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Capsule Endoscopy in Inflammatory Bowel Disease: A Systematic Review

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Abstract

The role of video capsule endoscopy (VCE) in inflammatory bowel disease (IBD) has evolved from small bowel to a panenteric evaluation tool over the past two decades. We systematically reviewed the techniques, applications, outcomes, and complications of VCE in IBD. A systematic literature search was performed using PubMed, Embase, and Medline. All relevant original articles involving VCE in IBD were included from 2003 to July 2022. After screening 3,089 citations, finally 201 references were included. The diagnostic yield of VCE in suspected Crohn's disease (CD) was highly variable (6–80%) with excellent sensitivity (77–93%) and specificity (80–89%). The diagnostic yield in known CD was 52 to 88.3% leading to a change in management (26–75%) and disease reclassification with variable retention rates. VCE was superior to small bowel series, computed tomography (CT) and could be better than magnetic resonance enterography (MRE), especially for proximal and superficial lesions. Colon or panenteric VCE has strong correlation to ileo-colonoscopy (IC) and combined magnetic resonance imaging and IC, respectively. The VCE retention rate in CD is higher in known CD which significantly decreases after the negative patency capsule test or CT/MRE. VCE can identify lesions beyond the reach of IC in postoperative CD. Colon Capsule Endoscopy is a noninvasive monitoring tool in ulcerative colitis (UC) having a strong correlation with IC and may uncover small bowel involvement. VCE is specifically useful in IBD-unclassified (IBD-U) which can lead to the diagnosis of CD in 16.7 to 61.5%. Various scoring systems have been established and validated for small bowel CD (Lewis score and capsule endoscopy CD activity index—CECDAI), UC (capsule scoring of UC: Capsule Scoring of Ulcerative Colitis), panenteric evaluation (Capsule Endoscopy Crohn's Disease Activity Index, Elaikim score), and flare prediction (APEX score). Technological advances include double head, three-dimensional reconstruction, sampling system, panoramic view (344 and 360 degree lateral), and panenteric capsule. Artificial intelligence and software like TOP100 and Quickview can help reduce capsule reading time with excellent sensitivity and specificity. VCE in IBD has widespread application in suspected and known small bowel CD, monitoring of UC, postoperative CD, IBD-U, and for panenteric evaluation. Patency capsule testing helps to reduce retention rates significantly. Artificial intelligence and technical advances can help evolve this novel technology.

Keywords

- video capsule endoscopy
- Crohn's disease
- ulcerative colitis
- inflammatory bowel disease
- patency capsule

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Introduction

Video capsule endoscopy (VCE) is a noninvasive, widely available, nonoperator-dependent imaging modality in inflammatory bowel disease (IBD) which avoids any radiation exposure and, hence, has high patient acceptability.[1,2] Although initially developed for detecting small bowel disease, the role of VCE has evolved to panenteric evaluation.[3] The role of VCE in postoperative Crohn's disease (CD) and treatment follow-up is being increasingly recognized. The drawbacks include risk of retention and inability to procure biopsy and to detect extraluminal disease.[4] The risk of retention can be substantially reduced by the use of patency capsule testing. A new recoverable sampling system (RSS) has shown the technical feasibility of obtaining biopsy with capsule technology, however still not in routine clinical use.[5] As newer methods of deep small bowel total enteroscopy like novel motorized spiral enteroscopy have evolved parallel to the development of capsule endoscopy, the positioning of VCE in the evaluation of IBD needs reconsideration.[6] Hence, we systematically reviewed the literature to understand the current role of VCE in evaluation and monitoring of IBD.

Materials and Methods

Search Strategy

Data Sources

For the purpose of the review, we used the PubMed, Embase, and Medline databases.

Study Selection

All relevant original research articles involving VCE in IBD were included for the review from 2003 to July 2022.

Interventions

We intended to evaluate the current role of VCE in the evaluation and monitoring of IBD. We included articles using keywords such as capsule endoscopy, inflammatory bowel disease, Crohn's disease, ulcerative colitis, indeterminate colitis, panenteric capsule, artificial intelligence, postoperative Crohn's recurrence, patency capsule, Lewis score (LS), and capsule endoscopy Crohn's disease activity index.

Main Outcome Measures

The role of VCE in suspected and known CD, ulcerative colitis, postoperative CD recurrence, IBD-unclassified (IBD-U), pouchitis, role of various scoring systems, role of artificial intelligence, and technological advances were assessed.

Results

We screened total 3,089 citations and 502 were screened for full test after the exclusion of articles based on title and abstract and exclusion of duplicates. Finally, 201 citations were included for our review excluding case reports/series/original articles with a small sample size (less than 10 subjects unless they are addressing special circumstances/describing novel technique or an unique complication)/letter to editor/editorials/conference abstracts (►**Fig. 1**) and including relevant articles with specific searches and selected cross references.

Limitations

The limitations include a qualitative review of all study types given the paucity of controlled or comparative studies and preexisting meta-analysis of prospective studies in a few aspects.

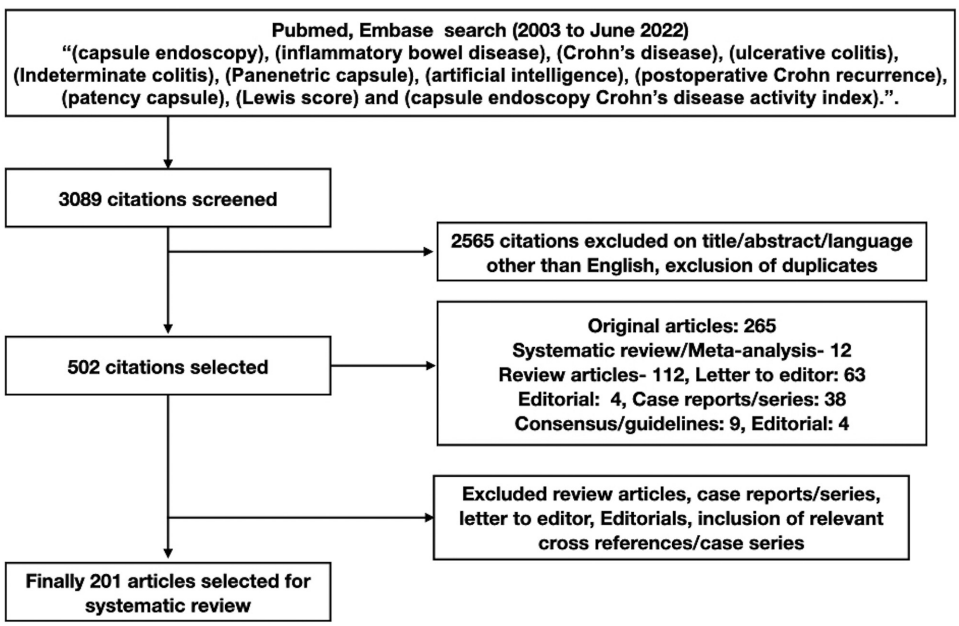

Fig. 1 Search strategy for systematic review.

Results

Role of Video Capsule Endoscopy in Inflammatory Bowel Disease

Video Capsule Endoscopy in Suspected Crohn's Disease

Study Selection and Study Characteristics

We have identified 30 original articles (13 prospective) which evaluated the role of VCE in suspected CD[7–36] (►**Table 1**).

Results

Suspicion of CD is the most common indication of VCE in IBD as per a Spanish physician survey.[37] The diagnostic yield was highly variable (6–80%) across these studies. This wide variability can be explained by the heterogeneity of study design, variable definitions of suspected CD, pretest probability in the subjects studied, and variable age groups (includes pediatric). The probability was higher with an increasing number of symptoms, elevated biochemical markers of inflammation, anemia, and hypoalbuminemia.

Three studies evaluated the sensitivity and specificity of VCE which were excellent (77–93% and 80–89%, respectively). The positive predictive values (PPVs) and negative predictive values (NPVs) varied from 50 to 77% and 92 to 96%, respectively. VCE retention rates varied from 0 to 12.5%. Two meta-analyses have shown that VCE was superior to small bowel follow through (SBFT) and ileo-colonoscopy (IC) and comparable to computed tomography enterography (one meta-analysis showed inferiority to VCE and another comparable to VCE)/MRE in the evaluation of suspected CD (see comparative yield section).[38,39]

3.1.1. Capsule Endoscopy Differentiating Crohn's Disease from Mimics (e.g., Small Bowel Tuberculosis)

Capsule endoscopy findings should be interpreted in correlation with other findings to differentiate from other similar appearing lesions like small bowel tuberculosis (SBTB), nonsteroidal anti-inflammatory drugs enteropathy, Behcet's disease, vasculitis, and also normal variation (10%). In a prospective study, out of 37 suspected CD patients on VCE, only 13% were subsequently diagnosed to have CD on 1 year follow-up.[18] On the contrary, 19% patients with nonspecific enteritis develop CD on follow-up. High baseline LS (>135) and clinical suspicion were predictors of the subsequent development of CD.[40]

To address the aforementioned issue, a prospective study from India in which VCE was done in 26 patients after proving bowel patency showed that ileo-cecal valve involvement and aphthous ulceration were universal in SBTB (100% compared with 33% in CD) and CD (100% compared with 25% in SBTB), respectively. Large ulcers were more common in SBTB as compared with CD (75 vs. 47%).[41]

3.1.2. Factors Affecting Yield of Video Capsule Endoscopy in Suspected Crohn's Disease

Based on clinical symptoms, the combination of abdominal pain and diarrhea was shown to be highly predictive of CD on VCE. Nearly, one-third with the combination of symptoms had CD in this retrospective analysis.[42] The diagnostic yield with only chronic abdominal pain was 20.9% based on a systematic review.[43] The independent predictive factors of proximal small bowel involvement were ileal involvement, stricturing behavior, and significant weight loss.[44] In suspected CD with negative IC and SBFT, the combination of anemia and increased platelet count was a significant predictor of CD on VCE.[45] Fecal calprotectin as a predictor of the lesion in VCE has shown variable results in several studies with variable cutoffs.[46–60]

Fecal calprotectin level >194 µg/g had a sensitivity and specificity of 47 and 90%, respectively, for diagnosing CD on VCE.[57] On the contrary, fecal calprotectin <50 µg/g had a negative predictive value of 91.8% of having CD on VCE based on a systematic review.[52]

Two studies have evaluated multiple parameters for the prediction of CD. A Spanish multicenter study developed and validated a scoring index based on fecal calprotectin (score 10), c-reactive protein (CRP; score 6), thrombocytosis (score 3), anemia (score 2), leukocytosis (score 2), and high erythrocyte sedimentation rate.[1] Score ranges 0 to 5, 6 to 15, and ≥16 predicted low, intermediate, and high risk of inflammatory lesions on VCE, respectively.[61]

Another elegant study has shown the incremental yield of VCE with an increasing number of International Conference on Capsule Endoscopy (ICCE) criteria. Suspected CD was defined as clinical symptoms (chronic abdominal pain/diarrhea, weight loss, and growth failure) plus any one or more extraintestinal manifestations, inflammatory markers, and abnormal imaging (SBFT/CTE). The prevalence of CD in those with suspected CD not supported by ICCE criteria, two criteria, and three criteria was 21.4, 52.6, and 77.8%, respectively. In those with LS ≥135, 82.6% had CD.[62]

3.1.3. Value of Repeat Video Capsule Endoscopy in Suspected Crohn's Disease

In a letter to the editor, Robertson et al have reported findings of 18 patients with suspected CD who underwent repeat VCE on follow-up. Those with nonspecific inflammation on initial VCE (33%) were more likely to have repeat VCE suggestive of CD (33%) along with those with higher fecal calprotectin levels.[63]

3.1.4. Role of Video Capsule Endoscopy in Presymptomatic Patients

VCE has been used in first-degree relatives of CD patients to identify those with subclinical small bowel inflammation. A cross-sectional study in 2017 by Teshima et al showed increased intestinal permeability, and small bowel ulceration (≥3) was seen in 30 and 24% of the first-degree relatives ($n = 223$) with CD. However, increased intestinal permeability did not correlate with small bowel inflammation.[64] Later, another study by Taylor et al in 2019 involving 480 asymptomatic first-degree relatives of CD has shown a risk tool comprising family history of CD, genetic variants associated with CD, and high level of fecal calprotectin predicted risk of presymptomatic small bowel inflammation.[65]

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Table 1 Summary of studies evaluating role of video capsule endoscopy in suspected Crohn's diseases

Author	Indication	Study type	*N*	Diagnostic yield	Sensitivity	Specificity	PPV	NPV	Adverse events
Fireman et al 2003[7]	Suspected CD, negative conventional imaging	Prospective	17	71%	–	–	–	–	
Herrerías et al 2003[8]	Suspected CD, negative conventional imaging	Prospective	21	43%	–	–	–	–	None
Ge et al 2004[10]	Suspected CD, negative conventional imaging	Prospective	20	65%	–	–	–	–	–
De Bona et al 2006[12]	Suspected CD, negative conventional imaging	Prospective	38	39.5% (46.2%with symptoms+ biochemical markers of inflammation)	–	–	–	–	2.6%
van Tuyl et al 2006[13]	Suspected small bowel disorders including CD	Retrospective	57	49%	–	–	61%	92%	–
May et al, 2007[15]	Abdominal pain+ diarrhea weight loss/anemia/elevated inflammatory markers	Prospective	50	54% Additional symptom increased diagnostic yield	–	–	–	–	Retention (4%)
GIrelli et al 2007[14]	Suspected CD: pain and diarrhea >3 mo + fever/ weight loss/anemia/EIM	Prospective	27	59%	93%	84%	–	–	Retention requiring surgery (11.1%)
Tukey et al 2009[18]	Suspected CD or pain and/or diarrhea	Retrospective	102	37% (13% final diagnosis of CD on follow up)	77%	89%	50% (depends on selection criteria)	96%	–
Figueiredo et al 2010[19]	Suspected CD	Retrospective	78	39.8% (56% for those with negative ileoscopy)	93%	80%	77%	94%	Retention (4%)
Adler et al 2012[21]	Perianal disease, normal ileo-colonoscopy/SBFT/CTE/MRE	Prospective	26	24%	–	–	–	–	0%
Kalla et al 2013[24]	Suspected CD	Retrospective	265	12%	–	–	–	–	–
Egnatios et al 2015[27]	Chronic abdominal pain	Retrospective	90	24.4% (27.1% with additional symptoms, 19.4% only pain)	–	–	–	–	None
Mitselos et al 2016[29]	Chronic abdominal pain and/ or diarrhea	Retrospective	91	17.6%	63.6%	92.5%	–	–	–
Lee and Lim 2016[28]	Symptomatic patients with Isolated ileitis	Retrospective	137	85.4% (high with ileal ulcer/ erosion and high ESR)	–	–	–	–	–
Song et al 2017[30]	Chronic diarrhea	Retrospective	91	42.9% (hematochezia and hypoalbuminemia were predictors)	–	–	–	–	1%

Table 1 (*Continued*)

Author	Indication	Study type	*N*	Diagnostic yield	Sensitivity	Specificity	PPV	NPV	Adverse events
Huang et al 2018[32]	Chronic abdominal pain >3 mo	Retrospective	341	28.15% (33.3% for abdominal pain + associated symptoms) (half had inflammatory pathology)	–	–	–	–	0%
Magalhaes et al 2019[33]	Suspected CD	Prospective	220	44.5% (high CRP, low iron increased yield)	–	–	–	–	–
Min et al 2013[25]	Suspected CD (pediatric)	Retrospective	17	6%	–	–	–	–	0%
Gralnek et al 2012[23]	Suspected CD (pediatric)	Prospective	10	80%	–	–	–	–	0%
Argüelles-Arias et al 2004[9]	Suspected CD (pediatric, ≥12–16 y)	Prospective	12	58.3%	–	–	–	–	0%
Wu et al 2020[34]	Symptomatic patients (abdominal pain, obscure GI bleed, diarrhea etc.) (Pediatric)	Retrospective	825	19.9% CD	–	–	–	–	Retention requiring surgery (0.4%)
Nuutinen et al 2011[20]	Suspected CD (pediatric) (8–188 mo)	Retrospective	26	62%	–	–	–	–	0%
Moy and Levine 2009[17]	Suspected CD (pediatric) (growth failure)	Retrospective	7	57.1% Improvement in height after small bowel CD treatment	–	–	–	–	1 retained in stomach
Cohen et al 2012[22]	Suspected CD (pediatric)	Retrospective	184	15%	–	–	–	–	1 retention
Esaki et al 2014[26]	Suspected CD	Retrospective	80	72.5%	–	–	–	–	6.3% retention
van Tuyl et al 2007[16]	Suspected CD	Retrospective	22	71% definitive diagnosis, 14% probable diagnosis	–	–	–	–	–
Mow et al 2004[16]	Suspected CD	Retrospective	8	37.5%	–	–	–	–	12.5%
Eliakim et al 2018[31]	Suspected CD (panenteric capsule)	Prospective	7	57.1%	–	–	–	–	None
Broderson et al 2022[36]	Suspected CD (panenteric capsule)	Prospective	59	44.8% Better image quality with increased volume of PEG but no change in diagnostic yield (43.9% versus 47.1%)	–	–	–	–	Not mentioned clearly
Tai et al 2020[35]	Suspected CD (panenteric capsule)	Prospective	22	13.6%	–	–	–	–	0%

Abbreviations: CD, Crohn's disease; CRP, c-reactive protein; ESR, erythrocyte sedimentation rate; NPV, negative predictive values; PEG, polyethylene glycol; PPV, positive predictive values.

Role of Video Capsule Endoscopy in Spondyloarthropathy
Three prospective studies have shown a high yield of VCE (12.5–42.2%) to diagnose CD in the established case of spondyloarthropathy (SpA) with bowel symptoms.[66–68] Elevated fecal calprotectin (>100 µg/g) was the predictor of small bowel CD (odds ratio = 4.5).[68] In a case series of three juvenile idiopathic arthritis, all cases were diagnosed to have CD.[69]

Video Capsule Endoscopy in Known Crohn's Disease

Study Selection and Study Characteristics
A total of 29 original articles were identified (12 prospective) evaluating the role of VCE in known CD.

Results
Overall diagnostic yield varied from 52 to 88.3%. The yield was high for symptomatic CD (highest for diarrhea—73%), whereas it was 21.1 and 4.7% only in those with clinical remission and clinico-biochemical remission, respectively.[16,20,22–26,31,35,70–88] The incremental yield over SBFT was 32 to 32.7% and 7% over IC. In a prospective study in pediatric CD, the diagnostic yield of VCE (41%) was higher than magnetic resonance imaging (MRI)/small intestinal contrast ultrasonography (SICUS; 18.2%).[75] The incremental yield in the proximal small bowel was 28 to 50%.[23,83,85] The overall change in management after VCE varied from 21 to 71% which included treatment escalation, deescalation, initiation of new medications (biologics/immunomodulators), and decision for surgery.[16,24,85,87] Other implications of VCE in known CD are reclassification of disease phenotype (11%), assessment of mucosal healing posttherapy, and prediction of relapse (higher with jejunal disease).[78,82,84] Clinical and biochemical improvement can predict mucosal healing in less than half (none at 2 weeks, 42% at 52 weeks) of the patients.[89–91] The rate of retention varied from 2.1 to 18.6% (►**Table 2**).

3.3. Video Capsule Endoscopy Compared with Other Imaging Technologies in Suspected or Known Crohn's Disease

Study Selection and Study Characteristics
In total, 9 studies including 378 patients compared the diagnostic yield of VCE with various other modalities (IC, SBFT, CTE, MRE, SICUS) in suspected CD.

Results
VCE was better than all the other modalities with regard to diagnostic yield except MRE (►**Table 3**)[29,92–98]. An earlier meta-analysis and a recent meta-analysis have also shown the same for both suspected and established CD.

Similar results were found in known CD (10 articles and 2 meta-analysis)[3,99–107]. However, SICUS had comparable sensitivity (90%) and specificity (93%) to VCE for small bowel involvement in pediatric CD.[102] Panenteric colon capsule endoscopy (PCCE) has been compared with MRE plus IC and was found that MRE + IC had 100% sensitivity (94% with VCE) but low specificity (22% compared with 74% with PCCE).[106] PCCE has been compared with reference endoscopic standard (bidirectional double balloon enteroscopy), and diagnostic accuracy was 88.3 and 77.1% for small and large bowel, respectively.[3] Compared with colonoscopy, the sensitivity and specificity of CCE were 86 and 40%, respectively.[101] Moreover, risk prediction for future flare was better with the VCE LS (AUC—area under the curve: 0.79) compared with MRE risk prediction (AUC: 0.71). Among 11 studies ($n = 439$) comprising both suspected and known CD, VCE had higher sensitivity compared with CTE, IC, and SBFT but lower specificity (53% compared with 100% with others).[108–118] Comparing the specificity of VCE according to the regions of small intestine, the specificity of VCE was lower in jejunum (61%) and proximal/mid-ileum (74%), but higher in terminal ileum (90%) compared with MRE and SICUS (►**Table 3**).[117] VCE was better compared with MRE for proximal and superficial lesions.

3.4. Risk of Retention in Suspected or Known Crohn's Disease

The risk of retention of VCE is 13% in established CD and 1.6% in suspected CD based on the earlier retrospective study by Cheifetz et al.[119] The overall retention rate in CD is 3.32% (2.35% suspected CD and 4.63% known CD) based on an updated systematic review and meta-analysis.[120] This is the reason why VCE is not generally preferred in established CD except for patients with anemia, obscure GI bleed, or assessment of mucosal healing. Retention rates were lower in pediatric CD (1.64%) compared with adult CD (3.49%).[120]

3.4.1. Predictors of Capsule Retention

Negative patency capsule testing and negative CT/MRE are negative predictors of capsule retention. The retention rates of patency capsule varied between 15.2 and 28% in known CD.[121,122] A retrospective study showed that the retention rates after positive and negative patency capsule testing were 11 and 2.1%, respectively.[123] Similarly a prospective study showed 28.9% retention rates with active inflammation on MRE.[122] Based on meta-analysis, the retention rates in established CD remained 2.88% even after patency capsule testing and 2.32% after CT/MRE. The risk of retention is reduced after CT/MRE by 50%. MRE has a sensitivity of 92.3% and specificity of 59% to evaluate capsule retention as compared with 97 and 83%, respectively, for patency capsules. MRE tends to overdiagnose the risk of capsule retention. If only MRE is used to predict retention instead of patency capsule, nearly 40% patients (specificity—59%) would not undergo VCE due to fear of capsule retention.[122]

Other predictors were obstructive symptoms, stricturing/penetrating disease, BMI≤ 5th percentile, suspected stenosis on SBFT, restricted diffusion on diffusion-weighted MRI, extensive small bowel thickening on small bowel ultrasound, longer stricture length and higher number of prestenotic dilatations, high CRP, and history of abdominal surgery according to several studies[119–136] (►**Supplementary Table S1**, available in the online version).

Table 2 Summary of studies evaluating role of video capsule endoscopy in known Crohn's diseases

Author	Indication	Study type	*N*	Yield/Incremental yield	Impact on management	Adverse events/retention
Cotter et al 2014	Known CD	Retrospective	50	Incremental yield- 66%	Initiation of immunomodulators/biologics increased by 26%	6% retention
Dussault et al 2013	Known CD	Retrospective	77	Overall yield - 62%	53.5% 60% in unexplained anemia 58% when performed for assessing disease location 20% when performed for discordance between symptoms and morphology	4.2% transient retention after negative patency testing
Elosua et al 2022	Known CD	Retrospective	432	Overall yield - 63.7%	51.4%, Escalation- 46.1%, De-escalation-5.3% Escalation:89.5% in moderate-severe disease, 57.8% mild disease	2.5% retention, all managed nonsurgically
Flamant et al 2013	Known CD	Retrospective	108	Jejunal lesions -56%	Increased risk of relapse with jejunal lesions	5.5% retention
Hansel et al 2018	Known CD	Prospective	50	Proximal small bowel incremental yield- 28%	Altered management- 34% New medication initiated- 29% Exclusion of active small bowel disease- 24%	None reported except dysphagia in one
Kopylov et al 2015	Known CD	Retrospective	187	Overall yield- 71.6%	52.3%	Retention 2.1%
Mehdizadeh et al 2010	Known CD	Retrospective	134	Overall yield - 52% (highest for diarrhea -73%) Incremental yield- 32% (to SBFT) 7% (to IC)	Not evaluated	None
Melmed et al 2018	Known CD	Prospective	53	Proximal small bowel -85%	Not evaluated, high correlation with IC No correlation with clinical severity indices (CDAI)	None were capsule related
Niv et al 2014	Known CD	Prospective	19	78.9% at week 0 84.6% at week 4	Not evaluated, No correlation with sequential clinical severity indices (CDAI)	No retention
Park et al 2007	Known CD	Retrospective	52	32.7% (over-SBFT)	28.8%	Retention-9.6% Surgery- 3.8%
Petruzziello et al 2010	Known CD	Prospective	32	50% (in CD involving distal ileum)	Not evaluated	3% retention
Santos-Antunes et al 2015	Known CD	Retrospective	106	Proximal small bowel -46% (incremental yield)	40% Immunomodulator therapy post-VCE 44 vs. 21% pre VCE	None
Lorenzo-Zúñiga et al 2010	Known CD	Prospective	14	85.7%	64%	None
Long M et al 2011	Known CD, indeterminate	Retrospective	86 (CD)	77.9%	Change in medication: 51.1% New IBD medication: 39.5% Surgery: 12.8%	16 cases of retention 8 required operative intervention

(*Continued*)

Table 2 (*Continued*)

Author	Indication	Study type	*N*	Yield/Incremental yield	Impact on management	Adverse events/retention
	colitis and pouchitis					
Nardo et al 2011	Known pediatric CD	Prospective	44	41% with VCE vs. 18.2% with MRI/SICUS	Not evaluated	None
Kalla et al 2013	Known CD	Retrospective	50	66%	Management was altered in 48%	None
Greener et al 2016	Known CD	Prospective	56	51%	Reclassification of disease phenotype in 11%	1 patient had temporary patency capsule retention
Min et al 2013	Known pediatric CD	Retrospective	50	70% (43% extensive disease compared with other imaging)	75% Improved growth, BMI, HBI, and ESR on follow-up	None
Gralnek et al 2012	Known pediatric CD	Prospective	4	50% more proximal involvement detected	75% change in management	None
Oliva et al 2019	Known pediatric CD	Prospective	48	71% (panenteric capsule endoscopy)	71% change in management Mucosal healing achieved at 24 and 52 wk were 54 and 58% respectively compared with 21% at baseline	No serious event except for nausea and vomiting in 3 patients
Nuutinen et al 2011	Known pediatric CD	Retrospective	9	56%	–	1 had retention requiring elective surgery
Cohen et al 2012	Known pediatric CD	Retrospective	61	57.3%	–	9.8%
Cohen et al 2008	Known pediatric CD	Retrospective	21	62%	23.8% change in management	1 had retention
Esaki et al 2014	Known CD	Retrospective	94	88.3%	75% (8/12) of colonic disease reclassified as ileo-colonic disease	7.4% retention
Tuyl et al 2007	Known CD	Retrospective	14	71% definitive diagnosis 14% probable diagnosis	21% changed management	None
Mow et al 2004	Known CD	Retrospective	20	70%	60%	5% retention
Eliakim et al 2018	Known CD	Prospective	29	55.17% (panenteric capsule) 31% proximal disease	Not evaluated	None
Tai et al 2020	Known CD	Prospective	71	67.6%	38.7% had change in management Upstaging of Montreal classification 33.8% Mucosal healing 15.5%	2.8%
Kopylov et al 2015	Known CD (clinical remission or mild symptoms)	Prospective	56	21.1% in those in clinical remission 4.7% in clinico-biochemical remission	Mucosal healing and deep remission are rare in CD in clinical remission and hence may require escalation of therapy	0%

Abbreviations: BMI, body mass index; CD, Crohn's disease; CRP, c-reactive protein; ESR, erythrocyte sedimentation rate; HBI, harvey bradshaw index; MRI, magnetic resonance imaging; NPV, negative predictive values; PEG, polyethylene glycol; PPV, positive predictive values; SBFT, small bowel follow through; SICUS, small intestinal contrast ultrasonography; VCE, video capsule endoscopy.

Table 3 Video capsule endoscopy compared with other diagnostic modalities in suspected and known Crohn's disease

Author	Study type	*N*	Indication	Diagnostic yield	Comparator	Diagnostic yield of competing technology
Eliakim et al 2002	Prospective	20	Suspected CD	70%	Barium meal follow through (BMFT) Entero-CT	BMFT: 37% EnteroCT: 50%
Di Nardo eta 2010	Prospective	18	Suspected IBD	50%	MRI and/ or SICUS	22.2%
Eliakim et al 2004	Prospective	35	Suspected CD	77%	Barium meal follow through (BMFT) Entero-CT	BMFT: 23% EnteroCT: 20%
Voderholzer et al 2004	Prospective	41	Known CD	60.9	CTE	29.2%
Albert et al. 2005	Prospective	27	Suspected CD ($n=14$) + known CD ($n=13$)	93%	MRI Fluoroscopic enteroclysis	MRI: 78% Enteroclysis: 33%
Chong et al 2005	Prospective	43	Suspected CD ($n=21$) + known CD ($n=22$)	Suspected CD:19% Known CD 77% Change in management 70%	Push enteroscopy Enteroclysis	Enteroclysis (19% known CD, 6% suspected CD) Push enteroscopy: 16% known CD, 0% suspected CD)
Marmo et al 2005	Prospective	31	Known CD	71% 89% (with terminal ileal involvement) 46% (proximal small bowel)	Enteroclysis	25.8% 37% (with terminal ileal involvement) 13% (proximal small bowel)
Hara et al 2006	Prospective	17	Suspected CD	71%	IC CTE SBFT	IC: 65% CTE: 53% SBFT: 24%
Efthymiou et al 2008	Prospective	55	Suspected CD ($n=26$) + known CD ($n=29$)	Suspected CD:65% Known CD 74.1%	Enteroclysis	Enteroclysis (3% suspected CD, 40.7% known CD) ($p<0.05$)
Solem et al 2008	Prospective	28	Suspected CD + known CD	Sensitivity:83% Specificity:53%	CTE IC SBFT	CTE Sensitivity: 67% Specificity:100% ($p=0.02$) IC Sensitivity:67% Specificity:100% ($p=0.03$) SBFT Sensitivity:50% Specificity:100% ($p=0.2$)
Bocker et al 2010	Prospective	21	Suspected or known CD	42.9%	MRI	28.6%
Petruzziello et al 2010	Prospective	30	Suspected CD	50% Incremental yield: 33%	IC SICUS SBFT	IC: 63% SICUS: 40% SBFT: 50%
Casciani E et al 2011	Prospective	37	Pediatric suspected CD	Sensitivity: 97.6% Specificity: 92.3% Accuracy: 98.3%	MRE	Sensitivity: 91.9% Specificity: 90.9% Accuracy: 100%

(*Continued*)

Table 3 (*Continued*)

Author	Study type	*N*	Indication	Diagnostic yield	Comparator	Diagnostic yield of competing technology
Jensen et al 2011	Prospective	93	Suspected or newly diagnosed CD	Sensitivity: 100% Specificity: 91% (terminal ileum)	CTE MRE	CTE Sensitivity: 76% Specificity: 85% MRE Sensitivity: 81% Specificity: 86%
Wiarda et al 2011	Prospective	38	Suspected CD ($n=20$) + known CD ($n=18$)	Sensitivity: 57% Specificity: 89% PPV: 67% NPV: 84%	MRE	Sensitivity: 73% Specificity: 90% PPV: 88% NPV: 78%
Kovanlikaya et al 2013	Retrospective	23	Children with suspected or known IBD	Sensitivity 77.8%	MRE	Sensitivity: 75%
Aloi M et al, 2014	Prospective blinded, comparative	25	Pediatric suspected CD ($n=6$) + known CD ($n=28$)	Sensitivity in jejunum, proximal /midileum and terminal ileum were 92, 100, and 81%, respectively	MRE SICUS	Sensitivity: MRE: jejunum: 75%, Proximal/mid ileum: 100%, terminal ileum: 81% SICUS: jejunum: 92%, Proximal/mid ileum: 80%, terminal ileum: 94% Specificity of capsule lower in jejunum (61%) and proximal/mid ileum (74%) but higher in terminal ileum (90%)
Leighton et al 2014	Prospective	80	Suspected small bowel CD	VCE + IC (small bowel + colon)- 97.3% VCE (terminal ileum+ cecum) - 49.2% VCE (small bowel)- 93%	1. IC (terminal ileum + cecum) 2. SBFT + IC (small bowel + colon) 3. SBFT (small bowel)	1. IC (terminal ileum + cecum) −70.5% ($p=0.09$) 2. SBFT+ IC (vs. IC + VCE) − 57.3% ($p<0.001$) 3. SBFT (small bowel) (vs. VCE) − 25.6%
Oliva et al 2015	Prospective	40	Pediatric known CD	Colon Sensitivity: 89% Specificity:100% PPV: 100% NPV: 91% Small bowel Sensitivity: 90% Specificity: 94% PPV: 95% NPV: 90%	SICUS MRE	SICUS (small bowel) Sensitivity: 90% Specificity: 93% MRE (small bowel) Sensitivity: 85% Specificity: 89%
Leighton et al 2016	Prospective	114	Known active CD with proven bowel patency	Panenteric capsule endoscopy: 83.3%	IC	69.7%
Mitselos et al 2016	Retrospective	91	Suspected CD	Sensitivity: 81.82% Specificity: 77.50% PPV: 53.85% NPV: 94.87% AUC: 0.781	IC	Sensitivity: 63.64% Specificity: 92.50% PPV: 33.33% NPV: 96.88% AUC: 0.797

Table 3 (*Continued*)

Author	Study type	*N*	Indication	Diagnostic yield	Comparator	Diagnostic yield of competing technology
Carter D et al, 2018	Prospective	50	Suspected CD-negative ileocolonoscopy	38%	IUS	38%, Sensitivity: 72%, specificity: 84% compared with capsule endoscopy which was considered gold standard
Gonzalez-Suarez et al 2018	Prospective	47	Suspected CD ($n=15$) + known CD ($n=32$)	76.6% (higher in jejunal, ileal and terminal ileal lesions)	MRE	44.7% (capsule significantly better for superficial and proximal lesions)
Hijaz et al 2019	Prospective	27	Children with CD or indeterminate colitis	Sensitivity: 83% Specificity: 78.6%	MRE	Sensitivity: 100% Specificity: 57.14% Capsule has lower sensitivity but high specificity
Bruining DH et al 2020	Prospective	99	Known CD (Panenteric capsule)	Sensitivity 94% (proximal small bowel 97%) Specificity: 74%	MRI + IC	Sensitivity: 100% Specificity: 22% ($p=0.021$; similar specificity in terminal ileum and colon)
Yamada et al 2021	Prospective	20	Known CD, Colon capsule endoscopy	Diagnostic accuracy (detecting ulcers) Small bowel-88.3% Large bowel-78.1%	Bidirectional double balloon enteroscopy	Reference standard
Dubsenco et al 2005	Prospective	39	Known and suspected CD	Sensitivity: 89.6% Specificity-100.0%, Positive predictive value:100% Negative predictive value: 76.9	Small bowel series	Sensitivity: 27.6% Specificity: 100.0% PPV: 100.0% NPV: 32.3%.
D'Haens et al 2015	Prospective	40	Colonic CD (paneneteric capsule PCCE-2)	Sensitivity: 86% Specificity: 40%	Colonoscopy	Reference standard Better estimated the disease severity compared with PCCE-2 PCCE-2 better tolerated
Papalia et al 2021	Prospective	47	Known ileo-colonic, nonstricturing CD for mucosal healing	Strong correlation with SES-CD scores in colonoscopy ($r=0.77$), strongest in terminal ileum	Colonoscopy	PCCE-2 identified additional ulcers PCCE-2 was complete in 68% cases compared with 89% colonoscopy PCCE-2 noninvasive modality for monitoring
Ben Horin et al 2019	Prospective	61	Clinically quiescent known CD for predicting flare	Lewis score >350 predicted risk of flare with AUC 0.79	Fecal calprotectin MRE	Fecal calprotectin (AUC) 2 y flare: 0,62 6 mo flare: 0.81 MRE risk prediction (AUC) 2 y:0.71

Abbreviations: AUC, area under the curve; CD, Crohn's disease; IC, ileo-colonoscopy; CTMRI, magnetic resonance imaging; IUS, intestinal ultrasound; MRE, magnetic resonance enterography; PCCE, panenteric colon capsule endoscopy; SES- CD, simple endoscopic score Crohn's disease; SICUS, small intestinal contrast ultrasonography.

3.4.2. Management of Retained Capsule

Capsule retention is asymptomatic in 85% which can be managed conservatively with enteroscopy-guided removal electively. Partial air complete small bowel obstruction occurs in the rest which requires endoscopic retrieval with or without balloon dilation. There are several reports of retrieval by double-balloon enteroscope (success rate 80–92%) and recently novel motorized spiral enteroscopy which can avoid surgery in the majority.[137–139] Moreover, it can help take surgical decisions as some of the patients may require surgery even after capsule removal for treating the underlying disease.

3.4.3. Other Complications of Video Capsule Endoscopy

Although known CD substantially increases the risk of capsule retention, other complications of VCE like swallow disorder, aspiration, and technique failure can be substantial and clinically important. However, we could not find specific citations pertaining to IBD with regard to this. Meta-analysis, which included IBD patients, showed that the pooled rates of aspiration, technical failure, and swallow disorders were 0, 0.94, and 0.75%, respectively.[140]

3.4. Video Capsule Endoscopy in postoperative Crohn's Disease

Study selection and study characteristics

Five prospective and one retrospective study including 313 patients have compared VCE with colonoscopy in postoperative CD (►**Supplementary Table S2**, available in the online version).

Results

Except for the one retrospective study,[141] all the studies concluded that the yield of VCE was higher than colonoscopy in detecting postoperative recurrence especially for proximal involvement out of the reach of the colonoscopy.[142–147] Another prospective study has compared capsule endoscopy or no capsule endoscopy in postoperative settings and has shown that VCE arm had lower hospitalization or surgery[147] (►**Supplementary Table S2**, available in the online version).

3.5. Video Capsule Endoscopy in UC

Study Selection and Study Characteristics

In total, 14 prospective and 3 retrospective studies involving 612 patients have evaluated the role of VCE in ulcerative colitis (UC) (►**Table 4**).[11,20,23,31,75,148–159]

Results

Overall results indicate that VCE had an excellent correlation with colonoscopy for severity/extent of inflammation and is better than fecal biomarkers. Patient acceptability was better than colonoscopy. Small bowel involvement in UC with VCE is variable (4.8–80%) and is dependent on the pretest probability (80% for those with suspicion of CD in a small series).[11,23,31,149,150,156] In postproctocolectomy cases, extensive colitis, pouchitis, and age less than 20 years were predictors of small bowel involvement.[150] Active UC was also a predictor of small bowel involvement (40% compared with overall 36.6%).[150] No adverse events are reported except those related to bowel preparation and one case of retention due to unexpected rectal tumor (►**Table 4**).[157] Bowel preparation was acceptable in 62 to 90% cases (►**Table 4**).

3.5.1. Role of Video Capsule Endoscopy in Pouchitis

A single-center prospective study has shown that all of the patients with chronic antibiotic refractory pouchitis have small bowel lesions from duodenum to ileum detectable on VCE which ranges from aphthous to deep, fissuring ulcers. None of the patients have any prior evidence of CD on review of surgical biopsy. These patients need to be followed up further, and the significance of such lesions is still unknown.[160] In a retrospective study, small bowel capsule endoscopy in pouchitis showed positive findings in 65.2%. Initiation of new IBD medications was noted in 56.5%, and small bowel resection was done in 4.4% following VCE.[76]

3.6. Video Capsule Endoscopy in Inflammatory Bowel Disease-Unclassified

Study Selection and Study Characteristics

VCE could be particularly helpful in the IBD unclassified subgroup, where up to 16.7 to 50% patients can be diagnosed with CD after undergoing VCE as per four retrospective and five prospective studies in 177 adult and pediatric patients (►**Supplementary Table S3**, available in the online version).[23–25,75,148,161–164]

Results

However, VCE can miss a diagnosis of CD as five of the aforementioned studies have shown that 0 to 16.7% patients develop CD on follow-up.[23,148,161,162,164] A change in existing treatment after CD diagnosis may not be necessary in all the patients as the reported change in treatment after CD diagnosis was seen in 0 to 100%.[24,163,164] A confirmed diagnosis of UC after exclusion of small bowel involvement in IBD-U can occur in 5.5 to 59.3%.[23,161–164] No change in diagnosis of IBD-U can occur in 0 to 75% cases (►**Supplementary Table S3**, available in the online version). LS >135 is a predictor of CD diagnosis with a sensitivity and specificity of 90 and 100%, respectively.[164]

3.7. Scoring Systems for Video Capsule Endoscopy

Scoring systems in VCE may help predict disease severity and disease course similar to conventional endoscopic scoring. There are various validated scores for small bowel, colon, and panenteric evaluation.

3.7.1. Lewis Score

Study Selection and Study Characteristics

Total 9 studies (2 prospective) including 811 patients evaluated the role of the LS alone.[62,165–172]

Results

LS was initially developed by Gralnek et al based on edema, ulceration, and stenosis in three tertiles with the

Table 4 Summary of studies evaluating role of video capsule endoscopy in ulcerative colitis

Author	*N*	Study type	Small bowel involvement	Correlation with colonoscopy	Cleanliness	Adverse events
Ye et al 2013	26	Prospective		Excellent correlation with extent and severity of UC	80%	None
Higurashi et al 2011	23 UC and 23 healthy volunteers	Prospective	57%, correlated with disease activity	Not studies	Not evaluated	None
Hisabe et al 2011	30	Prospective	36.6% (40% in active UC and 33% in postproctocolectomy) (extensive colitis, pouchitis and age <20 y are predictors)	Not evaluated	–	None
Hosoe et al 2013	42	Prospective	Not evaluated	Strong correlation with colonoscopy	<50% good or excellent cleansing level	None
Juan Acosta et al 2014	42	Prospective	3 out of 42 patients	Good correlation for severity and extent of inflammation	80%	None
Matsubayashi et al 2020	41	Prospective	Not evaluated	Capsule Scoring of Ulcerative Colitis (CSUC) better than fecal biomarkers for predicting relapse	Not mentioned	None
Meister et al 2013	13	Prospective	Not evaluated	Colonoscopy detected vessel vulnerability, granulated mucosa, mucosal damage and disease extension better than capsule endoscopy	90% good or fair	None
Okabayashi et al 2018	33	Prospective	Not evaluated	Good correlation with endoscopic indices of severity. Active disease had longer transit time with resultant poor acceptability	77.2% acceptable	5.1% from laxatives, 7.7% delayed excretion (> 24 hours)
Oliva et al 2014	30, Pediatric	Prospective	Not evaluated	High sensitivity (96%), specificity (100%), positive predictive value (100%), negative predictive value (85%)	62% adequate, 24% fair	None
Shi et al 2017	150	Prospective	Not evaluated	Good correlation ($R = 0.64$–0,67) for severity of mucosal inflammation (sensitivity: 97%)	66%	21% mainly related to bowel preparation, one serious adverse event due to retention by unexpected rectal tumor

(*Continued*)

Table 4 (*Continued*)

Author	*N*	Study type	Small bowel involvement	Correlation with colonoscopy	Cleanliness	Adverse events
Sung et al 2012	100	Prospective	Not evaluated	High sensitivity (89%), specificity (75%), positive predictive value (93%), negative predictive value (65%)	64% acceptable, 31% fair	No serious adverse events, all related to bowel preparation
Nardo et al 2011	29	Prospective	No incremental yield	Not evaluated	Not evaluated	None
Gralnek et al 2012	2	Prospective	50%, diagnosis changed to CD	Not evaluated	Not evaluated	None
Nuutinen et al 2011	21	Retrospective	4.8%	–	–	None
Cohen et al 2011	5	Retrospective	80% (UC with suspicion of CD)	–	–	None
Mow et al 2004	20	Retrospective	59%	Not evaluated	Not evaluated	None
Eliakim et al 2018	5	Prospective	40% (panenteric capsule)	Not evaluated	Not mentioned separately	None

Abbreviation: CD, Crohn's disease.

establishment of cut-off values (►**Table 5**; ►**Fig. 2**).[165] Later, the incremental number of ICCE criteria was found to be the predictive factor of significant inflammatory activity (LS >135) on VCE.[62] LS $\geq$ 135 was shown to have a positive predictive value of 73.9%, and a score <135 had a negative predictive value of 91.8%.[168] Similar findings were seen in another validation study. A strong agreement was seen for global as well as for each tertile score in interobserver study.[166] Recent studies have evaluated the prognostic role of LS to predict CD-related emergency hospitalization and risk of cumulative relapse.[171,172] Correlation of VCE with disease activity and small bowel transit time was weak in adults, whereas correlation with inflammatory markers was moderate in both pediatric age group and adults.[169] LS score correlates well with the MRE global score ($r=0.71$) except the proximal LS score ($r=0.55$).[170]

3.7.2. Capsule Endoscopy Crohn's Disease Activity Index

Capsule Endoscopy Crohn's Disease Activity Index (CECDAI) or Niv score was also developed at the same time as the LS (2008) which was simpler and based on severity of inflammation, extent of disease, and narrowing in proximal and distal small bowel. Interobserver agreement was strong ($k=0.87$) in single center and good between different centers ($k=0.767$).[173,174] The score has been validated by Ponte et al in 2018 which showed that the corresponding cut-off value of CECDAI for LS between 135 and 790 was 7.7 to 10.3.[175] Another study showed the cut-off value to be 3.8 to 5.8 which also showed that LS better correlates with fecal calprotectin ($<100\,\mu g/g$) than CECDAI.[176,177] In comparison to LS, a retrospective study has shown that CECDAI may better predict intestinal inflammation. Those with high LS and normal CECDAI may reflect strictures rather than active inflammation.[58]

3.7.3. Panenteric Capsule Endoscopy Scores

As panenteric evaluation became feasible with VCE, panenteric scores were developed. The first one was CECDAlic which was an extension of CECDAI score into colon. Inflammation, extent of disease, and narrowing were evaluated in proximal small bowel, distal small bowel, right colon, and left colon. The concordance was high for small bowel (Kendell's coefficient: $k=0.85$) and panenteric evaluation ($k=0.77$) except for strictures in proximal small intestine and distal colon.[178] Later, it was validated and was shown to have excellent interobserver agreement ($k=0.94$).[179]

The second panenteric score was based on novel PillCam Crohn's (PCC) (Medtronic, Dublin, Ireland) capsule. Panenteric scores were calculated from five areas: three tertiles of small intestine, right, and left colon. Each subscore was calculated using most common lesion (1), most severe lesion (2), extent of disease (3), and stricture (4) (each parameter rated from 0 to 3). Each segmental score was $([A+B]\times C)+D$. This score also named as the Elaikim score was shown to have an excellent correlation with LS and had excellent interobserver agreement ($k=0.9$).[180]

Table 5 Summary of studies on video capsule endoscopy scoring systems

Author and year	Scoring system	Area of bowel	*N*	Study type	Study objective	Results
Granlek et al 2008	LS	Small bowel	44	Prospective	Development of scoring index	Based on villous edema, ulcer and stenosis in three tertiles, LS was developed, score <135: clinically insignificant,135–790: mild, ≥790: moderate to severe.
Rosa et al 2012	LS	Small bowel	56	Retrospective	Usefulness of LS in suspected CD as per the ICCE criteria	Patients with suspected CD based on one or more ICCE criteria were more likely have inflammatory activity (LS > 135) compared with those in whom none of the ICCE criteria were present (incremental increase with increase in the number of ICCE criteria)
Cotter et al 2015	LS	Small bowel	70	Retrospective	Interobserver agreement	Strong interobserver agreement in each tertile and global score ($k = 0.852–0.960$; $p < 0.0001$)
Monteiro et al 2015	LS	Small bowel	95	Retrospective	Diagnostic accuracy of the LS in patients with suspected CD undergoing capsule endoscopy	LS > 135 had an overall diagnostic accuracy of 83.2% with a sensitivity, specificity, positive predictive value, and negative predictive value of 89.5, 78.9, 73.9, and 91.8%, respectively for the diagnosis of CD.
De Castro et al 2015	LS	Small bowel	53	Retrospective	Assess prognostic value of the severity of inflammatory lesions quantified by the LS	Increased need for steroid (RR: 5) and hospitalization (RR: 13.7) on multivariate analysis
He et al 2017	LS	Small bowel	150 (30 pediatric)	Retrospective	Correlation of LS with disease activity, inflammatory markers and small bowel transit time (SBTT)	Correlation with disease activity: moderate (pediatric), weak (adults) Correlation with inflammatory markers: Moderate (both) Correlation with SBTT: none (pediatric), weak (adults)
Nishikawa et al 2019	LS	Small bowel	125	Retrospective	Predicting emergency hospitalization and clinical relapse	An LS of 264 was an useful cutoff value that could predict CD-related emergency hospitalization and cumulative risk of relapse (AUC: 0.92)

(*Continued*)

Table 5 (*Continued*)

Author and year	Scoring system	Area of bowel	*N*	Study type	Study objective	Results
Nishikawa et al 2021	LS	Small bowel	102 (retrospective) + 66 (prospective)	Retrospective + prospective	Predicting emergency hospitalization and clinical relapse based on retrospective analysis followed by prospective validation	LS $\geq$ 270 or prognostic nutrition index (PNI) $<$ 45 had a significantly higher risk of Crohn's disease-related emergency hospitalization. Additional treatment in these patients
Klang et al 2018	LS for validation of MRE global score	Small bowel	50	Prospective	Validation of MRE global score using LS and fecal biomarkers	Significant correlation of LS with global MRE score ($r = 0.71$, $p < 0.001$), the correlation of MRE global score with Proximal LS score ($r = 0.55$). Correlation with fecal calprotectin was higher with MRE global score compared with LS
Gal et al 2008	CECDAI	Small bowel	20	Prospective	Assessment and validation	Strong interobserver agreement ($k = 0.87$) Convenient, reliable and reproducible diagnostic and follow-up tool
Niv et al 2012	CECDAI	Small bowel	62	Prospective	Validation of CECDAI score	The correlation between endoscopists between different centers was good ($r = 0.767$)
Miyazu et al 2021	CECDAI	Small bowel	21	Prospective	To assess use of CECDAI to predict need of additional treatment for patients in clinical remission	CECDAI was useful in assessing requirement of additional treatment for CD patients in clinical remission (more in those with CECDAI $\geq$ 5.8)
Koulaouzidis et al 2012	LS and CECDAI	Small bowel	49	Retrospective	Comparison of correlation with fecal calprotectin with LS and CECDAI	In patients with fecal calprotectin $<$100 µg/g, correlation was better with LS compared with CECDAI. In patients with elevated fecal calprotectin ($>$100 µg/g), neither LS and CECDAI correlated with fecal calprotectin.
Omori et al 2019	CECDAI and LS	Small bowel	132	Retrospective	Compare the usefulness of CECDAI and LS	CECDAI better reflect the status and severity of intestinal inflammation than LS Those with high LS but normal CECDAI may reflect strictures rather than active inflammation
Ponte et al 2017	CECDAI and LS	Small bowel	53	Retrospective	To identify cut off values of CECDAI as corresponding to LS cut offs	LS threshold values of 135–790 in LS corresponds to CECDAI cutoff values of 7.7–10.3, both scores did not have any correlation to CRP or Harvey–Bradshaw index

Table 5 (*Continued*)

Author and year	Scoring system	Area of bowel	*N*	Study type	Study objective	Results
Elaikim et al 2020	Elaikim score	Panenteric	41	Substudy of a RCT	Correlation with LS and reliability	Excellent interobserver agreement ($k = 0.9$) and strong correlation with calprotectin levels ($r = 0.54$) which was better than with LS ($r = 0.32$)
Niv et al 2016	CECDAIic	Small bowel and colon	10	Prospective	Extension of Niv score into colon to establish a new score for small bowel and colon	Concordance high (0.85 for small bowel and 0.77 for entire bowel) except for proximal small bowel and distal colonic strictures
Arieira et al 2019	CECDAIic	Panenteric	22	Retrospective	Interobserver agreement and the correlation with inflammatory parameters.	Excellent interobserver agreement ($k = 0.94$) and strong correlation with calprotectin levels ($r = 0.82$) moderate correlation with CRP ($r = 0.5$)
Hosoe et al 2018	Capsule Scoring of Ulcerative Colitis (CSUC)	Large bowel	40	Prospective	Development of endoscopic score for UC with colon capsule endoscopy 2	Correlation of newly developed CSUC (score 0–14 based on with fecal calprotectin and Lichtiger index)
Macedo Silva et al 2022	APEX score	Small bowel	47	Retrospective	Prediction of flare in small bowel CD	Age $\leq$ 30 y ($+$ 3 points), platelet count $\geq$ 280×10^3/L ($+2$ points) and extraintestinal manifestations ($+2$ points) to calculate APEX score (low: 0–3, high: 4–7) to predict CD flare during the first year after achieving mucosal healing

Abbreviations: CD, Crohn's disease; CECDAIic, Capsule Endoscopy Crohn's Disease Activity Index; CRP, c-reactive protein; ICCE, International Conference on Capsule Endoscopy; LS, Lewis score; MRE, magnetic resonance enterography.

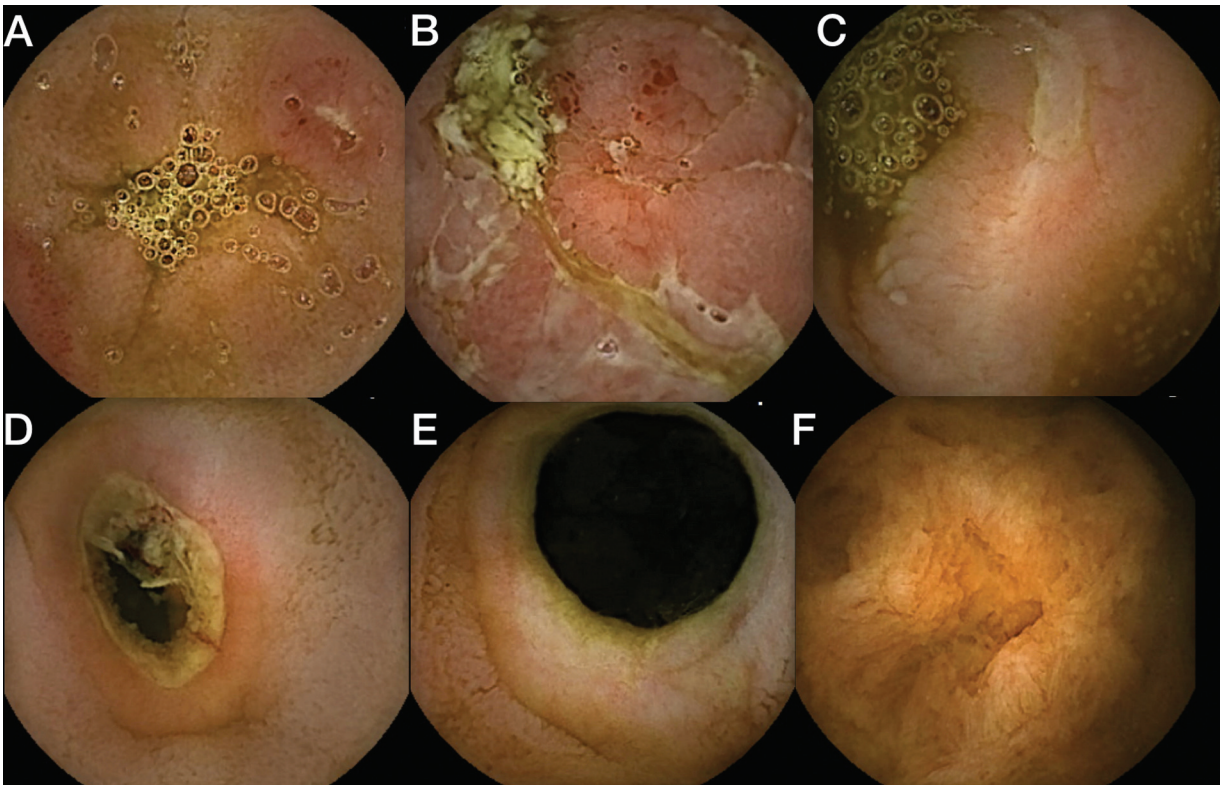

Fig. 2 Video capsule endoscopy in Crohn's disease. (**A**) Aphthous ulcers, (**B**) linear ulcer, (**C**) transverse hemicircumferential ulcer, (**D**) circumferential ulcerated stricture, (**E**) fibrotic stricture, and (**F**) mucosal edema.

3.7.4. Capsule Scoring of Ulcerative Colitis

Similar to ulcerative colitis endoscopic activity index (UCEIS), Capsule Scoring of Ulcerative Colitis (CSUC) is based on parameters like vascular pattern (0: none, patchy obliteration[1] <30%, obliterated[2] >30%), bleeding (0: none, automated suspected blood indicator $<10=1$, $>10=2$), and erosions/ulcers (0: none, 1: <5 mm erosion, 2: >5 mm superficial ulcer, 3: excavated deep ulcer ± excavation/raised margins) in second-generation colon capsule endoscopy. Each item was subdivided into proximal and distal parts with the reference point being the splenic flexure. The total score was 0 to 14. Its correlation with fecal calprotectin, CRP, and clinical Lichtiger index was similar to UCEIS.[181]

3.7.5 APEX Score

This is based on age (≤30 years) (+3), platelet count ($\geq 280 \times 10^3$/L) (+2), and extraintestinal manifestations (+2) which were shown to predict risk of 1 year relapse after achieving mucosal healing in small bowel CD based on a recent retrospective study.[182]

3.8. Interobserver Agreement in Diagnosing Small Bowel Crohn's Disease with Video Capsule Endoscopy

There is substantial interobserver agreement (IOA) for the detection of small bowel CD with VCE ($k=0.68$). IOA was moderate for localization ($k=0.44$) and only fair for aphthous ulcers ($k=0.38$). Although small bowel CD can be diagnosed confidently with VCE, diagnosis can be observer dependent in those with few lesions. Differentiating ileal from cecal lesions can be difficult in a minority of patients.[183]

3.9. Artificial Intelligence

Study Selection and Study Characteristics

We found nine original articles on the use of artificial intelligence in VCE related to IBD.

Results

AI technology was used for Pillcam SB 3, panenteric capsule, and colon capsule. A variable number of training images (469–483,444) were used to develop the various AI technology followed by validation. The sensitivity and specificity of the AI models were 80 to 97.1% and 89 to 98.1%, respectively[184–192] (►**Supplementary Table S4**, available in the online version). Hence, AI can significantly reduce the examination time with excellent sensitivity and specificity.

3.10 Novel Techniques and Future Directions

Study Selection and Study Characteristics

We found eight original articles describing various technical advances for VCE in IBD[5,193–199](►**Table 6**).

Results

To increase the visibility and diagnostic yield, double head capsule and 344 degree panoramic view capsules have been developed.[198] For rapid review, the QuickView mode of RAPID capsule view software can reduce the reading time with excellent diagnostic accuracy up to 98%.[194] 3D reconstruction can help in the estimation of size of lesions.[197]

Table 6 Summary of studies studying technological advances in video capsule endoscopy pertaining to inflammatory bowel disease

Author and year	Indication	*N*	Capsule technology	Basic principle	Advantages	Drawbacks
Yung et al 2021	Small bowel inflammation and reassessment of known IBD	84	MiroCam MC2000	Double head capsule instead of conventional single head capsule	13.1% clinically significant different finding with new technology	Potential to overreport if the same lesion is visualized at different time points by different camera heads
Yau et al 2021	IBD	Pre-clinical	Recoverable sampling system	Automatic sampling of gastrointestinal fluids and storage of analytes using preservatives to stabilize DNA and proteins	May enable sampling of GI fluid without endoscopy	Intact ileo-cecal valve is mandatory for triggering tissue sampling
Tontini et al 2020	Suspected or known CD	41	PillCamTM Crohn's System, PCS; Medtronic, Dublin, Ireland	344 degree panoramic view	Higher diagnostic yield (56 vs. 39%) Better clinical management (48.8 vs. 31.7%)	Overestimation of lesion Higher reading time Lower image quality
Nam et al 2020	Suspected or known CD	14	MiroCam MC4000	3D reconstruction using stereo camera-based technology	3D reconstruction Size estimation for lesions	The value in altering clinical management not clear Size estimation function needs validation
Koulaouzidis et al 2012	Suspected or known CD	81	QuickView (QV) mode RAPID capsule view software	Rapid capsule video review	Reduction in capsule reading time	Blue mode does not add any advantage over white light Decreased overall diagnostic yield
Halling et al 2013	Suspected CD	40	QV mode RAPID capsule view software	Rapid capsule video review	Reduction in capsule reading time Sensitivity 94% Diagnostic accuracy 98%	False negative in terminal ileal lesions Significant number of missed lesions
Freitas et al 2020	Suspected or known CD	115	TOP 100 software tool of the RAPID Reader	Automatic selection of 100 images that will most likely contain abnormalities	Prompt calculation of Lewis score and high agreement in moderate to severe inflammatory activity	Needs further validation Agreement less in mild inflammatory activity
Tontini et al 2014	CD	1	CapsoCam SV-1 (Capso- Vision, Inc. Saratoga, CA, United States)	Lateral panoramic 360 degree viewing	Improved diagnostic yield	Needs further validation

Abbreviations: CD, Crohn's disease; IBD, inflammatory bowel disease.

A novel RSS capsule technology has been developed which may allow noninvasive sampling, preservation, and storage of analytes found in gastrointestinal fluids which can correlate with inflammation and gut permeability. The preservative contained in the novel capsule stabilizes DNA and proteins for analysis after expulsion.[5]

3.11. Cleansing Regimen

A randomized controlled trial in pediatric patients has shown that 25 mL/kg of polyethylene glycol (PEG) solution plus 20 mL (376 mg) of oral simethicone was superior to high volume PEG (50 mL/kg), oral simethicone, and low-dose PEG alone (25 mL/kg) with regard to better visualization but not diagnostic yield.[200] According to a prospective study, the addition of 15 mL of castor oil to 1 L of Moviprep and 10 mg bisacodyl significantly improved colon capsule endoscopy completion rates (87 vs. 73%) and polyp detection (82 vs. 44%)[201].

4. Discussion

VCE is indicated in suspected small bowel CD after negative IC (nearly 10% of small bowel CD) if there are no obstructive symptoms or known stenosis/history of bowel surgery. If these are present, cross-sectional imaging (CT/MRE) is warranted. In those with positive findings in IC, VCE may still be indicated for mapping of the disease as one-third may have proximal bowel involvement.[44] The inherent limitation of VCE to evaluate the extraluminal involvement can be an additional reason to use cross-sectional imaging upfront especially in tuberculosis endemic regions where distal small bowel involvement often leads to TB and CD dilemma. The long duration of symptoms should also be kept in mind as it may indicate stricturing complications with high risk of retention.[6] VCE is also helpful to exclude differential diagnosis like TB and diagnose CD in presymptomatic patients.

The role of VCE in known CD ranged from diagnosis of active disease (highest in symptomatic patients), change in treatment decisions (escalation or deescalation of treatment and surgical decision), reclassification of disease, assessment of mucosal healing, and prediction of relapse. The yield was noninferior to MRI. However, the risk of retention is higher in known CD. PCCE has high agnostic accuracy in detecting active disease in small and large bowels.

VCE can also be useful in postoperative settings. However, the drawbacks of VCE in postoperative settings are lower yield in neoterminal ileum, inability to perform in those with positive patency testing, and poor correlation of endoscopic activity in VCE and clinical recurrence.

Capsule endoscopy can have role in relatively noninvasive monitoring of disease activity in UC with excellent correlation with colonoscopy. It has the advantage of identifying small bowel involvement although the preparation may be poor in a third of the patients.

VCE scores have a good correlation with cross-sectional imaging (e.g., MRI scores) and can be helpful to establish the extent of small bowel, panenteric, and large bowel involvement with the existing scores (Lewis, CECDAI, Capsule Endoscopy Crohn's Disease Activity Index [CECDAIic], CSUC). Scores like APEX can predict the risk of relapse in small bowel CD.

Technical advances in the form of artificial intelligence, technical modification, and various software packages can reduce reading time with high diagnostic accuracy. Technology like RSS has the potential to guide therapy by disease monitoring and characterization and may also help in developing novel therapeutic targets.

The limitations of the review include qualitative nature and inclusion of primarily uncontrolled, noncomparative studies. The highest quality citations included good-quality prospective studies. Individual meta-analysis of the different outcomes is out of the scope of this broader systematic review. The strength of this review is the inclusion of all relevant articles pertaining to the role of VCE in IBD. The review implies the need for further comparative studies such as comparing MRI with VCE in suspected and known CD or comparison of VCE with other modalities like IC for diagnosing postoperative recurrence. In areas where randomized controlled trials are not available, high-quality prospective studies can give true estimates of VCE yield in scenarios such as IBD-U and pouchitis and their implications in future disease courses.

Conclusion

Capsule endoscopy is indicated in the evaluation of suspected small bowel CD irrespective of findings of IC to map small intestinal involvement, and the diagnostic yield is superior to other modalities except MRE. Hence, VCE should be the preferred investigation in suspected CD in the absence of obstructive symptoms or known stenosis. A cross-sectional imaging (CTE/MRE) or patency capsule testing should be done prior to CE in suspected stricturing CD or established CD. In known CD, VCE should not be preferred over cross-sectional imaging due to the risk of retention. It can be done in established CD to evaluate unexplained anemia, obscure GI bleed, and sometimes assessment of mucosal healing. Capsule retention is usually asymptomatic, however, symptomatic cases can be treated with balloon or spiral enteroscopy-guided retrieval failing which surgery is warranted. Various scoring systems are available for small bowel, colon, and panenteric evaluation. Scoring systems at VCE can help to determine severity and disease course similar to endoscopic scoring. VCE is useful to assess postoperative CD, IBD-U, and noninvasive monitoring of UC. Artificial intelligence and newer technologies increase the diagnostic yield and reading time of VCE and are the future avenues in this evolving field.

Authors' Contribution

P.P. was responsible for conceptualization, literature review and writing original draft, and illustrations. P.P., R.G., and P.M.R. were responsible for images. M.T., R.B., R.G., P. M.R., and D.N.R. were responsible for proof reading and critical review. M.T., P.P., R.B., R.G., P.M.R., and D.N.R. were responsible for approving final manuscript.

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None declared.

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