Video Capsule Endoscopy in Inflammatory Bowel Disease

23

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Introduction

Traditionally, ileocolonoscopy and biopsies along with radiological studies have served as the imaging "gold standards" for the evaluation of patients with suspected or known inflammatory bowel disease (IBD), both in adult and pediatric cases. Ideally, complete small bowel (SB) imaging should be included at the initial evaluation to establish the diagnosis and to assess the location, extent, and severity of disease. In pediatric-onset cases, we reported that esophagogastroduodenoscopy (EGD) with biopsies were of clinical value in order to ascertain the presence of findings suggestive of Crohn disease (CD) in the upper gastrointestinal tract [1]. This has long been incorporated in the diagnostic "Porto" guidelines of the European Society for Pediatric Gastroenterology Hepatology and Nutrition [2]. Realistically, it is uncommon to inspect the small bowel mucosa beyond 25 cm in either direction with bidirectional endoscopy. This translates to meters of small bowel mucosa not visualized endoscopically.

Other imaging techniques employed in IBD are extensively discussed elsewhere in this book. These include transabdominal ultrasound (US), with or without contrast enhancement (CEUS), endoscopic ultrasound (EUS), enterography by computed tomography (CTE), magnetic resonance imaging (MRE), balloon-assisted endoscopy, as well as nuclear scans and positron emission tomography. Despite these techniques, complete assessment of the small bowel has remained a challenge.

Whereas push enteroscopy surpasses EGD, it only affords visualization of the proximal jejunum and is relatively invasive in young children. Intraoperative enteroscopy is even more invasive, necessitating a laparotomy or laparoscopy. Potential complications that may ensue include prolonged ileus, obstruction, perforation, bleeding, or fistula formation. Ballon assisted enteroscopy (BAE) is a technique that can achieve diagnostic, as well as therapeutic, enteroscopy for the entire bowel, without requiring surgery [3]. However, BAE requires a long period of manipulation, and few centers have experience in pediatric patients. Early experience with BAE in pediatric patients dealt with biliary strictures, rarely IBD cases [4]. Data on the choice and timing of BAE vs. video capsule endoscopy (VCE) in pediatric IBD are discussed later in this chapter.

The small bowel had long been considered a relatively inaccessible "black box" for pediatric endoscopy specialists. All this changed rather dramatically with the development of VCE. This innovative technique is no longer considered an emerging technology [5]. It is now embraced as an essential small bowel imaging method that has truly revolutionized enteroscopy. VCE, more than any other test, provides a noninvasive method for the complete endoscopic evaluation of the small bowel mucosa [6–12].

The extremely short focal length of the lens permits incredibly precise imaging of the intestinal mucosa as the capsule transits along the lumen, without requiring insufflation of air. The astounding resolution of the lens yields extraordinarily detailed, high-quality images of the mucosa and offers the ability to visualize normal villi, easily identifying focal areas of villous edema or atrophy (Fig. 23.1). Other recent technological advances include longer battery

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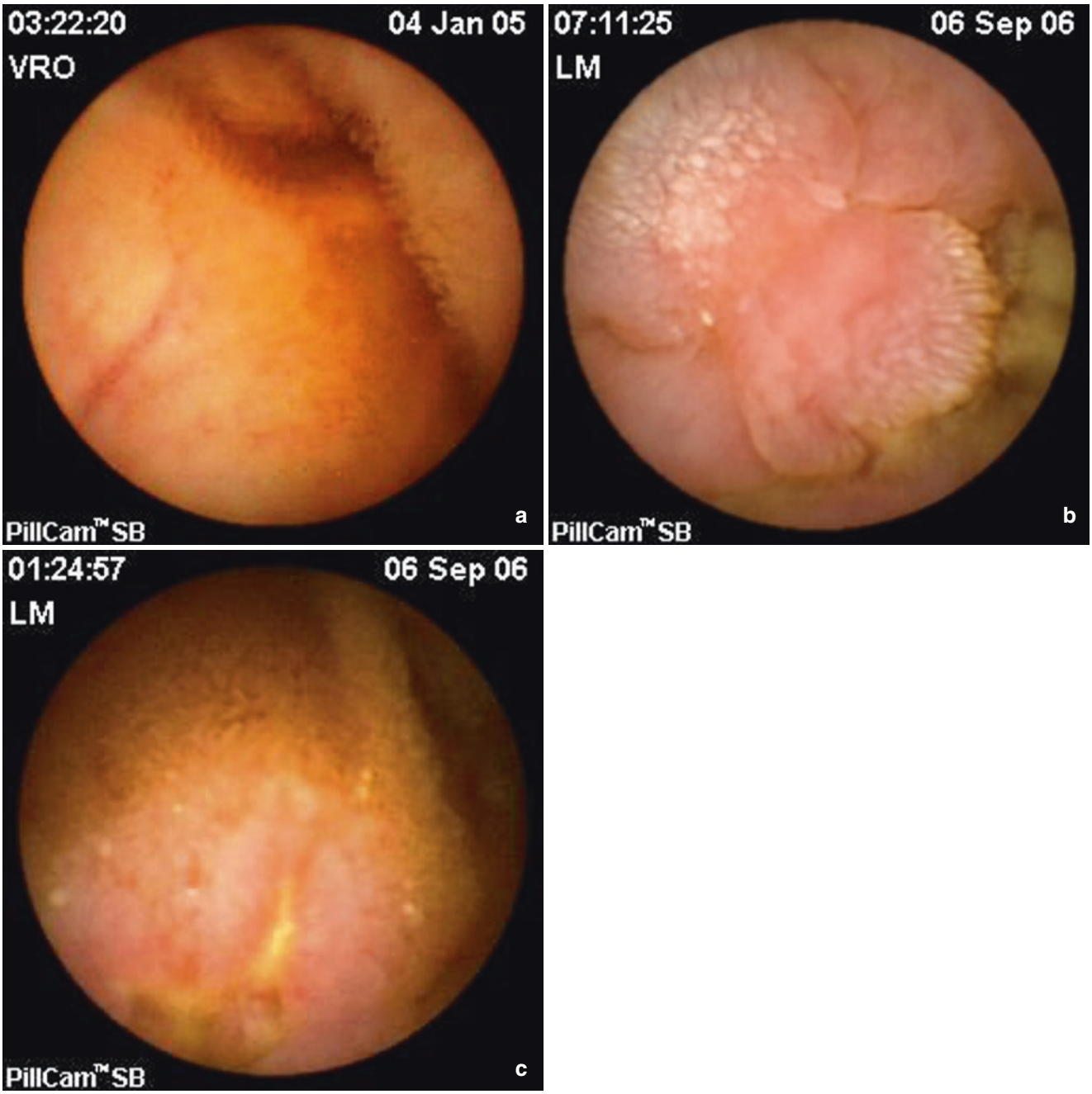

Fig. 23.1 Normal mucosal findings (**a**) in the mid-small bowel as seen by wireless capsule endoscopy in a child suspected of Crohn disease. The astonishing resolution of the capsule's lens (0.1 mm) affords visualization of normal villi and mucosal blood vessels. In contrast, subtle inflammatory changes of the small bowel mucosa that were not visualized radiologically can readily be seen focally by capsule endoscopy. These include areas of mucosal nodularity with focal villous atrophy and "white tipped villi, signifying inflammatory edema (**b**), as well as superficial linear ulcerations (**c**). Whereas these lesions detected by capsule endoscopy are typical of Crohn disease, they may be caused by other etiologies, including the use of medications such as nonsteroidal anti-inflammatory drugs

life, wider angle of vision, increased dynamic imaging speeds, and even real-time viewing to assure the capsule has traversed the pylorus [7]. The goals of this review are to provide an update on the clinical utility of VCE for IBD in the pediatric age group, as well as information on the practical applications of VCE in children.

Potential Uses of Capsule Endoscopy for Inflammatory Bowel Disease

The diagnosis of IBD entails the documentation of the extent as well as severity of the inflammation affecting segments of the gastrointestinal tract, as well as the exclusion of other

Table 23.1 Potential indications for small bowel capsule endoscopy in IBD

1. Diagnosis of suspected small bowel Crohn disease
2. Determination of the extent and severity of small bowel disease in established Crohn disease[a]
3. Evaluation of unexplained symptoms in established IBD
4. Evaluation of the presence of small bowel lesions in patients with colonic inflammatory bowel disease (ulcerative or indeterminate colitis, IBD-U)
5. Evaluation of mucosal healing of small bowel Crohn disease after treatment
6. Assessment of postoperative recurrence of small bowel Crohn disease
7. Incomplete colonoscopy
8. Assessment of pouchitis

[a]Particularly in cases of small bowel Crohn disease with symptoms potentially attributable to functional bowel disease

etiologies. There is no single test that is pathognomonic for ulcerative colitis (UC) or Crohn disease (CD). Bowel imaging techniques, whether endoscopic or radiological, are employed to support the diagnosis. The combination of ileocolonoscopy and EGD with multiple biopsies can usually differentiate between UC and CD based on the distribution and pattern of mucosal inflammation [2]. Endoscopic procedures provide invaluable information regarding the anatomic extent and severity of the mucosal inflammation. However, the vast majority of the small bowel is inaccessible to standard endoscopy or even enteroscopy. Over the past few years, several studies have established the utility of VCE to evaluate the small bowel in patients with IBD [6]. Whereas in adults, obscure bleeding is the most common indication for VCE, known or potential CD constitutes the majority (>60%) indication in children [13]. The potential uses of VCE in established or known IBD are summarized in Table 23.1, and discussed below.

Diagnostic Utility in Suspected Crohn Disease

Contrast small bowel radiography (SBR) and upper endoscopy (EGD and ileocolonoscopy) have long been the standard methods for evaluating known or suspected small bowel CD [2]. However, SBR has relatively low sensitivity for early and superficial lesions of CD in the small bowel [8, 11, 12]. Ileoscopy, when achieved, generally only affords examination of the distal and terminal ileum. Push enteroscopy can be employed to examine the proximal regions of the small bowel that cannot be examined by EGD. However, it too has a rather limited range. A recent Spanish consensus guideline recommends VCE as a far more promising tool for the evaluation of the small bowel in suspected IBD [14]. In cases where prior traditional investigations including EGD, ileocolonoscopy, and SBR were generally negative or nondiagnostic, VCE is vastly superior to establish, or exclude a diagnosis of "obscure" CD limited to the small bowel [6]. A meta-analysis reported a pooled odds ratio (OR) for VCE of 13.0 (95% confidence interval (CI) 3.2–16.3; $p < 0.0001$) compared with SBFT in detecting small-bowel abnormalities in patients with known or suspected CD [8]. The pooled OR for detecting lesions in known or suspected Crohn disease was 5.4 (95%CI 3.0–9.9) for VCE compared with enteroclysis. Another meta-analysis focused on 11 prospective comparative studies comparing VCE to other modalities for the diagnosis of established or suspected nonstricturing CD [15]. VCE was compared to multiple diagnostic modalities (ileoscopy, push enteroscopy, and small bowel radiography, including SBFT and enteroclysis, CT enterography, and small bowel MRI) in a total of 228 patients. The yield for VCE was significantly higher compared to barium small bowel radiography (63% vs. 23%, respectively). Similarly, the yield for VCE versus ileoscopy was 61% and 46%, whereas that for VCE versus CT was 69% and 30%, respectively. Subset analysis of patients with established CD showed that VCE had a higher yield compared to the other modalities. Ongoing issues include the lack of standardization between studies in terms of inclusion and exclusion criteria, as well as the widely variable capsule reading experience. Overall however, VCE is now established as more sensitive for small bowel mucosal lesions than other traditional imaging modalities. Moreover, a normal VCE examination has a very high negative predictive value, essentially ruling out small bowel CD.

Other techniques for small bowel imaging such as CT enterography (CTE) and MR enterography (MRE) are capable of evaluating bowel wall thickness and enhancement, supporting a diagnosis of CD. In addition, these techniques can also detect the presence of extraintestinal abnormalities, such as abscess formation. Also, CTE and MRE have been shown to correlate with disease activity. A small study compared VCE with MRE in 36 adults with known or suspected small bowel CD [17]. Among the 18 patients with known CD, VCE detected inflammatory lesions in the proximal and mid-small bowel (jejunum and ileum) in 12, compared to only one with MRI ($p = 0.016$). There was no significant difference in sensitivity between the two studies for terminal ileal involvement. The authors suggested that VCE is better

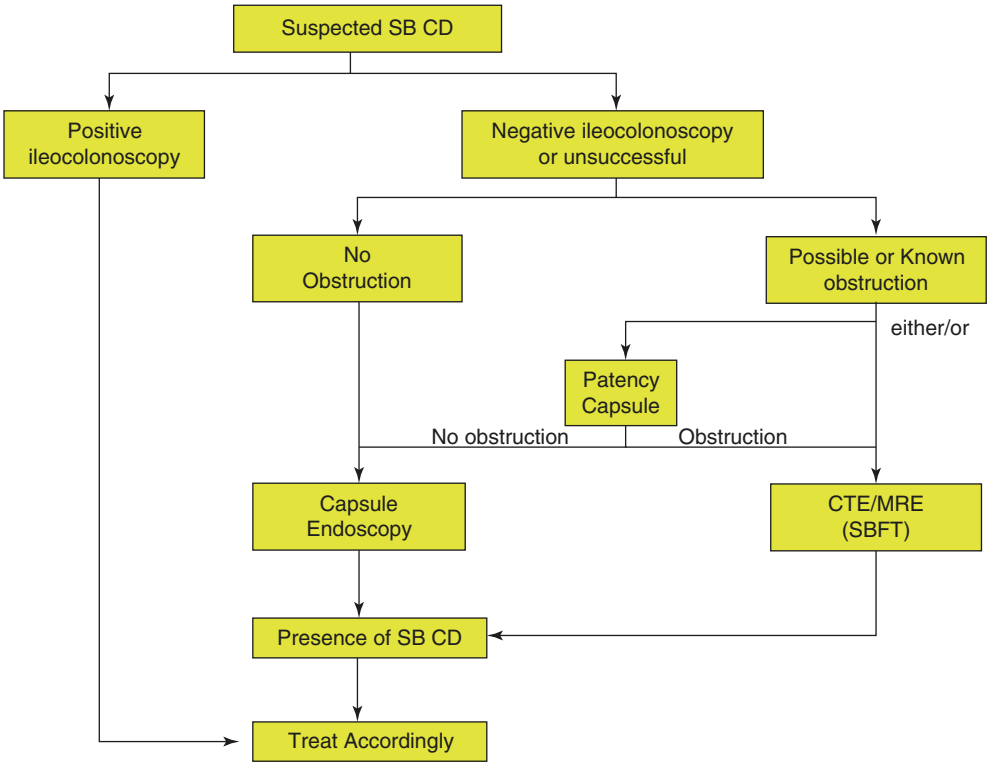

Fig. 23.2 Algorithm for the approach to suspected small bowel Crohn disease (CD). The absence of any mucosal lesions demonstrated by a complete assessment of the small bowel by capsule endoscopy essentially excludes active CD of the small bowel. Patients with symptoms suggestive of or known to have a stenosis should undergo either a patency capsule exam or evaluation by CTE or MRE prior to capsule endoscopy (From: Leighton et al. [12]; with permission). *Abbreviations*: *CD* small bowel Crohn disease, *CTE* CT enterography, *MRE* MR enterography, *SB* small bowel, *SBFT* small bowel follow through

to assess the severity and extent of small bowel inflammation. Another study compared MRE and VCE in 27 patients with established and 25 with suspected CD [10]. Among those with established CD, the yield for VCE was 93% compared to 79% with MRE. In those with suspected CD, VCE was more sensitive and specific (92%/100% vs. 77%/80%, respectively). Another small study (28 cases) used data analysis by consensus diagnosis, comparing VCE with CTE, SBFT, and ileocolonoscopy [11]. Although VCE had the highest sensitivity (83%) for CD, the specificity was lowest of the four modalities (53%).

A recent prospective study [16] in a tertiary pediatric center compared MRE, small intestine contrast US, and VCE in a cohort of 25 pediatric cases of known or suspected CD. The performance of each method was compared blinded to a reference standard for the upper small bowel and ileocolonoscopy. The authors concluded that all three methods were effective in assessing the small bowel. They recommended an integrated approach using more than one tool to achieve a complete assessment of the small bowel in known or suspected pediatric CD. Major limitations to the study are the limited cohort size ($n = 25$), combining known and suspected cases and the use of a consensus reference to the upper small bowel.

Additional prospective studies are required to define the roles of VCE vs. CTE or MRE in the diagnostic algorithm for known and suspected CD [6]. A recommended approach, based on available data [12], is illustrated in Fig. 23.2. An economic analysis comparing VCE to the traditional modalities for diagnosing CD [17] concluded that VCE was a less costly strategy if its diagnostic yield was 64% or greater, based on average diagnostic yields in the literature of 70% for VCE and 54% for SBFT and colonoscopy/ileoscopy. The authors suggested that VCE may also be less costly as a first-line test in this situation.

Detection of Postoperative CD Recurrence

The number of indications for VCE in established CD has been recently extensively reviewed [18]. Among them is to determine the presence of early postoperative recurrence of CD. Recurrence has been documented in the neo-terminal ileum in 73–93% of cases after resection [19]. A prospective comparison of VCE and ileocolonoscopy 6 months after surgery was carried out in 32 adult CD patients, 21 (68%) of whom had recurrent disease [20]. VCE was better able to identify proximal small bowel disease. However, ileocolonoscopy was more sensitive overall (90% vs. 62%). Other studies [19, 21] favored VCE or VCE and abdominal ultrasound. Overall, ileocolonoscopy remains the procedure of choice. However, in view of its noninvasive nature, VCE may be considered as an alternative approach in this clinical situation in the pediatric age group. VCE would be particularly helpful when the surgical anastomosis is not accessible by endoscopy [19].

Indeterminate Colitis

Indeterminate colitis (IC), referred to as IBD of undetermined type (IBD-U), may be defined as a chronic inflammatory bowel disease limited to the colon, without clear endoscopic or pathologic features diagnostic for either CD or UC. Pilot studies [18, 22] reported that VCE led to a change in diagnosis in 29–40% of patients. In a study involving 120 cases of UC and IBD-U, VCE revealed findings compatible with CD in 19 cases (15.8%), whereas barium small bowel imaging found just one case [23]. In a pediatric study in 26 cases of IBD-U [24], small bowel lesions typical of Crohn disease were detected by imaging in 7 and by VCE in 16 ($p < 0.05$). Overall, VCE appears to have utility as a diagnostic tool for CD in patients with IBD-U, as over 30% will be reclassified as CD (G). Larger prospective studies are needed to confirm the usefulness of VCE in this setting.

Use of VCE to Evaluate Mucosal Healing

Symptom assessment is a poor indicator of severity and extent of disease. Mucosal healing after treatment is predictive of reduced subsequent disease activity and decreased hospitalizations and surgery [25]. The high diagnostic precision of VCE can be useful to evaluate small bowel mucosal healing after treatment and thus impact upon disease management and clinical outcomes. Efthyemiou et al. [26] conducted a prospective, multicenter, case-series study. Forty patients with clinically active known or suspected CD were included, all with nonstricturing, nonpenetrating CD. All patients underwent VCE prior to the initiation of any treatment. Treatment was selected according to the treating physician. For the evaluation of mucosal healing, three endoscopic variables were collected: number of apthous ulcers, number of large ulcers, and period of time that any endoscopic lesion was visible (erythema, edema, ulcers). When patients achieved clinical response (after at least a month of treatment) they underwent a second VCE, with evaluation of the same parameters. The number of large ulcers before and after treatment were 8.3 ± 1.4 and 5 ± 0.8, respectively (mean ± SEM) (mean difference 3.3 ± 1.2, 95% confidence interval (CI) 0.8–5.9, $p = 0.01$).

Another pilot study aimed to determine the efficacy of infliximab in treatment of chronic refractory pouchitis complicated by ileitis, using capsule endoscopy [27]. VCE was repeated at week 10 and the Pouchitis Disease Activity Index score was determined. Clinical remission was achieved in 9/10 patients. At VCE and pouch endoscopy, a complete recovery of lesions was observed in eight patients.

In an ongoing study, we are evaluating VCE to assess mucosal healing of the small bowel in a cohort of adult patients with moderate to severe jejunal and or ileal CD [28]. After 6 months of adalimumab monotherapy a second VCE was carried out blinded to the initial severity score, using the Lewis Index [29]. The evaluation of the first ten cases showed complete mucosal healing in five and partial healing in four others (Lewis score decrease >50 %). Although promising, further study of the use of VCE to determine mucosal healing of the small bowel after therapy is needed. This concept is particularly appealing for pediatric onset disease, given the noninvasive nature of VCE.

Utility of VCE in "Obscure" Pediatric Onset CD

VCE was approved as a safe and beneficial in the pediatric population after the first trial [5]. Potential roles for VCE in suspected CD are substantiated by

- Isolated involvement of the small bowel in ~30% of CD cases.
- Normal findings on ileocolonoscopy and upper endoscopy are not sufficient to exclude jejunal or nonterminal ileal CD.
- Although cross-sectional imaging can detect transmural inflammation, superficial mucosal inflammatory lesions are frequently missed.

An early study used VCE in 12 adolescent patients with a clinical suspicion of CD despite negative EGD and colonoscopy [30]. Ileoscopy, achieved in 50% of the patients, was normal in all. Lesions suggestive of CD were identified by VCE in 7/12 (58%) cases. In our comparative and prospective, self-controlled pediatric trial, 30 patients from 10 to 18 years of age were evaluated for obscure small bowel disease [5]. Lesions consistent with a diagnosis of CD were found only by VCE in 10/20 (50%) patients suspected of CD, whereas the diagnosis was formally ruled out in 8. Two remaining cases were found to have eosinophilic gastroenteropathy (by histopathology obtained via subsequent enteroscopic assessment), for an overall VCE diagnostic yield of 60%. Other reports suggest that VCE is potentially useful in the evaluation of possible CD among young patients presenting with a protein-losing enteropathy [31] and/or growth failure when other studies are negative.

Specificity of VCE Findings

No gold standard test exists for the diagnosis of CD. The diagnosis is based on a compilation of clinical, endoscopic, histological, radiological, and biochemical findings. There is a justifiable concern that normal variant capsule findings in the small bowel may be overinterpreted. In adults, up to

13% of normal, asymptomatic individuals can have mucosal breaks and other minor lesions of the small bowel detected by VCE. Therefore, VCE findings of minor mucosal lesions of the small bowel are alone not sufficient for a diagnosis of CD. Other causes to be considered include celiac disease, infectious, ischemic, autoimmune as well as immunodeficiency-related, allergic and drug-induced etiologies. Nonsteroidal anti-inflammatory drug (NSAID) induced enteropathy is common and should be excluded, as it is generally conceded that lesions detected by VCE in NSAID enteropathy cannot be reliably distinguished from those due to CD. The chronicity of the lesions may assist is the differential diagnosis of CD and NSAID induced enteropathy [32].

A standard terminology system has been developed along with a VCE scoring index for small bowel inflammatory lesions such as seen for CD [29]. The parameters that were found to have the necessary inter- and intraobserver consistency were villous edema, mucosal ulcerations and the presence of stenotic lesions. This "Lewis Score" [29] provides an aid to diagnosis and a validated measure of mucosal damage:

- Combined with other clinical parameters the Lewis score could provide a threshold for establishing a positive exam and potentially for the diagnosis of CD.
- Provides an objective measure of assessing small bowel disease extent and severity, as well as the presence of stenotic lesions (whether or not ulcerated or traversed).
- Assists in determining appropriate patient management.
- Facilitates communication and standardization for assessing disease states.
- May be utilized to monitor drug therapy effectiveness.

In our experience, although scoring the mucosal lesions (villous edema, ulcers, strictures) to compile the "Lewis Score" are not specific for CD, they do accurately discriminate normal from a positive exam, and gauge the severity of mucosal inflammation (mild, moderate, severe) for each small bowel tertile [29]. Hopefully, such a standardized scoring system will be utilized by clinical investigators carrying out VCE so that the data from future trials are standardized and comparable. It is will also be important to develop a system for classifying the extent and severity of inflammatory lesions seen on VCE in normal individuals and to develop reliable criteria for the diagnosis of CD. Further validation studies in pediatric patients are needed.

An alternative, albeit more invasive endoscopic approach to VCE, is ballon assisted enteroscopy (BAE). Although used much less frequently in the pediatric age group, it has the distinct advantage to provide histological specimens for analysis [33]. A recent retrospective review examined the accuracy if BAE after VCE in 36 pediatric cases [34]. Overall, both VCE and BAE had a high sensitivity for histologically significant findings (100 vs. 87%, respectively). However, the specificity was higher for BAE (20% vs. 65%). Given the high diagnostic yield of both tests and in view of the high negative predictive value of VCE, the authors recommended carrying out VCE first [34].

Impact of VCE on Management

In the assessment of any diagnostic technology, a critical evaluation of the impact or added value of the test must be considered. A retrospective review of VCE in 83 children was reported by a single tertiary care center [35]. Among these approximately 60% were established CD, 20% IBD-U, and 20% suspected IBD. One year after VCE, patients with known CD had significant improvements in growth, higher body mass index, lower ESR and Harvey Bradshaw index. VCE also revealed more extensive disease extent in 43% of CD compared to other modalities used. The negative predictive value for suspected IBD was 94%. Moreover, 50% of IBD-U cases had their diagnosis changed to CD after VCE [35].

Practical Capsule Issues in Pediatric Patients

Capsule Retention

The major contraindication to VCE is the presence of a known or suspected gastrointestinal tract obstruction and/or small bowel strictures, because of the risk of capsule retention [6, 7, 13, 17]. The incidence of capsule retention varies widely between reports, from 0.75% to 5%. Most episodes of capsule retention are caused by NSAID, CD, or radiation induced strictures. In adult patients, tumors are more often implicated as a cause of capsule retention than in pediatrics. Most cases of retention are transitory and remain asymptomatic. However, it may rarely cause symptomatic small bowel obstruction and require endoscopic or surgical removal. To minimize the risk of capsule retention in the small bowel, a careful history should be taken regarding obstructive symptoms. Patients with established CD are generally at higher risk for stricture formation, and this risk increases with duration and severity of small bowel disease. The rate of capsule retention in patients with suspected CD appears to be quite low. In our pediatric prospective trial of VCE for suspected CD, capsule retention was seen in 10% (2/20) of cases, despite normal imaging by SBR [5]. In both cases, the capsule passed the unsuspected inflammatory stenosis subsequent to treatment with oral corticosteroids. The rate of capsule retention in patients with known CD is typically higher, in the range of 4–7% [18]. However, a retrospective review

of over 1000 tests in pediatric patients reported retention in only 2.2% of CD cases, compared to 2.3% overall [13]. An example of a retained capsule is shown in Fig. 23.3.

Studies support the utility of a patency capsule to screen for the risk of retention in patients suspected of having a stricture or obstruction. The newer Agile Patency Capsule (Given Imaging Inc) has been approved in Europe, Canada as well as by the FDA in the United States for use in patients with suspected small or a known stricture. It is identical in size to the conventional imaging capsule, but rather than being inert, it is designed to dissolve spontaneously in the small bowel lumen. Its body is comprised of lactose with barium, a radiofrequency identification (RFID) tag, and two side timer plugs with exposed windows. It remains intact for a minimum of 30 h, and then begins to disintegrate. The system offers an RFID patency scanning device that can detect the RFID tag. If the patient witnesses excretion of the patency capsule intact or the scanner does not detect the RFID tag at or prior to 30 h, it is generally safe to proceed with the conventional VCE [36]. We employ an abdominal plain film at ~30 h to determine if the patency capsule has been excreted or is in the small vs. large bowel. If the patency scanner is contraindicated (due to a pacemaker or implanted cardiac defibrillator), fluoroscopy may be employed to check for the presence of the patency capsule or RFID tag. Although there have been rare cases of abdominal pain associated with the patency capsule, as well as exceptional episodes of temporary intestinal occlusion [37], it is generally very safe. In the unlikely event that a capsule is retained and induces symptoms, one can use ballon assisted enteroscopy (BAE) to dilate the stenosis and retrieve the capsule without surgery.

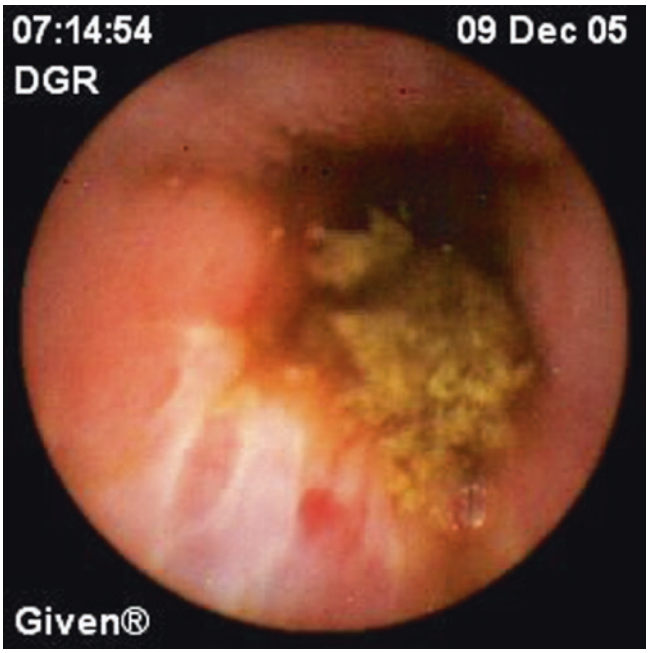

Fig. 23.3 Capsule endoscopy image of an ulcerated stricture in an adolescent patient with known Crohn disease. The patient had ongoing anemia and elevated markers of inflammation, despite a normal ileocolonoscopy and a barium small bowel follow through. The ulcerated stenosis of the mid-small bowel was seen only by capsule endoscopy. The patient presented with symptoms of partial bowel obstruction within 24 h of ingesting the capsule. All symptoms and radiological signs of bowel obstruction cleared promptly with intravenous corticosteroids, and the capsule was expelled shortly thereafter

A recent multicenter study [38] evaluated the clinical utility of the systematic use of a patency capsule in known CD (our center) compared to selective use (only if obstructive symptoms, history of intestinal obstruction or surgery, or per treating physician's request). In this cohort of over 400 adult cases, the risk of retention was 1.5% without a prior patency capsule and 2.1% after a negative patency test ($p = 0.9$). However, 18 patients underwent VCE after a positive patency capsule test, with a retention rate of 11.1% ($p = 0.01$).

Preparations and Prokinetics

Given the inability to suction, wash, insufflate air or gas, the quality of the preparation is critical to adequately visualize the small bowel mucosa. Yet, the ideal preparation for VCE in the setting of IBD remains unknown. There is no universally accepted consensus on the "ideal" prep, or a validated scale with which to grade the utility of various preparations. Various trials have examined the use of oral sodium phosphate based or polyethylene glycol (PEG) based preparations, without reaching a firm conclusion. A consensus guideline for the use of bowel preparation in adults prior to colonoscopy and small bowel video capsule endoscopy was published [39]. In summary, the recommendations for VCE were to utilize a PEG-based regimen as first line (Grade A); sodium phosphate (NaP) based prep was not recommended in view of potential for renal damage and other adverse events (Grade B), unless PEG or sodium picosulfate is ineffective or not tolerated (Grade D); NaP should be avoided in chronic kidney disease, preexisting electrolyte disturbances, congestive heart failure, cirrhosis or a history of hypertension (Grade D). The authors furthermore stated [39] that there is insufficient evidence to support the use of prokinetics (Grade D) or simethicone (Grade D). No recommendation was made regarding timing of the dose (Grade D).

PEG-based regimens are generally recommended for children undergoing colonoscopy. A recent prospective, randomized single blinded pediatric study for preps in VCE was reported [40]. The effect of different preparation regimens was compared in 198 cases evaluated for bleeding or IBD by VCE. The primary outcome was the calculated percentage of visualized surface area. Patients were randomized to one of 5 groups: (A) 12 h liquid diet day prior to VCE; (B) high

volume PEG (50 ml/kg up to 2 L; (C) low volume PEG (25 ml/kg up to 1 L0; (D) 3.76 mg simethicone; or (E) low dose PEG and simethicone as above. The highest visualization score achieved was for the combination preparation used in group E ($p < 0.01$). Overall diagnostic yield and tolerability were not different [40]. Inter-observer agreement was $\kappa = 0.89$; 95% CI 0.83 ± 0.71.

Two very recent studies examined the use of bowel preps prior to VCE in adults. A retrospective analysis of data from two tertiary care medical centers in Israel [41] compared 2-L PEG ($n = 360$) with a clear liquid diet plus 12-h fast protocol ($n = 500$). SB completion rates were higher in the PEG protocol (96% vs. 83%, $p < 0.001$) and SB passage time was significantly faster in the PEG protocol (mean 217 ± 73 vs. 238 ± 77 min, $p < 0.001$). However, bowel preparation quality was similar between groups (8% vs. 7% inadequate preparation). Overall positive SB findings were also similar between the two groups (57% vs. 51%, respectively, $p = 0.119$).

A randomized, blinded controlled trial comparing 3 prep regimens was reported by a Canadian group (42). Patients ($n = 198$) were randomized to clear fluids only, 2 sachets of Na picosulfate plus magnesium sulfate, or 2 L PEG the evening before VCE. No benefit was found for either prep compared to clear fluid diet in terms of visualization or diagnostic yield. Moreover, a significantly higher proportion of patients on clear fluids rated tolerance as easy or very easy ($p < 0.0001$).

In general, about 85% of VCE studies obtain images of the complete small bowel, including the terminal ileum and or cecum in large pediatric series [13]. However, in the randomized pediatric study on various preps described above, the cecum was seen in at least 95% for all five groups [40]. Some studies have thus examined the use of prokinetic agents to improve transit times and completeness of the small bowel evaluation [43]. In general, prokinetic agents may shorten gastric and/or small bowel transit times, but the ideal regimen remains controversial.

The adult consensus described above [39] did not support a prokinetic agent routinely. We recommend using a real-time viewer about an hour post capsule ingestion to determine whether it has exited the stomach. If not, we employ a single dose of erythromycin (2–4 mg/kg) to promote gastric motility. Rarely, if the capsule is still in the stomach 2 h after ingestion, we use gastroscopy to advance it into the duodenum.

One should routinely ascertain if there is any history suggestive of gastroparesis, if the patient is sedentary, or if medications are being used which may interfere with gastric emptying. Patients should be fasting for a minimum of 8 h prior to the test. We allow patients to drink clear fluids 1–2 h after the study has begun and to eat a light meal about 2 h after ingesting the capsule.

Endoscopic Placement of the Capsule

Patients of any age may be unable to swallow the capsule. This problem is very common in children under age 8. Patients can practice by swallowing similar sized jelly beans or other candies. If a parent has any doubt as to their child's ability to swallow the capsule, it is worthwhile having the child demonstrate that they are indeed capable of swallowing a similar sized object (vitamin tablet or jelly bean), prior to undergoing VCE.

For patients unable or unwilling to swallow the capsule, VCE can be safely performed by introducing the capsule into the proximal duodenum endoscopically, under direct vision. This can be accomplished by "front loading" the capsule on a gastroscope [42]. A specific capsule delivery device (Fig. 23.4) has been developed ("AdvanCE™", US Endoscopy, Mentor, Ohio, USA) which affords the secure delivery of the

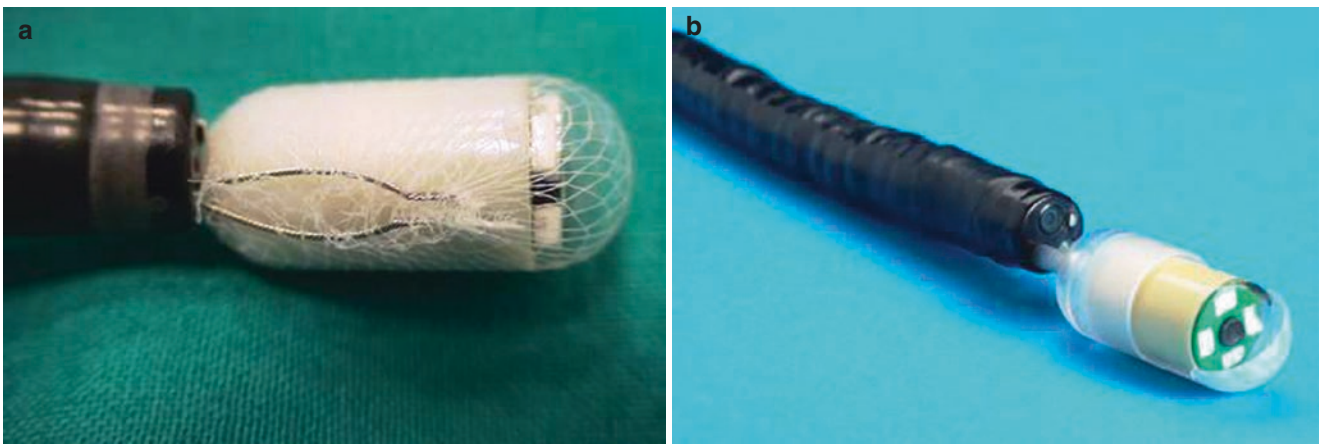

Fig. 23.4 Methods of "front loading" the capsule endoscope onto a gastroscope: (**a**) using a foreign body net, and (**b**) employing the US Endoscopy patency launching device (From: Keuchel et al. [44] (with permission))

capsule into the duodenum. As with the Roth net however, it may be difficult to launch the capsule into the duodenum in young children (Fig. 23.4). The same technique can be used in patients with severe gastroparesis.

Age and Size Limitations

Aside from swallowing issues, the capsule may be too large to cross the esophageal sphincters or pass through the pylorus and/or ileocecal valve. One study evaluated the feasibility of VCE in 83 children under age 8 [44]. It showed that VCE is feasible and safe to age 1.5 years. Overall, 24% swallowed the capsule (aged >4). Use of a foreign body net was associated with more mucosal trauma (50%) compared to the Advance™ capsule delivery device [45]. More recently a smaller retrospective study compared children unable to swallow the capsule (group A, $n = 11$) with those who were (group B, $n = 15$) [46]. Median ages [range] were 2 [10 months–9 years] and 12 [8–16 years]. The smallest child weighed 7.9 kg. Median [range] small bowel transit of 401 min [264–734] was significantly longer ($p = 0.0078$) for group A compared to group B's 227 min [56–512]. The authors attributed this to the effects of anesthetic agents. However, diagnostic yield was not different and no cases of capsule retention or adverse events occurred. Although the above study [44] did not employ endotracheal intubation, we caution to protect the child's airway, particularly for patients incapable of independently swallowing the capsule, or in those with neurological impairment.

Future Directions

After more than 15 years since small-bowel VCE was first reported, its use as a noninvasive tool that allows visualization of the entire small-intestinal mucosa has expanded momentously. In patients of all ages VCE has also been applied to other organs including the esophagus, stomach, and colon [47, 48]. The main indications for esophageal CE (ECE) are screening for gastroesophageal reflux disease/Barrett's esophagus, and esophageal varices. However, the clinical benefit of ECE remains unconfirmed. Magnetically guided CE (MGCE), developed to visualize the gastric mucosa, is a new concept of capsule navigation and preparation protocol. First-generation colon CE (CCE) had moderate sensitivity and specificity compared with colonoscopy for colorectal neoplasia surveillance. To obtain higher accuracy, a second-generation CCE was developed with a high sensitivity for detecting clinically relevant polypoid lesions. Possible applications of CCE in pediatrics are IBD (or IBD-U) or polyposis syndromes.

A recent pediatric study prospectively enrolled 40 consecutive cases of established CD to evaluate the accuracy of CCE compared to MRE, CEUS, and ileocolonoscopy [49]. The sensitivity, specificity, positive, and negative predictive values for CCE were extremely high for colonic findings (89, 100, 100, and 97%, respectively). The accuracy was superior to MRE and CEUS. Similarly, the accuracy for small bowel findings exceeded for the other two modalities (90, 94, 95, and 90%, respectively) [49].

The results of the latter study along with the substantive evidence of the clinical accuracy of small bowel VCE raises the question as to whether we should consider reversing the investigative paradigm and screen the gastrointestinal tract using wireless capsules. Advantages include being less invasive and lower cost, anesthesia and radiation free [13]. In the not too distant future, VCE may include diagnostic and therapeutic functions such as magnifying endoscopy systems, targeted biopsy forceps, and drug delivery systems.

Conclusions

In summary, the advent of VCE has revolutionized the field of small bowel enteroscopy. It has led to improvements in the diagnosis and evaluation of small bowel disorders, including IBD, in a noninvasive manner and without exposing patients to radiation. Studies suggest that VCE is particularly useful in the evaluation of patients with small bowel CD and is considered to be superior to other imaging modalities. The availability of a standardized and validated scoring system is clinically useful to classify studies as normal or showing mucosal inflammation, and the severity of disease. Larger, prospective randomized controlled trials are still needed to further understand its role in the evaluation of pediatric IBD, reassessment of mucosal healing, and how it should be used in conjunction with other modalities, such as CT or MR cross-sectional imaging. In order to assure quality of care and interpretation, a more formalized approach to training will be required for credentialing pediatric trainees as has been initiated in adult GI programs [50].

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