CLINICAL STUDY

Intraprocedural Parenchymal Blood Volume Is a Predictor of Treatment Response for Chemoembolization in Hepatocellular Carcinoma: Results of a Prospective Study

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ABSTRACT

Purpose: To evaluate cone-beam parenchymal blood volume (PBV) before and after embolization as a predictor of radiographic response to transarterial chemoembolization in unresectable hepatocellular carcinoma (HCC).

Materials and Methods: A phase IIa prospective clinical trial was conducted in patients with HCCs > 1.5 cm undergoing chemoembolization; 52 tumors in 40 patients with Barcelona Clinic Liver Criteria stage B disease met inclusion criteria. Pre- and postembolization PBV analysis was performed with a semiquantitative best-fit methodology for index tumors, with a predefined primary endpoint of radiographic response at 3 months. Analyses were conducted with Wilcoxon signed-rank tests and one-way analysis of variance on ranks.

Results: Mean tumoral PBV measurements before and after embolization were 170 mL/1,000 mL ± 120 and 0 mL/100 mL ± 130, respectively. Per modified Response Evaluation Criteria In Solid Tumors, 25 tumors (48%) exhibited complete response (CR), 13 (25%) partial response (PR), 3 (6%) stable disease (SD), and 11 (21%) progressive disease (PD). Statistically significant changes in median PBV (ΔPBV) were identified in the CR ($P = .001$) and PR ($P = .003$) groups, with no significant difference observed in SD ($P = .30$) and PD groups ($P = .06$). A statistically significant correlation between ΔPBV and tumor response was established by one-way analysis of variance on ranks ($P = .036$; CR, 200 mL/100 mL ± 99; PR, 240 mL/100 mL ± 370; SD, 64 mL/100 mL ± 99; PD, 88 mL/100 mL ± 129).

Conclusions: Intraprocedural PBV can be used as a predictor of response in index HCC tumors of > 1.5 cm.

ABBREVIATIONS

CR = complete response, DEE = drug-eluting embolic, ΔPBV = change in median parenchymal blood volume, HCC = hepatocellular carcinoma, mRECIST = modified Response Evaluation Criteria In Solid Tumors, PBV = parenchymal blood volume, PD = progressive disease, PR = partial response, ROI = region of interest, SD = stable disease

The evolution of hepatic arterial embolic therapies have centered around the development of newer and more advanced carriers; however, imaging and angiography have remained largely unchanged. In most situations, procedures are typically performed to an endpoint of angiographic stasis without consideration of penetration, tissue drug delivery, or internal distribution within the tumor (1).

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Fluoroscopic cone-beam CT is a recent technologic advancement that allows for intraprocedural 3-dimensional imaging (2). The present study assesses its ability to provide, in a semiquantitative fashion, assessment of tumoral vascular capacitance through the measurement of parenchymal blood volume (PBV) (3). Analogous to cerebral blood volume imaging in the brain, hepatic PBV can be measured to assess the volume of blood in a given volume of liver tissue (4). The intent of the present study is to prospectively evaluate the prognostic value of intraprocedural cone-beam PBV measurement for transarterial chemoembolization in patients with unresectable hepatocellular carcinoma (HCC) in a single-arm prospective trial.

MATERIALS AND METHODS

Approval for this prospective nonrandomized phase IIa study of patients with nonresectable HCC diagnosed by computed tomography (CT) or histopathology was obtained from the review ethics board. All patients were reviewed and approved for chemoembolization at the study institution's multidisciplinary liver tumor rounds. Written informed consent for study participation was obtained from all patients in advance of the procedure. Inclusion criteria were as follows: histologic or cytologic diagnosis or fulfillment of American Association for the Study of Liver Diseases criteria for diagnosis of HCC and at least one unidimensional tumor measurable according to modified Response Evaluation Criteria In Solid Tumors (mRECIST) on CT; willingness to undergo to embolization as adjuvant, neoadjuvant, or definitive (ie, curative or palliative) therapy; age greater than 19 years and estimated life expectancy of more than 3 months; Eastern Cooperative Oncology Group performance status less than or equal to 1; adequate hematologic function (hemoglobin $>$ 5.6 mmol/L, absolute neutrophil count $>$ 1500/uL, and platelet count $> 50\times10^9$/L); adequate renal function (serum creatinine level $<$ 1.7 mg/dL); bilirubin level no greater than 2.9 mg/dL and aspartate aminotransferase or alanine aminotransferase level no more than 5 times the upper normal limit; International Normalized Ratio no greater than 1.5; Child–Pugh score no greater than 7; and ability to provide written informed consent.

The exclusion criteria were as follows: active gastrointestinal bleeding, encephalopathy, ascites refractory to diuretic therapy, pregnancy or breastfeeding, allergy to contrast media, contraindication to hepatic artery catheterization (eg, severe peripheral vascular disease precluding catheterization), psychiatric or other disorder likely to impact informed patient consent, and inability and/or unwillingness to comply with treatment and study instructions.

The study population included 40 consecutive consenting patients who met the study criteria (Fig 1), who had a total of 52 tumors meeting inclusion criteria. The study population consisted of 34 men and 6 women, with a mean age of 65.6 years (range, 56–78 y). Three patients were lost to follow-up and were excluded from evaluation for treatment response. One patient was excluded because the target tumor was an atypical hemangioma incorrectly diagnosed as an

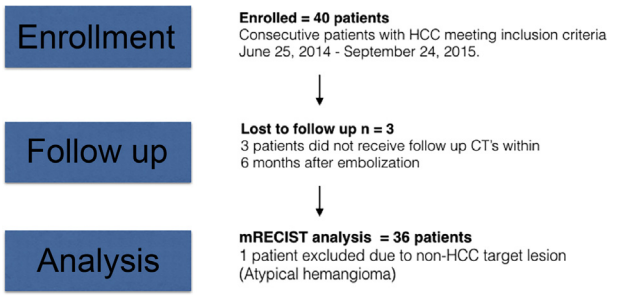

Figure 1. Study flowchart.

Table 1. Demographic and Procedural Details of the Study Population (N = 40)

Characteristic	Value
Sex	
Male	34
Female	6
Mean age (y)	65.6
ECOG PS	
0	30
1	8
2	2
Child–Pugh class	
A	30
B	10
C	0
Index tumors	52
Embolic agent	
Drug-eluting beads	30
Lipiodol	6
Bland microspheres	1
Tumor biology	
Hepatitis C	21
Hepatitis B	9
Alcohol abuse	4
Cryptogenic	3
NASH	1
PBC	1

ECOG = Eastern Cooperative Oncology Group; NASH = nonalcoholic hepatic steatohepatitis; PBC = primary biliary cirrhosis; PS = performance status.

HCC. All patients had Barcelona Clinic Liver Cancer stage B disease, Child–Pugh class A (n = 30) or B (n = 10) disease, and Eastern Cooperative Oncology Group performance status of 0 (n = 32), 1 (n = 8), or 2 (n = 2). Embolization was performed with the use of drug-eluting embolic (DEE) agents in 33 patients, 6 patients underwent conventional transarterial chemoembolization, and 1 patient underwent bland embolization. Early during the course of this prospective study, the local standard of care shifted from conventional chemoembolization to the use of DEE agents, which is reflected in the distribution. Tumor biology was secondary to hepatitis C (n = 21), hepatitis B (n = 9), alcohol abuse (n = 4), cryptogenic hepatic disease