# Transcatheter Oily Chemoembolization of the Extrahepatic Collaterals in Hepatocellular Carcinoma

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**Abstract**

Twenty patients with hepatocellular carcinoma who had hepatic artery occlusion from repeated transcatheter oily chemoembolization (TOCE), were treated with additional TOCE through extrahepatic collaterals.

Repeated TOCE were performed through the inferior phrenic artery (10 patients), branches of the gastroduodenal artery (6 patients), the internal mammary artery (2 patients), the pancreaticoduodenal arcade (1 patient), the accessory hepatic artery (1 patient), the capsular branch of the right renal artery (1 patient) and the 12th intercostal artery (1 patient). The TOCE was unsuccessful in 4 patients with accessory hepatic artery, one patient with cystic artery arising from superior mesenteric artery, one patient with omentoepiploic artery and one patient with left gastric anastomose with right gastric artery. The success rate of TOCE in the extrahepatic arteries was 76.67 per cent while there was a 23.33 per cent failure rate. The overall cumulative survival rates were 80 per cent (6 months), 50 per cent (12 months) and 18.8 per cent (18 months).

One patient developed skin necrosis at the right chest wall following TOCE of the right internal mammary artery for HCC. One patient developed hemiplegia following TOCE of the right 12th intercostal artery. The extrahepatic collaterals are important alternative routes for continuous transcatheter management of hepatocellular carcinoma following hepatic artery occlusion.

**Key word** : Extrahepatic Collaterals, Hepatocellular Carcinoma, Transcatheter Oily Chemoembolization

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**J Med Assoc Thai 2000; 83: 1393-1401**

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Hepatocellular carcinoma (HCC) is a highly malignant tumor of liver cell origin and is known to be exclusively supplied by the hepatic artery. Recently, transcatheter oily chemoembolization (TOCE) of the hepatic artery has been widely accepted as an effective means of palliation for inoperable or postoperative recurrent HCC[1-5]. When the hepatic arteries are interrupted by mechanical injury during catheter placement or arteritis are induced by TOCE or thrombosis from embolization, extrahepatic collateral pathways frequently develop[6-8]. Our experience with these alternative routes for the continuation of TOCE of hepatocellular carcinoma is presented.

## MATERIAL AND METHOD

From July 1989 to June 1999, 20 patients were chosen from 100 patients who had undergone repeated transcatheter oily chemoembolization (TOCE) of hepatic arteries with occlusion of the hepatic arteries. The extrahepatic collateral pathways then developed in these 20 patients. We excluded those who had extrahepatic collaterals demonstrated at the first session of TOCE (11 patients). We also excluded those patients whose hepatic arteries were still patent at the time of developing the extrahepatic collateral pathways (2 patients). The twenty patients were 15 men and 5 women, 40 to 82 years of age. All patients were histologically proved by liver biopsy to have hepatocellular carcinoma (HCC). All patients had TOCE performed through hepatic arteries for about 4 sessions or 5 months prior to developing extrahepatic collaterals with occlusion of common or proper hepatic arteries demonstrated by angiography.

A lipiodol CT scan was obtained in every patient prior to TOCE of the extrahepatic collaterals which demonstrated residual HCC[9] from TOCE of the previous hepatic artery.

For angiography, the celiac and superior mesenteric arteries were used in all patients. We considered development of extrahepatic collateral pathways possible when there was occlusion of either the common hepatic artery or proper hepatic artery or both and every attempt was made to search for new perihepatic collateral networks. These arteries were introduced with a 5 French preshaped catheter as peripheral as possible. When it was difficult to insert the catheter into these collaterals, we used the coaxial system with a 3 French tracker -18 catheter or SP catheter inserted into a 5 French preshaped catheter and advanced as far as possible into the feeding artery. For TOCE of these collaterals, we used a mixture of an iodised oil (Lipiodol; Andre' Guerbet, Aulnay-Sous-Bois, France) 10 ml with Mitomycin C 20 mg and final gelatin sponge embolization of the feeding artery until cessation of blood flow was demonstrated under fluoroscopic control. The periodic follow-up was obtained with $\alpha$ - fetoprotein titer and lipiodol CT scan every month. A repeat TOCE of these vessels was performed every 6 weeks if recurrent or residual tumor was demonstrated.

**Table 1. Frequency of extrahepatic collaterals for TOCE in 20 patients.**

| Type of Collateral | | No. of vessels | No. vessels with TOCE | No. vessels failed TOCE |
|---|---|---|---|---|
| Inferior phrenic a. | (Rt) 8 (Lt) 2 | 10 | 10 | 0 |
| Pancreaticoduodenal arcade | | 1 | 1 | 0 |
| Branches from Gastroduodenal a. | | 6 | 6 | 0 |
| Accessory hepatic a. (from SMA) | | 5 | 1 | 4 |
| Internal mammary a. | | 2 | 2 | 0 |
| Right paracolic gutter a. | | 1 | 1 | 0 |
| Cystic a. (from SMA) | | 1 | 0 | 1 |
| Capsular branch of right renal a. | | 1 | 1 | 0 |
| Intercostal a. | | 1 | 1 | 0 |
| Omentoepiploic a. | | 1 | 0 | 1 |
| Left gastric route | | 1 | 0 | 1 |
| | Total | 30 | 23 | 7 |
| | % | 100% | 76.67% | 23.33% |

## RESULT

Table 1 reveals the frequency of the extrahepatic collateral pathways after repeated TOCE of hepatic artery in 20 patients. The inferior phrenic artery was the major extrahepatic collateral pathway for TOCE with no failure (Figures 1, 2, 3, 4 and Table 1). The periportal route or epicholedocal arteries were the second most common extrahepatic collaterals for TOCE; they included one case with pancreaticoduodenal arcade (Table 1) from dorsal pancreatic artery which was successfully treated with TOCE (Figures 5, 6) and 6 cases which had branches from the gastroduodenal artery. Only one out of five patients with HCC supplied by accessory hepatic artery was successfully treated with TOCE (Figures 7, 8, 9, 10, 11 and Table 1). This artery was one of the periportal routes mentioned by Charnsangavej et al[6].

TOCE was successfully performed in one patient with capsular branch from the right renal artery, one patient with $12^{th}$ intercostal artery and in one patient with right paracolic gutter artery

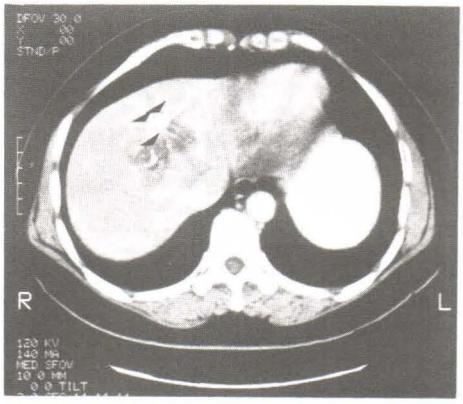


Fig. 1. Lipiodol CT scan after repeated TOCE of hepatic artery shows unopacified portion of HCC in right lobe liver (arrow) representing viable tumor, with only minimal lipiodol stain in tumor from TOCE (two arrows).

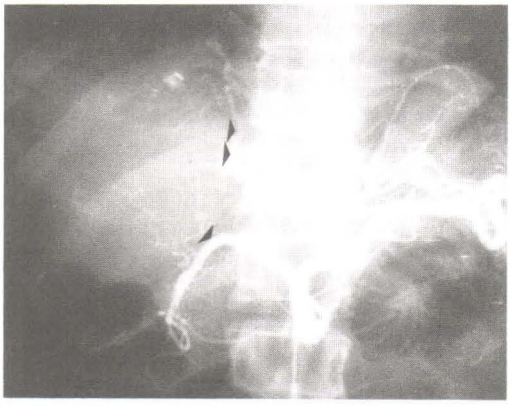

Fig. 2. Same case as in Figure 1, celiac angiogram reveals complete occlusion of proper hepatic artery from TOCE (arrow). The inferior phrenic artery is enlarged (two arrow) supplying HCC adjacent to dome of diaphragm.

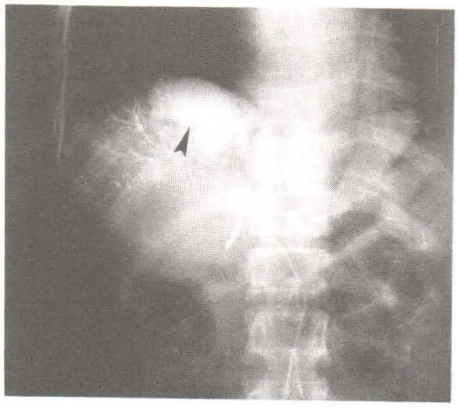

Fig. 3. Same case as in Figure 1, delayed inferior phrenic angiogram post TOCE of this artery shows retained lipiodol in HCC (arrow) adjacent to dome of diaphragm.

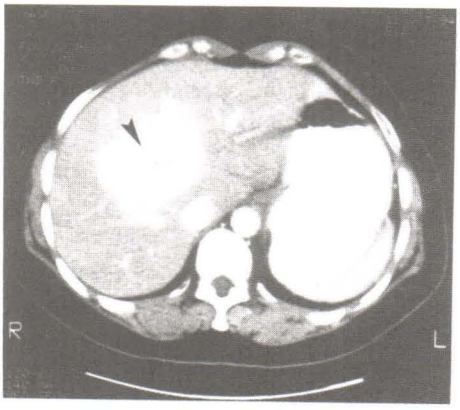


Fig. 4. Same case as in Figure 1, follow-up Lipiodol CT scan after TOCE of inferior phrenic artery shows complete opacification with lipiodol of HCC (arrow).

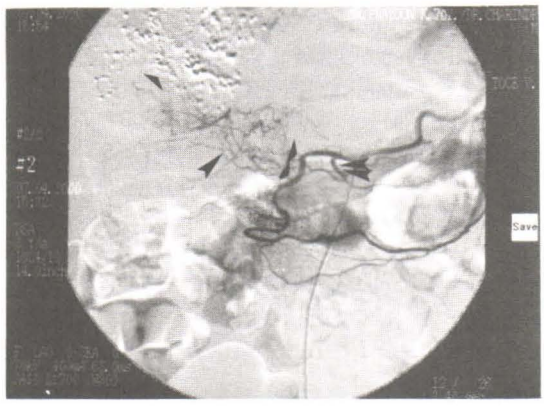

Fig. 5. Hepatic angiogram post repeated TOCE of hepatic artery with staining of lipiodol in HCC (small arrow), there is occlusion of proper hepatic artery (two small arrows), tumor feeders (big arrow) arising from dorsal pancreatic artery (two big arrows).

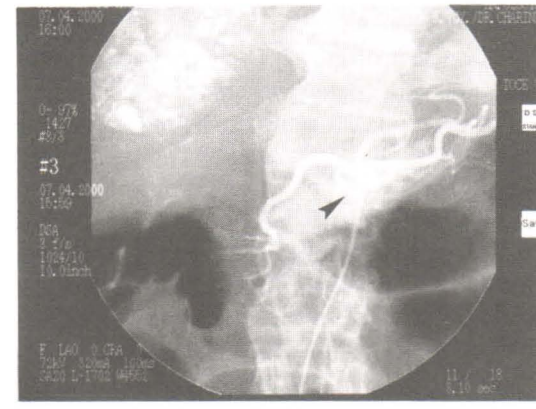

Fig. 6. Same case as in Figure 5, celiac angiogram post TOCE of dorsal pancreatic artery with complete occlusion of feeders and dorsal pancreatic artery (arrow).

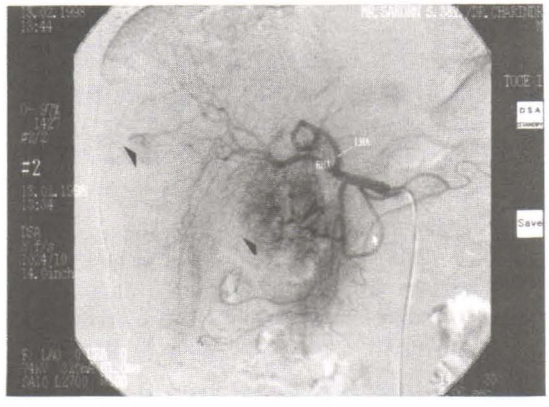

Fig. 7. Hepatic angiogram shows HCC supplied by both hepatic arteries and gastroduodenal artery (big arrow) tumor stain of HCC noted (small arrow).

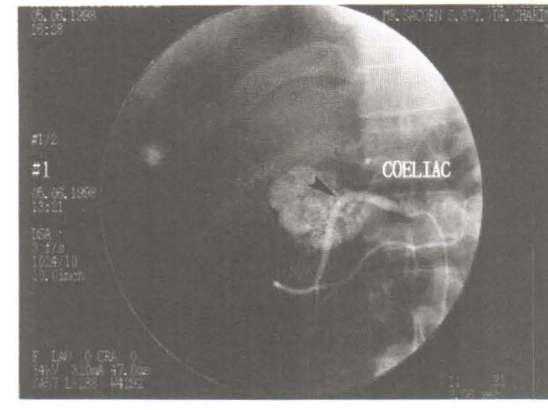


Fig. 8. Common hepatic angiogram same case as in Figure 7, post TOCE shows lipiodol staining of HCC (small arrow). There is occlusion of the proper hepatic artery (big arrow).

(Figures 12, 13, Table 1). Two patients had collateral from the right internal mammary artery supplied HCC who underwent treatment with TOCE of this collateral (Figures 14, 15, 16).

Figure 17 shows the cumulative survival calculate from the time of first session of hepatic artery chemoembolization compared to that calculated from the last session of TOCE of extrahepatic collaterals. There was no significant difference between the two. The median survival of both of them were 6 months and 7 months respectively. The survival rates of hepatic artery chemoembolization were 34.9 per cent (6 months), 10.5 per cent (12 months) and of TOCE of extrahepatic collaterals were 55 per cent (6 months), 19.3 per cent (12 months).

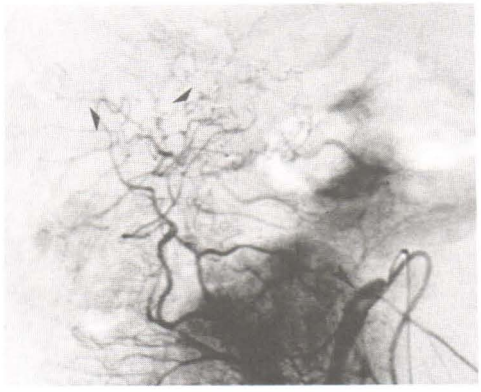

Fig. 9. Same case as in Figure 7, superior mesenteric angiogram shows multiple tumor feeders (small arrow) arising from accessory hepatic artery (big arrow).

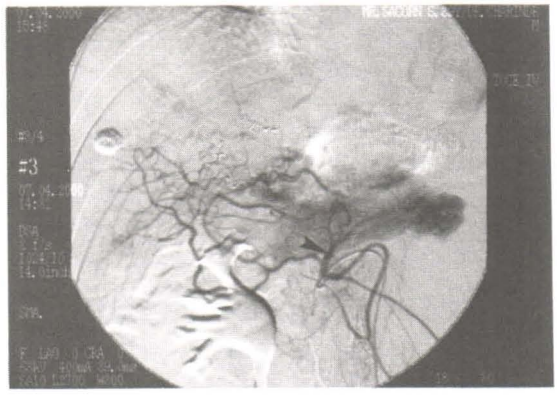

Fig. 10. Same case as in Figure 7, angiogram of the accessory hepatic artery arising from superior mesenteric trunk (arrow) enter HCC in right lobe.

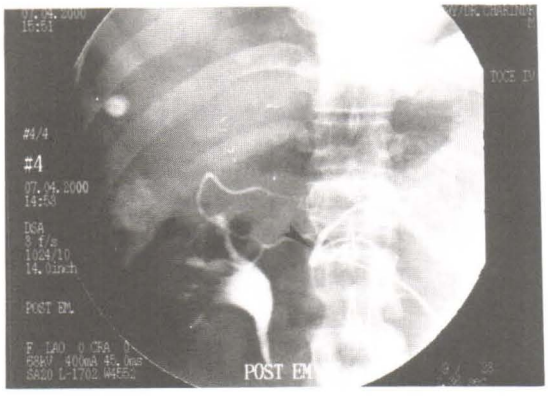


Fig. 11. Same case as in Figure 7, angiogram post TOCE of accessory hepatic artery (arrow) and its tumor feeder arteries with complete occlusion of the tumor feeder arteries.

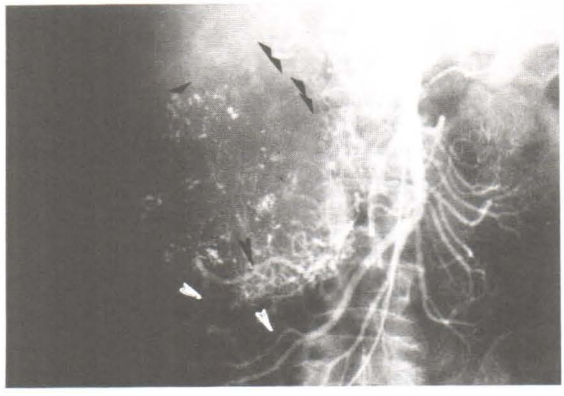

Fig. 12. Superior mesenteric angiogram post repeated TOCE of hepatic artery with lipiodol stain in HCC (small arrow). There is right paracolic gutter collaterals (big arrow) arising from right colic artery supplying HCC, also there is cystic artery arising from superior mesenteric artery supplying the tumors (two small arrows).

Figure 18 shows the overall survival rates of patients from the first session of TOCE of hepatic artery to the last session of TOCE of extrahepatic collateral pathways. The median survival was 12 months which was much longer than TOCE of the hepatic artery (6 months) (see Figure 17). The overall survival rates were 80 per cent (6 months), 50 per cent (12 months) and 18.8 per cent (18 months).

The complication of all patients with TOCE of extrahepatic collaterals were mostly minor with low grade fever, abdominal pain and ileus, and elevated liver function test as seen in TOCE of hepatic artery.

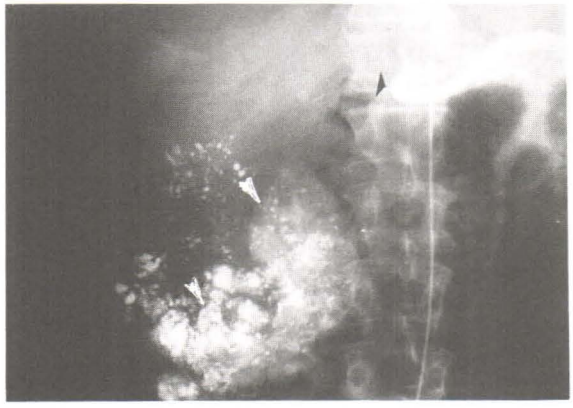

Fig. 13. Same case as in Figure 12, post TOCE of right paracolic gutter artery (not shown) reveals more opacification with lipiodol of HCC right lobe (big arrow) compared to Figure 12. Note occlusion of common hepatic artery (small arrow) in celiac angiogram.

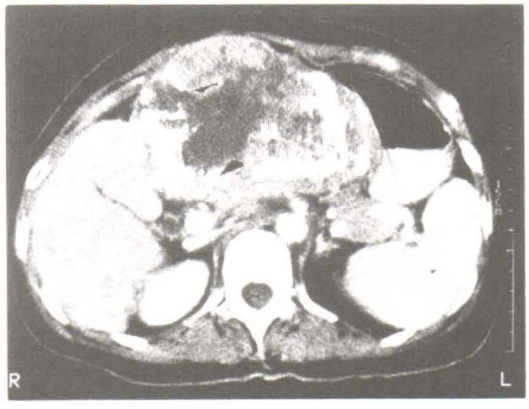


Fig. 14. Lipiodol CT scan post repeated TOCE of hepatic artery shows nonopacified portion by lipiodol at right and left liver lobes at anterosuperior portion adjacent to diaphragm representing residual HCC (arrow).

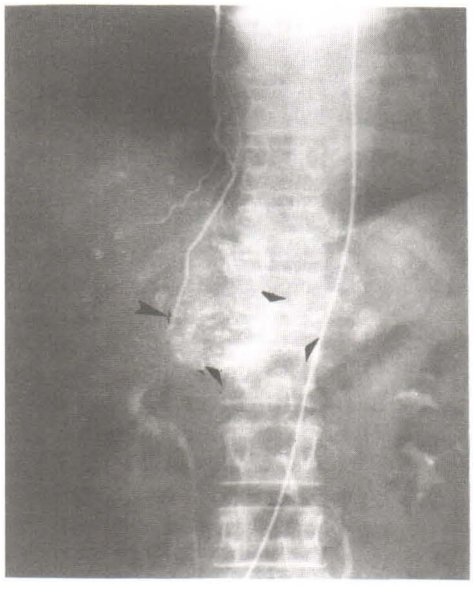

Fig. 15. Same case as in Figure 14, post TOCE of right internal mammary artery supplying the HCC (big arrow) with lipiodol stain in HCC (small arrow).

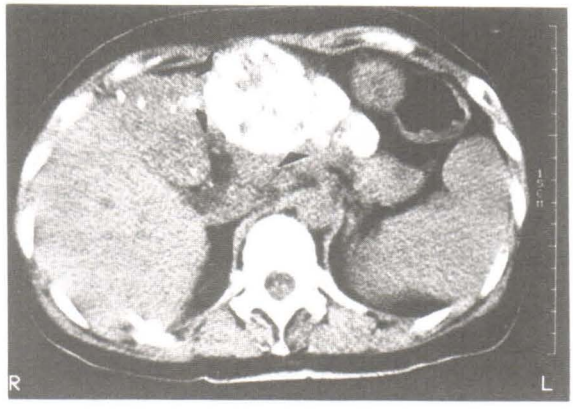


Fig. 16. Same case as in Figure 14, follow-up 1 month post TOCE. Lipiodol CT scan shows complete opacification of HCC by lipiodol (arrow) with significant decrease in tumor size compared to last exam (compared to Figure 14).

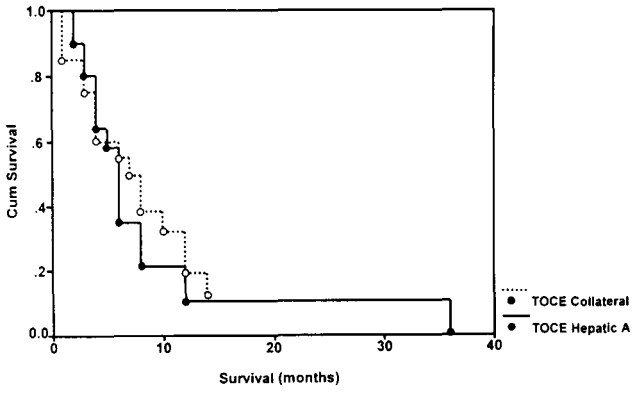


Fig. 17. **Comparing cumulative survival of 20 patients with TOCE of hepatic artery (median survival 6 months) to that of TOCE of extrahepatic collaterals (median survival 7 months) shows no significant difference.**

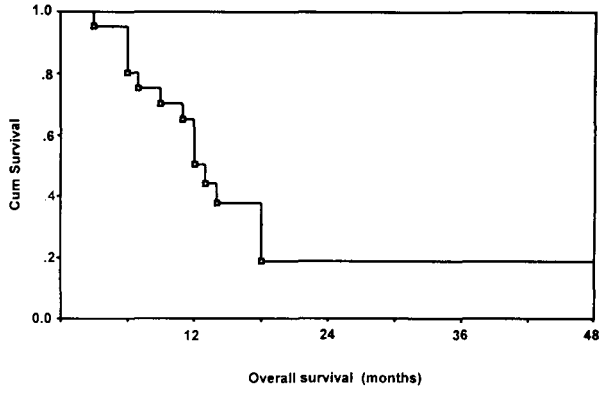


Fig. 18. **Overall cumulative survival of 20 patients from 1st session of TOCE of hepatic artery to last session of TOCE of extrahepatic collaterals shows improved survival rates from TOCE of hepatic artery alone. The median survival of overall cases was 12 months.**

One patient developed hemiplegia after TOCE of the right 12th intercostal artery probably due to reflux of gelatin sponge into the spinal artery during TOCE. The patient died eventually from hepatic failure 6 months after TOCE of this artery. One patient who had treatment of HCC by TOCE of the right internal mammary artery had sharp pain along the distribution of the superior epigastric artery which is a branch of the internal mammary artery and developed skin necrosis that was treated with surgical excision of the lesion.

## DISCUSSION

Although TOCE is a useful therapy for HCC, the necrosis rate of the tumor cells after TOCE is estimated at about 90-95 per cent from pathological examination[10,11]. The objective of TOCE should be tumor control rather than eradication, and multiple TOCE is usually needed. Certain problems related to repeat TOCE in these patients have arisen. They include the development of extrahepatic collateral pathways. These collateral pathways usually develop from a potential network of various small anastomotic branches of the adjacent organs secondary to alteration of the hemodynamics of the liver after TOCE. Therefore, the diameter of these collaterals is not usually large enough and it is difficult to pass the catheter close to the lesion. The incidence of extrahepatic collateral pathways in our cases was 20 per cent which was close to that reported in the literature[12,13]. With the use of a small preshaped catheter or by using coaxial catheter systems with either tracker -18 or SP catheter, the success rate of TOCE in these extrahepatic collaterals was 76.67 per cent (Table 1). Also, experience with catheter manipulation and skill of the angiographers are needed to achieve a high success rate.

TOCE of the extrahepatic collaterals were suggested when there was unopacified portion of lipiodol demonstrated with iodized oil CT scan (Figure 14) or persistent elevation of the level of serum α - fetoprotein, even after TOCE of the hepatic artery. The inferior phrenic artery was the most common extrahepatic collateral. Inferior phrenic, internal mammary and the intercostal arteries were all suspected to be the major collateral pathways when there was a defect in iodized oil CT scan at or near the dome of the diaphragm. When these collateral vessels are chemoembolized, there is a risk of embolization of the nontarget branches, which can lead to a variety of complications, depending on their location. Chemoembolization of the inferior phrenic artery has resulted in shoulder pain, pleural effusion and basal atelectasis[14]. Paraplegia or hemiplegia can result from inadvertent embolization of spinal branches arising from intercostal or

lumbar arteries[15] as seen in one of our patients. The cutaneous complication that occurred after nontarget embolization of extrahepatic collaterals is similar to the description of skin injuries caused by extravasation of chemotherapeutic drugs binding to tissue DNA, producing necrosis and a permanent loss of the wound's ability to heal[16]. This was demonstrated in our patient with chemoembolization of the internal mammary artery with a painful area of violaceous discoloration and induration including skin necrosis which was a worrisome complication, also reported in the literature[17]. In this patient, the specific artery supplying the area of the tumor should be thoroughly demonstrated angiographically and the catheter should be advanced directly avoiding the nontarget artery by using a microcatheter. Embolization to complete stasis should be avoided so that the chemomixture does not reflux into a nontarget blood vessel in order to avoid reflux and inadvertent embolization of nontarget organs. Therefore, to achieve a complete TOCE of HCC, a good quality angiography for visualization of the collateral feeding arteries, selection of the most effective branches to embolize and avoidance of potential complications from inadvertent embolization to the nontarget organs are necessary. From our study, chemoembolization or TOCE of the extrahepatic collaterals should be performed in order to prolong the patient's survival. The overall cumulative survival rates, when calculated from the first session of hepatic artery TOCE were 80 per cent (6 months), 50 per cent (1 year) and 18.8 per cent (18 months). The median survival increased from 6 months with TOCE of the hepatic artery to 12 months, with additional TOCE of extrahepatic collaterals.

(Received for publication on May 23, 2000)

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# การอุดกั้นหลอดเลือดแดงภายนอกตับเพื่อการรักษามะเร็งตับชนิดปฐมภูมิ

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ตั้งแต่กรกฎาคม 2532 จนถึงมิถุนายน 2542 มีผู้ป่วยที่รับการยืนยันจากผลชิ้นเนื้อตับที่เจาะตรวจว่าเป็นมะเร็งตับชนิดปฐมภูมิ จำนวน 20 ราย เป็นชาย 15 ราย หญิง 5 ราย อายุ 40 ถึง 82 ปี ได้รับการรักษาด้วยการใส่หลอดสวนเข้าหลอดเลือดแดงของตับและฉีดสารต้านมะเร็งพวกไมโตไมซิน ซี 20 มิลลิกรัม และสารทึบรังสีลิพิโอดอล 10 ซีซี และอุดกั้นหลอดเลือดด้วยสารเจลโฟม การรักษาด้วยวิธีนี้โดยเฉลี่ย 5 เดือน ประมาณ 4 ครั้ง จนหลอดเลือดแดงของตับเหล่านี้อุดกั้นไปและเกิดหลอดเลือดแดงภายนอกตับขึ้นมาเลี้ยงมะเร็งตับ ได้ทำการรักษามะเร็งตับด้วยการอุดกั้นหลอดเลือดแดงภายนอกตับที่เกิดมาใหม่เหล่านี้ด้วยวิธีดังที่กล่าวมาแล้ว มีผลสำเร็จในการสอดหลอดสวนประมาณ 76.67 เปอร์เซ็นต์ ผู้ป่วยเหล่านี้ได้รับการติดตามผลการรักษาด้วยการถ่ายรูป ซี ที สแกน และดูระดับแอลฟาฟีโตโปรตีนในเลือด พบว่าอัตราการอยู่รอดของผู้ป่วยเหล่านี้มีมากกว่าการอุดกั้นหลอดเลือดแดงของตับที่เกิดขึ้นตอนแรก ๆ อยู่มาก คือ ใน 6 เดือน มีอัตราการอยู่รอด 80%, 1 ปี มี 50% 1 1/2 ปี มี 18.8% ผลแทรกซ้อนจากการรักษาโดยมากพบเหมือนการอุดกั้นหลอดเลือดแดงตับ คือมีไข้ต่ำ ๆ ปวดท้อง เบื่ออาหาร ฯลฯ ผลแทรกซ้อนที่รุนแรงมี 2 ราย รายหนึ่งเป็นอัมพฤกษ์ชั่วคราวจากการหลุดรอดของเจลโฟมเข้าไปในหลอดเลือดของกระดูกสันหลัง มีผู้ป่วย 1 ราย มีแผลที่ผิวหนังบริเวณหน้าอกจากการอุดกั้นหลอดเลือดแดงที่ไปเลี้ยงมะเร็งที่มาจากหลอดเลือดแดงที่ไปเลี้ยงผนังหน้าอก

**คำสำคัญ** : หลอดเลือดแดงภายนอกตับ, มะเร็งตับ, การรักษาด้วยการอุดกั้นหลอดเลือด

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