CLINICAL STUDY

Cone Beam CT–Guided Chemoembolization of Probable Hepatocellular Carcinomas Smaller than 1 cm in Patients at High Risk of Hepatocellular Carcinoma

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ABSTRACT

Purpose: To evaluate the effectiveness and safety of cone-beam computed tomography (CT)–guided chemoembolization for probable hepatocellular carcinomas (HCCs) smaller than 1 cm in patients at high risk for HCC.

Materials and Methods: From December 2009 to May 2014, 57 patients (43 male and 14 female; mean age, 61.1 y) at high risk for HCC underwent cone-beam CT–guided conventional chemoembolization for 79 treatment-naive probable HCCs < 1 cm. Probable HCCs were diagnosed when hepatic nodules showed arterial enhancement and washout on dynamic CT or magnetic resonance images. The Kaplan–Meier method and Cox proportional-hazards regression were used to evaluate the time to local progression (TTLP), time to progression (TTP), and overall survival (OS).

Results: Initial follow-up images obtained 2–3 months after chemoembolization showed complete response in all 79 tumors. The 1-, 2-, and 3-year local progression rates were 10.4%, 21.7%, and 35.7%, respectively. Subsegmental catheterization ($P < .001$; hazard ratio [HR] = .041) and segmental catheterization ($P = .001$; HR = .049) were significantly associated with longer TTLP. The 1-, 2-, and 3-year progression rates were 40.5%, 66.7%, and 78.6%, respectively. Tumor multiplicity ($P = .004$; HR = 2.612) was a significant risk factor for shorter TTP. The 1-, 2-, and 3-year OS rates were 100%, 98.2%, and 88.5%, respectively. Child–Turcotte–Pugh class B disease ($P = .029$; HR = 5.989) was significantly associated with shorter OS. No complications occurred after chemoembolization.

Conclusions: Cone-beam CT–guided chemoembolization can be a useful and safe option for probable HCCs < 1 cm in patients at high risk for HCC.

ABBREVIATIONS

CI = confidence interval, CTP = Child–Turcotte–Pugh, DSA = digital subtraction angiography, HCC = hepatocellular carcinoma, HR = hazard ratio, MELD = Model for End-stage Liver Disease, TTLP = time to local progression, TTP = time to progression

For the surveillance of populations at high risk for hepatocellular carcinoma (HCC), it has recently become more common to use dynamic computed tomography (CT) or magnetic resonance (MR) imaging, which have superior sensitivity and specificity compared with ultrasonography (US) (1–3). In addition, the advent of hepatocyte-specific MR contrast agents and the propagation of diffusion-weighted imaging make it possible to provisionally diagnose even subcentimeter-sized tumors such as HCCs (4–8). The Liver Imaging Reporting and Data System, developed by the American College of Radiology to interpret and report CT and MR images of the liver in patients at high risk for HCC, also categorizes subcentimeter-sized tumors with sufficient imaging evidence as "probably HCC" (9).

In this context, the "wait-and-see" policy for subcentimeter-sized tumors detected on US screening

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may need to be adjusted in response to the higher probability of tumors identified on CT or MR imaging. When clinicians encounter a probable HCC based on sufficient imaging evidence, but of a small size, and a further imaging study does not seem to be beneficial, several options can be considered: (*i*) waiting until the tumor grows, (*ii*) performing a diagnostic intervention, or (*iii*) administering immediate treatment. The waiting strategy may be inappropriate because the tumor has a very high probability of being an HCC, and some locally aggressive HCCs show vascular invasion despite their small size (8). The possibility of a diagnostic intervention (ie, image-guided percutaneous biopsy) is limited for probable HCCs smaller than 1 cm, considering false-negative results caused by sampling error, technical difficulty depending on the target location, coagulopathy, ascites, and the prevalence of needle tract seeding (2.7% incidence according to a meta-analysis [10]).

Percutaneous image-guided ablation techniques have limitations similar to those of diagnostic interventions, and surgical management may be too aggressive. In such cases, cone-beam CT–guided chemoembolization, in conjunction with selective catheterization, may be the treatment of choice for small HCCs in view of its therapeutic effectiveness and safety (11). Therefore, the present retrospective study was conducted to evaluate the effectiveness and safety of cone-beam CT–guided chemoembolization for probable HCCs smaller than 1 cm in patients at high risk for HCC.

MATERIALS AND METHODS

Patients

The institutional review board approved this retrospective study and permitted the waiving of informed consent. Based on a search of electronic medical records and chemoembolization reports generated from December 2009 to May 2014, this study initially archived the records of 2,852 patients who received their initial chemoembolization at the authors' institution. According to the procedural records, 155 patients initially underwent cone-beam CT–guided conventional chemoembolization for presumed HCCs $\geq$ 5 mm and $<$ 10 mm in size. The diagnosis of HCC was based on four-phase dynamic CT or gadoxetic acid–enhanced MR imaging obtained within 2 months before chemoembolization. Hepatologists could consult with interventionalists about the technical feasibility of chemoembolization and image-guided ablation, but the final decisions regarding the need for treatment and the choice of therapeutic modality were left to the discretion of each hepatologist. Patients who had HCCs $\geq$ 10 mm in size, marginal recurrence following hepatic resection, or local tumor progression after image-guided ablation were excluded from the analyses. Patients with insufficient imaging evidence of HCC on a retrospective review, vascular invasion, extrahepatic spread, Child–Turcotte–Pugh (CTP) class C disease, or a low risk of HCC were also excluded. Patients at high risk of HCC were defined as those with cirrhosis, hepatitis B carriers with active hepatitis or a family history of HCC, hepatitis C carriers with stage 3 liver fibrosis, and patients with a history of HCC (12,13). A total of 57 patients with 79 probable HCCs smaller than 10 mm were finally included in the study (**Fig 1**). The baseline characteristics of the final study population are summarized in **Table 1**.

Imaging Diagnosis of Probable HCC

On four-phase dynamic CT or gadoxetic acid–enhanced MR images, subcentimeter-sized hepatic nodules with typical arterial enhancement and washout on portal venous and/or delayed phases were judged as probable HCCs (ie, Liver Imaging Reporting and Data System category 4A) (9,14). On CT and MR images (dynamic three-dimensional fat-saturated T1-weighted sequences), the *x*-, *y*-, and *z*-axis resolutions were 1.2–1.9 mm, 1.2–1.9 mm, and 2.4–3.0 mm, respectively.

Cone-Beam CT–Guided Chemoembolization

Conventional chemoembolization was conducted by, or under the supervision of, two experienced interventional radiologists (H.C.K. and J.W.C, with 10 and 24 y of experience in interventional oncology, respectively). After obtaining digital subtraction angiography (DSA) images at the level of the common hepatic artery or celiac trunk, a single series of three-dimensional rotational cone-beam CT hepatic arteriography images was acquired at the proper hepatic artery or equivalent by using a flat-panel detector angiography unit (Axiom Artis dTA/VB30 or Artis Zee; Siemens, Forchheim, Germany). The parameters of the cone-beam CT system were as follows: 0.5° increment, 211° circular trajectory for 7–8 seconds, 512 × 512 matrix in projections, system dose of approximately 0.36 μGy per frame, and a total of 419 projections. Iodinated contrast agent (Ultravist 300; Bayer Schering, Berlin, Germany) was administered by a power injector at a flow rate of 2–4 mL/s for 12 seconds, and the cone-beam CT images were obtained 4 seconds after the start of the injection (15,16). In cases of anatomic variation, such as the right hepatic artery arising from the superior mesenteric artery, the cone-beam CT scan of each hepatic artery was conducted separately, and the amount of contrast agent was adjusted depending on the arterial territory. The cone-beam CT data were then transferred to a dedicated workstation (Leonardo with DynaCT; Siemens) and immediately reconstructed with axial, coronal, and sagittal images of 0.3-mm section thickness and maximum-intensity-projection reformatted images.