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Incidence and therapeutic frequency of extrahepatic collateral arteries in transcatheter arterial chemoembolization of hepatocellular carcinoma: Experience from 182 patients with survival time more than 3 years

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ABSTRACT

Purpose: To retrospectively evaluate the incidence of each extrahepatic collateral artery (EHCA) supplying to hepatocellular carcinoma (HCC) in sessions of transcatheter arterial chemoembolization (TACE) and its therapeutic frequency.
Materials and methods: Between February 2002 and May 2008, 182 patients with HCC underwent TACE and survived more than 3 years. For TACE procedure, angiographic evaluation of all suspected EHCAs that could supply the tumor were performed. The incidence of EHCAs in TACE sessions and therapeutic frequency were analyzed. Correlations between the number of collaterals and the number of TACE sessions were investigated.
Results: 162 patients showed 647 EHCAs supplying tumors in a total of 795 sessions of TACE. The initially confirmed EHCAs in TACE sessions were the right inferior phrenic artery (RIPA, $n = 150$), left inferior phrenic artery (LIPA, $n = 8$), right internal mammary artery (RIMA, $n = 4$), right adrenal artery (RAA, $n = 2$) and left gastric artery (LGA, $n = 5$), respectively. The incidences of EHCAs were 51.1%, 68.1%, 50.0%, 50.0%, 42.3%, 34.6%, 29.1%, 19.8%, 6.6%, 3.3% and 0.6% from 1 to 11 session of TACE, respectively. The RIPA was accounted for 62.5% of EHCAs and other EHCAs often occurred after the attenuation of RIPA. There were correlations between the number of TACE sessions and either the sum number of collaterals ($r = -0.961$; $p < 0.001$), the number of RIPA ($r = -0.948$; $p < 0.001$) or the number of LGA ($r = -0.670$; $p = 0.024$). The mean therapeutic frequencies of TACE were 2.6, 1.5, 1.6, 1.3, 1.5, 1.2, 3.3, 1.1, 1.0 and 7.0 times for the RIPA, LIPA, RIMA, left internal mammary artery (LIMA), omental artery (OMA), LGA, right intercostal artery (RICA), RAA, right renal capsular artery (RRCA) and colic artery (COA), respectively.
Conclusions: The RIPA angiography should be routinely performed in TACE procedure. EHCAs should be searched during the sessions of TACE in the following order: RIPA, RIMA, LIPA and other collaterals of lower incidence.

1. Introduction

Transcatheter arterial chemoembolization (TACE) is recommended by the Society of Interventional Radiology as a first line treatment for nonsurgical treatment of hepatocellular carcinoma (HCC) [1]. The development of extrahepatic collateral pathways is one of the causes of local tumor recurrence. It prohibits effective control of the tumor with chemoembolization of the hepatic artery (HA). Chemoembolization through some collaterals has been attempted as means of continuing treatment [2–5]. The incidences of extrahepatic collateral arteries (EHCAs) reported were various because they may easily change according to each patient's characteristics, in particular tumor location and size, as well as the choice of angiography of EHCAs subjected to the operator's experience [6–9]. Michels [10] described 26 possible extrahepatic collateral pathways after dissection of 200 cadavers. Considering the wide spectrum of extrahepatic collateral arteries and the time-consuming process of selective angiography of individual collateral, it is impossible to perform all potential collateral feeders in one session of TACE. We retrospectively analyzed the incidence and the

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therapeutic frequency of every collateral supplying HCCs on 182 patients who survived more than 3 years. The aim is to investigate the incidence and possible order of EHCAs developed in repeated TACE and whether chemoembolization through collateral can affect the development of EHCAs.

2. Materials and methods

This study has been approved by the hospital review boards. Written informed consents were obtained from all patients for the TACE procedure. The written informed consent for each patient was documented in her or his medical chart.

2.1. Patients

From February 2002 to May 2008, TACEs were performed in 2451 patients with HCC in our hospital. A diagnosis of HCC was rendered on the basis of the results of a percutaneous needle biopsy, surgical resection, laboratory tests (e.g. α-fetoprotein > 200 μg/L and the sustained time is more than 8 weeks or α-fetoprotein > 400 μg/L and the sustained time is more than 4 weeks) in combination with typical appearances of computed tomography (CT) or magnetic resonance (MR), which was routinely performed except in the cases of emergency transarterial embolization and disease progression on follow-up images. Of the 2451 study subjects, 182 patients (7.4%) survived more than 3 years. The survival time of each patient was calculated by the interval between the first and last session of TACE. There were 158 males and 24 females with ages ranging from 25 to 80 years (mean 56.3 years) at their initial TACE session. All patients had preprocedural laboratory data, including complete blood count, liver function tests, α-fetoprotein measurement, and coagulation profile. Triple-phase CT or gadolinium-enhanced MR imaging was performed within 30 days before embolization. All patients had liver cirrhosis, which were associated with hepatitis B virus in 178 patients (97.8%) and hepatitis C virus in 2 patients (1.1%). The etiology was unknown in 2 patients (1.1%). The patient profiles and the baseline tumor characteristics prior to the first TACE session are summarized in Table 1.

Table 1
Baseline characteristics of patients.

Characteristics	Value
No. of patients	182
Gender	
Male	158 (86.8%)
Female	24 (13.2%)
Mean age (*y*)	56.3 ± 11.6
Liver cirrhosis	
HBV related	178 (97.8%)
HCV related	2 (1.1%)
Etiology unknown	2 (1.1%)
Child-Pugh class	
A	142 (78.0%)
B	40 (22.0%)
Tumor number	
Multiple	70 (38.5%)
Single	112 (61.5%)
Growth pattern of primary tumors	
Diffuse	1 (0.5 %)
Nodular	181 (99.5%)
Maximum diameter of primary tumor	
<10 cm	143 (78.6%)
≥10 cm	39 (21.4%)
Portal vein tumor thrombus	
No	176 (96.7%)
Right	6 (3.3%)
Left	2 (1.1%)
Main	2 (1.1%)
Distant metastasis (/)	
No	180 (98.9%)
Yes (lung)	2 (1.1%)
Previous treatments	
No	134 (73.6%)
Surgery	33 (18.1%)
RFA	7 (3.8%)
MWA	9 (4.9%)

HCV: hepatitis C virus; HBV: hepatitis B virus; RFA: radiofrequency ablation; MWA: microwave ablation. Values in parentheses are percentages.

2.2. Angiography

Arteriograms of the celiac and superior mesenteric arteries were performed in all patients from a common femoral approach with a 4- or 5-F angiographic catheter to establish hepatic arterial anatomy, location of lesion(s), and portal vein patency. Selective angiography was performed in each case with extrahepatic collateral arteries suspected of supplying HCCs. Aortography helped to locate the individual vessels arising from the aorta, if necessary.

2.3. Determination of the presence of extrahepatic collateral arteries

Extrahepatic blood supply to the lesion(s) was suspected [6]: when the size of tumor demonstrated on angiograms of these arteries is not concordant with CT/MR; a tumor located near the diaphragm or the ligaments; the HA is not the major vessel of blood supply or is occluded; a tumor grew exophytically or invaded adjacent organs; there was a history of spontaneous rupture, previous abdominal operation or percutaneous therapy; a peripheral defect of iodized oil retention within a tumor was seen during chemoembolization or on a follow-up CT scan; a sustained elevation in serum α-fetoprotein level was noted despite adequate embolization of the HA. Several extrahepatic collaterals were sought when extrahepatic blood supply to the tumor was suspected. An arteriogram/fluoroscopic image of the right inferior phrenic artery (RIPA) was routinely performed and other suspected extrahepatic collateral pathways were sought mainly depending on the tumor locations. When a tumor was located in the bare area of the liver, a selective angiography was performed on the right adrenal artery (RAA). When a tumor was located in the superoanterior portion of the liver, selective angiographies of the right internal mammary artery (RIMA) and left internal mammary artery (LIMA) were performed. When the tumor was in contact with the right kidney, selective angiographies of the right renal capsular artery (RRCA) and RAA were performed. When the tumor was in contact with omental fat with an exophytic growth pattern or the patient has a history of spontaneous rupture, previous abdominal operation or percutaneous therapy, selective angiographies of the gastroduodenal artery and spleen artery were conducted to seek whether the omental artery (OMA) was supplying the tumor. When a tumor invaded or was in contact with the right lateral thoracic wall, the selective angiography was performed on RIMA, the lower right intercoastal artery (RICA) and the right lumbar artery. When an exophytic tumor was located in the left lateral segment of the liver, the selective angiography was performed on the left gastric artery (LGA), left inferior phrenic artery (LIPA) and LIMA. When an exophytic tumor was in contact with the colon and angiography of the superior mesenteric artery demonstrated that the branch supplied to the tumor, the selective angiography of the colic artery (COA) was performed. The cystic artery was derived from the hepatic artery and was not considered as the extrahepatic collateral artery in the present study.