REVIEW

Optimising the use of small bowel endoscopy: a practical guide

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ABSTRACT

The wireless nature of capsule endoscopy offers patients the least invasive option for small bowel investigation. It is now the first-line test for suspected small bowel bleeding. Furthermore meta-analyses suggest that capsule endoscopy outperforms small bowel imaging for small bowel tumours and is equivalent to CT enterography and magnetic resonance enterography for small bowel Crohn's disease. A positive capsule endoscopy lends a higher diagnostic yield with device-assisted enteroscopy. Device-assisted enteroscopy allows for the application of therapeutics to bleeding points, obtain histology of lesions seen, tattoo lesions for surgical resection or undertake polypectomy. It is however mainly reserved for therapeutics due to its invasive nature. Device-assisted enteroscopy has largely replaced intraoperative enteroscopy. The use of both modalities is discussed in detail for each indication. Current available guidelines are compared to provide a concise review.

INTRODUCTION

Capsule endoscopy is a wireless pill camera designed to visualise the small bowel (SB). Since its introduction, several prototypes have been developed. CapsoCam (Capso-Vision, Saratoga, Germany) provides panoramic views of the SB and allows for remote small bowel capsule endoscopy (SBCE).¹

Double balloon enteroscopy (DBE) was first introduced in 2001, followed by single balloon enteroscopy (SBE). The device allows deep intubation of the SB by means of an overtube and a single or double balloon. Spiral enteroscopy uses a helical overtube to examine the SB, which shortens procedure time. Literature on the use of device-assisted enteroscopy (DAE) is mostly available for DBE as it has been available for the longest time. Most centres worldwide provide a DBE service rather than SBE despite the latter being cheaper.²

One possible explanation is the reported higher rate of complete enteroscopy for DBE in one meta-analysis.³ This was however shown to be the same in another meta-analysis. Otherwise, DBE and SBE are equivalent in diagnostic and therapeutic yield, complication rate and extent of SB examined.⁴ Total enteroscopy is rarely required as the pathology may be reached with a single antegrade or retrograde route.

There are no trials comparing the diagnostic yield (DY) of SBCE and DBE. However ample evidence exists that provides an indirect comparison of DY of both procedures. The pooled DY for SBCE and DBE is 60%–61% and 55%–57%, respectively.⁵ Evidence for a low rebleeding rate following a negative SBCE adds further to the reliability of SBCE.⁶ The DY of SBCE in Crohn's disease (CD) is similar to the DY of magnetic resonance enterography (MRE) and CT enterography (CTE). In coeliac disease, the sensitivity of SBCE in detecting macroscopic changes is comparable with the gold standard, which is duodenal histology.

This review summarises the common indications for SB endoscopy and provides a practical guide on how to optimise its yield. The DY of SBCE is also compared with that of other modalities including DAE and radiological investigations according to different SB pathologies.

OVERT AND OCCULT OBSCURE GASTROINTESTINAL BLEEDING

In a proportion of patients (5%–10%) in whom no source of bleeding is found, a SB source is usually suspected.⁷ SB bleeding may be occult (iron deficiency anaemia [IDA]) or overt with melaena or haematochezia. In IDA, the European Society of Gastrointestinal Endoscopy (ESGE) guidelines recommend that prior to SBCE, all the following are undertaken:

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Figure 1 (A) Non-bleeding and (B) bleeding angioectasias on small bowel capsule endoscopy in 2 patients presenting with iron deficiency anaemia.

acquisition of a complete medical history, gastroduodenoscopy with duodenal and gastric biopsies, and ileocolonoscopy.⁸

The American College of Gastroenterology guidelines on the management of SB bleeding recommend a repeat gastroscopy in patients with overt obscure gastrointestinal bleeding (OGIB)⁷ as most lesions can be reached with a standard endoscope. However, this approach is not cost-effective.⁹ We advocate a repeat gastroscopy if previously carried out by an inexperienced endoscopist, if suboptimal views were obtained or if more than 6 months have elapsed since the index gastroscopy.

SBCE should be first line to investigate OGIB as it has a better DY than push enteroscopy (PE) and SB radiography (online supplementary appendix table 1). SBCE can detect flat lesions such as angioectasias and ulcers, which can be missed by other modalities. However, CT angiography (CTA) is still preferred in unstable patients. The DY of SBCE is similar to that of DBE in patients with OGIB.¹⁰ The DY of DBE is improved if carried out after a positive SBCE (75% vs 28%).¹⁰

Early SBCE improves DY in OGIB. The ESGE recommends the performance of SBCE as soon as possible after the bleeding episode (hot SBCE), ideally within the first 14 days.⁸

The DY of SBCE for SB angioectasias (figure 1) is higher in elderly patients with multiple comorbidities.¹¹ They commonly occur in the proximal SB.

Most evidence exists on the treatment of angioectasias with argon plasma coagulation (APC) during DAE¹² as it can reduce transfusion requirement and improves haemoglobin. However, the rate of rebleeding following APC is high and can be similar to natural history cohorts, begging the question of its long-term efficacy.¹³ It is not unreasonable to treat patients with multiple comorbidities who have SB angioectasias and mild IDA conservatively, as DAE is not without risks. PE can be better tolerated by some patients due to the requirement of less sedation and the procedure being shorter. There is some evidence for the addition¹⁴ of somatostatin analogues to APC to reduce rebleeding rate. Antiangiogenic drugs can be considered but with more side effects.

Following a negative SBCE, it is safe to treat patients conservatively as the rate of rebleeding after a negative SBCE is very low.⁶ A watch and wait policy with a low threshold to repeat SBCE if haemoglobin drops (≥ 0.4 g/dL) or if there is a change in presentation from occult to overt OGIB is advised. There is a much higher rate of rebleeding after a positive SBCE in patients with OGIB (32% vs 17%). This emphasises the need for aggressive management of these patients with DAE, CTA and/or surgery.⁶

Intraoperative enteroscopy (IOE) is still useful in persistent OGIB where the culprit lesions are identified on SBCE but fail to be reached at DAE. IOE is no longer the first-line investigation because of its invasive nature and the high morbidity and mortality.

Figure 2 Flow chart summarizing the management of small bowel bleeding.

Figure 3 Small bowel stricture in patients with Crohn's disease (A) on Pillcam Crohn's and (B) at double balloon enteroscopy.

Figure 2 summarises the treatment of occult gastrointestinal bleeding.

Summary points

- ▶ SBCE should be the initial investigation in patients with OGIB.
- ▶ The yield of SBCE is higher in patients who are elderly and with multiple comorbidities and best done as close to the bleeding episode as possible.
- ▶ DAE is useful for therapeutics in patients with SB causes, such as angioectasias, by using APC, haemoclips and epinephrine injection.
- ▶ Patients with a negative SBCE can be managed conservatively with a low threshold to repeat SBCE if haemoglobin drops or if there is a change in presentation from obscure to overt OGIB.
- ▶ IOE is reserved for cases of unsuccessful management of bleeding with DAE and should only be undertaken in specialist centres.

RETENTION OF SBCE

Capsule retention is the main risk of SBCE and is defined as the persistence of the capsule within the

gastrointestinal tract for more than 2 weeks or retention requiring endoscopic or surgical retrieval.¹⁵ The risk of SBCE retention varies from 2% to 8% depending on indication and presence of underlying inflammatory bowel disease (IBD).¹⁶ Patency of SB can be confirmed by a patency scanner 30–33 hours after ingestion of a soluble patency capsule, or if this is positive by carrying out a limited CT scan. There is a good concordance between a negative patency capsule and subsequent SBCE.¹⁷ Capsule retention does not always result in SB obstruction. A capsule is very often retained proximal to a stricture or within a diverticulum. It will only result in obstruction requiring emergency surgery if it gets impacted within a stricture. Several therapeutic options exist if a SBCE is retained: endoscopic retrieval and dilatation of strictures, pharmacological treatment of inflammation with subsequent passage of capsule or surgical intervention. Retention of a capsule can at times be beneficial for patients as it leads to localisation and management of underlying pathology due to secondary procedures. Retention of SBCE is also discussed further under SB CD.

SB ULCERS

SB ulcers are picked up on SBCE in patients with persistent gastrointestinal symptoms following negative bidirectional endoscopy. Weight loss, hypoalbuminaemia and raised inflammatory markers are associated with a higher rate of positive findings on SBCE.¹⁸ Causes of SB ulcers include medications such as non-steroidal anti-inflammatory drugs (NSAIDs), infections such as tuberculosis and CD.

Ulcers secondary to infective causes will resolve once the underlying condition is treated. Medications such as NSAIDs need to be stopped for SB healing. This

Figure 4 Flow chart for the diagnosis and management of small bowel ulcers and Crohn's disease.

can take months if there has been extended use, and a repeat SBCE should only be considered after 6–8 months of stopping NSAIDs.

Raised inflammatory markers and faecal calprotectin and a positive family history increase the likelihood of SB CD and improve the diagnostic accuracy of SBCE.⁸ If SB CD is likely, empirical budesonide can be considered and a SBCE repeated in 6–8 months to assess mucosal healing or obtain histology via DAE, although histology can be negative in up to 77% of cases.¹⁹

SBCE can change management of patients with suspected CD and with other negative investigations. In two studies, patients with suspected CD on SBCE were studied and followed up for 12 months. Prevalence for the eventual diagnosis of CD was 12%–13% and the positive predictive value ranged between 31% and 69%.^{20,21} Management was altered in 4%–30% of patients with established CD who underwent SBCE and with evidence of proximal disease, missed on other modalities. These patients were commenced on thiopurines and/or biologics at a year of follow-up.²² While SBCE has been shown to improve detection of lesions in the proximal SB when compared with cross-sectional imaging, implications of these findings on management remain under debate.

The European Crohn's and Colitis Organisation guidelines recommend SBCE if clinical suspicion of CD remains high despite negative ileocolonoscopy and radiological investigations.²³ The ESGE guidelines recommend SB imaging in patients with CD diagnosed at colonoscopy. Only if this is negative should one proceed to SBCE with a patency capsule.⁸ SBCE is equivalent to CTE and MRE in suspected and established non-stricturing CD (online supplementary appendix table 2). However, patency capsule and SBCE can still pick up subtle strictures missed on SB imaging. SB involvement is reported in 66% of patients with CD.²⁴ We recommend SBCE in patients with colonic CD irrespective of a positive ileoscopy or in those patients where the suspicion of CD remains high despite negative endoscopy.

SBCE can be used to monitor disease activity in patients with CD after treatment modification or after surgery. This can help direct additional pharmacological therapy to aid mucosal healing. Disease activity can be graded by capsule endoscopy CD activity index⁸ or Lewis score²⁵ which is embedded in the capsule reading software. Both are strongly correlated and perform similarly.

A new panenteric capsule endoscopy (PillCam Crohn's; Medtronic, Dublin, Ireland) has been introduced in Europe. The main aim is to assess the entire gastrointestinal tract using one capsule. The DY of panenteric capsule endoscopy in patients with active CD has been shown to be higher than ileocolonoscopy.²⁶

Capsule retention in patients with suspected and established CD can be up to 3.6% and 8.2%, respectively.¹⁶ The ESGE does not recommend routine use of

patency capsule before SBCE in patients with suspected CD but in patients with established CD and negative cross-sectional imaging.⁸ In cases of SBCE retention, the ESGE recommends medical treatment prior to attempting capsule retrieval using DAE.⁸

DAE is also useful for dilatation of SB strictures with high success rates (figure 3). Symptomatic strictures less than 5 cm in length without active ulceration or fistulation or acute angulation have the best outcome.¹⁵ However there have been no trials comparing the long-term efficacy of dilatation at DAE versus surgery. Risks of SB dilatation include bleeding, perforation, death, stent migration and acute pancreatitis.²⁷

Figure 4 summarises the management of SB CD.

Summary points

- ▶ Patients with a clinical suspicion of IBD should be referred for SB imaging and/or SBCE despite negative ileocolonoscopy.
- ▶ A careful history to look for symptoms of obstruction is pertinent.
- ▶ Screening for use of NSAIDs before making a diagnosis of SB CD on SBCE is important.
- ▶ DAE offers the ability to dilate strictures with the best outcome in those less than 5 cm in length, without active ulceration or fistulation or acute angulation.

COELIAC DISEASE

The gold standard for diagnosing coeliac disease in adults remains duodenal histology.²⁸ However, SBCE has a high sensitivity (89%) and specificity (95%) in coeliac disease.²⁹ Its wider angle of view, better magnification than conventional endoscopy, lack of insufflation and underwater navigation make coeliac disease features such as scalloping of folds, fissuring of mucosa, villous atrophy and mosaic appearance more prominent.

SBCE can be used to detect macroscopic changes in patients who refuse gastroscopy.⁸ It can also be helpful in equivocal cases where coeliac disease-related changes are present on histology but serology is negative or vice versa.³⁰

When complications are suspected in patients with refractory coeliac disease (RCD), SBCE should be carried out.³¹ Abnormalities that are suspicious for coeliac disease-related complications should be followed by DAE for confirmative histology.

Data on the use of patency capsule in coeliac disease is very sparse. If malignancy is suspected as a complication of RCD, it is sensible to suggest a patency capsule.

Summary points

- ▶ SBCE is recommended in patients in whom a diagnosis of coeliac disease is suspected but cannot be confirmed on duodenal histology or in equivocal cases of coeliac disease.
- ▶ Patients with RCD should undergo SBCE to rule out potential complications.

- DAE should be reserved for patients in whom a histological diagnosis to confirm a complication is needed.

SB POLYPS

SBCE is equivalent to MRE in polyp (>10 mm) detection in Peutz-Jegher syndrome (PJS).³² Patients with PJS should undergo 3 yearly SBCE from 8 years of age. If few or no polyps are found at initial examination, screening should be deferred to 18 years.³³ Polyps larger than 10–15 mm should be removed⁸ to avoid intussusception and adenocarcinoma transformation. DAE allows safe polypectomies with minimal complications of bleeding and perforation. DAE has mainly replaced IOE, although this technique can still be useful if polyps cannot be reached during DAE.

SB TUMOURS

SB tumours (SBT) account for about 2% of all gastrointestinal tract malignancies.³⁴ Several types of SBT including carcinoids/neuroendocrine tumour (NET) and gastrointestinal stromal tumours (GISTs) exist. They can present with persistent anaemia, overt OGIB, abdominal pain or persistent diarrhoea.¹⁸ Lymphomas can appear as ulcerated, thickened mucosa or stricture. GISTs are smooth submucosal tumours. NETs can appear as submucosal tumours with central umbilication and ulceration. Suspected SBT on SBCE will require DAE for histology and allow a submucosal tattoo to be placed close to the lesion to help direct surgery.

There are no meta-analyses to compare cross-sectional imaging and SBCE for the diagnosis of SBT. CT and MRI can miss SBT.³⁵ The DY of SBCE is reported to be higher than that of CT in some studies.³⁶ In view of this evidence, cross-sectional imaging should be complementary to SBCE whenever suspicion of malignancy remains high despite a negative SBCE. It can also play an important role in staging and to guide further treatment such as chemotherapy.

Summary points

- SBCE and cross-sectional imaging should be complementary in the detection and staging of SBTs.
- DAE can be useful for histological diagnosis and to guide surgery.

FUTURE DIRECTION

Recent studies have investigated the use of SBCE beyond the usual indications. Early SBCE following presentation with obscure gastrointestinal bleeding in the emergency department has been shown to be superior to standard investigations in the identification of vascular lesions with no additional costs.³⁷ The role of SBCE has also been investigated in an intensive care setting.³⁸ SBCE can be performed at the bedside and requires no preparation or sedation. It is safe and can have a higher DY if performed close to the bleeding episode.

Attempts at image modification following image capture using capsule reading software to improve delineation of SB lesions have been unsuccessful. However, in a recent study, a contrast capsule (EC Type 1, Olympus) equipped with a special white light LED (light-emitting diode) was used to study the effect on SB lesion detection. Contrast images were equivalent or superior to white light in the detection of angioectasias and ulcers.³⁹

A few studies have shown the usefulness of endoscopic ultrasound combined with DAE to evaluate depth of invasion in malignant SB lesions and assess vascularity of lesions where biopsy can be complicated by haemorrhage.⁴⁰

CONCLUSION

SBCE can localise and potentially diagnose most SB pathologies including malignancies, vascular lesions, strictures, ulcers and diverticuli. The overall DY is equivalent to that of DAE, and given its non-invasive nature and its lack of radiation it should be the first investigative modality when SB pathology is suspected. It is also equivalent to CTE and MRE but has the added benefit of providing mucosal views in patients with CD. Variation in concordance of SBCE and DAE is however reported in SBT with radiological investigations being superior in some cases. DAE is complementary to SBCE. Since it is more invasive and exposes patients to greater risks, it should be reserved for those requiring diagnostic confirmation of SB pathology by allowing for a histological diagnosis and in patients requiring therapeutic intervention such as dilatation of SB strictures or management of angioectasias with APC. Careful selection of patients can help ensure both modalities have the highest yield.

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