IBD REVIEWS REVIEW ARTICLE

Utility of Video Capsule Endoscopy and Device Assisted Enteroscopy in Inflammatory Bowel Disease

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Abstract

Introduction: *There is no single gold standard test for the diagnosis of Crohn's disease. The diagnosis is based on a constellation of findings: clinical history and physical examination, laboratory tests, radiologic and endoscopic examinations, and histopathology. Most patients diagnosed with Crohn's disease have small bowel involvement. A colonoscopy with visualization of the terminal ileum may not identify involvement of the disease in proximal segments because of its patchy pattern. Complete evaluation of the small bowel is needed in order to establish a definitive diagnosis of Crohn's disease and determine the extent and severity of the disease and its activity at baseline so it can be monitored.* ***Objective:*** *To review the role of video capsule endoscopy in different clinical situations of inflammatory bowel disease (IBD): suspicion of IBD; established IBD; unclassified IBD; ulcerative colitis (including ileorectal anastomosis); complications related to the use of video capsule endoscopy in IBD.* (IBD Rev. 2016;2:30-7)

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Small bowel video capsule endoscopy in patients with suspected Crohn's disease

Suspicion of Crohn's disease (CD) in the small bowel is the second indication for use of video capsule endoscopy (VCE) of the small intestine after evaluation for midgut bleeding (obscure gastrointestinal bleeding) and, in the evaluation of midgut bleeding (obscure gastrointestinal bleeding), whether occult or overt, inflammatory findings have been reported in up to 35% of cases[1].

The diagnostic yield of VCE has been compared to other diagnostic modalities in patients with suspected CD. A meta-analysis by Dionisio, et al.[2] showed VCE had a significantly higher diagnostic performance in patients with

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suspected CD than intestinal transit studies, computed tomography enterography, and colonoscopy with ileoscopy, and similar performance to magnetic resonance enterography. Recent studies have shown the superiority of the diagnostic performance of VCE versus magnetic resonance enterography[3]. The findings in this meta-analysis support the fact that VCE is a first-line diagnostic tool in patients with suspected small bowel CD, especially when the ileocolonoscopy is unsuccessful or non-diagnostic. The increase in performance is not synonymous with diagnostic reliability. The high diagnostic yield may increase true and false positives, especially in clinical inflammatory disorders. Video capsule endoscopy has high diagnostic sensitivity in inflammatory diseases or conditions of the small bowel, but very low diagnostic specificity[4] so it is difficult to determine the cause of an inflammatory disease in the absence of a histological evaluation. So therefore, to increase specificity, it is necessary to supplement its findings with a clinical history suggestive of inflammatory bowel disease (IBD) and other laboratory tests for markers of inflammation or radiologic exams such as magnetic resonance enterography.

Among the other types of inflammatory lesions to be considered in the differential diagnosis, enteropathy induced by nonsteroidal anti-inflammatory drugs (NSAID) is the most important due to the high rate of small bowel lesions seen in people who use NSAIDs, 75% of whom present with lesions after two weeks of taking them[5,6].

It is important to remember that more than 13% of normal asymptomatic persons present with inflammatory lesions in the small intestine that are seen on VCE and whose significance is unknown, i.e. the definition of "normal" in small bowel mucosa in relation to inflammatory findings is unclear.

The spectrum of inflammatory findings seen on VCE (Fig. 1) is very similar in all inflammatory diseases. The patient's clinical history is imperative for determining specificity in these findings, particularly the history of use of NSAIDs. The lesions identified on VCE are nonspecific and are not sufficient for a diagnosis of CD. The history of NSAID use is crucial to image interpretation.

To improve the diagnostic accuracy of VCE in patients with suspected CD, there should be a careful selection of the patients who will be referred for the test, made on the basis of a clinical history suggestive of IBD, i.e. symptoms of chronic abdominal pain, chronic diarrhea, weight loss, stunting of growth, iron deficiency anemia, extraintestinal manifestations such as fever, arthritis, arthralgia, pyoderma, perianal disease, sclerosing cholangitis, inflammatory markers such as iron deficiency, increased sedimentation rate, increased C-reactive protein levels, leukocytosis, serum and fecal markers, abnormal imaging studies that can complement and increase the diagnostic accuracy of the VCE results in this population (Fig. 2).

European Society of Gastrointestinal Endoscopy Guidelines

The European Society of Gastrointestinal Endoscopy (ESGE) recommends ileocolonoscopy as the first endoscopic examination for investigating patients with suspected CD (strong recommendation, high quality evidence)[7].

In patients with suspected CD and negative ileocolonoscopy findings, the ESGE recommends small bowel video capsule endoscopy (SBVCE) as the initial diagnostic modality for investigating the small bowel, in the absence of obstructive symptoms or known stenosis (strong recommendation, moderate quality evidence).

The ESGE does not recommend routine small bowel imaging or use of a patency capsule prior to SBVCE in these patients (strong recommendation, low quality evidence).

In the presence of obstructive symptoms or known stenosis, the ESGE recommends that small bowel cross-sectional imaging modalities, such as magnetic resonance or computed tomography enterography, or enteroclysis, be used first (strong recommendation, low quality evidence).

In suspected CD, the ESGE recommends careful patient selection (using the clinical history and

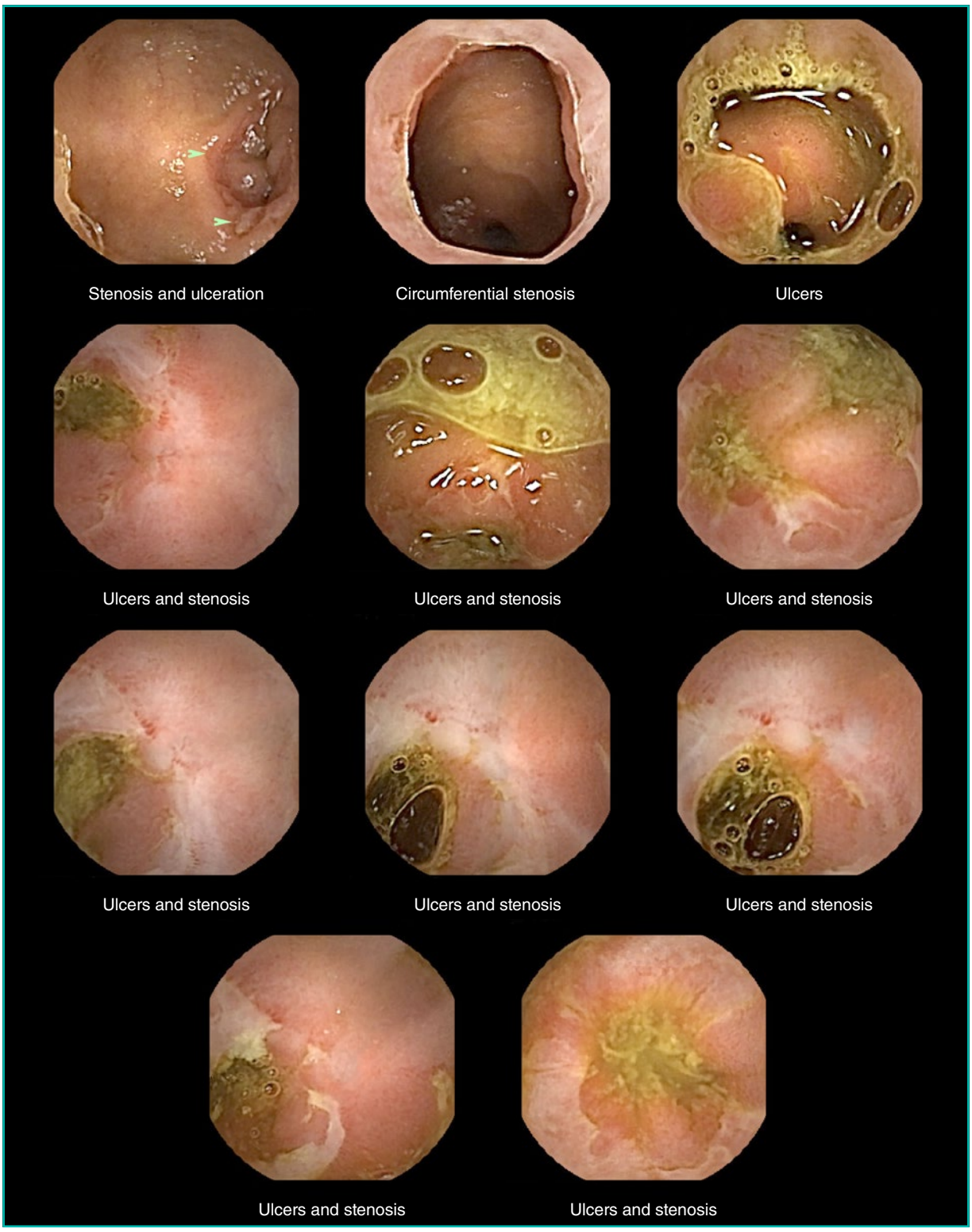

Figure 1. Images of video capsule endoscopy findings in inflammatory bowel disease.
Description: A 56-year-old female patient with iron deficiency anemia of six years duration, with positive occult blood in stool. Upper gastrointestinal endoscopy procedures with normal duodenal biopsy and normal colonoscopy plus ileoscopy procedures were performed on two occasions. Following a diagnosis of occult obscure gastrointestinal bleeding, a video capsule endoscopy was requested, with the following findings in the small bowel: findings compatible with inflammatory bowel disease, Crohn's disease, elevated C-reactive protein and erythrocyte sedimentation rate. Treatment with immunomodulators and biologic therapy is started with adequate clinical response of anemia and inflammatory markers. *Source: Own practice.*

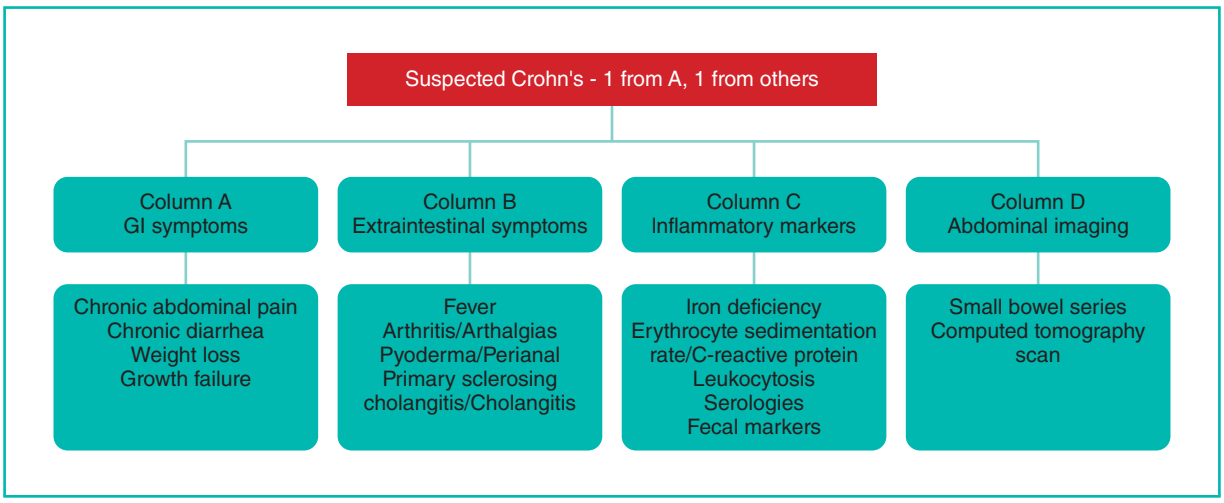

Figure 2. There are many inflammatory diseases of the small bowel and they present with similar lesions on video capsule endoscopy *(source: ICCE criteria for suspected Crohn's disease. Gastrointestinal Endoscopy. 2007;66(3):533-40)*.

fecal inflammatory markers) prior to SBVCE in order to improve the diagnostic accuracy of capsule endoscopy for lesions consistent with active small bowel CD (strong recommendation, low quality evidence).

The ESGE recommends discontinuation of NSAIDs for at least one month prior to SBVCE since these drugs may induce lesions in the small bowel mucosa that are indistinguishable from those caused by CD (strong recommendation, low quality evidence).

Small bowel video capsule endoscopy in patients with established Crohn's disease

The meta-analyses by Triester, et al.[8] and Dionisio, et al.[2] also demonstrated the diagnostic superiority of VCE in comparison with intestinal transit studies, computed tomography enterography, and push enteroscopy, and similar performance to ileocolonoscopy and magnetic resonance enterography. However, the question is, How does the use of VCE affect the management of patients with established CD? It can probably be used to assess unexplained abdominal pain and anemia and to monitor mucosal healing after treatment, to guide treatment, and to map the extent of disease. Studies that establish and demonstrate the utility of this procedure in this group of patients are needed since it is the small bowel disease in which retention of the capsule endoscope occurs most frequently.

A recent study that used biomarkers, capsule endoscopy, and imaging to detect small bowel mucosal healing and deep remission in patients with known small bowel CD showed that capsule endoscopy is a very safe procedure for the assessment of small bowel mucosal healing in CD. Use of this procedure showed that a high percentage of patients with CD in clinical remission or in clinical and biomarker remission have inflammatory mucosal lesions[9].

European Society of Gastrointestinal Endoscopy Guidelines

In patients with established CD, based on ileocolonoscopy findings, the ESGE recommends cross-sectional imaging for small bowel evaluation, since this has the potential to evaluate the extent and location of any CD lesions, identify stenosis, and assess extraluminal disease (strong recommendation, low quality evidence)[7].

In patients with normal small bowel cross-sectional imaging, the ESGE recommends SBVCE as the next procedure, if deemed to influence patient management (strong recommendation, low quality evidence).

Table 1. Lewis score

Parameters	Number	Longitudinal extent	Descriptors
Villous appearance (worst-affected tertile)	Normal-0	Short segment-8	Single-1
	Oedematous-1	Long segment-12	Patchy-14
	Whole tertile-20		Diffuse-17
Ulcer (worst-affected tertile)	None-0	Short segment-5	b1/4-9
	Single-3	Long segment-10	1/4-1/2-12
	Few-5	Whole tertile-15	Nl/2-18
	Multiple-10		
Stenosis (whole study)	None-0	Ulcerated-24	Traversed-7
	Single-14	Non-ulcerated-2	Not traversed-10
	Multiple-20		

Lewis score: score of the worst affected tertile ([villous parameter × extent × descriptor] + [ulcer number × extent × size]) + stenosis score (number × ulcerated × traversed).
Longitudinal extent: short segment: b10% of the tertile; long segment: 11% to 50% of the tertile; whole tertile: N50% of the tertile.
Ulcer number: single: 1; few: 2-7; multiple: ≥ 8.
Ulcer descriptor (size) is determined by how much of the capsule picture is filled by the largest ulcer.
Adapted from Gralnek, et al.
Adapted from Annese V, et al.[13].

When capsule endoscopy is indicated, the ESGE recommends use of the patency capsule to confirm functional patency of the small bowel (strong recommendation, low quality evidence).

Scoring systems for small bowel video capsule endoscopy in patients with established Crohn's disease

Determination of the diagnosis based on VCE findings in the small bowel has been very diverse and not established in the various papers that have been published, with the most commonly used being Mow's Criteria[10], which considers the presence of diffuse or multiple ulcerations (three or more) as diagnostic for CD. So for this reason, systems for classifying VCE findings have been developed, one of which is the Lewis Score (Table 1)[11,12], which has been incorporated in the Given System and the Capsule Endoscopy CD Activity Index (CECDAI) that was devised by Niv and recently validated (Table 2)[13].

European Society of Gastrointestinal Endoscopy Guidelines

The ESGE suggests the use of activity scores (such as the Lewis score and the Capsule Endoscopy Crohn's Disease Activity Index) to facilitate prospective SBVCE follow-up of patients for longitudinal assessment of the course of small bowel CD and its response to medical therapy (using mucosal healing as an end point) (weak recommendation, low quality evidence)[7].

Small bowel video capsule endoscopy in patients with established Crohn's disease: Special situations

Small bowel video capsule endoscopy in patients with colonic inflammatory bowel disease type unclassified

After an ileocolonoscopy, it may be impossible to distinguish between CD and ulcerative colitis in up to 10% of patients with IBD in the

Table 2. Capsule Endoscopy Crohn's Disease Activity Index

Inflammation score
0 = None
1 = Mild to moderate edema/hyperemia/denudation
2 = Severe edema/hyperemia/denudation
3 = Bleeding, exudate, aphtae, erosion. small ulcer (b 0,5 cm)
4 = Moderate ulcer (0.5-2 cm), pseudopolyp
5 = Large ulcer (N2 cm)
Extent of disease score
0 = No disease
1 = Focal disease (single segment)
2 = Patchy disease (2-3 segments)
3 = Diffuse disease (more than 3 segments)
Stricture score
0 = None
1 = Single-passed
2 = Multiple-passed
3 = Obstruction (non-passage)

CECDAI = proximal ([AI × BI] + CI) + distal ([A2 × B2] + C2).
Adapted from Niv Y, et al.; Annese V, et al.[13].

colon. So therefore, VCE may be important for establishing a definitive diagnosis for these patients. VCE has shown lesions in the small bowel that are compatible with CD in between 17 and 70% of patients with unclassified IBD. Negative VCE findings do not exclude a future diagnosis of CD[14].

Small bowel video capsule endoscopy in patients with inflammatory bowel disease after surgery

A diagnosis of recurrence after surgery is made after performing an ileocolonoscopy and using the Rutgeerts score to predict symptomatic disease relapse[14,15]. VCE has been compared to ileocolonoscopy and allows detection of proximal lesions similar to those achieved with colonoscopy in two-thirds of all patients. The clinical relevance of these findings is unknown.

Video capsule endoscopy should be considered for postsurgical recurrence only when ileocolonoscopy is contraindicated or unsuccessful. VCE can identify lesions in the small bowel that have not been identified by ileocolonoscopy after ileocolic resection.

Small bowel video capsule endoscopy in patients with inflammatory bowel disease before surgery

There is no statistical association between the results of pre-operative VCE and the prognosis after surgery in patients with ulcerative colitis or unclassified colitis. There seems to be little value in using VCE for the preoperative assessment of these patients[13].

Video capsule endoscopy of the small bowel and colon in patients with ulcerative colitis

ECCO statement

To date, there is insufficient data to support the use of capsule endoscopy in the diagnostic work-up or in the surveillance of patients with ulcerative colitis (EL5) (voting results: 100% agreement)[13].

Complications of small bowel video capsule endoscopy in patients with inflammatory bowel disease

Our goal should be to perform these procedures only when they are expected to provide data relevant to the management of our patients' disease. We must choose the procedures that have the best safety profiles and diagnostic yield. When using VCE in patients with IBD, especially those with established small bowel CD, we need to be aware of the possibility of capsule retention[16], which has been reported to be up to 13% in this group

of patients. For this reason, use of the patency capsule prior to performing VCE can be of great assistance, as can cross-sectional imaging, such as magnetic resonance enterography, since they allow us to identify stenosing lesions that would contraindicate the performance of this procedure, i.e. we must always balance the benefits against the potential risks.

European Society of Gastrointestinal Endoscopy Guidelines

The ESGE recommends initial conservative treatment in case of capsule retention. If the capsule does not pass spontaneously after medical therapy, the ESGE recommends device-assisted enteroscopy (strong recommendation, low quality evidence)[7].

Device-assisted enteroscopy in inflammatory bowel disease

Due to its invasive nature and the potential risk of complications, device-assisted enteroscopy (DAE) is indicated in patients with suspected CD when histological assessment is required in order to determine the cause of the inflammatory lesions and when the findings have an impact on the therapeutic management of this group of patients[17-19]. The clinical impact of positive findings of DAE on patients with CD has been examined in prospective trials[20-22]. In experienced hands, the treatment of CD-related stenoses is safe and effective[23,24]. Dilation of stenoses is recommended for those that are less than 4 cm, non-inflammatory, and with no angulation.

European Society of Gastrointestinal Endoscopy Guidelines

The ESGE recommends DAE with small bowel biopsy in patients who have had a negative ileocolonoscopy but suspicion for CD remains on small bowel cross-sectional imaging or SBVCE[25]. The DAE with small bowel biopsy is more likely to provide definitive evidence of CD than cross-sectional imaging, but small bowel cross-sectional imaging is less invasive and better define transmural complications (strong recommendation, high quality evidence).

The ESGE recommends DAE if small bowel therapeutic endoscopy is indicated (including dilation of CD small bowel stenoses, retrieval of foreign bodies, and treatment of small bowel bleeding) (strong recommendation, low quality evidence).

The ESGE recognizes SBVCE, DAE, and magnetic resonance or computed tomography enterography or enteroclysis as complementary strategies (weak recommendation, low quality evidence).

There are no cost-effectiveness data regarding optimal investigation strategies for diagnosis of small bowel CD.

Conclusions

Video capsule endoscopy is a good method for evaluating the small bowel in IBD, improving the diagnosis and classification, guiding treatment, and for impacting the prognosis of our patients. However, we need prospective studies to help us increase the specificity of inflammatory findings on VCE and studies that show us the impact of its use in the management of patients with established CD, especially of its role in monitoring response to drugs.

Device-assisted enteroscopy in patients with suspected CD allows us to perform biopsies that provide specificity to the inflammatory findings, which has an impact on the clinical management of these patients and can be used in follow-up of established IBD to guide treatment management. Therapeutic device-assisted enteroscopy with dilation of stenoses plays an important part in the treatment of IBD.

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