CLINICAL STUDY

Transarterial Chemoembolization with Small Drug-Eluting Beads in Patients with Hepatocellular Carcinoma: Experience from a Cohort of 421 Patients at an Italian Center

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ABSTRACT

Purpose: To assess the safety, tolerability, and efficacy of small drug-eluting embolic (DEE) agents (70–150 μm) for chemoembolization of hepatocellular carcinoma (HCC).

Materials and Methods: This single-center, single-arm, retrospective study involved 421 patients (mean age, 66.1 y ± 9.8 [standard deviation]) with Barcelona Clinic Liver Cancer (BCLC) stage A (n = 88), B (n = 140), or C (n = 193) HCC and Child–Pugh class A (n = 233) or B (n = 188) cirrhosis. Patients had a mean of 7.2 lesions ± 4.8 (range, 1–21; mean diameter of target lesion, 21.4 cm ± 8.1; unilobar, n = 132; bilobar, n = 289; portal vein involvement, n = 193). One (n = 320) or 2 (n = 101) vials of small DEEs loaded with doxorubicin 50 mg per vial were delivered selectively (ie, segmentally) or superselectively (ie, directly into the tumor-feeding vessel) until complete delivery or stasis/near-stasis. Treatment was repeated in patients with partial response or stable disease at 1- or 3-month follow-up (mean, 2.0 cycles ± 0.9). Adverse events within 30 days of chemoembolization, response per modified Response Evaluation Criteria In Solid Tumors (mRECIST), and survival were assessed.

Results: Within 30 days after treatment, no deaths or bleeding events occurred, but all patients had at least 1 episode of postembolization syndrome (pain, fever, and/or nausea/vomiting; 27.1% grade 3/4 per National Cancer Institute Common Terminology Criteria for Adverse Events, version 3.0) and increased bilirubin and liver aminotransferase levels (0.2% and 5.9% grade 3/4, respectively). Overall response rates were 94.5% at 3 months and 99.5% at 6 months. Median overall survival was 42.0 months (95% confidence interval, 38.0–43.0 mo).

Conclusions: Chemoembolization with small DEE agents is well tolerated and an effective treatment for a broad range of patients with liver-confined HCC.

ABBREVIATIONS

BCLC = Barcelona Clinic Liver Cancer, CI = confidence interval, DEE = drug-eluting embolic, EASL = European Association for the Study of the Liver, HCC = hepatocellular carcinoma, mRECIST = modified Response Evaluation Criteria In Solid Tumors, ORR = overall response rate, PES = postembolization syndrome

Drug-eluting embolic (DEE) agents are an established method of delivering sustained drug release at target sites during transarterial chemoembolization of liver tumors (1). Particles are available in a range of diameters, with the smallest sizes potentially allowing embolization of the narrowest vessels feeding the tumors (2). In comparison with larger DEE particle sizes, animal studies (3) indicate that DEE particles with a diameter range of 70–150 μm are associated with greater tumor coverage, more distal penetration, higher doxorubicin concentration in the tumor with no increase in systemic exposure, and greater uniformity of DEE particle and drug distribution.

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Published evidence on these small DEE particles in clinical practice is still limited (4–10). Tumor response rates and tolerability have shown promise, but the studies typically involved low patient numbers or were restricted to specific subpopulations, such as patients with small tumors. In the authors' experience, small DEE particles offer optimal efficacy, and therefore they have been used in all chemoembolization procedures performed in the authors' institution since October 2013, with data from more than 500 patients with liver-confined hepatocellular carcinoma (HCC) to date. The purpose of the present report is to assess the safety, tolerability, and efficacy of chemoembolization with small DEE particles, with a view to addressing some of the questions about this technique in a large cohort of patients.

MATERIALS AND METHODS

This single-center, single-arm, retrospective study is based on data derived from patients' routinely collected hospital medical records. The study protocol was approved by the institute's ethics committee, and all patients provided written informed consent to the procedure and to the use of their anonymized data for research purposes.

Patients

Records were searched for patients who met the following criteria: age at least 18 years, liver-confined HCC diagnosed according to European Association for the Study of the Liver (EASL) guidelines (11), Child–Pugh class A or B cirrhosis, treatment with transarterial chemoembolization with small DEE particles (70–150-μm DC Bead M1; BTG, London, United Kingdom), and at least 6 months of follow-up data. In total, 421 patients (341 men, 80 women) treated between October 2013 and May 2015 were identified who met these criteria. Their mean age was 66.1 years ± 9.8 (standard deviation), and their median age was 67.0 years (range, 34.0–88.0 y). Their disease characteristics are summarized in **Table 1**.

Table 1. Baseline Disease Characteristics of 421 Patients Treated with Small DEE Particle Chemoembolization

Characteristic	Incidence/Value
Etiology	
Hepatitis C	221 (52.5)
Hepatitis B	76 (18.1)
Alcohol	47 (11.2)
Other	77 (18.3)
Child–Pugh class	
A	233 (55.3)
B	188 (44.7)
BCLC stage*	
A	88 (20.9)
B	140 (33.3)
C	193 (45.8)
Okuda tumor stage	
I	314 (74.6)
II	107 (25.4)
MELD score	
0–9	84 (20.0)
10–19	140 (33.3)
20–29	124 (29.5)
30–39	73 (17.3)
No. of tumor nodules	
Mean ± SD	7.2 ± 4.8
Median (range)	6.0 (1.0–21.0)
Maximum index tumor diameter (mm)	
Mean ± SD	21.4 ± 8.1
Median (range)	20.0 (4.0–45.0)
Sum of tumor diameters (mm)	
Mean ± SD	89.3 ± 53.2
Median (range)	74.0 (5.0–425.0)
Lobar involvement	
Unilobar	132 (31.4)
Bilobar	289 (68.6)
Portal vein involvement†	
Yes	193 (45.8)
No	228 (54.2)

Note–Values in parentheses are percentages of patients unless specified otherwise.
BCLC = Barcelona Clinic Liver Cancer; DEE = drug-eluting embolic; MELD = Model for End-stage Liver Disease; SD = standard deviation.
*Estimated retrospectively.
†Branch portal vein only; involvement of main portal vein is a contraindication for chemoembolization with DC Bead.

Procedure

The decision to use transarterial chemoembolization was made by a multidisciplinary team (including a hepatobiliary surgeon, radiologist, oncologist, and hepatologist) as the most appropriate treatment on the basis of standard EASL criteria (including tumor size and number, degree of cirrhosis, and performance status [11]), together with an individualized assessment of the patient's overall clinical status and preferences. Hence, patients with BCLC stage A or C disease could be considered for chemoembolization if alternative treatments were not deemed suitable for that individual (eg, on the basis of tumor number).

Each procedure was performed by one of four interventional radiologists in the department, who had between 3 and 15 years of experience in performing transarterial chemoembolization. Patients underwent a single procedure in each session; if not all lesions could be treated in one session, the remaining lesions were treated at the next cycle after approximately 4 weeks. The standard treatment per session was one vial (2 mL) of small DEE particles loaded with 50 mg doxorubicin. Depending on tumor number, size, and vascularity, selected patients (eg, those with Child–Pugh class A cirrhosis or whose disease met the Milan criteria for transplantation and were aged less than 70 y and deemed suitable for "bridging" to transplantation) received two vials (4 mL) of small DEE particles loaded with doxorubicin at a