CLINICAL STUDY

Chemoembolization of Hepatocellular Carcinoma with Drug-Eluting Polyethylene Glycol Embolic Agents: Single-Center Retrospective Analysis in 302 Patients

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ABSTRACT

Purpose: To evaluate the efficacy and safety of transarterial chemoembolization with polyethylene glycol (PEG) drug-eluting embolic agents in the treatment of hepatocellular carcinoma (HCC).

Materials and Methods: A single-center retrospective study of 302 patients (258 men; 85.4%) with HCC treated during a 20-month period was conducted. The mean patient age was 66 years ± 10; 142 (47%) had Barcelona Clinic Liver Cancer stage A disease and 134 had (44.4%) stage B disease; 174 (57.6%) had a single HCC tumor, 65 (21.5%) had 2, and 62 (20.9%) had 3 or more. Mean index tumor size was 36.6 mm ± 24.8. One-month follow-up computed tomography (CT) response per modified Response Evaluation Criteria In Solid Tumors and clinical and biochemical safety were analyzed. Progression-free and overall survival were calculated by Kaplan–Meier method.

Results: Median follow-up time was 11.9 months (95% confidence interval, 11.0–13.0 mo). One-month follow-up CT revealed complete response in 179 patients (63.2%), partial response in 63 (22.3%), stable disease in 16 (5.7%), and progressive disease in 25 (8.8%). The most frequent complications were postembolization syndrome in 18 patients (6%), liver abscess in 5 (1.7%), and puncture-site hematoma in 3 (1%). Biochemical toxicities occurred in 57 patients (11.6%). Survival analysis at 12 months showed a progression-free survival rate of 65.9% and overall survival rate of 93.5%. Patients who received transplants showed a 57.7% rate of complete pathologic response.

Conclusions: Chemoembolization with PEG embolic agents for HCC is safe and effective, achieving an objective response rate of 85.5%.

ABBREVIATIONS

CI = confidence interval, CR = complete response, DEE = drug-eluting embolic, EASL = European Association for the Study of the Liver, HCC = hepatocellular carcinoma, mRECIST = modified Response Evaluation Criteria In Solid Tumors, PEG = polyethylene glycol, PR = partial response, RF = radiofrequency, ROC = receiver–operating characteristic

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Transarterial chemoembolization is currently indicated for the treatment of patients with intermediate-stage hepatocellular carcinoma (HCC) according to the American Association for the Study of Liver Diseases and European Association for the Study of Liver Diseases (EASL)/European Organization for Research and Treatment of Cancer recommendations on the management of HCC (1,2). Chemoembolization, either conventional or with the use of drug-eluting embolic (DEE) agents (3), is also one of the recommended options as a "bridge" therapy for liver transplantation candidates with stage T1 and T2 HCC tumors while on the waiting list based on assessment of the patient's liver function, expected waiting time, and the organ allocation policy of each country or region (2). However, no specific locoregional therapy has been recommended over the others, including thermal ablation, combination treatments, or radioembolization, raising the need for continuous research in this area. Currently, there are a number of DEE agents available on the market, and an in vitro comparison of a variety of characteristics of each of the microspheres was published recently (4), describing their drug-loading and elution properties, diameter changes after loading, changes after 2 weeks in storage, and time in suspension. Two preliminary studies by the same group (5,6) have reported clinical experiences with the recently developed polyethylene glycol (PEG) LifePearl microspheres (Terumo, Tokyo, Japan) for DEE chemoembolization in a cohort of 20 patients with primary and metastatic liver cancer (5) and in a cohort of 42 patients with HCC (6).

The purpose of the present study is to evaluate the efficacy and safety of DEE chemoembolization with the use of PEG embolic agents in the treatment of HCC in 302 patients during a 20-month period of time.

MATERIALS AND METHODS

Study Design

The present study was conducted in a single liver transplantation center and retrospectively reports a 20-month experience between September 2015 and April 2017, during which 302 patients with HCC were treated with DEE agent chemoembolization. The time frame of the study was chosen to allow an extensive number of patients to be included to strengthen the analysis. This study was approved by the local ethics committee. The manuscript was written based on the Strengthening the Reporting of Observational Studies in Epidemiology Statement.

Patients

Eligible participants included 333 patients with inaugural HCC, referred from a multidisciplinary tumor board, consecutively treated with DEE chemoembolization at a single interventional radiology (IR) unit. Only the 302 patients who had 1-month follow-up contrast-enhanced computed tomography (CT) after treatment and/or follow-up blood tests, obtained as long as 3 months after treatment, were included (Fig 1). The indication for chemoembolization was HCC diagnosed per EASL/American Association for the Study of Liver Diseases criteria. Contraindications for chemoembolization included extrahepatic disease, bilirubin levels greater than 2 mg/dL, and complete portal vein thrombosis or tumor portal vein invasion. During the 20-month study period, 302 patients were treated with DEE chemoembolization: 258 men (85.4%) and 44 women (14.6%), with a mean age of 66 years ± 10. The baseline characteristics of the patients and tumors are summarized in Table 1.

DEE Chemoembolization Procedure

All DEE chemoembolization procedures were performed by three interventional radiologists with 4–25 years of experience. One day before treatment, patients were admitted to the hospital and evaluated according to the admission protocol, including clinical and biochemical evaluation. At the IR unit, patients received intravenous prophylactic antibiotic therapy (cefazolin 2 g) and sedative/analgesic therapy (midazolam 1 mg, paracetamol 1 g, metamizole magnesium 2 g). Vascular access was achieved through the common femoral artery. A 5-F Simmons catheter (Cordis, Somerset, New Jersey) was used to catheterize the celiac trunk or anatomic variant to gain access to the hepatic arteries, which was achieved with a 2.7-F Progreat microcatheter (Terumo). Diagnostic angiographic runs were obtained at the celiac trunk and proper hepatic and right and left hepatic arteries to define tumor arterial supply. DEE chemoembolization was performed after superselective catheterization of the tumor-feeding artery (or arteries), and 1 or 2 vials of LifePearl microspheres (Terumo), charged with 75 mg of doxorubicin each for a maximum dose of 150 mg per session, were administered until near-stasis was achieved, defined as stasis of contrast medium during 5 heartbeats (7). A final manual angiographic run was performed to confirm effective embolization. In patients with large tumors and remaining arterial feeding vessels on control angiography, a second chemoembolization procedure was planned 3–4 weeks later.

Evaluation of Tumor Response

The efficacy of DEE chemoembolization was the primary outcome of this study. Efficacy was measured as the response on 1-month follow-up contrast-enhanced CT according to modified Response Evaluation Criteria In Solid Tumors (mRECIST) (8), categorized into four groups: complete response (CR), partial response (PR), stable disease, or progressive disease. Evaluation of response was performed by three radiologists with 4–25 years of experience in reading follow-up CT images for the purpose of evaluation of tumor response after DEE chemoembolization.

Evaluation of Safety

Safety was measured clinically, with symptoms (pain, nausea, vomiting) and vital signs (heart rate, blood pressure,