Guideline

Clinical Practice Guideline for Enteroscopy

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Management of small bowel diseases has evolved since the advent of capsule endoscopy (CE) and balloon-assisted enteroscopy (BAE). One of the most common indications for enteroscopy is obscure gastrointestinal bleeding (OGIB), followed by small bowel stenosis, tumors, and inflammatory bowel disease. Although enteroscopes have been regarded as useful tools, correct guidelines are required to ensure that we manipulate these enteroscopes safely and efficiently in clinical practice. Herein, the Japanese Gastroenterological Endoscopy Society has developed ‘Clinical Practice Guidelines for Enteroscopy’ in collaboration with the Japanese Society of Gastroenterology, the Japanese Gastroenterological Association, and the Japanese Association for Capsule Endoscopy. These guidelines are based on the evidence available until now, but small bowel endoscopy is a relatively new technology, so the guidelines include recommendations based on a consensus reached among experts when the evidence has not been considered sufficient. These guidelines were not designed to be disease-based, but focus on how we should use small bowel CE and BAE in everyday clinical practice.

Key words: balloon-assisted endoscopy, obscure gastrointestinal bleeding, patency capsule, small bowel capsule endoscopy, small bowel disease

INTRODUCTION

HISTORICALLY, DEVELOPMENT OF the small bowel enteroscope started almost simultaneously with that of the colonoscope without lagging behind. In 1971, Hiratsuka et al. reported the first success of total enteroscopy using the ropeway method. Total enteroscopy was also achieved with the ‘sonde’ method. Both methods, however, were too tortuous, time-consuming, and technically difficult to be widely adopted. Afterwards, ‘push’ enteroscopy went mainstream for approximately 30 years, when the deep portion of the small intestine was virtually inaccessible by endoscopy. At the beginning of the 21st century, the advent of capsule endoscopy (CE) and balloon-assisted endoscopy (BAE) enabled observation of the entire small intestine and, nowadays, these enteroscopes have been widely used in daily practice. It is not an exaggeration to say that these two enteroscopic procedures have brought about a revolution in the diagnosis and the treatment of small bowel diseases.

The guideline committee of Japanese Gastroenterological Endoscopy Society (JGES) decided to develop the Clinical Practice Guidelines for Enteroscopy to ensure that enteroscopes are used correctly in clinical practice. Unlike the handbook previously issued under the supervision of JGES as a form of expert guidance (‘Gastroenterological Endoscopy Handbook’ compiled by JGES Postgraduate Education Committee and issued in May 2012), these guidelines have been compiled as authoritative guidelines based on the available evidence and consensus reached through scientific methodologies. These guidelines are not composed in a clinical question (CQ)-style but consist of a general discussion and a more specific discussion: they first outline the features, procedures, and adverse events associated with the use of small bowel CE and BAE in the general discussion section before summarizing the statements and descriptions for each item in the form of a review paper.

In fact, only a few academic papers with a high level of evidence have been published because small bowel endoscopy is a new procedure. Accordingly, these guidelines contain relatively more expert consensus statements, but it is nevertheless an authoritative document that developed through scientific methodologies. It is expected
to provide useful guidance in the clinical practice of enteroscopy.

**PROCESS OF DEVELOPING THE GUIDELINES**

**Committee members**

The JGES Guideline committee selected members for the development of the Clinical Practice Guidelines for Enteroscopy in cooperation with the Japanese Society of Gastroenterology, the Japanese Gastroenterological Association, and the Japanese Association for Capsule Endoscopy. Table 1 lists all the members.

**Evidence level, strengths of recommendations, statements, and description**

Based on discussion among the members, the committee selected the following important enteroscopy-related topics: (i) obscure gastrointestinal bleeding (OGIB); (ii) stenosis; (iii) tumors; (iv) inflammatory diseases; and (v) others. Two committee members were assigned to each topic. Each pair of committee members drafted CQ appropriate for each topic. Draft CQ were discussed at the committee meeting prior to preparation of the final CQ. The members conducted a literature search of academic papers concerning each topic using PubMed and the Japan Medical Abstract Society database and prepared evidence-based statements and descriptions. The committee members determined the evidence level of the articles and the recommendation strengths of the statements based on the grades recommended by the Medical Information Network Distribution Service (MINDS) (Table 2). In each statement, the evidence levels of the articles were determined according to the relevance to each statement. Therefore, the same article could have different levels of evidence for different statements. When each committee member completed the statements and descriptions for each topic, all of the members gathered and held a meeting to evaluate each statement using the Delphi method. All the members evaluated each statement by voting on a scale from 0 to 9. Modifications and votes were repeated until at least a median scale of 7 was obtained. Once the draft guidelines were completed, the evaluation committee evaluated them.

**Table 1** Committee members for development of the Clinical Practice Guidelines for Enteroscopy

<table>
<thead>
<tr>
<th>Japan Gastroenterological Endoscopy Society Guideline Committee</th>
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<tr>
<td><strong>Director:</strong> Kazuma Fujimoto (Department of Internal Medicine and Gastrointestinal Endoscopy, Saga Medical School, Faculty of Medicine, Saga University)</td>
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<tr>
<td><strong>Chairman:</strong> Kazuma Fujimoto (Department of Internal Medicine and Gastrointestinal Endoscopy, Saga Medical School, Faculty of Medicine, Saga University)</td>
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<tr>
<td><strong>Working Committee Chairman:</strong> Hironori Yamamoto (Department of Medicine, Division of Gastroenterology, Jichi Medical University)</td>
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<tr>
<td><strong>Chairman of Development Committee:</strong> Haruhiko Ogata (Center for Diagnostic and Therapeutic Endoscopy, Department of Internal Medicine, School of Medicine, Keio University)</td>
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<td><strong>Committee members:</strong> Takayuki Matsumoto (Division of Gastroenterology, Department of Internal Medicine, Iwate Medical University)</td>
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<td><strong>Committee members:</strong> Naoki Ohmiya (Department of Gastroenterology, Fujita Health University School of Medicine)</td>
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<td><strong>Committee members:</strong> Kazuo Ohtsuka (Department of Endoscopy, Tokyo Medical and Dental University)</td>
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<td><strong>Committee members:</strong> Kenji Watanabe (Department of Gastroenterology, Osaka City General Hospital)</td>
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<td><strong>Committee members:</strong> Tomonori Yano (Department of Medicine, Division of Gastroenterology, Jichi Medical University)</td>
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<tr>
<td><strong>Chairman of the Evaluation Committee:</strong> Toshiyuki Matsui (Clinical Research Center for Medical Science, Department of Gastroenterology, Fukuoka University Chikushi Hospital)</td>
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<td><strong>Evaluation Committee member:</strong> Kazuhide Higuchi (Second Department of Internal Medicine, Osaka Medical College)</td>
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<td><strong>Evaluation Committee member:</strong> Tetsuya Nakamura (Department of Medical Informatics, Dokkyo Medical University)</td>
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2Japanese Society of Gastroenterology.
3Japanese Gastroenterological Association.
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Table 2  Evidence level and strength of recommendations (grades recommended by MINDS)

<table>
<thead>
<tr>
<th>Evidence level</th>
<th>Description</th>
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<tbody>
<tr>
<td>I</td>
<td>Systematic review/meta-analysis</td>
</tr>
<tr>
<td>II</td>
<td>Based on at least one randomized controlled study</td>
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<tr>
<td>III</td>
<td>Based on a non-randomized control study</td>
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<tr>
<td>IVa</td>
<td>Analytical epidemiological study: Cohort study</td>
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<tr>
<td>IVb</td>
<td>Analytical epidemiological study: Case-control study, Cross-sectional study</td>
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<tr>
<td>V</td>
<td>Descriptive study (case report or case series)</td>
</tr>
<tr>
<td>VI</td>
<td>Expert committee opinions or personal expert opinions not based on patient data</td>
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Strength of recommendation

- **A**: It is strongly recommended based on sound scientific evidence
- **B**: It is recommended based on scientific evidence
- **C1**: It is recommended without scientific evidence
- **C2**: It is not recommended without scientific evidence
- **D**: It is not recommended based on scientific evidence that shows ineffectiveness and/or harmfulness

MINDS, Medical Information Network Distribution Service.

When reimbursement for small bowl CE was first approved by the national medical insurance system in Japan in 2007, its indication was restricted to OGIB; that is, gastrointestinal bleeding of unknown origin that persists or recurs after negative results of upper endoscopy and colonoscopy. This restriction was based on concerns over possible capsule retention at stenotic lesions. When Covidien’s patency capsule was approved for the health insurance system in 2012, the indications for CE were expanded to ‘patients known to have or suspected of having small bowel disease’ on the condition that the patency of the gastrointestinal tract was confirmed with the patency capsule (PillCam® patency capsule; Covidien, Dublin, Ireland) for patients with suspected stenosis before CE was carried out. CE, however, is contraindicated or its use should be carefully considered when patients have known severe stenosis in the gastrointestinal tract, intestinal obstruction, a history of abdominal irradiation and when patients are pregnant or not willing to agree to possible endoscopic or surgical retrieval of the retained CE. Since a study reported that the frequency of complications such as retention in the body did not differ regardless of the age of the patients who were able to swallow a CE, patients under the age of 18 years were approved in Japan as additional candidates for CE in January 2015.

**Target patients**

These guidelines apply to the medical care of patients who are suspected of having small bowel disease and in whom enteroscopy with a small bowel CE or a BAE is considered an effective option.

These guidelines are intended to be used by clinicians and their advising doctors who treat patients with small bowel diseases. These guidelines provide standards for practice only; thus, careful consideration should be given to each patient’s own will, age, possible complications, and social circumstances.

**CAPSULE ENDOSCOPY (CE)**

Features and indications for CE

Capsule endoscopy (CE) was reported to achieve total enteroscopy in 85% of patients with OGIB. Recent advances in the technology of CE have enabled improved image quality, wider viewing angle, adaptive frame rate according to motion, increased image reading efficiency, and extended recording time. Development of the patency capsule has expanded the indications for CE for small bowel disease.

Current status of small bowel CE

Small bowel CE that are approved in Japan for clinical use are PillCam SB2 and SB3 from Covidien and EndoCapsule from Olympus (Tokyo, Japan). Small bowel CE is relatively simple, safe, and comfortable for patients; however, some lesions can be missed or are depicted only partially. Thereby, doctors should understand its drawbacks and interpret the results.

Patency of the small bowel should be confirmed with a patency capsule 30–33 h after its ingestion. When a patency capsule is excreted, intact capsule (body and timer plugs are virtually intact) or intact body (body is intact and hard but timer plugs have eroded) should be confirmed by inspection and palpation (Fig. 1). If the patency capsule remains in the body but is detected in the large bowel on X-ray examination, the gastrointestinal tract is also considered to be patent; however, entry into the large bowel should be verified by further examinations such as a CT scan if necessary, because plain X-ray can be deceptive. The PillCam patency capsule now available in Japan has been modified from its European version (Agile™ patency capsule, Covidien, Dublin, Ireland) for the Japanese market by removing the radiofrequency
Identification (RFID) tag from the capsule. As the patency capsule contains barium sulfate, it cannot be used in patients who are allergic to barium.

Adverse events associated with small bowel CE

The main adverse event associated with CE is capsule retention. It is defined as retention of the capsule in the gastrointestinal system for more than 2 weeks or retention possibly requiring subsequent endoscopic or surgical retrieval. Incidence of capsule retention was reported to be 1.4% in OGIB patients, 7.4% in patients with documented Crohn’s disease, and 6.3% in suspected Crohn’s disease. Capsule retention almost never results in symptomatic events such as intestinal obstruction, but if the capsule is not excreted spontaneously or with medical intervention, BAE or surgery is carried out to retrieve it.

Aspiration into the respiratory tract and capsule dysphasia are also reported adverse events. In patients with dysphagia, the assistance of upper gastrointestinal endoscopy should be considered.

REFERENCES

BALLOON-ASSISTED ENDOSCOPY (BAE)

Features of BAE

The basic principle of balloon-assisted endoscopy (BAE) is that the balloon on the tip of the overtube grips the intestinal tube from the inside to prevent unwanted extension of the intestine and allows the maneuver to be transferred precisely to the tip of the endoscope. In addition, pulling both the endoscope and the overtube while holding the intestine enables the intestine to be pleated over the overtube and shortened. This grip and pull allows the endoscope to advance through the intestine, the length of which far exceeds the working length of the endoscope. Equipped with an accessory channel, it can carry out biopsy, endoscopic ultrasonography (EUS), marking, and various endo-therapies because the balloon endoscope maintains good maneuverability even deep in the small intestine.

There are two types of BAE system: double-balloon endoscopy (DBE) having a second balloon at the tip and single-balloon endoscopy (SBE) without a balloon at the tip. DBE was first reported by Yamamoto et al. in 2001 and launched for commercial use by Fujinon (currently Fujifilm, Tokyo, Japan) in 2003. Along with the CE system, which came onto the market around the same period, the BAE system gained widespread global acceptance and greatly advanced the diagnosis and treatment of small bowel diseases. SBE launched by Olympus Corp. (Tokyo, Japan) in 2007 has been widely used like DBE and has contributed to the increasing use of BAE.

BAE procedure

Either a transoral or a transanal approach is decided depending on the patient’s symptoms and other imaging examination results. The preparation differs depending on the route of insertion as with the case of conventional upper and lower gastrointestinal endoscopy: transoral BAE requires overnight fasting only, whereas transanal BAE involves giving a laxative and bowel preparation. BAE is commonly carried out under deep sedation when the transoral route is chosen and under conscious sedation when the transanal route is used.

Balloon-assisted endoscopy is commonly carried out by two persons: the operator who controls the endoscope and the assistant who operates and holds the overtube. However, single-operator methods are also available: using a unique technique or an auxiliary tool allows a single operator to carry out BAE.

Insufflation with carbon dioxide (CO₂) has been reported to be effective in BAE as in other endoscopic procedures. An excessive amount of gas in the bowel prevents the shortening procedure, making it difficult to insert the endoscope deeper. CO₂ gas dissolves in water at a rate more than 100-fold higher than air and is rapidly absorbed and exhaled through the breath, so insufflation of CO₂ allows for deeper intubation of the scope in BAE and increases the total enteroscopy rate. It also minimizes post-endoscopy discomfort.

Until physicians completely master the techniques of the BAE, they may use fluoroscopy to verify the position of the scope during insertion. As physicians become more adept in the technique, the less frequently fluoroscopy needs to be used. Once the technique is mastered, fluoroscopy is used only when the scope position needs to be checked in patients in which insertion into the small bowel is challenging and when a water-soluble contrast medium is used to visualize a tumor, stricture, or fistula.

Adverse events associated with BAE

Adverse events associated with BAE include perforation, bleeding, aspiration pneumonia, infection, and mucosal damage, which are similar to those for upper and lower gastrointestinal endoscopy, and acute pancreatitis, an adverse event unique to BAE.

Concerning adverse events associated with DBE, in their systematic review, Xin et al. collected data on 9047 cases and reported that major adverse events occurred in 0.72% of cases (61): 0.2% (20) were cases of perforation, 0.2% (17) were cases of acute pancreatitis, 0.09% (8) were cases of aspiration pneumonia, 0.07% (6) were cases of bleeding, and 0.1% (10) were others. Adverse events associated with SBE have been reported only in studies involving a small number of patients.

The incidence of acute pancreatitis after transoral DBE was reported to be 0.3–0.5% in large retrospective studies. In a prospective study, hyperamylasemia and acute pancreatitis after transoral DBE were reported to account for 25–50% and 3–12%, respectively, with long procedure time cited as a factor contributing to the occurrence of hyperamylasemia.

Most post-BAE pancreatitis occurred mainly in the tail of the pancreas, suggesting that it was caused by the
physical load applied to the duodenum and pancreas.\textsuperscript{15} Acute pancreatitis after transoral DBE is reported in most studies, but there are studies reporting the occurrence of acute pancreatitis after transoral SBE\textsuperscript{16} and very rarely cases of acute pancreatitis after transanal DBE\textsuperscript{17} and transanal SBE.\textsuperscript{18}

**Total enteroscopy with BAE**

Total enteroscopy may be successfully carried out by the transoral or transanal route in BAE. In most cases, however, transoral BAE and transanal BAE are combined to achieve total enteroscopy: clipping or tattooing is done for sites when insertion becomes difficult by one of the routes and then the marked sites are accessed by the other route.

The systematic review carried out by Xin \textit{et al.}\textsuperscript{10} up until 2010 showed that the total enteroscopy rate for DBE was 44.0\% (569 of 1243 cases) and that total enteroscopy was achieved in nine cases (1.6\%) by the transoral route only.

Data on the total enteroscopy rate collected by Takano \textit{et al.}\textsuperscript{19} showed that the total enteroscopy rate for SBE was 16.7\% (20 of 120 cases). Takenaka \textit{et al.}\textsuperscript{20} reported that total enteroscopy was achieved only by the transanal route in 11 out of 90 Crohn’s disease patients (12.2\%).

Comparative studies between DBE and SBE were reported in Japan\textsuperscript{19} and Europe\textsuperscript{21} and showed that the total enteroscopy rate was significantly higher in DBE than in SBE.

Total enteroscopy rate for DBE had been considerably lower in reports from the USA and Europe than in those from Japan. However, as far as recent prospective studies are concerned, no differences exist: 71\% (34 of 48 cases) in Japan\textsuperscript{22} versus 71\% (45 of 63 cases) in Europe and the USA.\textsuperscript{21,23}

**REFERENCES**

20. Takenaka K, Ohtsuka K, Kitazume Y \textit{et al.} Comparison of magnetic resonance and balloon enteroscopic examination of
patients with lesions from the upper gastrointestinal tract reported that black stool was commonly observed in a center study using DBE in Japanese patients with OGIB depending on gastrointestinal tract transit time, a multi-center study using DBE in Japanese patients with OGIB.1


### DETAILED DISCUSSION

**Obscure gastrointestinal bleeding (OGIB)**

**Statement: 1-1**

The cause and site of bleeding in the small bowel can be estimated by asking patients about the following points;

- presence/absence of hematemesis
- color, consistency, and frequency of stool
- abdominal symptoms
- presence/absence of epistaxis
- past medical history, comorbidities or medications given
- family history

These questions are also useful in designing diagnosis/treatment strategies.

Median Delphi score: 9, Minimum score: 8, Maximum score: 9

Evidence level: IVb–V, Strength of recommendation: C1

### REFERENCES


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**STATEMENT: 1-2**

It is known that the diagnostic yield of enteroscopy for OGIB will be reduced if not performed within 2 weeks after the bleeding episode. Even if it is performed timely, in often cases evidence of bleeding cannot be obtained or the bleeding source cannot be identified. Therefore enteroscopy should be performed as quickly and repeatedly as possible until the aim is achieved.

Median Delphi score: 9, Minimum score: 8, Maximum score: 9
Evidence level: IV–V, Strength of recommendation: C1

**COMMENTARY**

Bresci et al. reported that the diagnostic yield of small bowel CE for OGIB which was carried out within 15 days in 32 patients was 91%, whereas it was reduced to 34% in 32 patients who underwent CE at least 15 days after OGIB. Esaki et al. reported that small bowel CE carried out within a week after OGIB contributed to a better diagnostic yield in a retrospective analysis of 68 patients with OGIB. Shinozaki et al. reported that they carried out DBE in 200 patients with OGIB and the diagnostic yield in 170 patients with overt bleeding was 84% when endoscopy was carried out within 1 month following the last day of bleeding and it was significantly reduced to 57% if carried out after 1 month following the last bleeding day. In addition, even in cases of ongoing overt bleeding such as when blood was noted in the small intestine, the bleeding source could not be identified in 10–23% of patients. Repeating examinations leads to identifying and treating the source of bleeding and results in prevention of subsequent rebleeding.

References


COMMENTARY

A RETROSPECTIVE STUDY with PillCamSB, Coviden, Dublin, Ireland, in 911 patients with OGIB (372 patients with overt bleeding and 539 patients with occult bleeding) conducted at two sites in France reported that significant abnormal findings were observed in 509 patients (56%) by small bowel CE, of which 464 patients (51%) had bleeding or bleeding lesions in the small intestine: a total of 203 patients were diagnosed with vascular lesions, 88 patients with ulcers, 70 patients with tumors, 24 patients with varices, six patients with diverticula, and 73 patients with blood pooling only. Total enteroscopy rate was 85%. In addition, three patients could not swallow the CE, nine patients (1%) had retention (three patients with Crohn’s disease, three patients with small intestinal tumors, and three patients with gastric retention), and six patients with Crohn’s disease/small intestinal tumors underwent surgery to retrieve the CE.1

In a multicenter randomized comparison of the Endocapsule and the PillCamSB, Coviden, Dublin, Ireland, in 51 patients with OGIB at four academic medical centers in the USA, Endocapsule detected abnormalities in 24 patients (47%) and PillCamSB detected abnormalities in 17 patients (33%), which was not significantly different.2

A Japanese single-center study in which 74 OGIB patients underwent both small bowel CE (PillCamSB) and DBE reported that the diagnostic yields of CE and DBE were 54% and 64%, respectively, which was not significantly different.2 Vascular lesions in the duodenum/jejunum, gastrointestinal stromal tumor (GIST), intussuscepting lipoma, Roux-en-Y limb varices, and Meckel’s diverticulum, however, were not detected by CE.3

Consequently, non-invasive small bowel CE is considered an appropriate method for screening and follow up after treatment, and is recommended as the first-line endoscopic method for overt and occult OGIB as in the European Society of Gastrointestinal Endoscopy Guidelines (2009)4 and the American Society for Gastrointestinal Endoscopy Guidelines (2010). However, we should note that CE has some disadvantages, including the inability to provide endoscopic treatment and accurately identify the site of lesions, and false-positive and false-negative results, and it does not always allow observation of the entire small intestine within the recording time.5

REFERENCES


STATEMENT: 1–4

BAE is very useful as it enables many issues;
• the identification of the origin of bleeding
• detailed observation of the lesion with image-enhanced endoscopy or endoscopic ultrasonography
• biopsy
• endoscopic treatment.

However, the invasiveness of this procedure and possible adverse events should be kept in mind.

Median Delphi score: 9, Minimum score: 8, Maximum score: 9
Evidence level: IVb–VI, Strength of recommendation: C1

COMMENTARY

BAE CAN BE advanced deep within the small intestine, where it enables accurate diagnosis and endoscopic treatment through the accessory channel as with conventional endoscopy. As opposed to CE that passes by peristalsis, BAE can be advanced to the afferent limb of the postoperative reconstructed intestine1 and it can be used even when small bowel stenosis or obstruction is suspected.

The diagnostic yield of BAE for OGIB is reported to be 55–78%.2–8

As BAE has good maneuverability deep in the small bowel, after the origin of bleeding is identified, the site can be carefully examined with water immersion or lavage, chromoendoscopy,9 and an ultrasound miniature probe.10,11 Tumors or stenosis can be selectively imaged by injecting contrast medium through the accessory channel while the

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scope balloon of DBE is inflated. BAE enables the collection of biopsy specimens and intestinal juice for histopathological, bacteriological, and genetic examinations.

It enables endoscopic hemostasis\(^\text{12}\) using various methods. In cases that require surgical treatment, it can mark the site of lesions with tattooing or clips.

Because BAE is more invasive than small bowel CE, its indication should be carefully determined, especially in very elderly patients or in patients with cardiopulmonary dysfunction.

**REFERENCES**


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**STATEMENT: 1-5**

The indications for endoscopic hemostasis include vascular lesions and bleeding lesions (ulcers, tumors or diverticula) with a visible vessel. The hemostatic method is similar to that used for upper or lower gastrointestinal endoscopy. When endoscopic hemostasis is unsuccessful, surgical treatment or interventional radiology is indicated.

Median Delphi score: 9, Minimum score: 8, Maximum score: 9
Evidence level: IVb–VI, Strength of recommendation: C1

**COMMENTARY**

Endoscopic hemostasis is indicated for bleeding from vascular lesions, tumors, and diverticula/ulcers. Surgical treatment or interventional radiology, however, is indicated when endoscopic hemostasis is impossible or in the case of varix or large arteriovenous malformations. Surgical resection is the curative treatment of benign tumors in the muscle layer or deeper, malignant tumors invading into the submucosa or deeper, and diverticula.

Endoscopic hemostasis includes mechanical therapy (e.g. clipping, ligation, and balloon compression), electric cauterization (e.g. argon plasma coagulation, heater probe coagulation, and high-frequency coagulation), drug injection (e.g. polidocanol, histoacryl, hypertonic Na-epinephrine, and anhydrous ethanol), and the topical spray of drugs (e.g. thrombin). The hemostatic method should be selected depending upon the type of lesion or available treatment tools. Moreover, the method should be selected considering the risk of iatrogenic perforation, because the small intestinal wall is thinner than other parts of the gastrointestinal tract. Accordingly, argon plasma coagulation that allows superficial cauterization over a wide area and clipping by mechanical compression are commonly recommended.

In cases of bleeding from hemorrhagic polyps, hemostasis can be achieved by endoscopic mucosal resection/polypectomy or blocking the bloodstream with detachable snares or clips.
REFERENCES


Diagnostic algorithm for OGIB

1) In hospitals or clinics without CT, CE may come first, but CT should be performed later in another facility.
2) Dynamic CT is preferable because some lesions can be visualized only by dynamic CT.
3) In patients with suspected CoI’s disease, abdominal symptoms (pain, distension, etc.), past medical history of abdominal radiation therapy or surgery, and on long-term NSAIDs, a gastrointestinal patency test with a patency capsule should be performed first. Note that patients with bowel obstruction (including suspected obstruction) should not even undergo the patency capsule test or CE.
4) In case of emergency that enteroscopy is impossible to perform immediately or in hospitals or clinics where enteroscopy is unavailable.

CE, capsule endoscopy; CT, computed tomography; IVR, interventional radiology; NSAIDs, non-steroidal anti-inflammatory drugs.

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STATEMENT: 1-6

COMMENTARY

I F WE ENCOUNTER patients with obscure gastrointestinal bleeding without abnormalities at upper gastrointestinal endoscopy or colonoscopy, we should first carry out a high-resolution computed tomography (CT) scan from the chest to the pelvis in an emergency setting. If patients have no allergy to contrast media and no renal insufficiency, contrast-enhanced (preferably dynamic) CT should be carried out to detect abnormalities in intramural and extramural structures as well as extra-intestinal lesions (e.g. lung lesions, tumors in other organs). In addition to abdominal scanning, chest scanning should be obtained at the same time because the etiology of small bowel bleeding consists of secondary intestinal tuberculosis, metastasis of lung cancer, and arteriovenous malformation in hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber disease). In hospitals or clinics where CT is unavailable, CE may be carried out first, but CT should be done later in another facility.

In patients with established Crohn’s disease, medical treatment including fasting, hemostatic drugs, and anti-tumor necrosis factor (TNF)-alpha antibody agents should be started. If abnormalities are found on CT, BAE should be carried out by the route closest to the lesion. Common causes of bleeding in the small bowel that require emergency treatment are arteriovenous malformation and Meckel’s diverticulum. They do not occur frequently, but in cases of massive bleeding that require massive blood transfusions, BAE should be done after hemodynamics become stable. With respect to insertion route, the transanal approach is selected for bright red stool or dark red stool and the transoral approach for black stool. In the event of massive bleeding, the transoral approach is generally preferable to the transanal approach through the large intestine filled with blood because of poor bowel preparation. If no abnormalities are found using one approach, the other approach should be carried out immediately or as soon as possible. In case of massive bleeding when urgent BAE is unavailable, or in case the patient’s condition is too unstable to undergo BAE, transcatheter artery embolization (interventional radiology) should be carried out. In case of massive bleeding where the bleeding site cannot be identified by BAE, is inaccessible by BAE, or when endoscopic hemostasis fails, interventional radiology or intraoperative enteroscopy, if surgical treatment is indicated, should be considered.

When there are no abnormalities on abdominal contrast-enhanced CT, small bowel CE should be selected. After overt bleeding has stopped, CE should be carried out as soon as possible. In patients at risk of capsule retention such as suspected or documented Crohn’s disease, obstructive symptoms (pain or distension), previous history of abdominal radiation therapy, abdominal surgery, bowel obstruction, and in chronic NSAIDs users, the gastrointestinal patency test with a patency capsule should be done before CE. We should note that one of the most common bleeding origins in young patients is Meckel’s diverticulum, which may sometimes be overlooked at CE. In particular, in young children including infants, less invasive ectopic gastric mucosa scintigraphy (Meckel’s scan) may be carried out. Transanal BAE is the best modality to detect Meckel’s diverticulum, thereby endoscopic marking with India ink also can be done for subsequent laparoscopic surgery. The progress indicator of CE may be useful when deciding whether to choose the oral or the anal route for BAE. In case BAE is unavailable, if a lesion is found in the proximal jejunum or in the distal ileum, the transoral approach with a pediatric colonoscope or the transanal approach with a long-type colonoscope can be an alternative.

If no abnormalities are found on small bowel CE, follow-up should be done, or in patients who have a history of frequent hemorrhage/massive bleeding/severe anemia, BAE is recommended as the optimal diagnostic modality. If further examinations are not required or refused by patients, antithrombotic agents should be resumed in case their use had been suspended, as should an ordinary diet. If recurrent bleeding occurs over the follow-up period, upper gastrointestinal endoscopy or colonoscopy should be repeated. If there are no upper gastrointestinal or colonic lesions, small bowel CE should be carried out.

REFERENCES

STENOSIS

STATEMENT: 2-1

When performing enteroscopy the following issues should be asked to the patient in addition to those listed in the Statement: 1-1 in the section on OGIB;

- the intensity and the onset of symptoms which suggest the presence of stenosis
- history of medication
- history of abdominal surgery
- history of radiation therapy
- presence/absence of anal lesion

Median Delphi score: 8, Minimum score: 6, Maximum score: 9
Evidence level: IVb–VI, Strength of recommendation: C1

REFERENCES


STATEMENT: 2-2

CE is contraindicated when the patient presents with obstructive symptoms. Indication for CE should be carefully determined if the patient has, or is suspected to have, gastrointestinal stenosis.

Median Delphi score: 9, Minimum score: 8, Maximum score: 9  
Evidence level: IVa–VI, Strength of recommendation: C1

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COMMENTARY

SMALL BOWEL CE is contraindicated, without the need to consider a patency capsule pretest, in patients with known gastrointestinal obstruction based on the findings of abdominal X-ray or ultrasonography, medical or surgical history, and clinical symptoms. It is also contraindicated in patients with known gastrointestinal stenosis in whom retention of the CE is an obvious possibility. Moreover, small bowel CE is basically contraindicated in patients with a history of bowel obstruction who have not received treatment to improve the stenosis even if current symptoms of bowel obstruction are less frequent. If patients without obstructive symptoms have gastrointestinal stenosis, whether small bowel CE can be carried out should be determined based on other diagnostic modality findings or the results of patency capsule as pretest.\(^1,2\) Length, morphology, and proximal dilatation of the stenosis as well as the presence of fistulas should be confirmed by precise diagnostic imaging examination.\(^3\) As the first step of confirmation of gastrointestinal patency using a patency capsule, a simple abdominal X-ray that covers the imaging range up to the inferior border of the pubic symphysis should be done. It is crucial that this judgment for gastrointestinal patency is carried out correctly. It is often difficult to accurately distinguish between the small intestine and the large intestine using simple X-ray only. This may lead to misdiagnosis of the location of the patency capsule. Taking this into account, abdominal CT scan or other imaging modality should be added if appropriate. In addition, the patency capsule itself sometimes causes bowel obstruction within a few days after ingestion. Caution therefore should be exercised when considering its use in patients with suspected stenosis. Although it is very rare, retention of the small bowel CE in patients with Crohn’s disease has been reported after patency was confirmed using a patency capsule. Therefore, it is important to carry out CE as soon as possible after confirming patency before changes in gastrointestinal patency occur as a result of changes in the disease condition.\(^4-7\)

REFERENCES


STATEMENT: 2-3

When deciding the route (per-oral or per-anal) for BAE insertion, the one closer to the site of stenosis should be selected based on the results of other imaging modalities. If the diagnosis cannot be made using the initially selected route, BAE via the other route should be considered.

Median Delphi score: 9, Minimum score: 9, Maximum score: 9
Evidence level: IVb, Strength of recommendation: C1

COMMENTARY

FOR THE INSERTION of BAE, the route that enables easier reaching of the lesion should be selected based on the results of CT scan, contrast X-ray examination, and other imaging modalities.

In a report by Fukumoto \textit{et al.},\(^1\) in which the underlying causes in 179 patients who were diagnosed with small intestine stenosis by BAE were summarized, inflammatory disease (e.g. Crohn’s disease, chronic enteropathy associated with SLCO2A1 gene (CEAS; previously known as chronic non-specific multiple ulcers of the small intestine [CNSU]),\(^2\)
intestinal tuberculosis, NSAIDs-induced enteritis, and simple ulcer accounted for 55.8%, more than half of the patients, whereas postoperative inflammation and adhesions accounted for 17.3%, and neoplastic disease was the cause in 16.7%. In a report of 66 patients by Ohmiya et al., Crohn’s disease accounted for 34.8%, malignant tumors 22.7%, ischemic enteritis 10.6%, intestinal intussusception and inflammatory adhesion 6.1% each, and diaphragm disease caused by NSAIDs-induced enteritis and postoperative adhesion were 4.5% each. Thus, because the underlying cause was Crohn’s disease in a high proportion of cases, insertion through the anus was most commonly selected.

If a diagnosis cannot be made using the initially selected route for BAE, the other route should be considered. When transanal BAE is carried out, considering the presence of stenosis, transanal preparation including high-pressure enema or slower and longer dosing of bowel preparation should be planned.

REFERENCES

STATEMENT: 2-4
If the BAE can reach the site responsible for the obstruction in the small bowel, many kinds of intervention can be achieved; direct observation of the obstructive lesion, endoscopic ultrasonography, taking biopsy, selective radiological enteroclysis, balloon dilation, etc.

Median Delphi score: 9, Minimum score: 7, Maximum score: 9
Evidence level: IVb–V, Strength of recommendation: C1

COMMENTARY
If the BAE can reach the site responsible for the obstruction in the small bowel, direct visualization, endoscopic ultrasonography,1,2 and tissue biopsy can be carried out.

In order to confirm the shape and length of a stenosis, selective imaging should be carried out by injecting contrast medium through the accessory channel. D BE allows a relatively wide range of imaging because reflux of contrast medium can be prevented by dilating a balloon on the tip of the scope. This allows contrast medium to flow easily over the stenosis.

If the accessory channel diameter of the balloon endoscope is not less than 2.8 mm, balloon dilation for stenosis1–8 can be carried out by inserting a balloon dilator. In the case where the accessory channel diameter of the diagnostic scope is smaller, balloon dilation can be carried out by inserting a balloon dilator under fluoroscopic guidance after removing the scope, leaving the overtube and guidewire in place.9

If direct visualization of the far side of a stenosis—through which the scope cannot pass through—is required, the scope should be passed through the stenosis after balloon dilation or it should be inserted from the opposite side.

REFERENCES
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### SMALL BOWEL TUMORS

**Statement: 3-1**

> It is recommended that large tumors in the small intestine be examined first with CT, MRI or enteroclysis rather than CE, because the latter can result in a false negative finding. On the other hand small neoplasms or flat lesions are better detected with CE.

Median Delphi score: 9, Minimum score: 8, Maximum score: 9
Evidence level: I–VI, Strength of recommendation: C1

**COMMENTARY**

According to the US and EU guidelines, small bowel CE is recognized as useful for gastrointestinal polyposis and small bowel tumors as it has higher detectability than other examinations including small bowel X-ray, CT, and MRI.1 The American Society for Gastrointestinal Endoscopy states that it is indicated for surveillance of polyposis syndrome and suspected small bowel tumors.2 In a systematic review of small bowel CE (24 papers, 1,960 patients), small bowel tumors were detected in 7.95% in a group of patients with iron-deficiency anemia alone and in 2.25% of the entire patient group including other reasons, with the difference being significant. Therefore, CE is particularly useful in patients with iron-deficiency anemia when hemorrhage from other organs has been excluded.3 Moreover, since small bowel tumors have been detected in 124 of 5,129 patients (2.4%) undergoing small bowel CE for a variety of reasons, it is necessary to keep in mind that small bowel tumors exist in a certain percentage of patients indicated for small bowel CE.4

On the other hand, if a tumor is strongly suspected, other examinations should also be considered.1 Since small bowel CE may produce false-negative results in segments of rapid intestinal passage, such as the proximal small intestine,5–8 in the US and EU, it is recommended to perform CT or MRI for the initial examination.9 In Japan, small bowel X-ray has a high accuracy and is recommended for the initial examination. In addition, some tumors that have not been detected by small bowel CE may be detected by other modalities.10 For this reason, combined use of CE and contrast-enhanced CT is also recommended for screening of small bowel tumors.8,11 However, small bowel CE has higher sensitivity for detecting small lesions of ≤10 mm and flat lesions, which are difficult to detect by other examination methods.12,13

### REFERENCES

11 Yamada A, Watabe H, Obi S et al. Surveillance of small intestinal abnormalities in patients with hepatocellular

STATEMENT: 3-2

BAE is superior to other imaging modalities and therefore recommended for the detection and characterization of small intestinal neoplasm. It also enables endoscopic treatment.

Median Delphi score: 9, Minimum score: 8, Maximum score: 9
Evidence level: I–V, Strength of recommendation: C1

COMMENTARY

For small bowel tumors, the capacity of BAE to diagnose the presence of lesions is excellent, independent of size, compared with small bowel X-ray and CT. The diagnostic yield of BAE is significantly superior to small bowel CE, which sometimes misses tumors located in segments of rapid intestinal passage such as the duodenum and the proximal jejunum, and submucosal tumors even sized ≥10 mm. Endoscopic ultrasonography with BAE is effective in some cases. Endoscopic treatment includes tumor resection, argon plasma coagulation for the management of hemorrhage, and sclerotherapy for the treatment of hemangioma.

REFERENCES

STATEMENT: 3-3

Endoscopic biopsy is useful for making a definitive diagnosis or determining a management strategy. However, it should be performed carefully in a case with GIST or tumor of vessel origin because it may cause massive bleeding requiring blood transfusion.

Median Delphi score: 9, Minimum score: 8, Maximum score: 9
Evidence level: IVb–VI, Strength of recommendation: C1

COMMENTARY

Taking pathological specimens is essential for diagnosing neoplastic disease and for deciding the management strategy. BAE can reach lesions and take biopsy specimens deep within the small bowel. The diagnostic yield of biopsy is high for epithelial tumors, malignant lymphoma, and neuroendocrine tumors (NET), but tends to be low for metastatic small bowel tumors and GIST. Biopsy from GIST should be carefully taken because it is hypervascular and may cause pulsatile bleeding, potentially requiring blood transfusion. There is a report of bleeding as a result of biopsy from capillary hemangiomas which could not be stopped and resulted in emergency surgery. Refer to the atlas for diagnosis of individual diseases.
REFERENCES

STATEMENT: 3-4

Endoscopic resection is indicated for epithelial neoplasm confined within the mucosa and a subepithelial tumor limited to the submucosal layer. However, tumors of vessel origin or invaginated tumors are high risk for bleeding or perforation, and therefore surgical resection should also be considered.

Median Delphi score: 9, Minimum score: 8, Maximum score: 9
Evidence level: IVb–V, Strength of recommendation: C1

COMMENTARY

Endoscopic resection has been reported to be useful for epithelial benign tumors/polyps (e.g. adenoma, hamartoma, inflammatory fibroid polyp) and intramuscular carcinoma. Unlike in the esophagus, stomach, and large intestine, there are no reports on whether endoscopic resection is indicated for cancers invading the submucosal layer in the small intestine and, therefore, it is not recommended at this time.1–4 Endoscopic resection is also useful for submucosal tumors confined to the submucosal layer (e.g. lipoma, aberrant pancreas, fibroma, hemangioma). The European Society of Gastrointestinal Endoscopy Guidelines for flexible endoscopy recommend a submucosal injection prior to small bowel polypectomy. For large polyps, piecemeal resection is also recommended to avoid perforation. Risk of adverse events of endoscopic resection in the small bowel was reported to be similar to that in the right colon.5,6 Hemorrhagic vascular tumors pose a risk of hemorrhage as a result of intratumoral dissection and dissection of feeding vessels. Endoscopic resection of large intussuscepted polyps may cause perforation as a result of involvement of the serosa, and surgical resection may be required in some cases.7,8 Sclerotherapy using polidocanol has been reported to be useful for hemangioma, especially for multiple hemangiomas associated with blue rubber-bleb nevus syndrome.9

REFERENCES
STATEMENT: 3-5

Hamartomatous polyps associated with Peutz-Jeghers syndrome most commonly develop in the small intestine. Enteroscopy is useful for their diagnosis, treatment, and follow up. Endoscopic polyp resection can preclude complications such as intussusception, bleeding or malignant transformation and can obviate the need for surgery.

Median Delphi score: 9, Minimum score: 8, Maximum score: 9
Evidence level: IVb–V, Strength of recommendation: C1

COMMENTARY

THE PRINCIPLE FEATURES of Peutz-Jeghers syndrome are gastrointestinal polyposis and melanin spots on the oral mucosa, the lips, and the digits. It is transmitted as an autosomal dominant trait. STK11/LKB1 has been identified as one of the responsible genes. Peutz-Jeghers polyps occur in the stomach and throughout the small and large intestines but are most common and numerous in the jejunum and the ileum (at least 90% of cases). The polyps are mostly hamartomas, but, in a few polyps, adenomatous changes and foci of adenocarcinoma are present.1 The most frequent complications include intussusception and bleeding because of ulceration or infarction of a polyp in young patients, and malignant tumors in patients aged ≥30 years. Polyps sized ≥15 mm (≥10 mm, if possible) should be resected endoscopically because 1% of small bowel polyps sized ≤20 mm and 30% of polyps sized >20 mm are complicated by adenoma or carcinoma, and polyps sized ≥15 mm may be complicated by intussusception.2 By repeating resection using BAE, it may be possible to prevent the above-mentioned complications and avoid surgery. However, as endoscopic resection of large intussuscepted polyps may cause perforation as a result of involvement of the serosa, surgical resection should be considered in some cases. The diagnostic yield of small bowel CE for small bowel polyps is significantly higher than small bowel X-ray; therefore, CE is useful for screening and follow up after treatment. Peutz-Jeghers syndrome is associated with high risk of cancer not only in the gastrointestinal tract but also in the mammary glands, pancreas, ovary, and uterus etc. In this regard, periodic whole body surveillance is necessary.1–8

REFERENCES


STATEMENT: 3-6

In addition to numerous colorectal polyps, patients with familial adenomatous polyposis may harbor epithelial neoplasms commonly in the small intestine, especially in the duodenum (including the duodenal papilla) and jejunum. Enteroscopy is useful for the diagnosis and follow up of their small bowel neoplasm.

Median Delphi score: 9, Minimum score: 8, Maximum score: 9
Evidence level: IV, Strength of recommendation: C1

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COMMENTARY

FAMILIAL ADENOMATOUS POLYPOSIS (FAP) is a hereditary disease characterized by multiple adenomatous polyps in all parts of the large intestine, and is associated with a high incidence of colorectal carcinoma. One of the two genes responsible is the APC gene, which is inherited in an autosomal dominant pattern, and is classified into classic type, severe type, and attenuated FAP (AFAP). The other gene is the MUTYH gene, which is inherited in an autosomal recessive pattern, and gives rise to so-called MUTYH-associated polyposis (MAP). Epithelial tumors commonly occur in the duodenum and jejunum in particular and the incidence of concomitant small bowel carcinoma is 7–8%. Presence of duodenal polyps can be an indicator of the existence of polyps deep within the small bowel. BAE is useful for the diagnosis, endoscopic resection, and follow up of small bowel tumors. Small bowel CE is useful for surveillance of jejunal/ileal polyps, but it is not suitable for surveillance of the duodenum because of its low diagnostic performance for duodenal polyps and papillary tumors.1–11

REFERENCES


INFLAMMATORY DISEASES

Statement: 4-1

The importance of enteroscopic examination has been confirmed for inflammatory diseases including the following.

- Crohn’s disease
- Intestinal Behcet’s disease/simple ulcer
- Ulcerative colitis
- Chronic enteropathy associated with SLCO2A1 gene (CEAS)
- Eosinophilic gastrointestinal diseases
- Drug-induced enteritis
- Intestinal tuberculosis
- Ischemic enteritis
- Radiation enteritis

Median Delphi score: 8, Minimum score: 8, Maximum score: 9
Evidence level: IVa, Strength of recommendation: C1

COMMENTARY

DETAILS OF EACH disease are described.

Crohn’s disease: Crohn’s disease is a chronic inflammatory disease of unknown cause, which develops at a young age. Although the initial phase of this disease is mainly characterized by persistent inflammation in the gastrointestinal tract, intestinal complications including stenosis, fistula, and perforation develop during the course of the disease, which frequently lead to intestinal resection. Small bowel lesions associated with Crohn’s disease are characterized by longitudinal ulcers predominantly on the side of

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Intestinal Behcet’s disease/simple ulcer: Behcet’s disease is a recidivating and recurrent inflammatory disease of unknown cause, and its major symptoms are recurrent oral aphtha, skin symptoms, ocular symptoms, and ulceration of the vulva. When gastrointestinal lesions occur as the main clinical manifestation of this disease, the condition is called intestinal Behcet’s disease. Typical lesions are also observed even in those patients who do not meet the diagnostic criteria for Behcet’s disease. This condition is referred to as simple ulcer, but there is no consensus about how it differs from Behcet’s disease. There is a report of enteroscopic evaluation of diminutive small bowel lesions associated with intestinal Behcet’s disease and simple ulcer.14

Ulcerative colitis: Ulcerative colitis is a non-specific inflammatory intestinal disease of unknown cause leading to diffuse erosion and ulceration in the large bowel mucosa. Although backwash ileitis has been regarded as a small bowel lesion of ulcerative colitis, the existence of other lesions extending over a wide area of the small intestine has also been pointed out, and there is a report of small bowel lesions associated with ulcerative colitis (aphtha, erosion, small ulcer) being evaluated by small bowel CE.15,16

Chronic enteropathy associated with SLCO2A1 gene (CEAS): CEAS is previously known as chronic non-specific multiple ulcers of the small intestine (CNSU), mainly characterized by chronic iron-deficiency anemia and hypoproteinemia. Multiple superficial ulcers presenting with non-specific histological findings occur in the ileum other than the terminal ileum. Transanal BAE is an effective means for diagnosing this disease, and endoscopic findings are characterized by ramification or fusion of multiple circular or oblique zonal ulcers.17–19

Eosinophilic gastrointestinal diseases: Eosinophilic gastrointestinal diseases generally refer to chronic inflammatory allergic diseases causing infiltration of eosinophils into the gastrointestinal tract, and are classified into eosinophilic esophagitis and eosinophilic gastroenteritis. Eosinophilic gastroenteritis is characterized by eosinophilia in the peripheral blood, as well as infiltration of eosinophils into the mucosal tissue mainly of the stomach and small intestine. There are a certain proportion of patients with lesions confined to the small intestine with negative upper and lower gastrointestinal tract lesions. Enteroscopic examination is expected to be valuable for these cases.20

Drug-induced enteritis: NSAIDs including low-dose aspirin are the most important among drugs that potentially cause drug-induced enteritis. NSAID-induced small bowel damage can be observed by BAE or small bowel CE, and the lesions present various morphologies, such as circular ulcer, longitudinal ulcer, and erosion.21–28

Intestinal tuberculosis: Intestinal tuberculosis is an inflammatory disease as a result of infection by Mycobacterium tuberculosis. It commonly occurs in the section from the lower ileum to the right colon, where the lymph system is prominent.29 On endoscopy, circular/zonal ulcers are most typically observed in the active phase. It presents in various ways with a mixture of active and healing lesions including multiple ulcers and scars, flattened ileocecal valve, pseudodiverticulum formation, and the presence of an atrophic scarring area around the ulcer. There are reports of proximal small bowel lesions detected by BAE or small bowel CE.30–33

Ischemic enteritis: Ischemic enteritis is a small bowel lesion as a result of disturbance in blood flow in the small bowel. Many cases manifest the stenotic type, which may lead to obstruction of intestinal passage. Enteroscopy makes it possible to observe tubular stenosis as a result of circumferential ulcer, small intestine dilation at the oral side, and granular mucosa with an irregular surface.33–36

Radiation enteritis: Radiation enteritis develops as a complication when radiation therapy is used to treat intrapelvic malignant tumors. Endoscopic findings include reddening, hyperemia, edema, erosion, hemorrhage, white villi, vasodilation, mucosal congestion with edema, ulceration, and strictures as a result of fibrosis.33,36,37

REFERENCES


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STATEMENT: 4-2

Although endoscopic findings of NSAID-induced small bowel injuries can be varied, circular ulcers on the Kerckring’s folds are typical and almost pathognomonic. In cases of diaphragmatic stenosis, endoscopic balloon dilation is an effective therapy.

Median Delphi score: 8.5, Minimum score: 8, Maximum score: 9
Evidence level: IV, Strength of recommendation: C1

COMMENTARY

IMPORTANT OF BAE 1–3 and small bowel CE4–8 in NSAID-induced small bowel injuries has been reported. Using biopsy tissues, the presence of apoptotic bodies and eosinophilic infiltration in the deep part of the crypt are diagnostic, but the positive rates for these are low at 30% and 19%, respectively. However, apoptotic bodies are found in 100% of cases of surgical resection.9 Among NSAID-induced small bowel injuries, perforation and serious hemorrhage may require surgical treatment, but most small bowel injuries are minor, such as a mucosal defect or ulcer, and most improve after discontinuation of the drug and follow up.10,11 NSAID-induced small bowel injuries cause ulcerative lesions more commonly in the ileum than in the jejunum.5 Users of oxicam, arylacetic acid, and coxib NSAIDs and carriers of genetic polymorphisms in the metabolic enzyme CYP2C9 are at higher risk of NSAID-induced diaphragm disease.12 In cases of diaphragm disease complicated by bowel obstruction, small bowel endoscopic balloon dilation is effective.1,12 Refer to the atlas for the diagnosis of individual diseases.13

REFERENCES

STATEMENT: 4-3

BAE is useful for the diagnosis and evaluation of the pathological condition of Crohn’s disease. However, since it is an invasive method, other forms of diagnostic imaging should also be considered. In addition, surgery may be avoided by performing endoscopic balloon dilation for strictures. Small bowel CE is useful for the diagnosis and follow-up of Crohn’s disease. However, since the procedure is associated with a risk for retention in cases with Crohn’s disease (including cases where the diagnosis is suspected), it is necessary to perform a patency capsule examination prior to real CE in order to verify the patency of the gastrointestinal tract.

Median Delphi score: 8, Minimum score: 8, Maximum score: 9
Evidence level: I, Strength of recommendation: C1

COMMENTARY

BAE1–3 AND SMALL bowel CE4–13 which allow direct visual inspection of the lesion, are useful in the diagnosis and evaluation of the pathological condition of Crohn’s disease. For use of CE in Crohn’s disease, however, a patency capsule (capsule for verifying the patency of the gastrointestinal tract) is inevitable for the prediction and prevention of retention.10,14–16 Balloon dilation has been reported to be an effective way to avoid surgery in cases of stricture.17–19 In the EU guidelines, CT/MR enterography is recommended for evaluation of the pathological condition. Based on a comparison between MR enterography and BAE, however, it has been reported that MR enterography can be used to evaluate inflammation, but BAE is warranted for the evaluation of stenosis.20

REFERENCES

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STATEMENT: 4-4

Balloon dilation for small bowel lesions of Crohn’s disease is indicated when the following conditions are all met:

- The patient presents with symptoms related to the stricture or the images show dilation of the bowel proximal to the stricture.
- The longitudinal length of the stricture is ≤5 cm.
- The stricture is not associated with fistula, fissure, abscess, deep ulcer, or severe adhesion/fixure.

Possible complications associated with balloon dilatation include bleeding and perforation.

Median Delphi score: 9, Minimum score: 8, Maximum score: 9
Evidence level: I, Strength of recommendation: B

Evidence level: IVb, Strength of recommendation: C1

REFERENCES


OTHERS

Statement: 5-1

Enteroscopy is useful for the following systemic diseases:

- Amyloidosis
- Collagen diseases
- Congenital diseases
- Gastrointestinal polyposis
- IgA vasculitis (former names: Schoenlein-Henoch purpura, allergic purpura)
- Satoyoshi disease

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COMMENTARY

Amyloidosis

Amyloidosis is characterized by dysfunction of organs caused by deposits of amyloid, which is an insoluble protein having a fibrous structure. The gastrointestinal tract, especially the small bowel, is the site of the most predominant amyloid deposits. Among amyloid proteins, AL (amyloid light chain) type, AA (amyloid A) type, AF2M (Beta2-microglobulin) type, and ATTR (trans-thyretin-related amyloid) type show high affinity for the gastrointestinal tract. The deposition leads to various enteroscopic findings including granular mucosa and submucosal tumor-like protrusion.

Collagen diseases

Collagen diseases that involve the small bowel are systemic lupus erythematosus (SLE), systemic scleroderma (SSc), rheumatoid arthritis (RA), polyarteritis nodosa (belonging to vasculitis syndrome), microscopic polyangiitis, eosinophilic granulomatosis with polyangiitis (formerly known as Churg-Strauss syndrome), and granulomatosis with polyangiitis (formerly known as Wegener’s granulomatosis) etc. Small bowel lesions of lupus enteritis in association with SLE and vasculitis syndrome consist of multiple erosions and ulcers, which may lead to gastrointestinal perforation. In addition, SLE may be complicated by intestinal lymphangiectasia presenting as protein-losing enteropathy. SSc causes intestinal dilation in the circumferential axis direction mainly in the duodenum and jejunum, leading to chronic pseudo-obstruction. RA may be complicated by secondary amyloidosis (AA type).

Congenital diseases

Both Meckel’s diverticulum and intestinal duplication commonly develop in the lower ileum (Meckel’s diverticulum occurs on the anti-mesenteric side, whereas intestinal duplication occurs on the mesenteric side), causing bleeding, bowel obstruction, and intussusception. Hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber disease) is an autosomal dominant hereditary disease, which leads to recurrent epistaxis and arteriovenous malformation/arteriovenous fistula in the skin, oral mucosa, and parenchymatous organs (lung, liver, and brain), as well as telangiectasia (arteriovenous malformation) in the stomach and small and large intestines, which may be the source of gastrointestinal hemorrhage. Neurofibromatosis type 1 (Recklinghausen’s disease) is an autosomal dominant hereditary disease characterized by multiple neurofibromas, and cafe-au-lait spots on the skin, which may complicate gastrointestinal stromal tumors (GIST) in the small and large intestines, and sometimes in the stomach.

Gastrointestinal polyposis

Polyposis occurring in the small intestine includes neoplastic (e.g. familial adenomatous polyposis, MUTYH-associated polyposis, Turcot syndrome, and Lynch syndrome), hamartomatous (e.g. Peutz-Jeghers syndrome, Cowden disease, and juvenile polyposis), and non-hereditary non-neoplastic polyposis (Cronkhite-Canada syndrome).

IgA vasculitis

This vasculitis is related to IgA immunocomplex. In the gastrointestinal tract, it affects most frequently the small intestine including the duodenum. Multiple irregular ulcers, hematoma-like ulcer floor, edema, and erosion are observed.

Satoyoshi disease

A disease of unknown cause characterized by the triad of progressive muscle spasm (cramp), systemic loss of hair, and diarrhea. Lesions are found throughout the entire length of the small intestine, disappearing Kerckring’s folds, fine granular mucosa, and white villi are observed.

REFERENCES

STATEMENT: 5-2

Malabsorption syndrome/protein-losing enteropathy is classified into primary and secondary types and can be induced by a variety of causes. Enteroscopic observation, pathological examination of the biopsy specimen, and microbiological examination are possibly useful for its diagnosis.

Median Delphi score: 9, Minimum score: 8, Maximum score: 9

Evidence level: V, Strength of recommendation: C1

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AUTHORS’ CONFLICTS OF INTEREST IN RELATION TO THE CONTENTS OF THE PRESENT ARTICLE

WITH REGARD TO the conflicts of interest of the committee members involved in the preparation and evaluation of the present guidelines, each member was requested to make a declaration with regard to the following.

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FUNDING

COSTS ASSOCIATED WITH the formulation of the present guidelines were subsidized by the Japan Gastroenterological Endoscopy Society (JGES).
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