Original Article

Magnetic resonance enterography and bowel ultrasonography in Saudi Arabian patients with Crohn's disease: A correlation study

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Abstract

Background: Crohn's disease (CD) is a complex autoimmune disease that results in chronic inflammation of the gastrointestinal tract. CD activity is determined through clinical, laboratory, endoscopic, and radiological evaluations. Studies that examine the data of radiological modalities of evaluation are lacking, particularly in Saudi Arabia. This study compares magnetic resonance enterography (MRE) and ultrasonography (US) findings among patients diagnosed with CD, to uncover a possible correlation between these techniques.

Methods: All patients were assessed for disease activity using MRE and US.

Results: A total of 376 patients with CD were recruited. The mean age was 14.9 ± 4.3 years (range, 8–27 years), and males constituted 64% (n = 239) of the cohort. Overall, a strong positive correlation was found between US and MRE evaluations of disease activity ($r = 0.83$, $P < 0.001$). US activity correlated positively with MRE findings of enlarged lymph nodes ($P < 0.001$), bowel wall enhancement ($P < 0.001$), distal jejunal thickness ($P < 0.001$), and distal ileal thickness ($P < 0.001$). The mean difference in wall thickness was significant based on gender ($P < 0.001$), age in proximal jejunal thickness ($P < 0.001$), and distal ileal thickness ($P = 0.011$).

Conclusions: MRE and US correlate significantly as imaging techniques for the assessment of CD activity.

Keywords: Clinical score, imaging, inflammatory bowel disease, radiology, ultrasonography.

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INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory disorder that can affect any part of the gastrointestinal tract, from mouth to anus. CD is clinically heterogenous and its degree of severity can vary, resulting in a highly unpredictable course.[1] Recent studies suggest that pharmacological intervention at an early stage can prevent disease progression and irreversible damage.[2,3] The incidence of CD has been increasing worldwide

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according to recent reports, with a rapid rise in Middle Eastern countries, including Saudi Arabia.[4,5] Despite the widespread occurrence of the disease, its exact etiology remains unknown, although it has been suggested that the disease results from interactions between environmental, genetic, and immunological factors.[6] Identification of CD problems, particularly fistulae, is critical for effective clinical treatment. For instance, there is an increased prevalence of internal fistula as a cause of malabsorption and intestinal failure in CD patients, although such enteroenteric fistulas are difficult to detect.

A family history of CD, ethnicity, young age at onset, cigarette smoking, use of non-steroidal anti-inflammatory drugs, and specific dietary patterns has been associated with various prognostic outcomes of CD.[7] Even though 8 out of 10 autoimmune diseases are associated more commonly with females, this is not the case with inflammatory bowel disease (IBD), where there is no gender difference.[8] Similarly, in CD, there is no gender-based difference in terms of incidence rate.[9] One study has found that the incidence of CD in children is increasing,[10] and one study has suggested that incidence is also increasing in older people.[11]

In the recent past, radiological evaluation of CD activity was commonly carried out through a barium small bowel follow-through (SBFT).[12] However, presently, the most common types of radiological imaging techniques used to evaluate patients with CD are computed tomography (CT), magnetic resonance imaging (MRI), and ultrasonography (US).[13] In one study, a CT scan had the advantage of providing a high degree of temporal resolution, with a good capability of detecting enlarged lymph nodes, abscesses, and masses, but with the disadvantage of exposing the patient to radiation, which is a problem not encountered with US or MRI scans, which do not emit radiation.[14] A number of studies suggest that US assessment of the small bowel has a high level of specificity and sensitivity for CD,[15,16] but US is a challenging technique that requires well-trained sonographers with access to high-resolution equipment.[17] MRE, by contrast, is effective in evaluating transmural lesions and is known to provide accurate assessments of penetrating and structuring disease,[17] although it is the least efficient technique in evaluating superficial ulcerations, and its diagnostic accuracy can be hindered by imaging artifacts caused by bowel peristalsis and inadequate intake of oral contrast.[17]

A study by Rispo *et al*.[18] on the concordance between magnetic resonance-based Lémann index (MR-LI) and US-based Lémann index (US-LI)—the two methods used to evaluate the degree of bowel damage—has found a high concordance rate.[18] Also, in a population-based cohort, it was found that the incidence rate of IBD (consisting of CD and UC) and its temporal trends vary between racial and ethnic groups.[19] However, there have been no studies conducted in Saudi Arabia that have tested for a correlation between US and MRE evaluations of CD. Thus, the present study sets out to explore possible correlations in this regard, from radiological data of MRE and US in Saudi patients with CD. It also aims to find the jejunal and ileal thickness with respect to gender and age.

METHODS

We conducted a retrospective study to investigate possible correlations between MRE and US in Saudi patients, with a confirmed diagnosis of CD, according to standard clinical and histological criteria. Ethical approval was provided by the affiliated university of King Abdulaziz University Hospital in Jeddah, Saudi Arabia.

All patients with CD that were followed up between 2013 and 2018 were identified and included. Demographic and clinical characteristics were collected. The results of MRE and US evaluations were collected from the radiology information system 'SPECTRA', and the values assessed included the following: wall thickness, presence of enhancement, lymphadenopathy, free fluid, narrowing or dilatation, obstruction, fistula, abscess, fat, ulceration, and other signs of disease.

Magnetic resonance enterography and ultrasonography evaluations

MRE was performed using a standardized clinical protocol on one of two static magnets: 1.5 Tesla (Avanto; Siemens Medical Systems, Erlangen, Germany) or 3 Tesla (Achieva; Philips, Best, Netherlands). Patients then fasted for at least 4 hours and ingested 1-1.5 L of 0.2% locust bean gum and 2.5% mannitol solution over 45 min, immediately before imaging. Twenty milligrams of intravenous hyoscine butylbromide (Buscopan; Boehringer Ingelheim, Ingelheim, Germany) was administered together with 0.1 mmol/kg of gadolinium (3 ml/s injection using a power injector).

A real-time ultrasonic apparatus (Aloka Prosound 5000 or Hitachi 6500) with a conve × 3.5–6 MHz transducer and linear 7.5–10.0 MHz probe was used to carry out the US scans. Measurements in longitudinal and transverse sections were taken and intestinal thickness of greater than 4 mm were considered to be pathological. Two independent radiologists re-evaluated the findings. Information such as thickness of

the small bowel, including proximal jejunum thickness (th1), distal jejunum thickness (th2), proximal ilium thickness (th3), and distal ilium thickness (th4), was measured. In addition, the presence of abnormal wall enhancement and enlarged lymph nodes was recorded [Figure 1].

To evaluate the activity of CD by MRE in this study, we adapted the simplified magnetic resonance index activity (MARIAs) to assess CD, which has been previously validated, and is an efficient method to evaluate CD activity.[20] The original scoring system, MARIA (not simplified), requires the calculation of relative contrast enhancement (RCE), which used a rather complicated equation that may be considered too subjective for assessment. RCE is calculated by measuring the signal intensity of the enhancement of the bowel wall segment pre- and post-IV contrast administration, along with measuring the standard deviation of the signal noise within the image, which can be at risk of subjective selection of the areas of interest.[21] Thus, for the purpose of avoiding subjectivity, the current study selected MARIAs, which is based on evaluating each bowel segment alone by identifying the presence of wall edema, fatty stranding, ulceration, and thickened bowel wall of more than 3 mm, using the following simpler and arguably less subjective equation:

MARIAs = (1 × thickness > 3 mm) + (1 × edema) + (1 × fat stranding) + (2 × ulcers)

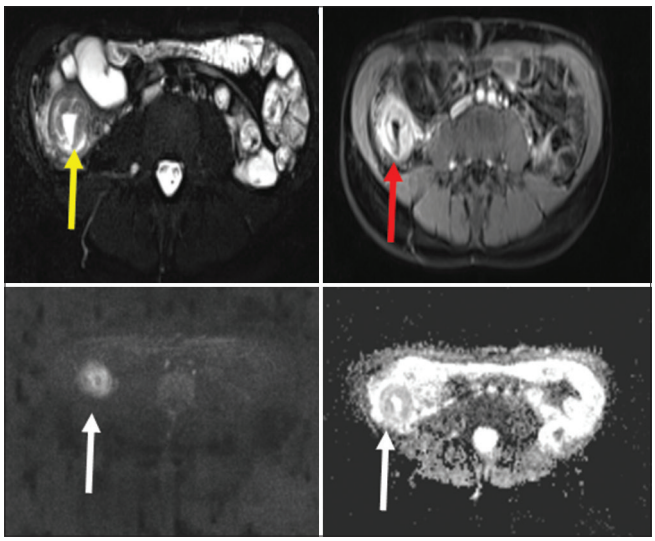

Figure 1: MRI of the abdomen in T2WI fat saturated axial sequence and axial T1WI fat saturated axial sequence with post contrast of active Crohn's disease demonstrates circumferential transmural distal ileum wall thickening (yellow arrow), submucosal edema, inflamed surrounding fat, trace of free fluid, and enlarged lymph node. The post contrast image showed avid mucosal enhancement consistent with active disease. The corresponding diffusion weighted image and apparent diffusion coefficient sequences (white arrows) demonstrate restricted diffusion, secondary to disease activity

All the elements that comprise this equation are relatively easy to obtain. The disease was considered active when on MRE the sum of the calculated indices of all bowel segments reached a value ≥7. The same radiologists also re-evaluated the radiological findings of US. Both of these radiologists had >5 years of experience in radiology. Both radiologist were blinded while interpreting the MRE and US data of the same patients. In case of any disagreement, the opinion of another experienced radiologist was taken. For the prediction of disease activity of CD using ultrasonographic features, the study selected the presence of significant wall thickening of >5 mm[22] and the presence of grade 3 or 4 hyperemia of the wall. This follows Sasaki *et al*.[23] which reports that protracted stretches of increased vascularity is seen in the wall of the affected segment, or when abnormal flow is seen at both sides of the wall and surrounding fat [Figure 2].

Outcomes

The primary outcome of the study was to explore a possible correlation between CD radiological activity in MRE and US. The secondary outcome was to test for a correlation between US activity and various elements of MRE-based evaluations.

Statistical analysis

A statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) Version 23 (SPSS, Inc., Chicago, III). A Chi-squared test was used to compare categorical variables, and the Spearman's correlation coefficient (r) was incorporated to quantify a possible correlation between MRE and US activity. An independent samples *t*-test was conducted to find the difference in mean for jejunal thickness and ileal thickness, based on gender and age. A value of $P < 0.05$ was set as statistically significant.

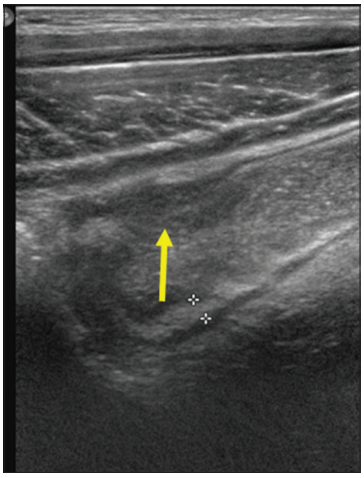

Figure 2: High-frequency ultrasound probe of active Crohn's disease demonstrates dilated bowel loop, transmural distal ileum wall thickening (yellow arrow), submucosal edema and inflamed surrounding fat

RESULTS

Baseline characteristics

A total of 376 patients with IBD were included in the analysis. The radiological characteristics of the study cohort are shown in Table 1.

Radiological assessments

MRE demonstrated active disease in 60.1% of patients, and early small bowel enhancement in 59.8% of patients. Enlarged mesenteric lymph nodes were detected by MRE in 30% of patients and intestinal wall thickening was seen more frequently in the distal ileum. A box plot was used to analyze variability among the upper and lower quartiles and to observe possible outliers in the data [Figure 3]

Correlation between US and MRE evaluation of CD activity

Table 2 shows the correlations between US activity assessment and different elements of MRE assessments. It shows a positive correlation between US activity assessment and the presence of enlarged lymph nodes (r = 0.6, P < 0.001), intestinal wall enhancement (r = 0.83, P < 0.001), and distal jejunal wall thickening (r = 0.35, P = 0.047). However, US activity correlated negatively with the presence of distal ileal wall thickening (r = –0.57, P < 0.001).

Table 1: Radiological characteristics (MRE and US) of the total study cohort (*n*=376)

Demographic Characteristics	*N* (%) or Means
Male	239 (64%)
Female	137 (36.4%)
Age (Between 8-27 years)	14.9±4.3 years
Radiological Characteristics	*n* (%) or Means
Pattern of enhancement (MRE)	
Early enhancement	225 (59.8%)
Late enhancement	1 (0.2%)
No enhancement	150 (39.8%)
Lymph node enlargement (MRE)	
Positive	120 (31.9%)
Negative	256 (68.0%)
Intestinal wall thickening (MRE)	
Proximal Jejunal	3.3±1.9
Distal jejunal	2.8±2.3
Proximal ileal	2.9±1.4
Distal ileal	4.1±2.1
MRE activity	
Active	226 (60.1%)
Inactive	150 (37.4%)
Pattern of enhancement (US)	
Early enhancement	195 (51.8%)
Late enhancement	10 (2.6%)
No enhancement	171 (45.4%)
Lymph node enlargement (US)	
Positive	147 (39.0%)
Negative	229 (60.9%)
Intestinal wall thickening (US)	
Proximal Jejunal	3.2±1.8
Distal jejunal	2.7±2.2
Proximal ileal	2.8±1.3
Distal ileal	4.0±2.0
US activity	
Active	190 (50.5%)
Inactive	186 (49.4%)

Difference between Jejunal and Ileal thickness based on gender and age

Table 3 shows the mean difference between jejunal and ileal thickness based on gender and age. The mean proximal and distal ileal and jejunal thickness was found to be significantly different between males and females. Surprisingly, jejunal thickness was found to be greater in females (P = 0.000), whereas ileal thickness was found to be greater in males (P = 0.000). The largest difference in thickness was found in proximal jejunal thickness (1.469`0.11 mm). However, not all results were found to be significant when analyzed from the perspective of gender. Proximal jejunal had a mean thickness of 3.468 ± 1.17 mm in patients >13 years, and 2.969 ± 1.24 mm in children ≤13; the mean difference was 0.499 ± 0.13 (P = 0.000). By contrast, the distal ileal thickness was found to be high in children ≤13, i.e., 4.222 ± 1.09 mm, and low in patients >13 years, i.e., 3.924 ± 1.11 mm; the mean difference (0.298 ± 0.12 mm) was found to be statistically significant (P = 0.011).

DISCUSSION

Radiological assessment of disease activity plays an important role in the practice of gastroenterologists, which routinely manage patients with CD. Physicians rely on radiological tests to determine disease activity, uncover the presence of complications, carry out risk stratification, and make pre-operative assessments. The use of several modalities to evaluate CD patients is advantageous yet can be confusing for some physicians. A preferred test must have the characteristics of being safe, accurate, cheap, available,

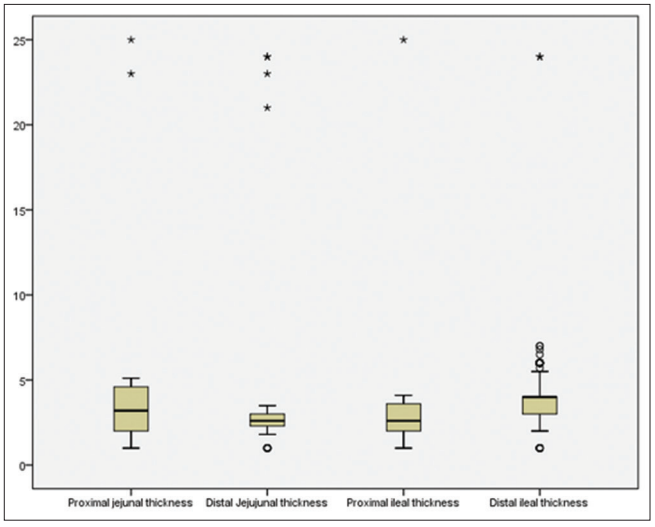

Figure 3: A box plot of median wall thickness detected by MRE at different locations of the small bowel

Table 2: Correlation between MRE and US activity

MRE findings	Ultrasound activity
Lymph nodes	r=0.6, P<0.001
Enhancement	r=0.83, P<0.001
Proximal jejunal thickness	r = -0.08, P=0.11
Distal jejunal thickness	r=0.35, P=0.047
Proximal ileal thickness	r=0.05, P=0.28
Distal ileal thickness	r = -0.57, P<0.001

and efficient. Bowel US is considered the safest and most time-efficient radiological examination modality, but has the disadvantage of being operator-dependent.[24] The use of US as a validated modality to identify CD has been established, although whether to use it as a substitute for endoscopy, to establish inter-rater variability, requires further research.[25] While highly reliable, the waiting times for MRE is usually prolonged owing to the limited availability of MRI machines and the relatively long examination times. It is therefore prudent to establish a correlative relationship between these different techniques toward enhanced evaluation.[26,27]

The most common age group with CD found in the present study were children and young adults, which coheres with one previous study where first onset of CD is commonly diagnosed at childhood.[7] However, there are studies that indicate that late onset or second onset can also occur, although this was not the case in the Saudi Arabian population of the present study.[28] Since the incidence rate also varies among populations with ethnicity,[19] further study is required on a larger population to have a clearer picture of average disease onset age in Saudi populations. Also, the thickness of wall varied among the age groups. Wall thickness has previously been shown to be associated with sensitivity to inflammation.[29] Similarly, in the present study, thicker ileal and jejunal walls were found to be associated with disease activity. However, the thickness found was lower than the 6 mm reported by Zappa *et al*.[30]

This study has explored possible correlations between MRE and US analysis in patients with CD. The results indicate a strong correlation between MRE and US in terms of accuracy of assessment of CD activity. This is in line with some previously published literature[31-34] and provides further evidence that bedsides bowel, US could replace MRE examinations in cases where a quick assessment of disease activity is required, rather than a detailed examination of the abdominal cavity. Another common scenario where US may be beneficial is where patients require an evaluation but suffer from claustrophobia, which complicates the use of MRE. In this study, it was also important to know if US-based disease activity assessments correlate with findings that are currently usually only elucidated through MRE, since it may be the case that MRE uncovers features that may be missed on a US examination.

In the domains of US and MRE, comparable improvements in diagnosis are currently being made. In US, point-of-care usage is becoming a possibility; MRE, alternative sequences in small bowel evaluation are being broadened to include diffusion-weighted imaging and dynamic contrast.[34]

Another important factor to consider when choosing an imaging method is the degree of radiation exposure. MRE and US have traditionally been favored owing to the lack of radiation exposure emitted by these modalities; efforts are now being undertaken to reduce the radiation exposure linked with diagnosis techniques such as computer tomography enterography (CTE), which has long been seen as a major disadvantage associated with the disease. However, owing to the issue of high picture noise, any reduction in radiation dosage might limit the validity of diagnostic information. However, the use of CT reconstruction techniques based on iterative approaches has been used to reduce excessive picture noise. This method enables the acquisition of pictures at lower radiation doses while reducing image noise. This method has been used in the diagnosis of CD, with results showing that in efficiency and effectiveness it is comparable to conventional CTE.[35,36]

Regarding reduction of radiation exposure, preliminary results on the diagnosis of active CD showed that model-based iterative reconstruction (MBIR) was a non-inferior method in comparison to filtered back projection and adaptive statistical iterative reconstruction.[37] MBIR was found to be non-inferior to adaptive statistical iterative reconstruction in terms of radiation dose

Table 3: Difference between mean of wall thickness based on age and gender

		Proximal jejunal thickness	Distal jejunal thickness	Proximal ileal thickness	Distal ileal thickness
Gender	Male (mean±SD)	2.739±0.79	2.415±0.34	3.428±0.57	4.200±1.33
	Female (mean±SD)	4.207±1.28	3.071±0.14	2.049±0.12	3.752±0.41
	Difference (mean±SD)	1.469±0.11	0.656±0.30	1.379±0.05	0.448±0.12
	P-value	0.000	0.000	0.000	0.000
Age	≤ 13 (mean±SD)	2.969±1.24	2.654±0.43	2.926±0.81	4.222±1.09
	> 13 (mean±SD)	3.468±1.17	2.657±0.42	2.927±0.81	3.924±1.11
	Difference (mean±SD)	0.499±0.13	0.026±0.04	0.006±0.08	0.298±0.12
	P-value	0.000	0.954	0.995	0.011

reduction, resulting in a roughly 70% reduction in total radiation exposure compared to the standard approach of filtered back projection. This low-dose approach has the potential to improve patient care by addressing the radiation concern with CTE.

Our analysis identified a positive correlation between US activity assessment and various MRE findings, including the presence of enlarged lymph nodes, disease enhancement, and intestinal wall thickening. However, there was no correlation for detecting proximal jejunal thickness and proximal ileal thickness. According to Pallotta *et al*.,[38] small intestine contrast ultrasonography (SICUS) is highly sensitive and accurate for detecting proximal ileal thickness in pediatric CD compared to conventional transabdominal US. Further study may be conducted to compare SICUS with MRE in the detection of CD in adult and pediatric populations.

According to the Montreal and Paris classifications, patients with CD are classified based on disease localization, behavior, and onset. The behavior is subdivided into penetrating, nonstricturing/nonpenetrating, and stricturing.[39] Penetrating and stricturing behavior of the disease can be associated with unfavorable prognosis. Disease activity is usually grouped into severe, moderate, and mild, although there is no objective process of categorization. The clinical importance of subtype differentiation resides in the different selection of medical treatment of active inflammation required for each subtype, unless there are symptoms related to the development of complications, such as obstructive symptoms that characterize fibrostenotic disease, which is usually an indication that surgery is required.[40] In addition, CD is classified into three subtypes based on disease behavior: inflammatory, fibrostenotic, and fistulizing/perforating. These correlate with the clinical classifications and are important to distinguish disease behavior radiologically. MRE is the preferred choice by clinicians that require detailed images showing CD phenotype.

This study may be limited by its small sample size, retrospective design, and lack of assessment of disease activity in terms of clinical, biochemical, and endoscopic measurements. Another possible limitation was that two different machine models were used for the MRE analysis, which might have made a nominal difference between radiological findings. Further larger prospective studies that address these factors are warranted to establish further correlations.

In summation, the strongest correlation was found in detecting distal jejunal thickness, followed by distal ileal thickness, and the weakest correlation was found in detecting enhancement. Thus, overall, a strong correlation exists between MRE and US with regards to the assessment of CD activity, and so US and MRE may both be important in the assessment of CD activity in clinical practice.

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Conflicts of interest

There are no conflicts of interest.

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