

Modified Cisplatin-based Transcatheter Arterial Chemoembolization for Large Hepatocellular Carcinoma: Multivariate Analysis of Predictive Factors for Tumor Response and Survival in a 163-Patient Cohort

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ABSTRACT

Purpose: To evaluate the safety and efficacy of modified cisplatin-based transcatheter arterial chemoembolization for inoperable hepatocellular carcinomas (HCCs) larger than 5 cm in diameter, and the factors associated with tumor response and survival.

Materials and Methods: From January 2007 to November 2009, 163 patients who underwent modified cisplatin-based chemoembolization for inoperable large HCCs were evaluated. Predominant tumors were as large as 25 cm (median, 8.6 cm). Seventy-nine patients had a solitary tumor, and 84 had two or more tumors. Tumor response was evaluated per modified Response Evaluation Criteria In Solid Tumors.

Results: After chemoembolization, 65% of patients showed a tumor response. On multivariate analysis, tumor size ($P < .001$) and portal vein (PV) invasion ($P = .017$) were significant factors for tumor response. After chemoembolization, 97% of patients (56 of 58) with PV invasion received additional radiation therapy for PV tumor thrombosis. Median survival time was 15.8 months. On multivariate analysis, Child–Pugh class ($P = .001$), surgical resection ($P = .003$) or radiofrequency (RF) ablation ($P = .018$) after chemoembolization, and tumor response ($P = .002$) were significant factors for patient survival after chemoembolization. Major complications ($N = 5$) included acute renal failure ($n = 3$), cholecystitis with hepatic abscess ($n = 1$), and intractable pleural effusion ($n = 1$).

Conclusions: Transcatheter arterial chemoembolization is safe and effective for large HCCs. Tumor size and PV invasion are significant predictors of tumor response and, Child–Pugh class A disease, surgical resection after chemoembolization, RF ablation after chemoembolization, and tumor response are good prognostic factors for survival.

ABBREVIATIONS

AFP = α -fetoprotein, BCLC = Barcelona Clinic Liver Cancer, HCC = hepatocellular carcinoma, HR = hazard ratio, PV = portal vein, RF = radiofrequency, RT = radiation therapy

The management of large hepatocellular carcinomas (HCCs; ie, > 5 cm) in patients who are not candidates

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for surgical resection remains a major medical challenge. Transcatheter arterial chemoembolization has been used for palliative treatment in patients with unresectable HCC, regardless of the size or number of tumors, and it has been shown to improve the rate of patient survival (1–4). Although there are studies that have shown higher complications rates when chemoembolization is performed in patients with main portal vein (PV) invasion (2,5), additional studies have shown that, in selected patients, chemoembolization may be safe and effective as long as a superselective embolization technique is used (6,7). However, the prognosis for patients with

large HCCs treated with chemoembolization may be limited (8,9): large HCCs are usually fed by multiple tumor-feeding arteries, and large HCCs generally produce intrahepatic metastases and/or PV tumor thrombosis (10).

The present study was performed to investigate the safety and efficacy of modified cisplatin-based transcatheter arterial chemoembolization for inoperable HCCs larger than 5 cm in diameter, as well as the factors associated with tumor response and patient survival.

MATERIALS AND METHODS

Patient Population

The present retrospective study was approved by our institutional review board, and informed consent was obtained for chemoembolization. Indications for chemoembolization for HCC at the authors' institution are (i) HCC that is unresectable because of advanced stage or insufficient hepatic reserve and (ii) tumors that are unsuitable for other local treatments such as radiofrequency (RF) ablation or percutaneous ethanol injection because of tumor size, presence of multiple lesions (ie, more than three), vascular invasion, or subcapsular lesions. Exclusion criteria for chemoembolization treatment include any contraindication to the use of an arterial procedure, such as impaired clotting (platelet count < 50,000/mm³ or prothrombin activity < 50%), bacterial infection, or renal failure. Advanced liver disease (ie, Child–Pugh class C), PV thrombosis, and extrahepatic metastasis were not considered to be contraindications to chemoembolization. The inclusion criteria of the present retrospective study were (i) single or multiple HCCs larger than 5 cm in largest diameter and (ii) newly developed HCC without any previous treatment. The exclusion criteria were (i) previously treated HCCs, (ii) lack of imaging before or after chemoembolization, and (iii) infiltrative HCCs (ie, with indistinct borders and a lack of typical enhancement pattern).

Between January 2007 and November 2009, a total of 163 patients with large HCCs met the aforementioned criteria. The patients' baseline characteristics are summarized in **Table 1**. A diagnosis of HCC was made based on the histologic evaluations achieved by image-guided percutaneous needle biopsy (n = 27) or by clinical or laboratory tests, eg, elevated α -fetoprotein (AFP) levels and viral markers, combined with the typical appearance seen on computed tomography (CT) and angiography (n = 136).

The numbers of patients with Child–Pugh class A, B, and C disease (referring to the degree of liver function) were 113, 46, and four. Of 163 patients, 16 (9.8%) had extrahepatic metastases detected before the initial chemoembolization. Seventy-nine patients had a solitary tumor, and 84 patients had two or more tumors. The

Table 1. Summary of Baseline Patient Characteristics

Characteristics	Value
Sex	
Male	139
Female	24
Mean age (y) \pm SD	58.3 \pm 11.4
Viral marker	
HBsAg	117 (71.8)
Anti-HCV	15 (9.2)
Child–Pugh classification	
A	113
B	46
C	4
AJCC stage	
I	24
II	17
IIIA	33
IIIB	40
IIIC	7
IVA	11
IVB	31
Tumor number	
Single	79
Multiple	84
\leq 3	26
$>$ 3	58
Additional treatment	
Surgical resection	17
RF ablation	10
RT for PV invasion	56

Values in parentheses are percentages.

AJCC = American Joint Committee on Cancer, HBsAg = hepatitis B surface antigen, HCV = hepatitis C virus, SD = standard deviation.

predominant tumor size ranged from simply “greater than 5 cm” to 25 cm (median, 8.6 cm; interquartile range, 7–12.3 cm) in maximum dimension before the initial treatment. PV invasion was identified in 58 of the 163 patients (36%; main PV, n = 10; lobar PV, n = 17, segmental PV, n = 31).

Chemoembolization

We used the terminology of the Society of Interventional Radiology (SIR) reporting standards (11). All patients received intravenous fluid and premedications (antiemetic agents or steroids) before treatment. Superior mesenteric and celiac arteriography was initially performed to assess the anatomy, tumor burden, and PV patency. Our method is somewhat different than classical transcatheter arterial chemoembolization: 0.5 mg/mL of cisplatin dissolved in distilled water was infused for 15 minutes into the right lobar, left lobar, or proper hepatic artery according to tumor location, but without embolic particle administration (12,13). The infused dose

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