Table 1 Clinicopathological characteristics of colorectal neoplasia

Gender	
Male	637
Female	392
Age(mean ± SD), years	65.2 ± 11.7
Tumor size (mean ± SD), mm	26.4 ± 8.6
Tumor location	
Rectum	162
Sigmoid colon	300
Descending colon	38
Transverse colon	161
Ascending colon	231
Cecum	137
Gross appearance	
Ip	239
Is	231
LST-G	352
LST-NG	164
Others	43
Treatment method	
EMR	866
Polypectomy	163
Pathology	
Category 1 or 2	24
Category 3	502
Category 4 or 5	503

Ip pedunculated type, *Is* sessile type, *LST-G* laterally spreading tumor granular type, *LST-NG* laterally spreading tumor non-granular type, *EMR* endoscopic mucosal resection

classification category 4–5 and en bloc resection were significant risk factors for perforation (Table 3). No procedure-related mortality was reported. The overall complication rate was 2.3 %.

Discussion

EMR and polypectomy are well-tolerated and cost-effective procedures in the management of large colorectal lesions. Our multicenter study also shows that CER is a safe and effective therapy for large colorectal lesions. Until recently, surgery has been a standard treatment for large early neoplasms. However, these lesions are frequently detected in elderly patients who are often associated with comorbidities and higher surgical risk. Endoscopic treatment of large sessile polyps is less invasive, avoids a major operation, and is also associated with fewer complications.

Clinically, post procedure bleeding and perforation remain the most common complications. According to the literature, the rate of post procedure bleeding after CER is reported to be between 0.4 and 7.0 % although the size of the subject lesions was varied [17–19]. In the present study, the post procedure bleeding rate for colorectal lesions sized ≧20 mm was 1.6 %. The multivariate analysis of the data revealed that the age under 60 years old is a risk factor for post procedure bleeding (OR = 6.53, 95 % CI 2.38–17.92). Kim et al. [20] reported that the average age of patients was lower in bleeding patients after colorectal endoscopic resection, but the difference was not statistically significant.

Table 2 Multivariable analysis of lesion characteristics, odds ratio, and 95 % confidence interval concerning post procedure bleeding

		Bleeding	No bleeding	Odds ratio	95 % Confidence interval
Gender	Male = 0	12	625	0.74	0.27–2.05
	Female = 1	6	386		
Age	≧60 = 0	6	730	6.53	2.38–17.92
	<60 = 1	12	281		
Tumor size	≧30 mm = 0	6	294	0.90	0.31–2.66
	20–29 mm = 1	12	717		
Tumor location	Proximal = 0	12	517	0.46	0.16–1.32
	Distal = 1	6	494		
Gross appearance	LST-NG = 0	5	159	1.28	0.27–6.01
	Non LST-NG = 1	13	852		
Treatment method	EMR = 0	17	849	0.27	0.03–2.25
	Polypectomy = 1	1	162		
Resection type	en bloc = 0	10	576	0.89	0.32–2.52
	Piecemeal = 1	8	435		
Insufflation	CO2 = 0	9	409	0.81	0.30–2.18
	Room air = 1	9	602		
Pathology	Category 1–3 = 0	7	519	1.83	0.67–4.97
	Category 4–5 = 1	11	492		

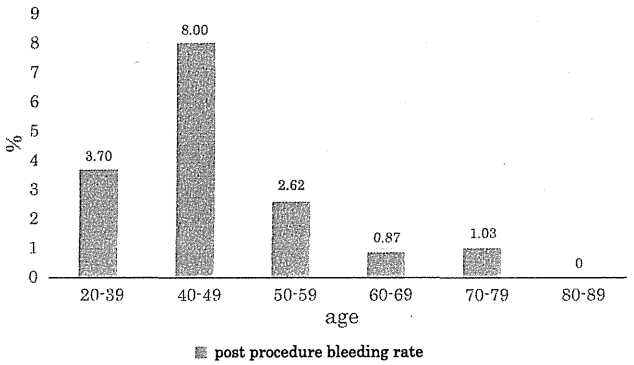

Fig. 1 Age-specific post procedure bleeding rate

To our best knowledge, this study is the first to show statistically higher incidence of bleeding in younger patients. No statistically significant difference of bleeding rate was found regarding gender, tumor size (between 20–29 mm and ≥30 mm), treatment method, gross appearance, kind of insufflation (CO2 or room air), and pathology. Lim et al. [21] reported that complications were encountered more frequently when the lesion size was larger. In our study, we included only lesions ≧20 mm. There was no difference of bleeding rate between the lesions 30 mm or larger in diameter and those less than 30 mm. Bleeding rate is probably different between lesions <20 mm and those ≧20 mm, but may not increase any more even if the size becomes 30 mm or larger. Metz et al. reported that proximal location of the lesion is a highly significant risk for delayed bleeding following colonic EMR of large colonic lesions [20]. In our study, the bleeding rate in the proximal and distal colon (including the rectum) was not significantly different. Fettata et al. reported that bleeding incidence was related to malignancy ($P = 0.01$) [22]. In the present study, 11 of 18 bleeding cases were encountered in lesions of Vienna classification category 4–5, but the rate was not significantly high (category 1–3 = 0, category 4–5 = 1, OR = 1.83, 95 % CI 0.67–4.97).

Araghizadef et al. [23] reported that the perforation rate of standard diagnostic colonoscopy was 0.09 %. Perforation related to endoscopic resection has been reported to be between 0.7 and 4 % [24–26] and higher than in diagnostic colonoscopy. The perforation rate was 0.78 % in the present study. Though we enrolled only lesions sized 20 mm or larger, the perforation rate was as low as the previous reports including smaller lesions. In this study, perforation was encountered in 8 lesions, all of which had been resected with EMR technique. Risk factors for perforation in multivariate analysis were en bloc resection (en bloc = 0, piecemeal = 1, OR = 0.08, 95 % CI 0.01–0.78) and category 4–5 (category 1–3 = 0, category 4–5 = 1, OR = 9.11, 95 % CI 1.03–80.79). According to our results, it is not recommended to adhere to en bloc resection in colorectal lesions ≧20 mm, as it may lead to perforation. No statistically significant differences of perforation rate were found regarding gender, size, tumor location, gross appearance, and kind of insufflation (CO_2 or room air).

Preference has been suggested in some studies for en bloc resection compared with piecemeal resection because it provides more accurate histological assessment and reduces the risk of local recurrence [27]. Hotta et al. reported that the en bloc resection rates were 91.5 % for colorectal neoplasms sized less than 20 mm and 43.0 % for

Table 3 Multivariable analysis of lesion characteristics, odds ratio, and 95 % confidence interval concerning perforation

		Perforation	No perforation	Odds ratio	95 % Confidence interval
Gender	Male = 0	5	632	0.89	0.20–3.96
	Female = 1	3	389		
Age	≧60 = 0	6	730	1.06	0.20–5.58
	<60 = 1	2	291		
Tumor size	≧30 mm = 0	3	297	0.53	0.11–2.47
	20–29 mm = 1	5	724		
Tumor location	Proximal = 0	6	523	0.27	0.05–1.48
	Distal = 1	2	498		
Gross appearance	LST-NG = 0	3	161	0.22	0.03–1.37
	Non LST-NG = 1	5	860		
Resection type	en bloc = 0	7	579	0.08	0.01–0.78
	Piecemeal = 1	1	442		
Insufflation	CO2 = 0	6	412	0.27	0.05–1.59
	Room air = 1	2	609		
Pathology	Category 1–3 = 0	1	525	9.11	1.03–80.79
	Category 4–5 = 1	7	496		

those sized 20 mm or larger [28]. Colorectal ESD technique is spreading gradually, but it is still very demanding due to its technical difficulty, long procedure time, and high rate of perforation. Nakajima et al. [29] reported that the en bloc resection rate for ESD was significantly higher than for CER. On the other hand, according to Kunihiro et al. [27], there was no statistically significant difference in the recurrence rate between en bloc and piecemeal resection groups. Endoscopic piecemeal mucosal resection for colorectal neoplasms ≧20 mm is usually useful. However, the area that suggests submucosal invasion should not cut in piece because it would interfere with a correct pathological diagnosis and because it might result in a local recurrence. In such cases, magnifying colonoscopy is very useful as it enables us to distinguish between neoplasia and non-neoplasia or between adenoma and carcinoma and to predict the degree of invasion. It is especially important to see if the lesion presents with type V pit pattern as it would indicate the lesion may be invasive [30].

In conclusion, CER is a safe, efficient, and effective minimally invasive therapy for large colorectal lesions. However, care should be taken for post procedure bleeding in patients under 60 years of age and for perforation in lesions with higher categories (4, 5) or when en bloc resection is tried.

The limitation of this study is rather small number of complications. It could not be avoided due to two reasons. One is that the present study is the subanalysis of the prospective study which was designed for a different main endpoint, and the power calculation was performed for that goal. The other reason is that the complication rate is sufficiently low enough in our endoscopic treatment and it would require vast number of lesions to establish a statistically significant difference among certain subgroups. In spite of the limitation, we believe that the results of this study are valuable as it is a multicenter prospective study which dealt with the largest number of colorectal lesions ≧20 mm so far to our best knowledge. Another study with larger scale is warranted.

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Original Article

Double-balloon endoscopy is safe and effective for the diagnosis and treatment of small-bowel disorders: Prospective multicenter study carried out by expert and non-expert endoscopists in Japan

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Background and Aim: Double-balloon endoscopy (DBE) has enabled direct, detailed examination of the entire small bowel with interventional capabilities. Although its usefulness is recognized, efficacy and safety have not been extensively evaluated by prospective multicenter studies. To evaluate the efficacy and safety of DBE carried out by expert and non-expert endoscopists, a prospective, multicenter study was conducted in five university hospitals and a general hospital in Japan.

Methods: A total of 120 patients who underwent 179 procedures were enrolled in the study. Experts carried out 129 procedures and non-experts carried out 50 procedures. Primary and secondary end points were evaluation of safety, the rate of achievement of procedural objectives, namely, identification of a new lesion, detailed examination to establish a therapeutic strategy, or exclusion of significant lesions by total enteroscopy, and rate of successful examination of the entire small bowel and evaluation of safety.

Results: Overall rate of achievement of procedural objectives was 82.5% (99/120). Overall success rate for examination of the entire small bowel was 70.8% (34/48). Incidence of adverse events was 1.1% (a mucosal injury and an episode of pyrexia in two of 179 examinations). No severe adverse events were encountered. There were no significant differences in any of the outcome measures comparing expert and non-expert operators.

Conclusions: DBE is effective and safe for patients with suspected small bowel diseases, and can be safely carried out even by a non-expert under the supervision of an expert, following a simple training program.

Key words: digestive system endoscopy, double-balloon endoscopy, enteroscopy, small intestinal disease, training program

INTRODUCTION

DOUBLE-BALLOON ENDOSCOPY (DBE), which uses balloons fitted to the tips of both an endoscope and an overtube was developed to realize direct, detailed examination of the entire small bowel.[1] DBE allows detailed examination of the target area, endoscopic interventions, and definitive diagnosis by biopsy because the balloons fitted to the tips of both the endoscope and the overtube fix the small bowel in place. DBE is currently used in more than 65 countries worldwide, and its usefulness is widely recognized. However, an advanced insertion technique is considered necessary to carry out DBE, and its use is still limited to tertiary medical facilities.

Many studies[2] have been published on the safety and efficacy of DBE, but most were single-center retrospective studies. There are few multicenter prospective studies.[3] In addition, the efficacy and safety of DBE carried out by non-expert endoscopists have not been sufficiently verified.[4,5] Non-expert endoscopists may be able to carry out

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DBE safely if they thoroughly understand the principles of DBE insertion and participate in an appropriate training program.

We conducted a prospective, multicenter study of the efficacy and safety of DBE in Japan, and also examined the efficacy and safety of DBE when carried out by expert and non-expert endoscopists.

METHODS

Patient selection

PATIENTS ELIGIBLE FOR inclusion in the present study had to meet the following criteria: a patient with suspected small-bowel disease based on symptoms and other examinations who is considered to require endoscopic examination and/or treatment of the distal small bowel (a suspected case of gastrointestinal bleeding of unknown cause, a suspected case of apparent small-bowel bleeding, a patient with other suspected small-bowel disease, or a patient requiring foreign body removal from the small bowel), of either gender, aged between 13 and 79 years, and in whom previous examinations determined that DBE is appropriate.

Any patient meeting any of the following criteria was excluded from the study: (i) acute abdomen; (ii) serious acute inflammation; (iii) hypersensitivity to natural latex; (iv) poor general condition; (v) a suspected case of perforation of the intestines; (vi) any serious blood coagulation abnormality; (vii) serious hepatic dysfunction; (viii) any serious respiratory or circulatory disorder; (ix) pregnancy or possible pregnancy; (x) insertion from a stoma; and (xi) a patient determined ineligible by a physician.

Among the inpatients and outpatients who visited six medical institutions between October 2008 and April 2009, 120 patients who met the above criteria were enrolled. The study was conducted in accordance with the Declaration of Helsinki and the Ministerial Ordinance on the Good Clinical Practice for Medical Devices in Japan. Written informed consent was obtained from all patients.

Study devices

Two types of endoscopes were used in this study: XP-45 (Fujifilm Corporation, Tokyo, Japan; diagnostic endoscope equivalent to EN-450P5/20 by Fujifilm Corporation, outer diameter of the distal end 8.5 mm, forceps channel diameter 2.2 mm), and XT-45 (Fujifilm Corporation; therapeutic endoscope equivalent to EN-450T5/W by Fujifilm Corporation, outer diameter of the distal end 9.4 mm, forceps channel diameter 2.8 mm). Their corresponding overtube and a balloon on the tip of the endoscope were combined to make a double-balloon endoscope.

Table 1 Efficacy and safety of DBE conducted in one general and five university hospitals

Study site	No. patients enrolled	No. examinations	
		First	Second
Jichi Medical University Hospital	20	20	5
Nippon Medical School Hospital	20	20	10
Nagoya University Hospital	26	26	10
Hiroshima University Hospital	20	20	14
Showa University Fujigaoka Hospital	18	18	8
Sendai Kousei Hospital	16	16	12
Total	120	179	

DBE, double-balloon endoscopy.

Study design

The study was designed as a multicenter, single-arm, open-label study, and conducted at a total of six institutions including five university hospitals and a general hospital (Table 1).

The protocol was approved by the independent ethics committee of each institution. The study was registered within the University Hospital Medical Information Network Clinical Trials Registry (UMIN-CTR) under registration number UMIN000005137.

Experts and non-experts participated in the present study. All institutions in this study were high-volume DBE centers. Experts were teaching staff of these institutions. Non-experts were selected from trainees of these institutions who had completed training of regular endoscopies including colonoscopy. The non-expert in this study was defined as a physician who had carried out <10 DBE (excluding experience in assisting with DBE). Non-experts carried out DBE in this study after a simple training session. During this training session, a 24-page simple manual, which was abstracted from a published textbook,[6] was provided. Non-expert participants read the manual to understand how DBE works and how to carry out DBE. Experts helped the non-experts understand the text when necessary. No hands-on training was provided.

An expert observed endoscopy procedures carried out by any non-expert. To ensure safety, the expert took over when an adverse event necessitated intervention, when insertion time >40 min and insertion was not efficient, when endoscopic therapy required a high level of skill, or when the expert determined that it was necessary to take over. Each institution was advised to assign patients to non-experts in approximately every three patients. However, the final decision regarding the selection of operator (expert or non-expert) was left to the discretion of the physicians at each

institution. Maximum insertion time by non-experts was limited to 40 min because excessive procedure time could increase the risk of complications such as pancreatitis.

All DBE procedures were carried out with room air insufflation. The insertion route was selected according to the site of the lesion, inferred from information including the patient's clinical history or from other examinations prior to endoscopy. Peroral insertion was used for a suspected jejunal lesion and transanal insertion was used for a suspected ileal lesion. The final decision regarding the route of insertion was left to the discretion of the physicians at each institution. Depending on the individual patient, both peroral and transanal endoscopies were carried out as needed.

When both peroral and transanal endoscopies were carried out on a patient, they were spaced 1 to 8 days apart. Therefore, the examinations were carried out not necessarily by the same endoscopist. Before and during endoscopy, suitable sedation was given as needed. To identify adverse events, pulse rate, blood pressure, electrocardiogram (ECG), interview (pain, bowel movement), palpation (abdominal tenderness), and clinical tests (hematology, blood biochemistry, urinalysis) were evaluated before endoscopy and no more than 3 days after endoscopy, or at discontinuation of participation in the study. Abdominal computed tomography (CT) scan was done as needed. During endoscopy, fluoroscopy was used as indicated and the patient's respiratory and circulatory condition was observed by monitoring the blood pressure, ECG, and SpO_2.

When disease condition necessitated endoscopic observation of the entire small bowel, both peroral and transanal endoscopies were done. Physicians at each institution determined the route that was used for the first examination in each patient. With endoscopic observation of the entire small bowel, a tattoo was applied to the deepest part reached during the first examination and, at the second examination, an endoscope was inserted in the opposite direction and had to reach the tattoo placed during the first examination to confirm successful observation of the entire small bowel. When a new tattoo was considered unnecessary because of an apparent, existing pointer such as a previous tattoo or stricture, that pointer was used.

Depth of insertion, duration of examination, performance of interventions, findings, provision of a diagnosis, reason for terminating an insertion and other data were recorded for both peroral and transanal insertions, as survey items for evaluation of efficacy. In addition, success or failure of observation of the entire small bowel was recorded when endoscopies were carried out by both insertion routes.

Depth of insertion was defined as the distance from the pyloric ring with peroral insertion, and from the ileocecal valve with transanal insertion, to the deepest insertion point. According to the study[7] by May *et al.*, depth of insertion was calculated as the sum of the estimated length inserted at each stroke when the endoscope was pushed while the overtube was fixed in place. When the target lesion was reached and further insertion was considered unnecessary, insertion was terminated even if deeper insertion was possible. The distance to the deepest lesion was used as the depth of insertion.

Statistical analysis and outcomes

Primary end points were safety and efficacy of the procedure. Safety was evaluated based on incidence of adverse events, overall safety, and changes in laboratory values. Efficacy was evaluated based on the rate of achievement of the procedural objectives. Achievement of the procedural objectives was defined as follows: (i) identification of a lesion in patients with unknown small intestinal lesions; (ii) determination of necessity for endoscopic interventions or surgical procedure/drug treatment by a detailed examination of the lesion in patients with known or highly suspected small intestinal lesions; and (iii) confirmation of the absence of a significant lesion by endoscopic observation of the entire small bowel.

Any significant findings other than normal findings during endoscopic observation were considered positive findings. When positive findings were considered lesions, identification of the findings was defined as the endoscopic diagnosis.

Secondary end points were rate of successful observation of the entire small bowel, depth of insertion, duration of insertion, and rates of execution of endoscopic interventions as adjuncts to efficacy evaluation.

Experts and non-experts were compared in terms of efficacy and safety. Analysis of efficacy was conducted using the full analysis set which excluded patients in whom no efficacy evaluation was carried out from all patients in which endoscopy was carried out. Analysis of safety was conducted for all patients in which endoscopy was carried out.

RESULTS

THE STUDY EVALUATED a total of 120 patients in six institutions, as shown in Table 1. A complete analysis was carried out for all 120 patients, which included 77 males (62.4%). Average age was 52.4 years and three patients were minors (14–19 years of age).

Sixty-one patients underwent a single examination, and 59 underwent a second examination by a different insertion route. The total number of examinations was 179, including 78 peroral insertions and 101 transanal insertions. Experts carried out 129 examinations and non-experts carried out 50 examinations. Among the 50 examinations (34 patients) carried out by non-experts, 17 examinations (15 patients)

Table 2 Achievement of procedural objectives in 99 patients undergoing DBE

Objective achieved	No. patients	%
Identification of a new lesion	16	16.2
Examination of the entire small bowel confirmed the absence of a lesion by endoscopy	18	18.2
Necessity for treatment was assessed by a detailed examination of the lesion	65	65.7

DBE, double-balloon endoscopy.

Table 3 Achievement of objectives according to proficiency of endoscopist

	No. patients in whom objectives were achieved	Total no. patients	Rate of achievement of objectives (%)
Total	99	120	82.5
Expert	67	80	83.8
Non-expert	29	34	85.3
Other†	3	6	–

†Patients for whom an expert carried out the first or second examination and a non-expert carried out the other.

were taken over by the supervising expert during the examination. Reasons for the takeovers included 'endoscopic therapy required a high level of skill' in two examinations, 'insertion time exceeded 40 min and the insertion was not efficient' in six examinations and 'the expert determined that it was necessary to take over' in nine examinations.

Clinical usefulness

Procedural objectives were achieved in 99 patients with an achievement rate of 82.5% (99 out of 120 patients). Breakdown of the achievement of procedural objectives is given in Table 2.

Rates of achievement of objectives by proficiency of the endoscopist

Rates of achievement of procedural objectives according to proficiency of the endoscopist are shown in Table 3. No statistically significant difference in the rate of achievement of the procedural objectives was found between experts and non-experts ($P = 1.000$). Non-experts achieved the objectives in 85.3% (29/34) of patients. Even after excluding the 17 examinations that were taken over by experts during the procedure, the objectives were achieved in 18 patients (85.7%) among 21 patients completed by non-experts alone.

Table 4 Achievement of objectives according to device and insertion route

	No. patients in whom objectives were achieved	Total no. patients	Rate of achievement of objectives (%)
Endoscope			
XP-45 (diagnostic)	68	85	80.0
XT-45 (therapeutic)	27	31	87.1
Combination of two types	4	4	100
Insertion route			
Peroral	13	19	68.4
Transanal	36	42	85.7
Peroral and transanal	50	59	84.7

XP-45, Fujifilm Corporation, Tokyo, Japan; XT-45, Fujifilm Corporation, Tokyo, Japan.

Rates of achievement of objectives by type of endoscope and insertion route

Rates of achievement of the procedural objectives by type of endoscope and insertion route are shown in Table 4. No significant differences were found based on these factors.

Rates of successful observation of the entire small bowel

Among the 59 patients who underwent bidirectional enteroscopy, observation of the entire small bowel was attempted in 48 patients. Success was achieved in 34 patients, with a 70.8% (34/48) success rate for observation of the entire small bowel. No significant difference in the success rates was found between experts and non-experts (Table 5).

Peroral insertion

Analysis of procedural outcomes with peroral insertion are shown in Table 6. Mean depth of insertion from the pyloric ring was 219 ± 109 cm and maximum depth of insertion was 465 cm. Endoscopic interventions were carried out in 74.4% (58/78) of the examinations.

Endoscopic findings were positive in 62.8% (49/78) of examinations and an endoscopic diagnosis was made in 53.8% (42/78) of examinations. Mean total duration of examination was 67.3 min.

Transanal insertion

Procedure outcomes after transanal insertion are shown in Table 7. Mean depth of insertion from the ileocecal valve

Table 5 Success rates for examination of the entire small bowel

	No. successful examinations of the entire small bowel	No. patients	Success rate (%)
Total	34	48	70.8
Expert	24	35	68.6
Non-expert	7	8	87.5
Other†	3	5	–

†Patients for whom an expert carried out the first or second examination and a non-expert carried out the other examination.

was 159 ± 100 cm and maximum depth of insertion was 455 cm. Endoscopic interventions were carried out in 91.1% (92/101) of the examinations.

Endoscopic findings were positive in 62.4% (63/101), and an endoscopic diagnosis was made in 61.4% (62/101) of the examinations. Mean total duration of examination was 74.5 min.

Adverse events

Adverse events were observed in two patients – a mucosal injury and an episode of pyrexia (1.1%: 2/179 examinations), but no severe adverse events occurred (Table 8). Eleven patients had an increase in serum amylase and lipase levels; however, no clinical findings were noted that suggested acute pancreatitis, such as abdominal or back pain.

DISCUSSION

THE EFFICACY AND safety of DBE were demonstrated in this multicenter prospective study. To examine the usefulness of DBE in the clinical setting, the study was conducted in patients who required endoscopic examination or treatment of suspected small bowel disease. Whereas diagnostic yield is often used as an index to evaluate the efficacy of diagnostic medical devices such as endoscopes, the present study adopted the rate of achievement of specific procedural objectives as an index of efficacy. The use of diagnostic yield is appropriate when a study has a limited target population such as patients with obscure gastrointestinal bleeding. We considered that use of the rate of achievement of procedural objectives as an index was more appropriate for this study because of the broad target population; namely, patients with suspected small bowel disease. In the evaluation of patients suspected to have small bowel disease, the procedural objectives included not only making a diagnosis but also providing treatment and ruling out disease. As disease prevalence in such patients greatly affects the diagnostic yield, and patients with a known, definitive diagnosis were also included in the study, we concluded that use of diagnostic yield for efficacy evaluation was inappropriate. The high achievement rate of 82.5% in this study indicates the excellent efficacy of DBE.

A prospective, comparative study of DBE and push enteroscopy[8] reported that the depth of insertion was significantly greater in DBE than in push enteroscopy, with mean depths of insertion from the pyloric ring of 230 cm and 80 cm, respectively. The present study also demonstrated the great depth of insertion in DBE either by peroral insertion or transanal insertion. Success rate of total enteroscopy by the combination of both routes was also high (70.8%).

Endoscopic interventions were carried out at high rates in this study. All patients requiring endoscopic interventions were able to undergo them. This finding shows the excellent intervention capability of DBE.

The results of the present study also demonstrate the safety of DBE. An overall rate of adverse events was as low as 1.1% with no severe events. We believe that this low incidence of adverse events in the study patients, many of whom underwent endoscopic interventions, adequately confirms the safety of DBE.

Developments of acute pancreatitis and increases in serum amylase levels have been reported after DBE.[9,10] Pancreatitis was observed in 0.3% of 2362 patients who underwent DBE in a single review.[9] The suggested mechanism was as follows: (i) obstruction of the duodenal papilla as a result of compression; (ii) reflux of pancreatic secretions as a result of increased internal pressure in the duodenum; and (iii) mechanical stimulation of the pancreas on insertion.[11] In the present study, 11 patients had an increase in serum amylase and lipase levels. However, it was transient, and no clinical findings suggested acute pancreatitis.

In the present study, efficacy and safety were comparable in procedures carried out by both experts and non-experts. This indicates that DBE can be safely and effectively carried out by non-experts under the supervision of experts, provided the non-experts complete a simple training course, as was done in this study.

Limitations of the present study include that it was a single-arm study without a control group and that conduct of a procedure by an expert or non-expert was not randomized. Taking patient safety into consideration, difficult cases could not be assigned to non-experts. We cannot exclude the possibility that relatively easy cases were unevenly assigned to non-experts. Even taking this fact into consideration, however, the high efficacy and safety shown by non-experts suggests that acquisition of technical skill at DBE is relatively easy as long as DBE is done with proper guidance and with an understanding of the procedure.

In conclusion, DBE is effective and safe for patients with suspected small bowel diseases, and can be safely carried out

Table 6 Analysis of procedural outcomes after peroral insertion

	No. examinations (%)	Mean	SD	Maximum value	Minimum value
Depth of insertion from pyloric ring (maximum depth of insertion or distance to deepest lesion: cm)	78	219.01	109.40	465.0	37.0
Duration of examination (min)					
Total duration of examination	78	67.28	25.97	191.0	15.0
Duration of insertion (min)					
From pyloric ring to 100-cm point	67	14.06	8.00	36.0	5.0
From pyloric ring to final observation site	78	38.51	17.74	78.0	5.0
Endoscopic interventions done	58 (74.4%)				
Positive endoscopic findings	49 (62.8%)				
Endoscopic diagnosis	42 (53.8%)				

Table 7 Analysis of procedural outcomes after transanal insertion

	No. examinations (%)	Mean	SD	Maximum value	Minimum value
Depth of insertion from ileocecal valve (maximum depth of insertion or the distance to the deepest lesion: cm)	101	158.68	99.56	455.0	2.0
Duration of examination (minutes)					
Total duration of examination	101	74.50	25.16	148.0	24.0
Duration of insertion					
From the anal canal to ileocecal valve	101	12.30	8.05	58.0	2.0
From ileocecal valve to the 50 cm point	92	13.29	10.72	58.0	2.0
From ileocecal valve to the final observation site	101	39.50	19.96	96.0	1.0
Endoscopic interventions were done	92 (91.1%)				
Positive endoscopic findings	63 (62.4%)				
Endoscopic diagnosis	62 (61.4%)				

Table 8 Incidence of adverse events

	No. adverse events	No. examinations	Incidence of adverse events (%)
Total	2	179	1.1
Expert	2	129	1.6
Non-expert	0	50	0

Among the 50 examinations initially carried out by non-experts, 17 examinations were taken over by an expert during the examination.

even by non-experts under the supervision of experts, following a simple training program.

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CONFLICT OF INTERESTS

AUTHOR H.Y. WAS supported by donations from FUJIFILM Corporation, Tokyo, Japan, and has patents for double-balloon endoscope and endoscopic submucosal dissection (ESD) devices produced by FUJIFILM Corporation. He also has a consultant relationship in FUJIFILM Corporation and has received honoraria, grants and royalties from the company. Authors T.M., M.I and K.S. were paid consultants of this study. No other authors had personal financial relationships with a commercial entity producing health-care-related products and/or services relevant to this article. FUJIFILM Corporation, Tokyo, Japan, which was to receive approval for manufacture of the endoscopes XP-45 and XT-45 from the Ministry of Health, Labor, and Welfare of Japan, supported this clinical study. Fujifilm Corporation contracted and paid all hospitals on the basis of good clinical practice as a clinical trial.

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COMMENTARY
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Narrow Band Imaging as an Efficient and Economical Tool in Diagnosing Colorectal Polyps

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See "A Randomized Controlled Clinical Study Comparing the Diagnostic Accuracy of the Histologic Prediction for Colorectal Polyps Depending on the Use of Either Magnified or Nonmagnified Narrow Band Imaging" by Jin Joo Kim, Kyoung Sup Hong, Joo Sung Kim and Hyun Chae Jung, on page 528-533.

INTRODUCTION

Colorectal cancer (CRC) is one of the leading causes of cancer-related death in males and females of the Western world, and is one of the most prevalent cancers amongst populations (including within Asian countries).[1] Screening for CRC should be considered a medical priority in all health systems and reduced mortality from CRC could be achieved by improving the available screening methods. The early detection and removal of neoplastic polyps is essential in this challenge because the sequential development of an adenoma into a carcinoma has become a well-understood process. This sequential model describes the development of cancer in relation to the stepwise pattern of mutational activation of oncogenes and inactivation of tumor suppressor genes. Colonoscopy is the only available technique that allows for removal of adenomas, thereby preventing progression towards CRC. Unnecessary risks associated with polyp removal should be avoided. Since Gono and colleagues[2] designed narrow band imaging (NBI), this digital optical enhancement method of gastrointestinal endoscopy has become a popular imaging technique. Importantly, it can distinguish between neoplastic and non-neoplastic lesions without requiring the use of a dye.[3,4] Magnifying endoscopy, in combination with the digitally enhanced method, provides an obvious advantage in analyzing the epithelial pit pattern and the vascular network.[5] No guidelines have been established for the application of image enhancing techniques, and issues have recently been identified regarding the selection of neoplastic lesions in the colorectum.

The use of NBI enhances the identification of both the vascular and surface pattern of tumors. There have been many reports evaluating NBI for the diagnosis of colorectal lesions, most of which have focused on the diagnostic accuracy of magnified NBI.[6-8] In Western countries, the magnifying endoscope has not been extensively used in clinical practice until recently. Only limited studies have been conducted on non-magnified NBI evaluation,[9-11] possibly due to the complicated variety of magnified appearances of the tumor surface. Given this context, a simple system was proposed to categorically classify NBI findings from close observations with a high-resolution electronic endoscope. The NBI International Colorectal Endoscopic (NICE) classification was proposed by the Colon Tumor NBI Interest Group—an organization for promoting international collaboration and wide utilization of NBI. The NICE classification is a simple category classification consisting of three types (1, 2, and 3) based on three separate characteristics: (1) lesion color, (2) microvascular architecture, and (3) surface pattern.[12] The in-

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ternational study group has tested the validity of this classification in multiple studies, including a pilot evaluation during real-time colonoscopy; this evaluation demonstrated the predictive validity of NICE with a high degree of confidence.[13,14]

In an issue of *Clinical Endoscopy*, Kim et al.[15] reported that non-magnified NBI colonoscopy, using the NICE classification, distinguishes neoplastic lesions from non-neoplastic colorectal polyps with at least the same accuracy as magnified NBI. In this randomized controlled study, the efficacy of magnified and non-magnified NBI was compared in real-time. While this is an advancement on other studies, it is worth noting that the analysis was conducted by a single experienced endoscopist. A total of 236 polyps were evaluated by NBI in real time during therapeutic colonoscopy, with the decision on whether or not to use NBI made at random. After a real-time endoscopic histological prediction, all lesions were endoscopically excised and retrieved for pathological diagnosis. The 236 isolated lesions had an average size of 5.6 mm (range, 2.5 to 12.0). The sensitivity, specificity, positive predictive value, and negative predictive value in differentiating neoplastic from non-neoplastic lesions with magnified NBI were 97.5%, 83.3%, 94.0%, and 92.6%, respectively; meanwhile, in the non-magnified group, the values were 97.5%, 85.1%, 91.7%, and 95.2%, respectively. Considering that based on clinical experience and opinions from expert committees,[2] it is recommended that colonic polyps 5 to 9 mm in size be removed, these data suggest that non-magnified NBI could help in performing risk stratification for these middle-sized polyps. The findings of this study are significant because they have the potential to be incorporated into the algorithm for therapeutic colonoscopy. It is obvious that the costs of magnifying colonoscopy are much higher than those of a more standard type. Moreover, detailed observation with magnification is likely to require longer time, especially during therapeutic colonoscopy, which could lead to increased work and endoscopist exhaustion in hospital units. In an era of large scale CRC screening, establishing both efficient and economical procedures is an important matter. This is not only important for patients, but also for medical providers. It is noted that the quality of this study would have been enhanced if the procedure time had been assessed and included.

In this study, the authors aimed to adopt a 'resect and discard strategy,' which may result in cost saving for screening and surveillance colonoscopy.[16] Fortunately, no small invasive carcinomas were found. However, there is a certain risk of small invasive carcinomas accompanied by lymph node metastasis amongst polyps that are 10 mm or less in size.[17] In a recently conducted prospective trial, magnifying NBI was proved useful in discriminating small invasive carcinomas from discardable lesions.[18] If small invasive carcinomas were resected and discarded without careful evaluation, regardless of whether the technique required complete or incomplete resection, additional lymph node dissection surgery might also be missed. It is perhaps too premature to establish a 'resect and discard' protocol using non-magnified NBI as a more efficient and economical way of managing the rate of CRC. Along with the evolution of NBI technology, we will need to wait until a multicenter, prospective randomized study of non-magnifying NBI in colonoscopy (with a large number of polyps) has been conducted. This work would need to show a validated reduction in CRC, efficiency, and favorable costs.

Conflicts of Interest

The authors have no financial conflicts of interest.

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