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Medical Review Report

Role of ElastoScan™ for the patients with Crohn's Disease

RS80A with Prestige

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Introduction

Crohn's disease (CD) is a relapsing and remitting form of transmural inflammatory bowel disease that affects the gastrointestinal tract and diffuses into the mesenteric fat. Whereas endoscopy with biopsy remains the gold standard for CD's diagnosis, imaging plays a central role in the assessment of intestinal and extra - intestinal involvement, in the surveillance and assessment of response to treatment, and in the detection of complications. Magnetic Resonance Enterography (MRE), including Diffusion-Weighted Imaging (DWI), helps in identifying bowel wall thickening, hyperperfusion, and active inflammation.

The evaluation of elasticity using Strain Elastography (SE), is a non-invasive method that allows assessment of tissue stiffness. SE is currently used for the evaluation of liver, breast, and thyroid diseases. By applying a manual compression with the Ultrasound (US) transducer, SE provides a real-time elastography colorimetric map according to the degree of stiffness. Recent clinical studies reported promising results for distinguishing inflamed from fibrotic bowel by using the US-SE (Ultrasound-Strain Elastography).

The purpose of our study was to assess whether SE and DWI could be used to detect mesenteric and bowel wall fibrosis and differentiate it from edematous/inflammatory changes.

Material and Methods

Thirty-five patients (mean age 33.12; 16/19 F/M) were selected for this study. All patients had a previous ileocolonoscopy diagnosis of CD. Typical MRE imaging appearance of CD was defined as bowel wall thickening (> 1 cm) and bowel wall enhancement, while the extramural disease was defined as fibro-fatty proliferation (infiltration of the submucosa with fat and thickening of extramural fat which separates the bowel loops), or vascular engorgement ('comb sign' - hypervascular appearance of mesentery which forms linear densities on the mesenteric side of the affected segments of small bowel giving the appearance of the teeth of a comb).

Typical US imaging appearance of CD was defined as bowel wall thickening (> 3 mm), lost or preserved gut signature. The extramural disease was defined as perienteric fluid and creeping fat which separates bowel loops due to fibrofatty proliferation.

MR imaging protocol

All 35 patients were imaged with a 1.5T MR imaging unit (Achieva, Philips Healthcare, Best, Netherlands). A dedicated abdominal multi-channel surface coil was used for all patients. All patients were scanned after oral administration of 1.5-2 L of polyethylene glycol solution, MoviPrep® (Norgine, Amsterdam, The Netherlands) or Selg-Esse 1000 (Promefarm, Milan, Italy), as oral contrast agent over the course of 30 minutes.

Imaging protocol included axial pre-contrast images acquired with T2-weighted fast-spin echo sequence (TR/TE, 4000/76 ms; section thickness 5–6 mm) and T1-weighted axial in-phase and out-of-phase gradient-recalled-echo sequence (TR/TE, 140/2.2 – 4.4 ms; section thickness, 5–6 mm). Dynamic studies were performed with three-dimensional fat-suppressed T1-weighted gradient echo sequence (TR/TE, 3.8/1.2 ms; FA 12°; slice thickness: 4.4 mm; intersection gap 2 mm; FOV: 44 cm; matrix 256 × 256) by using a bolus tracking system.

Images were acquired on the coronal plane immediately before and after intravenous injection of either 0.1 mmol/kg body weight of gadoterate meglumine (Dotarem®, Guerbet GmbH, Sulzbach, Germany) at 2 mL/s or 0.1 mmol/kg body weight through a 20-gauge intravenous catheter by means of a power injector (Medrad® Spectris Solaris® EP MR Injection System, Bayer Healthcare, Whippany, NJ, USA), followed by a 20 mL saline flush at the same injection rate.

Scanning delays after automatic detection of contrast bolus were 18, 60, and 180 s, respectively for the acquisition of the arterial, portal venous and three minutes phase. Before contrast medium injection, 20 mg hyoscine-N-butylbromide (Buscopan®, Boehringer Ingelheim, Germany) was intravenously injected unless contra-indicated (e.g. history of cardiac arrhythmia, narrow-angle glaucoma, or prostatism). Diffusion-weighted imaging single-shot echo planar images with b-values of 0, 600 and 800 s/mm^2 were acquired with free breathing method using slice thickness of 8 mm.

US-SE imaging protocol

All US examinations were conducted by an abdominal staff radiologist with 15 years of experience and a fifth-year radiology resident, respectively, by using an RS80A with Prestige ultrasound unit (Samsung Medison Co. Ltd., Seoul, Korea) equipped with and ElastoScan™ technology (Samsung Medison Co. Ltd).

All patients underwent abdominal US examination immediately after the MRE. For each patient, B-mode US coronal and axial images were obtained of the last ileal loop and of the relative mesenteric fat. In the same locations, the US-SE was performed and relative strain measurements were obtained from the mesenteric fat.

Image analysis

All MR images were evaluated on a commercial picture archiving and communication system station (PACS - IMPAX, Agfa - Gevaert, N.V., Belgium).

An acute inflammatory change of CD appearance was defined as bowel wall-thickening greater than 3 mm, hyperintense bowel wall on T2-weighted FAT-SAT images, and increased enhancement on post-contrast T1-weighted images appearing either as stratified contrast enhancement pattern or as transmural enhancement pattern.

While the mesenteric was characterized by edema (intermediate-to-high signal intensity on T2-weighted FAT-SAT images) and by the presence of inflammatory mesenteric lymph nodes. While a fibrotic change of CD appearance was defined as a bowel wall-thickening greater than 3 mm, hypointense bowel wall on T2-weighted FAT-SAT images, and increased enhancement on post-contrast T1-weighted images appearing as low-level inhomogeneous contrast enhancement pattern. While the mesenteric was characterized by creeping fat (hyperplasia of the mesenteric fat adjacent to the inflamed segments of intestine producing a mass effect) which presented a slightly decreased signal intensity on T2-weighted FAT-SAT images.

Two observers graded jointly their degree of confidence in diagnosing the presence of acute inflammatory or fibrotic appearances in volumetric T1-weighted GRE images on post-contrast phases, in T2-weighted FAT-SAT and DWI images (1=no changes; 2=probably acute inflammatory; 3=definitely acute inflammatory; 4=probably fibrotic; 5=definitely fibrotic). If there was any discordance, the determination was reached by means of consensus. Observers also analyzed the number and diameter of bowel wall lesions and the presence of any complications.

Observers analyzed the US-SE of the patients and they categorized jointly their degree of confidence in diagnosing the presence of an acute inflammatory or fibrotic appearance of the mesenteric fat in colorimetric map images (Red=no changes; Yellow=probably acute inflammatory; Green=definitely acute inflammatory; Light Blue=probably fibrotic; Blue=definitely fibrotic).

Statistical analysis

Values are expressed as mean (range) or percentages, as appropriate. Fisher's exact test was used to compare differences in discrete or categorical variables and the Student's T - test was used to compare differences between mean values. Statistical significance was defined as p less than 0.05. All statistical tests were 2-sided. All statistical analyses were performed by using GraphPad Prism for Mac (Version 6, GraphPad Software Inc., La Jolla, CA, USA).

Result

A total of 41 affected bowel segments (35 ileum and 6 colon segments), and 35 unaffected bowel segments (35 ileum) in 35 patients were evaluated. In 29 patients, the ileum was affected, while in 6 patients the ileum and colon were involved. The affected segment's extension mean was 8.1 cm (range 2.1 cm – 25.2 cm) and the wall-thickening mean was 1 cm (range 0.6 cm – 1.3 cm).

We found 9 stricture segments, while intra-wall abscess and ileoileal fistulas were detected in 11 and 7 patients, respectively. A fibrotic mesenteric and bowel wall change was present on MRE and US-SE in 12/35 (34.29%), 23/35 (65.71%), 15/35 (42.85%) and in 20/35 (57.15%) respectively, while an acute inflammatory mesenteric and bowel wall change was present on MRE and US-SE in 23/35 (65.71%), 12/35 (34.29%), 20/35 (57.15%) and in 15/35 (42.85%), respectively (Fig. 1 and Fig. 2).

In all unaffected bowel segments and relative mesenteric fat, the US-SE color-coded scale showed a red and/or yellow color variation. Moreover, the signal of the bowel wall and mesenteric fat was iso-/hypo-intense on T2-weighted sequence in the fibrotic pattern (23/35 and 12/35 patients) and hyperintense in the edematous pattern (12/35 and 23/35 patients).

The correlation between US-SE color-scale and T2 signal intensity was statistically significant ($p < 0.05$). There was a significant diffusion restriction in 18 patients with CD in the active phase (mean apparent diffusion coefficient [ADC] values for the fibrotic mesentery: 2.58 ± 0.33 x 10 - 3, mean ADC values for edematous mesentery: 2.14 ± 0.28 x 10 - 3).

There was a statistical correlation between the US-SE color - scale and ADC maps ($p < 0.05$). However, 3/35 patients were defined as acute inflammatory pattern by US-SE but MRE through both T2 - weighted sequence and ADC map classified them in fibrotic pattern. No significant diffusion restriction was encountered in 35/35 unaffected bowel segments and relative mesenteric fat (mean ADC values: 2.92 ± 0.15 x 10 - 3).

Statistically significant correlations between the presence of enlarged lymph - nodes and the edematous change ($p < 0.05$) and between the presence of stricture and the fibrotic changes ($p < 0.05$) were found.

Discussion : compared to edematous

In the management of CD, assessment of disease activity and the differentiation between inflammatory/ edematous and fibrotic patterns play a pivotal role to guide therapeutic choices. Magnetic Resonance Imaging (MRI) examination showing high signal on DWI sequences helps in the detection of active CD and also in the differentiation between fibrotic and edematous changes of bowel loops, showing higher ADC values in case of fibrotic changes compared to the edematous or normal mesentery. Differentiation between active edematous inflammation, that needs just conservatory treatment, and progression towards fibrosis, that usually needs endoscopic dilatation or surgery, is crucial.

Our results show that on MRE, fibrotic changes of the mesentery are characterized by higher ADC values and lower T2 signal compared to the edematous mesentery (Figure 1 and 2). However, MRI is time and money consuming and not widely available. US, which is more widely available and less time consuming than MRI, may evaluate the localization and the length of the affected intestinal segments in CD (bowel thickening from the superficial layer which is hyperechoic to the mucosal layer > 5 mm in a non-distended bowel; > 3 mm in a distended bowel, loss of multi-layer pattern is sign of active inflammation).

Concerning the mesenteric changes, US may assess the presence of creeping fat (an echogenic area separating bowel loops representing the fibro-fatty proliferation of adipose tissue that extends around active inflammation). With US elastography, it is possible to grade the fibro-fatty changes of the mesentery from grade 1 and 2 (red), grade 3 (green) edematous changes, to grade 4 and 5 (blue) which indicate fibrotic changes. In our study, concerning the changes in the stiffness using US-SE, the pathological ileal loop showed edematous changes (grade 3 - green) in 20 patients, fibrotic changes in 15 patients (grade 4 and 5 - light and dark blue), while all the non-pathological ileal loops did not show any edematous or fibrotic change (grade 1 and 2 - red and yellow color). These differences proved to be statistically significant in the identification of the pathological loop and in the differentiation of the fibrotic and edematous changes. In 3 patients, US-SE did not correctly grade the bowel and mesenteric changes as fibrotic. This could be explained by the fact that a qualitative assessment of US-SE leads to incomplete separation of edematous and low-fibrosis pattern, and of high– and low–fibrosis pattern, while on MRI, the combination of the quantitative datum of ADC map and the T2 signal allow a more precise categorization. Albeit this overlap is minimal, a quantitative assessment through shear wave US elastography could theoretically overcome this limit.

Our study revealed a statistically significant correlation between the MRI and the US-SE findings during the evaluation of bowel wall and mesenteric changes. The evaluation of the mesenteric changes in CD through US-SE can be considered an additional tool in the differentiation of the edematous or fibrotic changes to distinguish acutely inflamed from fibrotic intestine in patients with CD. Increased ADC values and blue color in inflammatory stricture bowel is likely due to differences in bowel wall collagen and water content compared to edematous bowel wall. US strain imaging quantifies the 'hardness' or 'softness' of a tissue as a function of tissue compressibility. This differentiation is mandatory for the therapeutic management.

In conclusion, US-SE and MRI, including ADC values and signal intensity on T2 - weighted sequences, are useful tools for the evaluation of CD pattern. In particular, US-SE allows the evaluation of the fibrotic or edematous changes of the mesentery and bowel wall, thus suggesting an important potential clinical impact, mainly for therapy.

Figure Legend

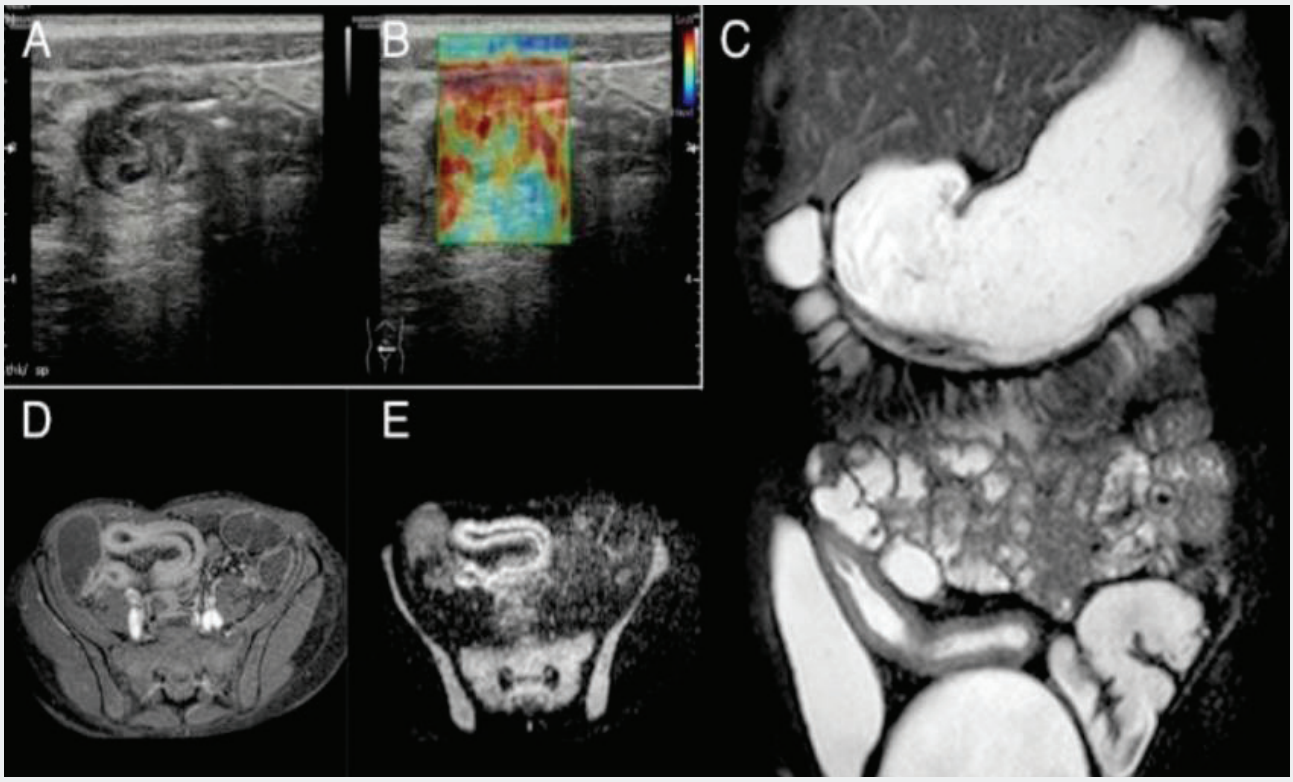

Figure 1. Longitudinal US-scan of the last ileal loop in a 33-years old male shows wall thickening with prominence of submucosa and hyperechoic appearance of perivisceral fat. The gray scale (A) findings and US-SE (B) aspect performed at this level are suggestive for of active inflammation pattern. The MR study (C, D and E) confirmed these suspicions: T2-weighted coronal view revealed hyperintensity of the bowel wall, T1-weighted axial post-contrast showed stratification of the bowel wall, DWI with 800 b-value showed hyperintensity of the bowel wall and an aspect of the last ileal loop very similar with US findings.

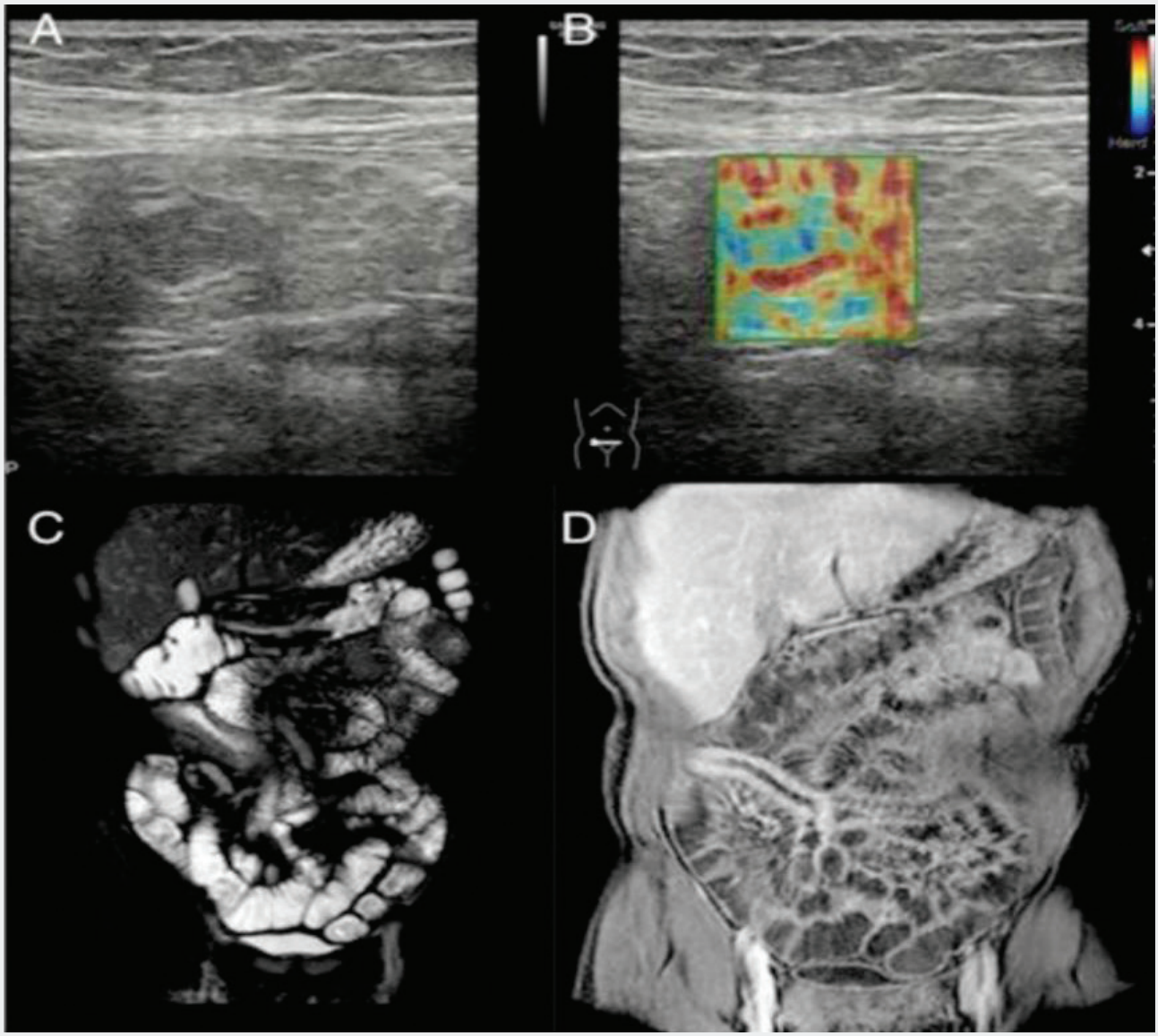

Figure 2. Transverse US-scan of the last ileal loop in a 26-years old female shows wall thickening in which stratification was completely lost and hypo-isoechoic appearance of perivisceral fat. The gray scale (A) findings and US-SE (B) aspect performed at this level are suggestive for fibrotic pattern. The MR study (C and D) confirmed these suspicions: T2-weighted coronal view revealed hypointensity of the bowel wall, T1-weighted coronal post-contrast showed enhancing of the bowel wall without stratification.

Supported Systems

- RS80A with Prestige

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