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Small bowel diagnostics: Current place of small bowel endoscopy

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A B S T R A C T

The small intestine has been difficult to examine by traditional endoscopic and radiologic techniques. Until the end of the last century, the small bowel follow through was the primary diagnostic tool for suspected small bowel disease. In recent years capsule endoscopy, deep enteroscopy using balloon-assisted or spiral techniques, computerized tomography and magnetic resonance enteroclysis or enterography have facilitated the diagnosis, monitoring, and management of patients with small bowel diseases. These technologies are complementary, each with its advantages and limitations. In the present article, we will discuss the different options and indications for modern diagnostic methods for visualization of the small bowel. We also try to provide a clinical rationale for the use of these different diagnostic options in less established, newly emerging, indications for small bowel evaluation.

Introduction

The first part of the small bowel, up into the third part of the duodenum, is in a standard fashion intubated and assessed by regular upper endoscopy. The same applies for the last part of the small bowel, i.e. the terminal ileum, which is in general easily intubated and assessed with a regular ileo-colonoscopy procedure. While intubating the terminal ileum with the colonoscope the distal

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segment of the ileum can be examined, varying from a minimal segment of five centimetres, up to a maximum of 50 cm in to the distal ileum. The remaining 'in between' part of the small bowel may vary in length from four to up to eight m, and is more difficult to access with endoscopy procedures. Due to its total length and tortuous anatomy, the mid-gut part of the small bowel has historically been a difficult area to examine. Until the end of the last century, the small bowel follow through (SBFT) was the primary diagnostic tool for suspected small bowel disease. However, the SBFT has shown to have a relatively low diagnostic yield for small bowel disease [1,2]. In recent years, there have been significant innovations in radiological small bowel imaging using a variety of techniques, such as computed tomography (CT) or magnetic resonance imaging (MR or MRI) enteroclysis and/or enterography. Moreover, in the past decade new small bowel endoscopy techniques have been introduced, which have revolutionized daily gastroenterological practice worldwide. The introduction of capsule endoscopy (CE), followed by double balloon enteroscopy (DBE), single-balloon enteroscopy (SBE) and more recently spiral enteroscopy (SE) have opened the 'black box' of the small bowel. The aim of this review is to discuss the different options and indications for modern diagnostic methods for visualization of the small bowel. We also try to provide a clinical rationale for the use of these different diagnostic options in less established, newly emerging, indications for small bowel evaluation.

Radiological imaging of the small bowel

Radiological imaging tools of the small bowel are defined as any investigations using radiological techniques to visualize the intraluminal space of the small bowel and small bowel wall, with the use of intravenously and/or intraluminal contrast agents. Currently, the radiological options for visualization of the small bowel are the small bowel follow through, computerized tomography and magnetic resonance imaging, whether using enterography or enteroclysis technique. Enterography is being defined as using only oral contrast, and enteroclysis as a 'double contrast' technique involving oral contrast as well as intraluminal air insufflation. The latter is often combined with spasmolytic agents to improve visualization of the small bowel lining.

Small bowel follow through (SBFT) and enteroclysis

The development of newer forms of small bowel imaging and endoscopy has dramatically reduced the employment of conventional barium studies for the evaluation of the small bowel. One of the main reasons being the low diagnostic yield of small bowel follow through (SBFT) series and enteroclysis, ranging between an in general disappointing diagnostic yield of estimated 0–21% [3–7]. Especially, the diagnostic yield of mucosal lesions such as angiodysplasias, as well as mild to moderate active inflammatory lesions, is reported to be disappointingly low. Unfortunately, vascular malformations and minor inflammatory changes are both reported as the most common causes of small bowel pathology in daily clinical gastroenterology practice [8,9]. Currently, emerging diagnostic tools in assessment of small bowel disease are computerized tomography (CT)- and magnetic resonance (MR)-based enterography or enteroclysis studies. These modern diagnostics offer an alternative means of detecting mass lesions as well as improved visualization of small bowel mucosa, including vascular lesions such as angiodysplasias, previously poorly or non-visualized using conventional radiography studies.

CT-enteroclysis or -enterography (CTE)

The development of multidetector-row technology has introduced new opportunities for the CT guided evaluation of the gastrointestinal tract, owing to the use of thinner collimation and faster acquisition times. CTE combines the advantages of barium enterography or enteroclysis and conventional abdominal CT examinations using intravenous administration of iodine contrast agents, allowing simultaneous evaluation of intraluminal bowel content, bowel wall, bowel mesentery, and extra-intestinal abdominal organs and vessels. In CT enteroclysis insertion of nasojejunal tube is required for administration a total volume of 1500–2000 mL of enteral contrast medium at a rate of 60–120 mL/

min with a pressured-controlled electric pump directly into the proximal jejunum. CT enterography is more patient-friendly not requiring a nasojejunal tube insertion for enteral contrast infusion. During CT enterography the contrast agent is orally administered, and often divided into multiple doses given every 20 min, beginning 60 min before the actual scanning. Due to the fact that oral contrast intake is often slower, a larger total volume of enteral contrast medium intake might be required, which can be again challenging for patients. CT enteroclysis provides better bowel distension than CT enterography, and for this reason enteroclysis is in general regarded the preferred method. Therefore, CT enterography is therefore mainly used in patients not tolerating a nasojejunal tube. Nevertheless, studies have shown no significant differences in diagnostic accuracy between CT enteroclysis and CT enterography in patients with suspected bowel disease [10,11]. The main drawback of CTE is the increased exposure to radiation, being reported consisting of up to 63 mSv in different studies, which is a major concern in younger and pregnant patients [12,13]. Furthermore, CTE is a purely diagnostic tool, not allowing biopsies of suspect gastrointestinal lesions and not allowing direct therapeutic intervention [14].

MR-enteroclysis and -enterography (MRE)

Recent improvements in MRI soft- and hardware have extended the role of MR imaging in the evaluation of the small bowel, allowing demonstration of intraluminal, mural, and extra-intestinal diseases simultaneously, with improved image quality and resolution. As with CTE, an adequate contrast enhancement with or without bowel distension is required for optimal visualization; intraluminal contrast agents may be administered orally, defined as MR-enterography, or through a nasojejunal tube, defined as MR-enteroclysis using the 'double contrast' technique, in a more or less similar fashion as with the CTE procedure. At this stage, MRE is often used in patients with known or suspected Crohn's disease, but they have an emerging role in the detection of other small bowel diseases, including small bowel tumours. In the aforementioned settings, the major advantages of the MR examinations include information revealing intra- and extramural small bowel disease at the same time, and the lack of radiation exposure. Current limitations of MRE include costs, accessibility, variability in examination quality, and, as with CTE, the impossibility to perform biopsies from suspected lesions and not allowing therapeutic interventions [15].

Small bowel endoscopy

Small bowel endoscopy is defined as any endoluminal visual examination of the small bowel, including laparotomy assisted enteroscopy, push enteroscopy, capsule endoscopy, and balloon- or device-assisted endoscopy.

Laparotomy assisted or intraoperative enteroscopy

Laparotomy assisted or intraoperative enteroscopy is defined as an endoscopic examination of the small bowel during abdominal surgery with manual external assistance of the surgeon for endoscope progression. The endoscope can be introduced either orally or via an enterotomy during a laparotomy performed by a surgeon. The advantage of intraoperative enteroscopy is the fact that with this technique the complete small bowel can be evaluated, and during the same procedure, if indicated, surgical therapy can be performed. The main disadvantages of intraoperative enteroscopy are its invasiveness, the need for surgical assistance and the high complication rate. Morbidity associated with intraoperative enteroscopy has been reported in 3–42% of cases, including serosal tears, avulsion of the superior mesenteric vein, anastomotic leakage, intra-abdominal abscess, and prolonged ileus [16]. After the introduction of balloon- or device assisted enteroscopy, intraoperative enteroscopy has become rarely needed. Currently, the role of intraoperative enteroscopy seems to be limited to selected patients in which balloon- or device assisted enteroscopy fails to achieve the diagnostic and/or therapeutic goal. For example due to limited insertion depths by balloon- or device-assisted enteroscopy as a result of adhesions often as result of earlier abdominal surgery.

Push enteroscopy

Push enteroscopy (PE) is a trans oral endoscopic examination technique using a 200- to 250-cm long flexible endoscope, often combined with an overture system to avoid intragastric looping. PE allows tissue sampling, polypectomy, and treatment of bleeding lesions of the proximal jejunum [17]. The main advantages of PE are that it is easy and quick to perform technique, and that it is readily available as there is no need to acquire a specific endoscopic and/or pump control system. All these facts avoid extra costs and, therefore, PE seems a cost-effective technique for diagnostic and therapeutic endoscopy of the proximal small bowel [18]. The main disadvantage is its limited insertion depth, reported maximally up to 130–150 cm in the proximal jejunum. In recent years, balloon-assisted endoscopic techniques have largely replaced PE in diagnostic and therapeutic procedures of the small bowel [19].

Capsule endoscopy

Capsule endoscopy (CE), introduced in 2000, is a method of endoluminal examination of the small bowel using a wireless capsule shaped tool. In most patients the capsule is swallowed and then propelled through the gastrointestinal tract by gut motility. If the patient is unable to swallow the capsule or the anatomy of the proximal gastrointestinal tract is altered due to earlier surgery, the capsule can be introduced via a gastroduodenoscopy. Special endoscopic delivery devices have been introduced to provide easy direct placement of the capsule in the proximal small bowel. Capsule endoscopy can be performed using the Given M2A video capsule system (Given Imaging Ltd, Yoqneam, Israel), the Olympus Endocapsule (Olympus America Inc., Center Valley) or MiroCam (IntroMedic Co., Seoul, Republic of Korea). The most commonly used Given capsule consists of a 26 by 11 mm device, containing a battery-powered complementary metal oxide silicon imager (CMOS), a transmitter, antenna and four light emitting diodes [20]. During the battery life of the capsule, images are recorded, and these images are reformatted into a continuous video file that can be reviewed on a normal computer using specially adapted software. After eight–ten hours, the antenna and storage unit are removed and the images transferred to a computer for analysis and reviewed by an experienced capsule endoscopist.

The main advantages of CE are the ability to visualize, in theory, the complete small bowel with minimal discomfort for the patient. The procedure also requires less physician training than advanced endoscopic techniques. The main disadvantages of this technique are the inability to manoeuvre the capsule, the lack of therapeutic options, and the relative contraindication of possible strictures, because of the risk of capsule impaction [21,22]. Furthermore, although most images are excellent, they are still not comparable to the view achieved at conventional endoscopy with gas insufflation. Moreover, incomplete small bowel visualization has been reported in approximately 30% of CE investigations, leaving especially the distal part of the ileum uninspected. The combination of suboptimal and incomplete visualization of the small bowel lining, have been put forward as the main cause of false-negative outcomes of CE procedures [23].

Balloon- and device-assisted enteroscopy techniques

Balloon assisted enteroscopy (BAE) is a generic term for endoluminal examination of the small bowel by any endoscopic technique using balloons to promote deeper insertion into the small bowel, including single balloon enteroscopy (SBE) and double balloon enteroscopy (DBE). Device assisted enteroscopy (DAE) is a generic term for endoluminal examination of the small bowel by any endoscopic technique that includes assisted progression, i.e. by a balloon, overtube, or other stiffening device. Currently, DAE is considered the 'gold standard' diagnostic tool for small bowel pathology. The main advantage of DAE is the fact that it combines the possibility to perform additional biopsies for histopathological evaluation, together with the ability to perform therapeutic interventions during the same procedure. These DAE therapeutic options cover the whole range of widely used upper endoscopy and colonoscopy interventions, including electrocoagulation, argon plasma coagulation, polypectomy, balloon dilation of strictures, and retrieval of foreign bodies, including removal of retained wireless

capsules. In majority of DAE therapeutic interventions, specially manufactured devices are used, which in general are longer and limited in external diameter, as compared to regular endoscopy devices. Another exciting and innovative diagnostic tool is the use endoscopic ultrasound for evaluation of small bowel tumours. The latter is performed using a specialized longer, and smaller in diameter, ultrasound catheter probe, which allows differentiation between gastrointestinal stromal tumours (GIST) and adenocarcinoma of the small bowel wall.

Double balloon enteroscopy (DBE)

The DBE system, first introduced by Yamamoto and colleagues in 2001, allows deep intubation of the small bowel by pleating the bowel onto a long, flexible endoscope fitted with an overtube. The DBE system consists of a diagnostic and therapeutic endoscope, the EN-450P5 and EN-450T5 (Fujinon, Saitama, Japan) respectively, in combination with a special balloon sufflation device and remote control of the latter device [24]. The endoscope and the accompanying overtube have both an in- and deflatable balloons at their distal end. By intermittent inflation and deflation of these two balloons, combined with instrument insertion and retraction, large portions of the small bowel can be pleated on the overtube using the so-called "push and pull technique" [24,25]. During withdrawal of the endoscope, small parts of the small bowel are 'released' from the overtube, enabling the endoscopist to assess the small bowel lining and, if indicated, perform biopsies and/or therapeutic interventions. In theory, this enables the endoscopist to achieve complete visualization of the small bowel. However, in general practice a combination of the anterograde, i.e. proximal or oral, route and the retrograde, i.e. distal or anal, route is used to achieve complete small bowel examination. The procedure is performed using conscious sedation or general anaesthesia. A range of accessories has been developed to allow tissue sampling and to perform 'thought the endoscope' therapeutic procedures. DBE is a complex examination and should only be carried out by trained and experienced endoscopists. The standard method requires two individuals: an operator who handles the enterosocope and an assistant who handles the overtube. Complete evaluation of the small bowel, or total enteroscopy, performed by single approach or combined antero- and retrograde approaches, have a reported success rate ranging from 16 up to 86% [24,26]. However, DBE is not without limitations. The prolonged duration of the procedure, increased amounts of sedation used, and the frequent requirement of additional assistance are all potential problems that impact widespread use of this challenging technique. Furthermore, the overall complication rate of diagnostic DBE procedures is reported to be up to 1%, and is therefore higher as compared to other diagnostic endoscopic procedures. The most reported significant complication during or after diagnostic DBE procedures is acute pancreatitis. Two large multi-centre, one national and one internationally, conducted studies both showed a comparable incidence of this serious complication. The range of incidence of acute pancreatitis was respectively reported to be 0.2 and 0.3% after anterograde DBE procedures [27,28]. Quite some studies have addressed the issue of the relation of acute pancreatitis and anterograde DBE, by investigating the pancreatic enzyme levels (serum amylase and/or lipase levels) before and after anterograde DBE procedures. All these published studies seem to agree on the fact that there is an evident relation between a prolonged total procedural duration time and hyperamylasemia. Moreover, there seems to be a role for early insufflation of the DBE balloons, i.e. in the proximal part of the duodenum and/or jejunum. The clinical significance of this reported post-procedural hyperamylasemia is still open for debate: elevation of enzymes is reported in 13–51% of procedures, while the incidence of clinical acute pancreatitis is much lower, ranging from 1 to 13% of cases [29–33]. Whilst interpreting the data of these studies, one should take in mind that three studies, out of in total five, consisted of a relatively small number of patients, ranging from 13 to 48 procedures in total [29,30,32]. In the two larger studies, including a total of 135 and 92 patients, both the incidence of hyperamylasemia and acute pancreatitis were reported to be the lowest, 17–39% and 0.7 and 3%, respectively [31,33]. The current advice to minimize the risk of acute pancreatitis during or after anterograde DBE procedures is to prevent longer duration of the anterograde DBE procedure, and to insufflate both DBE balloons only after introduction beyond ligament of Treitz. The overall risk of acute pancreatitis during or after retrograde DBE seems to be very low, or even non-existent. In a prospective study

no post-procedural rise of serum amylase or lipase was found in 8 patients during or after a retrograde DBE procedure [32]. Until now, no cases of acute pancreatitis after retrograde DBE have been published. In line with the reported complication rates with conventional diagnostic and therapeutic endoscopy, the risk of significant complications is higher in therapeutic DBE procedures, as compared to diagnostic DBE procedures. The rate of complications after therapeutic DBE procedures is estimated to be around 3–4%, comparable or slightly higher than the reported complication rates of conventional therapeutic colonoscopy procedures [27,28].

Single balloon enteroscopy

The SBE system was introduced in 2007 as a simplification of the DBE system. The enteroscope (X SIF-Q160Y or -Q180, Olympus Optical Co, Tokyo, Japan]) is also a high-resolution video endoscope. The system uses only one balloon, which is attached to distal end of the overtube. In contrast to the DBE, the SBE system uses angulation of the tip of the enteroscope instead of the inflated balloon as 'fixation' of this point. In theory, the same 'push and pull technique' as advocated by the DBE system is used to pleat the small bowel on to the overtube, and to inspect on withdrawal [34]. At present, fewer data are available with regards to the complication rates in diagnostic and therapeutic SBE. The largest prospective study to date, suggests that the risk of post procedural hyperamylasemia and acute pancreatitis following anterograde SBE procedures is comparable to that after anterograde DBE procedures, being reported after 16 and 0% of procedures, respectively [35]. The risk of deep mucosal tears or perforation is estimated between 0 and 3% in diagnostic procedures [34,35]. It is suggested that the 'hooked tip' technique used during SBE procedures increases the risk of small bowel perforation during this procedure. Therefore, an alternative fixation technique of the tip of the SBE endoscope was suggested, named the 'power suction technique', which in theory should reduce the risk of this complication [36]. Until now, no data have been published to compare these different fixation techniques used during SBE procedures, in regards to performance, outcome and/or complication rates. The complication rate of therapeutic SBE procedures seems comparable to the rate of therapeutic DBE procedures, varying between 0 and 5%. However, in interpreting these therapeutic SBE complication data, one should realize that so far all presented studies consisted of a limited number of therapeutic SBE procedures [34,35,37].

To date, one case of acute pancreatitis after a retrograde, i.e. anal, SBE has been published. The authors of the latter case suggest that insufflation of the overtube balloon in the colon, resulting in local compression and irritation of the pancreas, as being the cause of to the pancreatitis. The authors suggest to postpone insufflation of the overtube balloon until the terminal ileum is reached, to prevent this rare and unlikely complication of retrograde SBE [38].

Spiral enteroscopy

Spiral enteroscopy (Spirus Medical Inc., Stoughton, MA, USA) is the most recently introduced device assisted enteroscopy technique. An enteroscope is passed through a disposable overtube, which has raised helical spirals of 5 mm in height at its distal 21 cm end, facing the tip of the endoscope. The enteroscope can be locked in the overtube allowing the option of spiralling the overtube and enteroscope, in to the small bowel using clockwise rotation. Alternatively, the overtube can be unlocked, allowing the endoscope to be advanced into the small bowel through the overtube [39,40]. One of the advantages of the spiral enteroscopy system is that it requires no further specific equipment. The spiral overtubes can be used both with 'older types' enteroscopes and paediatric colonoscopes. Another advantage seems the 'speed' of introduction during the anterograde spiral enteroscopy procedure: experienced endoscopists are able to perform deep enteroscopy procedures within a time frame of 30–45 min. The latter being fairly quick, as compared to DBE and SBE procedures which require at least 60 min for completion. Until now, no cases of acute pancreatitis after spiral enteroscopy have been published. The main complication with diagnostic spiral enteroscopy seems to be perforation of the small bowel, occurring in 0.3% in a retrospective analysis of 1750 anterograde spiral enteroscopy cases [41]. A prospective study performed in the USA showed that spiral enteroscopy was feasible and safe in an elderly population, only four mild complications and no

perforations were reported [42]. A recently published study showed that retrograde spiral enteroscopy was feasible and successful in 22 patients, one minor complication and no perforation was reported [43].

Indications and choice of small bowel imaging and/or endoscopy

Obscure gastrointestinal bleeding (OGIB)

The most common indication for small bowel imaging and/or endoscopy is obscure gastrointestinal bleeding (OGIB). OGIB is defined as occult or overt bleeding of unknown origin that persists or reoccurs after an initial negative endoscopic evaluation including upper endoscopy and colonoscopy, the latter both often repeatedly performed. OGIB has been shown to be defined to occur in approximately 5% of all patients who present with gastrointestinal haemorrhage [44]. In the evaluation and treatment of OGIB, capsule endoscopy and DAE are considered complementary procedures [45,46]. DBE and CE have shown comparable diagnostic yields in patients evaluated for OGIB (see Table 1 below). A recent updated and revised meta-analysis of ten studies, of in total 642 patients, demonstrated that the pooled overall diagnostic yield for CE and DBE was 62 and 56%, respectively [47]. Unless contra-indicated, CE is usually the initial diagnostic test in patients with suspected OGIB, because of its minimally invasive nature and therefore excellent tolerability, and theoretical the ability to visualize the entire small bowel. A secondary DAE is indicated if CE detects a lesion requiring biopsy or endoscopic intervention, or in patients whom have a high suspicion of small bowel bleeding despite a negative initial CE. This approach leads to a significant clinical improvement in over 75% of treated patients, including reduced transfusion and iron requirement needs [48]. However, from a cost minimization perspective, an initial DAE approach is the least expensive strategy when the need for therapeutic intervention or definitive diagnosis is highly probable [49]. As the fast majority of lesions responsible for OGIB are located in the proximal small bowel, it is reasonable to start with an anterogradel DBE in these cases [48,50]. An initial capsule endoscopy study remains the preferred initial strategy because of its relative non-invasive nature and acceptable diagnostic yield in OGIB patients. Current guidelines, including the ASGE guideline, advocate the use of CE as primary diagnostic tool for evaluation of the small bowel in OGIB patients [51].

Currently, the use of modern non-invasive diagnostic radiological investigations, as CTE or MRE in context of OGIB seems to be limited. The diagnostic yield of multidetector CT enterography or enteroclysis in OGIB patients is overall disappointing, ranging from 22 to 42%. A higher sensitivity, up to 55%, was reported in patients with massive bleeding or recurrent overt OGIB [52,53]. There are limited data concerning the use of MR enterography or enteroclysis in OGIB patients. A recently published prospective study comparing CE, DBE and MRE in a total of 38 consecutive OGIB patients, showed a disappointing sensitivity of only 21% for MRE as compared to the findings with DBE, the latter diagnostic tool which was considered the 'gold standard' in this study [54]. The relatively low sensitivity of CTE and MRE in OGIB patients may not come as a surprise, as the most coming finding in these particular patients group is reported to be small bowel angiodysplasia or vascular malformations. The latter vascular lesions are, in general, small in size and do not show as 'masses' and therefore are easily missed by these radiological investigations, which mainly focus on identification

Table 1
Comparison of diagnostic yield for different techniques in OGIB or CD patients.

Diagnostic yield	OGIB	CD
SBFT	0–21%	0–32%
MRE/CTE	22–48%	21–39%
CE	38–83%	60–71%
DAE	43–80%	50–57%

OGIB, obscure gastrointestinal bleeding; CD, Crohn's disease; SBFT small bowel follow through; MRE/CTE, MR/CT-enteroclysis or enterography; DAE, device assisted enteroscopy.

on small bowel masses and/or differences in contrast enhancement. In future, further refinements of the CT and MR techniques might improve resolution and therefore the detection rate of these lesions.

Suspected or known Crohn's disease (CD)

Most cases of CD affect the distal small bowel, i.e. terminal ileum, and right colon, whereas 20–30% of patients may have disease limited to upper gastrointestinal tract, including the small bowel. Especially the paediatric CD population is well known to present with a higher incidence of proximal small bowel involvement as compared to the adult CD population [55]. Small bowel involvement of CD is known as an independent risk factor for complicated disease. CD patients with small bowel activity more often need step-up medical treatment and surgical interventions [56]. Therefore, it seems critical to evaluate the small bowel in all patients with suspected inflammatory bowel disease to assess small bowel disease activity, and to 'stage' the extent and severity of disease. Until recently, the diagnosis of small-bowel CD was made on the basis of ileocolonoscopy and/or small bowel radiological diagnostics. The newer endoscopic techniques have improved the clinician's ability to identify, often subtle, lesions that may be associated with small bowel CD (see Table 1) [51,52]. A recently published large meta-analysis of 12 studies, of in total 552 included patients, compared the diagnostic yield of CE with other diagnostic modalities, including ileocolonoscopy, push enteroscopy, SBFT, CT enterography and MR enterography in both suspected and established CD patients. CE demonstrated to be superior to SBFT, CTE, and ileocolonoscopy in suspected CD patients. Moreover, CE also proved to be more effective in established CD patients, as compared to SBFT, CTE and push enteroscopy [57]. A recently published prospective study in 38 patients compared the use of CE, MR enteroclysis and DBE in patients with suspected or known CD. The results of the latter study demonstrate a better performance for MRE as compared to CE, especially due to the fact that a high incidence of significant small bowel stenosis prohibited the use of CE as a diagnostic modality in this patient group. MRE was recommended as the first-choice, and non-invasive, diagnostic procedure in patients with suspected small bowel CD. Guided by the outcome of the MRE, a CE can be conducted to assess mild to moderate ulcerative small bowel disease, or a BAE can be scheduled to arrange histopathological confirmation or to perform therapeutic intervention, i.e. dilation therapy [58]. The risk for CE retention in CD patients is estimated to be 5–13%, which is a notable limitation for this procedure in this patient group [59]. European guidelines, published by the ECCO and ESGE, both state that CE is the first choice diagnostic procedure for evaluation of small bowel mucosal lesions in suspected and known CD, and that small bowel imaging or a patency capsule should precede CE to minimize the risk of capsule retention [60,61]. The ECCO guideline specifically states that it is important to realize that the clinical significance of these small bowel mucosal lesions identified with CE in patients with known CD remains unclear. Furthermore, it mentions that there might be a role for CE in inflammatory bowel disease unclassified patients, to identify patients with lesions compatible with CD. The ECCO guideline also states that the potential role for CE in paediatric patients with suspected or known CD, is comparable to that of the adult population. CE seems to have a comparable diagnostic yield in paediatric patients, and can be used safely in this specific patient population [61]. DAE is indicated in patients with suspected small bowel CD disease, in order to confirm the diagnosis of CD and to exclude alternative diagnosis, i.e. abdominal tuberculosis, small bowel lymphoma, or carcinoma. Adequate endoscopic evaluation of small bowel strictures with additional biopsies for histopathology or dilation of medical therapy refractory strictures can be successfully performed using DAE [62]. Also DAE is indicated for endoscopic removal of foreign bodies such as a capsule or bezoar, and can in this way prevent the necessity for surgical intervention [63].

(Inherited) Polypoid syndromes

Peutz-Jeghers syndrome (PJS) is an inherited, autosomal dominant disorder distinguished by pigmented mucocutaneous lesions and hamartomatous polyps in the gastrointestinal tract. Prevalence of PJS is estimated to range from one in 8300–280,000 individuals. The two main challenges in the management of gastrointestinal tract related complications in PJS patients are firstly to prevent

polyp related complications, such as intussusception and bleeding, and secondly to reduce the long term cancer risk. Therefore, regular assessment of the gastrointestinal tract, including the small bowel, is part of the screening program in these patients. Currently, there is discussion about at what age small bowel screening should be initiated, taking into account that over two-thirds of PJS patients already had at least one intussusception at a median age of 16 (range 3–50) years [64]. Two studies have confirmed that CE has a significant improved diagnostic yield for small bowel polyp detection in PJS patients, as compared to SBFT [65,66]. Comparative studies using CE and MRE in PJS patients has already shown that CE is superior for detection of smaller polyps, both modalities seem to have comparable diagnostic yields for polyps 15 mm, or larger in size. MRE demonstrated improved determination of localization and actual size of the small bowel polyps [67]. However, a recent study showed that MRE may be superior for detection of larger small bowel polyps, which are clinically more relevant, and may be more reliable in size assessment of small bowel polyps, as compared to CE [65]. DBE has already shown to be of use in detection and removal of small bowel polyps in PJS patients [68]. However, long-term prospective studies on the outcomes of PJS patients screened with CE and/or DAE are currently lacking. In theory, DAE combines the 'gold standard' diagnostic and therapeutic tool, to prevent small bowel polyp related complications, but it invasiveness inhibits it use as a primary diagnostic in PJS patients. Centers of excellence with larger PJS patient cohorts, currently promote the use of CE and/or MRE as the first diagnostic procedure for screening of small bowel polyps, this followed by a guided DAE procedure for endoscopic removal of small bowel PJS polyps. According to a group of European PJS experts it is recommended to a perform small bowel surveillance every three years if polyps are found at the initial examination, starting from the age of 8 years, or earlier if the patient is symptomatic [69]. SBFT is currently regarded obsolete in surveillance of PJS, since it has shown a lowered diagnostic yield for small bowel polyps and due to its significant radiation exposure.

Until now, the use of CE and/or DAE for small bowel screening in patients with familial adenomatous polyposis (FAP) has only been reported in smaller patient cohorts. Using CE in up to 87% of patients small bowel polyps were detected, as with DBE in up to 75% of patients adenomatous polyps were found and resected [70,71]. There seems to be a potential role for new endoscopic imaging techniques, i.e. chromoendoscopy and/or narrow band imaging, for improved detection and staging of small bowel polyps in these particular patients [72].

Summary

Currently, various radiological, endoscopic and surgical options are available for assessment of the small bowel, each with their own advantages and shortfalls. To date the classical SBFT has completely been replaced by newer radiological and endoscopic techniques for evaluation of the small bowel. Currently, the first line radiological diagnostics for small bowel evaluation are CTE and MRE. Both seem to have comparable diagnostic yields, and clinical applicability mainly depends on the availability of techniques. The introduction of CE and DAE procedures has transformed the approach to the evaluation and management of small bowel diseases over the past decade, especially for the indication obscure gastrointestinal bleeding. CE is generally accepted as the first choice investigation in the latter patient group. CE combines a minimal invasive approach with an acceptable diagnostic yield. DAE is in this patient group reserved for patients with abnormal findings on previous CE, i.e. a 'guided DAE'. DAE has already shown to be the 'gold standard' endoscopic investigation of the small bowel, with the superior capacity to perform additional diagnostics, i.e. biopsies for histopathology, and to ability to perform endoscopic therapeutic interventions. These properties make DAE the first choice in patients with known small bowel pathology, needing histopathological confirmation and/or endoscopic therapeutic intervention. The potential clinical benefit of DAE therapeutic intervention has already been shown in patients with Crohn's disease related small bowel strictures and Peutz-Jeghers syndrome related small bowel polyps.

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Practice points

1. Small bowel follow through is obsolete in modern small bowel imaging due to its low sensitivity.
2. Capsule endoscopy is the first line diagnostic choice in OGIB patients.
3. Capsule endoscopy and MR enteroclysis or enterography can both be used as first line small bowel diagnostic in patients suspected for or with known Crohn's disease.
4. Device assisted enteroscopy is best performed complementary to capsule endoscopy, or MR of CT enteroclysis or enterography, to provide additional histopathology or to perform endoscopic therapeutic interventions.
5. To date device assisted enteroscopy remains the 'gold standard' for small bowel pathology.

Research points

1. Larger prospective studies comparing CE, BAE and newer CT and MR techniques for diagnostic yield and long-term outcomes in the different patient groups.
2. Cost-effectiveness studies for patient selection and strategies in OGIB patients.
3. Prospective, preferably placebo-controlled, studies to clarify the clinical significance of small bowel mucosal lesions in patients with known Crohn's disease.
4. Long-term prospective studies to provide evidence-based guidelines for small bowel screening for familiar polypoid syndrome; including the evaluation of newer endoscopic imaging techniques as chromoendoscopy, narrow band imaging and FICE in these patients.

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