

Capsule Endoscopy in Inflammatory Bowel Disease

Evolving Role and Recent Advances



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KEYWORDS

- Video capsule endoscopy • Crohn's disease • Pan-enteric capsule
- Artificial intelligence • Inflammatory bowel disease

KEY POINTS

- Video capsule endoscopy (VCE) has a high diagnostic performance in both suspected and established Crohn's disease (CD).
- VCE plays a crucial role in predicting future clinical flares among patients with CD, even those in clinical and biochemical remission, as well as for post-operative surveillance.
- Artificial intelligence-based VCE reading may shorten capsule reading time and provide accurate prognostication information regarding lesion severity and classification.
- Up to 43% of inflammatory bowel disease-unclassified patients may be reclassified to CD based on VCE findings.
- Although colon capsule performs well compared to ileocolonoscopy in detecting mucosal inflammation in ulcerative colitis, issues with bowel preparation and colorectal cancer surveillance remain.

INTRODUCTION

Introduced in 2000, small-bowel capsule endoscopy (SBCE) marked a significant advancement in small bowel (SB) assessment,¹ enabling a reliable, non-invasive evaluation of the entire SB in a single procedure.^{2,3} The accumulated data on SBCE use and advantages have led to new patient monitoring models in gastroenterology^{2,4} and specifically among Crohn's disease (CD) patients.^{2,5,6}

Given that up to 75% of CD patients have SB involvement, with almost a third having exclusive SB disease⁷ the value of SBCE in CD is considerable. SBCE is effective in diagnosing and monitoring CD, identifying remission states, predicting flares and postoperative recurrence.^{5,8} Unlike SBCE, the use of pan-enteric capsule (ie, PillCam Crohn's

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capsule [PCC]) is not yet included in current guidelines, although its ability to assess both the SB and colon in one procedure is promising.⁹ Video capsule endoscopy (VCE) has proven effective in classifying inflammatory bowel disease-unclassified (IBD-U) patients and shows a strong correlation with ileocolonoscopy (IC) in detecting mucosal inflammation in ulcerative colitis patients.^{10–13}

In recent years, artificial intelligence (AI) applications including convolutional neural network (CNN) have been widely studied in patients undergoing VCE.¹⁴ Its use may shorten VCE reading time and improve the accurate identification and classification of CD-related lesions^{15,16} in this population.

Of the available capsule endoscopy systems,¹⁷ the vast majority of the existing literature on CD has focused on Medtronic capsules. However, there are other notable capsules in use, as detailed in [Table 1](#).

In this manuscript, we aimed to review the existing literature regarding the evolving role and recent advances of VCE in IBD, especially CD, including innovative fields of AI-assisted VCE reading and interpretation.

SMALL BOWEL CAPSULE ENDOSCOPY

Suspected Crohn's Disease

CD diagnosis typically combines clinical symptoms, inflammatory biomarkers, and endoscopic evaluation, often confirmed by histology from IC biopsies.¹⁸ However, about 30% of CD patients have exclusive proximal SB involvement, beyond IC's reach.^{19,20} In these cases, IC's diagnostic yield is limited,¹⁹ and patients with normal IC results are usually diagnosed using cross-sectional imaging studies.

Several studies^{21–23} have shown SBCE's effectiveness in diagnosing SB-CD. Leighton and colleagues demonstrated SBCE's superiority over SB follow-through (SBFT) in detecting SB inflammation, performing comparably to IC.²² Combined use of SBCE and IC identified SB inflammatory lesions in 107/110 patients with suspected CD, compared to 63/110 using SBFT and IC ($P < .001$). A meta-analysis by Dionisio and colleagues,²³ demonstrated that SBCE had higher diagnostic yield compared to SBFT (52% vs 16%) and computed tomography enterography (CTE) (68% vs 21%) for CD-related lesions in suspected CD patients. SBCE and magnetic resonance enterography (MRE) had comparable performance (50% vs 43%, $P = .23$) for detecting CD-related lesions. Choi and colleagues's meta-analysis confirmed SBCE's superiority over SBFT but demonstrated similar yield between SBCE and both CTE and MRE for the detection of mucosal inflammation in suspected CD.²⁴ Notably, SBCE outperformed IC in detecting terminal ileum (TI) lesions (47% vs 25%, $P = .009$ ²³); but was comparable to CTE in the same anatomic locale (40% vs 32%, 95% confidence interval [CI] $-0.02 = 0.19$).²⁴ Kopylov and colleagues's²⁵ meta-analysis, showed that SBCE and MRE had similar diagnostic performance for CD-related lesions in suspected CD patients (odds ratio [OR] 3.24, 95% CI 0.14 to 72.76, $P = .46$).

Of the prime benefits of SBCE is its high diagnostic performance for detecting proximal SB inflammation. As demonstrated by Kopylov and colleagues,²⁵ among 251 patients, SBCE was superior to MRE in detecting proximal SB inflammation (OR 2.79, 95% CI 1.2–6.48, $P = .02$). Therefore, SBCE is at least equivalent to MRE/CTE for SB-CD diagnosis, with a notable advantage in proximal SB locales. A practical CD diagnostic algorithm is provided in [Fig. 1](#).

Established Crohn's Disease

SBCE's diagnostic performance in patients with established CD has been well-documented. A meta-analysis by Dionisio and colleagues²³ showed the superiority of

Table 1
Technical features of the most commonly used video capsules in Crohn's disease

	PillCam SB3 (Medtronic, Given Imaging)	PillCam COLON2 (Medtronic, Given Imaging)	PillCam Crohn's (Medtronic, Given Imaging)	EndoCapsule (Olympus)	MiroCam (Intromedic)	OMOM (Jinshan Science and Technology)	CapsoCam (CapsoVision)	NaviCam (Ankon, AnX Robotica)
Dimensions (mm)	11.4 mm × 26.2 mm	11.6 mm × 31.5 mm	11.6 mm × 31.5 mm	11 mm × 26 mm	11 mm × 24.5 mm	13 mm × 27.9 mm	11 mm × 31 mm	11.8 mm × 27 mm
Resolution	340 × 340	256 × 256	256 × 256	512 × 512	320 × 320	640 × 480	221 × 184	640 × 480
Field of view	156°	344°	336°	145°	170°	140°	360°	160°
FPS	2–6	4–35	4–35	2	3	2	20	0.5–6
Battery life	≥8 h	≥10 h	≥10 h	≥8 h	≥10 h	≥6 h	≥12 h	≥16 h
Optical domes	1	2	2	1	1	1	4	1

Abbreviations: SB, small bowel; FPS, frames Per Second.

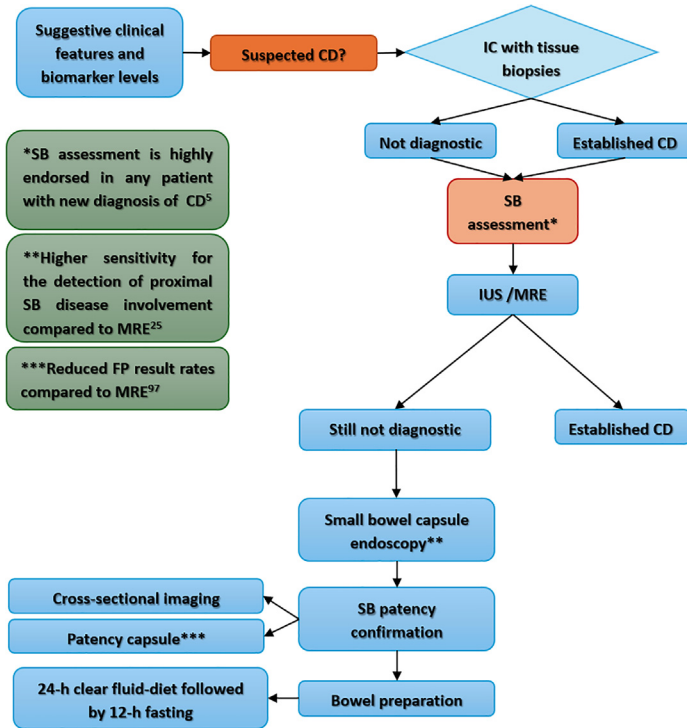


Fig. 1. Practical algorithm in diagnosing Crohn's disease. *Abbreviations:* CD, Crohn's disease; FP, false positive; IC, ileocolonoscopy; IUS, intestinal ultrasound; MRE, magnetic resonance enterography; SB, small Bowel.

SBCE over SBFT (diagnostic yield: 71% vs 36%, $P < .001$) and CTE (diagnostic yield: 71% vs 39%, $P < .001$), but a comparable one to MRE (70% vs 79%, $P = .65$). Recently, meta-analyses by Choi and colleagues demonstrated the comparable diagnostic yield of SBCE to SBFT, CTE, IC and MRE.²⁴ as Kopylov and colleagues,²⁵ showed SBCE and MRE to have a comparable diagnostic performance in this population.

In the following paragraphs we present the current data on the main indications for SBCE use in CD, including determining accurate anatomic extent, monitoring mucosal healing (MH), predicting future clinical flares, and postoperative surveillance.

Crohn's Disease Anatomic Extent

Accurate anatomic extent assessment is crucial in evaluating CD patients, as proximal SB involvement is linked to poor clinical outcomes in CD.^{26,27} SBCE is superior to MRE in detecting proximal SB inflammation, while MRE is better for determining disease phenotype and structural damage.^{28–31}

In a study by Hansel and colleagues,³² SBCE detected proximal SB disease in 28% of CD patients, undetected by MRE or CTE, leading to treatment changes in 34% of cases. Greener and colleagues,³³ showed that SBCE superior to MRE for determining disease extent in CD with undetermined location (51% vs 25%, $P < .001$), though less accurate in identifying disease phenotype (11% vs 26%, $P = .005$).

Gonzales-Suarez and colleagues compared SBCE and MRE for assessing CD's anatomic extent.³⁴ SBCE detected active CD in 36/47 patients, while MRE detected it

in 21/47 patients. SBCE showed superior performance to MRE in detecting jejunal and ileal inflammation, leading to changes in disease extent in 53.1% of patients compared to 12.7% with MRE ($P<.001$). Elosua and colleagues found proximal SB activity in 131/432 (30.3%) of patients using SBCE, resulting in changes in disease extent in 92 patients, and subsequent treatment modifications in more than half of the patients.³⁵

McCurdy and colleagues³⁶ evaluated SBCE for detecting luminal CD in 45 patients with isolated perianal fistula (IPF) and normal IC and abdominal enterography. CD-related inflammatory lesions were found in 26% of these patients, compared to 3% of controls ($P<.001$). Immunosuppressive agents were recommended for 70% of patients with IPF versus 15% of controls, with treatment modifications made in 58% of patients with active luminal CD detected by SBCE.

Mucosal Healing Monitoring in a Treat-To-Target Approach

MH is a paramount goal in managing CD, as it is linked to improved clinical outcomes.³⁷ Baert and colleagues showed that early-stage CD patients achieving MH had over 70% steroid-free remission after 4 years.³⁸ Meta-analyses by Reinink and colleagues³⁷ and Shah and colleagues³⁹ showed that MH was associated with higher long-term clinical remission rates and lower surgery and hospitalization rates. The STRIDE-II initiative emphasizes this goal, using IC or VCE for lesions beyond IC's reach.⁴⁰ For many CD patients, SBCE is crucial for accurately assessing MH.

Kopylov and colleagues⁴¹ found that only one-third of CD patients in clinical and biochemical remission achieved MH as determined by SBCE. Another study by Kopylov and colleagues⁴² indicated that VCE should not be limited to CD patients with elevated inflammatory markers, as these markers were not reliable predictors of CD inflammation detected by SBCE.⁴² Similarly, Aggarwal and colleagues⁴³ showed that 60% of CD patients in clinical remission had mucosal inflammation detected by SBCE, whereas only 85% had elevated fecal calprotectin (FC) levels. Melmed and colleagues⁴⁴ demonstrated a strong correlation between SBCE and IC mucosal activity scores, but no correlation between clinical/biochemical measures and endoscopic activity scores. Thus, mucosal visualization is crucial, even in CD patients in clinical and biochemical remission.

Few studies have used SBCE to assess MH in response to treatment. Hall and colleagues⁴⁵ prospectively examined 43 CD patients on immunomodulators/biologics, finding that 42% achieved MH after 52 weeks. Nakamura and colleagues,⁴⁶ reported SB mucosal inflammation (ie, Lewis score [LS]>135) in 40 patients, with only 28 (70%) patients showing clinical symptoms. Following SBCE results, treatment was modified in 38/40 patients, and 23/29 patients who underwent SBCE at 6-month follow-up showed LS improvement.

A study by Wetwittayakhlang and colleagues⁴⁷ found adalimumab to induce MH in 47% of patients with proximal SB-CD, defined as LS less than 350. Niv and colleagues's meta-analysis,⁴⁸ confirmed that VCE-scoring systems (ie, Capsule Endoscopy Crohn's Disease Activity Index [CECDAI] and LS) effectively predicted MH during 24-month follow-up (OR 11, 95% CI 3.74–32.73, $P<.001$ for improved outcomes).

Prediction of Future Flares in Patients with Crohn's Disease

Identifying high-risk CD patients for future clinical flares is promising, to better optimize disease management. Ben-Horin and colleagues.⁶ demonstrated that in CD patients in clinical remission, LS greater than or equal to 350 predicted clinical flares within 2 years (Hazard ratio [HR] of 10.7, 95% CI 3.8 to 30.3, $P<.001$). SBCE-LS's predication remained stable over time (6 months: Area under the curve [AUC] – 0.82, 24 months: AUC – 0.79), while FC's decreased (6 months: AUC – 0.81, 24 months: AUC – 0.62),

suggesting different roles in short/medium-term and long-term prediction. An extended follow-up (ie, median follow-up ≤ 5 years) found that middle SB-LS greater than or equal to 135 identified high-risk CD patients for treatment failure (HR 6.317, 93% negative predictive value), regardless of disease phenotype.⁴⁹

A recent study presented by our group, showed proactive treatment modification in high-risk CD patients (ie, $LS \geq 350$) in clinical remission significantly reduced clinical flares within 24 months compared to standard-of-care treatment (OR 0.14, 95% CI 0.04–0.57, $P < .001$).⁵⁰

Nishikawa and colleagues⁵¹ found that LS greater than or equal to 270 predicted clinical flares, hospitalization, and endoscopic/surgical interventions in CD patients within 2 years. Patients whose treatment was modified based on SBCE findings experienced fewer clinical flares and hospitalizations.

Postoperative Surveillance of Patients with Crohn's Disease

Yung and colleagues's meta-analysis showed that SBCE, MRE and intestinal ultrasound accurately evaluated postoperative endoscopic recurrence in CD patients,⁵² SBCE had 100% sensitivity, 69% specificity, OR of 30.8 (95% CI, 6.9–138), and AUC of 0.94 for detecting endoscopic recurrence.

Han and colleagues,⁵³ found that patients who underwent both IC and SBCE post-resection had lower clinical recurrence rates within 1 year compared to IC alone (2.7% vs 21.7%, $P = .019$). SBCE detected 11/37 endoscopic recurrences missed by IC. Shiga and colleagues found that monitoring with SBCE in a treat-to-target approach led to lower rates of composite outcome (ie, hospitalization, re-operation, endoscopic dilation) during 26-month follow-up ($P = .028$).⁵⁴ **Table 2** summarizes SBCE's value in established/suspected CD.

COLON CAPSULE AND PAN-ENTERIC CAPSULE ENDOSCOPY IN CROHN'S DISEASE

Colon Capsule Use in Crohn's Disease

The performance of the second-generation colon capsule endoscopy system (CCE-2) was first assessed in a case series by Negreanu and colleagues in 2014.⁵⁵ The use of CCE-2 allowed for a thorough examination of the TI and colon in a single procedure among CD patients who either declined IC or had failed to complete this procedure, leading to significant alterations in disease management.

D'Haens and colleagues⁵⁶ showed that among 40 patients with active CD, CCE-2 underestimated the severity of mucosal inflammation compared to IC as a reference method, using the Crohn's Disease Endoscopic Index of Severity⁵⁷ with sensitivity and specificity rates of 86% and 40%, respectively. Carvalho and colleagues⁵⁸ demonstrated the feasibility and safety of CCE-2. This study included 12 patients with quiescent non-complicated (B1) CD, undergoing CCE-2 following SBCE with IC at least 1 year apart. Pan-enteric visualization was available in 10/12 of patients.

Hausmann and colleagues⁵⁹ showed that CCE-2 may serve as an eligible tool for postoperative surveillance in CD patients. Out of 15 patients who underwent IC, active disease (ie, Rutgeerts⁶⁰ index (RI) $\geq i2$) was identified in 5 individuals, all of whom were also detected using the CCE-2. CCE-2 revealed active disease in one patient in the proximal SB that was missed during IC.

Yamada and colleagues⁶¹ demonstrated a high diagnostic performance of CCE-2 in detecting inflammatory lesions using double balloon enteroscopy as a reference method, with sensitivity and specificity rates of 95.5%, 90.0%, for detecting ulcers.

Papalia and colleagues,⁶² demonstrated lower completion rates (ie, TI to rectum visualization) for CCE-2 compared to IC among CD patients (68% vs 89%), attributed to

Table 2
Clinical applications using small-bowel capsule endoscopy in suspected or established Crohn's disease

SBCE Features	Significant Findings
Diagnostic yield	Higher diagnostic performance of SBCE compared to SBFT (52% vs 16%) and CTE (68% vs 21%) ²³ A comparable diagnostic performance between SBCE and MRE (10 studies, 400 patients, OR 1.17; 95% CI 0.83–1.67) in the detection of CD-related lesions in the SB. However, SBCE was significantly more effective than MRE in identifying proximal SB CD (7 studies, 251 patients, OR 2.79; 95% CI 1.2–6.48) ²⁵
Determining anatomic extent	SBCE led to changes in anatomic extent in 51%–53.1% of patients compared to 12.7%–25% using MRE among patients with CD ($P<.05$) ^{34,35}
Treatment modifications	SBCEs' findings led to treatment alternation in 34%–51.3% of CD patients ^{33,36}
Clinical flare prediction	Among CD patients in clinical remission, LS $\geq$ 350 predicted a future clinical flare within 2-y follow-up ⁶ LS $\geq$ 270 was associated with future clinical flares and hospitalization among CD patients within 2-y follow-up ⁵¹ Middle small bowel LS of $\geq$ 135 predicted treatment failure during follow-up of up to 5 y, regardless of disease-phenotype ⁴⁹
Mucosal healing (MH) assessment	Achieving MH and maintaining a low capsule endoscopy activity index (Niv or LS) significantly predicted endoscopic improvement within a 12-wk to 24-mo follow-up period (OR 11.06 ($P<.001$)) ⁴⁸ Among CD patients who were treated with adalimumab, MH was achieved in 27% of them at week 12 and in up to 50% at week 52 ^{2,45}
Post-operative endoscopic recurrence	SBCE provided precise evaluations of endoscopic recurrence during postoperative surveillance in CD undergoing intestinal resection (sensitivity-100%, specificity-69%, and OR of 30.8 compared to IC as a reference method) ⁵² Repeated SBCE procedures following surgery allowed for precise evaluation of residual and recurrent lesions prior to the onset of clinical symptoms ⁵⁴
IBD-U	Studies indicated that VCE can reclassify 15%–43% of IBD-U patients to CD based on mucosal findings during SBCE procedure ^{11,12,134–136}

Abbreviations: CD, Crohn's Disease; CTE, computed tomography enterography; IBD-U, inflammatory bowel disease–unclassified; IC, ileocolonoscopy; LS, lewis score; MH, mucosal healing; MRE, magnetic resonance enterography; OR, odds ratio; SBCE, small bowel capsule endoscopy; SBFT, small Bowel follow through

inadequate bowel preparation. CCE-2 had better diagnostic performance, detecting additional lesions primarily located in the TI and ascending colon, while IC detected more lesions in the distal colon and rectum which were overlooked by CCE-2.

PAN ENTERIC CAPSULE AND ITS USE IN CLINICAL PRACTICE IN PATIENTS WITH CROHN'S DISEASE

Encouraged by the advantages of colon capsule in detecting proximal SB inflammatory lesions, a novel pan-enteric VCE was introduced in 2017, known as the PCC (Medtronic, Yokneam, Israel), which has been tailored for patients with CD. PCC features include a dual-headed capsule with an extensive field of view spanning 344°. ⁶³ The PCC system,

inclusive of both hardware and software components, offers a unique approach for evaluating mucosal inflammation in the entire small and large intestines in patients with CD. Its software divides the SB into 3 anatomical-equivalent segments based on length, and the colon into 2 segments (ie, right and left colon segments). Subsequently, 3 key parameters are evaluated: disease distribution, lesion severity, and linear extent.⁶³

PillCam Crohn's Capsule Feasibility

Eliakim and colleagues⁶³ prospectively enrolled 41 patients with suspected or established CD aiming to examine PCC functionality in this population. The PCC completion rate was 100%, with excellent image quality (95%) and entire bowel coverage, and without any event of capsule retention (CR). Bowel cleanness was excellent/good in 97.5% and 75.6% of cases for the SB and colon, respectively, using 4 L of purgative sulfate-free polyethylene glycol (PEG) in 2 divided doses (ie, the evening before, and the day of examination). This study showed that the PCC system may enable a comprehensive assessment of the entire small and large bowel in a single procedure.⁶³

PillCam Crohn's Capsule Diagnostic Performance

Leighton and colleagues^{65, 61} compared the diagnostic yield of PCC and IC in patients with active CD. PCC detected inflammatory lesions in 83.3% of patients, compared to 69.7% by IC, a yield difference of 13.6% (95% CI, 2.6%–24.7%). PCC identified CD-related lesions in 12 patients with normal IC results: 5 in the TI, 3 in both TI and colon, and 4 in the colon.⁶⁴ IC detected mucosal inflammation in 3 cases that were missed by the PCC (2-TI, 1-colon).

In a multicenter study by Bruining and colleagues⁶⁵ 99 CD patients underwent PCC, IC, and MRE. PCC showed higher sensitivity and specificity than MRE for proximal SB disease (97% vs 71%, $P = .021$ and 87% vs 66%, $P = .020$). PCC and IC had comparable performance in the colon, but PCC had higher specificity for TI inflammation than MRE or IC (82% vs 37%, $P < .001$).⁶⁵ Our recent study found that PCC detected active CD in 93% of patients compared to 74% with MRE ($P = .04$).⁶⁶ PCC also performed better for proximal SB disease than MRE (46% vs 2.3%, $P < .001$).⁶⁶

Tontini and colleagues,⁹ conducted a prospective multicenter study with 41 patients with suspected/established CD, comparing PCC to a standard 172°-view capsule. PCC had a 90% completion rate and detected more lesions (56.1% vs 39.0%, $P = .023$), resulting in a higher LS (222.8 vs 185.7, $P = .031$) and improved disease management (48.8% vs 31.7%; $P = .023$).

Determination of Crohn's Disease Anatomic Extent

PCC has proven to be a valuable diagnostic tool for accurately determining disease anatomic extent, and to optimize disease management. Tai and colleagues⁶⁷ found that PCC altered anatomic extent in 27/71 (33%) patients with established CD and led to treatment escalation in 36/93 (39%) patients with suspected/established CD. Both FC and C-reactive protein (CRP) were less effective than PCC in detecting active disease.⁶⁷

In 2024, Oliva and colleagues⁶⁸ published a study of 194 CD patients (144-adults, 50-pediatric) who underwent 249 PCCs. Pediatric patients had a higher likelihood of extensive anatomic involvement and more prominent colonic involvement compared to adults.⁶⁸

Mucosal Healing Monitoring in a Treat-to-target Approach Using PillCam Crohn's Capsule

Oliva and colleagues⁶⁹ evaluated PCC's diagnostic yield for monitoring MH and remission in 48 pediatric patients with quiescent CD. PCC prompted treatment changes in

71% at baseline and 23% at 24-week timepoint. By week 52, 58% of patients achieved MH, up from 21% at baseline. An extension follow-up showed that, after 104 weeks, 93.5% of patients who achieved MH at week 52 maintained it. The latter was associated with improved clinical outcomes.⁷⁰

In 2022, Volkers and colleagues⁷¹ examined PCC's performance in identifying mucosal inflammation at baseline and after initiating biologic treatment in 28 CD patients. At baseline, 22 patients had mucosal inflammation; after 10 to 12 weeks, 27% achieved endoscopic remission (ie, absence of ulcers), and 59% showed endoscopic response. This study reinforced PCC's responsiveness to mucosal changes under biologic treatment.

The Predictive Role of PillCam Crohn's Capsule

Oliva and colleagues⁶⁸ found that a higher most common lesion (MCL) score on PCC was an independent predictor of the need for treatment escalation in CD patients (OR: 4.09, 95% CI, 1.80–9.25; $P = .001$). Disease anatomic extent involving greater than 30% predicted future clinical/endoscopic relapse (OR: 2.98, 1.26–7.08; $P = .013$) as well. For pediatric CD patients, disease anatomic extent was the only factor associated with endoscopic recurrence (OR: 4.50, 95% CI, 1.47–13.77; $P = .008$). In adult CD patients, the degree of lesion severity, described by both MCL and most severe lesion (MSL), was the best predictor of treatment escalation (OR: 4.31, 5% CI, 1.52–12.1; $P = .006$).⁶⁸ Fig. 2 summarizes the value of PCC use in CD.

VIDEO CAPSULE ENDOSCOPY-INFLAMMATORY SCORING SYSTEMS

Activity Scoring-Systems for Small Bowel Capsule Endoscopy

There are 2 main VCE-inflammatory scoring systems to quantitate the degree of mucosal inflammation during SBCE procedure. The LS,⁷² which is the most commonly used VCE-inflammatory score divides the SB into 3 tertiles based on SB transit-time in which each tertiles' LS composed of 3 SB capsule built-in parameters (ie, mucosal edema, presence of ulcers, and the presence of strictures). Both grade severity and disease anatomic extent are taken into account upon LS calculation (Table 3). The degree of inflammation is then classified into one of 3 categories: LS less than 135—normal or clinically insignificant mucosal inflammation; greater than or equal to 135 and less than

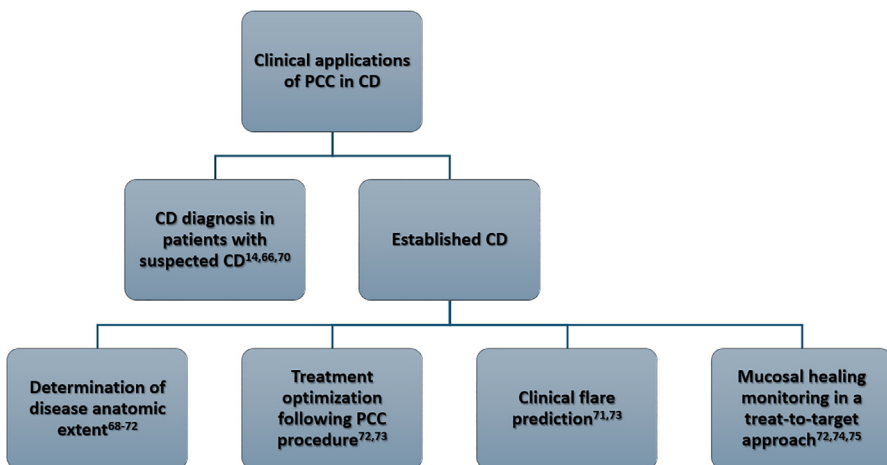


Fig. 2. Clinical applications using PillCam Crohn's capsule (PCC) in Crohn's disease (CD).

Table 3
Video capsule endoscopy's scoring-system

Scoring System	Calculation	Notes
Lewis score (LS) ⁷²	Mucosal inflammation is quantified for each Of the small bowel tertiles, which are equally divided based on capsule transit time. Key parameters: edema, ulcer, stricture. The LS is the highest score of the 3 tertiles.	LS key parameters: • Villi ([normal-0/edematous-1]+[short-8/long-12/whole tertile-20]+[single-1/patchy-14/diffuse-17]) • Ulcer ([none-0/single-3/few-5/multiple-10] + [short-5/long-10/whole tertile-15] + [$\frac{1}{4}$-9/$\frac{1}{4}$-12/>$\frac{1}{2}$-18]) • Stenosis ([none-0/single-14/multiple-20] + [ulcerated-24/nonulcerated-2] + [trasversed-7/not trasversed-10]) <i>Classification</i> -Normal/clinically insignificant (<135), mild (135≤ and<790), and moderate-to-severe (≥790).
The Capsule Endoscopy Crohn's Disease Activity Index [that is, Niv score] ⁷⁶	3 aspects evaluated: A. Inflammation score 0 → None 1 → Mild to moderate edema/hyperemia/denudation 2 → Severe edema/hyperemia/denudation 3 → Bleeding, erosion, small ulcer (<0.5 cm) 4 → Moderate ulcer (0.5–2 cm), pseudo polyp 5 → Large ulcer (>2 cm) B. Extent of disease 0 → None 1 → Focal disease (ie, single segment) 2 → Patchy disease (ie, multiple segments) 3 → Diffuse disease C. Stricture score 0 → None 1 → Single passed 2 → Multiple passed 3 → Obstruction	$CEDCAI = (A1 \times B1 + C1) + (A2 \times B2 + C2) + (A3 \times B3 + C3) + (A4 \times B4 + C4)$, where 1- Proximal small bowel 2- Distal small bowel, 3- Right colon, 4- Left colon.

Crohn's Disease Activity in Capsule Endoscopy [CDACE]⁷⁹

The small bowel is divided into 4 quartiles. Severity of inflammation in each quartile is graded on a scale from 0 to 4:

- 0 → Normal mucosa
- 1 → Edematous/reddish appearance
- 2 → Erosion (<0.5 cm)
- 3 → Irregular/circular ulcer (0.5–2 cm)
- 4 → Longitudinal/large ulcer/cobblestone appearance
- Scores are summed to obtain the location of inflammatory (Li) score (0–16).
- Number of quartiles with inflammatory lesions: reflects the range of inflammation; R score (0–4).
- The stenosis (S) score is graded from 0–3:
 - 0 → No stenosis
 - 1 → Single passage
 - 2 → Multiple passages
 - 3 → No passage

The CDACE score is calculated as:

Li score × 100 + R score × 10 + S score, with a range of 0–1643.

The first 2 digits indicate the location of inflammation along the small intestine, whereas the third digit represents the extent of inflammation, and the fourth digit indicates the presence/absence of stenosis

PillCam Crohn's capsule score [that is, Eliakim score]⁸⁰

- A. MCL
 - 0 → none
 - 1 → mild
 - 2 → moderate
 - 3 → severe
- B. MSL
 - 0 → none
 - 1 → mild
 - 2 → moderate
 - 3 → severe
- C. Anatomic extent of disease
 - 0 → none
 - 1 → 0%–10%
 - 2 → 10%–30%
 - 3 → 30%–60%
 - 4 → >60%
- D. Stricture
 - 0 → none
 - 1 → one traversed
 - 2 → >1 traversed
 - 3 → retention

S score (SB1/SB2/SB3/RC/LC) = [(A + B) × C] + D

SB PCC score = SB1 + SB2 + SB3.

Pan-enteric PCC score = SB1 + SB2 + SB3 + RC + LC

790—mild inflammation; and greater than or equal to 790—moderate-to-severe inflammation. LS has been widely validated for the diagnosis and monitoring of patients with CD.^{73–75} In addition, a higher LS was significantly linked to an increased need for treatment escalation, intestinal resection, and hospital admission within the first year following diagnosis in newly diagnosed CD patients.⁷⁵ An additional VCE inflammatory scoring-system is the CECDAI/NIV score.⁷⁶ Using NIV score the SB is divided into 2 segments, and the degree and extent of mucosal inflammation are the key operators of the score, along with the presence of strictures.⁷³ Previously published study including patients who were evaluated for suspected CD, demonstrated that while LS correlation to FC was quite strong (ie, $r = 0.68$), CECDAI to FC correlation was weak (ie, $r = 0.24$).⁷⁷ A study by Yablecovitch and colleagues⁷⁸ demonstrated that both inflammatory scores were strongly correlated ($r = 0.81$, $P = .0001$) and equally effective in the evaluation and monitoring of mucosal inflammation in patients with established CD. Recently, Omori and colleagues,⁷⁹ developed the Crohn's Disease Activity in Capsule Endoscopy (CDACE) score, a novel scoring method aiming to assess SB-CD mucosal inflammation. This scoring system puts more emphasis on inflammatory lesions with the representation of the inflammation grade (ie, Li score) and its range (ie, R score), rather than the presence of strictures, which has a high influence on LS calculation. CDACE had a strong correlation to both LS and CECDAI ($r = 0.737$, $P < .0001$ and $r = 0.915$, $P < .0001$, respectively) among patients with quiescent CD. Additionally, the CDACE showed significant correlations with Crohn's Disease Activity Index (CDAI) ($r = 0.36$) and CRP levels ($r = 0.23$).⁷⁹

Activity Scoring-System for PillCam Crohn's Capsule

The PCC score (ie, Eliakim score [ES]) has been developed for CD patients undergoing PCC procedure. In a prospective, single-center study conducted in 2020, Eliakim and colleagues⁸⁰ presented this novel scoring-system using the principle parameters of the PCC system (ie, MCL, MSL, disease extent, presence of strictures). This study included 41 CD patients with quiescent disease who underwent PCC. ES was proven as a reliable scoring system with an excellent degree of agreement between readers (inter-class classification of 0.9, $P < .0001$). A moderate correlation was observed between ES and FC, while LS to FC correlation was weak ($r = 0.54$ and 0.32 , respectively; $P = .001$ for both).⁸⁰ Recently, our group published a study⁶⁶ which further corroborated ES reliability for CD patients with active disease who underwent PCC prior to biologic initiation. We found that ES had a better responsiveness to biochemical changes during follow-up, compared to LS (CRP: $r = 0.306$ vs $r = 0.138$, $P = .057$ and FC: $r = 0.479$ vs $r = 0.297$, $P = .034$). Furthermore, ES was better correlated to CDAI than LS ($P = .036$).⁶⁶ We believe that the cumulative nature of ES better reflect the true inflammatory burden than LS, and therefore ES should be the preferable scoring system among CD patients who undergo PCC procedure. **Table 3** details all VCE-inflammatory scoring system in CD.

VIDEO CAPSULE ENDOSCOPY SAFETY PROFILE

CR is defined as a capsule remaining in the SB for greater than 2 weeks, often identified by X-ray or CT scan, as the accuracy of X-ray to precisely locate the retained capsule is limited.⁸¹ While CR is a serious complication of VCE, it is usually asymptomatic or causes mild self-limiting symptoms, and rarely present as SB obstruction/perforation.^{82,83} CR infrequently requires intervention, as up to 50% of patients will excrete the capsule after 2 weeks, and steroids may help in 30% of cases.⁸¹ For capsule that has remained in the colon for 3 to 6 months, retrieval should be considered. Although

surgery was previously considered the first choice for capsule retrieval, device-assisted enteroscopy has emerged as an acceptable tool for this purpose, with 90% to 100% success rate.⁸¹

CD patients with stricturing disease phenotype, previous SB obstruction or abdominal surgeries have an increased risk of CR.^{84,85} Older studies reported CR rates of up to 8.2% for VCE,^{85,86} but these rates decreased to 2.3% to 4.63% with prior SB patency confirmation.⁸⁷ A recent meta-analysis by Cortegoso Valdivia and colleagues, including 328 studies and 86,930 patients, showed a 2% CR rate overall, with a 2 fold increase (ie, 4%) in CD patients.⁸⁸ Another meta-analysis by Pasha and colleagues⁸³ reported a 4.63% CR rate in patients with established CD and a 2.35% rate in those with suspected CD, following SB patency confirmation with patency capsule (PC), CTE or MRE.

In 2022, we reviewed CR rates among CD patients undergoing PCC procedure in 6 studies.^{63–65,67,69,80,89} Out of 386 patients, 12 experienced serious adverse events following PCC ingestion. There were 3 cases of CR (<1%), despite SB patency confirmation via PC in one patient, MRE in another, and one instance where the capsule was retained in the colon due to a colonic stricture despite SB patency confirmation.⁸⁹ Recently, we published a study on 108 patients with active CD who underwent PC ingestion prior to PCC.⁶⁶ 14 cases of unpassed PC precluded PCC ingestion, and no CR cases were observed during follow-up.

Current US and European guidelines highly endorse SB patency confirmation before VCE ingestion,^{5,8} using either cross-sectional imaging or PC ingestion. PC is an ingestible capsule similar in size to VCE but dissolves after 30 hours, posing minimal harm.^{90,91} A meta-analysis by Zhang and colleagues⁹² demonstrated PC's accuracy in identifying high-risk patients for CR, with 97% sensitivity and 83% specificity. CTE and MRE are also commonly used for this purpose. A retrospective study by Yadav and colleagues,⁹³ found comparable sensitivity and specificity rates for PC and cross-sectional imaging in detecting significant SB strictures (57% vs 71%; $P = 1.00$, 86% vs 97%; $P = .22$).⁹³ While SB patency confirmation is recommended for patients with established CD, it is not routinely advised for those with suspected CD.⁸²

A major limitation of SB patency confirmation is its high false positive (FP) rate, which prevents VCE use in many CD patients. Although PC may have lower FP rates than CTE^{94,95} and MRE⁹⁶ it can still be as high as 87%.^{95,97–99} Constipation can increase FP rates, as delayed bowel movements (>30 hour) may trigger PC self-dissolution.⁹⁹ Watanabe and colleagues¹⁰⁰ found that extending PC excretion time to 72 hours significantly increased confirmed SB patency rates with similar safety. Notably, X-ray have less than 50% accuracy in determining PC location,¹⁰¹ and CT may be needed for clarification. Our group observed that PC ingestion might predict high-risk CD patients for future poor clinical outcomes,¹⁰² independently of disease phenotype. Therefore, PC can serve as a prognostic tool in monitoring and managing CD patients, in addition to screening for VCE ingestion.

BOWEL PREPARATION PRIOR AND DURING VIDEO CAPSULE ENDOSCOPY INGESTION

Achieving an adequate degree of bowel cleanliness is of prime importance to provide an adequate mucosal visualization during VCE procedure. The consumption of PEG prior to VCE ingestion has been shown to optimize mucosal visualization,¹⁰³ however its influence on VCE completion rate and diagnostic yield has not yet been well-established.^{104–106} In clinical practice SB preparation with PEG agents is not commonly used for VCE that is primarily confined to the SB, and patients usually instructed to

adhere to low-fiber diet and clear fluid-diet only the day before the procedure followed by a 12-h fast the evening before VCE ingestion. Additionally, the current US and ESGE guidelines do not address these issues.^{8,82}

As the use of PCC has not yet been incorporated to the current guidelines, there are no recommendations regarding bowel preparation prior to PCC ingestion. In a narrative review including several PCC's studies by our group,⁸⁹ protocols of PEG-based solution of 1.5 to 2 L were employed. SB cleansing was generally more effective than colon cleansing, with 90% of good/excellent cleanliness¹⁰⁷ for the SB compared to up to 75% for the colon.^{63,65,80} There was no difference in SB cleansing between PCC and IC, but colon cleansing was significantly better with IC.^{64,65} These data have been further solidified in a more recent study by our group⁶⁶ where out of 142 PCCs reviewed, SB preparation was rated as excellent or good in 128 cases (90%) while colon cleanliness was rated as excellent or good in 58% of the procedures.⁶⁶ Therefore, the use of bowel preparation seems to be a crucial part of PCC procedure, to afford a feasible and accurate assessment of the colonic mucosa. However, PEG consumption prior to PCC ingestion makes it more complex and less patient-friendly.

ARTIFICIAL INTELLIGENCE-BASED VIDEO CAPSULE ENDOSCOPY READING

A single VCE procedure typically captures and transmits an average of 12,000 images per patient, which are usually read by a single interpreter, who should read the entire VCE film without distraction. Thus, cases of missed diagnosis are inevitable,^{108,109} and are estimated to be as high as up to 10%.¹¹⁰ Other challenges are related to technical features of the capsule, where there is no option to self-direct or refocus the camera during reading process.¹¹⁰ Reading a single VCE film may take 30 to 40^{108,111} minutes on average, even for experienced VCE readers, and there is still a substantial rate of disagreement between readers (ie, 20%)¹¹² in the detection of inflammatory lesions. AI-based VCE reading methods, including CNN algorithms, have emerged to offer automated image analysis and interpretation.¹¹³ These CNN algorithms automatically identify typical characteristics of raw data (ie, VCE frames), using a training dataset of frames. These features are integral elements of the running algorithms, and often cannot be perceived by humans.¹¹⁴ Then, their accuracy is examined on an internal dataset of frames (ie, testing dataset). Ideally, an external dataset (ie, validated dataset) is used to independently assess this model's performance.^{115,116} **Table 4** summarizes the current literature addressing AI-based VCE reading in CD.

Artificial Intelligence-Based Detection of Crohn's Disease Lesions

Overall, CNN-based VCE reading demonstrated an excellent accuracy rate (ie, >95%)¹¹⁷ and sensitivity¹¹⁸ in the detection of ulcers and erosions, with a higher sensitivity for the former than the latter. Adding a bounding box for lesion localization by Wang and colleagues¹¹⁹ led to 10% of improvement in the detection performance of small SB ulcers, with larger ulcers (>1% of the whole image) more commonly detected (92% vs 85%) than others.¹¹⁹ Yet, FP events are still prevailed (5%),¹¹⁷ with a great advantage in identifying missed pathologic frames by conventional readers.¹¹⁸ Another limitation, as demonstrated by Klang and colleagues,¹²⁰ was a lower diagnostic yield for unseen frames, ranging from 73.7% to 98.2% which probably reflect the challenges in real-world practice.

Several CNN models dealt with ulcer detection among other pathologic lesions.¹²¹ Ding and colleagues showed a marginal improvement rate in the detection of SB ulcers (2%) compared to other SB pathologies (20%), while Otani and colleagues¹²²

Table 4
Summary of current literature addressing artificial intelligence-based video capsule endoscopy reading in Crohn's disease

Reference, Year of Publication	Field of Application	Algorithm	Number of Patients	Primary Outcome	Results
Fan et al, ¹¹⁷ 2018	Small bowel inflammatory lesions	AlexNet CNN	144 patients	The detection of small bowel ulcers and erosions	Ulcer detection accuracy - 95.16%, Erosion detection accuracy - 95.34%
Aoki et al, ¹¹⁸ 2019	Various small bowel pathologic findings	CNN	180 patients	The detection of small bowel ulcers and erosions	Ulcers and erosions detection accuracy - 90.8%
Wang et al, ¹¹⁹ 2019	Small bowel inflammatory lesions	Modified RetinaNet	1504 patients	The detection of small bowel ulcers	Accuracy - 90.1%
Ding et al, ¹²¹ 2019	Small bowel inflammatory lesions	CNN-based auxiliary model	6970 patients	Differentiation between normal and pathologic VCE frames	Sensitivity and specificity of ulcer detection - 99.73% and 100%, respectively
Otani et al, ¹²² 2020	Small bowel inflammatory lesions	Modified RetinaNet	194 patients	Differentiation between normal and pathologic VCE frames	Ulcers and erosions detection accuracy - 98.6%–99.3%
Nakada et al, ¹⁶ 2023	Various small bowel pathologies	Revised RetinaNet	1234 patients	Detection of erosions, ulcers, vascular lesions, and tumors in the small bowel	AUC of 0.997 for the detection of erosions/ulcers, 0.998 for the detection of vascular lesions, and 0.998 for the detection of tumors in the small bowel
Klang et al, ¹²⁰ 2020	CD-related ulcerated lesions	CNN	49 patients	Detection of small bowel ulcers	Per-lesion analysis accuracy - 95.4%–96.7%. Per-patient analysis accuracy 73.7%–98.2%

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Table 4
(continued)

Reference, Year of Publication	Field of Application	Algorithm	Number of Patients	Primary Outcome	Results
Barash et al, ¹²⁷ 2021	CD-related ulcerated lesions	CNN	49 patients	Detection and grading of small bowel ulcers	An accuracy rates of 91%, 78%, 62.4% in classifying grade 1 vs grade 3 ulcers, grade 2 vs grade 3, and grade 1 vs grade 2, respectively.
Klang et al, ¹²⁸ 2021	CD-related ulcerated lesions and strictures	Google's EfficientNet networks	NA	Detection of small bowel strictures	An accuracy rates of 93.5% and 78.9% in the detection and classifying ulcerated and non-ulcerated strictures
Hwang et al, ¹²³ 2021	Small bowel inflammatory and hemorrhagic lesions	VGGNet	NA	Classification of hemorrhagic and ulcerative small bowel lesions	An accuracy rates of 96.62%–96.83%.
Mascarenhas Saraiva et al, ¹³⁰ 2021	Various small-bowel pathologies	Xception	4319 patients	Classification and prediction of bleeding high-risk lesions	AUC of 0.99 and 1.00 for P1 and P2(>20 mm) ulcers.
Afonso et al, ¹²⁹ 2022	Small bowel inflammatory and hemorrhagic lesions	CNN	NA	Classification and prediction of bleeding high-risk lesions	An accuracy of 95.6% in the detection and classification of erosions and/or ulcers.
Majtner et al, ¹²⁶ 2021	CD-related ulcerated lesions in patients with suspected/established CD undergoing PCC	ResNet-50	38 patients	The detection and grading of small bowel and colonic ulcers and erosions	An accuracy rate of 98.4%–98.6% in identifying inflammatory lesions in the small bowel and/or colon.

Ferreira et al, ¹²⁵ 2022	Small bowel and colon inflammatory lesions in patients undergoing PCC	Xception	NA	The detection and grading of small bowel ulcers and erosions	An accuracy of 98.8% in the detection of small bowel and/or colonic ulcers and erosions.
Kratter et al, ¹²⁴ 2022	Established and suspected Crohn's disease	EfficientNet	NA	Small-bowel and colon ulcer detection and grading	The detection and grading accuracy of mucosal ulcers across various types of VCE reached 97.4%
Brodersen et al, ¹⁵ 2024	Patients with suspected Crohn's disease undergoing PCC	Axaro	131	The sensitivity and specificity of small bowel CD-related inflammatory lesions following AI-based frame number reduction (<i>real-world implementation</i>)	Sensitivity rates of 96% and 92%, and specificity rates of 93% and 90% for reader 1 and reader 2, respectively.
O'hara et al, ¹³² 2023	Various small-bowel pathologies	OMOM HD capsule	40 (18-CD)	Real-world performance of AI-based VCE reading vs standard reading	AI-based VCE reading reduced the reading time compared to standard reading by 92.3% (2.29 min vs 29.69 min, $P<.001$), and had a higher sensitivity rate in the detection of ulcers and erosions (98.6% vs 89.3%, $P<.001$)
Oh et al, ¹³³ 2024	Various small-bowel pathologies	OMOM HD capsule	90 (43-CD)	Real-world performance of AI-based VCE reading following a removal of VCE frames with poor visualization vs conventional reading	Both reading methods resulted in a detection rate of 42.2%.

Abbreviations: AI, artificial intelligence; AUC, area under the curve; CNN, convolutional neural network; GIB, gastrointestinal bleeding; IBD, inflammatory bowel disease; NA, not applicable; PCC, PillCam Crohn's Capsule; SSD, single-shot detector; VCE, video capsule endoscopy

demonstrated an accuracy rate of 99%, for the detection of ulcers, erosions, and vascular lesions employing a modified RetinaNet CNN model. In 2023, Nakada and colleagues¹⁶ utilized a revised version of the AI model RetinaNet, which achieved a mean AUC of 0.997 for erosions/ulcers, 0.998 for vascular lesions, and 0.998 for tumors.

Hwang and colleagues¹²³ examined 2 different CNN-based model training modes. In the first one, a combined model (ie, hemorrhagic and ulcerative lesions were trained independently), and in the second, a binary model (ie, all abnormal images trained together). Though both training models demonstrated high accuracy rates in lesion detection (96.83% vs 96.62%, for the combined versus the binary models, respectively, $P = .122$), the former exhibited higher sensitivity and negative predictive value rates than the latter, with decreased likelihood of missed diagnoses (23 cases vs 47 cases, respectively).

Kratter and colleagues¹²⁴ focused on a combined multi-model CNN algorithm aiming to read and interpret 2 distinct capsule types (ie, PCC and SB3 capsules by Medtronic), which may reflect the real-world practice. This innovative approach resulted in an accuracy of 97.4% in the detection of CD lesions.

3 studies evaluated the accuracy of AI-based PCC reading in the detection of CD lesions. Ferreira and colleagues¹²⁵ demonstrated a sensitivity rate of 83% and specificity rate of 98% for the detection of ulcers, and sensitivity rate of 91% and specificity rate of 93% for the detection of erosions. Majtner and colleagues,¹²⁶ employed 2 distinct methods of data splitting: random allocation and per-patient allocation. There were minimal misclassifications, with only 4/558 colon images incorrectly identified as SB, and 7/1000 SB images misclassified as colon. Remarkably high accuracy rates were achieved with both the per-patient and random-split methods (98.4% and 98.6%, respectively) for lesions detected in either the SB or colon. Recently, Brodersen and colleagues¹⁵ further corroborated the efficacy of AI-assisted PCC reading which resulted with sensitivity and specificity rates of 92% to 96% and 90% to 93%, respectively.

Lesion Classification Using Artificial Intelligence-Based Video Capsule Endoscopy Reading

In the realm of identifying inflammatory lesions such as ulcers and erosions, numerous studies have focused on categorizing and classifying these lesions based on specific parameters to better predict disease severity and subsequently optimize disease management in this population.

In 2021, Barash and colleagues¹²⁷ utilized an ordinal CNN model for grading the severity of ulcers in patients with CD. Severity grading was based on the PCC system (1-the mildest, 3-the most severe ulcer). The model best distinguished between grade 1 and grade 3 ulcerations (ie, accuracy rate of 91%), but to a lesser degree between grade 2 and grade 1/grade 3 (ie, accuracy rates of 65% and 79%, respectively). Consistent with these findings, Kratter and colleagues¹²⁴ showed an AUC of 0.99 for classifying ulcers into grade 1 or grade 3.

Another AI-based application by Klang and colleagues¹²⁸ aimed to classify intestinal strictures as inflammatory or fibrotic. This CNN-based model exhibited an average accuracy of 93.5% in distinguishing stricture versus non-stricture lesions, but only 78.9% accuracy in distinguishing between ulcerated versus non-ulcerated ones.

2 studies showed a novel CNN-based model which classified SB ulcers by their potential risk of bleeding,^{129,130} based on Saurin classification system¹³¹ (ie, P1–small ulcers, P2–ulcers>20 mm). Consistent with the study by Wang and colleagues,¹¹⁹ which

showed that the larger the ulcer, the higher the sensitivity to detect it, Mascarenhas Saraiva and colleagues¹³⁰ demonstrated impressive sensitivity rates of 81% for P1 lesions and 94% for P2 lesions in identifying mucosal ulcers. Finally, an accuracy of 95.6% was achieved by Afonso and colleagues¹²⁹ in AI-based interpretation of VCE film to identify and classify ulcers' bleeding risk, as well, using an independently developed CNN for automatic identification.

Real-World Use of Artificial Intelligence-Based Video Capsule Endoscopy Reading

The real-world performance of AI-based VCE reading in CD was recently described by several studies.^{15,132,133} Using the OMOM type SBCE, O'Hara and colleagues included 40 patients, among them 18 patients with suspected/established CD¹³⁴. AI-based VCE reading reduced the reading time compared to standard reading by 92.3% (2.29 minutes vs 29.69 minutes, $P<.001$), and had a higher rate of sensitivity to detect ulcers and erosions (98.6% vs 89.3%, $P<.001$). Jun Oh and colleagues utilized AI-based VCE reading process to identify and subsequently remove VCE frames with poor visualization prior to conventional VCE interpretation.¹³³ Out of 90 patients who underwent OMOM type SBCE ingestion, there were 43 patients with suspected CD. Both reading methods resulted in 42.2% CD diagnosis using the AI-based removal of poorly visualized frames or not. Consistent with these studies, Brodersen and colleagues¹⁵ demonstrated the high sensitivity and specificity rates using AI-based application aiming to reduce the number of PCC frames to be read by conventional readers. The noted sensitivity rates of 96% and 92%, and specificity rates of 93% and 90% for reader 1 and reader 2, respectively. **Fig. 3** provides the key applications of AI-based/assisted VCE reading, and the current challenges in this field to be solved in the future.

VIDEO CAPSULE ENDOSCOPY USE IN INFLAMMATORY BOWEL DISEASE UNCLASSIFIED

The prevalence of IBD-U is up to 20%.¹² Serology was previously widely used to distinguish between ulcerative colitis (UC) and CD, but many patients test negative.¹² Accurate classification is crucial since IBD-U patients may have a worse prognosis than UC.¹² Studies indicated that VCE can reclassify 15% to 43% of IBD-U patients to CD based on mucosal findings (eg, LS $\geq$ 135, ulcers $\geq$ 3, irregular ulcers, stenosis).^{11,12,134–136} VCE may be particularly useful for patients with atypical clinical features or post-colectomy.¹¹

VIDEO CAPSULE ENDOSCOPY USE IN ULCERATIVE COLITIS

Overall, VCE, particularly CCE-2, performs well in UC, with up to 97% sensitivity and 100% specificity in detecting mucosal inflammation compared to IC.^{10,13,137} VCE is highly tolerable, with higher patient satisfaction rates, especially in pediatric patients.^{13,137} It is also safe, with most adverse events related to bowel preparation.¹³⁸ VCE can detect SB inflammatory lesions in up to 36% of UC patients, which IC cannot.¹³⁹ Inadequate bowel cleanliness, even with 2 L of PEG, can hinder mucosal visualization.¹⁴⁰ However, due to UC's diffuse rather than patchy inflammation, the severity can usually still be assessed despite inadequate bowel preparation.¹⁴¹ For colorectal cancer screening in UC patients, CCE-2 has 80% to 95% sensitivity for detecting polyps greater than or equal to 6 mm, but it cannot perform biopsies or resections,¹⁴² necessitating follow-up colonoscopy and repeat bowel preparation, reducing patient friendliness.

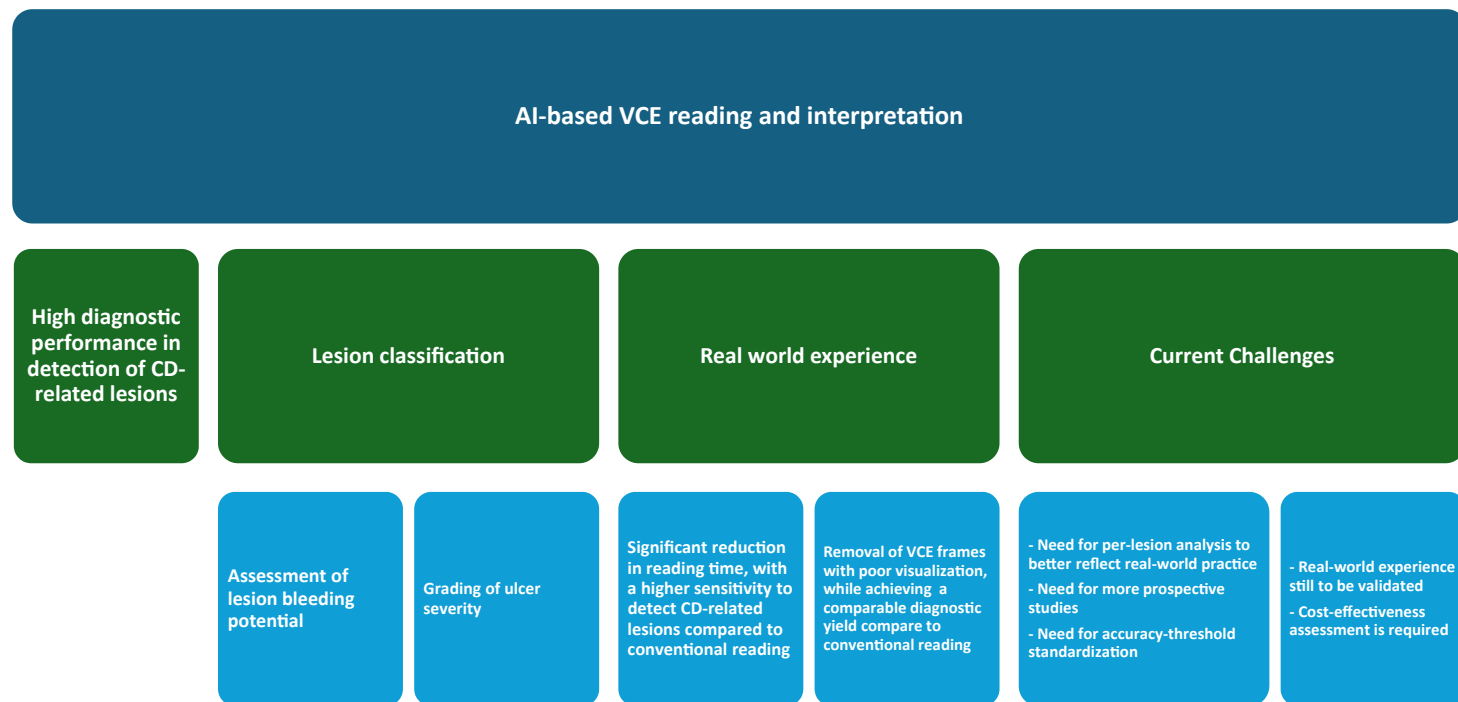


Fig. 3. Where we stand today in the field of AI-based video capsule endoscopy reading? *Abbreviations:* AI, artificial intelligence; VCE, video capsule endoscopy; CD, Crohn's disease.

SUMMARY

In this review paper, we provide a comprehensive update on the use of VCE in patients with IBD. Since its introduction, VCE has become crucial for diagnosing and monitoring CD, particularly as most CD patients have SB involvement and IC is limited in about 20% of cases where the disease is beyond its reach. VCE is the most sensitive and accurate tool for identifying proximal SB-CD. VCE is also effective in assessing MH, determining disease extent, postoperative surveillance, and predicting clinical flares in this population.

The inclusion of PCC in CD guidelines is promising, as PCC allows visualization of the entire SB and colon, offering superior diagnostic performance in the proximal SB compared to MRE and a comparable diagnostic yield in the colon to IC. However, bowel preparation is necessary for adequate colon visualization during PCC, making it less patient-friendly. VCE has been proven to accurately classify patients with IBD-U, and has a strong correlation with IC in detecting mucosal inflammation among UC patients.

The safety profile of VCE is acceptable, with the risk of CR being preventable by confirming SB patency before VCE ingestion using PC or cross-sectional imaging.

Recently, AI-based developments have shortened capsule reading time and shown excellent diagnostic performance. AI-based VCE applications for structural assessment and prognostication, such as severity grading and bleeding potential show promise for better disease management. Few studies have reported real-world experiences with AI-based VCE reading in CD patients, and the results are encouraging. AI-driven VCE interpretation and prediction models using CNN architecture could significantly enhance disease management strategies for CD patients.

CLINICS CARE POINTS

- Patients with suspected CD who have normal results from both IC and cross-sectional imaging should undergo VCE.
- Patients with a new diagnosis of CD should undergo SB assessment by cross-sectional imaging or VCE, with the latter having a higher sensitivity in detecting proximal SB involvement compared to the former.
- Patients with CD should undergo cross-sectional imaging or patency capsule ingestion prior to VCE procedure to preclude a CR event.
- VCE does not require bowel preparation with PEG unless pan-enteric capsule endoscopy is performed in order to ensure adequate colon cleanliness.
- Patients with IBD-U should undergo VCE in order to accurately classify their disease and better optimize disease management in this population.

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