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ROLE OF MAGNETIC RESONANCE IMAGING IN PREDICTING INFECTION IN PANCREATICO-BILIARY DISEASES

Radiodiagnosis

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ABSTRACT

Background: Acute Pancreatitis has been defined as an acute, mainly diffuse, inflammatory process of the pancreas with associated intermediate (2-5 weeks) complications like infected necrosis, pancreatic abscesses, etc. Biliary infections or ascending cholangitis is a clinically defined syndrome caused by complete / or partial biliary obstruction with associated ascending infection from the intestine.

Materials and Methods: Study comprised of 31 patients [22 with biliary system collections and 9 with pancreatic collections were prospectively scanned using an integrated MR examination that included T1 weighted, T2 weighted, and Diffusion weighted echo planer imaging (DW-EPI) sequences. All the patients were subjected to radiological intervention drainage/aspiration procedure within 48-72 hrs of the imaging study for their management.

Results: DW-EPI data of 31 patients with pancreatico-biliary collections 12 were microbiologically proven infected and 19 were sterile. 8 among the 12 showed diffusion restriction on ADC while 4 showed T2-shine through effect. Remainder of 19 patients with microbiologically proven sterile collections reveals absence of any restriction.

Conclusions: Based on Receiver operator curve (ROC) analysis, at ADC levels <3, the sensitivity of the test was 75% while specificity was 63.16%. The negative predictive value was reasonably high (80%). Thus the test could be used efficiently as a screening tool.

KEYWORDS

DW-EPI, ADC, ROC.

INTRODUCTION

Acute Pancreatitis

has been defined as an acute, mainly diffuse, inflammatory process of the pancreas that exhibits great variations in the degree of involvement of gland, the adjacent retroperitoneal tissues and other distal organs.[1-3] The classification proposed in 1992 by the Atlanta International Symposium on Acute Pancreatitis has classified it into – Mild Acute Pancreatitis which occurs in majority 75-80% and Severe Acute Pancreatitis seen in minority of patients.[1-3] Various associated intermediate (2-5weeks) complications of Acute Pancreatitis, are – infected necrosis, pancreatic abscesses, pseudocyts, local retroperitoneal infections, gastrointestinal and biliary complications, and solid organ involvement[4]

The early detection and treatment of local complications is essential because they are responsible for > 50% of the mortality reported in Acute Pancreatitis.[5-9]

Infectious cholangitis

is bacterial ascending infection is a clinically defined syndrome caused by complete / or partial biliary obstruction with associated ascending infection from the intestine.[10] While it can be caused by variety of organisms most often it is due to E. Coli infection.[11] The most consistent imaging findings in infectious cholangitis is generalized / or segmental biliary dilatation that can be mild / or severe but does not correlate well with the severity / or stage of the disease.[12]

Reddy et al (2006) carried out the study with the objective to evaluate the sensitivity and specificity of DWI in differentiating brain abscesses from other intracranial cystic lesions.

Lesions appearing hyperintense on DWI with the ADC values of lower than 0.9 +/- 0.13 x 10(-3) mm(2)/s (mean +/- SD) were considered as brain abscess, whereas hypointense lesions on DWI with the ADC values 2.2 +/- 0.9 x 10(-3) mm(2)/s were categorized as nonabscess cystic lesions. The sensitivity of DWI for the differentiation of brain abscesses from nonabscesses was 96%; specificity, 96%; positive predictive value, 98%; negative predictive value, 92%; and accuracy of the test, 96%. They concluded that diffusion-weighted imaging has high sensitivity and specificity for the differentiation of brain abscess from other nonabscess intracranial cystic lesions.[13]

Magnetic resonance imaging (MRI) has the potential for early detection of infection in pancreatic and biliary diseases. Therefore this study has been under taken to assess feasibility of MRI to detect infection at earlier stage for accurate timing of their management.

AIMS AND OBJECTIVES

To confirm the findings of MRI by image guided aspiration/drainage and its microbiological examination from the suspected site of pancreatic or biliary infection.

MATERIAL AND METHODS

The present study was conducted over the period of two years at the Department of Radiodiagnosis, Dr. Ram Manohar Lohia Institute of Medical Sciences (DRRMLIMS), Lucknow in patients with pancreatico-biliary diseases.

There were 31 patients with pancreatico-biliary collections (13 male & 18 female). Among which12 were microbiologically proven infected. The final diagnosis of infection in aspirated fluid was considered when it fulfilled the one or more of the following criteria:

1. Demonstration of organism on gram-staining, and
2. Growth of organism on culture
3. Pus cell count more than or equal to 5 pus cells per high power field

In remaining 19 patients the fluid collection did not grow any microorganism and was termed sterile. Microorganisms cultured were Escherichia coli, Enterococcus faecium, Staphylococcus aureus, Pseudomonas aeruginosa, Enterobacter cloacae. Some of these patients were on antibiotics for the variable period of time prior to study.

The MR imaging was performed on a 3T MR scanner (Signa LX, General Electrical Medical systems, Milwaukee, US) equipped with high-speed gradients. A torso-phased array coil and body coil were used for data acquisition.

Single shot fast spin echo (SS-FSE) T2 three-plane localizerT2 weighted FSE pulse sequences in axial plane. Pre-contrast axial T1 weighted FSPGR sequences (FA-100, TR-6.7ms, TE-2.8ms, FOV-35 x 26 , effective slice thickness 5 mm, matrix 256 x 128) were also obtained. No oral contrast was given.

Images were acquired in coronal or coronal oblique planes using

heavily T2-weighted single shot FSE pulse sequences with the following imaging parameters, for thick slice: effective TE 1400 ms; TR 4800 ms; matrix size-256 x 224, field of view-28 x 28 cm, slice thickness 30-40 mm 3D. For thin slices: effective TE 90 ms; TR 4000 ms; matrix size-256×224, field of view-28 x 28 cm, slice thickness 3.0 mm.

Diffusion–weighted echo-planar imaging (DW-EPI) in the axial plane (using body coil) was performed using a single shot EPI-SE pulse sequence with TR/TE = 6-10 sec/110ms (minimum), Field of view = 24×24 cm, slice thickness=10mm, matrix size of 128×256. Diffusion sensitizing gradients were sequentially applied along the three orthogonal directions with diffusion- weighing factor (b) of b=1000 and 800 s/mm^2. Ramp sampling was done to reduce the echo spacing thereby minimizing the geometric distortion.

In view of research work to evaluate the ability of MRI to detect presence or absence of infection in pancreatico-biliary collections we had tried to found the relationship between the ADC values and micro-biological nature (infected or sterile) in collection fluid (pancreatic fluid or bile). Image guided aspiration / or drainage procedure was performed in all 31 cases and aspirated fluid was collected. In all cases, collection fluid (pancreatic/biliary) was used as inoculus for BACTEC culture bottles for culture (aerobic and anaerobic).

Image analysis of the DW-EPI data: ADC map was generated on a pixel-by-pixel basis using: $ADC = b^{-1} \ln (S0/S)$

Where: S0 and S represent the signal intensities of the image without and with diffusion weighted gradients. Using the segmentation procedure, the mean ADC's from the restricted, non-restricted and the whole abscess area were calculated. The unrestricted regions presumably represented the pus with necrotic inflammatory and neuronal cells. The restricted regions presumably represented inflammatory cells with intact cell membrane and nucleus and are referred to as viable cells. A region of interest (ROI) of ~ 0.5 cm2 in the area of high or low signal intensity was drawn on DWI images of each collection, and the mean ADC in the ROI from the restricted area will be referred to as the mean restricted ADC in the remainder of this research.

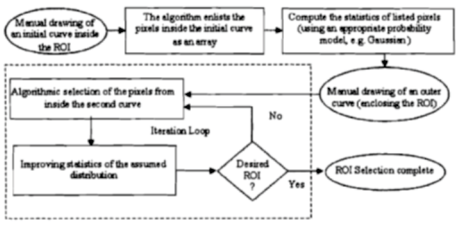
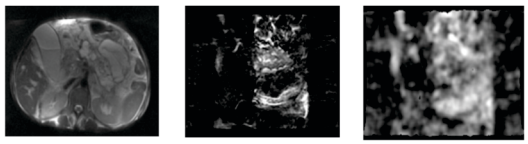


Figure 1: Flow chart of the procedure for calculating lesion volumes from a particular region of interest.

Microbiological Analysis of collection fluid: Culture of aspirated fluid: Immediately after aspiration from the abscess cavity, pus was injected into BACTEC plus aerobic, anaerobic media (Becton, Dickinson and company, Sparks: MD, USA) to isolate the aerobic, facultative anaerobic and anaerobic bacteria for diagnosis of the etiologic agents. The inoculated media were incubated at 3°C and growth was monitored in BACTEC 9050 for 5 days. Media with positive growth were sub-cultured on appropriate solid media and incubated aerobically and anaerobically at 3°C. Anaerobic incubation was carried out in jars filled with the gas mixture N2 (80-90%), C02 (5-10%) and H2 (5-10%) through an Anoxomat system (Mart® BV Microbiology, Holland). All the isolates were identified by standard biochemical tests.

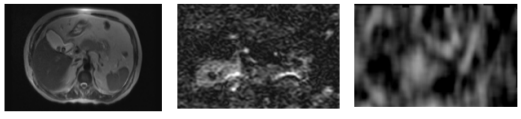
OBSERVATION AND RESULTS

DW-EPI data was acquired in 31 patients with pancreatico-biliary collections. There were 12 microbiologically proven infected pancreatico-biliary collections, heterogenous hyperintensity was seen in majority (n=8) of patients with collections on T2-weighted images (fig. 2a & 3a) as well as on DW images (fig. 2b & 3b) with corresponding heterogenous hypointensity on the ADC maps (fig. 2c & 3c) suggestive of restriction, while rest of minority (n=4) of patients with collections showed heterogenous hyperintensity on T2-weighted and DW images but no corresponding hypointensity, this probably because of "T2 shine through effect" on DW images. Remainder of 19 patients with microbiologically proven sterile collections, however, showed homogenous hyperintensity in all cases (n=19) on T2-weighted images (fig. 4a & 5a) as well as on DW images (fig. 4b & 5b) with no corresponding hypointensity on ADC maps (fig. 4c & 5c) suggestive of absence of any restriction.



2A 2B 2C

Fig. 2 Heterogenous pancreatic collections (acute fluid collections) in anterior relation to body and tail of pancreas in a patient with acute pancreatitis. T2-weighted axial MR image (a) shows an ill-defined varying sized hyperintense lesions that appear heterogeneously hyperintense on the diffusion-weighted image (b) and corresponding heterogenously hypointense on ADC map ©, suggesting heterogenous restricted diffusion in the collections.

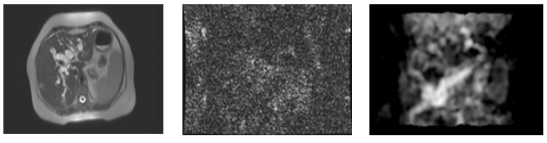


3A 3B 3C

Fig. 3Empyema gallbladder with few intraluminal calculi show homogenous hyperintense signal. T2-weighted axial MR image (a) shows a hyperintense signals from galbladder lumen. The lumen shows homogenously hyperintense signals on the diffusion-weighted image (b) and shows corresponding homogenous hypointense signals on the ADC map ©, suggesting homogenous restricted diffusion in the gallbladder lumen

4A 4B 4C

Fig. 4Pancreatic pseudocyst with homogenous hyperintensity in lesser sac. T2-weighted axial MR image (a) shows a well defined hyperintense lesion in lesser sac. The lesion appear homogenously hypointense on diffusion-weighted image (b) and shows corresponding homogenous hyperintensity on the ADC map (c) , suggestive of absence of any restricted diffusion in pseudocyst.



5A 5B 5C

Fig. 5Bilobar intrahepatic dilatation of biliary tree in a of patient carcinoma gall bladder and subsequent hilar block. T2-weighted axial MR image (a) shows homogenous hyperintense signals from biliary tree. The biliary tree appear homogenous hypointense on the diffusion-weighted image (b) and shows corresponding hyperintense signals from biliary tree on the ADC map ©, suggestive of absence of any restricted diffusion in biliary tree.

Evaluation of data done with the usage of the Receiver operator curve (ROC) analysis MRI data of all the 31 patients was reviewed for the topographical location of these lesions to ensure pancreatico-biliary location. In collection areas, with microbiologically proven infection on DW images shows two patterns (a) heterogeneously hyperintense signals – when the lesion contains both high and low signal intensities intermixed in variable proportion in collection cavity and (b) homogenous hypointense when the signal intensity of the lesion was homogenously low in the collection area and corresponding hypointensity or absence of hypointensity on ADC maps respectively.

The lesion was considered as bright if signal intensity on DWI over the lesion was higher as compared to the adjacent parenchymal tissue.

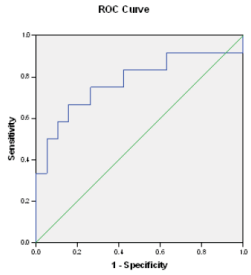


Fig: 6 Receiver-Operator Curve Analysis

Area Under the Curve

Test Result Variable(s): ADC ($x10^{-3}$ mm^2/sec.)

Area	Std. Error(a)	Asymptotic Sig.(b)	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.776	.096	.011	.589	.964

a. Under the nonparametric assumption
b. Null hypothesis: true area = 0.5

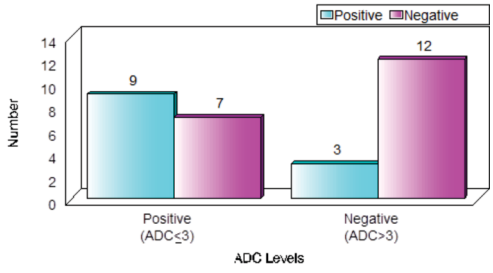
Receiver operator curve analysis showed an area of 77.6% under the curve, thus showing it to be a good predictor for diagnosing infection.

Table: Diagnostic Efficacy of Test at ADC cut-off <3.0

ADC Levels	Microbiological Findings		Total
	Positive	Negative	
Positive (ADC<3)	9 (a)	7 (b)	16 (a+b)
Negative (ADC>3)	3 (c)	12 (d)	15 (c+d)
Total	12 (a+c)	19 (b+d)	31

x^2=4.288 (df=1); p=0.038

Sensitivity= a/(a+c) = (9/12)x100=75%
Specificity= d/(b+d) = (12/19)x100=63.16%
PPV= a/(a+b) = (9/16)x100=56.25%
NPV= d/(c+d) = (12/15)x100=80%



At ADC levels ≤3, the sensitivity of the test was 75% while specificity was 63.16%. The negative predictive value was reasonably high (80%). Thus the test could be used efficiently as a screening tool, though high proportion of false negative (25%) are still an obstacle in its use as a routine marker to establish infection, however, with continuing studies on larger sample size, it is expected that a more efficient cut-off will be established.

DISCUSSION

Diffusion weighted imaging now forms the standard armory of MRI pulse sequences due to the impact it has made in the diagnosis of a number of neuropatholgies (Moseley *et al*., 1995, Schaefer *et al*., 2000 Sener RN, 2001, Mishra *et al*., 2004, Bukte *et al*., 2005). In this study we have assess the role of MR imaging in pancreatico-biliary disease and we have extrapolated the study and evaluated the results for the Pancreatico-biliary diseases.

Based on ROC analysis, at ADC levels ≤3, the sensitivity of the test was 75% while specificity was 63.16%. The negative predictive value was reasonably high (80%). Thus the test could be used efficiently as a screening tool, though high proportion of false negative (25%) are still an obstacle in its use as a routine marker to establish infection, however, with continuing studies on larger sample size, it is expected that a more efficient cut-off will be established. The current study has a few limitations. The number of patients in the study was relatively small, and we only studied symptomatic individuals. However, with continuing studies on larger sample size, it is expected that a more efficient results will be established.

CONCLUSION:

The result from the microbiologically proven sterile collections corresponds to observed high values of ADC on MR imaging. Thus proving absence of infection in collections. In conclusion, MRI in special reference to DWI and the calculation of the ADC may facilitate the quantitative analysis of infection in pancreatico- biliary diseases. Considering its relative light patient burden and non-invasiveness MRI may contribute to the early and timingly management of patients with pancreatico-biliary diseases.

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