CLINICAL STUDY

Three-Dimensional Quantitative Color-Coding Analysis of Hepatic Arterial Flow Change during Chemoembolization of Hepatocellular Carcinoma

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ABSTRACT

Purpose: To evaluate feasibility of using three-dimensional (3D) quantitative color-coding analysis (QCA) to quantify substasis endpoints after transcatheter arterial chemoembolization of hepatocellular carcinoma (HCC).

Materials and Methods: This single-institution prospective study included 20 patients with HCC who had undergone segmental or subsegmental transcatheter arterial chemoembolization between December 2015 and March 2017. The chemoembolization endpoint was a sluggish anterograde tumor-feeding arterial flow without residual tumor stains. Contrast medium bolus arrival time (BAT) was used as an indicator of arterial flow. BAT of the proper hepatic artery was obtained as a reference point. BATs of the proximal right lobar artery, proximal left lobar artery, and segmental artery that received embolization were analyzed before and after chemoembolization. Wilcoxon signed rank test was used to evaluate the difference between BATs before and after chemoembolization.

Results: BATs before and after chemoembolization of the segmental artery that received embolization were 0.47 seconds (interquartile range [IQR], 0.31–0.70 s) and 1.04 seconds (IQR, 0.78–2.01 s; $P < .001$), respectively. BATs before and after chemoembolization of the proximal left lobar hepatic artery (0.35 s [IQR, 0.11–0.55] and 0.13 s [IQR, 0.05–0.32], $P = .025$) and right lobar hepatic artery (0.23 s [IQR, 0.13–0.65] and 0.22 s [IQR, 0.08–0.39], $P = .027$) exhibited no significant change.

Conclusions: 3D QCA is a feasible method for quantifying sluggish segmental arterial flow after transcatheter arterial chemoembolization in patients with HCC.

ABBREVIATIONS

BAT = bolus arrival time, CHA = common hepatic artery, DSA = digital subtraction angiography, HCC = hepatocellular carcinoma, IQR = interquartile range, PHA = proper hepatic artery, QCA = quantitative color-coding analysis, 3D = three-dimensional, 2D = two-dimensional

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An optimal embolization endpoint for transcatheter arterial chemoembolization is crucial for successfully treating hepatocellular carcinoma (HCC). Underembolization of tumor-feeding arteries leads to a poor tumor response to treatment (1–3). By contrast, overembolization has a negative prognostic effect on survival (4). Therefore, substasis flow of a tumor-feeding artery is slightly preferred by interventional radiologists as a transcatheter arterial chemoembolization endpoint (5). A subjective angiographic grading system was proposed as a qualitative scale for an embolization endpoint (6), but substasis flow was difficult to define using a subjective grading scale. Therefore, two-dimensional (2D) digital subtraction angiography (DSA) and fluoroscopy quantitative color-coding analysis (QCA) can be implemented as objective tools for substasis flow

measurement as transcatheter arterial chemoembolization endpoints (7,8). However, a limitation of 2D QCA is that it entails obtaining data from 2D source images. Overlapping vasculature or hypervascular tumors in 2D projections accentuate the contrast medium attenuation on the vessels of interest, which produces misleading QCA results.

A time-resolved three-dimensional (3D) DSA technique has been applied to diagnose neural vascular diseases (9,10). A rotational mask is acquired and fill projection flat-panel images are computed to generate 3D vascular anatomy with temporal information. The seed point can be placed at the vessel of interest, which can be confirmed using different projection angles to avoid unwanted vessel overlap. The contrast medium bolus arrival time (BAT) in each voxel can be assigned a particular color (i.e., 3D QCA) as an indicator of blood flow. The goal of this study was to evaluate the feasibility of using 3D QCA to objectively quantify a substasis transcatheter arterial chemoembolization endpoint and resolve the problem of vessel overlap that is prevalent in 2D QCA.

MATERIALS AND METHODS

Patient Selection

This prospective, single-institution study was approved by the institutional review board. Consecutive patients with HCC who underwent conventional transcatheter arterial chemoembolization between December 2015 and March 2017 were enrolled in this study. All patients provided written informed consent. HCC was diagnosed either through biopsy or by established diagnostic imaging criteria using 4-phase computed tomography (CT) or magnetic resonance imaging. Patients were selected for transcatheter arterial chemoembolization by the institutional multidisciplinary HCC tumor board. The inclusion criteria for transcatheter arterial chemoembolization were as follows: Child-Pugh A or B liver disease, Eastern Cooperative Oncology Group performance status of ≤ 2, no major ascites, total bilirubin < 2.5 mg/dL, serum creatinine < 2.0 mg/dL, international normalized ratio ≤ 1.5, and alanine aminotransferase and aspartate aminotransferase < 5 times the upper normal limit. The exclusion criteria for imaging analysis were as follows: inability to maintain an end-expiratory breath hold for 18 seconds and hepatic arterial anatomy other than Michels classification type I (to standardize the catheter tip location at the common hepatic artery [CHA]) (11).

Of 69 enrolled patients who received conventional transcatheter arterial chemoembolization, 27 did not receive 3D QCA image acquisition owing to vascular variance. Of the remaining 42 patients who received 3D QCA image acquisition, 22 patients were excluded because of an inability to maintain a breath hold for 18 seconds. Consequently, 20 patients with a mean age of 66.7 years (range, 52–82 y) were analyzed. Of these 20 patients, 19 (95%) had Child-Pugh A liver disease, and 1 (5%) had Child-Pugh B liver disease. Most patients (70%) were classified as having Barcelona Clinic Liver Cancer stage B. Other relevant clinical characteristics are summarized in the Table.

Table. Patient Demographics and Clinical Characteristics (n = 20)

Characteristic	Value
Sex	
Male	18 (90%)
Female	2 (10%)
Age, y, mean (range)	66.7 (52–82)
Body mass index, mean (range)	25.2 (17.1–35.7)
Cause of disease	
HBV	8 (40%)
HCV	8 (40%)
Alcoholic liver cirrhosis	1 (5%)
Others	3 (15%)
Child-Pugh class	
A	19 (95%)
B	1 (5%)
Barcelona Clinic Liver Cancer stage	
A	5 (25%)
B	14 (70%)
C	1 (5%)
AFP	
$\leq$ 200 ng/mL	19 (95%)
$>$ 200 ng/mL	1 (5%)
Tumor burden	
Single, $\leq$ 5 cm	3 (15%)
Single, $>$ 5 cm	0 (0%)
Multiple, largest tumor $\leq$ 5 cm	16 (80%)
Multiple, largest tumor $>$ 5 cm	1 (5%)
Biologic parameters, mean ± SD	
AST, U/L	54.20 ± 36.51
ALT, U/L	49.40 ± 35.19
Total bilirubin, mg/dL	0.82 ± 0.60
Albumin, g/dL	4.03 ± 0.53
INR	1.09 ± 0.09

Note–Values are reported as the number (%) of patients unless otherwise specified.
AFP = alpha fetoprotein; ALT = alanine aminotransferase; AST = aspartate aminotransferase; HBV = hepatitis B; HCV = hepatitis C; INR = international normalized ratio

Chemoembolization Procedures

To minimize interoperator variance of the subjective embolization endpoint, all chemoembolization procedures and image acquisitions were performed by 1 interventional radiologist with 6 years of experience (E.Y.L.). Arterial access was acquired in the right common femoral artery by using the Seldinger technique. A 4-F J-curve catheter (TEMPO; Cordis Corp, Milpitas, California) was used for initial visceral angiography. To identify tumors and tumor-feeding arteries, hepatic angiography was performed using cone-beam CT in all cases. After identifying the target tumors and their tumor-feeding arteries, a 2.5-F microcatheter (Renegade; Boston Scientific,