CLINICAL STUDY

Safety and Efficacy of Doxorubicin Drug-Eluting Embolic Chemoembolization of Hepatocellular Carcinoma Supplied by Extrahepatic Collateral Arteries

R. Peter Lokken, MD, MPH, Nicholas Fidelman, MD, K. Pallav Kolli, MD, and Robert K. Kerlan, Jr, MD

ABSTRACT

Purpose: To assess safety and efficacy of doxorubicin drug-eluting embolic (DEE) transarterial chemoembolization of hepatocellular carcinoma (HCC) by extrahepatic collateral arteries.

Materials and Methods: Records of 177 patients with HCC who underwent 338 consecutive DEE chemoembolization procedures from 2011 to 2014 were retrospectively reviewed. A subgroup of 16 patients (13 men, 3 women, median age 66 y) underwent 24 procedures for 17 HCCs via extrahepatic arteries and was included in the study. Median tumor size was 3.1 cm (range, 1.0–10.3 cm). Extrahepatic collaterals included right inferior phrenic (19 procedures; 12 patients), adrenal (4 procedures; 3 patients), and cystic arteries (2 procedures; 2 patients). Radiographic response was assessed by Modified Response Evaluation Criteria in Solid Tumors criteria. Complications were defined by National Cancer Institute Common Terminology Criteria for Adverse Events.

Results: DEE chemoembolization achieved stable disease in 6 (35.3%), partial response in 6 (35.3%), and complete response in 4 (23.5%) HCCs. Disease progression was ultimately observed in 8 tumors (47.1%), with mean time to progression of 8.3 months after chemoembolization (range, 2–13 mo). Three minor and 5 major complications occurred in 8 patients; 2 minor complications were rash in vascular distribution after right inferior phrenic artery DEE chemoembolization. The 5 major complications were transient hepatotoxicity that resolved within 4–80 days; 1 was accompanied by pleural effusion requiring hospitalization. A mean 13.4 months after DEE chemoembolization, 67% of transplant candidates proceeded to liver transplant.

Conclusions: DEE transarterial chemoembolization via extrahepatic collaterals was effective and facilitated bridging to transplant. It was generally well tolerated; transient hepatotoxicity was the most common major complication.

ABBREVIATIONS

DEE = drug-eluting embolic, DSA = digital subtraction angiography, HCC = hepatocellular carcinoma, LIPA = left inferior phrenic artery, RIPA = right inferior phrenic artery

Hepatocellular carcinoma (HCC) is typically vascularized by branches of the hepatic artery (1). However, extrahepatic arterial supply has been reported in 17% of intrahepatic HCCs on initial presentation (2). Prior intrahepatic transarterial chemoembolization; tumor diameter; extracapsular, subcapsular, or bare area location; and adjacent organ invasion are risk factors for extrahepatic supply (1–4). Conventional transarterial chemoembolization with emulsified ethiodized oil and chemotherapy of extrahepatic arteries, such as the inferior phrenic, adrenal, and intercostal arteries, has been reported (1,5). Although generally safe, complications from embolization of the skin, diaphragm, gallbladder, and other organs have occurred (6–11).

Department of Radiology (R.P.L.), University of Illinois Hospital and Health Sciences System, 1740 West Taylor Street, Mail Code 931, Chicago, IL 60612; and Department of Radiology and Biomedical Imaging (R.P.L., N.F., K.P.K., R.K.K.), University of California, San Francisco, San Francisco, California.
Received January 26, 2016; final revision received April 26, 2016; accepted April 28, 2016. **Address correspondence to** R.P.L.; E-mail: r.p.lokken@gmail.com

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Doxorubicin-loaded drug-eluting embolic (DEE) agents have potential advantages of prolonged drug delivery and tumor ischemia as well as increased tumoral concentration and lower systemic concentration of doxorubicin compared with conventional ethiodized oil transarterial chemoembolization (12). Cholecystitis and cutaneous complications have been reported after DEE transarterial chemoembolization of hepatic arteries (13–15), but the effect of DEE chemoembolization of extrahepatic arteries is unknown. In this study, we evaluated the safety and efficacy of DEE transarterial chemoembolization of HCC via extrahepatic collateral arteries.

MATERIALS AND METHODS

Study Population

This single-center retrospective study was compliant with the Health Insurance Portability and Accountability Act. Institutional review board approval was obtained with waiver of informed consent for retrospective review of records. Medical records and imaging studies were reviewed of 177 patients with HCC who underwent 338 consecutive DEE transarterial chemoembolization procedures between June 2011 (when DEE transarterial chemoembolization was first administered at this institution) and July 2014. Included in the study were 16 patients (13 men, 3 women) with median age 66 years (range, 54–83 y) who underwent 24 DEE transarterial chemoembolization procedures for 17 HCCs via extrahepatic arteries (Table 1).

DEE chemoembolization was performed via the right inferior phrenic artery (RIPA) for 12 tumors, left superior adrenal artery for 2 tumors, cystic artery for 2 tumors, and a combination of the right inferior adrenal artery and RIPA for 1 tumor (Table 2). In 11 of 24 procedures (45.8%), additional hepatic segments were treated via hepatic artery branches; 1 additional segment was treated in 7 procedures (29.2%), 2 additional segments were treated in 3 procedures (12.5%), and 4 additional segments were treated in 1 procedure (4.2%). Median lesion size was 3.1 cm (range, 1.0–10.3 cm) at the time of extrahepatic arterial supply detection. Prior locoregional therapy was performed upon 14 tumors (82.4%); 14 tumors (82.4%) had been treated with a median of 1.5 transarterial chemoembolization procedures (range, 1–6 procedures), 2 tumors (11.8%) had been previously treated with yttrium-90 radioembolization, and 3 tumors (17.6%) had been treated with radiofrequency ablation.

Table 1. Characteristics of 16 Patients with HCC Perfused by Extrahepatic Arteries

Characteristic	n (%)
Age (y)	
< 65	7 (43.8)
65–75	6 (37.5)
> 75	3 (18.8)
Sex	
Male	13 (81.3)
Female	3 (18.8)
Etiology of HCC	
HCV cirrhosis	6 (37.5)
Alcoholic cirrhosis	2 (12.5)
HCV/alcohol	1 (6.3)
NASH	2 (12.5)
Primary HCC	2 (12.5)
HBV	2 (12.5)
PBC	1 (6.3)
Child-Pugh class	
A	8 (50.0)
B	6 (37.5)
C	2 (12.5)
BCLC stage	
0	0 (0)
A	3 (18.8)
B	5 (31.3)
C	6 (37.5)
D	2 (12.5)
UNOS stage	
1	1 (6.3)
2	4 (25.0)
3	4 (25.0)
≥ 4A	7 (43.8)

BCLC = Barcelona Clinic Liver Cancer; HBV = hepatitis B virus; HCC = hepatocellular carcinoma; HCV = hepatitis C virus; NASH = nonalcoholic steatohepatitis; PBC = primary biliary cirrhosis; UNOS = United Network for Organ Sharing.

DEE Transarterial Chemoembolization Technique

All patients were discussed in a multidisciplinary tumor board before DEE transarterial chemoembolization, and written informed consent was obtained. DEE chemoembolization was performed by fellowship-trained interventional radiologists with experience ranging from 2 to > 20 years.

Two vials of 100–300 μm LC Bead microspheres (Biocompatibles UK Ltd, Farnham, United Kingdom) were admixed with 50–75 mg of doxorubicin hydrochloride per vial overnight. After discarding the supernatant, the microspheres were suspended in 10 mL of iodinated contrast agent (Omnipaque 350; GE Healthcare, Little Chalfont, United Kingdom) per vial before intraarterial administration. DEE transarterial chemoembolization was performed after digital subtraction angiography (DSA) of celiac and superior mesenteric arteries with a 5-F catheter and selective angiography of higher order branches with a coaxially placed 2.4- to 2.8-F microcatheter (Renegade STC-18 and Renegade HI-FLO; Boston Scientific, Marlborough, Massachusetts). Extrahepatic arterial supply was determined by computed tomography (CT) and magnetic resonance (MR)