European Journal of Radiology 92 (2017) 145–152

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Research paper

Differentiation of small intrahepatic mass-forming cholangiocarcinoma from small liver abscess by dual source dual-energy CT quantitative parameters

Ji Eun Kim[a], Hyun Ok Kim[b,*], Kyungsoo Bae[a], Jae Min Cho[a], Ho Cheol Choi[a], Dae Seob Choi[a]

[a] Department of Radiology, Gyeongsang National University School of Medicine, 79 Gangnam-ro, Jinju 52727, Republic of Korea
[b] Department of Internal Medicine, Gyeongsang National University School of Medicine, 79 Gangnam-ro, Jinju 52727, Republic of Korea

ARTICLE INFO

Keywords:
Intrahepatic cholangiocarcinoma
Liver abscess
Computed tomography
Dual-energy
Quantitative evaluation

ABSTRACT

Purpose: To investigate the use of dual source dual-energy CT (DECT) quantitative parameters compared with the use of conventional CT for differentiating small (≤3 cm) intrahepatic mass-forming cholangiocarcinoma (IMCC) from small liver abscess (LA) during the portal venous phase (PVP).

Material and methods: In this institutional review board-approved, retrospective study, 64 patients with IMCCs and 52 patients with LAs who were imaged in PVP using dual-energy mode were included retrospectively. A radiologist drew circular regions of interest in the lesion on the virtual monochromatic images (VMI), color-coded iodine overlay images, and linear blending images with a linear blending ratio of 0.3 to obtain CT value, its standard deviation, slope (k) of spectral curve and normalized iodine concentration (NIC). Two radiologists assessed lesion type on the basis of qualitative CT imaging features.

Results: CT values on VMI at 50–130 keV (20 keV-interval), k, and NIC values were significantly higher in IMCCs than in LAs ($p < 0.0001$). The best single parameter for differentiating IMCC from LA was CT value at 90 keV, with sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of 89.1%, 86.5%, 87.9%, 89.1%, and 86.5%, respectively. The best combination of parameters was CT value at 90 keV, k, and NIC, with values of 87.5%, 84.6%, 83.6%, 87.5%, and 84.6%, respectively. Compared with CT value at linear blending images, CT value at 90 keV showed greater sensitivity (89.1% vs 60.9%, $p < 0.0001$) and similar specificity (86.5% vs 84.6%, $p = 1.0000$), and combined CT value at 90 keV, k, and NIC showed greater sensitivity (87.5% vs 60.9%, $p < 0.0001$) and similar specificity (84.6% vs 84.6%, $p = 1.0000$). Compared with qualitative analysis, CT value at 90 keV showed greater sensitivity (89.1% vs 65.6%, $p = 0.0059$) and specificity (86.5% vs 69.2%, $p = 0.0352$), and combined CT value at 90 keV, k, and NIC showed greater sensitivity (87.5% vs 65.6%, $p = 0.0094$) and similar specificity (84.6% vs 69.2%, $p > 0.05$).

Conclusion: Quantitative analysis of dual source dual-energy CT quantitative parameters showed greater accuracy than quantitative and qualitative analyses of conventional CT for differentiating small IMCCs from small LAs on single PVP scan.

1. Introduction

Intrahepatic cholangiocarcinoma is the second most common primary hepatic malignancy that arises from the epithelium of the bile duct [1]. Intrahepatic mass-forming cholangiocarcinoma (IMCC) accounts for a large percentage of intrahepatic cholangiocarcinomas [2], with the only curative treatment being complete surgical resection [1,3,4]. The typical imaging findings of IMCC on multiphase contrast-enhanced CT are well known. However, small (≤3 cm) IMCCs can manifest as hypoenhancing lesions with peripheral rim hyperenhancement or as iso- or hyperenhancing lesions without ancillary findings during the hepatic arterial or portal venous phases [5,6]. These features can lead to a misdiagnosis of microabscess or solid organizing abscess [7–9], respectively. Liver abscess (LA) is commonly observed in patients at high risk for IMCC or with IMCC who share the common features of chronic biliary inflammation and ascending cholangitis [8,9]. Under these circumstances, differentiation of two diseases can be more challenging on a single phase CT scan, such as portal venous

Abbreviations: IMCC, intrahepatic mass-forming cholangiocarcinoma; LA, liver abscess; PVP, portal venous phase; DECT, dual-energy CT; VMI, virtual monochromatic images; ROI, region of interest; PACS, picture archiving and communications system; SD, standard deviation; NIC, normalized iodine concentration; ROC, receiver operating characteristic; PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval

* Corresponding author.
E-mail addresses: wldmsrla80@hanmail.net (J.E. Kim), galleonok@hanmail.net (H.O. Kim), ksbae@gnu.ac.kr (K. Bae), jmcho@gnu.ac.kr (J.M. Cho), jaro2@hanmail.net (H.C. Choi), choids@gnu.ac.kr (D.S. Choi).

http://dx.doi.org/10.1016/j.ejrad.2017.05.012
Received 22 February 2017; Received in revised form 9 May 2017; Accepted 10 May 2017

phase (PVP), due to a lack of information regarding characteristic dynamic enhancement patterns. The accurate differentiation of IMCC from LA is important for patient care and treatment decisions.

Dual source dual-energy CT (DECT) acquires dual-energy datasets with two different x-ray energy spectra using two tubes operating at high and low voltages with corresponding detectors mounted orthogonally in one gantry. It generates virtual monochromatic images (VMI) at energy levels ranging from 40 to 190 keV and color-coded iodine overlay images from a single contrast-enhanced CT acquisition [10,11]. The VMI enable reduction of beam-hardening artifacts and more quantitatively accurate attenuation measurement [12]. The iodine-specific images improve detection and characterization of lesions with slight differences in attenuation and of small lesions [11]. Recently, a second-generation dual source CT equipped with a tin-filter and an integrated circuit detector was introduced. This CT could enhance the performance of DECT algorithms by improving the separation between the two energy spectra and by improving the fidelity of DECT data acquisition [10,13,14]. With regard to focal liver lesions, quantitative parameters derived from iodine-specific images or VMI have been researched for differentiation of HCC from hemangioma [15], focal nodular hyperplasia [16], or angiomyolipoma [17] and for lesion characterization, including metastases and simple cysts [18]. However, to our knowledge, the value of DECT for differential diagnosis of IMCC from LA of small sizes has not been well evaluated. The purpose of our study was to investigate the use of dual source DECT quantitative parameters compared with the use of conventional CT for differentiating small ($\leq$ 3 cm) IMCC from small LA during the PVP.

2. Materials and methods

2.1. Patients

The institutional review board approved this retrospective study, and written informed consent was waived. We searched our radiologic database for abdominal CT examinations performed between May 2015 and May 2016 using the search terms “cholangiocarcinoma,” “CC” (the abbreviation for cholangiocarcinoma), “mass-forming,” “liver abscess,” and “hepatic abscess,” and the search yielded 389 patients. To develop a study group of suitable cases, we used the following inclusion criteria: (a) patients who underwent contrast-enhanced DECT with PVP scanning in dual-energy mode; (b) patients with the lesion size of 3 cm or less, according to the largest diameter measured on the CT scans, determined by one experienced radiologist (J.E.K, with 11 years of abdominal CT imaging interpretation experience); (c) patients with pathologic diagnoses of IMCC or LA; and (d) patients with clinical diagnoses of LA and follow-up CT or MR imaging showing disappearance of the LA lesion with or without percutaneous aspiration of pus. On the basis of these inclusion criteria, 273 patients were excluded: because (a) PVP imaging in dual-energy mode was not available (n = 179); (b) the lesion size was greater than 3 cm (n = 76); (c) there was an inadequate pathologic diagnosis (n = 5); or (d) follow-up CT or MR imaging was not available (n = 13) (Fig. 1). Each patient had one lesion. A total of 116 patients (mean age, 64.5 years old ± 13.1 [standard deviation]; range, 40–89 years), including 69 men and 47 women were included in our study. The mean body mass index of 116 patients was 22.0 ± 2.8 kg/m^2 (range, 14.3–29.5). Sixty-four patients (42 men, 22 women; mean age, 69.8 years old; range, 52–87 years) with 64 lesions (mean diameter, 2.4 cm; range, 1.1–3.0 cm) had IMCC. Fifty-two patients (27 men, 25 women; mean age, 64.5 years old; range, 40–89 years) with 52 lesions (mean diameter, 2.4 cm; range, 1.0–3.0 cm) had LA. The diagnoses of 64 patients with IMCC were determined by surgery (n = 13) or percutaneous biopsy (n = 51). The diagnoses of 52 patients with LA were determined by clinical diagnoses and follow-up CT or MR imaging showing disappearance of the LA lesion with (n = 26) or without percutaneous aspiration of pus (n = 25). In the LA patients, the mean duration between the onset of symptoms, such as fever or right upper quadrant pain, and DECT was 17.5 days (range, 3–66 days). The mean follow-up period for these patients was 5.5 months (range, 0.5–12.0).

2.2. CT imaging protocol

Images were obtained using a 128-section dual source CT scanner (SOMATOM Definition Flash; Siemens Healthineers) equipped with an integrated circuit detector (Stellar; Siemens). Non-enhanced, late arterial and delayed phase scanning was performed in the conventional mode using an automated program (CARE kV; Siemens Healthineers) with reference tube voltage of 120 kVp and reference tube current-time products of 120, 180 and 180 mAs, respectively. The PVP was scanned in dual-energy mode with a dual source of 80 kVp and Sn140 kVp tube voltages using the following parameters: tube current-time product, 230 and 89 mAs, respectively; section collimation, 2 × 64 × 0.6 mm with a z-flying focal spot; rotation speed, 0.33 s; and helical pitch, 0.7. The scan range reached from the lower lung base to the iliac crest. The mean CT dose index volume was 25.0 mGy, which was comparable to a CT dose index volume of 24.6 mGy for conventional liver scanning in patients with normal body mass indices at our institution. Nonionic contrast material (iopromide [370 mg of iodine per milliliter], Ultravist 370; Bayer Schering Pharma, Berlin, Germany) was injected through antecubital vein at a rate of 3–4 mL/s; a 1.5 mL per kilogram of body weight was injected using an automated injector (Optivantage; Mallinckrodt, Cincinnati, Ohio, USA). The late arterial scanning began automatically at 17 s after the abdominal aorta at the level of hepatic dome reached the trigger attenuation threshold (100 HU), using automated scan-triggering software (CARE Bolus CT; Siemens Healthineers). The portal venous and delayed phase scanning began 60–65 s and 130 s after contrast material injection, respectively. The DECT images were reconstructed with a section thickness of 1.5 mm (increment of 1 mm) and using a dual-energy dedicated algorithm (Q40). The adaptive statistical iterative reconstruction algorithm with strength of 2–5 was applied to suppress image noise on the decomposition images.

2.3. Quantitative analysis

Quantitative analysis of DECT data was performed using software (syngo.via, VB10B, Siemens) and an application (CT Dual energy). Two types of reconstructed image sets were used for analysis: (a) 151 sets of VMI at energies ranging from 40 to 190 keV and (b) color-coded iodine overlay images. A circular region of interest (ROI) were drawn to encompass as much of the lesion as possible (mean area, 5.3 cm^2; range, 0.6–10.9 cm^2) on the 70 keV images [10,19,20]. A 2-cm^2 circular ROI was placed in the suprarenal abdominal aorta as a reference [15]. All of the ROIs were automatically copied onto all of the VMI. The 70 keV images with section positions and ROIs were saved in the picture archiving and communications system (PACS) (Impax 5.3, Agfa, Mortsel, Belgium). The ROIs with the same sizes and shapes as on the VMI were drawn on color-coded iodine overlay images using the saved 70 keV images on a separate screen. For each ROI, the CT value and its standard deviation (SD) and the iodine concentration (in milligrams per milliliter) were calculated automatically on the 40–190 keV images and color-coded iodine overlay images, respectively. CT and SD values were exported to a Microsoft Excel spreadsheet, and those at 40 keV and 50–130 keV (20-keV interval) were recorded. The syngo.via also automatically generated a spectral attenuation curve for each ROI. The slope (k) of spectral curve was calculated as follows: k = (CT value^{40} − CT Value^{110})/70 keV, where CT value^{40} and CT Value^{110} referred to the measured CT values in Hounsfield Units at the 40 and 110 keV images, respectively [18]. The iodine concentration (IC) of the lesions was normalized to values in the aorta to derive a normalized iodine concentration (NIC): NIC = IC^{lesion}/IC^{aorta} [15] (Figs. 2 and 3). The ROIs with the same sizes and shapes as on the VMI were also drawn