by OA were recorded): 1 case located at segment I, 2 cases at segment III, 3 cases at segment IV, 4 cases at segment V, 9 cases at segment VI, 7 cases at segment VII, and 6 cases at segment VIII (Couinaud classification of segments).

Twelve patients were found other extrahepatic parasitized arteries during angiography: the right phrenic artery (5 cases), the colic branch of the superior mesenteric artery (5 cases), the right inferior adrenal artery (1 case), and the left gastric artery (1 case). After superselective catheterization to these parasitized arteries, prone chemoembolization was performed successfully with microcatheter, except for 1 case from

the right diaphragmatic artery and 2 cases from the colic branch of the superior mesenteric artery.

A total of 97 POAs were found (all originated from the right gastroepiploic artery), which often formed sharp angle between the POA and the gastroduodenal artery. With microcatheter, 62 POAs underwent successful superselective catheterizations, giving a success rate of 63.9% (62/97). The angiographic appearance of POAs was as follows: (1) hypertrophy and circuitry of the POAs participated in positive tumor staining (28 cases); (2) the edge of the POA was stiff and distorted due to tremendous HCC directly infiltrated (11 cases), OA branches cambered displacement occurred due to the tumors' oppression (8 cases); and (3) tumor staining or lipiodol deposition deflection occurred close to either gastrocolic omentum distribution or the liver capsule nearby the HCC (7 cases) (Figure 1).



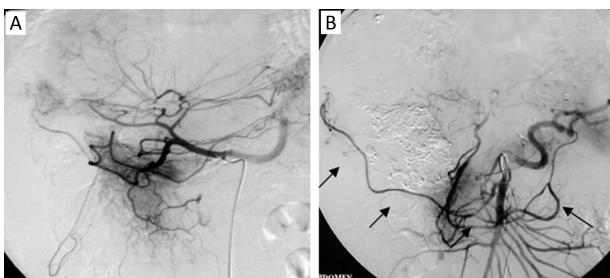
**Figure 1.** The angiographic appearance of POAs. **A, B:** The POA was hypertrophy and circuitry, pointing to HCC (arrow); after superselective catheterization with microcatheter, tumor staining could be observed during the parenchymal phase; **C, D:** The gastroduodenal artery and OA were displaced due to huge tumor' oppression. The POA participated in tumor staining on the edge of the tumor; **E, F:** After first chemoembolization, the deflection of tumor staining was observed at the second chemoembolization, close to the place which broke through the liver capsule. After superselective catheterization, the POA was convinced during the arterial phase.

### Complications from POA Interventions

The post-reaction after chemoembolization in A group included transient fever (18 cases), abdominal pain (15 cases), and nausea and vomiting (16 cases), and no intestinal ischemic necrosis, abscess or intestinal perforation occurred. One female patient experienced postoperative abdominal pain, and blood and urine's amylase increase, and was diagnosed with acute edema pancreatitis by emergency abdominal CT. She was subsequently cured with the drugs sandostatin, omeprazole, and pancreatinum etc for 3 weeks under diet and water forbidden condition. The post-chemoembolization course of B group included transient fever (10 cases), abdominal pain (4 cases), and nausea and vomit (12 cases). In both A and B groups, no chemoembolization-related deaths were recorded.

### Survival Rates

After chemoembolization treatment, the 6-, 12-, 18-, and 24-month cumulative survival rates were respectively 78.9%, 47.4%, 31.6% and 21.1% in A group, and 61.5%, 30.8%, 15.4% and 7.7% in B group. In B group, 2 patients died of ruptured HCC (US-guided abdominal paracentesis that reveals uncoagulatable blood confirmed the diagnosis) during follow-up.



**Figure 2.** POA occurrence was related to liver surgery and hepatic artery stenosis and occlusion. **A:** HCC recurrence was observed in one 55-year-old male patient who once underwent partial excision, and the POA and tumor staining could be observed at the surgical margin; **B:** Superior mesenteric artery angiography showed: the occlusion of the proper hepatic artery was found in one 64-year-old male patient who underwent multiple (3 times) chemoembolization, and the POA originated from gastroduodenal artery to nourish the HCC near the liver capsule (arrow).

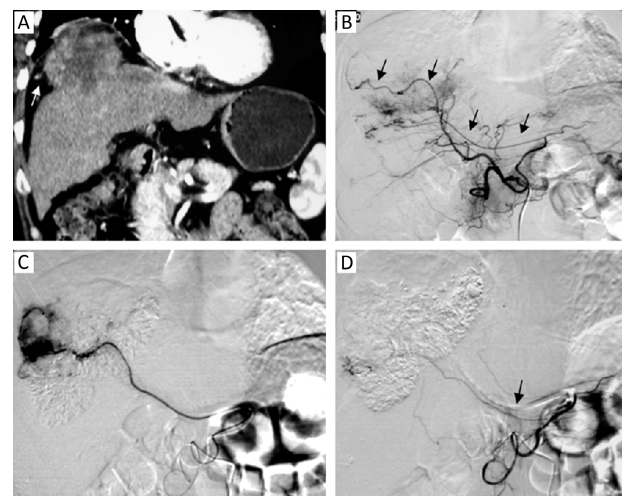
### DISCUSSION

The prevalence and causative factors of HCC's extrahepatic collateral and parasitized arteries were studied by some interventional radiologists<sup>[6,7,17,18]</sup>, and OA is a rare one, with an incidence rate of 1.4%–2.6%<sup>[19,20]</sup>, which is similar to 2.09% found in our study. The mechanism of POA occurrence may be related to huge-block HCC type, liver surgery with

omentum to suture and hemostasis at the surgical margin, hepatic artery stenosis and occlusion<sup>[10]</sup> (Figure 2). The occlusion (1 case) and stenosis (6 cases) of the hepatic artery were also found in our study, and avoiding hepatic artery stenosis and occlusion may decrease the incidence rate of the POA<sup>[17,18]</sup>.

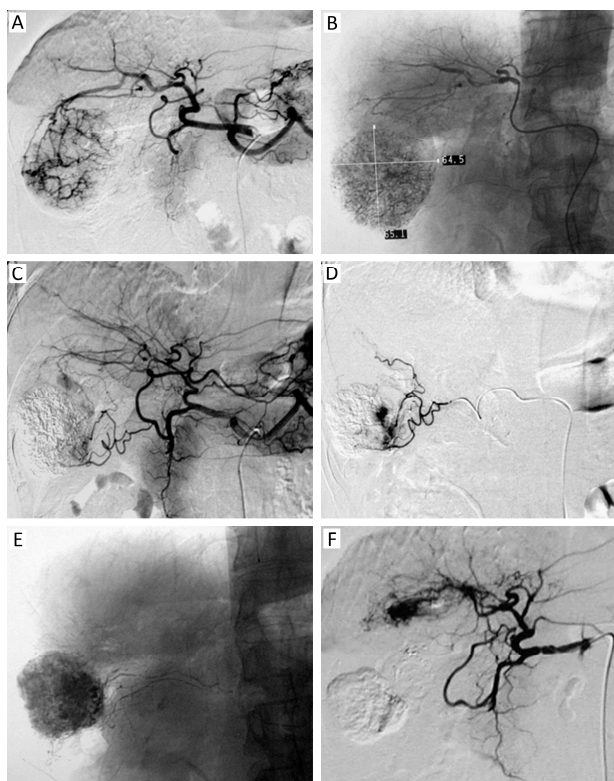
The extrahepatic parasitized arteries mainly traverse in the hepatogastric ligament, hepato-duodenal ligament, falciform ligament, coronary ligament, and the bare area of liver to feed the HCC<sup>[6]</sup>. However, due to its variable distribution, POA does not traverse via the above mentioned anatomical structures<sup>[7,19]</sup>. Where the HCC is covered by or adhered to omentum, where a POA may occur. In our study, except for the segment II of the liver, the POA was observed at all the other segments, and the most location was at the right lobe and left medial lobe.

A pre-chemoembolization contrast abdominal CT or MRI would be helpful for making the diagnosis whether the POA occurred or not: if the CT scan demonstrated tumor breaking through the liver capsule and an enlarged serpiginous artery was near the tumor edge (Figure 3), a POA may be strongly suggested<sup>[19]</sup>. When performing angiography, we should pay more attention to the hypertrophied artery which originates from the gastroduodenal artery or the dorsal pancreatic artery. Huge tumor compresses the nearby gastroepiploic artery and OA branches, and many plexiform



**Figure 3.** HCC supplied by POA in a 60-year-old women. **A:** Abdominal CT scan in hepatic arterial phase shows: the tumor breaks through the liver capsule, showing exogenous growth, an enlarged artery near the tumor edge (white arrow); **B:** Celiac artery angiography shows enlarged POA nourishes the edge of the tumor (black arrow); **C:** The 2.7F microcatheter was successfully used to perform the superselective catheterization for the POA. The tip of a microcatheter is beyond the stomach artery; **D:** After chemoembolization to the POA, another POA was found, however, it was too fine to fail the superselective catheterization.





**Figure 4.** HCC supplied by POA in a 73-year-old man. **A, B:** Celiac artery angiography in the first chemoembolization shows: HCC blood supply comes from the right liver artery, and no POA was found. After superselective catheterization, chemoembolization treatment was performed, and the lipiodol oil retention was compact; **C, D, E:** Two months later after the first chemoembolization treatment, a POA could be observed at the edge of the HCC and tumor staining in celiac artery angiography, coming from the gastroduodenal artery. The 2.7F microcatheter was used to perform the superselective catheterization for the POA successfully, and chemoembolization was performed. Compact lipiodol oil retention was observed; **F:** The POA was occluded after the chemoembolization treatment (celiac artery angiography 4 months later).

POAs may displace and be observed at the HCC's edge. In our study, the deflection of lipiodol oil deposition or tumor staining was close to either gastrocolic omentum areal area or the tumor which broke through the liver capsule, and further gastroduodenal artery or superior mesenteric artery angiography should be performed.

Chemoembolization is of significant benefit for the unresectable HCC, and the efficacy was not only associated with complete chemoembolization of the intrahepatic artery, but also with precise chemoembolization to extrahepatic parasitized artery (including POA), otherwise the therapeutic effect of chemoembolization will be reduced<sup>[6, 7]</sup>.

For the narrow lumen and sharp angle between the OA's origins and the gastroduodenal artery, in general,

5F catheters cannot be used to perform superselective OA catheterization. Microcatheter may help to improve the success rate of catheterization and decrease potential damage to the vessels<sup>[10]</sup>. But even with the 2.7F microcatheter, the success rate of our superselective OA catheterization was only 63.9%. More fine and flexible coaxial catheter may elevate the success rate of superselective catheterization. If damages to the POA such as vasospasm, dissection and occlusion occur, new extrahepatic parasitized arteries may emerge and may cause new difficulties for superselective catheterization<sup>[19]</sup>, in addition, the risks of reflux and mis-embolization will increase (Figure 4). Due to rich collateral branches, even if a small number of normal OAs were embolized, serious complications such as ischemia or infarction of the intestine (which usually is supplied by one of the mesenteric arteries) would not occur<sup>[7, 10, 19]</sup>. However, POAs may communicate with dorsal pancreatic artery, middle-colic artery, and mesenteric arteries. When huge tumor had encroached the nearby gastrointestinal tract wall prior to treatment, chemoembolization via POA may worsen the ischemia and edema of the intestine, consequently, gastrointestinal ulceration, perforation or intestinal infarction may occur<sup>[10]</sup>. In our opinion, it is important to advance the catheter tip until staining of the stomach or bowel wall is not demonstrated. When gastroepiploica vein and other portal vein branches displayed under fluoroscopy, chemoembolization should stop immediately. In our study, except 1 acute edema pancreatitis case, no other serious complications were found.

About 10% of HCC patients die of hemorrhage due to spontaneous rupture, and the arterial embolization is an effective emergency treatment<sup>[21]</sup>. In our study, no cases with HCC rupture were found in A group, but 2 cases in B group, because usually OA was involved in the marginal part of the tumor, where part of rupture is often located, so chemoembolization via the POA may have potential effect for preventing HCC rupture.

In our study, the 6-, 12-, 18- and 24-month cumulative survival rates in A group were somewhat higher than these in B group, suggesting the chemoembolization via a POA may have potential therapeutic value for HCC. However, we could not conclude this approach will prolong the survival time of HCC patients with blood supply from the POA significantly. Other factors, such as tumor size, AFP, pathological grading information, portal vein invasion, fistula extrahepatic metastasis, Child-pugh class, and Barcelona Clinic Liver Cancer (BCLC) stage, may also predict poor prognosis and affect the survival time<sup>[22-25]</sup>. This is why we didn't perform statistical comparison of these patients' survival outcomes between A and B groups. In addition, most HCC simultaneously fed by intrahepatic and extrahepatic arteries, it was difficult to

determine the degree of contribution of chemoembolization via the POA to the achievement of the complete or partial response, so we didn't analyze the radiologic response on CT or MRI. The two aspects were the main limitations of the retrospective study.

In conclusion, chemoembolization with microcatheter via the POA is feasible and relatively safe, and either may have potential therapeutic value or may help prevent rupture of HCC.

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#### Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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