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Research paper

Dual energy spectral CT imaging for the evaluation of small hepatocellular carcinoma microvascular invasion

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A R T I C L E I N F O

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A B S T R A C T

Objective: To study the clinical value of dual-energy spectral CT in the quantitative assessment of microvascular invasion of small hepatocellular carcinoma.

Methods: This study was approved by our ethics committee. 50 patients with small hepatocellular carcinoma who underwent contrast enhanced spectral CT in arterial phase (AP) and portal venous phase (VP) were enrolled. Tumour CT value and iodine concentration (IC) were measured from spectral CT images. The slope of spectral curve, normalized iodine concentration (NIC, to abdominal aorta) and ratio of IC difference between AP and VP (RIC_{AP-VP}: [$RIC_{AP-VP} = (IC_{AP} - IC_{VP})/IC_{AP}$]) were calculated. Tumours were identified as either with or without microvascular invasion based on pathological results. Measurements were statistically compared using independent samples *t* test. The receiver operating characteristic (ROC) analysis was used to evaluate the diagnostic performance of tumours microvascular invasion assessment. The 70 keV images were used to simulate the results of conventional CT scans for comparison.

Results: 56 small hepatocellular carcinomas were detected with 37 lesions (Group A) with microvascular invasion and 19 (Group B) without. There were significant differences in IC, NIC and slope in AP and RIC_{AP-VP} between Group A (2.48 ± 0.70 mg/ml, 0.23 ± 0.05, 3.39 ± 1.01 and 0.28 ± 0.16) and Group B (1.65 ± 0.47 mg/ml, 0.15 ± 0.05, 2.22 ± 0.64 and 0.03 ± 0.24) (all $p < 0.05$). Using 0.188 as the threshold for NIC, one could obtain an area-under-curve (AUC) of 0.87 in ROC to differentiate between tumours with and without microvascular invasion. AUC was 0.71 with CT value at 70 keV and improved to 0.81 at 40 keV.

Conclusion: Dual-energy Spectral CT provides additional quantitative parameters than conventional CT to improve the differentiation between small hepatocellular carcinoma with and without microvascular invasion.

Clinical Application/Relevance: Quantitative iodine concentration measurement in spectral CT may be used to provide a new method to improve the evaluation for small hepatocellular carcinoma microvascular invasion.

1. Introduction

Hepatocellular carcinoma is the most common primary malignant tumour in the liver; accounting for 19.33% of all malignant liver tumours [1]. With the improvement in imaging techniques, more and more small hepatocellular carcinomas are discovered early and treated in time. Currently, the radical resection is still the most effective way to treat small hepatocellular carcinoma, but the prognosis and long term effect varies dependent on patients. Roayaie [2] reported that up to 70% patients with small hepatocellular carcinoma would be in relapse at 5 years after hepatic resection. The main reason for liver cancer recurrence and poor prognosis is due to portal vein and tumour microvascular invasion [3]. Researchers have shown that tumours with positive microvascular invasion can more easily invade adjacent vessels and lymphatics, cause early dissemination and metastasis, and have greater influence on prognosis. So, accurate preoperative evaluation of tumour microvascular invasion is important for the treatment plan and the prognosis. Many scholars have used the hepatic artery CT angiography, dynamically enhanced MRI and superparamagnetic contrast enhanced MRI in the preoperative evaluation of hepatocellular carcinoma microvascular invasion [4,5].

Dual-energy CT performed during two consecutive scans or with a dual x-ray source, dual-detector can provide additional information that is used for material separation at imaging [6–8]. Spectral imaging

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is also reported as an excellent qualitative as well as a quantitative tool for assessing and predicting hepatocellular carcinoma in cirrhotic patients [9]. The spectral CT is based on the principle that this technique involves scanning at distinctly different energies (most commonly used energy levels are 80 and 140 kVp). This works best for post contrast CT scans due to the use of Iodine, which has a K-edge of 33.2 keV. The higher attenuation of Iodine suggests hypervascular (Iodine rich) nodules in contrast to rest of the liver parenchyma.

Therefore, we tried to applicate dual-energy spectral CT for evaluating the primary hepatic carcinoma microvascular invasion. The purpose of this study was to study the clinical value of dual-energy spectral CT in the quantitative assessment of microvascular invasion of primary small hepatocellular carcinoma.

2. Materials and methods

2.1. General information

This study was approved by our ethics committee, and patient consent was waived. We retrospectively analyzed the imaging information of 50 patients who came to our hospital between July 2013 and March 2015 for the diagnosis and treatment of primary small hepatocellular carcinoma. All patients had confirmed results of hepatocellular carcinoma by pathology. There were 36 male patients and 14 female patients with age ranged from 38 to 77 years and median age of 49 years. 34 cases had reported history of cirrhosis. All patients underwent the contrast-enhanced dual-energy spectral CT for definitive diagnosis of primary small hepatocellular carcinoma before surgical operation were enrolled in the study, if they meet the following criteria: (1) the maximum diameter of single tumour was under 3 cm; or (2) in the case of multiple tumours, the numbers were no more than two, and the maximum total diameter was below 3 cm, and there was no obvious signs of metastasis; (3) 1–3 weeks after CT examination the tumours were resected in our hospital with complete tumour resection and negative margins, and no metastasis findings in the 1 month follow up imaging; (4) imaging revealed lesions in the liver, but no obvious portal vein tumour thrombus; (5) there was no treatment for cancers before the operation. Patients with severe image artifacts were excluded. Patient information is summarized in Table 1.

Table 1
Patient information between the two pathological groups of small hepatocellular carcinoma in Spectral CT.

Parameter	Group		p-value
	Tumours with microvascular invasion (n = 37)	Tumours without microvascular invasion (n = 19)	
Gender (Number of patients)			
Male (n = 36)	21/36	15/36	
Female (n = 14)	8/14	6/14	0.939
Age	53 ± 26.3	55 ± 17.2	0.746
Location (Number of lesions)			
Left lobe of liver	16/24	8/24	
Right lobe of liver	21/32	11/32	0.935
History of cirrhosis (n = 34)	20/34	14/34	0.863
Degree of differentiation			
well-differentiated and moderate-differentiated HCC (n = 22)	8/22	14/22	
poorly differentiated HCC (n = 34)	29/34	5/34	0.000*

*$p < 0.05$.

2.2. Imaging methods

All patients underwent the non-contrast and two-phase contrast enhanced CT scans on a Discovery CT750HD scanner (GE Healthcare, Waukesha WI USA) using the dual-energy spectral CT acquisition mode. Patients fasted for 4 h and took 800–1000ML warm water orally 5–10 min before the scanning. The scan protocol included 5 mm slice thickness, 600 mA tube current, 0.5s/rot gantry rotation speed, and 0.984:1 helical pitch. The nonionic contrast agent Ioversol (300mgI/ml) (China, Jiangsu Hengrui medicine) was injected through the median cubital vein with a German ORICH high pressure syringe at a patient weight-dependent dose of 0.8–1.0 ml/kg and infusion rate of 4.0–5.0 ml/s. The contrast injection was followed by 40 ml physiological saline at the same injection rate. The arterial phase (AP) scan started 20–25 s after the contrast injection, and the portal vein phase (PV) scan started 30 s after AP scanning. The volumetric CT dose index (CTDIvol) was 21.8 mGy (which is comparable to the 21.5-mGy dose for the conventional contrast enhanced liver scanning for a normal size patient in our institution). Images were reconstructed at 1.25 mm slice thickness using filtered back-projection and standard reconstruction kernel and dual-energy spectral CT-specific software to generate both virtual monochromatic image sets with energy levels from 40 to 140 keV and material decomposition images with water and iodine as the basis material pair.

2.3. Observation and analysis method

2.3.1. Image analysis

Images were transferred to a GE AW4.6 Workstation equipped with Gemstone Spectral Imaging (GSI) Viewer software for post-processing and analysis. Region-of-interest (ROI) with diameter of about half of the tumour size was placed on tumour to measure the iodine concentration (IC) on the iodine-based material decomposition images and the CT value on the 101 sets of virtual monochromatic images (corresponding to photon energies from 40keV–140 keV at 1 keV interval) in both AP and VP. The copy and paste function was used to ensure measurement consistency between the two phases. To reduce measurement variation, ROI was placed 3 times on the tumour and the average of the 3 measurements was used as the final result. The iodine concentration measurement was repeated on the abdominal aorta at the same imaging level for generating normalized iodine concentration (NIC) for tumours: NIC(tumour) = IC(tumour)/IC(aorta). The ratio of the iodine concentration difference between AP and VP (RIC_{AP-VP}: [$RIC_{AP-VP} = (IC_{AP} - IC_{VP})/IC_{AP}$]) were calculated. The CT value measurements from the virtual monochromatic images from 40 keV to 90 keV were used to calculate the slope (λ_{HU}) for spectral HU curve (CT value as a function of virtual monochromatic energy level): λ_{HU} = [(CT(40keV)–CT(90keV)]/50. Since the 70 keV virtual monochromatic images in spectral CT have similar muscle CT value to the conventional 120kVp images in abdominal imaging, the 70 keV virtual monochromatic images in our study were used to simulate the results of conventional CT scans for comparison.

2.3.2. Pathological analysis

The tissues for pathological analysis were obtained from 50 patients with primary small hepatocellular carcinoma after surgical operation. The whole process followed the protocol edited by the Department of Health of China ("Diagnosis and treatment of primary liver cancer", edition 2011), including the location and the number for obtaining specimens. The specimen treatment and pathological analysis were performed by two experienced pathologists. The specimen treatment included formaldehyde fixation and paraffin fixation followed by section cutting with the thickness of 4 mm and conventional H–E staining. According to the Hyung standard [10], the presence of microvascular invasion was defined as satisfying the following situations after HE staining: (1) the formation of tumour thrombus were found in central