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Review

Subclassification of small bowel Crohn's disease using magnetic resonance enterography: a review using evidence-based medicine methodology

D.J. Murphy [a,*], A.E. Smyth [a], S.H. McEvoy [a], D.J. Gibson [b], G.A. Doherty [b], D.E. Malone [a]

[a] Department of Radiology, St Vincent's University Hospital, Elm Park, Dublin 4, Ireland
[b] Department of Gastroenterology, St Vincent's University Hospital, Elm Park, Dublin 4, Ireland

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Magnetic resonance enterography (MRE) has a growing role in imaging small bowel Crohn's disease (SBCD), both in diagnosis and assessment of treatment response. Certain SBCD phenotypes respond well to biologic therapy and others require surgery; MRE has an expanding role in triaging these patients. In this review, we evaluate the MRE signs that subclassify SBCD using evidence-based medicine (EBM) methodology and provide a structured approach to MRE interpretation.

Introduction

The small bowel is the most common part of the gastrointestinal tract affected in Crohn's disease. Small bowel Crohn's disease (SBCD) frequently affects young patients, and imaging plays an important role in assessing disease activity. Small bowel contrast studies and computed tomography (CT) were traditionally the mainstays of imaging, but there are concerns about cumulative lifetime ionising radiation dose.[1] Magnetic resonance enterography (MRE) is an attractive imaging technique with similar clinical utility in diagnosis and disease monitoring, and has a beneficial lack of ionising radiation.[2–4]

Why classify SBCD?

The medical treatment of SBCD has been transformed with the advent of biologic therapies. Certain groups of patients with SBCD, especially with acute inflammatory (AI) disease, appear to respond better to medical therapy than those with a chronic fibrotic disease who often require surgery.[5] Given the significant cost of the novel biologic medications, the accurate identification of patients with AI SBCD is desirable.[6] The emphasis in imaging in SBCD is changing from purely diagnostic into an effort to predict whether the balance of AI and chronic fibrotic changes favour medical or surgical therapy; thus, the ability to classify patients with SBCD into different disease phenotypes by their imaging characteristics can help inform therapeutic decisions.

How can we classify SBCD?

Maglinte *et al.*[7] proposed a classification of SBCD into four main disease patterns: 1) AI; 2) fibrostenotic; 3) perforating

* Guarantor and correspondent: D.J. Murphy, Department of Radiology, St Vincent's University Hospital, Dublin, Ireland. Tel.: +353 86 6047864.
E-mail address: murphy.84@gmail.com (D.J. Murphy).

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and 4) quiescent. This is a simple stratification and these patterns can be identified based on their MRE appearances.

Methodology

MRE signs that classify the SBCD patterns were evaluated as outlined using the evidence-based medicine (EBM) process of 'ask, search, appraise, apply, and evaluate'.[8] These five steps of EBM replace the introduction, methods, results and discussion sections of original research papers.[9,10]

Ask

A clinical question was devised using the PIO (patient, intervention, outcome) format[11]: *"In adults with SBCD, what MRE features characterise AI, fibrostenotic, and perforating patterns?"*

Search

The literature search followed assessment of the "evidence pyramid" paradigm.[12] A secondary literature search yielded no relevant returns. A primary literature search was performed of the Medline database using PubMed and Google Scholar. The search strategy employed linking medical index subject headings (MeSH terms) with the Boolean operators AND and OR: ([Crohn's disease OR inflammatory bowel disease] AND [small intestine OR small bowel]) AND (magnetic resonance imaging OR MRI) AND (severity of illness index OR fistula OR abscess OR inflammation OR subclassification OR intestinal obstruction OR stricture). In addition, a focused search of Google Scholar was carried out by using the "cited by" link for each item, a technique previously described as the "reverse citation trail".[13]

Appraise

The abstracts were reviewed and publications meeting inclusion criteria chosen. Inclusion criteria were adults, English text, MRE or MR enteroclysis protocol, assessment of small bowel, good reference standard (histopathological and/or endoscopic correlation), use of a 1.5/3 T magnet, and performance of MRE signs individually reported. As Crohn's disease is a transmural process, the strongest reference standard is histopathological assessment of surgically resected specimens as this allows complete interrogation of the entire small bowel wall. Endoscopy is a useful, if less robust reference standard, particularly adept at assessing mucosal disease. Although this has obvious limitations as a reference standard in a transmural pathology, inclusion of these studies results in patients with milder disease phenotypes being included, allowing a greater relevance of the results to routine clinical practice. Studies were excluded that were primarily paediatric, that did not include an assessment of small bowel, where individual MRE signs were not described, and which used reference standards other than histopathological and/or endoscopic correlation.

A number of meta-analyses were found that assessed MRE in SBCD,[4,14–17] but only a single meta-analysis that assessed the performance of the individual signs of SBCD.[18] In total 64 abstracts were reviewed, with 43 meeting inclusion criteria (Electronic Supplementary Material Appendix S1 for excluded studies). Included studies were assigned an Oxford Centre for EBM "level of evidence"[19]; the validity and strength of the best evidence was assessed using a radiology-specific critical appraisal sheet.[20] The studies were divided into those that assessed for AI disease (n=28), fibrostenotic (n=10), and perforating (n=19) disease and assessed the evidence behind each MRE sign in turn (Electronic Supplementary Material Fig S1). Where possible, raw data were extracted from studies with similar reference standards for calculation of pooled test properties for each MRE sign (sensitivity, specificity, likelihood ratios [LR]).[19,21]

Fibrostenotic disease

The presence of fibrostenotic disease is important in SBCD, as it represents a degree of chronicity that may not be reversible with medical therapy.[5,20] The development of fibrous tissue in the small bowel wall is postulated to result from recurrent episodes of inflammation and can eventually cause luminal narrowing leading to stricture formation(22). It is this continuum with acute inflammation that likely accounts for the strong correlation between wall enhancement, especially delayed enhancement, and fibrous tissue on full-thickness histopathological evaluation.[22–25] The differentiation of acute inflammation from chronic fibrotic disease is one of the crucial tasks of MRE.

Stricture

An enteric stricture is an abrupt narrowing of small bowel lumen (usually by approximately 50%) with the presence of pre-stenotic dilatation (Fig 1).[18] MRE performs well in both ruling in and ruling out enteric strictures (sensitivity 0.79, 95% confidence interval [CI]: 0.88–0.71; specificity 0.94, 95% CI: 1–0.89, positive LR 13.1, negative LR 0.2).[18,26–31]

AI disease

Mural thickness

Small bowel wall thickness can be accurately measured using electronic callipers at segments of small bowel with adequate distension, usually on T2-weighted axial images (Fig 2a). The majority of studies included used a cut-off value of >3 mm to define pathological thickening, but a small number of studies used 4 mm or higher. There is broad agreement that small bowel mural thickening is a consistent sign of acute inflammation in SBCD. In one of the initial studies that used full-thickness surgical histopathological evaluation as a reference standard, the authors found a useful correlation with increased mural thickening and acute inflammation on histology with a cut-off of 4 mm.[23] A meta-analysis of nine studies with good reference standards demonstrated a robust performance of wall thickness in identifying AI SBCD (sensitivity 0.91, 95% CI: 0.95–0.88; specificity 0.72, 95% CI: 0.81–0.64), positive LR