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**Role of capsule endoscopy in inflammatory bowel disease**

Kopylov U *et al*. Capsule endoscopy in inflammatory bowel disease

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**Abstract**

Videocapsule endoscopy (VCE) has revolutionized our ability to visualize the small bowel mucosa. This modality is a valuable tool for the diagnosis of obscure small bowel Crohn’s disease (CD), and can also be used for monitoring of disease activity in patients with established small-bowel CD, detection of complications such as obscure bleeding and neoplasms, evaluation of response to anti-inflammatory treatment and postoperative recurrence following small bowel resection. VCE could also be an important tool in the management of patients with unclassified inflammatory bowel disease, potentially resulting in reclassification of these patients as having CD. Reports on postoperative monitoring and evaluation of patients with ileal pouch-anal anastomosis who have developed pouchitis have recenty been published. Monitoring of colonic inflammatory activity in patients with ulcerative colitis using the recently developed colonic capsule has also been reported. Capsule endoscopy is associated with an excellent safety profile. Although retention risk is increased in patients with small bowel CD, this risk can be significanty decreased by a routine utilization of a dissolvable patency capsule preceding the ingestion of the diagnostic capsule. This paper contains an overview of the current and future clinical applications of capsule endoscopy in inflammatory bowel disease.

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**Key words:** Small bowel videocapsule endoscopy; Crohn’s disease; Pouchitis; Indeterminate inflammatory bowel disease; Ileal pouch-anal anastomosis; Patency capsule

**Core tip:** Videocapsule endoscopy has revolutionized our ability to visualize the small bowel mucosa. This modality is a valuable tool for the diagnosis of obscure small bowel Crohn’s disease (CD), and can also be used for monitoring of disease activity, detection of complications, evaluation of therapeutic response and postoperative recurrence in established CD, evaluation of the small bowel in patients with unclassified inflammatory bowel disease and pouchitis. Monitoring of colonic inflammation in patients with ulcerative colitis has also been reported. This manuscript contains an overview of the current and future clinical applications of capsule endoscopy in inflammatory bowel disease.

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**INTRODUCTION**

In the past, the small bowel has largely been inaccessible to direct endoscopic examination, with only the duodenum, proximal jejunum and terminal ileum being subject to direct visualization by a conventional endoscope. This paradigm changed dramatically with the invention and introduction of small bowel videocapsule endoscopy (VCE) in 2000[[1](#_ENREF_1)]. The first wireless capsule, manufactured by Given Imaging (Yokneam, Israel) was approved for clinical use in United States and Europe in 2001[[2](#_ENREF_2)]. Several other manufacturers subsequently released their own versions of VCE. This technology has been extensively used for the diagnosis and monitoring of patients with inflammatory bowel disease (IBD), mostly Crohn’s disease (CD). About 30% of the patients with CD have exclusive small bowel involvement[[3](#_ENREF_3)], and their diagnosis will frequently be missed if based solely on ileocolonoscopic findings. VCE is now also considered an important technique for monitoring small bowel CD, and has also been employed in management of patients with unclassified IBD and ulcerative colitis.

The aim of the current review is to outline the diagnostic role of VCE in the diagnosis and monitoring of inflammatory bowel disease, in particular small-bowel CD.

**DIAGNOSIS OF CD**

***Characteristic endoscopic findings***

Several VCE findings are frequently associated with CD: ulcerations, erythema, mucosal edema, loss of villi, strictures and mucosal fissures (Figure 1)[[4](#_ENREF_4)]. Unfortunately, none of these findings is specific for CD. In fact, minor small bowel lesions maybe present in upto 10% of normal subjects[[5](#_ENREF_5)]. As VCE lacks tissue-sampling capabilities, it cannot confirm the etiology of the observed lesions. The most common mimicker of CD in the small bowel is non-steroidal anti-inflammatory medication (NSAID)-induced enteropathy that may manifest with lesions indistinguishable from those of CD. Such lesions, appearing as early as 2 wk from the onset of NSAID therapy, can be demonstrated in 70% of chronic NSAID users[[6](#_ENREF_6),[7](#_ENREF_7)]. Thus, VCE should be reserved for patients with high clinical index of suspicion for CD. Patients who are candidates for VCE should be instructed to avoid NSAIDs for at least 1 mo before the examination. Similar bowel mucosal lesions may result from multitude of other pathologies, such as lymphoma, radiation enteritis, HIV with opportunistic infection, intestinal tuberculosis and Behcet’s disease[[5](#_ENREF_5)].

***Diagnostic scores***

The criteria for diagnosis of CD using VCE have not been well established. The most commonly used validated diagnostic index is the Lewis score[[8](#_ENREF_8)]. This score divides the small bowel into 3 tertiles (dividing the small bowel transit time in 3) and uses an algorithm that assigns points to various findings (mucosal edema, ulcers, strictures) characteristic for CD in each of the tertiles, taking in account the severity and the reproducibility of each finding. The final score represents the number of points accumulated by the most significantly involved tertile. The Lewis score is incorporated in the software used for decoding, reading and interpretation of VCE images obtained by PillCAM (RAPID). A score < 135 is designated as normal or clinically insignificant mucosal inflammatory changes, a score between 135 and 790 indicates mild, and a score ≥ 790 moderate to severe inflammation, respectively. An additional score known as capsule endoscopy CD activity index (CECDAI or Niv score), was recently proposed (Table 1)[[9](#_ENREF_9)]. This score incorporates three main characteristics of CD: inflammation, extent of disease, and strictures, in both the proximal and distal segments of the small bowel. It should be noted that while these scores attempt to quantify the severity and extent of small bowel (SB) CD, the lesions are not pathognomonic and may represent other causes of bowel inflammation.

VCE was also utilized for diagnosis of SB CD in patients primarily presenting with extraintestinal manifestations of IBD. Arhtropathy is the most common extraintestinal manifestation in IBD, occurring in 6%-46% of the patients[[10](#_ENREF_10)], and frequently manifesting even before the onset of bowel disease. Capsule endoscopy may be a valuable tool in evaluation of these patients, especially if conventional ileocolonoscopy is unappealing to the patient[[11](#_ENREF_11)]. Spondyloarthroathy can be diagnosed in up to 30% of IBD patients[[12](#_ENREF_12),[13](#_ENREF_13)]. Capsule endoscopy can demonstrate small bowel lesions consistent with CD in 33% of these patients (twice as many as conventional ileocolonoscopy[[14](#_ENREF_14)]).

***VCE vs other modalities for the diagnosis of CD***

The yield of VCE for the diagnosis of CD was compared to that of cross-sectional imaging modalities such as small bowel follow-through (SBFT), computer tomography enterography (CTE) and magnetic resonance enterography (MRE) in multiple studies (Table 2). Patients with suspected small bowel stenosis were excluded from VCE evaluation in these studies. The superiority of VCE over small bowel follow-through and enteroclysis has been repeatedly demonstrated in multiple studies[[15-18](#_ENREF_15)].

A recent meta-analysis demonstrated an incremental diagnostic yield (IY) of VCE in comparison to CTE in both suspected and established CD patients (IY, 47%; 95%CI: 31%–63%, *P* < 0.00001; and 32%; 95%CI: 16%–47%, *P* < 0.0001), respectively[[19](#_ENREF_19)]. A prospective trial evaluated the diagnostic accuracy of VCE, MRE and CTE in 93 patients with suspected CD as compared to ileocolonoscopy. The sensitivity and specificity for diagnosis of CD of the terminal ileum was 100% and 91% by CE, 81% and 86% by MRE, and 76% and 85% by CTE, respectively. There was statistical difference in sensitivity compared with CTE, but only a trend in comparison with MRE. Specificity was not significantly different between the modalities. Proximal small bowel CD was detected in 18 patients by using CE, compared with 2 and 6 patients using MRE or CTE, respectively (*P* < 0.05)[[20](#_ENREF_20)]. In earlier studies, VCE and MRE were reported to have comparable accuracy. Overall, VCE is more accurate in diagnosing subtle small bowel lesions and MRE in diagnosing intramural inflammation, stricturing complications and extra-intestinal manifestations[[19](#_ENREF_19),[21](#_ENREF_21),[22](#_ENREF_22)]. The superior sensitivity of VCE clinical for proximal small bowel disease is a potentially important diagnostic advantage, as proximal small bowel disease has recently been demonstrated to be a significant negative prognostic factor[[23](#_ENREF_23)].

Importantly, data acquired by different endoscopic and imaging modalities can be combined to improve the diagnostic accuracy, utilizing the specific advantages and strengths of each modality.

***VCE in established CD***

VCE is a potentially important but currently underutilized tool for monitoring of SB CD. In the latter years, the leading treatment paradigm in IBD has shifted form merely controlling symptoms to reversing the underlying inflammation, as expressed by objective surrogate markers such as laboratory inflammatory markers and endoscopic evidence of mucosal healing[[24](#_ENREF_24)]. Capsule endoscopy provides meaningful information on the inflammatory burden in the small bowel mucosa, similarly to the role of conventional ileocolonoscopy for the colon and the terminal ileum. Bowel stenosis should be ruled out before VCE is performed in established CD due to the increased risk of capsule retention (about 5%). Routine use of patency capsule diminishes the risk of retention to almost negligible (see below).

VCE could be particularly useful in the following clinical scenarios in known CD (Table 3): (1) Monitoring of mucosal healing; (2) Detecting postsurgical recurrence; and (3) Discrepancy between clinical and laboratory data and endoscopic findings.

**Mucosal healing:** Mucosal healing, defined as absence of visible endoscopic inflammation, has emerged as a very important marker of long-term clinical efficacy associated with decreased risk of long-term complications in both ulcerative colitis (UC) and CD[[24-27](#_ENREF_24)]. Conventional ileocolonoscopy is the current gold-standard modality for assessment of mucosal healing. A small prospective study had evaluated monitoring of mucosal healing with VCE performed before and after treatment for acute CD flare-up[[28](#_ENREF_28)]. Forty patients with CD flares were included in the study and all have responded to treatment within 4-8 wk of treatment. Three parameters (number of large ulcers, number of aphtous ulcers and percentage of time with lesions visible) were examined. Of these only the first one improved significantly. In a subgroup of patients treated with corticosteroids combined with immunomodulators or biologics, a significant improvement in all three parameters was demonstrated. The most important limitations of this study were a significant heterogeneity in the instituted treatment, with majority of patients treated with mesalamine or corticosteroids, along with absence of a validated scoring system for mucosal inflammation. The data from our center demonstrated a significant reduction in the Lewis score in 4 patients with spondyloarthropathy and newly diagnosed SB CD after 6 mo of treatment with Adalimumab[[14](#_ENREF_14)]. Importantly, no diagnostic score, including the commonly used Lewis score, has been validated for evaluation of mucosal healing in SB CD.

**Postoperative CD recurrence:** Recurrence of SB CD in the neo-terminal ileum following surgical resection can be demonstrated in 73%-93% of the patients within 1 year of ileocolonic resection[[29](#_ENREF_29),[30](#_ENREF_30)]. SB lesions associated with postoperative recurrence are frequently quantified using the Rutgeerts score[[29](#_ENREF_29)]. The accuracy of VCE in detection of postoperative recurrence was evaluated in 31 patients[[31](#_ENREF_31)]. Recurrence occurred in 21 patients (68%) and was detected by ileocolonoscopy in 19 patients. Sensitivity of VCE using the Rutgeerts score was 62%-76% and specificity was 90%-100%.The severity of lesions as assessed by both methods correlated significantly (*P* < 0.05). In an additional study, 24 patients with CD, neo-terminal ileum recurrence defined as Rutgeerts score > 2 was demonstrated by ileocolonoscopy in 25% and capsule endoscopy in 62% (VCE was performed in 22/24 patients due to failure to excrete the patency capsule in 2 patients). Capsule endoscopy detected proximal SB lesions inaccessible by ileocolonoscopy in 13 patients[[32](#_ENREF_32)]. VCE is an attractive monitoring modality for postoperative patients, providing a non-invasive and accurate visualization of the entire small bowel including the neo-terminal ileum.

**Unexplained symptoms:** Many symptoms of CD, such as diarrhea, abdominal pain, bloating, can be attributed to a multitude of etiologies other than active inflammation [underlying irritable bowel syndrome (IBS), bacterial overgrowth, bile salt diarrhea *etc*.]. Clear identification of inflammatory etiology is of crucial importance and may lead to significant changes in the treatment, such as initiation or escalation of anti-inflammatory treatment. Negative VCE results are also of clinical importance, as this would lead to diagnosis and initiation of treatment for a concomitant condition such as IBS, and prevent further unnecessary and expensive escalation of an anti-inflammatory regimen. Clinical indices and laboratory inflammatory markers may indicate ongoing inflammation, but lack sensitivity. In a study including 140 patients with CD, the Spearman’s rank correlation of Simple endoscopic index with fecal calprotectin, CRP, blood leukocyte count and CDAI was 0.75, 0.53, 0.42 and 0.38, respectively[[33](#_ENREF_33)]. Although ileocolonoscopy is a gold standard test for identification of active inflammation, it would potentially miss lesions located proximally to the ileocecal valve. Dubcenco *et al*[[34](#_ENREF_34)] have prospectively evaluated 28 symptomatic Crohn’s patients with ileocolonoscopy, barium radiography and capsule endoscopy. Active disease was identified by VCE, ileocolonoscopy and barium radiography in 82%, 49% and 32% of patients, respectively. In a study by Dussault *et al*[[35](#_ENREF_35)], in 25 out of the included symptomatic CD patients, VCE was indicated for a discrepancy between clinical symptoms and diagnostic findings. Abnormal SB findings were diagnosed in 44% of the patients, and in 45% of these patients the treatment was escalated following the performance of VCE.

VCE can also be used for monitoring of ileal recurrence in CD patients following bowel resection and ileocolonic anastomosis. In one study, VCE detected CD recurrence in 15 (62%) patients, whereas ileocolonoscopy detected inflammatory lesions in the neo-terminal ileum in only 6 (25%) patients[[32](#_ENREF_32)]. VCE was also evaluated for a potential role in the assessment of mucosal healing after drug therapy in CD[[28](#_ENREF_28)].

***Therapeutic yield of VCE in established CD***

VCE frequently produces clinically significant data that can lead to a change in a therapeutic management. In a retrospective series of 71 CD patients, medical treatment was changed in 38 (53%) of the patients within 3 mo of VCE performance[[35](#_ENREF_35)]. In an additional series that included 86 patients with established CD, 61.6% had a change in medication in the 3 mo after the CE, with 39.5% initiating a new anti-inflammatory medication[[36](#_ENREF_36)].

***VCE in unclassified IBD and ulcerative colitis***

Colonic inflammatory bowel disease cannot be classified as CD or ulcerative colitis using current colonoscopic and pathologic criteria in 10%-15% of the patients[[37](#_ENREF_37)]. At least 30% of these patients with unclassified IBD (IBDU) will be reclassified as CD during the course of their illness[[38](#_ENREF_38)], usually after identification of small bowel lesions. Correct classification of the patients is especially important when deciding on surgical intervention, as rates of chronic pouchitis, fistula formation and pouch failure after ileal pouch-anal anastomosis (IPAA) are significantly higher in patients with CD[[39](#_ENREF_39)].

Several small studies have evaluated the utility of VCE for reclassification of IBDU patients. Mow *et al*[[40](#_ENREF_40)] have described 22 patients with either isolated colitis or chronic symptoms following IPAA (*n* = 18) who were evaluated with VCE. All patients had prior unremarkable small bowel radiography. Multiple ulcerations (3 and above) considered diagnostic for CD were identified in 68 of 18 patients. Mehbizadeh *et al*[[41](#_ENREF_41)] described 120 patients with a history of UC or IBDU who underwent VCE. Findings consistent with SB CD were demonstrated in 15.8% of the patients. Eighteen/19 patients with CD diagnosed by VCE have previously underwent SBFT, with positive findings in only 1 patient. Another series included 30 patients with IBDU, in whom CD (defined as 3 or more SB ulcers) was identified in 5. Interestingly, in 6/25 VCE-negative patients CD was diagnosed on a subsequent ileocolonoscopy with biopsies[[42](#_ENREF_42)]. In a series of pediatric patients, 5/7 patients initially diagnosed as UC or IBDU were reclassified as having CD as a result of VCE findings[[43](#_ENREF_43)] (Table 4).

Higurashi *et al*[[44](#_ENREF_44)] evaluated small bowel inflammation in patients with established ulcerative colitis. Of the 23 UC patients, 13 (57%) showed small-bowel lesions, and 8 (35%) had erosions, as opposed to 2/23 (7%) and 1/23 (4%) in the control group. In 9/23 patients with UC, the Lewis score of inflammation was consistent with mild to moderate small bowel inflammation (between 135 and 790). The clinical and pathological significance of these lesions is unclear (repeated biopsies were performed in only 2 patients, but these results are of great interest and emphasize the possible risk of misdiagnosis in many IBD patients.

***VCE in evaluation of pouchitis in patients after IPAA***

IPAA provides a continence-preserving surgical option in patients with ulcerative colitis unresponsive or unwilling to continue anti-inflammatory therapy, or those who have developed complications (such as colonic stenosis, colonic dysplasia *etc.*) that require total colectomy. The procedure is technically demanding and is associated with a significant incidence of postoperative complications, the most common being chronic and acute pouchitis and “*de novo*” CD[[45](#_ENREF_45)]. Symptoms and endoscopic lesions consistent with chronic pouchitis are reported in 10%-59% in patients with UC, and even more frequently in patients with CD[[46](#_ENREF_46)]. It is commonly argued that at least a subgroup of these patients actually represent a previously undiagnosed CD. In a series of 15 UC patients with chronic pouchitis, diffuse lesions involving the stomach or different segments of the small bowel were demonstrated in all patients[[47](#_ENREF_47)]. Similar lesions were demonstrated in 27% of the control patients. Unfortunately, histological evaluation (showing non-specific inflammation) was available for only 2 patients with gastric involvement. The clinical significance of these lesions is unclear (Table 4).

The role of VCE in preoperative evaluation of UC/IBDU patients was examined in one retrospective series. The study evaluated the incidence of acute pouchitis, chronic pouchitis and *de novo* CD within 12 mo of the surgery in patients with and without pathological findings on a preoperative VCE. No significant difference was demonstrated for any of the outcomes[[48](#_ENREF_48)]. However, an important limitation of this study was the definition of “positive” VCE as any ulceration or lesion, possibly leading to a high false positive rate. In addition, a significant selection bias stemming from the retrospective design of the study (patients with a high preoperative probability of CD were not likely to undergo IPAA) interferes with the interpretation of the results. In our opinion, preoperative evaluation of IPAA candidates with VCE merits further evaluation in prospective studies.

Anemia is another frequent complication of IPAA surgery , occurring in about 17% of UC patients[[49](#_ENREF_49)]. Possible etiologies may include newly discovered CD, arteriovenous malformations, celiac disease and others. In a series of post-IPAA patients with chronic anemia, VCE detected the cause of anemia in 29.4%. Sixty percent of the patients were diagnosed as having a new-onset CD[[50](#_ENREF_50)].

**COLONIC CAPSULE ENDOSCOPY IN UC**

A colonic capsule [PillCam colonic capsule (PCCE) (Given Imaging, Yokneam, Israel] has been available for colorectal cancer screening for several years. This device includes 2 cameras which records 2 different sets of images. The colonic capsule was compared with colonoscopy with promising results, with the second-generation capsule reaching sensitivity of 88% for detection of polyps > 6 mm in comparison to colonoscopy[[51](#_ENREF_51),[52](#_ENREF_52)].

PCCE was evaluated for diagnosis and monitoring of ulcerative colitis. In the study by Ye *et al*[[53](#_ENREF_53)], 25 patients were evaluated for presence and severity (Mayo Score) of UC by PCCE and conventional colonoscopy. A significant correlation in the severity (*k* = 0.751, *P* < 0.001) and extent (*k* = 0.522, P < 0.001) of UC between the PCCE and conventional colonoscopy was demonstrated. Similar findings were reported by Hosoe *et al*[[54](#_ENREF_54)]. However, PCCE is not suitable for monitoring of dysplasia and cancer surveillance in UC patients due to its lack of tissue sampling ability.

***Contraindications and risks***

The main complication of CE is capsule retention, defined as a failure to excrete the capsule for 2 wk or more, requiring directed medical, endoscopic or surgical intervention[[55](#_ENREF_55)]. CE is contraindicated in patients with known bowel strictures or swallowing disorders, and history of bowel obstruction. Recent abdominal surgery is a relative contraindication[[56](#_ENREF_56)]. In patients with obstructive symptoms or one of the aforementioned risk factors, cross-sectional imaging should be performed before VCE; however, absence of strictures on cross-sectional imaging does not preclude capsule retention[[57](#_ENREF_57)]. The rate of capsule retention depends on the indication for performance of VCE[[58](#_ENREF_58)]: 0% in healthy controls[[59](#_ENREF_59)], 1.4% in obscure gastrointestinal bleeding[[60-62](#_ENREF_60)], 1.48% in suspected CD[[63-65](#_ENREF_63)], 5%-13% in known CD[[40](#_ENREF_40),[66](#_ENREF_66)] and 21% in suspected small bowel obstruction[[67](#_ENREF_67)]. Slow transit of the capsule, with delayed excretion of the capsule is very common, seen in up to 20% of the cases[[56](#_ENREF_56)]. A retained capsule is usually asymptomatic[[68](#_ENREF_68)], but may be associated with symptoms of partial or complete bowel obstruction. Only 6 cases of bowel perforation were reported[[56](#_ENREF_56),[69](#_ENREF_69)]. Usually, the retained capsule can be extracted with surgery or enteroscopy. If the cause is an inflammatory stricture, corticosteroids have been useful in some cases. No consensus on the timing of intervention exists, and it is unclear how long one should wait before intervention in asymptomatic patients.

***Patency capsule***

The patency capsule has the same shape and dimensions as the real videocapsule. It is constructed of cellophane with wax plugs at either end and it contains lactose mixed with 10% barium to make it radiopaque. The wax plugs have holes that allow succus entericus to dissolve the lactose , resulting in capsule disintegration[[70](#_ENREF_70)]. The dissolution of the patency capsule (Agile, Given Imaging) starts to occur after 30 h. The patency capsule can be detected by radiography or a portable radiofrequency scanner. When the patency capsule is successfully excreted or not detectable on radiography in the small bowel at 30 h post ingestion, it is usually safe to perform the diagnostic VCE. If the patency capsule location is uncertain, it is possible to localize it with the assistance of contrast or air enhanced fluorography or CT[[71](#_ENREF_71)]. The rate of excretion of the patency capsule varies from 45%-88%[[58](#_ENREF_58),[72-75](#_ENREF_72)], depending upon patient selection. In a series of 77 CD patients who underwent a patency capsule examination before proceeding to diagnostic VCE, the patency capsule was not excreted within 30 h in 7.8% of the patients[[35](#_ENREF_35)]. The main complication of patency capsule is mild abdominal pain, occurring in about 20% of the patients. Clinically evident intestinal obstruction requiring surgical intervention was reported in very few cases[[58](#_ENREF_58)]. This phenomenon may be explained by the lodging of the capsule in sites of obstruction not easily assessable by intestinal fluids necessary for the dissolution of the lactose in the patency capsule[[76](#_ENREF_76)]. The rate of uneventful completion of the VCE examination after successful excretion of the patency capsule approximates 100%, even though excretion times may vary between patients[[58](#_ENREF_58)]. In cases of unsuccessful patency capsule procedure, the small bowel should be investigated by alternative diagnostic modalities such as cross sectional imaging (MR-E).

**CONCLUSION**

VCE possesses several important diagnostic advantages for IBD patients, mainly excellent visualization of the entire small bowel mucosa and excellent tolerability .The main challenge for further implementation of VCE in monitoring of IBD patients is an establishment of a validated quantitative score for assessment of mucosal healing and postoperative recurrence, that would allow routine utilization of this modality in both clinical practice and clinical trials. This could be especially important in CD, where outcomes in clinical trials are frequently assessed using surrogate markers (clinical scores, inflammatory markers) and evaluation of the mucosal healing limited to the colon and terminal ileum , that frequently does not reflect the inflammatory burden of the small bowel.

Small bowel lesions are frequently diagnosed in patients initially diagnosed with ulcerative colitis or after IPAA. The true clinical significance of these lesions, and whether they actually represent undiagnosed cases of CD is an important question that merits further clinical and translational studies.

Another important pitfall limiting the use of VCE for CD monitoring is the clinician’s reluctance to perform VCE in these patients due to an exaggerated concern of retention. However, routine utilization of a patency capsule improves the safety of this procedure significantly, rendering the actual risk of retention extremely low. However, patency capsule frequently results in additional costs.

Further technological enhancements in the future may potentially lead to a further expansion of the indications for capsule endoscopy in IBD (Table 5). These improvements may include a development of an externally operated capsule, that has already been attempted[[77](#_ENREF_77),78]. An additional significant limitation of the capsule endoscopy is a lack of sampling ability, diminishing its usefulness for monitoring of neoplasms and colonic or small bowel dysplasia. In the future, additional technological features that are under development including tissue diagnosis capabilities, fluid aspiration, drug delivery and therapeutic (coagulation) capabilities may further increase the clinical utility of this modality[[79](#_ENREF_79)].

VCE is a very important tool for diagnosis of CD, and also has a potentially significant role in the therapeutic monitoring of these patients. Capsule endoscopy may also provide important clinical information for patients with IBDU, UC and pouchitis, with an excellent tolerability and safety profile. Indications for VCE in IBD are likely to increase in the future with further technological and clinical developments.

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**Figure 1 Videocapsule endoscopy findings.** A: Small ulcers (encircled); B: Edematous mucosa; C: Ulcerated stenosis (SBII capsule, RAPID and Imaging software, Given Imaging, Yokneam, Israel).

**Table 1 A comparison of 2 capsule endoscopy scoring indices for quantification of mucosal inflammation**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Lewis score[[8](#_ENREF_8)] | | | CECDAI[[80](#_ENREF_80)] | |
| **Parameter** | **Number/quality** | **Longitudinal extent** | **Descriptors** | **Parameter** | **Descriptors** |
| Villous appearance | Normal/edematous | Short segment/  long segment/  whole tertile | Single/  patchy/  diffuse | Inflammation score | None to large ulcer (>2 cm) |
| Ulceration | Non/single/  few/multiple | Short segment/long segment/whole tertile | < 25%, 25-50%, > 50% | Extent of disease | No disease to diffuse (3 segments) |
| Stricture | Non/single/  few/multiple | Ulcerated/non-ulcerated | Traversed/non-traversed | Stricture score | None to complete obstruction |
| Small bowel segmentation | Tertiles (strictures for the entire length of the examination) | | | Proximal to distal small bowel | |
| Score | < 135: normal or clinically insignificant inflammation | | | 0 (normal examination) -26 (severe inflammation) | |
| 135-790: mild inflammation | | |
| * 790 moderate to severe. | | |

CECDAI: Capsule endoscoy Crohn’s disease activity score.

**Table 2 Key studies evaluating the diagnostic yield of capsule endoscopy for Crohn’s disease**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Modality | Ref. | Number of patients | Diagnostic yield of VCE | Diagnostic yeild of the compared modality | IY | *P* value |
| CTE | Eliakim *et al*[[81](#_ENREF_81)] | 35 | 77% | 20% | 47% | < 0.05 |
|  | Hara *et al*[[82](#_ENREF_82)] | 17 | 71% | 53% | 18% | NA |
| Voderholzer *et al*[[83](#_ENREF_83)] | 41 | 61% | 49% (CT enteroclysis) | 12% | < 0.04 |
| Solem *et al*[[84](#_ENREF_84)] | 40 | 83% | 83% | 0 | NS |
| MRE | Albert *et al*[[85](#_ENREF_85)] | 27 | 93% | 78% | 15% | NS |
| Crook *et al*[[22](#_ENREF_22)] | 19 | 93% | 71% | 18% | NS |
| Jensen *et al*[[20](#_ENREF_20)] | 93 | 100% | 86% | 14% | NS |
| Ileocolonoscopy | Hara *et al*[[82](#_ENREF_82)] | 17 | 71% | 65% | 6% | NS |
|  | Solem *et al*[[84](#_ENREF_84)] | 40 | 83% | 74% | 9% | NS |
|  | Leighton*et al*[[86](#_ENREF_86)] | 80 | 55% | 25% | 30% | NA |

VCE: Videocapsule endoscopy; CTE: Computed tomography enterography; MRE: Magnetic resonance enterography; IY: Incremental yield; NA: Unavailable; NS: Non significant.

**Table 3 Key studies describing the role of videocapsule endoscopy in established Crohn’s disease**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Indication | Reference | *n* | Inclusion criteria | Diagnostic criteria | Results |
| Mucosal healing | Efthimyou *et al*[[28](#_ENREF_28)] | 40 | Patients with active CD (CDAI > 150) who responded to anti-inflammatory treatment, VCE was performed before and after treatment | Number of aphtous ulcers/large ulcers/ length of involved segment | Only number of large ulcers correlated with response (8.3 ± 1.4 and 5 ÷ 0.8, 95% CI 0.8–5.9, P < 0.01)\* |
| Postoperative recurrence | Bourreille *et al*[[31](#_ENREF_31)] | 31 | CD with ileocolonic anastomosis | Rutgeerts score ≥ 1 | VCE-21/31 (68%), IC- 19/31 (61%) |
| Beltran *et al*[[32](#_ENREF_32)] | 24 | CD with ileocolonic anastomosis | Rutgeerts score ≥ 2 | VCE-14/22 (55%), IC-6/24 (25%) |
| Unexplained symptoms | Dubcenco *et al*[[34](#_ENREF_34)] | 28 | Active CD patients | ≥3 ulcers | VCE- 23 (82%) ,IC-14 50% , barium radiography-9 (32%) |
| Dussault *et al*[[35](#_ENREF_35)] | 25 | Active CD patients with unexplained symptoms | Severity graded by number and appearance of ulcers and presence of stenosis | Active SB inflammation: 11/25 (44%) |

In 6 patients treated with immunomodulators, biologics or corticosteroids, a significant improvement was demonstrated in all 3 parameters. CD: Crohn’s disease;VCE: Vidoecapsule endoscopy; IC: Ileocolonoscopy; SB: Small bowel.

**Table 4 Key studies describing the role of videocapsule endoscopy in unclassified Inflammatory bowel disease pouchitis and ulcerative colitis**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Ref. | Indication | *n* | Definition of CD | Results |
| IBD-U | Mehdizadeh *et al* [[41](#_ENREF_41)] | IBDU | 6 | >3 ulcerations-diagnostic of CD, 1-2 ulcerations-suggestive of CD | 1 (17%)  SB findings |
| Maonoury *et al* [[42](#_ENREF_42)] | IBDU | 30 | >3 ulcerations-diagnostic of CD, 1-2 ulcerations-suggestive of CD | 5 (17%)-CD |
| Cohen *et al* [43] | IBDU | 2 | NA | 1 (50%)- CD |
| s/p IPAA | Mow *et al*[[40](#_ENREF_40)] | Isolated colitis | 6 | >3 ulcerations-diagnostic of CD, 1-2 ulcerations-suggestive of CD | 3 (50%)-definite CD ,2 (20%)- possible CD |
| Mehdizadeh *et al* [[41](#_ENREF_41)] | persistent symptoms after IPAA | 21 | >3 ulcerations-diagnostic of CD, 1-2 ulcerations-suggestive of CD | 7 (33%)  SB findings |
| Calabrese *et al* [[47](#_ENREF_47)] | Chronic pouchitis after IPAA | 15 | NA | Gastric or SB lesions -15 (100%) |
| Ulcerative colitis | | Mow *et al*[[40](#_ENREF_40)] | Isolated colitis | 12 | >3 ulcerations-diagnostic of CD, 1-2 ulcerations-suggestive of CD | 3 (25%)-definite CD, 3 (25%)- possible CD |
| Mehdizadeh (2008)[[41](#_ENREF_41)] | Treatment-resistant UC | 22 | >3 ulcerations-diagnostic of CD, 1-2 ulcerations-suggestive of CD | 2 (9%)- SB findings |
| Cohen(2008)[[43](#_ENREF_43)] | UC | 5 | NA | 4 (80%)- CD |
| Higurashi (2011)[[44](#_ENREF_44)] | UC | 23 | Lewis score | 13 (56.5%)- small bowel lesions  9 (39%)- Lewis score>135 |

IBDU: Unclassified inflammatory bowel disease; IPAA: Ileoanal pouch anastomosis; CD: Crohn’s disease; UC: Ulcerative colitis; SB: Small bowel.

**Table 5 Potential future technological developments in capsule endoscopy relevant to inflammatory bowel disease**

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| --- |
| Manually manipulated capsule[[77](#_ENREF_77)] |
| Electrically propelled capsule[[78](#_ENREF_78)] |
| Tissue sampling capabilities (brushing, cytology, fluid aspiration) [87] |
| Therapeutic capabilities (cautery)[87] |
| Drug delivery |