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The Role of Contrast-Enhanced Ultrasound in Guiding Radiofrequency Ablation of Hepatocellular Carcinoma: A Retrospective Study

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Abstract

Purpose: The objective of the study was to determine the efficacy of contrast-enhanced ultrasound (CEUS) using ultrasound (US)-specific microbubbles in guiding radiofrequency ablation (RFA) of hepatocellular carcinoma (HCC).

Methods: A retrospective analysis of 50 patients with HCC treated with CEUS guided RFA using perflutren at our institution was performed. CEUS images were first compared to B-mode US images performed at the same RFA session to determine the ability of CEUS to increase the conspicuity of lesions. A qualitative score (1 = poor, 2 = fair, 3 = excellent) was used to grade the ability to visualize the lesions. The preprocedure CEUS images were then evaluated using the most recent prior contrast enhanced computed tomography (CT) or magnetic resonance imaging (MRI). The efficacy of the treatment was evaluated with short-term follow-up imaging (median 1 month) for presence of residual or recurrent disease.

Results: CEUS allows at least fair visualization (score ≥ 2) in 78% (reader 1) and 80% (reader 2) of the lesions not visualized by B-mode US, and 50% (reader 1) and 42% (reader 2) of the lesions poorly visualized by B-mode US. Lesion appearances on CEUS are largely concordant with those on CT or MRI: 88% for reader 1, 96% for reader 2. With CEUS-guided RFA, complete response was achieved in the vast majority of the lesions at short-term follow-up: 82% for reader 1, 94% for reader 2.

Conclusions: CEUS increases the conspicuity and provides better characterization of hypervascular HCC that are either not seen or poorly seen on B-mode US, and CEUS provides real-time guidance of RFA with good short-term treatment responses.

Résumé

Objet : L'étude avait pour objectif de déterminer si l'échographie avec injection d'un produit de contraste (composé de microbulles) permettait de guider efficacement l'ablation par radiofréquence d'un carcinome hépatocellulaire.

Méthodes : Notre analyse rétrospective a porté sur 50 patients ayant subi une ablation de carcinome hépatocellulaire par radiofréquence sous échoguidage avec injection de perflutène au sein de notre établissement. Les images de l'échographie de contraste ont d'abord été comparées aux images de l'échographie en mode B (échographie de brillance) réalisée dans le cadre de la même séance d'ablation par radiofréquence afin de déterminer la capacité de l'échographie de contraste à accroître la perceptibilité des lésions. La perceptibilité des lésions a été évaluée au moyen d'une note qualitative (1 = faible, 2 = passable, 3 = excellente). Les images échographiques réalisées avant la chirurgie ont ensuite été analysées à l'aide d'images tirées du plus récent examen par tomographie assistée par ordinateur (TAO) ou d'imagerie par résonance magnétique (IRM) avec injection de produit de contraste. Enfin, l'efficacité du traitement a été déterminée à l'aide d'un examen de suivi à court terme (intervalle moyen d'un mois) visant à vérifier la présence d'une affection résiduelle ou récurrente.

Résultats : L'échographie de contraste a permis de visualiser dans une mesure qualifiée d'au moins « passable » (note égale ou supérieure à 2) 78 % (première lecture) et 80 % (deuxième lecture) des lésions n'ayant pas été discernées lors de l'échographie en mode B, et 50 %

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(première lecture) et 42 % (deuxième lecture) des lésions difficiles à discerner sur les images de l'échographie en mode B. L'aspect des lésions observées à l'échographie de contraste correspond la plupart du temps à l'aspect des lésions observées par TDM ou IRM (88 % à la première lecture, 96 % à la deuxième). Dans la grande majorité des cas, l'ablation par radiofréquence guidée par échographie de contraste s'est traduite par une réponse thérapeutique complète à l'examen de suivi à court terme (82 % à la première lecture et 94 % à la deuxième).

Conclusion : L'échographie de contraste accroît la perceptibilité et renforce la caractérisation des carcinomes hépatocellulaires hyper-vascularisés non visibles ou difficiles à discerner dans le cadre d'une échographie en mode B. Elle permet également le guidage en temps réel de l'ablation par radiofréquence, ce qui entraîne une bonne réponse thérapeutique à court terme.

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Key Words: Ultrasound; Contrast enhanced ultrasound; Radiofrequency ablation; Hepatocellular carcinoma; Gastrointestinal radiology; Interventional radiology

Hepatocellular carcinoma (HCC) is a common malignancy, with an increasing incidence due to hepatitis B and C viruses [1]. Chronic liver disease is the most important predisposing factor, accounting for 70%-90% of cases of HCC. Other common risk factors include alcohol, nonalcoholic fatty liver disease, tobacco, and diabetes [1]. Surgical resection or transplantation is the recommended treatment in patients with HCC and preserved liver functions. Unfortunately, less than 5% of cirrhotic patients with HCC fulfill these criteria [2]. Radiofrequency ablation (RFA) is a minimally invasive procedure that provides excellent local control of early stage HCC, allowing for lowered morbidity, thereby providing a treatment alternative for patients who are poor surgical candidates [3]. As a result, RFA has become an increasing important treatment modality for these patients.

Image guidance plays a crucial role in RFA in the targeting of the tumour and assessing treatment response. Although contrast-enhanced computed tomography (CECT) provides excellent visualization, ultrasound (US) is often the modality of choice for guidance due to its real-time capabilities [4]. Conventional B-mode US, however, may not adequately visualize the tumour for treatment, and in the setting of previous ablation, identifying residual/recurrent disease is often difficult [4–6]. With the introduction of second-generation microbubble US contrast agents, the sensitivity of contrast-enhanced US (CEUS) in detecting tumours is far superior to conventional B-mode US, and CEUS can be used to guide and monitor the RFA procedure to ensure successful treatment [6–19]. Finally, CEUS also has an important role in patients with renal impairment, where the uses of iodinated (CT) or gadolinium (magnetic resonance) contrast agents are relatively contraindicated.

Multiple studies from Europe and Asia have demonstrated the ability of CEUS to characterize HCC lesions and guide RFA treatments [6–19]; however, our institution is the first in North America to routinely perform CEUS guided RFA clinically, due to our large population of patients with hepatitis B/C and cirrhosis. The purpose of this study is to determine the efficacy of CEUS in guiding RFA of HCC.

Methods

Patient Selection and Study Design

Institutional review board approval was from both the research ethics board of the university and health authority. This retrospective analysis was conducted between January 2011 and June 2012; patients treated with percutaneous RFA between Oct 2008 and May 2010 were included initially. The inclusion criteria used by our liver tumour group (consisting of radiologists, hepatobiliary surgeons, hepatologists, and oncologists) to select patients with HCC to be treated with CEUS guided RFA is based on the American Association for the Study of Liver Diseases Practice Guideline on the Management of Hepatocellular Carcinoma [20]: 1) A lesion is diagnosed radiologically as HCC if its size is greater than 1 cm, has the typical appearance of hypervascularity in the arterial phase and washout in portal venous or delay phases on contrast-enhanced CT or magnetic resonance imaging (MRI) examination, and is present in patients with underlying cirrhosis or hepatitis; 2) Patients with early stage disease, either solitary HCC or up to 3 nodules ≤ 3 cm in size, and not suitable for surgical resection or transplantation. Exclusion criteria includes: 1) vascular invasion; 2) subcapsular/sub-diaphragmatic location, or adjacent to liver hilum, gallbladder, or gastrointestinal tract; 3) allergy to the CEUS contrast agent.

Analyses of images from the selected patients were performed by 2 radiologists with up to 4 years' experience in this field. Both readers were blinded to patient's identifying information and any clinical history. The CEUS images were first compared to the conventional B-mode images performed on the same session to determine the ability of CEUS to increase the conspicuity of lesions for delivery for RFA, with a qualitative visualization score (1 = poor, 2 = fair, 3 = excellent) used to grade the ability to visualize the lesion. The CEUS images were then evaluated against the most recent pretreatment cross-sectional imaging (contrast-enhanced CT or MRI) as the gold standard, during which the enhancement pattern of the lesions on both modalities were compared for concordance. Finally, the primary outcome of the study is the efficacy of CEUS guided RFA treatment at

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