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Diagnostic and Interventional Imaging (2016) $\mathbf{xxx},\,\mathbf{xxx}-\mathbf{xxx}$





ORIGINAL ARTICLE / Cancer Imaging

Evaluation of tumor response to intra-arterial chemoembolization of hepatocellular carcinoma: Comparison of contrast-enhanced ultrasound with multiphase computed tomography

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KEYWORDS

Contrast-enhanced ultrasound; Multiphase computed tomography (CT); Hepatocellular carcinoma; Trans-arterial chemoembolization; Comparative studies

Abstract

Purpose: To compare the diagnostic accuracy of contrast-enhanced ultrasound (CEUS) with that of multiphase computed tomography (CT) in the evaluation of tumor response to transarterial chemoembolization (TACE) of hepatocellular carcinoma (HCC).

Material and methods: Fifty patients (41 men, 9 women; mean age, 53 years \pm 12.5 [SD]) with a total of 70 HCCs (mean size, 5 cm \pm 3 [SD]) were evaluated. Post-TACE therapeutic assessment of HCC was done at 4 weeks. Patients with TACE done earlier and reporting with suspicion for recurrence were also included. Patients with hepatic masses seen on ultrasound were enrolled and subjected to CEUS, multiphase CT and magnetic resonance imaging (MRI). Hyperenhancing area at the tumor site on arterial phase of CEUS/multiphase CT/MRI was termed as residual disease (RD), the patterns of which were described on CEUS. Diagnostic accuracies of CEUS and MPCT were compared to that of MRI that was used as the reference standard.

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http://dx.doi.org/10.1016/j.diii.2016.09.002

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Please cite this article in press as: Paul SB, et al. Evaluation of tumor response to intra-arterial chemoembolization of hepatocellular carcinoma: Comparison of contrast-enhanced ultrasound with multiphase computed tomography. Diagnostic and Interventional Imaging (2016), http://dx.doi.org/10.1016/j.diii.2016.09.002

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Results: CEUS detected RD in 43/70 HCCs (61%). RD had a heterogeneous pattern in 22/43 HCCs (51%). Sensitivities of CEUS and multiphase CT were 94% (34/36; 95% CI: 81–99%) and 50% (18/36; 95% CI: 33–67%) respectively. Significant difference in sensitivity was found between CEUS and multiphase CT (P=0.0001). CEUS and multiphase CT had 100% specificity (95% CI: 83–100%).

Conclusion: CEUS is a useful technique for detecting RD in HCC after TACE. For long term surveillance, CEUS should be complemented with multiphase CT/MRI for a comprehensive evaluation. © 2016 Editions françaises de radiologie. Published by Elsevier Masson SAS. All rights reserved.

Transarterial chemoembolization (TACE) is a widely used therapeutic option for unresectable hepatocellular carcinoma (HCC) as a majority of patients with HCC are diagnosed at an advanced stage of the disease [1,2]. TACE involves the use of intra-arterial administration of chemotherapeutic drug emulsion containing iodized oil (Lipiodol[®]; Laboratoire Guerbet, Roissy-Charles de Gaulle, France) through the tumor feeding artery followed by embolization thus producing cytotoxic damage and ischemic necrosis of the tumor.

Accurate response evaluation following TACE is crucial for the management of patients with HCC. The decision of subsequent therapeutic planning (retreatment or resorting to other modes of therapy) is based on tumor response to TACE. Indicators of successful TACE are in the form of tumor necrosis appearing as early as 1-2 months while the changes of tumor shrinkage invariably takes longer to occur. Estimation of viable tumor tissue following TACE is done by the modified response evaluation criteria in solid tumor (mRE-CIST criteria) on multiphasic computed tomography (CT) or magnetic resonance imaging (MRI) [3,4]. These imaging modalities have high diagnostic accuracy in evaluating the entire liver during different phases of vascular enhancement [5–9].

However, both techniques have limitations as well. Multiphasic CT involves radiation exposure limiting its repetitive use and the masking effect of the viable tumor by hyperattenuating Lipiodol[®] used during TACE hinders accurate interpretation of response [4,5,10]. MRI is superior to multiphasic CT as the evaluation by highly sensitive T2 weighted sequences and the multiphasic contrast enhanced sequences are not hampered by the presence of Lipiodol[®]. This makes MRI a reference imaging modality for post TACE evaluation [11]. But high cost, infrastructure and limited availability poses a constraint in its wide usage. Thus, there emerges a need to explore alternative imaging modalities for therapeutic assessment.

Contrast-enhanced ultrasound (CEUS) can depict tumor vascularity based on the intranodular hemodynamics [12–14]. Earlier studies have focused mainly on the role of CEUS in the diagnosis of HCC and limited literature is available regarding tumor response to TACE [15,16]. Studies comparing CEUS with other imaging techniques are also scarce [17–21].

This study was designed to describe the patterns of residual disease on CEUS and compare the diagnostic accuracy of CEUS with that of multiphasic CT in the evaluation of tumor response to TACE of HCC.

Materials and methods

Study population

From February 2010 to June 2015, patients with HCC presenting to our Liver Clinic after undergoing TACE were included in this prospective study. Patients were of a mix of two types — those who had TACE one month prior and were assessed for the first time for tumor response and patients who had developed complete response to TACE earlier, and were reported on follow up with a clinical suspicion of recurrence such as like deterioration of liver function or raised serum alphafetoprotein (AFP) level. Ethics clearance was obtained from the Institute Ethics committee (IEC/NP-209/2010) and a written informed consent was obtained.

The inclusion criteria were: — Post TACE HCC patients of intermediate stage, Barcelona clinic staging classification (BCLC) B [5] with either a single mass or multinodular HCC (tumor burden < 50% of the liver), entire mass seen on ultrasound, and a mass not larger than 15 cm. Patients with diffuse disease (large mass or multiple nodules involving the entire liver), Child's C cirrhosis, comorbidities (coronary artery disease, cardiac or renal failure) and breast feeding women were excluded.

Enrolled patients underwent CEUS, multiphase CT and MRI in a random order not more than 1 to 2 weeks apart of each other after 4 weeks following TACE. For patients with multinodular HCC, the two largest masses (less than 15 cm) were evaluated. CEUS was tailored to the evaluation of post treatment tumor response indicating complete or partial response (residual/recurrent disease), whereas multiphase CT and MRI provided a comprehensive assessment of the liver. MRI was considered as the gold standard and further management was based on MRI findings. When TACE was repeated following partial response, then a repeat assessment of that patient was done by CEUS, multiphase CT and MRI at one month post-TACE. Each repeat evaluation was considered as a new observation.

TACE procedure

TACE was undertaken through a transfemoral arterial approach. A superior mesenteric artery and celiac axis angiogram were first obtained by using 5F RC1 (reverse curve, Cook, Bloomington, IN, USA) or C1 (Celiac, Cook,) diagnostic catheter and 0.035-inch J-tip guidewire (Terumo; Terumo Corporation, Tokyo, Japan). For approaching

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