Original Article

The Utility of Apparent Diffusion Coefficient in Diagnosis of Acute Cholecystitis

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Abstract

Background: Acute cholecystitis (AC) is a very common gastrointestinal pathology. Patient's history, physical examination, and laboratory investigations are usually not sufficient for accurate diagnosis. Moreover, imaging findings can overlap with that of many other gallbladder pathology especially chronic cholecystitis (CC). Therefore, there is a reasonable necessity for new diagnostic tools for AC. **Objective:** This study aimed to evaluate the efficiency of the apparent diffusion coefficient (ADC) as a diagnostic tool for AC and differentiating it from CC. **Materials and Methods:** During the period from April 2017 to March 2018, a total of 62 patients with suspected cholecystitis were enrolled in this prospective cross-sectional study. Patients were subjected to diffusion-weighted imaging, from which the ADC values were calculated. All patients were then undergone laparoscopic or open cholecystectomy, and the diagnosis of AC or CC was proven through histopathological examination. Receiver operating characteristic analysis was used to find out the area under the curve (AUC), sensitivity, and specificity of ADC in the diagnosis of AC. **Results:** The average value of ADC from three regions of interests from patients with AC was $1.434 \pm 0.31 \times 10^{-3}$ mm^2/s. On the other hand, the average ADC from CC was $2.032 \pm 0.31 \times 10^{-3}$ mm^2/s with significant difference ($P = 0.013$). The AUC was 0.803, 95% confidence interval = 0.702–0.905, $P < 0.001$, with a sensitivity and a specificity of the test at 1.94×10^{-3} mm^2/s cutoff value were 0.70 and 0.73, respectively. **Conclusions:** These results indicate a good diagnostic value of ADC in discrimination between acute and CC. Further studies using contrast media are required for more accurate evaluation of ADC as a diagnostic tool for AC.

Keywords: Acute and chronic cholecystitis, apparent diffusion coefficient, receiver operating characteristic

Introduction

Of most patients admitted with gastrointestinal diseases, acute cholecystitis (AC) is the major complaint.[1] These patients warrant urgent intervention, typically via prompt laparoscopic cholecystectomy.[2] Otherwise, there will be several serious complications such as gallbladder (GB) perforation, bile duct injury, and hemorrhage.[3] The accurate diagnosis of AC is usually challenging because the overlapped clinical manifestations and imaging findings with many GB pathologies especially chronic cholecystitis (CC).[4] In this regard, the sensitivity of abdominal ultrasonography and computed tomography in the detection of AC were found to be 37.5%–91% and 83%, respectively.[5,6] Furthermore, no individual history, physical examination, laboratory finding has adequate accuracy for diagnosis of AC.[7] As such, the proper detection and management of patients with AC, particularly those at risk of severe cholecystitis, is an utmost necessity.

Recent advances in imaging technology, of course, contribute significantly in better diagnosis of AC. Of particular interest is the advancement in magnetic resonance imaging (MRI) through the application of diffusion-weighted imaging (DWI). This technology is based on detection of changes in the tissue structure at the molecular levels.[8] DWI can identify the areas with a high signal intensity which correspond inflammatory and malignant lesions.[9] Images taken through this technique are quantitatively evaluated by their conversion into apparent diffusion coefficient (ADC) maps.[10]

The ADC was recently used as a diagnostic tool for detection of a large number of pathologies such as breast cancer, intervertebral disc generation and high-grade glioma and

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brain metastasis[11-13] with varying degree of efficiency. However, there is a paucity in reports about using ADC maps for diagnosis of AC. Thus, this study aimed to evaluate the diagnostic efficiency of ADC in the detection of AC among a sample of Iraqi patients.

Materials and Methods

The study population

During the period from April 2017 to March 2018, a total of 62 consecutive patients (32 females and 30 males) were enrolled in this prospective cross-sectional study. All those patients were admitted to the Gastroenterology and Hepatology Teaching Hospital/Medical City/Baghdad with preliminary diagnosis of AC based on clinical manifestations, laboratory findings, and ultrasonography. All patients were undergone cholecystectomy during which GB specimens were taken and fixed in 10% formalin for a histopathological examination. Inclusion criteria were patients with suspected AC who were scheduled to undergone cholecystectomy and those with thickened GB wall measuring >3 mm according to imaging finding. Exclusion criterion was patients with confirmed GB cancer.

Imaging technique

A written consent was obtained from all participants before MRI. Abdominal MRI was applied for all patients. MRI was performed on 1.5-T MR unit (Philips 1.5 Tesla scanner using Acheva software [Philips Medical System/Holland]). Patients were placed in a supine position on an extended table platform to allow full body scanning. The axial T1-weighted images were obtained with imaging parameters of 500/14–15 repetition time/echo time (TR/TE), a slice thickness of 5 mm, an interslice gap of 1.5 mm. For T2-weighted spin-echo, images with imaging parameters of 4000/102–105 (TR/TE), a slice thickness of 5 mm, an interslice gap of 1.5 mm, and DWIs with imaging parameters of 5000/101–118 (TR/TE), a slice thickness of 5 mm, an interslice gap of 1.5 mm, bandwidth of 79 kHz, duration of diffusion gradients of 31 ms, and gradient separation of 42 ms, in three directions.

Image analysis

In patients, the largest circular region of interest (ROI) was defined as the thickest hyperintensive GB wall compared to GB content on ADC maps. According to the application area, ROI was taken between 14 and 48 mm^2. In CC patients, ROIs were between 20 and 49 mm^2. The ADC maps and values were calculated on a workstation. The ADC values were calculated as average from ROIs using the exponential fitting algorithm as a function of b value (b = 0, 200 and 800).

Statistical analysis

Statistical package for social sciences (SPSS) version 2015 (IBM SPSS Statistics, IBM company, USA) was used for all analyses. Descriptive variables were expressed as mean, standard deviation, range, and median, and were analyzed with independent student's t-test. Binomial variables were expressed as number and percentages and analyzed with Chi-square which. Receiver operating characteristic (ROC) curve was used to find the area under the curve (AUC), sensitivity, specificity, and cutoff value of ADC. The level of significance was set at $P < 0.05$.

Results

Six patients out 62 were excluded because the diagnosis could not be made with histopathological examination. Furthermore, the histopathological examination revealed only 42 patients had AC while the other remaining 14 patients had CC. The main demographic, clinical and laboratory characteristics for the eligible patients are presented in Table 1. According to the data in the table, there were no significant differences between acute and CC in all the studied characteristics. Radiological signs of the AC and CC patients are shown in Table 2.

Patients with AC showed lower values of ADC compared to CC. The average value of ADC from three ROIs from patients with AC was $1.434 \pm 0.31 \times 10^{-3}$ mm^2/s (range $1.02–2.03 \times 10^{-3}$ mm^2/s). On the other hand, the average ADC from CC patients was $2.032 \pm 0.31 \times 10^{-3}$ mm^2/s (range $1.87–2.69 \times 10^{-3}$ mm^2/s) with significant difference ($P = 0.013$) as shown in Figure 1.

ROC analysis was performed for ADC maps [Figure 2]. The AUC was 0.803, 95% confidence interval = 0.702–0.905, $P < 0.001$. The sensitivity and specificity of the test at 1.94×10^{-3} mm^2/s cutoff value were 0.70 and 0.73, respectively, indicating a good discriminative value.

Discussion

The current study revealed the good diagnostic value of ADC to discriminate between AC and CC ($1.52 \pm 0.31 \times 10^{-3}$ mm^2/s

Table 1: Main demographic, clinical and laboratory characteristic for patients with acute and chronic cholecystitis

Variables	Acute cholecystitis (42)	Chronic cholecystitis (14)	P
Age, years (mean±SD)	52±14.8	48.2±12.6	0.139
Gender (%)			
Male	23 (54.76)	6 (42.86)	0.404
Female	19 (45.24)	8 (57.14)	
BMI, kg/m^2 (mean±SD)	27.18±4.46	26.9±6.14	0.476
Comorbidity (%)			
DM	13 (30.95)	2 (14.29)	0.202
HTN	9 (21.43)	2 (14.29)	0.55
ASA score ≥3	8 (19.05)	3 (21.43)	0.847
Lab results (%)			
WBC >18,000/mm^3	9 (21.43)	1 (7.14)	0.192
Serum bilirubin >50 IU/L	12 (28.57)	1 (7.14)	0.072

SD: Standard deviation, BMI: Body mass index, DM: Diabetes mellitus, HTN: Hypertension, ASA: American Society of Anesthesiologists, WBC: White blood corpuscle

Table 2: Radiological signs of acute and chronic cholecystitis

Radiological findings	Acute (total 42)	Chronic (14)
Plain X-ray abdomen	3 patients visible stones 2 patients dilated air-filled gallbladder with air in wall	One patient porcelain gallbladder seen as plaque of wall calcification
Ultrasound	39 patients have gall stones 35 patients wall thickening >3 mm 25 patients gallbladder distention 38 patients positive sonographic Murphy sign 21 patients pericholecystic 17 patients perihepatic (C sign) fluid	14 patients thick wall with gall stones 5 patients nonmotile contracted gallbladder
CT scan	23 patients Pericholecystic inflammatory fat stranding 30 patients hypo- or hyper-attenuating gallstones 26 patients had thick wall with edematous hyperattenuation of the hepatic gallbladder fossa 3 patients intramural gas emphysematous gallbladder 1 patient showed irregular or discontinuous mural enhancement (gangrenous gallbladder)	1 patient porcelain gallbladder seen on CT as plaques or punctate foci of mural calcification 1 patient mirizzi syndrome
MRI	36 patients showed Mural T2- hyperintensity 32 patients had mural hyperenhancement 27 patients mural striation 34 patients had low apparent diffusion coefficient	12 patients had thick gallbladder wall 8 patients showed low enhancement 11 patients had high apparent diffusion coefficient
Cholescintigraphy	Biliary excretion of radioisotope within10 min of injection in the absence of isotope accumulation in the gallbladder within 1 hour is typical of acute cholecystitis	Delayed gallbladder isotope accumulation, irregular gallbladder filling, or a gallbladder ejection fraction of <35% after the administration of cholecystokinin

CT: Computed tomography, MRI: Magnetic resonance imaging

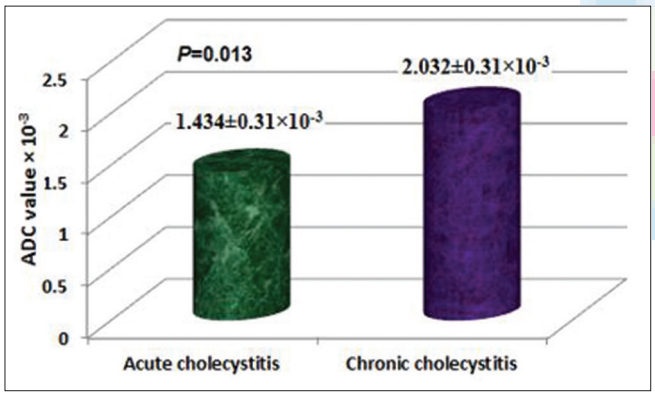

Figure 1: Mean apparent diffusion coefficient values in patients with acute and chronic cholecystitis

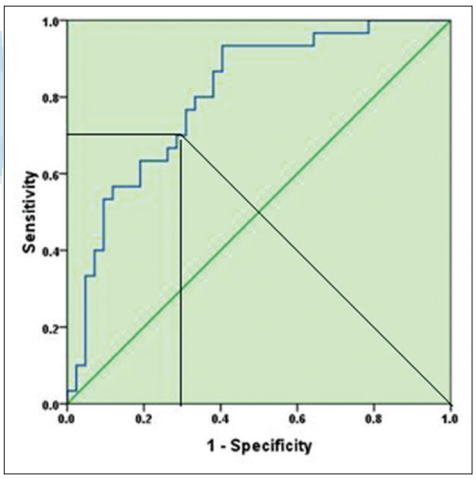

Figure 2: Receiver operating characteristic for the apparent diffusion coefficient as a diagnostic tool for acute cholecystitis

vs. 2.39 ± 0.31 × 10^{-3} mm^2/s) with 70% sensitivity and 73% specificity at cutoff value of 1.94 × 10^{-3} mm^2/s.

These results are comparable with that obtained in a Turkish study including 40 patients with AC and 18 patients who had a thickening in the GB wall due to cirrhotic ascites. The study revealed a significantly lower mean ADC among AC patients (1.68 ± 0.36 × 10^{-3} mm^2/s) than CC patients (2.35 × 10^{-3} mm^2/s). Using ROC curve, the authors demonstrated higher sensitivity and specificity for this technique (94% and 89.7%, respectively) than the current study.[14]

Also in agreement with the current study is a recent study conducted by Tomizawa *et al*.[9] who investigated 11 Japanese patients with AC using MRI with background signal suppression/T2 image fusion (DWIBS/T2). Ten/eleven patients were successfully detected by this technique, with 90.9% sensitivity. Consequently, the authors recommended the use of such technique for evaluation of the severity of AC. In the same regard, a recent study by Kitazume *et al*.[10] recommended using ADC to differentiate benign GB pathologies including AC from malignant disorders.

Another recent study aimed to evaluate the efficiency of DWI to discriminate between acute and CC in comparison to conventional MRI. In this study, 83 American patients with abdominal pain were recruited, and the imaging findings were read by two radiologists.[3] The quantitative ADC values did not differ significantly between acute and CC for either radiologists

(radiologist 1: $1.86 \pm 0.53 \times 10^{-3}$ mm^2/s vs. 2.04 ± 0.6110^{-3} mm^2/s, $P = 0.139$; radiologist 2: 1.8 ± 0.4610^{-3} mm^2/s vs. 1.63 ± 0.4910^{-3} mm^2/s, $P = 0.104$).

Finally, a retrospective study including 40 Japanese patients with different GB lesions was performed to assess the utility of ADC measured from high *b* value DWI in the differential diagnosis of cancer, adenoma, and inflammatory diseases affecting GB.[15] Interestingly, the study found significant differences in ADC values between these pathologies, where adenoma had the greatest value ($2.66 \pm 0.43 \times 10^{-3}$ mm^2/s) followed by inflammatory diseases ($1.47 \pm 0.54 \times 10^{-3}$ mm^2/s) and finally GB cancer ($1.31 \pm 0.5 \times 10^{-3}$ mm^2/s).

The technical principle of DWI is based on the motion of water molecules which is also known as Brownian movement. Within biological tissues, the microstructural barriers such as cell membranes, intracellular organelles, macromolecules, and other tissue compartments impede water movement.[16] Therefore, tissues with higher cellularity increased nuclear to cytoplasmic ratio, and the presence of intact cell membranes have a greater diffusion restriction with a corresponding decrease ADC value.[17] The significantly higher ADC value for CC than AC in the current study can be attributed to the nature of inflammatory infiltrate in GB wall in these two types of inflammation. In AC, the predominant feature is congestion; acute inflammatory infiltrates especially with neutrophils and macrophages, and fibroblast proliferation.[18,19] This feature with high cellular aggregation results in restricted diffusion, manifesting as high *b* value diffusion-weighted MRI and low corresponding ADC values. On the other hand, different degree of fibrosis, Rokitansky–Aschoff sinuses, and mild cellular infiltrate are the characteristic feature of CC.[19,20] With the relatively less cellular infiltrate, there will be low *b* value and high corresponding ADC.

Conclusions

These data indicate a good diagnostic value of ADC in discrimination between acute and CC. Further studies using contrast media are required for more evaluation of ADC as a diagnostic tool to differentiate AC from other pathologies associated with GB wall thickening other than CC such as pancreatitis, hepatitis, and pyelonephritis,[21] and to compare the efficiency of this technique with the other most common diagnostic methods such as ultrasound, computed tomography scan, and conventional MRI.

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Conflicts of interest

There are no conflicts of interest.

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