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Review

Double-balloon endoscopy: past, present, and future

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Double-balloon endoscopy (DBE) was developed as a new technique for visualization of and intervention in the entire small intestine. In DBE, the intestinal walls are held apart by a balloon attached to the distal end of a soft overtube. DBE has been reported worldwide to be very useful for not only diagnosis but also endoscopic therapy. Biopsy samples of small intestinal tumors can be obtained using DBE, and the appropriate treatment can be selected before a surgical procedure. For inflammatory diseases, DBE can reveal the localization of ulcers in the lumen (on the mesenteric or antimesenteric side), which is important for differential diagnosis. Some endoscopic therapies such as hemostatic procedures, polypectomy, and dilation therapy for benign strictures can be performed in the same manner as in the large intestine. DBE may also be suitable for colonoscopy for difficult insertion cases and therapeutic procedures such as endoscopic submucosal dissection. Furthermore, a double-balloon endoscope can be selectively inserted into the afferent loop to perform endoscopic retrograde cholangiopancreatography in patients with Roux-en-Y anastomosis, allowing various kinds of endoscopic treatments for biliary diseases to be successfully performed. Endoscopic therapy in the small intestine, whose wall is very thin, should be performed with special care to avoid complications such as bleeding and perforation. In the future, improvement is expected in terms of maneuverability, therapeutic capability, and imaging technology such as the addition of a magnifying function and flexible spectral imaging color enhancement. We anticipate that DBE will contribute to the establishment of medical science of the small intestine and to research elucidating the mechanisms of small intestinal diseases.

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Introduction

Since the first clinical application of double-balloon endoscopy (DBE) was reported in 1999,[1] numerous instances of its usability and application[2] have been reported by enthusiastic endoscopists around the world. The DBE base is becoming consolidated, including knowledge of insertion methods and safety issues a result of compilation of procedure-related complications. We would like to take this opportunity to consider the prospects of DBE by summarizing the present state of basic knowledge about DBE and its applications.

Path of DBE development

DBE was originally developed for enteroscopy. The development of the enteroscope started in 1970, on the back of the development of the colonoscope. In the same year, Itaru Oi et al.[3] succeeded in observing the jejunum by push enteroscopy, and Hideo Hiratsuka[4] succeeded in observing the ileum with a colon fiber endoscope using the string method for colonoscope guidance. Subsequently, in March 1971, Hiratsuka et al.[5] succeeded in performing a total enteroscopy using the ropeway method, which is an advanced guidance method based on the string method. It appeared that enteroscopy would progress with the development of endoscopes for other parts of the gastrointestinal tract; however, there was no significant progress for nearly 30 years after 1971. The standard enteroscopy method remained push enteroscopy, with the result that

most parts of the small intestine, where no standard endoscopes could reach, were called the "dark continent."

DBE was designed and developed as an endoscopic insertion method that would allow the depths of the small bowel to be reached. When a push enteroscope is inserted, extension of the small bowel causes difficulty, so an overtube with a balloon was used to prevent this small bowel extension. Then, to prevent the distal end of the endoscope from slipping backward when the overtube was inserted, a balloon was also attached to the distal end of the endoscope. That became the configuration of the double-balloon endoscope. For further details of the principles of DBE, please refer to a textbook describing the theory and practice of DBE.[6]

Improvement of the instrument

Current endoscopes for DBE

Currently, there are three models of endoscopes used for DBE. The slim-diameter EN-450P5 endoscope (working length, 2000 mm; external diameter, 8.5 mm; accessory channel, 2.2 mm) became commercially available in autumn 2003 and is used mainly for endoscopic observation. The EN-450T5 model (working length, 2000 mm; external diameter, 9.4 mm; accessory channel, 2.8 mm) was developed with a larger diameter accessory channel for compatibility with various endoscopic treatments. The EN-450BI5 endoscope (working length, 1520 mm; external diameter, 9.4 mm; accessory channel, 2.8 mm), with a short working length designed for compatibility with observation of colon and biliary disorders of the postoperative intestinal tract such as Roux-en-Y anastomosis, was released in November 2005 (Table 1). Ordinary accessory devices for the treatment of biliary disorders such as balloon dilation for biliary stenosis, lithotripsy, and stent placement can be used with the EN-450BI5 without modification.

Developing new endoscopes

There is controversy as to whether 200 cm is the most appropriate endoscope length. It has been suggested that a longer endoscope is needed to increase the success rate of examining the entire small intestine, especially in larger Western patients. However, 200 cm is considered a reasonable length in most cases because a longer endoscope might be difficult for endoscopists to handle, and it is possible to examine most of the small intestine with the current 200-cm endoscope, with some successful cases of total enteroscopy even in Western patients. The insertion difficulty experienced at the final stage of many examinations is not due to the endoscope length.

With regard to the endoscope diameter, thinner endoscopes are presumed to be more effective if the diameter of the forceps channel is sufficient and if technical problems of endoscope durability are solved.

Meanwhile, improvement of image processing is expected with the addition of enhanced imaging technologies, such as higher image quality super CCDs, magnifying functions, and flexible spectral imaging color enhancement (FICE).[7]

Developing peripheral equipment

The current balloon controller is more compact that that of the first model. The endoscopist can check the condition of the two balloons visually, and a monitor is attached to prevent improper operation.

There are currently three different kinds of overtube, depending on the endoscope. The inner and outer surfaces of the overtube are coated with hydrophilic polyvinyl pyrrolidone to reduce friction between the endoscope and overtube. In addition, an antireflux valve is attached to the proximal end of the tube as a skirt to prevent backflow of intestinal fluids from the inner part of the tube (Fig. 1). Friction may occur at the valve when the surface of the endoscope shaft becomes dry. In that case, lubricating jelly should be used to coat the surface. If the length of the overtube were shortened, the insertion length per stroke would become longer and insertion efficiency would increase; however, the length of the small bowel folding on the overtube in the final stage would be shorter, which would reduce the deepest distance reached. For the purpose of enteroscopy, the current length of the overtube is considered reasonable.

Table 1. Specifications of three models of double-balloon endoscope

	Endoscopes		
	EN-450P5	EN-450T5	EC-450BI5
Outer diameter (mm)	8.5	9.4	9.4
Accessory channel (mm)	2.2	2.8	2.8
Working length (mm)	2000	2000	1520
Total length (mm)	2300	2300	1820

Fig. 1. The antireflux valve attached at the proximal end of the overtube

For endoscopic treatments such as hemostasis, polypectomy, and dilation of strictures, an endoscopist using DBE can control the endoscope without the aid of an assistant if the overtube is stabilized with stabilizing tools. The assistant who used to hold the overtube can now assist in the treatment. These stabilizing tools are still in the experimental stage.

Improvement of the insertion technique in DBE

For the standard insertion method, refer to the aforementioned text.[6] Instructions for passing the ileocecal valve, where insertion requires some special tips, the technique in cases of intestinal adhesion, and new techniques for the postoperative intestinal tract have been introduced.

Techniques for passing the ileocecal valve

It is important to maintain air insufflation at a minimum during the passage through the colon for easy insertion past the ileocecal valve. After the distal end of the endoscope passes the ileocecal valve, the endoscope tip is angled upward. Before the endoscope is pushed in further, the endoscopic angle should be straightened. Then, the endoscope tip can be gently inserted further. However, when the angle between the ascending colon and the distal ileum is acute, even if the endoscope is inserted into the distal ileum as described, during further insertion the endoscope may slip out into the cecum. There are two ways of passing the ileocecal valve that solve this problem. First, the overtube should be slightly pulled back, with the overtube balloon inflated in the ascending colon, making the entrance angle from the ileocecal valve to the distal ileum obtuse and easing the insertion of the endoscope. Second, the endoscope should be inserted by pushing it and turning it around the cecum to reach the ileocecal valve from the opposite direction. In general, the most suitable patient posture for insertion through the ileocecal valve is supine. In some cases, however, it may be better to place the patient in the right lateral decubitus position and to use manual compression of the right lower lateral side of the abdomen if the endoscope cannot pass with the patient in the supine position.

Insertion method for patients with intestinal adhesions

It is sometimes difficult to insert the device after abdominal surgery or in patients with Crohn's disease because of fixed angulations due to adhesions between the intestinal tract and the abdominal wall or between parts of the intestinal tract. Selection of the EN-450P5 endoscope with an 8.5-mm outer diameter is best in such cases for observation purposes because it is easier to insert into the deeper parts of the intestine. The endoscope is basically inserted by making concentric circles, and for smooth insertion, it is important to insert it by drawing bigger loops. However, the loop becomes smaller or S-shaped if the lumen is followed with the distal end of the endoscope in patients with an adhesion, because the curvature of the lumen may be angulated and fixed by the adhesion. When the endoscope becomes stuck during insertion, it is better to correct it by making a bigger loop, after checking the configuration of the insertion loop by X-ray. When the endoscope is S-shaped, abdominal compression or changing the patient's position may be effective. If an attempt is made to pass the strongly bending curvature forcibly, the endoscope will not go forward and the overtube will be pushed back if the pushing force of the endoscope exceeds the grip force of the overtube. Therefore, it is important to operate the device without too much bending of the endoscope angle and to operate it by consciously transmitting the insertion force to the distal end of the endoscope by jiggling. Furthermore, it is important to pass small bends by using a slalom technique, shortening the endoscope linearly, similar to colonoscopic insertion in cases of adhesion.

One-man method

Basically, double-balloon endoscope insertion is performed by two people, but even one endoscopist can perform the insertion by holding the controller part of the endoscope with the left hand and holding the overtube with the first and second fingers of the right hand and the endoscope shaft with the palm and the fifth finger of the right hand (Fig. 2) for insertion and with-

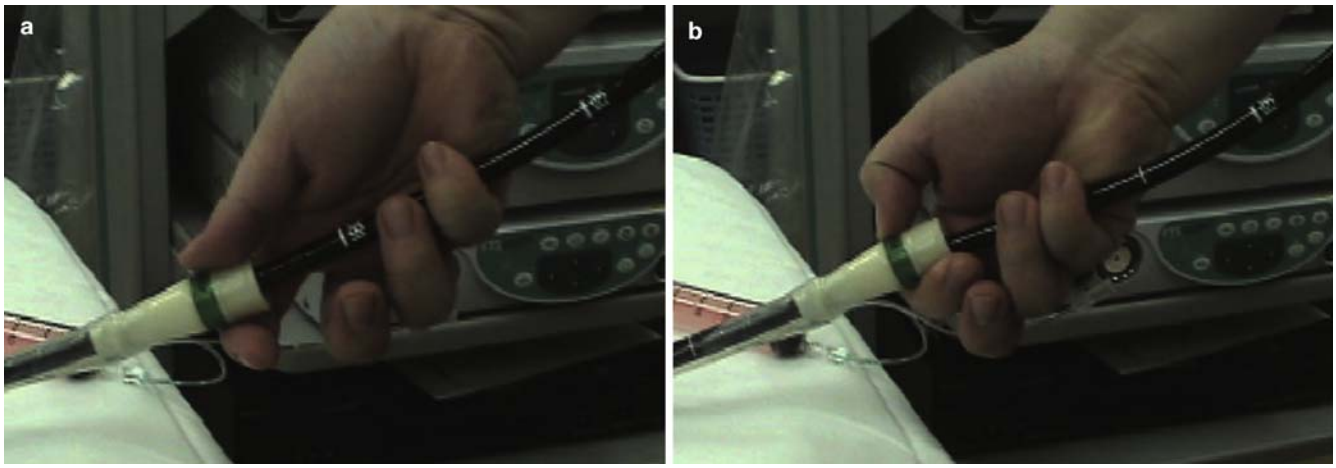

Fig. 2. a The overtube is held with the first and second fingers of the right hand and the endoscope shaft with the palm and the fifth finger. **b** The palm is closed to insert the endoscope or to withdraw the overtube relative to one another

drawal. The endoscopist must be ambidextrous, however. Nevertheless, further innovation could make insertion by a single endoscopist efficient.

Procedure for the postoperative intestinal tract

Prior to the examination, accurate information on the method of surgery needs to be collected. It is easier to find the bifurcation if it is known how it was anastomosed. In the postoperative intestinal tract, the anastomotic part must be identified. Expertise in finding the anastomotic part involves paying attention to a gap in the folds of Kerckring, dilation of the lumen, directional change of the peristalsis, and biliary interfusion.

For pancreaticobiliary treatment of patients with Roux-en-Y anastomosis, intubation of the afferent limb is necessary; however, identification of the afferent loop is sometimes difficult. In this case, tattooing one entrance first, then judging whether it is correct under fluoroscopic control by inserting the endoscope or by injecting contrast material into the lumen. The tattooing should be a guidepost for future examination.

Improvement in the diagnosis and treatment of diseases of the small intestine

Hemorrhagic lesion

Using DBE, identification of the source of bleeding is possible in 60%–70% of cases of obscure gastrointestinal bleeding (OGIB). In Japan, ulcers and erosions are the most common cause of OGIB, with vascular and neoplastic lesions next. However, according to reports from Europe and the United States, vascular lesions are the most common reason, and ulcers and erosions come next. The differences may reflect different modalities

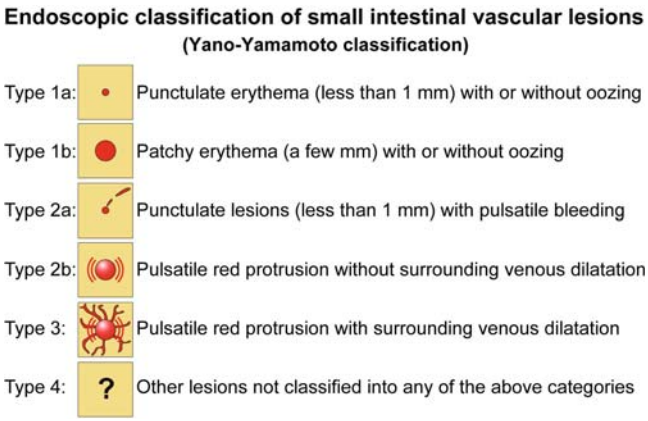

Fig. 3. Endoscopic classification of small intestinal vascular lesions[5]

used for diagnosis, or, possibly, differences between ethnic groups.

For vascular lesions of the gastrointestinal tract, no classification system has been related to pathologic findings, and definitions have been vague. Therefore, Yano et al.[8] classified types of endoscopic findings and related them with pathologic findings (Fig. 3) as follows.

Type 1a. Punctulate erythema (less than 1 mm) with or without oozing
Type 1b. Patchy erythema (a few mm) with or without oozing
Type 2a. Punctulate lesions (less than 1 mm) with pulsatile bleeding
Type 2b. Pulsatile red protrusion without surrounding venous dilatation
Type 3. Pulsatile red protrusion with surrounding venous dilatation
Type 4. Not classified above

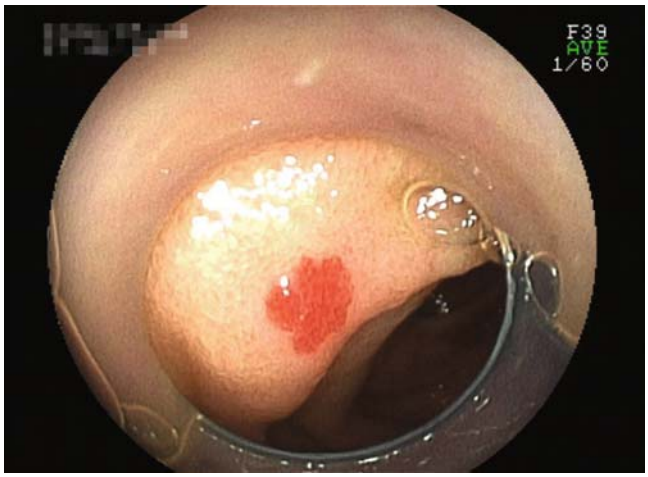

Fig. 4. A type 1b vascular lesion[8]

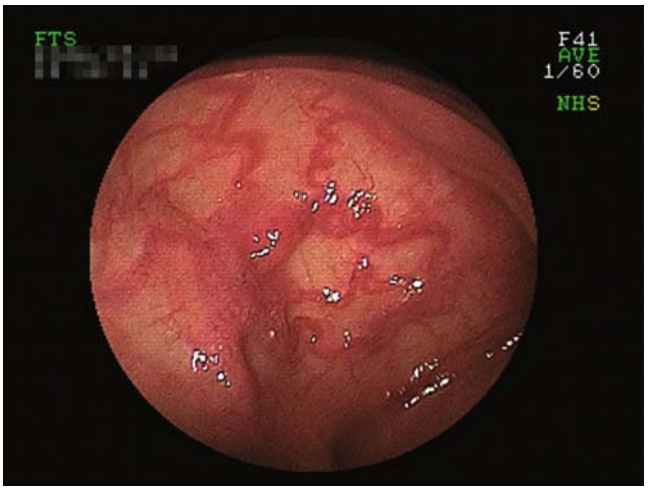

Fig. 6. A type 3 vascular lesion. From Yano et al.[8]

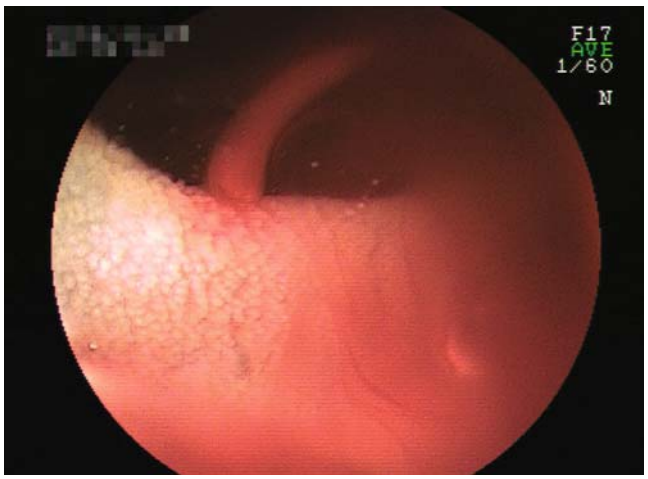

Fig. 5. A type 2a vascular lesion. From Yano et al.[8]

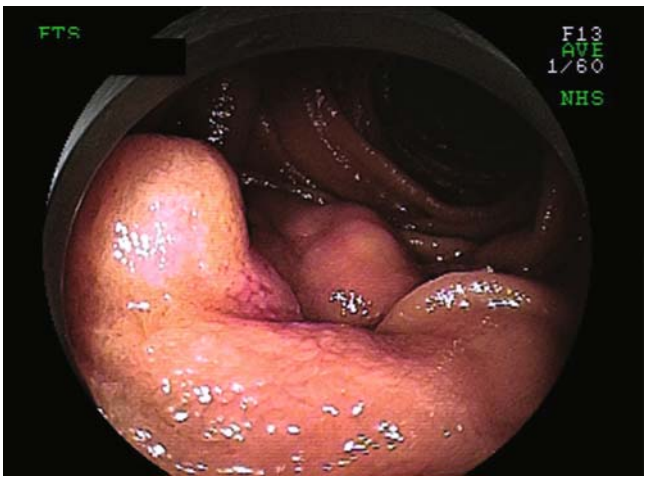

Fig. 7. A gastrointestinal stromal tumor in the small intestine

Types 1a and 1b (Fig. 4) are lesions up to a few millimeters in size made from a normal vein in the submucosal layer and dilation of capillary blood vessels in the lamina propria mucosae. The clinical condition is a tortuous abnormal blood vessel with pathologic venous characteristics corresponding to angioectasia. Types 2a (Fig. 5) and 2b correspond to Dieulafoy's lesion,[9] which can cause major hemorrhage because of an abnormally thick artery meandering in the submucosa contiguous with the surface mucosa, causing an erosion to form by mechanical pressure. Type 3 (Fig. 6) is a lesion within an anastomosis or in the transitional part between comparatively large arteries and veins. Such lesions are comparatively large, arteriovenous malformations (AVM), reaching the serosal surface and not limited to within the submucosa.

This classification is not just morphologic; it is possible to relate the types to pathologic features. Furthermore, it is practical for selection of treatment methods. In fact, coagulation of lesion types 1a and 1b with a high-frequency current such as argon plasma coagulation (APC), hemostasis of types 2a and 2b with clip placement, and, for type 3, placement of a clip to block the inflow blood vessel or surgical removal are recommended.

In the future, this classification should be verified by collecting data of endoscopic findings and comparing them with the corresponding pathologic findings, if available, at multiple facilities using this classification. At the same time, the selected treatment should be evaluated.

Neoplastic lesions

In general, neoplastic lesions of the small intestine are difficult to diagnose. Tumors of the small intestine are

rare, accounting for 5% or less of all tumors of the alimentary canal, and 60% or more[10] of tumors of the small intestine are thought to be benign. According to a report by Ohmiya et al.,[11] who collected data from seven facilities in Japan, neoplastic lesions were found in 21.7% of cases of OGIB, and the most common lesion was a gastrointestinal stromal tumor (Fig. 7). The next most common was a metastatic tumor of the small intestine, followed by malignant lymphomas and cancers of the small intestine.

Benefits of DBE for neoplastic lesions of the small intestine are (1) direct detailed observation is possible; (2) the extent of the lesion can be evaluated objectively by using selective contrast; (3) pathologic diagnosis is possible by biopsy; (4) tattooing of the tumor site to mark it for a surgical operation is possible; (5) the effects of chemotherapy can be evaluated; (6) endoscopic treatment (polypectomy[12] or endoscopic mucosal resection[13]) is possible for benign lesions or those without infiltration; and (7) for progressive tumors with stenosis, placement of a stent is possible, depending on the site (Fig. 8).[14]

Previously, definitive diagnosis of most small intestinal tumors was obtained only after surgical resection of the lesions. Using DBE, however, pathologic diagnosis as well as accurate diagnosis of the site or extent of the tumor can be done before surgery, thus helping avoid unnecessary surgery and in the selection of less-invasive surgical methods and the most appropriate treatment for the patients.

Ulcerative lesions

Differential diagnosis of ulcerative lesions in the small intestine includes benign inflammatory lesions, such as Crohn's disease, nonsteroidal anti-inflammatory drug enteritis, Behçet's disease, intestinal tuberculosis, ischemic enteritis, nonspecific multiple ulcers of the small intestine, and neoplastic lesions such as cancer and lymphoma. Neoplastic lesions can usually be diagnosed by biopsy. However, characteristic findings cannot be obtained only by biopsy of benign inflammatory ulcers in most cases; therefore, it is important to note the characteristics of an ulcer in terms of its shape, distribution, and localization. Localization of ulcers in the lumen of the small intestine (whether on the mesenteric or the antimesenteric side) is particularly important for differential diagnosis of some types of ulcerative lesions.[15] Ulcers typically are on the mesenteric side in Crohn's disease, and they are mainly on the antimesenteric side in Behçet's disease and intestinal tuberculosis. In DBE, the endoscope is inserted into the small intestine by making a concentric circles with its shaft, in either oral insertion or anal insertion. As a result, the mesentery is extended fanlike. In this situation, the mesenteric side is on the inside of the concentric circles. Therefore, when an endoscope is inserted by making circles at an upward angle, the upward direction tip movement indicates the mesenteric side. A radiograph clearly shows that the tip of an endoscope moves toward the center of the circle, and the wall near the tip is the mesenteric side.

However, the configuration of an inflammatory lesion is often not typical enough to reach a confirmed diagnosis with only one examination because of changes in the early phase of the disease or treatment. Therefore, diagnosis requires comprehensive consideration of the clinical course and observation of chronological changes of the lesions.

Treatment for Crohn's disease improved drastically with the use of immunosuppressive agents and anti-tumor necrosis factor α antibody, and the goal of medical therapy is shifting from clinical remission to mucosal healing (Fig. 9). The strategy centers on accurate periodic evaluation of the mucosal condition using capsule endoscopy or double-balloon endoscopy for selecting or adding treatment methods. By a strategy that aims at endoscopic remission (mucosal healing), the patient's quality of life will be improved with less possibility of complications in the intestinal tract such as stenosis or fistula.

Stenotic lesions

Using DBE, direct endoscopic observation of small intestinal stenosis is possible. From the endoscopic findings and pathologic findings of a biopsy specimen, the cause of the stenosis can be identified. The treatment strategy can be based on the condition and the cause of the stenosis.[16] In addition, endoscopic balloon dilation therapy may be possible, depending on the cause of the stenosis. (Fig. 10).[17]

Capsule endoscopy is efficient for diagnosing early-stage Crohn's disease and evaluation of disease progress; however, in patients with stenosis, retention is possible with capsule endoscopy. The patency capsule was developed to solve this problem; it is safer to perform a capsule endoscopic examination after discharge from the body of the patency capsule is confirmed. Before the availability of the patency capsule, a capsule endoscope retained at stenosis in a patient with Crohn's disease was retrieved by dilation of the stenosis by DBE.[18]

Application of DBE to the diagnosis of small bowel adhesions

After abdominal surgery or radiation therapy, adhesion sometimes occurs between parts of the intestinal tract or between the intestinal tract and the peritoneum. In

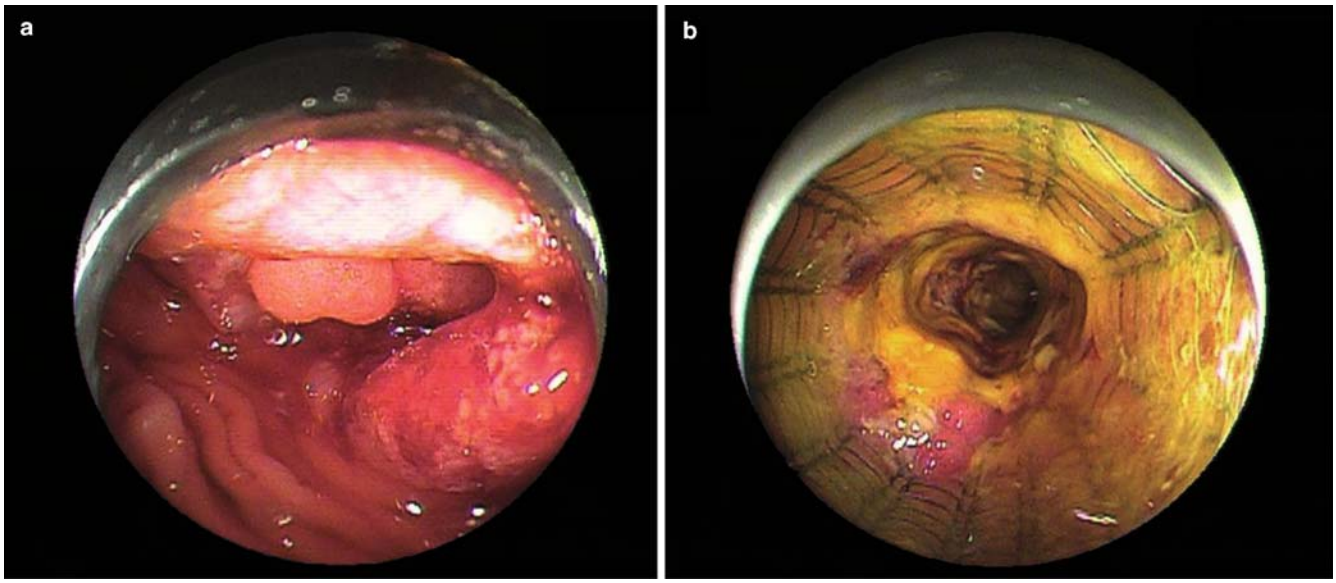

Fig. 8. **a** Advanced cancer in the jejunum. From Hayashi et al.[11] **b** Endoscopic view after metallic stent placement. From Hayashi et al.[14]

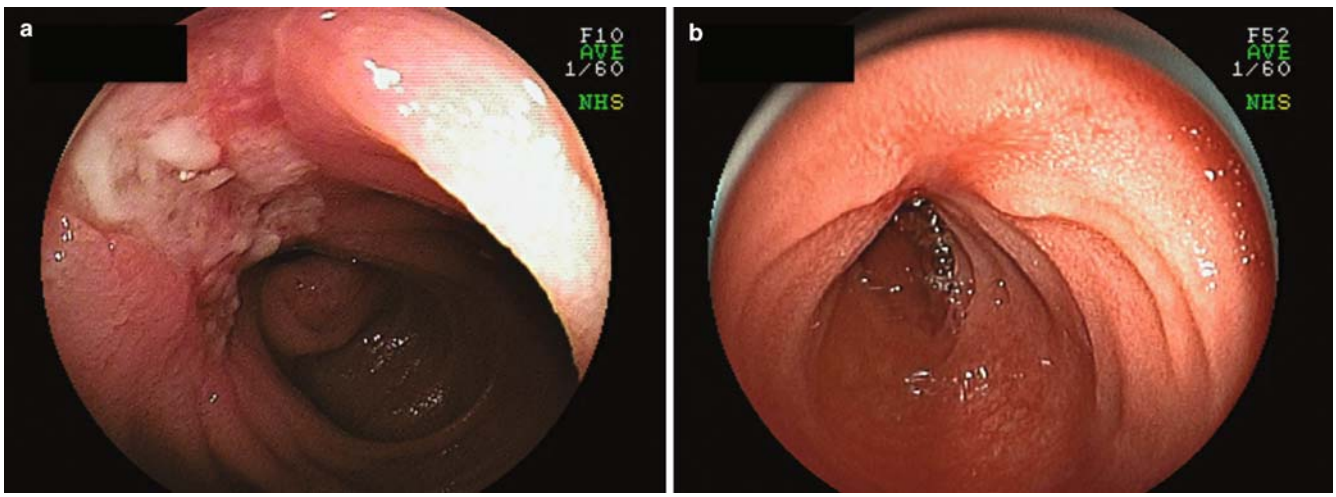

Fig. 9. **a** Active Crohn's ulcer observed in the ileum. **b** Healed ulcer after infliximab therapy

particular, in the event of severe inflammation in the peritoneal cavity, such as peritonitis, or after radiation therapy, adhesion occurs with high frequency. Adhesion causes bowel obstruction if the intestinal tract is distorted because of the adhesion or when fibrous strings are formed in the peritoneal cavity that press or pull the intestinal tract.

Emergency surgery is necessary if the bowel obstruction is associated with impaired blood circulation; however, many patients repeatedly show obstructive symptoms because of adhesion, which sometimes necessitates repeated hospitalization and strict diet restrictions.

In DBE, the endoscope is usually inserted by drawing a large concentric circles, but for patients with intestinal adhesions, the circles may suddenly becomes small or S-shaped, with the result that the endoscope does not move even after the endoscopist attempts to modify the shape of the intestinal tract by a shortening maneuver. In this situation, the presence of an adhesion at the site should be strongly suspected. In some cases, eccentric stenosis due to tightening by a fibrous string on the outside can be confirmed endoscopically. In these cases, no abnormality of the mucosal surface of the lumen is present at the stenotic site. After endoscopic identification and tattooing of the adhesion site, adhesiolysis

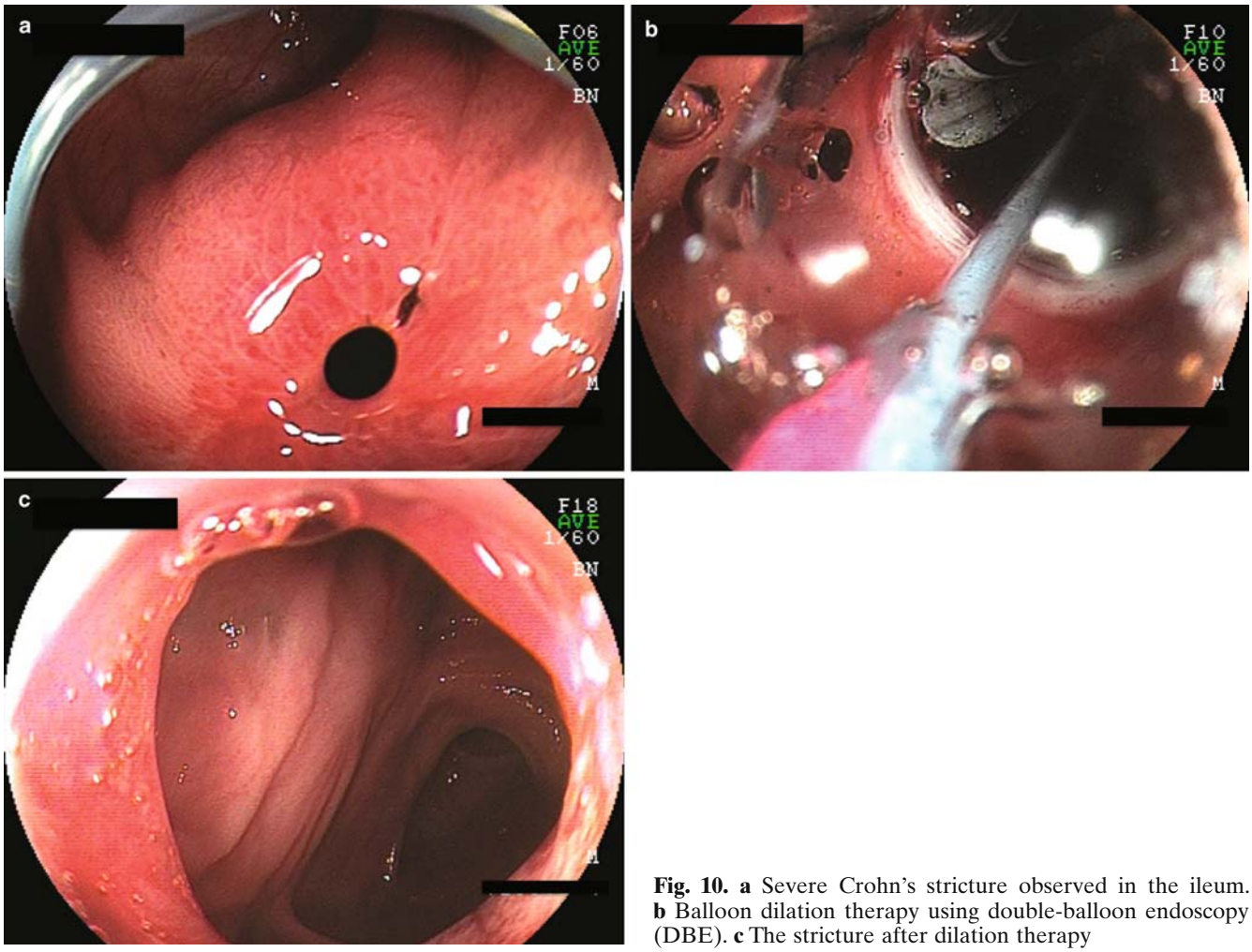

Fig. 10. a Severe Crohn's stricture observed in the ileum. **b** Balloon dilation therapy using double-balloon endoscopy (DBE). **c** The stricture after dilation therapy

during laparotomy or laparoscopy may be possible. These are less-invasive procedures involving only a small abdominal incision.

Therefore, DBE has several roles in clinical cases of adhesion of the small bowel: (1) exclusion of other causes (stenosis, etc.) such as tumors or inflammatory strictures;[19] and (2) support for the selection of less-invasive surgical methods by identifying and marking the adhesion site.

Application to the large intestine

Difficult colonoscopy

Colonoscopy is advancing with improvement of the successful insertion rate, reduction of the insertion time, and reduction in the degree of imposition on the subject by endoscope modifications and advances in insertion techniques. However, because of adhesions from abdominal surgery and the effects of gynecologic disorders, insertion during regular colonoscopy is occasionally very difficult and painful or insertion into the cecum may be impossible.

DBE was originally developed for observation and treatment of the deeper part of the small intestine. However, the ability to prevent extension of the intestinal tract, even at bends in the intestinal tract, by holding it with the overtube balloon during insertion of the endoscope is also a useful technique in the large intestine with an adhesion, making endoscopic insertion easy even in such cases.[20,21]

To date, we have experienced more than 150 cases of DBE used in difficult insertion colonoscopy cases. Using DBE, we have successfully completed a total colonoscopy in most of these cases. The EC450-BI5 endoscope is easy to handle because of its length, but another DBE for the small bowel can also be used for the colon as well, and the EN-450P5 is recommended for the most difficult cases with high-level and complicated adhesions.

Furthermore, DBE is useful not only for difficult insertion cases but also more widely for regular colo-

noscopies, as a method of painless insertion causing less discomfort to the patient.

Application to therapeutic colonoscopy

Although the use of endoscopic submucosal dissection (ESD) for early-stage gastric cancer has been expanding, ESD in the colon is regarded as more difficult technically because of the thin wall of the colon and the presence of plication and strong bending. However, ESD for a laterally spreading tumor, for which en bloc resection by snaring is difficult, has advantages over piecemeal resection, because recurrence after the resection is less likely and an accurate pathologic diagnosis is possible. We have been using a local injection of sodium hyaluronate together with a small caliber tip transparent hood (ST hood) and have been safely performing en bloc resection even of larger lesions (Fig. 11).[22,23]

We sometimes experience difficulty with endoscopic treatment in the deep part of the large intestine because of paradoxical movement. This means that even with the endoscope shaft inserted, the distal end of the endoscope is actually withdrawn because of extension of the flexure of the sigmoid and transverse colon. Especially for ESD, which requires precise treatment, the operator's intended detailed movements must be accurately transmitted to the distal end of the endoscope. By using a DBE, the overtube with the balloon prevents extension of the intestinal tract, and operation of the endoscopic shaft is directly transmitted to the distal end of the endoscope, enabling accurate and stable operation without paradoxical movement. In addition, the slim diameter of the double-balloon endoscope makes retroflex operation of its distal end possible not only in the rectum but also in the ascending and transverse colon. Therefore, incision and dissection on the oral side of the lesion would be easy as well.

The features of DBE can be applied to other colonoscopic treatments, such as polypectomy, hemostasis, and safe retrieval of foreign bodies. Therefore, further broadening of its application is expected.

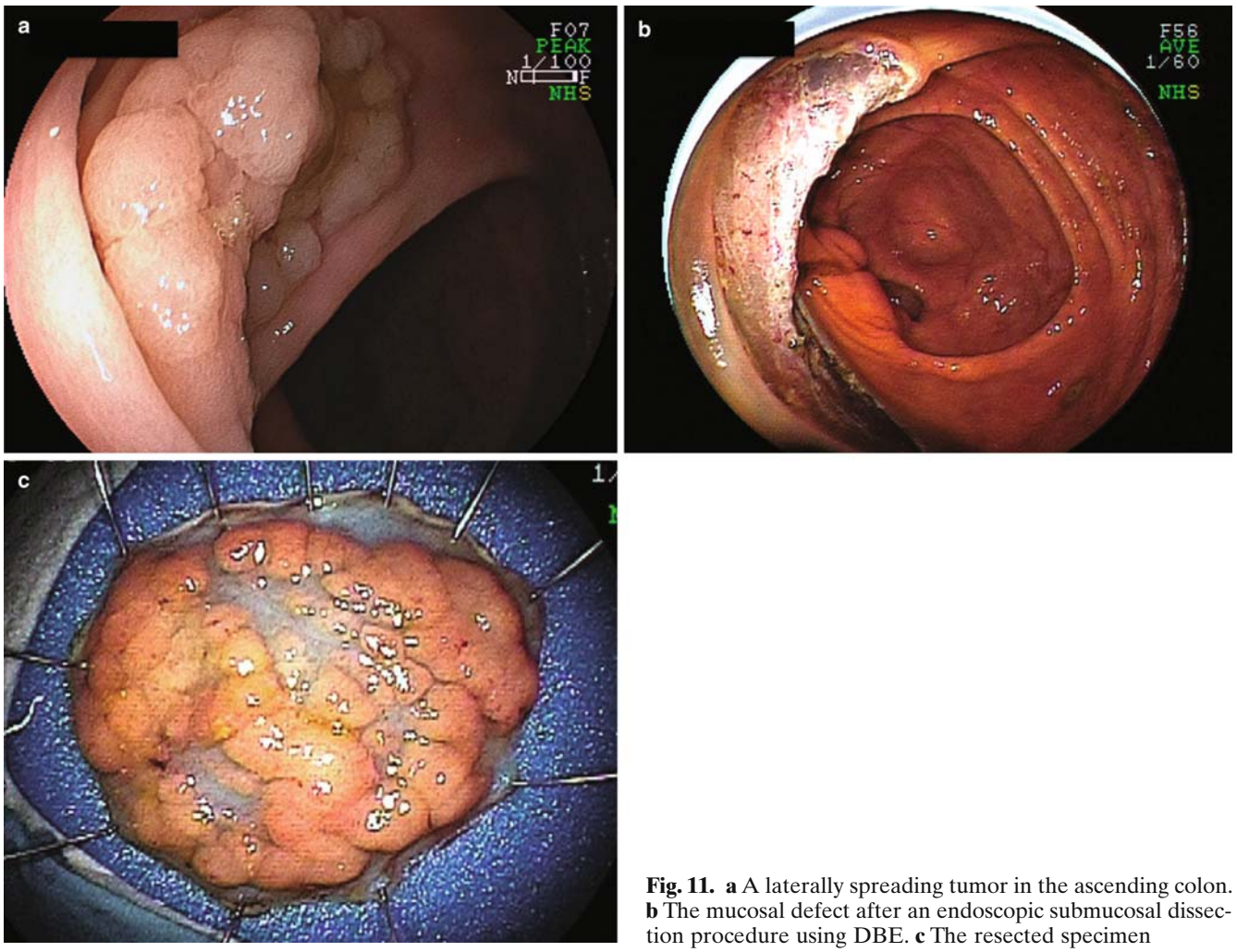

Fig. 11. **a** A laterally spreading tumor in the ascending colon. **b** The mucosal defect after an endoscopic submucosal dissection procedure using DBE. **c** The resected specimen

Application to pancreaticobiliary treatment

Examination of the afferent loop of the intestine with Roux-en-Y anastomosis is difficult by capsule endoscopy or contrast studies. In addition, in cases where the divergence is precipitous or the afferent loop has a long bend, even an endoscope with a long working length cannot reach the afferent loop. A double-balloon endoscope, however, can be selectively inserted into the afferent loop and can reach to the end in most cases. In particular, the EC450-BI5 model has great practical use because of the various pancreaticobiliary accessory devices available currently. Up to now, we have successfully performed various kinds of endoscopic procedures such as cholangiography,[24] dilation of the stenosis of a choledochojejunostomy,[25] and stent placement[24,26] in patients with Roux-en-Y anastomosis after liver transplantation.

In addition, selective insertion is possible in an intestinal tract with a bypass for a bowel obstruction, where multiple ulcers in the intestinal tract of the blind loop can be recognized, contributing to pathologic clarification of blind-loop syndrome.

Complications

DBE has been widely used and complications have been reported. Mensink et al.[27] compiled reports of complications from ten facilities in four countries. They reported that the incidence of complications was 0.8% (13/1728) for diagnostic DBE and 4.3% (27/634) for therapeutic DBE, and there were no fatal cases.

Perforation

In our department, we experienced four cases (0.4%) of perforation among 1091 small intestinal DBE examinations up to October 2007. (1) In a patient with active small bowel Crohn's disease, penetration at the base of a deep ulcer was recognized after the DBE examination, and localized peritonitis occurred, which could be managed conservatively. (2) A perforation was recognized after DBE in a patient with malignant lymphoma of the small intestine. The procedure was performed to determine the effect of chemotherapy, and the perforation was attributed to the chemotherapy rather than to the DBE procedure because the perforation was found on the side of the intestinal tract distal to the insertion site (the tissue was assumed to be weak because of the chemotherapy). (3) A perforation was recognized due to balloon dilation performed for stenosis of the small intestine of Crohn's disease. (4) Another perforation due to balloon dilation performed for stenosis of the small intestine of unknown cause was recognized. After an emergent operation, the cause of the stenosis turned out to be invasive pancreatic cancer.

From these experiences, we recommend the following to avoid perforation. (1) In the case of deep ulcerations such as in Crohn's disease, further insertion of the endoscope may be risky and forceful shortening should be avoided; (2) DBE examinations to judge the effect of chemotherapy should be performed only after a sufficient interval after final treatment so that the tissue can regenerate; (3) DBE should not be performed for dilation treatment in Crohn's disease if active ulceration is present at the stenosis, and in cases of prominent fibrosis, it should be started with a small dilating diameter and then gradually increasing the size; and (4) dilation therapy for a stenosis of unknown cause may carry considerable risk. In addition, because the wall of the small intestine is very thin, a local injection of physiologic saline should be made beneath the mucosa for polypectomy, except for pedunculated polyps, and a local injection of physiologic saline should be considered for APC and high-frequency ablation as well.

Bleeding

We have experienced bleeding after polypectomy when many polypectomy procedures were performed all at once. If the coagulation status is normal, bleeding may stop spontaneously, but in the case of continuous bleeding, consider reinserting the double-balloon endoscope for hemostasis by clip placement.

Acute pancreatitis

Acute pancreatitis after DBE examination has been reported.[28,29] According to the multicenter survey by Mensink et al.,[27] pancreatitis occurred in six of 1728 (0.3%) diagnostic DBE, and in one of 643 (0.2%) therapeutic DBE. In our department, we experienced two cases of pancreatitis in 1092 (0.18%) small intestinal DBE procedures up to October in 2007 (acute pancreatitis diagnosed by endoscopic retrograde cholangiopancreatography[30]). However, if pancreatitis cases diagnosed by CT imaging and an increase of amylase to less than three times the upper limit of normal, then we experience four cases (0.37%) in 1092 procedures. Possible mechanisms are (1) compressional obstruction of the papillary area of the duodenum; (2) reflux of intestinal fluid into the pancreatic duct by an increase of intraduodenal pressure; and (3) mechanical torsion of the pancreatic body during insertion (probably the primary mechanism). Therefore, for oral insertion, extreme shortening should not be done, and counterclockwise rotation is better. In addition, even if pancreatitis does not occur, the serum amylase level often increases after a DBE examination.[31]

Conclusion

By development and adoption of DBE, diagnosis of diseases of the small bowel, which used to depend to a great extent on radiologic diagnosis, has been significantly advanced because direct observation and qualitative diagnosis became possible. In addition, a variety of endoscopic treatments became possible for the small intestine as well as for the stomach and the colon. On the other hand, the capsule endoscope, developed around the same time, made noninvasive small bowel examinations possible. As a result of these two advances, diagnostic performance is becoming excellent for various diseases of the small intestine. In the future, integrated diagnosis and treatment of diseases of the small intestine, taking advantage of the features of both modalities, will be established.

In the future, DBE is expected to be useful for not only diagnosis and treatment of intestinal diseases but also for clarification of the underlying etiology. Because DBE can be used to obtain biopsy tissue, it is useful for not only histological but also microbiological and molecular biological investigations. In addition, many of the effects of various medications on the small intestine used to be unknown; however, they will be clarified through prospective clinical studies in the near future. Furthermore, DBE will likely contribute to the development of new medical agents for treating small intestinal disease.

With the cooperation of many endoscopists, DBE is expected to be an efficient modality for patients with various intestinal diseases and to contribute to the establishment of the medical science of small intestinal diseases in the future.

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