

# Video Capsule Endoscopy in Gastroenterology

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## Abstract

Video capsule endoscopy (VCE) is a wireless technology used by gastroenterologists for various indications in their clinical practice. There has been significant improvement in this technology since its start about two decades ago. Specific video capsules have been made to evaluate the small bowel, colon, and esophagus. Now pan-enteric video capsule is available to assess both the small bowel and colon. VCE is a noninvasive procedure that has been tremendously evaluated for various gastrointestinal disorders, particularly small intestinal bleeding. There are specific contraindications and complications of VCE. This procedure has the technical part and video reading part. Newer software programs will come to reduce the reading time. Artificial intelligence is also coming for quick and accurate diagnosis of any positive findings during VCE. VCE is an important diagnostic test in the field of gastroenterology. Although it is an addition to optical endoscopic procedures to visualize the gastrointestinal mucosa, it has advantages and disadvantages.

**Keywords:** Wireless capsule endoscopy; Capsule endoscopy; Small bowel capsule endoscopy; Colon capsule endoscopy; Esophageal capsule endoscopy; Capsule endoscopy; Gastrointestinal bleeding

## Introduction

Video capsule endoscopy (VCE) is a relatively new diagnostic tool developed over two decades. By this technique, we can evaluate the esophagus, stomach, small bowel, and colon in physiological conditions without exposing the patients to external radiation. Video small bowel capsule endoscopy (SBCE) can evaluate various small intestinal disorders. Video colon capsule endoscopy (CCE) is one of the options for colon cancer screening. Video esophageal capsule endoscopy (ECE) is an option to diagnose certain esophageal diseases when patients cannot tolerate optical endoscopy. Video SBCE significantly impacts diagnostic evaluation in clinical gastroenterology. In this article, we will be discussing the diagnostic implications, contraindications, complications, and technical aspects of VCE and how to read capsule endoscopy.

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# Video SBCE

#### **Diagnostic implications**

The small bowel is the most extended gastrointestinal tract organ, with an average length of 9 - 15 feet [1]. It has three parts: duodenum (first 9 inches) followed by jejunum (proximal twofifth or 40%) and ileum (distal three-fifth or 60%). It was once regarded as the "dark world" or "black box" of the gastrointestinal tract because of incomplete visualization of the whole small bowel mucosa by the conventional upper endoscopy, colonoscopy, and push enteroscopy. SBCE revolutionized the entire small bowel mucosal visualization painlessly and remotely when it entered our clinical practice in 2001 [2]. This technology has improved over the years and is now considered a first-line powerful diagnostic tool in evaluating various small bowel disorders. Most of the time, it is done to assess the source of overt or occult obscure gastrointestinal bleeding (OGIB) when esophagogastroduodenoscopy (EGD) and colonoscopy are negative [3]. One study showed that in the case of overt OGIB, early use of SBCE within 3 days of hospital admission results in significantly higher diagnostic yield, therapeutic intervention rate, and associated reduced hospital stay [4]. In 2017, the clinical practice guideline of the American Gastroenterology Association (AGA) Institute recommended SBCE in patients with known, relapsed, or suspected Crohn's disease when the active disease is still suspected in the small bowel after negative imaging studies and normal ileocolonoscopy. The AGA guideline also recommended SBCE in patients with the known celiac disease having unexplained symptoms even after adequate treatment. The AGA guideline suggested SBCE for surveillance of patients with polyposis syndromes and small bowel tumors (neuroendocrine tumors, adenocarcinoma, gastrointestinal stromal tumors, lymphoma, and sarcoma) [5]. Schulmann et al did a prospective study on 29 patients with familial adenomatous polyposis (FAP) syndrome. They found that 24% of the patients with FAP with duodenal adenomas had more polyps in the distal jejunum or ileum seen by SBCE [6]. So SBCE should be considered in FAP patients with multiple duodenal adenomas. Caspari et al found a higher diagnostic yield of SBCE as compared to magnetic resonance imaging (MRI) in detecting small polyps (< 5 mm) in patients with Peutz-Jeghars syndrome (PJS) [7]. Considering this, SBCE should be considered for the initial diagnosis and follow-up of patients with PJS. SBCE is also an important test in evaluating the extent of small bowel involvement and assessing treatment efficacy in primary gastrointestinal lymphoma [8].

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Non-steroidal anti-inflammatory drugs (NSAIDs) can cause various proximal and distal small bowel injuries, including erosion, ulcers, bleeding, stricture, and "diaphragm disease" [9]. SBCE can evaluate NSAID-induced enteropathy [10]. Acute graft vs. host disease (GVHD) can involve the whole gastrointestinal tract, and the small bowel mucosa is involved in 75% of cases [11]. However, it is more pronounced in the ileum than in the jejunum. The endoscopic findings may vary widely, ranging from normal-looking mucosa to focal erythema, edema, friability, exudation, erosion, ulceration, mucosal denudations, mucosal sloughing, and active bleeding [12]. One prospective study found that either ileocolonoscopy with biopsy (from the rectosigmoid, descending colon, and ileum) or upper endoscopy plus sigmoidoscopy with biopsy (from the gastric antrum, gastric body, duodenum, distal esophagus, and rectosigmoid) are equivalent diagnostic tests for GVHD [13]. SBCE should be considered if the above tests are negative and GVHD is clinically suspected. SBCE should also be considered an alternative diagnostic test of GVHD if the patient is too sick to have endoscopy and colonoscopy. SBCE is also helpful in evaluating rare disorders like common variable immunodeficiency disorder (CVID - where diffuse small nodular lesions are seen throughout the small intestine) [14], abetalipoproteinemia (where the entire small intestinal mucosa shows a diffuse whitish pattern with occasional yellow areas in the absence of any villous atrophy) [15] and intestinal lymphangiectasia (where whitish spots due to collection of dilated lymphatics are seen in a localized segment or diffusely) [16].

SBCE is considered as the first-line test over device-assisted enteroscopy: (double balloon enteroscopy (DBE), single balloon enteroscopy (SBE) or spiral enteroscopy (SE)) or other imaging modalities: computerized tomography enterography (CTE) or magnetic resonance enterography (MRE) in evaluating small intestinal bleeding lesion or mucosal lesion for five reasons. 1) It is a non-invasive, well-tolerated test without the need for any sedation. In contrast, deviceassisted enteroscopies are invasive tests done under sedation or anesthesia with a higher complication rate. 2) The total enteroscopy completion rate of SBCE is 90.6%, whereas the total enteroscopy completion rate of device-assisted enteroscopy is much less (DBE: 66%, SBE: 22%) [17, 18]. 3) SBCE and DBE have similar (60% vs. 57%) diagnostic yields in OGIB due to small bowel diseases [19]. SE has a slightly (not statistically different) lower diagnostic yield as compared to SBE (43.4% vs. 59.6%) in patients with OGIB [20]. 4) SBCE can detect small bowel mucosal lesions missed by small bowel imaging (CTE and MRE). 5) SBCE can first localize the small bowel lesion that can be treated or biopsied by deviceassisted endoscopy later on.

## Contraindications

The contraindications of SBCE included the following: 1) Known small bowel stenosis or stricture is a definite contraindication for SBCE. A patency capsule should be administered in patients with suspected small bowel stenosis or stricture, known small bowel Crohn's disease, history of small bowel

resection, or abdominopelvic radiation. If an intact patency capsule is excreted within 30 h, it is assumed safe to perform SBCE [21]. In case of suspected Crohn's disease without obstructive symptoms, the use of a patency capsule before SBCE is not recommended by the European Society of Gastrointestinal Endoscopy (ESGE) [22]. 2) Small bowel obstruction. 3)Small bowel fistulae. 4) Cardiac devices included cardiac pacemakers (PMs), implantable electromedical devices like autoimplantable cardiac defibrillators (AICDs), and left ventricular assist devices (LVADs). The video capsule manufacturers (Covidien, Olympus, Medtronic, IntroMedic, and Chongqing Jinshan Science & Technology) and the US Food and Drug Administration (FDA) recommend that SBCE not be performed in patients with cardiac devices. According to The American Society of Gastrointestinal Endoscopy (ASGE), SBCE is relatively contraindicated in patients with cardiac devices. Several in vivo studies investigated the electromagnetic interference between SBCE and PMs and AICDs [23-25]. But no electromagnetic interference was found between SBCE, PMs, and AICDs. Again electromagnetic interference was not a problem between SBCE and left ventricular assist device (LVAD) shown in a few in vivo studies [26, 27]. Cardiac devices are no longer absolutely contraindicated in performing SBCE, but a multidisciplinary team should be involved. 5) The safety of doing SBCE has not yet been established in pregnancy. Gastrointestinal motility slows down during pregnancy's second and third trimesters, and an enlarged uterus presses on the gut. These physiological changes may also hamper SBCE [28].

Overall, SBCE is considered a safe and simple test. But certain complications can occur as well, which are discussed as follows.

## Complications

The complications of SBCE include the following: 1) Retention of the video capsule in the small bowel is the most worrisome complication. Seventy-five percent of the capsule reaches the cecum during the 8 h study period, and then the capsule is excreted in the stool after 10 to 48 h [29]. Video capsule retention is defined as a capsule remaining in the small bowel for more than 2 weeks, needing intervention to remove or pass the capsule [30]. The average risk is about 1-2% in patients with OGIB, but the risk could increase to 4-5% in patients with Crohn's disease [31, 32]. Capsule retention is also increased in patients with obstructive tumor, NSAID-induced enteritis, ischemic enteritis, radiation enteritis, tuberculous enteritis, and post-surgical stenosis [33, 34]. Most of the patients remain asymptomatic. The ESGE recommends that capsule retention be initially managed conservatively by medications (e.g., cathartics, prokinetics, steroids, immunomodulators, and biologics) in asymptomatic patients without bowel obstruction. If that fails, device-assisted enteroscopy should be done to retrieve the capsule. If enteroscopy fails to retrieve the capsule, the next step is surgical intervention (laparoscopy or open surgery with enterotomy) to remove the capsule [22]. 2) Incomplete examination of the small bowel means that the capsule has not reached the cecum. It occurs in 15% of studies [35]. As a result, the test needs to be repeated to avoid missing any small bowel lesions. Abdominal surgery, inpatient status, and a high degree of dependency are predictive factors for an incomplete SBCE. 3) Delayed transit: The capsule stays in the same part of the stomach or intestine for more than 2 h, and thus complete visualization of the small bowel becomes incomplete. Patients with delayed gastric emptying (diabetes mellitus, inpatient status, patients on opioids) and prolonged small bowel transit time are at increased risk of delayed capsule transit. 4) Poor quality images: During SBCE, air bubbles, mucus, intestinal fluid, bile, and food materials in the small bowel may decrease small bowel visualization. Male gender and increased small bowel transit time are predictive factors for poor quality images [36].

#### Prep for SBCE

On the day before the procedure, the patient should avoid taking any tobacco products and take a clear liquid diet after lunch and bowel prep at around 6 pm. A 2L polyethylene glycol (PEG) is the most commonly used small bowel cleansing agent for SBCE [37]. Other cleansing agents include magnesium citrate and Miralax (polyethylene glycol 3350) with Gatorade. Kim et al did a pilot study in 2014. They found that patients who received a combination of a coffee enema and 2L PEG had better efficacy in cleaning the mid to distal small bowel than patients who received PEG only [38]. Bowel prep should be selected according to the patient's clinical circumstances. Patients should be nothing by mouth after midnight. On the morning of capsule endoscopy, the patient should chew two Simethicon tablets to reduce intraluminal bubbles and increase the visibility of small bowel mucosa [39]. After ingesting the video capsule, the patient needs to be nothing by mouth for at least 2 h. A clear liquid diet is allowed 2 h after capsule ingestion and light snack 4 h after capsule ingestion. The patient remains ambulatory but should avoid strenuous exercise for 8 h after capsule ingestion. Patients are instructed to stay away from any strong electromagnetic field like MRI, amateur (HAM) radio, and airport security during this period.

Currently, there is no standardization of optimal bowel prep for SBCE. Rosa et al did a prospective study on patients who had bowel prep before SBCE and considered adequate bowel prep if more than 75% of small bowel mucosa had excellent visualization [40].

#### **Technical aspects**

The small bowel (SB) capsule, also known as PillCam SB, is similar to the shape of a pharmaceutical capsule and the size of a large vitamin pill, measuring  $11 \times 26$  mm and weighing less than 4 g. The PillCam SB system consists of an SB capsule, a data recorder, and a computer and appropriate software workstation. A tiny wireless camera inside the SB capsule takes two pictures/images per second as it passes through the SB and transmits about 50,000 photos to a data recorder attached to a belt worn around the patient's waist throughout 8 h study period. The PillCam SB (former M2A) was the first SBCE system

to the United States and Europe market in 2001. The viewing angle was 1,400, the image was eight times magnified, and the depth of view was 1 to 30 mm [41]. Over the last two decades, PillCam SB2 and PillCam SB3 came with enhanced features. The PillCam SB2 has better image resolution due to its wider viewing angle (1,560 vs. 1,400), more image capture per second (4 vs. 2), and longer battery life (9 vs. 8 h) in comparison to the old PillCam SB [42]. The PillCam SB3 can increase the number of images from 2 to 6 frames per second and has 30% more image resolution than PillCam SB2. The recorded data are stored in manual mode (four screens at 28 times speed) in the case of PillCam SB2, whereas the recorded data are stored in the review mode (four screens at 28 times speed) in PillCam SB3. The software (RAPID 8.0 or 8.3 system) of the PillCam SB3 system has at least 40% better image processing function, interface, and video reading capability than that of the Pill-Cam SB2 system [43]. The PillCam SB3 system is now used in most centers.

#### How to read SBCE

During capsule endoscopy, the first gastric image, the first duodenal image, and the cecal image are marked. The reviewer can gather an idea about gastric emptying time and the small bowel transit time from these landmarks. He or she should make a comment that the capsule reached the cecum. SBCE is a passive form of endoscopy. Capsule movement depends on gastric and small bowel motility. Gastroparesis can cause retention of the capsule of the stomach for a long time, and as a result, the study could be incomplete. Hyperperistalsis or rapid transit of the small bowel can result in incomplete small bowel evaluation or missed small bowel lesion [44]. As the capsule moves fast in the duodenum and proximal jejunum, the risk of missed lesions can be high in these locations [45].

Luminal contents in the small bowel cannot be suctioned and impair visibility. The reviewer must pay close attention while reading the images and not be distracted. The study can be monotonous as it may take more than 1 h. The viewing speed should not be more than 15 frames per second to improve the detection rate and avoid missing any significant lesion [46]. Although the reviewer can view the study in the single, double, or quadruple video, it is recommended to view the study in the double or quadruple video to improve the visibility of any lesion [47]. The diagnostic yield depends on the quality of the prep, clarity of the images, detection of the lesion, and interpretation of the lesion [48]. There are different software systems to shorten the small bowel capsule reading time. One is the QuickView mode, in which the number of images of interest can be set as a percentage (e.g., 5%, 15%, 25%, and 35%) of all images. Shiotani et al found that the QuickView mode could shorten the capsule reading time, but it had an unacceptably high missed rate [49]. Another software called suspected blood indicator (SBI) was developed to detect bleeding in the small bowel. But the performance of SBI is suboptimal as its sensitivity of detecting active bleeding is less than 60% [50]. Various automated reading software and artificial intelligence are being investigated to detect small bowel lesions during capsule endoscopy [51-53]. Currently, they are not approved to be used in clinical practice. The data recorder DR3 (by Medtronic) came to the market a few years ago. Its screen can show real-time images during capsule endoscopy. By watching the capsule progression in the real-time viewer, the reviewer can take appropriate action in case of gastroparesis and can terminate the procedure when the capsule reaches the cecum [44]. DR3 can also improve the diagnostic yield and capsule study completion rate.

# **Endoscopic Capsule Placement**

Endoscopic placement of video capsule is indicated for patients with dysphagia, inability to swallow the capsule, giant hiatus hernia, gastroparesis, and abnormal upper gastrointestinal anatomy, particularly dual intestinal loop anatomy (Rouxen-Y gastric bypass, Billroth II gastrojejunostomy, and Whipple surgery) [54].

# Video Capsule Delivery System

It allows endoscopic placement of a video capsule into the duodenum in an atraumatic way. The delivery system consists of a plastic-covered metal fiber passed through the biopsy channel of a standard endoscope. A clear plastic cap is screwed on the fiber, and then the video capsule is pressed into the cap. The endoscope with the frontloaded capsule is then introduced through the mouth into the esophagus and further advanced into the duodenal bulb. The capsule is released from the cap by pulling a handle outside the endoscope that moves the stiff inner wire into the cap [55].

# Video CCE

CCE is another new test modality by which the colon mucosa can be visualized directly by a video capsule. Like SBCE, the patient swallows the video capsule that travels through the gastrointestinal tract into the colon by peristalsis. Images are acquired and transmitted to a data recorder attached to a belt worn around the patient's waist. Then they are converted into a video format to be viewed on a computer.

## **Prep for CCE**

It is difficult to do adequate colon cleansing for CCE. There are different regimens of colon cleansing adopted in various centers. One regimen is: the patient is placed on a low residue diet for 3 days before the procedure and a clear liquid diet the day before the procedure. The patient ingests polyethylene glycol (PEG) solution 2 L in the evening before the day of the procedure and 2 L on the morning of the procedure. The patient swallows the video capsule around 9 am on the day of the procedure. A real-time viewer is used, and when the video capsule reaches the small bowel, the data recorder vibrates and buzzes and gives instructions on the liquid crystal display (LCD). A

booster dose of SUPREP (6 oz added to 10 oz of water) is given. The real-time viewer follows the further progression of the video capsule. A second booster dose of SUPREP (3 oz added to 5 oz water) is given to the patient if the video capsule is not excreted within 3 h of ingestion of the first booster dose. If the video capsule remains in the colon 2 h after ingestion of the second booster dose of SUPREP, 10 mg of bisacodyl suppository is given [56]. Oral sodium phosphate (NaP) was used as the booster solution in some studies [57, 58].

Meta-analysis showed that adequate bowel cleansing is possible in 77% of cases, as washing and suction are impossible during CCE [59].

CCE is nowadays performed by a second-generation pill-Cam COLON capsule 2, also called CCE-2, which has two cameras, each having a viewing angle of 1,720, giving nearly 3,600 views. The CCE-2 is 11.6 × 31.5 mm in size and contains a battery life-saving adaptive function. It takes four images per second when virtually static and 35 images per second when in motion. Instead of going into sleep mode, it takes 14 images per minute until the small bowel is recognized when it goes into adaptive frame mode. When CCE is viewed, polyp size can be estimated [60]. In one study, seven out of 11 small polyps (< 6 mm) detected by optical colonoscopy were seen by CCE [61]. Another study showed the sensitivity and specificity of detecting colon polyp  $\geq$  6 mm by CCE-2 were 81% and 93%, respectively [62].

## **Indications of CCE**

The USFDA approved CCE in 2014 to detect colon polyp only in patients with incomplete colonoscopy [63]. In 2017, the Multi-Society Task Force (MSTF) representing the American College of Gastroenterology, American Gastroenterology Association, and American Society of Gastrointestinal Endoscopy recommended CCE every 5 years as the third tier test for colon cancer screening. The ESGE also recommends CCE as a screening test for colon cancer screening in average-risk individuals when optical colonoscopy is contraindicated, vehemently opposed by the patient, or technically impossible [64].

## How to read CCE

The video is downloaded at the workstation. Then the CCE images are viewed the same way SBCE images are viewed. Generally, it takes a much longer time to read CCE images than SBCE images.

## **Contraindications and complications of CCE**

The contraindications and complications of CCE are similar to those of SBCE, as mentioned above [65]. Besides those, some difficulties related to taking bowel preparation can occur, including abdominal pain, nausea with or without vomiting, and rarely Mallory-Weiss tear. In about 4.1% of cases of CCE, these adverse events can occur [59].

## ECE

#### **Diagnostic implications**

PillCam ESO was developed by Given Imaging and approved by the FDA in 2004. Functional modification of the capsule can allow visualization of the mucosal surface of the esophagus. Diseases like esophagitis, Barrett's esophagus, esophageal cancer, and esophageal varices can be detected by ECE. In one study, the sensitivity and specificity of ECE in detecting esophagitis were 79% and 94%, whereas the sensitivity and specificity of recognizing Barrett's esophagus were 60% and 100%, respectively [66]. McCarty et al did a systemic review and meta-analysis in patients with portal hypertension. The diagnostic pooled sensitivity and specificity of detecting esophageal varices were 83% and 85%, respectively. The diagnostic accuracy of grading medium to large varices was 92% [67]. ECE can be an option for patients who are unwilling or unable to have an endoscopy. But ECE is not widely available and is much more expensive than optical endoscopy.

#### **Technical aspects**

Two lenses at each end of the PillCam ESO (first generation) can take 18 images per second for about 30 min. Its shape, size, and weight are similar to PillCam SB2. PillCam ESO (third-generation) can take 35 pictures per second and has a wider angle of view of 1,740 [68]. The images are transmitted to the recorder via three sensors on the chest.

#### **Procedure protocol**

Fasting for at least 2 h is required. First, the patient drinks 100 mL of water in a standing position. Then he or she swallows the capsule in the supine position. The patient can sip 10 mL of water at this time. The recording is done in the supine position for 2 min, at a 300° inclined position for 2 min, and at a 600° inclined position for 1 min. Then recording is done in a standing position for 15 min.

## Limitations of VCE

SBCE, CCE, and ECE are passive endoscopic procedures. The video capsule traverses passively by the peristaltic movement of the gastrointestinal tract. Lesions can be missed behind the mucosal folds. The video capsule does not have any suction power. So, visualization can be poor due to mucus, food, or blood.

Although SBCE, CCE, and ECE are excellent diagnostic tests, they are not therapeutic.

Biopsy cannot be taken from any suspected lesions.

Both SBCE and CCE require bowel preparation, but the bowel prep protocol is complicated and prolonged in CCE.

Air insufflation is necessary for good visualization of the

esophagus and recognition and grading of esophagitis, Barrett's esophagus, and esophageal varices. As a result, the sensitivity of diagnosing these lesions by ECE is low.

#### **Unmet Needs**

Pan-enteric VCE: Video capsule with long battery life can visualize the whole small bowel and colon. Recently, a new pan-enteric Crohn's capsule (PCC) has been developed. In a feasibility study, PCC was used to assess and follow up disease extent and activity. After bowel preparation, all established Crohn's patients were evaluated by a patency capsule, and if that was satisfactory, the PCC system was used. It allowed efficient visualization of mucosal inflammation and healing [69]. PCC system can be a cost-effective alternative to colonoscopy  $\pm$  MRE for surveillance patients with Crohn's disease [70].

Most of the Gastroenterology Fellowship Programs train the fellows about SBCE. ASGE organizes some formal courses. ACG also offers online modules on capsule endoscopy. There should be more accredited training courses to teach the practicing gastroenterologists who are not fellowship-trained in SBCE, CCE, and ECE. The training program should comprise didactic lectures and hands-on training. It should also test proficiency in reading before certifying the trainee. The findings of the trainee should correlate 90% or more with the reports of a credentialed capsule endoscopist [71]. CCE and ECE are not widely available, possibly because of limited indications, limited resources, and lack of training.

The video capsule reader should be confident in both the examination's endoscopic abnormalities and technical aspects.

Gastrointestinal capsule biopsy: A magnetic capsule endoscope carrying untethered microgrippers with biopsy capability was proposed. This innovative technology is not yet available for clinical use [72].

# Capsule Endoscopy and Artificial Intelligence

It takes a significant amount of time to review the images taken during capsule endoscopy. Artificial intelligence is being tested to reduce the review time and get the precise diagnosis without missing any lesion. Deep learning-based methods, particularly convolutional neural networks (CNNs), were applied in capsule endoscopy to detect bleeding, angioectasia, ulcer, cancer, and hookworms. The sensitivity and accuracy of detecting these lesions were close to 100% [73].

## Conclusions

VCE has tremendously improved the diagnostic approach in gastroenterology. The new knowledge about VCE is that the mucosal lesions of the small intestine, colon, and esophagus can be visualized wirelessly by this technology. The newer video capsules have better image processing functions and longer battery life. SBCE is the first-line test for visualization

Procedure	Indications	Contraindications	Complications
SBCE	Obscure gastrointestinal bleeding and iron deficiency anemia when EGD and colonoscopy are negative. Known celiac disease with unexplained symptoms even after adequate treatment. Surveillance of patients with polyposis syndromes and small bowel tumors. Evaluation of NSAID-induced enteropathy. Evaluation of acute GVHD. Evaluation of extent of primary gastrointestinal lymphoma. Evaluation of patients with rare disorders like CVID, abetalipoproteinemia and intestinal lymphangiectasia.	Small bowel stricture. Small bowel obstruction. Small bowel fistulae. Cardiac devices: PM, AICD, LVAD (relative contraindications as per ASGE). Pregnancy.	Retention of the video capsule in the small bowel. Incomplete examination of the small bowel. Delayed transit. Poor quality images.
CCE	To detect colon polyp only in patients with incomplete colonoscopy. Colon cancer screening in average-risk individuals as the third tier test every 5 years.	Similar to those of SBCE.	Similar to those of SBCE. Complications related to bowel prep.
ECE	Evaluation of esophagitis, Barrett's esophagus, esophageal cancer, and esophageal varices for patients who are unwilling or unable to have an endoscopy.	Similar to those of SBCE. Dysphagia. Esophageal stricture.	No known complication.

## Table 1. Indications, Contraindications and Complications of SBCE, CCE, and ECE

SBCE: small bowel capsule endoscopy; CCE: colon capsule endoscopy; ECE: esophageal capsule endoscopy; EGD: esophagogastroduodenoscopy; NSAIDs: non-steroidal anti-inflammatory drugs; GVHD: graft vs. host disease; CVID: common variable immunodeficiency disorder; PM: pacemaker; AICD: autoimplantable cardiac defibrillator; LVAD: left ventricular assist device; ASGE: American Society of Gastrointestinal Endoscopy.

of small bowel mucosal lesions. SBCE is most commonly used in clinical practice for various indications, particularly obscure gastrointestinal bleeding and iron deficiency anemia when EGD and colonoscopy do not reveal any bleeding source. CCE is comparable to optical colonoscopy in detecting colon polyps. CCE is done mainly in patients with incomplete screening colonoscopy. It has also been approved as a third-tier test for colon cancer screening. ECE is rarely done to detect esophagitis, Barrett's esophagus, and esophageal varices when patients are unable or unwilling to have optical esophagoscopy. The various indications, contraindications, and complications of SBCE, CCE, and ECE are summarized in Table 1. It is recommended that physicians apply this knowledge before considering VCE. Patients need bowel prep for both SBCE and CCE. PCC is coming mainly for surveillance of patients with Crohn's disease. Artificial intelligence is also on the horizon to reduce review time and human error and achieve a more accurate diagnosis. The capsule reader should be well trained and cognizant of capsule endoscopy's technical and diagnostic aspects. Innovative technology capable of doing gastrointestinal capsule biopsy is still experimental.

# **Financial Disclosure**

None to declare.

# **Conflict of Interest**

None to declare.

# **Author Contributions**

Monjur Ahmed, MD solely contributed to this work.

# **Data Availability**

The authors declare that data supporting the findings of this study are available within thearticle.

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None to declare.

# References

- Collins JT, Nguyen A, Badireddy M. Anatomy, abdomen and pelvis, small intestine. [Updated Aug 10, 2020]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; Jan 2020. Available from: https://www.ncbi. nlm.nih.gov/books/NBK459366/.
- 2. Adler SN. The history of time for capsule endoscopy. Ann Transl Med. 2017;5(9):194.
- 3. Liu K, Kaffes AJ. Review article: the diagnosis and investigation of obscure gastrointestinal bleeding. Aliment Pharmacol Ther. 2011;34(4):416-423.
- Singh A, Marshall C, Chaudhuri B, Okoli C, Foley A, Person SD, Bhattacharya K, et al. Timing of video capsule endoscopy relative to overt obscure GI bleeding: implications from a retrospective study. Gastrointest Endosc. 2013;77(5):761-766.
- Enns RA, Hookey L, Armstrong D, Bernstein CN, Heitman SJ, Teshima C, Leontiadis GI, et al. Clinical practice guidelines for the use of video capsule endoscopy. Gastroenterology. 2017;152(3):497-514.
- 6. Schulmann K, Hollerbach S, Kraus K, Willert J, Vogel T, Moslein G, Pox C, et al. Feasibility and diagnostic utility of video capsule endoscopy for the detection of small bowel polyps in patients with hereditary polyposis syn-

dromes. Am J Gastroenterol. 2005;100(1):27-37.

- 7. Caspari R, von Falkenhausen M, Krautmacher C, Schild H, Heller J, Sauerbruch T. Comparison of capsule endoscopy and magnetic resonance imaging for the detection of polyps of the small intestine in patients with familial adenomatous polyposis or with Peutz-Jeghers' syndrome. Endoscopy. 2004;36(12):1054-1059.
- Flieger D, Keller R, May A, Ell C, Fischbach W. Capsule endoscopy in gastrointestinal lymphomas. Endoscopy. 2005;37(12):1174-1180.
- 9. Lang J, Price AB, Levi AJ, Burke M, Gumpel JM, Bjarnason I. Diaphragm disease: pathology of disease of the small intestine induced by non-steroidal anti-inflammatory drugs. J Clin Pathol. 1988;41(5):516-526.
- 10. Gay G, Delvaux M, Frederic M. Capsule endoscopy in non-steroidal anti-inflammatory drugs-enteropathy and miscellaneous, rare intestinal diseases. World J Gastroenterol. 2008;14(34):5237-5244.
- Naymagon S, Naymagon L, Wong SY, Ko HM, Renteria A, Levine J, Colombel JF, et al. Acute graft-versus-host disease of the gut: considerations for the gastroenterologist. Nat Rev Gastroenterol Hepatol. 2017;14(12):711-726.
- 12. Ponec RJ, Hackman RC, McDonald GB. Endoscopic and histologic diagnosis of intestinal graft-versus-host disease after marrow transplantation. Gastrointest Endosc. 1999;49(5):612-621.
- Thompson B, Salzman D, Steinhauer J, Lazenby AJ, Wilcox CM. Prospective endoscopic evaluation for gastrointestinal graft-versus-host disease: determination of the best diagnostic approach. Bone Marrow Transplant. 2006;38(5):371-376.
- Mihaly E, Nemeth A, Zagoni T, Nemet A, Werling K, Racz I, Tulassay Z. Gastrointestinal manifestations of common variable immunodeficiency diagnosed by videoand capsule endoscopy. Endoscopy. 2005;37(6):603-604.
- Gay G, Barth E, Keuchel M. Involvement of the small intestine in systemic disease. In: Keuchel L, Hagenmuller F, Fleischer D. Atlas of video capsule endoscopy. Heildelberg: Springer; 2006. p. 136-144.
- Toth E, Keuchel M, Riemann JF. Intestinal lymphangiectasia. In: Keuchel M, Hagenmuller F, Fleischer D, editors. Atlas of video capsule endoscopy. Heildelberg: Springer; 2006. p. 101-106.
- Nakamura M, Niwa Y, Ohmiya N, Miyahara R, Ohashi A, Itoh A, Hirooka Y, et al. Preliminary comparison of capsule endoscopy and double-balloon enteroscopy in patients with suspected small-bowel bleeding. Endoscopy. 2006;38(1):59-66.
- ASGE Standards of Practice Committee, Khashab MA, Pasha SF, Muthusamy VR, Acosta RD, Bruining DH, Chandrasekhara V, et al. The role of deep enteroscopy in the management of small-bowel disorders. Gastrointest Endosc. 2015;82(4):600-607.
- Pasha SF, Leighton JA, Das A, Harrison ME, Decker GA, Fleischer DE, Sharma VK. Double-balloon enteroscopy and capsule endoscopy have comparable diagnostic yield in small-bowel disease: a meta-analysis. Clin Gastroenterol Hepatol. 2008;6(6):671-676.

- Khashab MA, Lennon AM, Dunbar KB, Singh VK, Chandrasekhara V, Giday S, Canto MI, et al. A comparative evaluation of single-balloon enteroscopy and spiral enteroscopy for patients with mid-gut disorders. Gastrointest Endosc. 2010;72(4):766-772.
- 21. Herrerias JM, Leighton JA, Costamagna G, Infantolino A, Eliakim R, Fischer D, Rubin DT, et al. Agile patency system eliminates risk of capsule retention in patients with known intestinal strictures who undergo capsule endoscopy. Gastrointest Endosc. 2008;67(6):902-909.
- 22. Pennazio M, Spada C, Eliakim R, Keuchel M, May A, Mulder CJ, Rondonotti E, et al. Small-bowel capsule endoscopy and device-assisted enteroscopy for diagnosis and treatment of small-bowel disorders: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy. 2015;47(4):352-376.
- Payeras G, Piqueras J, Moreno VJ, Cabrera A, Menendez D, Jimenez R. Effects of capsule endoscopy on cardiac pacemakers. Endoscopy. 2005;37(12):1181-1185.
- Bandorski D, Jakobs R, Bruck M, Hoeltgen R, Wieczorek M, Keuchel M. Capsule endoscopy in patients with cardiac pacemakers and implantable cardioverter defibrillators: (Re)evaluation of the current state in Germany, Austria, and Switzerland 2010. Gastroenterol Res Pract. 2012;2012:717408.
- 25. Cuschieri JR, Osman MN, Wong RC, Chak A, Isenberg GA. Small bowel capsule endoscopy in patients with cardiac pacemakers and implantable cardioverter defibrillators: Outcome analysis using telemetry review. World J Gastrointest Endosc. 2012;4(3):87-93.
- 26. Amornsawadwattana S, Nassif M, Raymer D, LaRue S, Chen CH. Video capsule endoscopy in left ventricular assist device recipients with obscure gastrointestinal bleeding. World J Gastroenterol. 2016;22(18):4559-4566.
- 27. Truss WD, Weber F, Pamboukian SV, Tripathi A, Peter S. Early implementation of video capsule enteroscopy in patients with left ventricular assist devices and obscure gastrointestinal bleeding. ASAIO J. 2016;62(1):40-45.
- 28. Lawson M, Kern F, Jr., Everson GT. Gastrointestinal transit time in human pregnancy: prolongation in the second and third trimesters followed by postpartum normalization. Gastroenterology. 1985;89(5):996-999.
- 29. Mishkin DS, Chuttani R, Croffie J, Disario J, Liu J, Shah R, Somogyi L, et al. ASGE Technology Status Evaluation Report: wireless capsule endoscopy. Gastrointest Endosc. 2006;63(4):539-545.
- Cave D, Legnani P, de Franchis R, Lewis BS. ICCE consensus for capsule retention. Endoscopy. 2005;37(10):1065-1067.
- Karagiannis S, Faiss S, Mavrogiannis C. Capsule retention: a feared complication of wireless capsule endoscopy. Scand J Gastroenterol. 2009;44(10):1158-1165.
- 32. Mata A, Llach J, Bordas JM. Wireless capsule endoscopy. World J Gastroenterol. 2008;14(13):1969-1971.
- Liao Z, Gao R, Xu C, Li ZS. Indications and detection, completion, and retention rates of small-bowel capsule endoscopy: a systematic review. Gastrointest Endosc. 2010;71(2):280-286.
- 34. Majeski J. Endoscopic capsule retention in an intestinal

anastomosis. Int Surg. 2009;94(3):254-257.

- 35. Ho KK, Joyce AM. Complications of capsule endoscopy. Gastrointest Endosc Clin N Am. 2007;17(1):169-178.
- 36. Ponte A, Pinho R, Rodrigues A, Silva J, Rodrigues J, Sousa M, Carvalho J. Predictive factors of an incomplete examination and inadequate small-bowel cleanliness during capsule endoscopy. Rev Esp Enferm Dig. 2018;110(10):605-611.
- Koulaouzidis A, Rondonotti E, Karargyris A. Small-bowel capsule endoscopy: a ten-point contemporary review. World J Gastroenterol. 2013;19(24):3726-3746.
- 38. Kim ES, Chun HJ, Keum B, Seo YS, Jeen YT, Lee HS, Um SH, et al. Coffee enema for preparation for small bowel video capsule endoscopy: a pilot study. Clin Nutr Res. 2014;3(2):134-141.
- 39. Albert J, Gobel CM, Lesske J, Lotterer E, Nietsch H, Fleig WE. Simethicone for small bowel preparation for capsule endoscopy: a systematic, single-blinded, controlled study. Gastrointest Endosc. 2004;59(4):487-491.
- 40. Rosa BJ, Barbosa M, Magalhaes J, Rebelo A, Moreira MJ, Cotter J. Oral purgative and simethicone before small bowel capsule endoscopy. World J Gastrointest Endosc. 2013;5(2):67-73.
- 41. Munoz-Navas M. Capsule endoscopy. World J Gastroenterol. 2009;15(13):1584-1586.
- 42. Flemming J, Cameron S. Small bowel capsule endoscopy: Indications, results, and clinical benefit in a University environment. Medicine (Baltimore). 2018;97(14):e0148.
- Omori T, Hara T, Sakasai S, Kambayashi H, Murasugi S, Ito A, Nakamura S, et al. Does the PillCam SB3 capsule endoscopy system improve image reading efficiency irrespective of experience? A pilot study. Endosc Int Open. 2018;6(6):E669-E675.
- 44. Goenka MK, Majumder S, Goenka U. Capsule endoscopy: Present status and future expectation. World J Gastroenterol. 2014;20(29):10024-10037.
- 45. Singeap AM, Stanciu C, Trifan A. Capsule endoscopy: The road ahead. World J Gastroenterol. 2016;22(1):369-378.
- McAlindon ME, Ching HL, Yung D, Sidhu R, Koulaouzidis A. Capsule endoscopy of the small bowel. Ann Transl Med. 2016;4(19):369.
- 47. Shim KN, Jeon SR, Jang HJ, Kim J, Lim YJ, Kim KO, Song HJ, et al. Quality Indicators for Small Bowel Capsule Endoscopy. Clin Endosc. 2017;50(2):148-160.
- 48. Kim SH, Yang DH, Kim JS. Current status of interpretation of small bowel capsule endoscopy. Clin Endosc. 2018;51(4):329-333.
- 49. Shiotani A, Honda K, Kawakami M, Kimura Y, Yamanaka Y, Fujita M, Matsumoto H, et al. Analysis of smallbowel capsule endoscopy reading by using Quickview mode: training assistants for reading may produce a high diagnostic yield and save time for physicians. J Clin Gastroenterol. 2012;46(10):e92-95.
- 50. Buscaglia JM, Giday SA, Kantsevoy SV, Clarke JO, Magno P, Yong E, Mullin GE. Performance characteristics of the suspected blood indicator feature in capsule endoscopy according to indication for study. Clin Gastroenterol Hepatol. 2008;6(3):298-301.

- 51. Karargyris A, Bourbakis N. Detection of small bowel polyps and ulcers in wireless capsule endoscopy videos. IEEE Trans Biomed Eng. 2011;58(10):2777-2786.
- Wang S, Xing Y, Zhang L, Gao H, Zhang H. Deep convolutional neural network for ulcer recognition in wireless capsule endoscopy: experimental feasibility and optimization. Comput Math Methods Med. 2019;2019:7546215.
- Pogorelov K, Suman S, Azmadi Hussin F, Saeed Malik A, Ostroukhova O, Riegler M, Halvorsen P, et al. Bleeding detection in wireless capsule endoscopy videos - Color versus texture features. J Appl Clin Med Phys. 2019;20(8):141-154.
- Holden JP, Dureja P, Pfau PR, Schwartz DC, Reichelderfer M, Judd RH, Danko I, et al. Endoscopic placement of the small-bowel video capsule by using a capsule endoscope delivery device. Gastrointest Endosc. 2007;65(6):842-847.
- 55. Keuchel M, Csomos G, Al-Harthi S, Bruhn JP, Hagenmueller F. Endoscopic placement of the video capsule with the AdvanCETM delivery device. Gastrointestinal Endoscopy (Abstract). 2006;63(5):M1373.
- 56. https://www.medtronic.com/content/dam/covidien/library/us/en/product/endoscopy-products/pillcam-colon-2-capsule-staff-prep-information-sheet.pdf.
- Toth E, Yung DE, Nemeth A, Wurm Johansson G, Thorlacius H, Koulaouzidis A. Video capsule colonoscopy in routine clinical practice. Ann Transl Med. 2017;5(9):195.
- Van Gossum A, Munoz-Navas M, Fernandez-Urien I, Carretero C, Gay G, Delvaux M, Lapalus MG, et al. Capsule endoscopy versus colonoscopy for the detection of polyps and cancer. N Engl J Med. 2009;361(3):264-270.
- Spada C, Hassan C, Marmo R, Petruzziello L, Riccioni ME, Zullo A, Cesaro P, et al. Meta-analysis shows colon capsule endoscopy is effective in detecting colorectal polyps. Clin Gastroenterol Hepatol. 2010;8(6):516-522.
- 60. Spada C, De Vincentis F, Cesaro P, Hassan C, Riccioni ME, Minelli Grazioli L, Bolivar S, et al. Accuracy and safety of second-generation PillCam COLON capsule for colorectal polyp detection. Therap Adv Gastroenterol. 2012;5(3):173-178.
- 61. Sieg A, Friedrich K, Sieg U. Is PillCam COLON capsule endoscopy ready for colorectal cancer screening? A prospective feasibility study in a community gastroenterology practice. Am J Gastroenterol. 2009;104(4):848-854.
- 62. Rex DK, Adler SN, Aisenberg J, Burch WC, Jr., Carretero C, Chowers Y, Fein SA, et al. Accuracy of capsule colonoscopy in detecting colorectal polyps in a screening population. Gastroenterology. 2015;148(5):948-957. e942.
- 63. Pasha SF. Applications of colon capsule endoscopy. Curr Gastroenterol Rep. 2018;20(5):22.
- 64. Spada C, Hassan C, Galmiche JP, Neuhaus H, Dumonceau JM, Adler S, Epstein O, et al. Colon capsule endoscopy: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2012;44(5):527-536.
- 65. Ladas SD, Triantafyllou K, Spada C, Riccioni ME, Rey JF, Niv Y, Delvaux M, et al. European Society of Gastrointestinal Endoscopy (ESGE): recommendations (2009) on clinical use of video capsule endoscopy to investigate small-bowel, esophageal and colonic diseases. Endosco-

py. 2010;42(3):220-227.

- 66. Galmiche JP, Sacher-Huvelin S, Coron E, Cholet F, Soussan EB, Sebille V, Filoche B, et al. Screening for esophagitis and Barrett's esophagus with wireless esophageal capsule endoscopy: a multicenter prospective trial in patients with reflux symptoms. Am J Gastroenterol. 2008;103(3):538-545.
- 67. McCarty TR, Afinogenova Y, Njei B. Use of wireless capsule endoscopy for the diagnosis and grading of esophageal varices in patients with portal hypertension: a systematic review and meta-analysis. J Clin Gastroenterol. 2017;51(2):174-182.
- 68. Park J, Cho YK, Kim JH. Current and future use of esophageal capsule endoscopy. Clin Endosc. 2018;51(4):317-322.
- 69. Eliakim R, Spada C, Lapidus A, Eyal I, Pecere S, Fernandez-Urien I, Lahat A, et al. Evaluation of a new panenteric video capsule endoscopy system in patients with

suspected or established inflammatory bowel disease - feasibility study. Endosc Int Open. 2018;6(10):E1235-E1246.

- 70. Lobo A, Torrejon Torres R, McAlindon M, Panter S, Leonard C, van Lent N, Saunders R. Economic analysis of the adoption of capsule endoscopy within the British NHS. Int J Qual Health Care. 2020;32(5):332-341.
- ASGE Training Committee 2011-2012, Rajan EA, Pais SA, Degregorio BT, Adler DG, Al-Haddad M, Bakis G, et al. Small-bowel endoscopy core curriculum. Gastrointest Endosc. 2013;77(1):1-6.
- 72. Yim S, Gultepe E, Gracias DH, Sitti M. Biopsy using a magnetic capsule endoscope carrying, releasing, and retrieving untethered microgrippers. IEEE Trans Biomed Eng. 2014;61(2):513-521.
- 73. Hwang Y, Park J, Lim YJ, Chun HJ. Application of artificial intelligence in capsule endoscopy: where are we now? Clin Endosc. 2018;51(6):547-551.