Small Bowel Video Capsule Endoscopy Guidance in Practice: Expert Opinion Report

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ABSTRACT

Capsule endoscopy, in clinical use since the 2000s, has disrupted the diagnosis of various small bowel diseases, especially obscuregastrointestinal bleeding. An overview of information on indications, contraindications, patient management, and patient preparationfor capsule endoscopy, which allows the evaluation of the entire gastrointestinal tract, will be helpful for both referrers and capsuleendoscopy. This review critically considers current evidence on the optimal clinical use of capsule endoscopy and addresses areas in the "gray zone."

Keywords: *Capsule endoscopy, Crohn's disease, obscure gastrointestinal bleeding, preparation, small bowel, suspected small bowel bleeding*

INTRODUCTION

Diagnosis of small bowel (SB) diseases is often tricky and delayed, but things have changed drastically with technological developments since the dawn of the century. Capsule endoscopy (CE) allowed clinicians to depart from the conventional tethered gastrointestinal (GI) endoscopy, making CE the preferred method in routine SB examination due to its noninvasive nature and ease of application. Furthermore, as CE platforms are apt for further development, therapeutic applications and drug delivery are the final frontier for this technology.[1]

Capsule endoscopy was developed by Idan[2] in 1981. Since its introduction in 2000, it has become an important method in the evaluation of SB pathologies. In Turkey, PillCam SB3 (Medtronic), MiroCam (Intromedic), EndoCapsule (Olympus), OMOM (Jinshan Science & Technology Co.), and Capsovision (China Medimetrics) capsules are available for routine clinical use. For all of the above CE models, save for the Capsovision system, the images are transmitted via radiofrequency to the external recorder worn by the patient. Then, the image analysis is performed by loading these data on the computer (Workstation). The CapsoCam system comes with an apparatus placed in the toilet bowl that allows for capturing the capsule. As images are stored onboard with this capsule, the former is necessary for capsule retrieval and eventually data are transferred to the system. Medtronic's armamentarium also includes patency capsules. Patency checks provide the opportunity to use capsules in patients who have high clinical suspicion for SB obstruction. There is a continuous effort from most manufacturers to better CE technological specifications. The above-described types of capsule endoscopes and their basic specifications are summarized in Table 1.

In this review, we aimed to determine the optimal clinical use of CE in Turkey and try to address issues that still lie in the "gray zone."

MATERIALS AND METHODS

To arrive at a consensus on best clinical practice in SB enteroscopy, we were asked to review and modify consensus statements in 6 different areas: optimal bowel

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Table 1. Types of Capsule Endoscopes[3,4]

Capsule	(CapsoCam Plus®) (CapsoVision, Inc.)	(PillCam® SB 3) (Given Imaging)	(EndoCapsule®) (Olympus America)	(MiroCam®) (Intromedic Company)	(OMOM®) (Jianshan Science and Technology)
Size (length × diameter)	Length: 31 mm Diameter: 11 mm	Length: 26.2 mm Diameter: 11.4 mm	Length: 26 mm Diameter: 11 mm	Length: 24.5 mm Diameter: 10.8 mm	Length: 27.9 mm Diameter: 13 mm
Weight (g)	4.00	3.00	3.50	4.70	6.00
Battery life (h)	≥15	≥8	≥8	≥11	≥6-8
Resolution (pixels)	221 × 884	340 × 340	512 × 512	320 × 320	640 × 480
Frames per second (fps)	3-5	2-6	2	3	2
Field of view	360°	156°	145°	170°	140°
Communication	Radiofrequency communication	Radiofrequency communication	Radiofrequency communication	Human body communication	Radiofrequency communication

preparation, indications for CE, contraindication for CE, clinical evaluation before CE, the optimal reporting in CE, and combined CE with double balloon enteroscopy (DBE). We aimed to generate a consensus report for CE.

Search Strategy Methodology

In PubMed/MEDLINE, the past and recent literature on CE was reviewed, and each team of experts wrote key statement opinions on CE in these 6 areas: ideal bowel preparation, indications for CE, contraindication for CE, clinical evaluation before CE, the optimal reporting in CE, and combination of CE with DBE, taking into account the guidelines and recommendations from European Society of Gastrointestinal Endoscopy (ESGE), American Society for Gastrointestinal Endoscopy (ASGE), American College of Gastroenterology (ACG), and European Crohn's and Colitis Organisation (ECCO) on CE. These issues were then discussed within the groups and the final statements were drafted. The manuscript based on these statements was then sent to the group members for comments and modifications.

WHAT IS THE OPTIMAL BOWEL PREPARATION FOR CAPSULE ENDOSCOPY?

The aim of performing CE is to provide diagnostic imaging of the SB, which otherwise is difficult to visualize. Poor visualization quality (VQ) is one of the important confounders caused by intestinal debris, biliary secretions, and air bubbles, leading to a low diagnostic yield (DY).[5] However, the optimal bowel preparation regime before CE is not clearly established. It is generally agreed that patients should fast at least overnight (12 hours) and ingest only clear fluids. Whether additional pharmacotherapy is needed for better VQ and higher DY is controversial because studies have shown different conclusions regarding the efficacy.[6-9] There are some points to consider regarding SB preparation for CE. First, the indication for performing CE can be equally crucial, along with the preparation type, timing, and patient compliance. For example, if CE is being performed to investigate the cause of a mild GI bleeding, bowel preparation may provide clear findings. Conversely, preparation may not be required before a CE procedure to detect the cause of heavy GI bleeding, and in severe cases, there may not be time for such practice. On the other hand, the presence of dense and/or fecalized intestinal content proximal to partial stenosis, or in cases of Crohn's disease (CD) where detailed examination of the terminal ileum is needed, bowel preparation may be essential to display target areas.

Fasting Time

The fasting period recommended by capsule manufacturers is usually 8-12 hours before capsule ingestion. Most relevant CE studies used 12 hours of preprocedure fasting. They are, furthermore, attempting to keep high VQ for CE by a clear fluid diet before an overnight fasting period. However, there is not enough literature to confirm the optimal diet or fasting time. In a study comparing different fasting times, there was a significant relationship between increased fasting time and improved SB mucosal visualization, and 12 hours of fasting was found to be superior, in terms of VQ, compared to shorter periods.[10] In a study conducted in Turkey examining outcomes of CE performed after an 10-12 hour fasting, DY was found to be satisfactory.[11] Concerning patient comfort and compliance, 12-hour overnight fasting after a day of clear fluid diet seems reasonable and can be recommended as a preparation for SB CE.

Drugs for Bowel Preparation

There are 3 peri-procedural groups of medications in use for CE. The group with more evidence behind it are purgative drugs. Among these commonly used are polyethylene glycol (PEG) preparations and sodium phosphate (NaP)-based solutions. The second group is drugs used as anti-foaming agents to reduce air bubbles. The most frequently used and researched drug here is simethicone. The third group of drugs, whose effectiveness has been investigated in CE, is prokinetics, of which metoclopramide is the most frequently used. Many studies and several meta-analyses have been conducted on SB preparation with PEG, but CE has achieved different results. Intestinal cleansing using PEG, the evening before the procedure, is associated with an increase in SB VQ, while any increase in DY was less pronounced, and some argue that this has not been demonstrated.[12-17] Also, in some meta-analyses, it has been shown that PEG contributes to VQ in the CE.[18-22] Although different amounts of PEG (1 L, 2 L, 4 L) have been used in different studies, there is not much data about the superiority of the amounts to each other. In a study comparing 2 L PEG to 4 L PEG, intestinal preparation with 2 L PEG was found to be sufficient,[23,24] and in another meta-analysis, PEG was found to be sufficient even at low volume, but it was also stated that VQ increased as the volume increased.[18] One study showed increased VQ and DY with intraprocedural (60 minutes post-capsule ingestion) administration of 500 mL PEG instead of the traditional preprocedural (evening before) laxative preparation with PEG.[22] Although the optimal time for bowel preparation remains unclear, it can be stated that 2 L PEG in the evening before the procedure is sufficient.[10,25-27] Nevertheless, pre-CE laxative preparation with PEG has been recommended in the recent Canada 2017 and ESGE 2018 guidelines.[28,29] NaP solutions as bowel preparation for CE have been recommended as the second most common after PEG. Although there are studies that point to that NaP solutions may increase VQ,[13,20,30,31] there are also results that suggest it is useless.[18,21] Studies comparing PEG preparations and NaP solutions often show a result in favor of PEG.[13,18,21] The risk of NaP solutions to cause electrolyte disturbances, nonspecific aphthous-like mucosal lesions, and renal toxicity should also be taken into consideration before using these preparations for intestinal preparation. While ESGE 2009 and Canada 2017 guidelines recommend the use of NaP solutions as well as PEG preparations, only PEG solutions are recommended in ESGE 2018.[28,29,32] Among the anti-foaming agents, simethicone is the most studied one. It is aimed to reduce foaming and increase VQ by giving it before the procedure. In most studies, it was observed that the addition of simethicone before the examination to either isolated fasting or PEG preparation caused an increase in VQ, but it did not yield any improvement in DY.[12,13,21,33-35] It is stated that the intake of simethicone should be just before the capsule. Dosage of 80-200 mg has been used in different studies and the ideal dose is not clear. Nevertheless, in the Canada 2017 and ESGE 2018 guidelines, the use of simethicone is recommended due to its contribution to VQ.[28,29] Studies investigating the potential effect of prokinetics such as metoclopramide on CE have shown that such agents do not contribute neither to VQ nor to DY. Although the results are contradictory, metoclopramide may assist the capsule to reach the cecum during the recording period[36,37] especially in patients with a prolonged gastric emptying. In particular, available data suggest that this contribution may become evident if treatment is planned according to real-time monitoring and the duration of capsule retention in stomach exceeds 30-60 minutes.[38]

As conclusions,

- Before CE, intestinal preparation with 2 L PEG solution after a day of clear liquid diet followed with 10-12 hours of overnight fasting and administration of simethicone (80-200 mg) is an appropriate strategy.
- However, physicians should keep in mind indications, patient characteristics, and possible side effects of laxatives as well as an increasing body of evidence of small dose intraprocedural laxative (PEG) use.

WHAT ARE THE MAIN INDICATIONS OF CAPSULE ENDOSCOPY?

Capsule endoscopy can be used as a noninvasive method in all pathologies involving the small intestine. Capsule endoscopy indications were as follows:

- Obscure GI bleeding (OGIB)
- Iron deficiency anemia (IDA) (unexplained)
- Inflammatory bowel disease (IBD)
- Abdominal pain
- Polyposis syndromes (Lynch syndrome, Peutz-Jeghers syndrome, or familial adenomatous polyposis)
- Malabsorption (Celiac disease, etc.)
- Assessment of possible SB tumors
- Follow-up of patients after SB transplantation

The primary indication for SB CE is an OGIB. It constitutes more than 60% of CE studies.[39,40] The term "obscure GI bleeding" should be used for patients with no evident a

source of bleeding after performance of standard upper and lower endoscopic examinations, SB evaluation with VCE and/or enteroscopy, and radiographic testing. Obscure GI bleeding can be classified to overt or occult.[41] However, in practice, it should be considered in a patient who underwent gastroscopy twice (including duodenum third and fourth part) and ileocolonoscopy. Capsule endoscopy is accepted as gold standard for SB imaging.[42] The diagnostic rate of OGIB was 90%, and its sensitivity in predicting re-bleeding in the long term was 100% and specificity was 93%.[43] Diagnostic capability of CE is high especially in overt OGIB. The most common detected lesions are angioectasis, tumors, varicose veins, diverticula, and ulcers. Pennazio et al[44] reported the sensitivity, specificity, positive, and predictive values in OGIB as 88.9%, 95%, 97%, and 82.6%, respectively. In this study, the highest diagnostic rate was found in active bleeding (92.3% vs. 44.2%). The lowest diagnosis was found in those with previous/non-active bleeding (12.9%). Therefore, CE should be performed as soon as possible, preferably within 2 weeks from the index episode. Performing CE within 48 hours is associated with greater therapeutic yield, less re-bleeding episodes, and a longer re-bleeding free time.[45] Recent meta-analyses showed that the pooled sensitivity and specificity for ulcer detection were 0.95 (95% CI, 0.89-0.98) and 0.94 (95% CI, 0.90-0.96), respectively; furthermore, pooled sensitivity and specificity for bleeding or bleeding source were 0.98 (95% CI, 0.96-0.99) and 0.99 (95% CI, 0.97-0.99), respectively.[46,47] In a multicenter study, Albert et al[47] evaluated CE data from 247 patients and found that they changed treatment management in 66% of patients. In another study, patient management changed in 70% of patients with positive CE.[48] Capsule endoscopy also have an important role for the management of IDA, especially in the younger age groups.[49] The capsule may bypass large polypoid lesions and occasionally misdiagnosis is possible. On the other hand, it can also detect the lesions where gastroscopy and colonoscopy are skipped. Detection rate of non-small bowel lesions (NSBL) is 10.8% (colon 4.6%, bulbus 3.6%, stomach 2.2%, and choledochal 0.7%).[50] In emergency services, angiography, scintigraphy, and imaging are at the forefront of the classical approach in patients with massive bleeding.[51] Lecleire et al[52] evaluated CE results in 55 patients presenting to the emergency department with massive bleeding with a negative endoscopic examination in the first 24-48 hours of presentation. Management benefit was noted in 67% of them after a CE procedure. Therefore, CE may be the first choice in selected massive bleeding patients after radiological imaging in emergency services. Double balloon enteroscopy was found to be cost effective in OGIB in 1 study.[53] However, CE is uncomplicated; it can determine the entry direction for DBE and give an idea about the entire small intestine. On the other hand, Jawaid et al[54] also reported that CE may be a more efficient diagnostic approach than the standard of care approach, since it detects bleeding significantly more often without an increase in healthcare costs in patients with non-hematemesis bleeding. In the long-term period, CE has also high predictive value for re-bleeding in OGIB. Lai et al[55] reported that re-bleeding rate was 32.7% in the first year. They showed that the risk of re-bleeding was low in patients with CE negative during the median follow-up of 19 months (12-31 months). Delvaux et al[56] found a positive predictive value of 94.4% and a negative predictive value of 100% for the risk of re-bleeding in patients with normal CE in a 1-year follow-up of 44 patients. Arakawa et al[57] showed no bleeding in any patient with normal CE. Iwamoto et al[58] found that the rate of re-bleeding was higher in overt bleeding (26.1% vs. 4%) in the 6-month follow-up of 78 negative patients with CE. In the long-term (median 32 months; 6-82 months) evaluation of 141 patients, the total diagnostic rate of CE was found to be 84.9% and the rate of re-bleeding in patients was 40.3%. The bleeding rate during the follow-up period was 46.6% and 4.8% of capsule positive and negative patients, respectively. In multivariate analysis, anticoagulant/antiaggregant use (OR: 5.8; 95% CI: 1.86-18) and vascular ectasia (OR: 6.02; 95% CI: 2.568-14.146) were found to be independent risk factors for re-bleeding. In the univariate analysis, advanced age, comorbidity, and overt bleeding were detected as predictors for re-bleeding.[59]

Capsule endoscopy is also increasingly used in the diagnostic work up of known or suspected CD.[58,60] Capsule endoscopy can be used in selected cases of IBD.[61] Other SB radiographic imaging is often required to assess stenosis prior to CE. If abdominal pain is accompanied by diarrhea or weight loss or elevated fecal calpotectin, the rate of diagnosis increases more.[62] Although routine use of CE is not recommended in patients with an established CD, it should be considered in cases of unexplained anemia, severe malnutrition, and cross-sectional imaging situations such as MRE that do not match the patient's symptoms and clinical findings. In addition, evaluation of mucosal healing, which is an important target in CD, with CE is not recommended in routine use, but it is important in terms of treatment approach.[59-62] The diagnostic value of the CE is low in abdominal pain and diarrhea and should not be the first examination to be requested, abdominal

pain in the absence of other objective symptoms is an approved indication for CE.[63] Diagnosis rate is higher in polyposis case especially for <15 mm polyps which can be skipped by radiologic imaging.[64] It may be effective in showing complications in celiac disease.[65-67] On the other hand, CE can help the differential diagnosis of nonresponsive celiac disease patients for gluten-free diet.[68]

As conclusions,

- Main indications of CE are OGIB (overt/occult) and IDA.
- Other indications should be carefully evaluated in case-by-case basis.

IS THERE ANY REAL CONTRAINDICATION FOR CAPSULE ENDOSCOPY?

Small bowel obstruction is the only absolute contraindication of CE. Capsule retention occurs in approximately 1%-2% of patients being evaluated for OGIB. In a meta-analysis, authors reported that the overall prevalence of retention was as low as 1.4% (95% CI, 1.2-1.6). Retention prevalence for OGIB was 1.2% (95% CI, 0.9-1.6), for CD (diagnosed or suspected), it was 2.6% (95% CI, 1.6-3.9), and for neoplastic lesions, it was 2.1% (95% CI, 0.7-4.3).[69] Retention prevalence in patients with established IBD (especially CD) was higher than that of the others.[70-71] In our experience, the capsule retention rate was 3.1%; it was retained in a malignant lesion area (18.2%), in the SB in an ulcerated area (45.5%), and in the esophagus/stomach due to dysmotility (36.4%). None of the patients had symptoms of obstruction. The GI tract was evaluated for blockages with computerized tomography in all patients.[72] Imaging methods cannot be predicting capsule retention. Even with capsule retention, no serious complication developed. Surgery was performed due to underlying disease. When the capsule endoscopy is inserted in the benign ulcer area, it can be removed with DBE, or medical treatment can be given. Capsule may also be retained for a long time safely in the absence of obstructive symptoms.[73] Although retention is accepted as a complication of CE, capsule can be retrieved by DBE. Recent meta-analysis reported that the estimated pooled successful retrieval rate was 86.5% (95% CI, 75.6%-95.1%). Therefore, DBE is feasible and safe for removing retained video capsule endoscopes, and its use could decrease the need for surgery in patients with benign strictures and facilitate subsequent surgery in patients with malignant strictures.[74] Therefore, even capsule retention is not a serious complication. Patients' symptoms should be evaluated carefully to decrease the risk of retention complications. Retention rate decreased with the development of capsule technology and completing the learning period in clinical practice. A significant increase in the rate of patients undergoing SBCE for suspected SB bleeding was observed from 2001-2008 to 2011-2013 (67.3 vs. 76.1%; $P < .001$). In this study, the retention rate (2.1 vs. 0.8%; $P < .001$) and the rate of patients undergoing SBCE for CD (11.5 vs. 5.5%; $P < .001$) decreased significantly. The overall diagnostic rate remained stable (50.6 vs. 48.4%; $P = .089$). They concluded, over 13 years, the SB CE safety profile and completion rate significantly improved over time.[75] Some authors also recommend using CE in determining the location of stenotic segment before surgery. History and questionnaire for obstructive symptoms is important before CE. Abdominal CT should be performed to exclude obstruction. Patency capsules can be preferred in patients suspected of SB obstruction. These are fusible tablets of the same size and shape as the capsule endoscope. It has a radiofrequency recognition chip that detects the capsule. Although clinical results are variable, newly developed capsules seem useful in evaluating patients at risk of capsule retention.

Motility disorders are other contraindications that can be skipped in clinical practice.[71] However, upper GI motility problems (achalasia, gastroparesis, etc.) cannot be accepted for contraindication. We can easily insert capsule by gastroscope in duodenal bulb. Intestinal pseudo-obstruction is an absolute contraindication for CE. Patients should be questioned carefully for dysmotility (especially diabetics). External viewer may help to check capsule localization in diabetics and immobilized intensive care unit patients. If we detect the capsule in stomach after 2 hours, we can move the capsule to the SB by gastroscopy.

Swallowing problems should be evaluated very carefully. Capsule aspiration is very rare complication of VCE with a presumed incidence of 1 in 600-700.[76,77] This risk can be high in children and geriatric population. Oral ingestion of CE is contraindicated for patients with known swallowing problem. Endoscopic replacement can be possible if there is absolute indication in this condition.

Implantable devices (pacemaker, defibrillator, or electromechanical device) are accepted as relative contraindications for CE. Kasia et al[78] evaluated 44 pacemaker, 18 cardiac defibrillator, 3 left ventricular assist device (LVAD),

17 cardiac defibrillator plus pacemaker, 19 left LVAD plus cardiac defibrillator, and 6 left LVAD plus cardiac defibrillator plus pacemaker patients retrospectively. They did not report any device-related complications during the procedure and in the 30-day post-procedure time period. Post-procedure analysis of the CE recordings demonstrated no interference in CE image quality (loss of images or gaps in video) or duration. In a pooled analysis study (16 studies included), interference on capsule images transmission was noted in 5 cases (LVAD) where few images were lost when the capsule was closest to the device. These studies included Pillcam, Endocam, and Mirocam capsules. Finally, interference between capsule and telemetry leads was noted in 6 cases (4 permanent pacemakers, 2 implantable cardioverter-defibrillator) leading to image artifacts. Adverse cardiac events were not seen in this study. Loss of images occurred when the CE was in proximity to the device (only with LVAD) or after telemetry leads installation without affecting the completion rate and DY of CE.[79] In our practice, we use CE safely with implantable devices with taken inform consent.

Pregnancy is a relative contraindication for CE. There is a very little data about pregnancy and CE.[80,81] According to our real-life experience, if there is an absolute indication for CE, we can use it safely.

Other, relative contraindications are large diverticulum, Zenker's diverticulum, long-term use of nonsteroid anti-inflammatory drugs (NSAIDs) (stenosis due to diaphragm ulcer), and previous major abdominal surgery. Capsule endoscopy is safe in these group of patients unless there is no obstructive intestinal symptoms or dysphagia. Although The United States Food and Drug Administration (FDA) approved CE for children of 2 years or older in 2009, CE is used in practice in younger patients when necessary.

As a conclusion,

- Small bowel obstruction is the only accepted contraindication for CE today.

HOW SHOULD WE PERFORM CLINICAL EVALUATION BEFORE CAPSULE ENDOSCOPY?

Capsule endoscopy is a frequently used noninvasive method to visualize the SB in patients with disorders involving the SB such as OGIB, CD, polyposis syndromes, and celiac disease. Before CE, initial assessment of patient includes a detailed medical history including drugs, full physical examination, and upper GI endoscopy and colonoscopy. In selected patients, cross-sectional imaging methods such as magnetic resonance enterography (MRE) should be considered.

History and Physical Examination

We recommend evaluation of the risk of capsule retention and the presence of swallowing disorders before CE.

A detailed medical history and physical examination is of upmost importance in the evaluation of a patient before CE. The determination of the true presenting symptom is necessary for deciding an effective evaluation plan. In patients presenting with hematemesis, initial investigation should be planned to evaluate the segments above the ligament of Treitz. Additionally, complicated abdominal pain may suggest small intestinal obstruction due to tumors or inflammation such as CD and intestinal tuberculosis. Unexplained weight loss may suggest a malignancy.

A detailed medical history should include comorbidities (diabetes mellitus, hemodialysis, portal hypertension, cardiovascular disease, etc.), past history of cancer, radiation therapy or abdominal surgery, past and family history of epistaxis.[82] All prescription drugs (i.e., NSAID, aspirin) and over-the-counter drugs (i.e., herbals) should be sought to exclude medication-related mucosal lesions.

For the risk of capsule retention, patients should be investigated for the presence of obstructive symptoms, a history of known bowel stenosis, or small intestine resection before CE. Additionally, patients should be evaluated for swallowing disorders to exclude the risk of aspiration.

Detailed physical examination evaluating the liver, heart, kidney, and the respiratory system should be sought to search for clues. Some skin lesions or cutaneous sings found upon physical examination may help to suspect the disorders associated with OGIB.[83,84] These disorders are hereditary hemorrhagic telangiectasia (vascular lesions on the lips, nasal mucosa, tongue, palms, and palate), Henoch Schoenlein purpura, neurofibromatosis (painless papules), celiac disease (dermatitis herpetiformis), Plummer Vinson syndrome (brittle spoon nails), acquired immunodeficiency syndrome (Kaposi's sarcoma), IBD (erythema nodosum), Peutz-Jeghers syndrome (freckles on the lips and in the mouth), and Ehlers Danlos syndrome (chicken skin appearance, angioid streaks in retina).

Endoscopic Examination

Obscure Gastrointestinal Bleeding: Obscure GI bleeding has been defined by Zuckerman et al[85] in 2000 as "bleeding of unknown origin that persists or recurs (i.e., recurrent or persistent IDA, fecal occult blood test positivity, or visible bleeding) after a negative initial or primary endoscopy (colonoscopy and/or upper endoscopy) result" but recently it is updated as "OGIB" should be used for patients not found to have a source of bleeding after performance of standard upper and lower endoscopic examinations, SB evaluation with VCE and/or enteroscopy, and radiographic testing.[41]

The lower and upper endoscopic evaluations remain the cornerstone for investigation of OGIB. The experience of the push enteroscopy studies in patients with OGIB recommended that repeat standard endoscopy should be considered before push enteroscopy.[81,82] In these studies, most of the lesions were found to be within reach of a standard endoscope. Zaman and Katon[86] showed that lesions at or above the main duodenal papilla as source of bleeding were missed at initial endoscopy at rates as high as 26.3% in patients with OGIB. Cameron ulcers and arteriovenous malformations were found as the most common lesions in this study. Descamps et al[87] reported that "missed" upper GI lesions were detected in 10.2% of patients. Half of these missed lesions were located in the fundus of the stomach. Wirsungorrhagia was determined in 2 patients.

Many factors may affect the success of endoscopic examinations.

- The experience of the endoscopist who carried out the initial GI endoscopy may affect the results of endoscopic examination. Especially, the lesions located at the fundus, posterior of the duodenum, the papilla, and the terminal ileum can be missed.
- Many vascular lesions such as angiodysplasia may disappear during conventional endoscopy due to drugs used during sedation or hypotension.
- The presence of blood clots in the GI tract may decrease the quality of initial endoscopic examination.
- Also, other factors such as the patient's age and cooperation of the patient may be effective.

Non-small bowel lesions were defined as visible lesions (at or above the main duodenal papilla and at or below the terminal ileum) detected during CE that are located within reach of upper GI endoscopy and colonoscopy. The studies that evaluate NSBLs detected by CE reported that the rates NSBLs missed at conventional upper GI and lower GI endoscopy ranged from 3.5% to 39%.[88] Only upper GI lesions were evaluated in 3 studies and only lower GI lesions were evaluated in one study, both upper and lower GI lesions were investigated in the remaining studies.[89-98] Studies are summarized in Table 2.

The first study that evaluated only upper GI lesions showed although all patients had at least 1 upper GI endoscopy before the CE, 38.8% (201/78) had an NSBL that was within the reach of upper GI endoscopy.[89] Non-small bowel lesions were believed to be the source of bleeding in 16.4% (201/33) of patients. The distribution of detected NSBLs was 7 gastric ulcers, 4 duodenal

Table 2. Studies Evaluating the Rate of NSBLs Detected by CE

References	CE (n)	NSBL (n)	Diagnostic Yield (%)	Upper GI Lesions, n (%)	Lower GI Lesions, n (%)
Elijah et al[89]	201	78	38.8	33 (16.4)*	—
Tacheci et al[90]	118	44	37.3	25 (21.2)*	—
Juanmartinena-Fernandez et al[91]	2217	566	25.5	196 (8.8)*	—
Juanmartinena-Fernandez et al[92]	464	47	9.0	—	24 (4.6)*
Kitiyakara and Selby[93]	140	9	6.4	4 (2.8)	5 (3.6)
Vlachogiannakos et al[94]	317	11	3.5	4 (1.3)	7 (2.2)
Hoedemaker et al[95]	595	85	14.3	41 (6.9)	44 (7.4)
Riccioni et al[96]	637	179	28.1	50 (7.8)*	38 (6.0)*
Akin et al[97]	114	8	7.0	3 (2.6)	5 (4.4)
Innocenti et al[98]	290	88	30.3	31 (10.7)*	19 (6.5)*

CE, capsule endoscopy; NSBL, non-small bowel lesion.
*Only NSBLs as source of bleeding.

ulcers, 14 angioectasias, 7 gastric antral vascular ectasias (GAVEs), and 1 Cameron lesion.

The second study that determined only upper GI lesions found that although NSBLs were determined in 37.3% (118/44) of patients by CE, NSBLs were considered to be the source of bleeding in 21.2% (118/25) of patients.[90] While the most commonly detected lesions were hemorrhagic erosions (15 patients), GAVEs were detected in 3 patients.

The third study that investigated only upper GI lesions evaluated data from 2217 patients. Capsule endoscopy found 696 gastroduodenal lesions in 566 patients (25.5%). The distribution of gastroduodenal lesions were only gastric lesions in 285 patients, only duodenal lesions in 151 patients, and both gastric and duodenal lesions in 130 patients. Up to 488 patients had a previous upper GI endoscopy. While overlooked lesions in the initial endoscopy were 257, 178 of overlooked lesions were found significant as source of bleeding. Only gastroduodenal lesions without SB lesions were shown in 196 patients (8.8%). The most frequent lesions detected both in the stomach and duodenum as source of bleeding were vascular lesions.[91]

In a study evaluating only colonic missed lesions, colonic lesions were detected by CE in 9.0% of patients.[49] Overlooked lesions in the initial colonoscopy were detected in 24 patients. These lesions were vascular lesions, colonic ulcers, polyps, and carcinoma in 10, 5, 8, and 1 patients, respectively.[92]

A study reported that although the patients had on average a mean of 2.3 upper endoscopies and 2.2 colonoscopies, suspected lesions were within the reach of upper GI or lower GI endoscopy in 6.4% (140/9) of patients. While 2.8% (9/4) of NSBLs were located at the upper GI tract, 3.6% (9/5) of NSBLs were located at the lower GI tract. The most common of NSBLs in the upper GI tract were GAVE.[93]

Another study showed although the patients had a median of 2 upper GI endoscopies and 2 lower GI endoscopies before CE, NSBLs were still detected in 3.4% (317/11) of patients by CE. Non-small bowel lesions were located in the upper GI system in 1.2% (11/4) of the patients (1 cardia tumor, 2 angiodysplasias, and 1 GAVE) and in the lower GI system (3 colon carcinomas, 2 angiodysplasias, 1 diverticula, and 1 CD) in 2.2% of the patients (11/7). Interestingly, while endoscopic examinations of 9 of patients with NSBLs have been performed in the referring center, only 2 patients with NSBLs have undergone endoscopic evaluations in their own center.[94]

A prospective study evaluated results of CE of 595 patients regarding the NSBLs that were identified within the reach of upper GI endoscopy and colonoscopy. Non-small bowel lesions were found in 14.3% (595/85) of patients. The most frequently missed lesions were vascular lesions such as angiodysplasias. Non-small bowel lesions were detected in the stomach in 15 patients, at the proximal SB in 22 patients, at the terminal ileum in 21 patients, at the colon in 19 patients, and multiple localizations were found in 8 patients. Interestingly, the terminal ileum had been previously intubated during colonoscopy in only about 30% of cases.[95]

Another prospective study showed that CE displayed a cause of OGIB in the upper GI tract in 21.7% (637/138) of patients and in the lower GI tract in 6.4% (637/41) of patients with an initial non-diagnostic upper and lower GI endoscopy. Non-small bowel lesions as source of bleeding were detected outside the SB in only 13.8% (637/88) of patients. Non-small bowel lesions as source of bleeding detected in the upper GI tract were 11 gastric or duodenal angioectasias, 13 GAVEs, 11 gastric or duodenal ulcers, 2 esophageal varices, 3 neoplasms, 8 polyps, and 2 spontaneous mucosal bleedings. Non-small bowel lesions as source of bleeding found in the lower GI tract were 24 colonic angioectasias, 8 colonic ulcers, 2 spontaneous mucosal bleedings, 1 neoplasm, 2 polyps, and 1 diverticular active bleeding.[96]

Our recently published study analyzed NSBLs detected by CE in patients with potential SB bleeding. We found NSBLs at a rate of 7% (114/8). Three of these lesions were located in the upper GI tract and capsule endoscopic findings were GAVE in 1 patient and active bleeding in 2 patients. Five lesions located in the lower GI tract were angiodysplasias in 3 patients, active bleeding in 1 patient, and ulcer in 1 patient. In none of the patients who were referred to CE from our center, an NSBL as source of bleeding was found by CE.[97]

Recently published retrospective study reported data of 290 patients who underwent CE for the evaluation for OGIB. Capsule endoscopy showed clinically significant NSBLs missed upon both upper GI and lower GI endoscopy in 30.3% (290/88) of patients. The identified lesions were determined involving only the non-SB in 17.2% (290/50) of patients and the SB plus the non-SB

in 13.1% (290/38) of patients. Non-small bowel lesions were located 10.7% (290/31) on the upper GI tract and 6.5% (290/19) on the lower GI tract. The most clinically significant NSBLs were angiodysplasias in this study. Table 2 studies evaluating the rate of NSBLs detected by CE.[98]

According to the guidelines published by the American Gastroenterological Association (AGA), the ACG, the ASGE, and the ESGE, CE should be the first-choice examination after a non-diagnostic conventional upper and lower endoscopy in OGIB.[29,40,99]

In patients with overt GI bleeding, AGA recommends CE as the next diagnostic step if result of high-quality upper and lower GI endoscopy is non-diagnostic or as soon as possible if patient has obscure bleeding episode.[29] American College of Gastroenterology recommends repeat conventional both upper and lower GI endoscopy after ruling out celiac disease, hematologic or gynecologic pathologies if the patient is hemodynamically stable.[99] American Society for Gastrointestinal Endoscopy recommends repeat endoscopy and colonoscopy if upper or lower GI source is suspected.[40] European Society of Gastrointestinal Endoscopy recommends CE as the first-line investigation in patients with OGIB.[44] The repeat endoscopic examination before CE routinely is not recommended by ESGE, but the decision to perform the repeat endoscopic examination before CE in patients with OGIB or IDA should be made on a case-by-case basis.[44]

As a conclusion,

- In patients with OGIB, we recommend second-look endoscopy before CE.

Crohn Disease

Up to one-third of patients with CD have small intestinal involvement at diagnosis and the terminal ileum is included in majority of small-bowel CD patients.[100] So, ileocolonoscopy should be the first endoscopic examination for investigating patients with suspected CD. Because of the skip lesions of the terminal ileum, ileocolonoscopy may give false negative results.

A meta-analysis including 19 prospectively designed trials demonstrated that CE gave equal or higher DY compared to other methods such as colonoscopy with ileoscopy (95% CI = 5%-39%; $P = .009$), push enteroscopy (95% CI = –23% to 59%; $P = .39$), SB radiography (95% CI = 16%-48%; $P < .0001$), computed tomography (CT) enterography (95% CI = 31%-63%; $P < .00001$), and MRE (95% CI = –14% to 34%; $P = .43$) in patients with suspected CD.[101]

Another meta-analysis including 24 trials showed that CE had superior DY compared to procedures such as SB follow-through (CE, 66.0% vs. SBFT, 21.3%; IY_w, 0.44; 95% CI, 0.29 to 0.59; I^2, 30%) and enteroclysis (CE, 75.7% vs. EC, 29.4%; IY_w, 0.50; 95% CI, 0.21 to 0.79; I^2, 52%), but no significant difference could be found compared to other modalities such as CT enterography (CE, 72.5% vs. CTE, 22.5%; IY_w, 0.36; 95% CI, 0.18 to 0.90; I^2, 68%) or MRE (CE, 85.7% vs. MRE, 100%; IY_w, -0.16; 95% CI, -0.63 to 0.32; I^2, 44%) in patients with suspected CD.[102]

Use of NSAIDs may cause drug-induced enteropathy with small-bowel mucosal erosions and ulcerations.[103] A few studies determined that the high incidence of small-bowel erosion and ulcerations may be related use of NSAIDs.[104,105] Although different suggestions can be seen in the current literature, NSAIDs should better be stopped for at least 1 month before CE if possible.[105,106]

European Society of Gastrointestinal Endoscopy recommends ileocolonoscopy before CE in patients with suspected CD. European Society of Gastrointestinal Endoscopy does not recommend routine small-bowel imaging studies or the use of the PillCam patency capsule before CE in patients with absence of obstructive symptoms or known stenosis. European Society of Gastrointestinal Endoscopy recommends discontinuation of NSAIDs for at least 1 month before CE since these drugs may induce small-bowel mucosal lesions indistinguishable from those caused by CD.[44]

American Gastroenterological Association recommends ileocolonoscopy and imaging studies before CE if patients had suspected CD, if patients with CD had unexplained clinical features, or if patients had suspected recurrence of CD at the SB after bowel resection.[29]

ECCO recommends ileocolonoscopy before CE in suspected CD. If stenotic disease is suspected, risk of retention should be assessed. As according to ECCO guidelines, the presence of at least 3 small intestine ulcers in CE highly suggests a diagnosis of CD, the patient should stop using NSAIDs for at least 1 month before CE.[37]

In patients with suspected CD, we recommend ileocolonoscopy and imaging study before CE.

We recommend discontinuing the use of NSAID or aspirin in patients with suspected CD.

Capsule Retention

The risk of capsule retention is low in patients who present with suspected CD without obstructive symptoms provided that there is no known stenosis or history of the small intestinal resection. The risk of capsule retention in these patients is similar to patients who are being investigated for OGIB.[15] Routine small-bowel imaging or use of the PillCam patency capsule before CE is not essential in patients of suspected CD in the absence of suspected clinical symptoms or known stenosis.

The risk of capsule aspiration is extremely low during CE.[75] Occasionally, the patient's ability to swallow the capsule safely can be difficult to predict. Since elderly patients may have risk factors for aspiration such as cerebral stroke, bleeding, or trauma, thorough history of these patients is required. These patients may be tested for swallowing function before CE.[107] The capsule may be placed endoscopically directly into the duodenum in patients who have increased risk of aspiration.[108]

In patients with known or suspected strictures of the SB, AGA suggests using of patency capsule before CE to reduce risk of retention.[29]

European Society of Gastrointestinal Endoscopy recommends that using of patency capsule should be offered to patients at increased risk of capsule retention before CE.[42] Additionally, ESGE recommends the use of endoscopic capsule placement in patients with a suspected or established non-obstructive swallowing disorder, in order to prevent capsule aspiration.[28]

In conclusion, patients should be evaluated for the risk of capsule retention and presence of swallowing disorders before CE. Second-look endoscopy should be performed in patients with OGIB and ileocolonoscopy, and imaging studies should be performed in patients with suspected CD before CE. Routine SB imaging study for capsule retention before CE is not necessary.

We do not recommend routine SB imaging studies for capsule retention before CE.

WHAT SHOULD BE THE IDEAL REPORTING IN CAPSULE ENDOSCOPY?

Capsule endoscopy is one of the most important technological advances of the last 2 decades that enabled the visualization of the SB for a variety of conditions in a non-invasive and painless manner. Nevertheless, as in the other fields of medicine, complete, accurate documentation, and reporting the findings are the vital part of the CE study though there is no evidence that specific parts of the CE study may change the patient outcome.[29] Several attempts have been made to standardize reporting of findings in CE reports; however, the paucity of publications about reporting CE studies shows there is a lack of consensus on this issue. We believe this is an important aspect of the CE study, shortly, no surprise, we will be doing all of our diagnostic endoscopies or even some therapeutic procedures with advanced CEs. Therefore, this section aims to provide an up-to-date description of key structures of the standard CE report framework to improve the quality for future research and resultant better patient outcomes.

All of the reports should include mandatory fields: patient identifiers such as name, medical record number, date

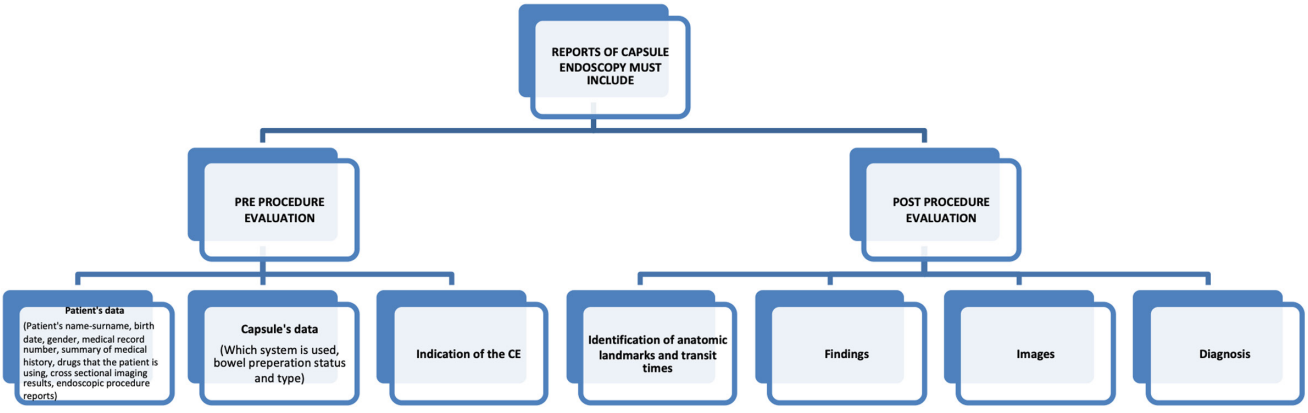

Figure 1. Summary of reports of CE must include.

of birth, date and time of the procedure, name(s) of the reader of capsule study output, patient demographics likewise in the endoscopy reports. Capsule endoscopy reports categorically could be subdivided into 2 domains: pre-procedure and post-procedure elements.[29,109] We summarized in Figure 1, what should be in CE report.

Pre-Procedure Elements

Pre-procedure elements are an indication of the CE study, system used, and bowel preparations, whereas post-procedure elements rely on CE digital output such as transit times, findings, images, and essential part of diagnosis and management recommendations.

Post-Procedure Elements

Identification of Anatomic Landmarks and Transit Times to Various Parts of Gastrointestinal Tract: Capsule endoscopy evaluation starts with the identification of the first gastric image, first duodenal image, and first cecal images, which should be recorded in the CE report. Visualization of the colon is essential for confirming total enteroscopy of the SB. Every report should include a statement on completion or extent of examination. Identification of these landmarks allows the software to calculate total gastric and small bowel transit times (SBTT). Rapid transit is associated with high rates of missing lesions, especially shorter than 2 hours. That is why rapid purge should be highlighted in the report to prompt the attending physician. The principal value of the SBTT is to determine accurate localization of findings and direct further management if needed, and guide therapeutic planning to the lesion. Currently, we localize the findings by dividing the SB into 3 segments as proximal, mid, or distal.[110] If the lesion is located within the first 2/3rd of the SBTT, an anterograde approach is the preferred one.[111] This recommendation should also find a place in the management section of the report.

Findings

Early efforts to create a common lexicon for the CE reports have begun soon after the introduction of CE systems. Capsule Endoscopy Structured Terminology (CEST) was a result of such effort, which was based on structured terminologies created by ASGE, ESGE, Japan Gastroenterological Endoscopy Society (JGES) and Organization Mondial d'Endoscopy Digestive (OMED) as Minimal Standard Terminology for digestive endoscopy, to develop a common language that represents the findings obtained in CE study.[26] Capsule Endoscopy Structured Terminology allows the reader to describe the majority of findings in terms of extent, number, or size with different attributes. The reader should use standard terminology to define the finding with a common nomenclature and minimum description. More detailed descriptions can be added to modify minimum terminology. For a description of a lesion, the reader should characterize the following aspects: villi, mucosa, lumen, and intestinal contents.[112,113] Professional associations recommend the use of CEST in reporting whenever possible.[28,29] Saurin classification system is simple and easy to use in CE reports, where P0 defines normal findings, P1 defines findings of unclear certainty (red spot or erosion), and P2 defines a definite lesion (angiodysplasia, ulceration, or neoplasm).[114] The Lewis score and Capsule Endoscopy Crohn's Disease Activity Index are rating scales used for the diagnosis or follow-up of CD besides, these scores can be used for objective reporting of any inflammatory changes in CE. However, we must remind the readers, studies on CE did not show any effect of using standard terminology on DY or image interpretation. Appropriate and ideal documentation of CE should include pre- and post-procedure elements as well as standardized rating scales to define CE findings.[29,115,116]

Images

Pathological findings of CE may require a sort of further investigation or treatment in some patients. To guide management, every finding should be marked as hours: minutes: seconds on the transit-time index of the study. Findings should be clearly described as outlined above and the report should include lesion (if any) size and estimated location. This information should be included for every identified lesion. Captured thumbnails of findings should be annotated and included in the report. There is no consensus on which part of the normal GI tract images should be included, or the number of images as well. Generally, we include normal mucosal and luminal images from the esophagus, stomach, duodenum, ileum, jejunum, and colon in our reports.[110,111,116]

Diagnosis

Capsule endoscopy report should include a diagnosis and interpretation of findings section. In this section, reader must summarize the significance of observed findings relevant to CE indication in an understandable manner, avoiding long and ambiguous description. Strategies including conservative follow-up or interventional methods based on findings and diagnoses may be recommended in the report to the referring physician to plan future therapeutic/diagnostic management.[29,110]

Future Directions

Reading and interpreting a CE examination is an intertwined time-consuming process and needs a careful evaluation of the visual data. Endoscopists are the natural candidate for such a difficult task because our job deals with visual data interpreting; on the other hand, specially trained nurses and technicians also read the CE with very same success rates. We believe we have to use this natural skill by implementing CE training in the core curriculum of gastroenterology education. The most important advantage of CE is that this procedure was a born-digital procedure and soon, we will see that all of the above-mentioned evaluations, gradings, and even report generation would be handled by Artificial Intelligence. Current CE systems allow both computer-generated and natural language entries. To generate an ideal report, the CE procedure should be documented appropriately in every aspect; patient-related factors, indications, comorbidities, and intraprocedural interventions, and the report should provide informative and clear documentation of CE findings that are interpreted as a consultant opinion instead of merely a technical report. The relevant findings would be described with CEST, or standard rating scales which may need more effort to integrate into the CE report.

WHAT IS THE IDEAL WAY TO COMBINE CAPSULE ENDOSCOPY WITH DOUBLE BALLOON ENTEROSCOPY? BEFORE OR AFTER?

Capsule endoscopy for disease of the small intestine was introduced into the clinical practice in 2001. Capsule endoscopy is a non-invasive, highly sensitive, and specific DY of small intestine disease.[32] Small bowel CE competition rate is almost 80%.[20] Retrospective studies have identified factors such as poor bowel cleaning, diabetes mellitus, previous abdominal surgery, long gastric transit time, or obstruction especially CD.[117-121] Other modalities such as balloon enteroscopy may be planned for patients at increased risk for complete examination.

Obscure GI bleeding, IDA, non-structuring SB CD, celiac disease, hereditary polyposis syndrome, and SB tumors are the main indications of SB CE. Obscure GI bleeding is the most frequent indication for CE examination. Small bowel CE in patients with OGIB is significantly higher for patients with ongoing overt bleeding compared with patients with obscure occult bleeding. The DY is also higher when the CE is performed within 48 hours of the bleeding episode.[120] Furthermore, in another study, it was shown that CE detected a source of bleeding in a greater proportion of patients (72%) than CT angiography (24%), or standard angiography (56%).[20] In a US multicenter trial, the agreement between CE and balloon endoscopy (BE) was about 74% for angioectasias, 96% for ulcerations, 94% for mucosal and submucosal polyps, and 96% for large tumors.[121] Two studies investigated the yield and the outcomes of BE following CE in patients with OGIB. Patients first underwent CE and then BE. The overall detection rates for both techniques were similar. Therefore, these 2 techniques may be considered complementary.[122,123] On the other hand, BE may permit endoscopic treatment of the bleeding lesion.[123]

The most frequent location of CD is in the terminal ileum and the colon. As such, an effective diagnosis can be made with the aid of ileocolonoscopy and biopsies in most cases. On the other hand, in one-third of all CD patients, the disease is confined to the SB.[124] Capsule endoscopy is the best diagnostic modality of SB CD,[125] however, retention of the capsule is the main problem in stenotic CD. The retention of the capsule is defined as the failure to progress along the GI tract (i.e., a capsule remains in the bowel for a minimum of 2 weeks or even permanently), unless extracted surgically or endoscopically.[126] Capsule retention occurs in 1% of patients with suspected CD, but retention ratios of between 2% and 6% have been reported in patients with confirmed CD.[127] Biodegradable capsules may be used to prevent retention of CE but using 2 capsules is still high price. Balloon endoscopy should not be the first-line procedure in the evaluation of suspected small-bowel CD. Capsule endoscopy can be complementary to BE, since findings may help direct the most effective route of intubation (oral vs. anal), in order to obtain a histopathological diagnosis or therapeutic intervention.[128] Unfortunately, CE still remains a purely visual technique with no ability to obtain biopsy specimens or perform therapeutic maneuvers. Computed tomography of SB may be useful for suspected stenotic CD, and BE that needing of therapeutic processing or biopsy, must be planned first.[129,130]

Population-based studies have demonstrated that in 4%-10% of adult patients with all IBD affecting the colon, it is impossible to distinguish between CD and ulcerative colitis using current diagnostic techniques. In IBD-type unclassified patients, CE is better than BE or enteroclysis at identifying mucosal lesions consistent with CD and is the first choice.[129,131]

The current gold standard diagnostic test for celiac disease is esophagogastro duodenoscopy with duodenal biopsies and SB histology demonstrating the presence of

villous atrophy (Marsh stage 3a to 3c). Capsule endoscopy may play a role in the investigation of cases with equivocal diagnosis of celiac disease. In the study of 30 patients by Kurien et al[132] with Marsh stage 1 or 2 changes, only 6 of whom had positive EMA or tissue transglutaminase (tTG) results, 1 patient was diagnosed with celiac disease and another with small-bowel CD on the basis of CE appearances. The other problematic area is complicated celiac disease. Ferretti et al[133] observed 130 CCD, and they underwent 137 CE and 21 BE. Disease duration <5 years were at higher risk of positive CE (RR 1.6, 1.7, and 1.5 respectively, $P < .05$) than their counter parts. They suggest, in suspected CCD, CE should be the first-line approach to detect complications and to identify patients deserving BE.

Small bowel malignancy is challenging to diagnose because the SB is difficult to evaluate. Most small-bowel tumors are detected during work-up for OGIB or IDA. According to a guideline for enteroscopy published in Japan in 2017, CE is recommended as a first-line diagnostic modality for GI malignancy but is contraindicated for obstructive disease. Regarding the study of Yoo et al, a total of 510 VCE and 126 DBE exams were performed on 438 patients, and diagnostic rate is higher CT and CE than BE.[134] A meta-analysis showed that CE has a significantly higher DY compared with push enteroscopy in patients with OGIB.[31] Abdominal CT and CE were used as screening examinations for SB malignancy, while BE was used for tissue biopsy and therapeutic interventions. For example, after achieving a diagnosis through abdominal CT and CE, DBE would be performed if a biopsy or therapeutic intervention is needed.

The capsules presently on the market are unable to localize or mark the location of detected lesions. Visualization may be impaired by the presence of food materials or bubbles and, in contrast with conventional endoscopy, CE cannot perform flushing, suctioning, or air insufflation to obtain better images. The rate of missed lesions is still high for those located in the duodenum and proximal jejunum, where the transit is more rapid than in the distal segment of the SB. Taking biopsy and therapeutic processing are impossible by using CE. Reading time for interpretation is another shortcoming of CE, as it takes more than 1 hour to read a full 8-hour examination.[135,136] Finally, the costs are still high. Although there are disadvantages, CE is still the first choice in small bowel diseases because it is noninvasive and safe. The rate of total enteroscopy is much higher than other invasive methods. It is well tolerated by patients with a high diagnosis rate. On the other hand, disadvantages associated with BE are the invasiveness of the examination, the need for

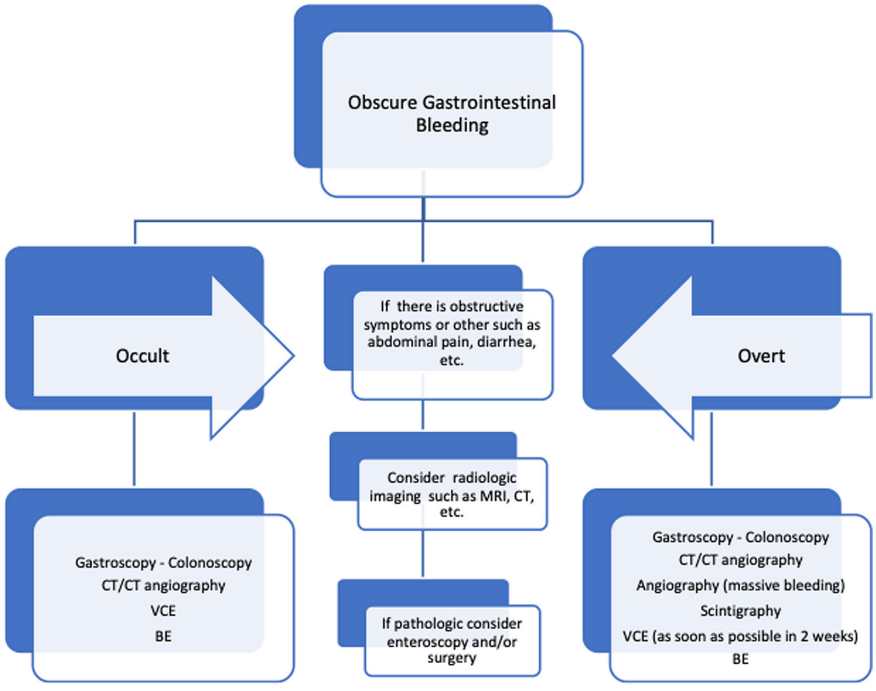

Figure 2. Management of OGIB.

sedation, limited availability of the procedure (specialized centers), difficulty in examining the entire SB, and the time and expense required for the procedure.[137,138] Nowadays, CE, BE, and abdominal CT are used to diagnose SB diseases. Each tool has its advantages and disadvantages. There is no single best way to diagnose SB disease because the currently available tools complement each other. Therefore, the choice of tool for evaluation should be made according to individual patient complaints and conditions (Figure 2).

CONCLUSION

- We need bowel preparation before CE, PEG solution after a day of clear liquid diet followed with 10-12 hours of overnight fasting, and administration of simethicone (80-200 mg) seem to be an appropriate strategy.
- Main indications of CE are OGIB (overt/occult) and IDA.
- Small bowel obstruction is the only accepted contraindication for CE today.
- We recommend evaluation of the risk of capsule retention and the presence of swallowing disorders before CE.
- In patients with OGIB, we recommend second-look endoscopy before CE.
- In patients with suspected CD, we recommend ileocolonoscopy and imaging study before CE.
- We do not recommend routine SB imaging studies for capsule retention before CE.
- To generate an ideal report, the CE procedure should be documented appropriately in every aspect: patient-related factors, indications, comorbidities, and intraprocedural interventions, and the report should provide informative and clear documentation of CE findings that are interpreted as a consultant opinion instead of merely a technical report.
- There is no single best way to diagnose SB disease because the currently available tools complement each other. Therefore, the choice of tool for evaluation should be made according to individual patient complaints and conditions.

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REFERENCES

1. *Vasilakakis MD, Koulaouzidis A, Marlicz W, Iakovidis DK. The future of capsule endoscopy in clinical practice: from diagnostic to therapeutic experimental prototype capsules. Prz Gastroenterol. 2020; 15(3):179-193.* [CrossRef]
2. *Iddan GJ, Swain CP. History and development of capsule endoscopy. Gastrointest Endosc Clin N Am. 2004;14(1):1-9.* [CrossRef]
3. *Van de Bruaene C, De Looze D, Hindryckx P. Small bowel capsule endoscopy: where are we after almost 15 years of use? World J Gastrointest Endosc. 2015;7(1):13-36.* [CrossRef]
4. *Melson J, Trikudanathan G, Abu Dayyeh BK, et al. Video capsule endoscopy. Gastrointest Endosc. 2021;93(4):784-796.* [CrossRef]
5. *Catalano C, Companioni RA, Khankhanian P, et al. Video capsule endoscopy: is bowel preparation necessary? J Investig Med. 2016; 64(6):1114-1117.* [CrossRef]
6. *Yung DE, Plevris JN, Leenhardt R, Dray X, Koulaouzidis A, Small E, et al. Poor quality of small bowel capsule endoscopy images has a significant negative effect in the diagnosis of small bowel malignancy. Clin Exp Gastroenterol. 2020;13:475-484.* [CrossRef]
7. *Yung DE, Rondonotti E, Sykes C, Pennazio M, Plevris JN, Koulaouzidis A. Systematic review and meta-analysis: is bowel preparation still necessary in small bowel capsule endoscopy? Expert Rev Gastroenterol Hepatol. 2017;11(10):979-993.* [CrossRef]
8. *Koulaouzidis A, Giannakou A, Yung DE, Dabos KJ, Plevris JN. Do prokinetics influence the completion rate in small-bowel capsule endoscopy? A systematic review and meta-analysis. Curr Med Res Opin. 2013;29(9):1171-1185.* [CrossRef]
9. *Dabos KJ, Giannakou A, Koulaouzidis A. Chewing gum and completion rate in small-bowel capsule endoscopy: meta-analyzing the data. Gastrointest Endosc. 2014;79(6):1032-1034.* [CrossRef]
10. *Giannakou A, Dabos KJ, Koulaouzidis A. Lubiprostone in small-bowel capsule endoscopy: meta-analyzing the data. Gastrointest Endosc. 2015;81(4):1047-1048.* [CrossRef]
11. *Ersoy O, Sivri B, Arslan S, Batman F, Bayraktar Y. How much helpful is the capsule endoscopy for the diagnosis of small bowel lesions? World J Gastroenterol. 2006;12(24):3906-3910.* [CrossRef]
12. *Gkolfakis P, Tziatzios G, Dimitriadis GD, Triantafyllou K. Meta-analysis of randomized controlled trials challenging the usefulness of purgative preparation before small-bowel video capsule endoscopy. Endoscopy. 2018;50(7):671-683.* [CrossRef]
13. *Niv Y. Efficiency of bowel preparation for capsule endoscopy examination: a meta-analysis. World J Gastroenterol. 2008;14(9): 1313-1317.* [CrossRef]
14. *Rokkas T, Papaxoinis K, Triantafyllou K, Pistiolas D, Ladas SD. Does purgative preparation influence the diagnostic yield of small bowel video capsule endoscopy?: A meta-analysis. Am J Gastroenterol. 2009;104(1):219-227.* [CrossRef]
15. *Belsey J, Crosta C, Epstein O, et al. Meta-analysis: efficacy of small bowel preparation for small bowel video capsule endoscopy. Curr Med Res Opin. 2012;28(12):1883-1890.* [CrossRef]
16. *Kotwal VS, Attar BM, Gupta S, Agarwal R. Should bowel preparation, antifoaming agents, or prokinetics be used before video capsule endoscopy? A systematic review and meta-analysis. Eur J Gastroenterol Hepatol. 2014;26(2):137-145.* [CrossRef]
17. *Yung DE, Rondonotti E, Sykes C, Pennazio M, Plevris JN, Koulaouzidis A. Systematic review and meta-analysis: is bowel preparation still necessary in small bowel capsule endoscopy? Expert Rev Gastroenterol Hepatol. 2017;11(10):979-993.* [CrossRef]
18. *Belsey J, Crosta C, Epstein O, et al. Meta-analysis: efficacy of small bowel preparation for small bowel video capsule endoscopy. Curr Med Res Opin. 2012;28(12):1883-1890.* [CrossRef]

19. Niv Y. Efficiency of bowel preparation for capsule endoscopy examination: a meta-analysis. World J Gastroenterol. 2008;14(9): 1313-1317. [CrossRef]
20. Rokkas T, Papaxoinis K, Triantafyllou K, Pistiolas D, Ladas SD. Does purgative preparation influence the diagnostic yield of small bowel video capsule endoscopy? A meta-analysis. Am J Gastroenterol. 2009;104(1):219-227. [CrossRef]
21. Kotwal VS, Attar BM, Gupta S, Agarwal R. Should bowel preparation, antifoaming agents, or prokinetics be used before video capsule endoscopy? A systematic review and meta-analysis. Eur J Gastroenterol Hepatol. 2014;26(2):137-145. [CrossRef]
22. Wu S, Gao YJ, Ge ZZ. Optimal use of polyethylene glycol for preparation of small bowel video capsule endoscopy: a network meta-analysis. Curr Med Res Opin. 2017;33(6):1149-1154. [CrossRef]
23. Kantianis A, Karagiannis S, Liatsos C, et al. Comparison of two schemes of small bowel preparation for capsule endoscopy with polyethylene glycol: a prospective, randomized single-blind study. Eur J Gastroenterol Hepatol. 2009;21(10):1140-1144. [CrossRef]
24. Hosono K, Endo H, Sakai E, et al. Optimal approach for small bowel capsule endoscopy using polyethylene glycol and metoclopramide with the assistance of a real-time viewer. Digestion. 2011; 84(2):119-125. [CrossRef]
25. Hookey L, Louw J, Wiepjes M, et al. Lack of benefit of active preparation compared with a clear fluid-only diet in small-bowel visualization for video capsule endoscopy: results of a randomized, blinded, controlled trial. Gastrointest Endosc. 2017;85(1):187-193. [CrossRef]
26. Pons Beltrán V, González Suárez B, González Asanza C, et al. Evaluation of different bowel preparations for small bowel capsule endoscopy: a prospective, randomized, controlled study. Dig Dis Sci. 2011;56(10):2900-2905. [CrossRef]
27. Gkolfakis P, Tziatzios G, Dimitriadis GD, Triantafyllou K. Meta-analysis of randomized controlled trials challenging the usefulness of purgative preparation before small-bowel video capsule endoscopy. Endoscopy. 2018;50(7):671-683. [CrossRef]
28. Rondonotti E, Spada C, Adler S, et al. Small-bowel capsule endoscopy and device-assisted enteroscopy for diagnosis and treatment of small-bowel disorders: European Society of Gastrointestinal Endoscopy (ESGE) Technical Review. Endoscopy. 2018;50(4):423-446. [CrossRef]
29. Enns RA, Hookey L, Armstrong D, et al. Clinical practice guidelines for the use of video capsule endoscopy. Gastroenterology. 2017;152(3):497-514. [CrossRef]
30. Wi JH, Moon JS, Choi MG, et al. Bowel preparation for capsule endoscopy: a prospective randomized multicenter study. Gut Liver. 2009;3(3):180-185. [CrossRef]
31. Niv Y, Niv G, Wiser K, Demarco DC. Capsule endoscopy - comparison of two strategies of bowel preparation. Aliment Pharmacol Ther. 2005;22(10):957-962. [CrossRef]
32. Ladas SD, Triantafyllou K, Spada C, 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. Endoscopy. 2010;42(3):220-227. [CrossRef]
33. Wu L, Cao Y, Liao C, Huang J, Gao F. Systematic review and meta-analysis of randomized controlled trials of simethicone for gastrointestinal endoscopic visibility. Scand J Gastroenterol. 2011; 46(2):227-235. [CrossRef]
34. Albert J, Göbel 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. [CrossRef]
35. Wei W, Ge ZZ, Lu H, Gao YJ, Hu YB, Xiao SD. Purgative bowel cleansing combined with simethicone improves capsule endoscopy imaging. Am J Gastroenterol. 2008;103(1):77-82. [CrossRef]
36. Selby W. Complete small-bowel transit in patients undergoing capsule endoscopy: determining factors and improvement with metoclopramide. Gastrointest Endosc. 2005;61(1):80-85. [CrossRef]
37. Almeida N, Figueiredo P, Freire P, et al. The effect of metoclopramide in capsule enteroscopy. Dig Dis Sci. 2010;55(1):153-157. [CrossRef]
38. Koulaouzidis A, Giannakou A, Yung DE, Dabos KJ, Plevris JN. Do prokinetics influence the completion rate in small-bowel capsule endoscopy? A systematic review and meta-analysis. Curr Med Res Opin. 2013;29(9):1171-1185. [CrossRef]
39. ASGE Technology Committee, Wang A, Banerjee S, et al. Wireless capsule endoscopy. Gastrointest Endosc. 2013;78(6):805-815. [CrossRef]
40. Sidhu R, McAlindon ME, Drew K, Hardcastle S, Cameron IC, Sanders DS. Evaluating the role of small-bowel endoscopy in clinical practice: the largest single-centre experience. Eur J Gastroenterol Hepatol. 2012;24(5):513-519. [CrossRef]
41. ASGE Standards of Practice Committee, Gurudu SR, Bruining DH, et al.The role of endoscopy in the management of suspected small-bowel bleeding. Gastrointest Endosc. 2017;85(1):22-31. [CrossRef]
42. Leighton JA. The role of endoscopic imaging of the small bowel in clinical practice. Am J Gastroenterol. 2011;106(1):27-36; quiz 37. [CrossRef]
43. Akyuz F, Ormeci A, Gokturk S, et al. What is the importance of capsule endoscopy in obscure gastrointestinal bleeding and its value in predicting bleeding in the long term? Gut. 2012;61(suppl 3):A 406.
44. Pennazio M, Spada C, Eliakim R, 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. [CrossRef]
45. Gomes C, Pinho R, Rodrigues A, et al. Impact of the timing of capsule endoscopy in overt obscure gastrointestinal bleeding on yield and rebleeding rate - is sooner than 14 d advisable? World J Gastrointest Endosc. 2018;10(4):74-82. [CrossRef]
46. Soffer S, Klang E, Shimon O, et al. Deep learning for wireless capsule endoscopy: a systematic review and meta-analysis. Gastrointest Endosc. 2020;92(4):831-839.e8. [CrossRef]
47. Albert J , Schulbe R, Hahn W. Therapeutic consequences of capsule endoscopy in obscure intestinal bleeding; a multicenter outcome study. in Proceedings of the 4th International Conference on Capsule Endoscopy. Miami, Florida, USA; 2005.
48. Katsinelos P, Chatzimavroudis G, Terzoudis S, et al. Diagnostic yield and clinical impact of capsule endoscopy in obscure gastrointestinal bleeding during routine clinical practice: a single-center experience. Med Princ Pract. 2011;20(1):60-65. [CrossRef]
49. Stone J, Grover K, Bernstein CN. The use of capsule endoscopy for diagnosis of iron deficiency anemia: a retrospective analysis. J Clin Gastroenterol. 2020;54(5):452-458. [CrossRef]
50. Akyuz F, Pınarbasi B, Akyuz U, et al. Kapsül endoskopi ile saptanan ince bağırsak dışı lezyonlar. Turk J Gastroenterol. 2011;22:261A.
51. Akyuz F, Mungan Z. Diagnostic capability of capsule endoscopy in small bowel Diseases. Gastroenterology Res. 2009;2(2):81-85. [CrossRef]
52. Lecleire S, Iwanicki-Caron I, Di-Fiore A, et al. Yield and impact of emergency capsule enteroscopy in severe obscure-overt gastrointestinal bleeding. Endoscopy. 2012;44(4):337-342. [CrossRef]

53. Gerson L, Kamal A. Cost-effectiveness analysis of management strategies for obscure GI bleeding. Gastrointest Endosc. 2008;68(5):920-936. [CrossRef]
54. Jawaid S, Marya NB, Hicks M, Marshall C, Bhattacharya K, Cave D. Prospective cost analysis of early video capsule endoscopy versus standard of care in non-hematemesis gastrointestinal bleeding: a non-inferiority study. J Med Econ. 2020;23(1):10-16. [CrossRef]
55. Lai LH, Wong GL, Chow DK, Lau JY, Sung JJ, Leung WK. Long-term follow-up of patients with obscure gastrointestinal bleeding after negative capsule endoscopy. Am J Gastroenterol. 2006;101(6):1224-1228. [CrossRef]
56. Delvaux M, Fassler I, Gay G. Clinical usefulness of the endoscopic video capsule as the initial intestinal investigation in patients with obscure digestive bleeding: validation of a diagnostic strategy based on the patient outcome after 12 months. Endoscopy. 2004;36(12):1067-1073. [CrossRef]
57. Arakawa D, Ohmiya N, Nakamura M, et al. Outcome after enteroscopy for patients with obscure GI bleeding: diagnostic comparison between double-balloon endoscopy and videocapsule endoscopy. Gastrointest Endosc. 2009;69(4):866-874. [CrossRef]
58. Iwamoto J, Mizokami Y, Shimokobe K, et al. The clinical outcome of capsule endoscopy in patients with obscure gastrointestinal bleeding. Hepatogastroenterology. 2011;58(106):301-305.
59. Ormeci A, Akyuz F, Baran B, et al. What is the impact of capsule endoscopy in the long term period? World J Gastrointest Endosc. 2016;8(7):344-348. [CrossRef]
60. Mehdizadeh S, Chen GC, Barkodar L, et al. Capsule endoscopy in patients with Crohn's disease: diagnostic yield and safety. Gastrointest Endosc. 2010;71(1):121-127. [CrossRef]
61. Pons Beltrán V, Nos P, Bastida G, et al. Evaluation of postsurgical recurrence in Crohn's disease: a new indication for capsule endoscopy? Gastrointest Endosc. 2007;66(3):533-540. [CrossRef]
62. Apostolopoulos P, Liatsos C, Gralnek IM, et al. Evaluation of capsule endoscopy in active, mild-to-moderate, overt, obscure GI bleeding. Gastrointest Endosc. 2007;66(6):1174-1181. [CrossRef]
63. Fry LC, Carey EJ, Shiff AD, et al. The yield of capsule endoscopy in patients with abdominal pain or diarrhea. Endoscopy. 2006;38(5):498-502. [CrossRef]
64. Mata A, Llach J, Castells A, et al. A prospective trial comparing wireless capsule endoscopy and barium contrast series for small-bowel surveillance in hereditary GI polyposis syndromes. Gastrointest Endosc. 2005;61(6):721-725. [CrossRef]
65. Petroniene R, Dubcenco E, Baker JP, et al. Given capsule endoscopy in celiac disease: evaluation of diagnostic accuracy and interobserver agreement. Am J Gastroenterol. 2005;100(3):685-694. [CrossRef]
66. Rondonotti E, Spada C, Cave D, et al. Video capsule enteroscopy in the diagnosis of celiac disease: a multicenter study. Am J Gastroenterol. 2007;102(8):1624-1631. [CrossRef]
67. Rokkas T, Niv Y. The role of video capsule endoscopy in the diagnosis of celiac disease: a meta-analysis. Eur J Gastroenterol Hepatol. 2012;24(3):303-308. [CrossRef]
68. Perez-Cuadrado-Robles E, Lujan-Sanchis M, Elli L, et al. Role of capsule endoscopy in alarm features and non-responsive celiac disease: a European multicenter study. Dig Endosc. 2018;30(4):461-466. [CrossRef]
69. Wang YC, Pan J, Liu YW, et al. Adverse events of video capsule endoscopy over the past two decades: a systematic review and proportion meta-analysis. BMC Gastroenterol. 2020;20(1):364. [CrossRef]
70. Singeap AM, Trifan A, Cojocariu C, Sfarti C, Stanciu C. Outcomes after symptomatic capsule retention in suspected small bowel obstruction. Eur J Gastroenterol Hepatol. 2011;23(10):886-890. [CrossRef]
71. Cheifetz AS, Kornbluth AA, Legnani P, et al. The risk of retention of the capsule endoscope in patients with known or suspected Crohn's disease. Am J Gastroenterol. 2006;101(10):2218-2222. [CrossRef]
72. Ormeci AC, Akyuz F, Baran B, et al. Retention during capsule endoscopy: is it a real problem in routine practice? J Int Med Res. 2016;44(4):968-975. [CrossRef]
73. Mungan Z, Pinarbaşi B, Akyüz F, Bektaş H, Akyüz A. Wireless endoscopy capsule remaining safely for a long time. Dig Dis Sci. 2008;53(5):1422-1423. [CrossRef]
74. Gao Y, Xin L, Wang YX, et al. Double-balloon enteroscopy for retrieving retained small-bowel video capsule endoscopes: a systematic review. Scand J Gastroenterol. 2020;55(1):105-113. [CrossRef]
75. Soncini M, Girelli CM, de Franchis R, Rondonotti E, SBCE Lombardia Study Group, On behalf AIGO, SIED and SIGE Lombardia. Small-Bowel Capsule Endoscopy in Clinical Practice: has Anything Changed over 13 years? Dig Dis Sci. 2018;63(9):2244-2250. [CrossRef]
76. Lucendo AJ, González-Castillo S, Fernández-Fuente M, De Rezende LC. Tracheal aspiration of a capsule endoscope: a new case report and literature complication of an increasingly reported complication. Dig Dis Sci. 2011;56(9):2758-2762. [CrossRef]
77. Tabib S, Fuller C, Daniels J, Lo SK. Asymptomatic aspiration of a capsule endoscope. Gastrointest Endosc. 2004;60(5):845-848. [CrossRef]
78. Kasia C, Appannagari A, Joshi A, Venu M. Safety of wireless capsule endoscopy in patients with implantable cardiac devices JGH Open. 2019;4(2):241-244.
79. Tabet R, Nassani N, Karam B, Shammaa Y, Akhrass P, Deeb L. Pooled analysis of the efficacy and safety of video capsule endoscopy in patients with implantable cardiac devices. Can J Gastroenterol Hepatol. 2019;2019:3953807. [CrossRef]
80. Hogan RB, Ahmad N, Hogan RB, et al. Video capsule endoscopy detection of jejunal carcinoid in life-threatening hemorrhage, first trimester pregnancy. Gastrointest Endosc. 2007;66(1):205-207. [CrossRef]
81. Wax JR, Pinette MG, Cartin A, Winn SS, Blackstone J. Cavernous transformation of the portal vein complicating pregnancy. Obstet Gynecol. 2006;108(3 Pt 2 Pt2):782-784. [CrossRef]
82. Ohmiya N, Nakagawa Y, Nagasaka M, et al. Obscure gastrointestinal bleeding: diagnosis and treatment. Dig Endosc. 2015;27(3):285-294. [CrossRef]
83. Raju GS, Gerson L, Das A, Lewis B, American Gastroenterological Association. American Gastroenterological Association (AGA) institute technical review on obscure gastrointestinal bleeding. Gastroenterology. 2007;133(5):1697-1717. [CrossRef]
84. Naut ER. The approach to occult gastrointestinal bleed. Med Clin North Am. 2016;100(5):1047-1056. [CrossRef]
85. Zuckerman GR, Prakash C, Askin MP, Lewis BS. AGA technical review on the evaluation and management of occult and obscure gastrointestinal bleeding. Gastroenterology. 2000;118(1):201-221. [CrossRef]
86. Zaman A, Katon RM. Push enteroscopy for obscure gastrointestinal bleeding yields a high incidence of proximal lesions within reach of a standard endoscope. Gastrointest Endosc. 1998;47(5):372-376. [CrossRef]

87. Descamps C, Schmit A, Van Gossum A. Missed. Endoscopy. Endosc 1999. 1999;31(6):452-455. [CrossRef]
88. Koffas A, Laskaratos FM, Epstein O. Non-small bowel lesion detection at small bowel capsule endoscopy: a comprehensive literature review. World J Clin Cases. 2018;6(15):901-907. [CrossRef]
89. Elijah D, Daas A, Brady P. Capsule endoscopy for obscure GI bleeding yields a high incidence of significant treatable lesions within reach of standard upper endoscopy. J Clin Gastroenterol. 2008;42(8):962-963. [CrossRef]
90. Tacheci I, Devière J, Kopacova M, Douda T, Bures J, Van Gossum A. The importance of upper gastrointestinal lesions detected with capsule endoscopy in patients with obscure digestive bleeding. Acta Gastroenterol Belg. 2011;74(3):395-399.
91. Juanmartiñena Fernández JF, Fernández-Urien Sainz I, Zabalza Ollo B, et al. Gastroduodenal lesions detected during small bowel capsule endoscopy: incidence, diagnostic and therapeutic impact. Rev Esp Enferm Dig. 2018;110(2):102-108. [CrossRef]
92. Juanmartiñena-Fernández JF, Fernández-Urién-Sainz I, Zabalza-Ollo B, Borda-Martín A, Vila-Costas JJ. Colonic lesions in patients undergoing small bowel capsule endoscopy: incidence, diagnostic and therapeutic impact. Rev Esp Enferm Dig. 2017; 109(7):498-502.
93. Kitiyakara T, Selby W. Non-small-bowel lesions detected by capsule endoscopy in patients with obscure GI bleeding. Gastrointest Endosc. 2005;62(2):234-238. [CrossRef]
94. Vlachogiannakos J, Papaxoinis K, Viazis N, et al. Bleeding lesions within reach of conventional endoscopy in capsule endoscopy examinations for obscure gastrointestinal bleeding: is repeating endoscopy economically feasible? Dig Dis Sci. 2011;56(6):1763-1768. [CrossRef]
95. Hoedemaker RA, Westerhof J, Weersma RK, Koornstra JJ. Non-small-bowel abnormalities identified during small bowel capsule endoscopy. World J Gastroenterol. 2014;20(14):4025-4029. [CrossRef]
96. Riccioni ME, Urgesi R, Cianci R, Marmo C, Galasso D, Costamagna G. Obscure recurrent gastrointestinal bleeding: a revealed mystery? Scand J Gastroenterol. 2014;49(8):1020-1026. [CrossRef]
97. Akin FE, Yurekli OT, Bolat AD, et al. Analysis of non-small bowel lesions detected by capsule endoscopy in patients with potential small bowel bleeding. Diagn Endosc. 2016;2016:9063293.
98. Innocenti T, Dragoni G, Roselli J, et al. Non-small-bowel lesions identification by capsule endoscopy: a single centre retrospective study. Clin Res Hepatol Gastroenterol. 2021;45(1):101409. [CrossRef]
99. Gerson LB, Fidler JL, Cave DR, Leighton JA. ACG clinical guideline: diagnosis and management of small bowel bleeding. Am J Gastroenterol. 2015;110(9):1265-87; quiz 1288. [CrossRef]
100. Van Assche G, Dignass A, Panes J, et al. The second European evidence- based consensus on the diagnosis and management of Crohn's disease: definitions and diagnosis. J Crohns Colitis. 2010; 4(1):7-27. [CrossRef]
101. Dionisio PM, Gurudu SR, Leighton JA, et al. Capsule endoscopy has a significantly higher diagnostic yield in patients with suspected and established small-bowel Crohn's disease: a meta-analysis. Am J Gastroenterol. 2010;105(6):1240-1248. [CrossRef]
102. Choi M, Lim S, Choi MG, Shim KN, Lee SH. Effectiveness of capsule endoscopy compared with other diagnostic modalities in patients with small bowel Crohn's disease: a meta-analysis. Gut Liver. 2017;11(1):62-72. [CrossRef]
103. Srinivasan A, De Cruz P. Review article: a practical approach to the clinical management of NSAID enteropathy. Scand J Gastroenterol. 2017;52(9):941-947. [CrossRef]
104. Maiden L, Thjodleifsson B, Theodors A, Gonzalez J, Bjarnason I. A quantitative analysis of NSAID-induced small bowel pathology by capsule enteroscopy. Gastroenterology. 2005;128(5):1172-1178. [CrossRef]
105. Goldstein JL, Eisen GM, Lewis B, et al. Video capsule endoscopy to prospectively assess small bowel injury with celecoxib, naproxen plus omeprazole, and placebo. Clin Gastroenterol Hepatol. 2005; 3(2):133-141. [CrossRef]
106. Maaser C, Sturm A, Vavricka SR, et al. ECCO-ESGAR Guideline for Diagnostic Assessment in IBD Part 1: Initial diagnosis, monitoring of known IBD, detection of complications. J Crohns Colitis. 2019; 13(2):144-164. [CrossRef]
107. Bandorski D, Kurniawan N, Baltes P, et al. Contraindications for video capsule endoscopy. World J Gastroenterol. 2016;22(45):9898-9908. [CrossRef]
108. Holden JP, Dureja P, Pfau PR, et al. Endoscopic placement of the small-bowel video capsule by using a capsule endoscope delivery device. Gastrointest Endosc. 2007;65(6):842-847. [CrossRef]
109. Armstrong D, Barkun A, Bridges R, et al. Canadian association of gastroenterology consensus guidelines on safety and quality indicators in endoscopy. Can J Gastroenterol. 2012;26(1):17-31. [CrossRef]
110. Mitselos IV, Christodoulou DK. What defines quality in small bowel capsule endoscopy. Ann Transl Med. 2018;6(13):260. [CrossRef]
111. Barkin JA, Barkin JS. Video capsule endoscopy: technology, reading, and trouble shooting. Gastrointest Endosc Clin N Am. 2017;27(1): 15-27. [CrossRef]
112. Delvaux M, Friedman S, Keuchel M, et al. Structured terminology for capsule endoscopy: results of retrospective testing and validation in 766 small-bowel investigations. Endoscopy. 2005;37(10):945-950. [CrossRef]
113. Korman LY, Delvaux M, Gay G, et al. Capsule Endoscopy Structured Terminology (CEST): proposal of a standardized and structured terminology for reporting capsule endoscopy procedures. Endoscopy. 2005;37(10):951-959. [CrossRef]
114. Saurin JC, Delvaux M, Gaudin JL, et al. Diagnostic value of endoscopic capsule in patients with obscure digestive bleeding: blinded comparison with video push-enteroscopy. Endoscopy. 2003;35(7): 576-584. [CrossRef]
115. Fernandez-Urien I, Panter S, Carretero C, et al. International core curriculum for capsule endoscopy training courses. Endosc Int Open. 2017;5(6):E526-E538. [CrossRef]
116. Spada C, McNamara D, Despott EJ, et al. Performance measures for small-bowel endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative. Endoscopy. 2019; 51(6):574-598. [CrossRef]
117. Ben-Soussan E, Savoye G, Antonietti M, Ramirez S, Lerebours E, Ducrotté P. Factors that affect gastric passage of video capsule. Gastrointest Endosc. 2005;62(5):785-790. [CrossRef]
118. Westerhof J, Weersma RK, Koornstra JJ. Risk factors for incomplete small-bowel capsule endoscopy. Gastrointest Endosc. 2009; 69(1):74-80. [CrossRef]
119. Triantafyllou K, Kalantzis C, Papadopoulos AA, et al. Video-capsule endoscopy gastric and small bowel transit time and completeness of the examination in patients with diabetes mellitus. Dig Liv Dis. 2007;39(6):575-580.

120. Paxoinis K, Triantafyllou K, et al. Does purgative preparation increase the diagnostic yield of small bowel video capsule endoscopy? A meta-analysis. Am J Gastroenterol. 2009;104(1):219-227.
121. Kamalaporn P, Cho S, Basset N, et al. Double-balloon enteroscopy following capsule endoscopy in the management of obscure gastrointestinal bleeding: outcome of a combined approach. Can J Gastroenterol. 2008;22(5):491-495. [CrossRef]
122. Kameda N, Higuchi K, Shiba M, et al. A prospective, single-blind trial comparing wireless capsule endoscopy and double-balloon enteroscopy in patients with obscure gastrointestinal bleeding. J Gastroenterol. 2008;43(6):434-440. [CrossRef]
123. Marmo R, Rotondano G, Rondonotti E, et al. Capsule enteroscopy vs other diagnostic procedures in diagnosing obscure gastrointestinal bleeding: a cost-effectiveness study. Eur J Gastroenterol Hepatol. 2007;19(7):535-542. [CrossRef]
124. Petruzziello C, Onali S, Calabrese E, et al. Wireless capsule endoscopy and proximal small bowel lesions in Crohn's disease. World J Gastroenterol. 2010;16(26):3299-3304. [CrossRef]
125. Redondo-Cerezo E. Role of wireless capsule endoscopy in inflammatory bowel disease. World J Gastrointest Endosc. 2010;2(5):179-185. [CrossRef]
126. Cave D, Legnani P, de Franchis R, Lewis BS, ICCE. ICCE consensus for capsule retention. Endoscopy. 2005;37(10):1065-1067. [CrossRef]
127. Legnani P, Kornbluth A. Video capsule endoscopy in inflammatory bowel disease 2005. Curr Opin Gastroenterol. 2005;21(4):438-442.
128. Pennazio M, Sprujevnik T, Arrigoni A, et al. Outcome of double-balloon enteroscopy after capsule endoscopy in patients with suspected small-bowel disease [abstract]. Gastrointest Endosc. 2006;63(5):90. [CrossRef]
129. Bourreille A, Ignjatovic A, Aabakken L, et al. Role of small-bowel endoscopy in IBD: international OMED–ECCO consensus report. Endoscopy. 2009;41(7):618-637. [CrossRef]
130. Sunada K, Yamamoto H, Kita H, et al. Endoscopic balloon dilation therapy for small intestinal strictures with Crohn's disease using double balloon endoscopy. Gastrointest Endosc. 2007;65(5):AB91. [CrossRef]
131. Maunoury V, Savoye G, Bourreille A, et al. Value of wireless capsule endoscopy in patients with in determinate colitis (inflammatory bowel disease type unclassified). Inflamm Bowel Dis. 2007;13(2):152-155. [CrossRef]
132. Kurien M, Evans KE, Aziz I, et al. Capsule endoscopy in adult celiac disease: a potential role in equivocal cases of celiac disease? Gastrointest Endosc. 2013;77(2):227-232. [CrossRef]
133. Ferretti F, Branchi F, Orlando S, et al. Effectiveness of capsule endoscopy and double-balloon enteroscopy in suspected complicated celiac disease. Clin Gastroenterol Hepatol. 2020;12:S1542-3565.
134. Yoo AY, Lee BJ, Kim WS, et al. Clinico pathological features of small bowel tumors diagnosed by video capsule endoscopy and balloon-assisted Enteroscopy: a single center experience. Clin Endosc. 2021;54(1):85-91. [CrossRef]
135. Triester SL, Leighton JA, Leontiadis GI, et al. A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with obscure gastrointestinal bleeding. Am J Gastroenterol. 2005;100(11):2407-2418. [CrossRef]
136. Singeap AM, Stanciu C, Trifan A. Capsule endoscopy: the road ahead. World J Gastroenterol. 2016;22(1):369-378. [CrossRef]
137. Tsujikawa T, Saitoh Y, Andoh A, et al. Novel single-balloon enteroscopy for diagnosis and treatment of the small intestine: preliminary experiences. Endoscopy. 2008;40(1):11-15. [CrossRef]
138. Cazzato IA, Cammarota G, Nista EC, et al. Diagnostic and therapeutic impact of double-balloon enteroscopy (DBE) in a series of 100 patients with suspected small bowel diseases. Dig Liver Dis. 2007;39(5):483-487. [CrossRef]