REVIEW ARTICLE

Capsule endoscopy for small-bowel evaluation in Crohn's disease

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Capsule endoscopy (CE) is increasingly accepted as a technique for small-bowel evaluation with a high diagnostic yield. Although the role of CE in evaluation of GI bleeding is now well established, its proper place in the evaluation of other small-bowel disorders, particularly Crohn's disease (CD), is less certain. The diagnosis of CD remains a clinical one and is based on the combination of clinical, radiologic, endoscopic, and histologic findings. Although there is no reference standard for the diagnosis of CD, endoscopic demonstration of mucosal lesions, with associated histologic findings of chronic intestinal inflammation, is often critical in reaching the diagnosis. Practice guidelines increasingly recognize that CE may play a role in the diagnosis and the evaluation of the extent and activity of small intestine CD. Recent comparative studies suggest that CE has a greater sensitivity for mucosal inflammatory changes than radiologic imaging modalities. However, the clinical significance of some of these mucosal lesions is unclear. The frequency of false-positive reporting of minor mucosal lesions and overdiagnosis of CD, in addition to an increased frequency of capsule retention in patients with known CD, may limit widespread application of CE in the workup of CD. This technical review examines published data on the utility of CE in CD to offer an evidence-based consensus framework for the safe and appropriate use of capsule examinations in patients with CD.

INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory disorder of the GI tract. The terminal ileum is the most common site of small-intestine involvement, accessible to endoscopic evaluation and biopsy by ileal intubation at the time of colonoscopy. However, isolated involvement of the proximal small intestine can occur in as many as one third of cases,[1] and therefore normal findings on ileocolonoscopy are not sufficient to exclude the diagnosis. Assessment of the full length of the small intestine, traditionally by means of a radiologic examination, is typically required to evaluate patients with both suspected and established CD.

Recent years have seen an expansion in both radiologic and endoscopic techniques available for small-bowel evaluation. Traditional contrast-enhanced radiology in the form of small-bowel follow-through (SBFT) or enteroclysis has been increasingly replaced by dedicated contrast-enhanced CT enterography (CTE) and more recently by magnetic resonance (MR) imaging (MR enterography [MRE]). Endoscopic techniques use either flexible video endoscopes, advanced through the small intestine by balloon or other intubation devices, or wireless video capsules (capsule endoscopy [CE]). CE, in particular, is increasingly advocated as an alternative to radiologic techniques for imaging the small intestine in CD, offering enhanced direct visualization of the small-bowel mucosa in a relatively noninvasive manner. However, debate persists about the proper place of CE relative to other techniques in the realm of inflammatory bowel disease (IBD).

This technical review critically evaluated the utility of CE relative to other imaging modalities in specific situations for patients with both suspected CD and established CD. We also review the complications of CE and ultimately propose a framework for the safe and appropriate use of CE in CD.

ROLE OF CE IN SUSPECTED CD

One of the perceived strengths of CE is its enhanced yield in the detection of small-bowel mucosal abnormalities in any symptomatic patient population. Some studies have demonstrated abnormal findings in more than one third of patient examinations, with an even higher yield in patients with suspected CD.[2,3] Although the yield of CE may be high, many of the abnormalities detected are not specific for CD. Minor mucosal abnormalities can be observed in almost one fifth of asymptomatic individuals[4] and in as many as two thirds of individuals regularly using nonsteroidal anti-inflammatory drugs (NSAIDs).[5] Thus, the value of CE in patients with suspected CD remains an area of debate and uncertainty. Consensus practice guidelines

Abbreviations: CD, Crohn's disease; CE, capsule endoscopy; CTE, CT enterography; IBD, inflammatory bowel disease; MR, magnetic resonance; MRE, magnetic resonance enterography; NPV, negative predictive value; NSAID, nonsteroidal anti-inflammatory drug; QALY, quality of life adjusted year; SBFT, small-bowel follow-through.

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in IBD have noted a potential role for CE in small-bowel CD but have not detailed particular indications for its use in IBD.[6,7]

A number of studies have assessed the utility of CE in patients with suspected small-bowel CD with previously negative (ileo)colonoscopy and SBFT findings with highly variable results. CD was confirmed in 26% to 71% of cases, depending on study definitions and design.[8-13] This wide variation in rates of diagnosis of CD is attributed to a number of factors, notably differences in how suspected small-bowel CD is defined and the variation in mucosal changes required for making a diagnosis of CD. In such studies, a diagnosis of CD is more common if symptoms are associated with abnormal findings on objective laboratory tests such as anemia or increased inflammatory markers.[3,8,10]

Recent consensus definitions should assist in promoting a degree of standardization in future studies.[14] The Lewis Index has been developed and validated as a means of defining an appropriate threshold for reporting the presence and degree of clinically significant mucosal inflammatory changes seen on CE.[15] The index scores 3 parameters: villous edema, ulceration, and stenosis (which are weighted based on extent and severity). A score lower than 135 is designated normal/clinically insignificant. Scores of 135 to 790 are classified as mild and scores higher than 790 as moderate to severe. The score does nothing, however, to specify the etiology of the mucosal inflammatory changes observed.

Increasing shifts toward standardizing the reporting of CE findings will assist in improving diagnostic accuracy.[14,16-18] However, caution will still be required when using findings on CE as the primary means of making a diagnosis of small-intestine CD. Interobserver agreement in the reporting of minor mucosal abnormalities representing CD is at best fair.[19] Using the presence of more than 3 ulcers found on CE as the threshold for a positive study in patients with suspected CD only yielded a positive predictive value of 50% for a diagnosis of CD on follow-up.[20] Interestingly, the predictive value of a negative study for the absence of CD at follow-up (NPV) was 96%, suggesting that CE serves much better to exclude CD than to confirm it. The significance of minor mucosal lesions is often uncertain, and caution must be used to avoid overdiagnosis of CD. Longitudinal studies based on similar lesions identified on ileoscopy suggest that although CD will eventually develop in a minority of patients, it will not develop in the majority of patients.[21,22] Undisclosed use of NSAIDs may be an important factor in interpreting many of these small mucosal lesions.[23] False-positive findings have the potential to expose patients to unnecessary medications with potentially serious toxicities, especially in the era of "top-down" biological therapy.[24]

Despite the high NPV of CE in suspected CD, the cost-effectiveness of tests of exclusion is questionable. Results of attempts to analyze the economic impact of CE use in CD diagnosis have been conflicting. Although some authors suggest that earlier use of CE in the evaluation of suspected small-bowel CD increases cost-effectiveness,[25] a more recent cost-effectiveness analysis better reflects the current decision model in daily clinical practice. This study suggests that although CTE is a cost-effective alternative to SBFT in evaluating suspected CD, the addition of CE after negative findings on ileocolonoscopy and SBFT or CTE incurs an additional cost of $500,000 per quality of life adjusted year (QALY) gained.[26] To put this cost into perspective, screening colonoscopy incurs an additional cost beyond no screening of $14,000 per QALY gained.[27] Given that CE is typically performed after the initial colonoscopy and small-bowel imaging examination (to exclude small-bowel strictures), it would seem unlikely that the additional costs can be routinely justified.

Before proceeding to examine in more detail the use of CE is patients with established CD, it is worth reviewing the data from studies comparing CE with other small-bowel imaging modalities. Head-to-head comparisons of CE with several radiologic techniques for assessing the small intestine and detecting CD have been performed. However, the majority of these studies include patients with both suspected and established CD.

COMPARATIVE STUDIES OF CE WITH OTHER SMALL-BOWEL IMAGING TECHNIQUES

Comparison with plain small-bowel radiology

Although both SBFT and enteroclysis remain widely available, CT and MR imaging are being increasingly used as primary diagnostic tools. A number of studies have compared small-bowel radiology with CE, and these are summarized in Table 1. Although some studies report reasonable correlation between SBFT and CE for detection of CD,[28] the majority suggest that SBFT misses a significant number of small-bowel mucosal lesions that are visualized on CE and identified by other imaging techniques.[29-33] The most recent prospective comparisons of CE with traditional enteroclysis showed similar results, with sensitivity of CE for detection of small-bowel lesions in patients with suspected CD more than twice that of enteroclysis.[34,35]

Comparisons with CT/MRE

Radiologic evaluation of the small intestine has been increasingly shifting toward the use of cross-sectional imaging techniques such as CTE and MRE. Of these 2 modalities, CTE is less expensive, faster, and more widely available, but has the clear disadvantage, compared with MRE, of significant ionizing radiation exposure. Several comparisons of CE and CT in the evaluation of the small intestine have been reported including 2 studies comparing CT enteroclysis with CE.[36,37] The larger of these 2 studies (n = 41) detected proximal small-bowel lesions in 25 patients by CE and in 12

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