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Computed Tomography Perfusion Imaging for the Diagnosis of Hepatic Alveolar Echinococcosis

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ABSTRACT

Objective: Alveolar echinococcosis (AE) is a rare life-threatening parasitic infection. Computed tomography perfusion (CTP) imaging has the potential to provide both quantitative and qualitative information about the tissue perfusion characteristics. The purpose of this study was the examination of the characteristic features and feasibility of CTP in AE liver lesions.

Material and Methods: CTP scanning was performed in 25 patients who had a total of 35 lesions identified as AE of the liver. Blood flow (BF), blood volume (BV), portal venous perfusion (PVP), arterial liver perfusion (ALP), and hepatic perfusion indexes (HPI) were computed for background liver parenchyma and each AE lesion.

Results: Significant differences were detected between perfusion values of the AE lesions and background liver tissue. The BV, BF, ALP, and PVP values for all components of the AE liver lesions were significantly lower than the normal liver parenchyma ($p<0.01$).

Conclusions: We suggest that perfusion imaging can be used in AE of the liver. Thus, the quantitative knowledge of perfusion parameters are obtained via CT perfusion imaging.

Keywords: Liver, alveolar echinococcosis; computed tomography perfusion imaging

Introduction

Alveolar echinococcosis (AE) is a rare parasitic infection that can be life threatening [1, 2]. The metacestode of *Echinococcus multilocularis* (EM) causes infection in humans. Their growth is slow and progressive similar to some liver tumors [3, 4]. This disease is seen in endemic areas of the northern hemisphere [2, 5, 6]. AE treatment includes benzimidazole derivatives, percutaneous drainage, and surgical resection. In non-resectable cases, liver transplantation is the last resort. This disease may lead to liver failure and even death if left untreated [3, 4].

Radiological imaging methods, including ultrasonography (US), magnetic resonance imaging (MRI), and computed tomography (CT) provide valuable information for the detection and characterization of AE lesions as well as for the determination of an appropriate treatment method [4, 7-9]. US is the first-line screening method for imaging in AE. However, US is constrained in recognizing AE sores with sanctums and broad calcification [3, 4, 9]. A CT is useful for evaluating lesions, particularly for dense peripheral calcification. Fibrous tissue calcifications seen in a CT scan might be useful for differentiating between liver AE lesions and other liver lesions. However, in some cases of AE, it may not be possible to completely differentiate a lesion from a tumor. MRI is useful for characterizing components of the parasitic mass [3, 4, 10]. It has been reported that the lesions' MRI findings are similar to other lesions, such as metastases and liver malignancies [3, 4, 10, 11].

Computed tomography perfusion (CTP) is a new imaging modality that allows functional assessment. CTP provides some parameters such as the portal liver perfusion (PLP), mean transit time (MTT), blood flow (BF), blood volume (BV), hepatic perfusion Index (HPI), and arterial liver perfusion (ALP). This imaging technique has the potential to provide both quantitative and qualitative information about tissue perfusion characteristics [12-21].

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Inspired by this information, our aim was to investigate the characteristic features and feasibility of CTP in hepatic AE lesions.

Materials and Methods

Patients

This was a prospective study performed on patients from September 2012 to September 2016. This study was approved by the local ethics committee, and written informed consent was obtained from all patients before starting the study. Patients diagnosed with AE, who had at least two of the following characteristics were included: (1) histopathological findings suggestive of EM; (2) EM-specific serum antibodies detected in a high-sensitive blood test; and (3) detection of nucleic acid from EM in a clinical specimen. A total of 52 consecutive patients (21 females and 32 males; median age, 52 years (3865 years]) were enrolled in the study.

Patients who had calcific components (n=−12), were allergic to the contrast material (n=2), recurrent disease following a percutaneous intervention or surgical resection (n=2), signs of vascular invasion (n=1), were unwilling to consent (n=1), a creatinine level above 2 mg/dL, heart failure (n=1), preexisting known liver disease (n=1), body mass index >35 kg/m^2 (n=3), chronic liver failure (n=1), or motion artifacts (n=3) were excluded.

Computed tomography perfusion imaging characteristics of the remaining 25 patients with 35 AE lesions were evaluated. The diagnosis of AE was confirmed by biopsy in all cases (Figure 1).

CTP technique

All CTP examinations were performed using a second-generation Somatom-Definition-Flash CT scanner (Siemens, Forchheim, Germany). The imaging protocol is provided in Table 1. Because the lesions showed lobar involvement in some cases and because there were multiple lesions in some others, the entire liver was included in the scanning area.

Imaging analysis

The maximum slope technique was used to compute the perfusion parameters [22, 23]. All the CTP image series were analyzed by two radiologists. The first reader (reader 1 [M.K]) who had 10 years of experience in hepatobiliary radiology and the second reader (reader 2 [R.S]) who had 4 years of experience in hepatobiliary radiology analyzed the CTP images. The size, localization, number, and perfusion characteristics of the lesions were evaluated. The interobserver agreement was also evaluated (Table 1). The functional maps had a color scale ranging from red to purple, with red showing the lowest and the purple showing the highest border of the display for the BF, BV, ALP, PLP, and HPI color maps.

Region of Interest (ROI) technique

Arterial liver perfusion, BF, BV, PLP, and HPI were used as CTP parameters with the help of a software. For AE lesions, the ROI (mean, 140 mm^2) was manually drawn from different sites of solid components of each lesion, which did not contain calcification, necrosis, normal parenchyma, and a vascular component (Figure 2). ROIs were drawn from 3 different areas if lesion was <5 cm and from 6 different areas if lesion was >5 cm. The mean values of all lesions were used in the analysis. For background liver, the ROIs were drawn from 3 different areas in the liver parenchyma (mean, 140 mm^2) that was far away from the capsule (>1 cm) and diaphragm (>2 cm) and did not contain vascular structures (Figure 3), and the mean perfusion parameters were calculated for 3 sections for the background normal liver in patients with AE.

Statistical analysis

The statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) 20.0 version (IBM Corp, Armonk.; NY, USA)). The normality of the data was analyzed using the Kolmogorov–Smirnov test.

The one-way Anova with Bonferroni correction method was used to compare the CTP parameters obtained from the different components of alveolar echinococcosis with background liver. All the values of the patients were calculated for each comparison; p values less than 0.05 were considered statistically significant.

Interobserver agreement was assessed adequate for inclusion in each patient by using the intraclass correlation coefficient (ICC) with 95% confidence intervals and applying one-way ICC to assess interobserver agreement [24]. The p values less than 0.05 were considered significant.

Results

We studied 35 AE lesions in 25 patients, which were proven by biopsy. The mean diameter of the AE lesions was 8.4 cm (range, 5.0–18.5 cm). All AE lesions had an irregular contour. Of the 35 AE lesions, 28 (80%) were located in the right lobe, while 7 (20%) were in the left lobe. Of 35, 12 (34.2%) AE lesions were solid without calcific and cystic components, while the remaining 23 (65.8%) had cystic components. In 17 patients, complete surgical excision and antihelmintic therapy (albendazol) was conducted. Three patients underwent a partial resection and albendazol therapy. Four patients underwent liver transplantation because the parasitic mass was unresectable.

Comparison of CTP Parameters between Alveolar Echinococcosis and Background Liver

Interobserver agreement was high for all perfusion parameters (Table 1).

The values of CTP for AE lesions are shown in Table 2. Background liver demonstrated higher BF, BV, ALP, and PVP values than all components of AE (p<0.001). No significant differences were found between the perfusion values of the background liver and AE with respect to HPI (p>0.05).

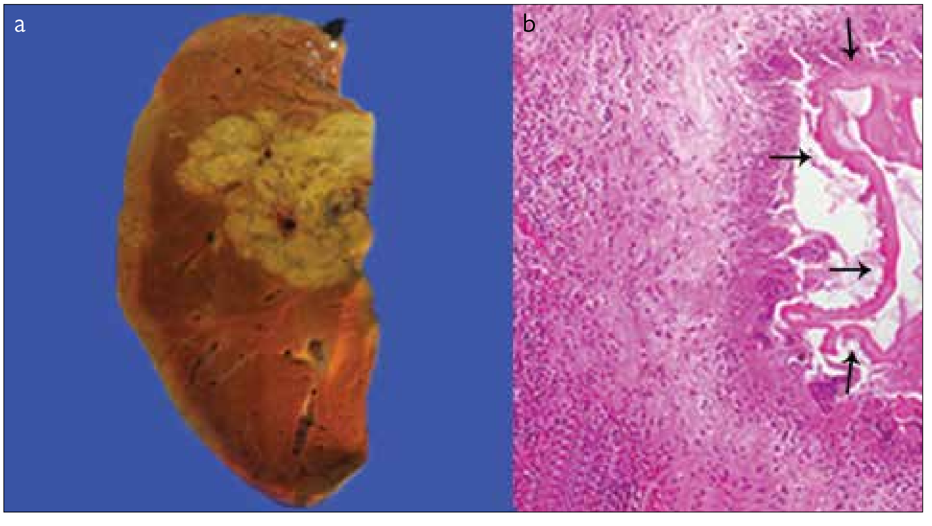

Figure 1. a, b. Photograph of an axial cross sectional (1 cm thickness) specimen enucleated from the liver shows a well-demarcated solid lesion and normal liver parenchyma (a), photomicrograph (original magnification, 10×; hematoxylin-eosin stain) shows alveolar echinococcosis vesicles with laminar membranes (arrows) (b)

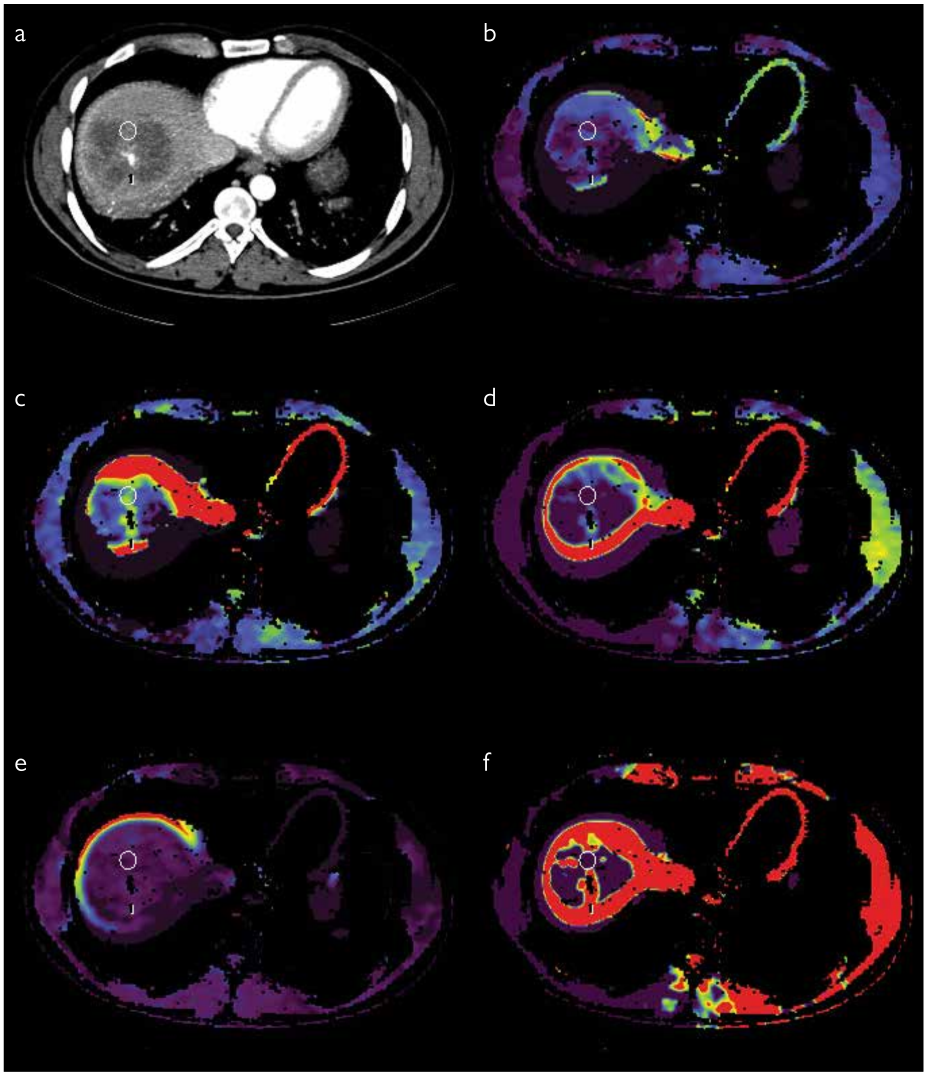

Figure 2. a-f. The patient has a non-well-circumscribed heterogeneous hypodense infiltrative lesion on the gray scale axial CT image (a), axial CTP functional maps of the BF (b), BV (c), ALP (D), PVP (E), and HPI (F) in a 59-year-old man show an alveolar echinococcosis (AE) lesion in the right lobe of the liver (A) that has a distinct range of colors compared with the background liver parenchyma. Perfusion values from an ROI (145 mm2) drawn in the solid component without calcification of AE (ROI 1)

Table 1. Contrast and computed tomography perfusion parameters

Contrast medium	iopromide (Ultravist 370 mg/mL, Bayer, Berlin, Germany)
Contrast volume	50 mL
Contrast velocity	4.5 mL/s
Scanning area	16-cm area (from the subdiaphragmatic area to the lower hepatic rim)
Tube potential	80 kVp
Effective tube current	100 mAs/rot
Slice acquisition	128 mm×0.6 mm
First scan time	6 seconds after contrast injection
Number of scans	26
Total examination time	45 seconds

Discussion

AE lesions of the liver are characterized by a multi-vesicular structure surrounded by a large, solid fibro-inflammatory tissue [3, 4]. The prognosis is dismal unless diagnosed and treated in a timely manner. Because there are no clinical signs accompanying this disorder, it may not be accurately differentiated from malignant lesions of the liver even with MRI and CT, particularly in non-endemic areas [7, 25].

Kodoma et al. [10] reported a marked contrast uptake in a small part of some AE lesions. Bredson Hadni et al. [3] also demonstrated an intense, prolonged peripheral contrast uptake characteristic of neovascularization in contrast-enhanced MRI of some AE lesions in the liver. Based on these findings, we employed the CTP technique to visualize AE lesions of the liver.

Computed tomography perfusion is a recently developed method that allows quantitative evaluation of hemodynamic changes in tissue. This imaging modality is used to calculate certain perfusion parameters in pathologic and normal tissues of many organs [13-15, 20]. Using CTP, parameters, such as the BF, BV and MTT can be evaluated noninvasively and quantitatively. In addition to these CTP parameters in the liver, the ALP, PLP, and HPI can be assessed noninvasively. We observed a significant drop in the CTP parameters including the BV, BF, ALP, and PVP in AE lesions compared with background liver. The HPI value was not significantly different. Therefore, we think that the AE lesions have less arterial and portal blood flow than background liver parenchyma. BV, BF, ALP values increase in HCC, cholangiocarcinoma, and liver tumor metastasis [26].

The differential diagnosis of liver AE includes other infiltrative hepatic lesions. Moreover, the percutaneous needle biopsy might be contraindicated in some cases, such as HCC; due to the presence of tumor seeding. Thus, we should distinguish between benign and malignant liver lesions before biopsy for histological diagnosis [10, 27].

This study has some limitations. First, it contained a limited sample size that reduced its statistical power. Further studies with a larger sample size may be needed. Second, we did not conduct a validation study or compare the results of CTP with a marker, such as microvessel density, which is a well-established marker for angiogenesis and used in many tumor studies. Third, the liver lesions in our study had different sizes. Therefore, no standard ROI of the same size could be drawn in every patient. Fourth, CTP imaging characteristics of benign hepatic lesions are less described in the literature. Therefore, we did not compare the results of CTP with other liver lesions. Fifth, CTP has a high radiation dose. Lastly, we were not able to follow-up with the patients because follow-up would have to be carried out over a prolonged period.

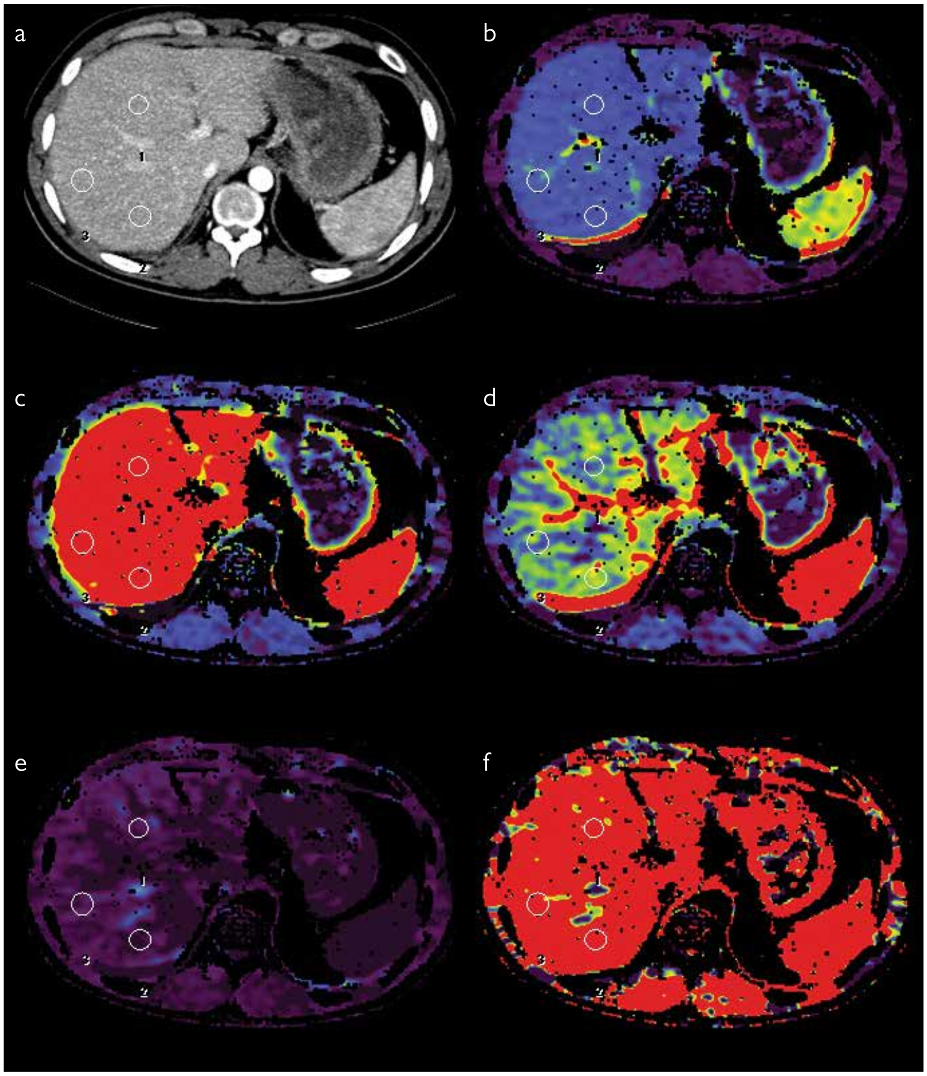

Figure 3. a-f. A 59-year-old man with an alveolar echinococcosis (AE) lesion. Axial CT image (a), axial CT perfusion functional maps of the BF (b), BV (c), ALP (d), PVP (e), and HPI (f) in the background liver parenchyma. Perfusion values from the ROI (135-142 mm2) drawn for normal liver parenchyma (ROI 1, 2, 3) that was far away capsule (>1 cm) and diaphragm (>2 cm) and did not contain vascular structures

Table 2. CT Perfusion Parameters of Alveolar echinococcosis and Background Liver

CT perfusion Parameters	Alveolar Echinococcosis	Background Liver	p Value* for AE and Background liver
BV (mL/100 ml)	2.11 (0.84-5.23)	11.47 (10.05-14.19)	<0.01
BF (mL/100 ml/min)	6.17 (3.51- 6.90)	30.37 (20.12-41.10)	<0.01
PVP (ml(100 ml/min)	4.30 (2.46-6.91)	14.58 (2.45-38.60)	<0.01
ALP (ml(100 ml/min)	4.34 (1.31-13.23)	16.14 (6.96-23.50)	<0.01
HPI (%)	61.05 (38.02-95.01)	50.51 (23.24-88.73)	<0.05

*p value of ≤ 0.05 indicates a significant difference

In conclusion, our study suggests that CTP is a feasible method for quantitatively assessing AE lesions of the liver. The current study showed lower BF, BV, ALP, and PLP values in AE lesions compared with background liver. Thus, CTP enables the quantitative evaluation of liver AE lesions and can facilitate a differential diagnosis between malignant liver lesions and AE by adding only a few seconds to a routine CT.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Atatürk University (15.08.2017/3/18).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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