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Diffusion-weighted imaging in quiescent Crohn's disease: correlation with inflammatory biomarkers and video capsule endoscopy

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AIM: To investigate the role of restricted diffusion in quiescent Crohn's disease (CD) patients and its association with inflammatory biomarkers and endoscopic disease.

MATERIAL AND METHODS: Fifty-two quiescent CD patients prospectively underwent magnetic resonance enterography (MRE) and video capsule endoscopy (VCE) and were tested for the inflammatory biomarkers, faecal calprotectin (FCP) and C-reactive protein (CRP). Restricted diffusion in the distal ileum was qualitatively (absence/presence) and quantitatively (apparent diffusion coefficient [ADC]) assessed by two readers. The VCE-based Lewis score was calculated for the distal ileum. Restricted diffusion sensitivity and specificity for VCE ulcerations were assessed for patients with elevated (>100 μg/g) or normal (<100 μg/g) FCP. Receiver operating characteristic (ROC) curve was used to assess the ability of ADC to identify patients with concurrent VCE ulceration and elevated FCP.

RESULTS: The sensitivity and specificity of restricted diffusion for patients with VCE ulceration were higher in patients with elevated FCP (reader 1: 71.4%, 80%, reader 2: 76.2%, 100%, respectively) compared to patients with normal FCP (reader 1: 46.2%, 61.5%; reader 2: 15.4%, 76.9%, respectively). The ADC had a high diagnostic accuracy for identifying patients that had concurrent VCE ulceration and elevated FCP (reader 1: AUC=0.819, reader 2: AUC=0.832).

CONCLUSION: In quiescent CD patients, the presence of restricted diffusion is suggestive of an active inflammation, associated with elevated FCP. Thus, DWI may serve as a clinical tool in the follow-up of these patients, implying subclinical inflammatory flares.

Introduction

Crohn's disease (CD) is a chronic, relapsing inflammatory disease characterised by transmural inflammation.[1] Accurate evaluation of disease activity encompassing radiographic, laboratory, and endoscopic techniques is crucial for treatment planning.[2] Magnetic resonance enterography (MRE) is increasingly used for evaluation of disease activity and is becoming the non-invasive technique of choice.[3]

Diffusion-weighted imaging (DWI) is based on the diffusion motion of water molecules, which displays information about the extracellular compartment, tissue cellularity, and the integrity of the cellular membranes.[4] In recent years, several studies investigated the role of DWI as a new imaging marker in CD.[2,3,5–16]

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Inflammatory biomarkers have a significant role in CD, and while many biomarkers have been evaluated, one of the most important is faecal calprotectin (FCP). This biomarker is a calcium and zinc binding protein constituting 60% of the neutrophil cytosolic proteins, and its production at sites of mucosal inflammation along the gastrointestinal tract allows for its detection in the feces.[17,18] FCP was shown to be useful for discriminating inflammatory bowel disease (IBD) patients from non-IBD diagnosis,[19] assessing disease activity,[20] and predicting relapses[21] and response to therapy in CD patients.[22,23]

To date, two studies have assessed the correlation between DWI and FCP in CD. One study found a correlation between ADC and FCP,[13] and a second study concluded DWI to be a reasonably sensitive tool for detection of bowel inflammation based on FCP, albeit with poor specificity.[24] FCP has been shown to correlate with three MRE-based quantitative scores: magnetic resonance index of activity (MaRIA), Clermont score, and the MRE global score (MEGS).[13,25,26] These scores aim to quantify CD burden at MRE using conventional (MaRIA and MEGS) and DWI (Clermont) series.

VCE was developed in 2000 (Given Imaging, Yoqneam, Israel) and allows direct visualisation of the entire small bowel in a minimally invasive procedure.[27]

In recent years, the treatment paradigm in CD has shifted from treating the symptoms to achieving mucosal healing, which was found to be associated with increased rates of clinical remission, fewer hospitalisations, and fewer abdominal surgeries.[28,29] Following this evolution in therapeutic endpoint, clinicians are facing a new population of quiescent patients who are clinically silent, with little or no symptoms, but may have an underlying active inflammatory disease. This group of patients increases the need for repeated imaging in order to detect subclinical flares, and it is the responsibility of the reading radiologist to suggest such a relapse.[14]

The purpose of the present study was to investigate the role of restricted diffusion in quiescent CD patients and its association with elevated FCP and endoscopic disease.

Material and methods

Study population

This work is a retrospective analysis of prospectively collected data that evaluate quiescent CD patients using MRE, VCE, and measurements of the inflammatory biomarkers FCP and CRP.[28,30,31] Institutional ethics review board approval (IRB) was granted for this study, and all patients signed an informed consent form. The study was performed during the years 2013–2015 and included male and female clinically quiescent CD adult patients (>18 years) with known small bowel disease in clinical remission or experiencing mild symptoms, with a CD activity index (CDAI) <220. Patients were treated with a stable medication dose and were in corticosteroid-free remission for at least 3 months.

Exclusion criteria were inability to understand or provide informed consent, presence of severe co-morbidities (liver, kidney, neurological, metabolic, or cardio-respiratory disorders), difficulty in swallowing, history of aspirations or dysphagia, inability to perform MRE due to claustrophobia, implanted metal objects or cardiac pacemaker, and known or suspected intestinal obstruction or severe stricture.

Study design

Upon enrolment, all patients underwent blood and stool work-up, VCE, and MRE. The interval between completing MRE and VCE examinations was up to 2 weeks in all patients.

MRE studies

MRE studies were performed on a 1.5 T GE Optima MR450w MRI machines with GEM Suite (GE Healthcare). Patients received oral and intravenous contrast medium. The MRE protocol was previously described[31,32] and is outlined in Table 1. Oral contrast medium was 360 ml mannitol (Osmitrol) 20% diluted in 1.5 l water. Patients were instructed to drink four doses of 465 ml every 15 minutes an hour before the MRE examination. During the last 15 minutes, patients received a slow drip of 150 ml saline containing 0.5 mg glucagon via infusion. Liver acquisition with volume acquisition (LAVA) sequences (axial and coronal) were acquired before and 40 seconds after injection of intravenous contrast medium (gadoterate meglumine, 0.5 mmol/ml by 0.2 ml/kg).

Table 1
Protocol for magnetic resonance enterography (MRE) image acquisition.

	Plane	Section width (mm)	Field of view	TR/TE
3-PI SSFSE		8	256×256	544.72/89.41
T2 SSFSE BH	Coronal	5	512×512	2000/59.33
T2 SSFSE BH + F	Coronal	5	512×512	4000/63.94
FIESTA	Coronal	5	512×512	4.97/200
FIESTA	Axial	6	512×512	5.39/200
FIESTA	Sagittal	6	512×512	4.81/200
FIESTA Dyn	Coronal	8	512×512	3.10/200
LAVA	Coronal	6	512×512	4.96/7
LAVA	Axial	6	512×512	4.16/7
LAVA + C	Coronal	6	512×512	4.96/7
LAVA + C	Axial	6	512×512	4.16/7
DWI MULT	Axial	6	256×256	12000/60.50
ADC	Axial	6	256×256	8000/0
Cal Body 48 AA	Axial	16	64×64	1.43/0.50
Cal TL Spine 36 4	Axial	16	64×64	1.43/0.50
MOD T2 FSE+FAT	Coronal	3	512×512	5757/67.26
Cal Body 24 AA2	Axial	15.8	64×64	1.44/0.50
MOD T1	Coronal	3	256×256	460/9.34
Cal Body 36 AA2	Axial	16	64×64	1.43/0.50
Cal Body 24 AA3	Axial	15.8	64×64	1.44/0.50
Cal Body 24 AA1	Axial	15.8	64×64	1.44/0.50

SSFSE, single shot fast spin echo; BH, breath hold; FIESTA, fast imaging employing steady state acquisition; LAVA, liver acquisition with volume acquisition; DWI, diffusion-weighted imaging; ADC, apparent diffusion coefficient; FOV, field of view; TR, repetition time; TE, Echo Time.

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