CLINICAL STUDY

Combined Cisplatin-Based Chemoembolization and Radiation Therapy for Hepatocellular Carcinoma Invading the Main Portal Vein

Sae Rom Chung, MD, Jin Hyoung Kim, MD, Hyun-Ki Yoon, MD, Gi-Young Ko, MD, Dong Il Gwon, MD, Ji Hoon Shin, MD, Ho-Young Song, MD, Heung Kyu Ko, MD, and Sang Min Yoon, MD

ABSTRACT

Purpose: To evaluate the safety and survival outcome of chemoembolization plus radiation therapy (RT) in patients with hepatocellular carcinoma (HCC) with main portal vein (PV) tumor thrombosis.

Materials and Methods: This retrospective study evaluated 151 patients with HCC and main PV involvement (101 with Child–Pugh class A liver function and 50 with Child–Pugh class B liver function) treated with combined cisplatin-based chemoembolization and RT. Medical records, imaging, and laboratory studies were reviewed, and complications, survival, and mortality rates were determined.

Results: After chemoembolization, major complications occurred in 19.9% of patients, with the rate of major complications significantly higher in Child–Pugh class B cases than in Child–Pugh class A cases (32% vs 13.9%; $P = .016$). The 30-day mortality rate was 0.7%. One hundred forty-seven patients received adjuvant RT an average of 17.4 days after chemoembolization for main PV tumor thrombosis. Adjuvant RT could not be performed in four patients because of intolerance of the initial chemoembolization. There were no major complications after RT. The objective tumor response at 6 months was 25.2%, with a median survival of 12 months (14 mo in Child–Pugh class A cases and 8 mo in Child–Pugh class B cases). Patients with Child–Pugh class B liver function with extrahepatic metastases, no tumor response, and absence of second-line sorafenib treatment had poor survival.

Conclusions: Chemoembolization combined with RT improves survival, with a median survival of 12 months in patients with HCC with main PV involvement.

ABBREVIATIONS

BCLC = Barcelona Clinic Liver Cancer, CR = complete response, HCC = hepatocellular carcinoma, PD = progressive disease, PR = partial response, PV = portal vein, PVTT = portal vein tumor thrombosis, RT = radiation therapy, SD = stable disease

Hepatocellular carcinoma (HCC) is the sixth most common malignancy worldwide and causes approximately 700,000 deaths each year (1,2). Potential curative therapies for HCC include partial hepatectomy, liver transplantation, and local ablative therapy. However, these curative treatments are applicable in only 30%–40% of patients, as most patients with HCC are diagnosed at intermediate or advanced stages despite surveillance programs (3).

HCC with main portal vein (PV) invasion is associated with a poor prognosis as a result of increased PV pressure, an increased risk of tumor spread, and ineligibility for curative therapies (4). With supportive care, the reported median survival time in these patients is 2.2 months (1).

HCC with PV invasion is classified as advanced-stage disease (stage C) according to Barcelona Clinic Liver Cancer (BCLC) staging. Chemoembolization is not recommended in these patients because of the high risk

From the Department of Radiology and Research Institute of Radiology (S.R.C., J.H.K., H.-K.Y., G.-Y.K., D.I.G., J.H.S., H.-Y.S., H.K.K.) and Department of Radiation Oncology (S.M.Y.), University of Ulsan College of Medicine, Asan Medical Center, 86 Asanbyeongwon-Gil, Song pa-gu, Seoul 138-736, Republic of Korea. Received September 30, 2014; final revision received April 11, 2015; accepted May 4, 2015. Address correspondence to J.H.K.; E-mail: jhkimrad@amc.seoul.kr

None of the authors have identified a conflict of interest.

J Vasc Interv Radiol 2015; XX:▮▮▮–▮▮▮

http://dx.doi.org/10.1016/j.jvir.2015.05.006

of complications, including acute liver failure. Instead, the BCLC group recommends that these patients be treated with the multikinase inhibitor sorafenib, which has shown survival benefits in patients with advanced HCC (5,6). However, sorafenib is not routinely used in some countries because of the high cost of the drug and the low degree of patient compliance; in addition, patients with HCC with PV tumor thrombosis (PVTT) showed poor response rates to sorafenib (only 2%–3.3%) in two randomized trials (5,6). Therefore, chemoembolization is often considered as an alternative treatment for unresectable HCC with main PVTT, with studies suggesting that chemoembolization could be safely performed in selected patients with main PV invasion (1,7,8). In addition, the recent advances with the combined treatment modality of chemoembolization with radiation therapy (RT) have shown superior results compared with those of chemoembolization alone (8–10). The present study evaluated the safety and survival outcome of chemoembolization plus RT in HCC with main PVTT. In addition, we assessed factors influencing survival after combination therapy.

MATERIALS AND METHODS

Patient Population

HCC was diagnosed per American Association for the Study of Liver Diseases criteria (11). The presence and extent of main PVTT were assessed by multiphase dynamic computed tomography (CT) with a routine slice thicknesses of 5 mm, and were confirmed by detection of enhancement of an intraluminal mass expanding the PV in the main PV on the arterial phase and the low-attenuation, intraluminal mass on the portal phase by three-phase dynamic CT (1).

Chemoembolization was recommended in patients with HCC and main PV involvement if the following criteria were met: (i) Child–Pugh class A or B liver function and (ii) an Eastern Cooperative Oncology Group performance status of 0–2. Chemoembolization was contraindicated in patients with HCC and main PV involvement if they had (i) Child–Pugh class C liver function, (ii) total bilirubin level $\geq$ 3 mg/dL, (iii) serum creatinine level $\geq$ 1.5 mg/dL, (iv) Eastern Cooperative Oncology Group performance status of 3/4, or (v) tumors occupying more than one half of the liver. Lymph node or distant metastases were not contraindications to chemoembolization. Patients with HCC with main PVTT who did not meet these criteria underwent other palliative treatments (eg, transarterial chemoinfusion or sorafenib therapy) or supportive therapy only.

Between February 2008 and January 2013, HCC with main portal invasion was newly diagnosed in 325 patients. Among them, 186 patients underwent chemoembolization first and were scheduled to undergo adjuvant RT (n = 151), pegylated interferon therapy (n = 12), sorafenib treatment (n = 9), or no further additional treatment (n = 14) by preference or because of cost considerations. Chemoembolization was not performed in the remaining 139 patients. Among these 139 patients, 60 underwent transarterial chemoinfusion only, 33 underwent transarterial chemoinfusion plus sorafenib treatment, 12 underwent sorafenib treatment only, and 34 received supportive treatment only. We reviewed the medical records of 151 patients who had been scheduled to undergo combined treatment with chemoembolization and RT for unresectable HCC and main PVTT. Our institutional review board approved this retrospective study and waived the requirement for informed patient consent.

The patient and tumor characteristics are listed in Table 1. Of the 151 patients, 101 (66.9%) had Child–Pugh class A liver function and 50 (33.1%) had Child–Pugh class B liver function, 23 (15.2%) had extrahepatic metastases detected before the initial chemoembolization, and 14 (9.3%) had hepatic or inferior vena cava invasion. Seventy-four patients (49%) had a solitary tumor, whereas

Table 1. Summary of Baseline Patient Characteristics

Characteristic	Value
Sex	
Male	132 (87.4)
Female	19 (12.6)
Mean age ± SD (y)	52.7 ± 9.4
Viral marker	
HBsAg positive	110 (72.8)
Anti-HCV positive	14 (9.3)
Child–Pugh classification	
A	101 (66.9)
B	50 (33.1)
Lymph node or distant metastasis	
Yes	23 (15.2)
No	128 (84.8)
Hepatic vein or IVC invasion	
Yes	14 (9.3)
No	137 (90.7)
Median maximum tumor size (cm)	10
IQR	7–13
Tumor multiplicity	
Single	74 (49)
Multiple	77 (51)
Bilobar involvement	
Yes	67 (44.4)
No	84 (55.6)
Median serum AFP level (ng/mL)	1,090
IQR	40.9–23,678
Median total bilirubin level (mg/dL)	0.8
IQR	0.4–1.3

Note–Values in parentheses are percentages.
AFP = α-fetoprotein, HBsAg = hepatitis B surface antigen, HCV = hepatitis C virus, IVC = inferior vena cava, IQR = interquartile range, SD = standard deviation.