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Endoscopy

Endoscopic balloon dilation for stenotic lesions in Crohn's disease

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ABSTRACT

Background/Aims: Endoscopic balloon dilation (EBD) can serve as an alternative to surgery for intestinal stenosis associated with Crohn's disease (CD). However, there has been controversy regarding the efficacy and safety of EBD. Here we sought to determine the therapeutic efficacy and safety of EBD for intestinal stenosis in CD.

Materials and Methods: Of 43 patients with CD accompanied by intestinal stenosis, 30 underwent EBD. These 30 patients were examined retrospectively in terms of the scope passage rate, surgery-free rate, and whether or not the observation of the distal intestinal tract influenced the therapeutic strategy.

Results: The overall scope passage and surgery-free rates were 90.0% and 76.7%, respectively. There were no statistically significant differences in the site of the dilated intestinal tract among groups. Patients who had inflammation in the distal intestinal tract alone after EBD accounted for 56.7%. The rate of re-dilation was 46.7%, and time until re-dilation was 6.6±3.6 months.

Conclusion: EBD was associated with favorable short-term and long-term outcomes and good safety. Observation of the distal intestinal tract influenced the decision-making process for therapeutic strategies. The results of this study suggest that EBD may allow the postponement or even avoidance of surgery, enabling not only intestinal dilation but also the evaluation of mucosal healing to be performed. Thus, EBD is considered to be an effective alternative treatment for intestinal stenotic lesions in patients with CD.

Keywords: Endoscopic balloon dilation, Crohn's disease, intestinal stricture

Original Article

INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory disease of unknown etiology. CD occurs more frequently in young persons, presenting as inflammation involving the entire gastrointestinal tract, though mainly the small and large intestines, and is associated with complications such as intestinal stenosis and fistulation. CD becomes advanced with recurrences and relapse, and the quality of life (QOL) deteriorates in patients unresponsive to treatment. Thus far, no treatment has achieved a complete cure for CD. The current treatment strategies aim to control disease activity and enhance QOL in patients. Introduction of anti-TNF-α antibodies has allowed not only clinical remission but also the achievement of mucosal healing, as evidenced by endoscopic remission (1-8).

In CD cases, surgery is not a radical treatment; rather, surgical treatment aims to manage intestinal inflammation that is refractory to medical therapy and to prevent complications, such as fistulae and stenosis, and should be chosen considering the long-term perspective of improvement in QOL, while avoiding short-bowel syndrome. Once the diagnosis is established, the cumulative recurrence rate is reportedly about 10% per year, and the cumulative surgery rate is 46–62% at 5 years and 61–75% at 10 years. In particular, relapse is likely to occur at the anastomotic site, postoperatively (9-13). Repeated surgery may cause short-bowel syndrome, raising the issue of decreased QOL again (14-16).

Endoscopic balloon dilation (EBD) has been widely employed in cases with stenotic lesions of the gastroin-

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testinal tract, regardless of whether such lesions are benign or malignant. The recent spread of small bowel endoscopy has allowed us to implement EBD for small bowel lesions in patients with CD, leading to the expansion of the indications for EBD.

Advancements in endoscopic techniques and drug therapy, especially biological products, have enabled endoscopic dilation to be applied for intestinal stenosis in patients with CD, followed by enhanced medical treatments and the postponement or even avoidance of surgery (17-25).

Although a number of studies have focused on EBD for intestinal stenosis in CD, its indications, safety, and therapeutic efficacy have not yet been completely clarified. This study was therefore conducted to elucidate the indications, therapeutic efficacy, and safety of EBD for intestinal stenosis in patients with CD.

MATERIALS AND METHODS

Patients and Dilation Definition

Of the 43 patients with CD accompanied by intestinal stenosis treated between August 2012 and September 2015, 30 actually underwent EBD (Figure 1). These 30 patients were investigated retrospectively. Patient information and records on the technique were obtained from electronic charts (Table 1).

Endoscopic balloon dilation was indicated for intestinal stenosis in CD cases under the following circumstances: a. there were symptoms or there was intestinal dilation on the oral side of the stenosis; b. the stenosis precluded a detailed examination of the distal intestinal tract; c. the length of the stenosis was less than 50 mm; d. there was neither fistulation nor abscess formation around the stenosis; e. there was no deep ulcer in the stenotic portion; or f. the stenosis was benign. EBD was not performed for cases in which the severity of the stenosis was mild and allowed the passage of the scope, the stenotic portion was severely flexed, the manipulation of the scope was difficult, or the guidewire could not be passed through the stenosis. All patients provided informed consent to undergo EBD, prior to the procedure, after the details of the endoscopic examination and the complications of sedation had been explained. This study was approved by the bioethics committee.

Scopes and Sedation

Although the stenosis in the large intestine or the terminal ileum was accessible by a colonoscope, a small bowel endoscope was used for cases in which insertion was difficult or the stenosis was present in a deep part of the small intestine. Endoscopy was performed from anal side in all patients except in one with small bowel lesions, for whom a small bowel endoscope was inserted orally. The scopes used were as follows: upper gastrointestinal endoscopes (GIF-Q260J, GIF-XQ260: OLYMPUS, Tokyo, Japan) in 4 cases, colonoscopes (PCF260A, PCF240AI, CFQ260AI, CSH260: OLYMPUS, Tokyo, Japan) in 13 cases, and small bowel endoscopes (EI-530B, EN-450T5/W:FUJINON, Saitama, Japan) in 13 cases. Balloons were passed to the site of dilation via the scope in all cases. The balloon instruments used were CRE (Boston Scientific Co., Natick MA, USA) in 29 cases and Hercules (Cook Japan, Tokyo, Japan) in one case. CO_2 was used for insufflation. EBD was performed under conscious sedation with midazolam, pentazocine, or pethidine hydrochloride.

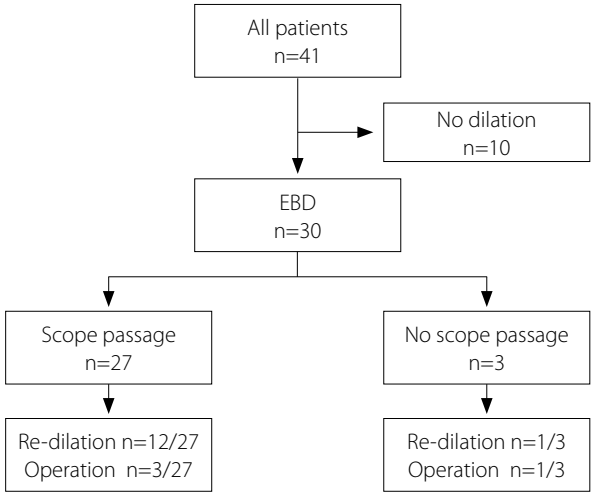

Figure 1. A flow-chart for outcomes of patients treated with EBD

Table 1. Patient characteristics

No. of patients	**30**
Gender (Male:Female)	21:9
Age (years)	36.9±10.7
Smoking (yes)	5
Disease duration (months)	160.1±106.0
History of surgery (present)	17
Disease type (small intestine: small/large intestine: large intestine)	4:21:5
Stenosis	
Site of stenosis (large intestine: small intestine: anastomotic site)	7:15:8
Length of stenosis (mm)	20.1±11.9
Treatment	
Anti-TNFα antibody	22
Adrenocortical steroid	3
Immunomodulator	19
Elemental diet therapy	22
Before EBD	
CDAI	131.4±99.8
CRP (mg/dL)	1.2±2.3
TP (g/dL)	7.1±0.7
Alb (g/dL)	3.8±0.6
ESR (mm/1hr)	22.4±20.6
Duration of hospital stay (days)	15.3±17.0
Median time for re-dilation (months) (n=13)	6.6±3.6
Median time for sugery (months) (n=7)	7.8±6.8
Observation period (months)	13.4±9.8

Patients who received 2 or 3 treatments were included.
Patients who received ≥600 kcal/day of enteral nutrition were included.

Dilation Methods

Stenotic lesions were visualized using Gastrografin to confirm the length, diameter, presence/absence of an associated fistula, and the severity of flexion in the stenotic portion. The

distal intestinal tract was defined as that on the oral side of the EBD site (on the anal side of the EBD site in patients undergoing peroral endoscopy), and the proximal intestinal tract was defined as that on the anal side of the EBD site. The length of the stenotic portion was regarded as the length of the stenosis up to the site that had the same luminal diameter as that of the proximal intestinal tract, and the diameter of the stenosis was measured at its narrowest portion in fluoroscopic images. Cases with malignant stenosis, as determined by biopsy, were excluded. When a case was judged to have an indication for EBD, the stenosis, if it was pinhole-like, was dilated to a target maximum balloon diameter of 10–12 mm; other types of stenoses were dilated stepwise to a diameter of 12–20 mm, according to the severity of the narrowing. The duration of the dilation procedure was 60 seconds. The dilation balloon was inflated under fluoroscopy using water-soluble contrast material diluted with water. For dilation, the internal pressure was gradually increased and maintained for 60 seconds at the target diameter. Thereafter, the balloon was deflated and then inflated again to a second target diameter. After EBD, the dilated portion was observed to examine for lacerations and the degree of bleeding. If the endoscope could be passed through the EBD site, the distal intestinal tract was observed.

Definitions of Short-Term and Long-Term Success

The short-term outcomes of EBD were evaluated in terms of the rate of scope passage after dilation of the stenotic portion, and differences in the rates of scope passage were examined in relation to the site of dilation. In addition, in order to determine whether or not the observation of the distal intestinal tract in the stenotic portion influenced the therapeutic strategy, therapeutic strategy alterations and related factors were analyzed in terms of the presence/absence of inflammation in the distal intestinal tract of patients in whom EBD allowed the passage of the scope.

The long-term outcomes of EBD were evaluated in terms of the surgery-free rate within 3 years after EBD, and the surgery-free rates were also analyzed in relation to the site of dilation. The rate of scope passage and related factors were studied in patients who have undergone surgery after EBD versus those who did not have. The re-dilation-free rate, the rate of scope passage, the surgery-free rate, and other related factors were examined in terms of the site of dilation in patients with or without re-implementation of EBD. To determine the differences in success rates between the two types of scopes, small bowel endoscopy and conventional endoscopy were compared with regard to the rate of scope passage, the surgery-free rate, and related factors.

Safety Profile

To evaluate the safety of EBD, complications such as gastrointestinal perforation and massive bleeding (requiring blood transfusion, accompanied by a hemoglobin decrease of at least 2.0 g/dL) were studied.

Statistical Analyses

IBM Statistical Package for the Social Sciences (IBM SPSS; Armonk, NY, USA) version 21.0 (International Business Machines Co., Tokyo, Japan) was used for the statistical analyzes of the data obtained. Unpaired samples were compared using the *t* test, Welch's test, Mann-Whitney U test, Pearson's χ^2 test, and Fisher's direct method, while paired samples were compared using the paired *t* test and Wilcoxon signed-rank test. Kaplan–Meier survival curves and the log-rank test were used for the analysis of the cumulative surgery-free rate and the cumulative re-dilation-free rate. Differences between variables with <0.05 were considered significant.

RESULTS

Short-Term Outcome

In the short term, the rate of scope passage was 90.0% for the overall intestinal tract, 100.0% for the large intestine, 93.3% for the small intestine, and 75.0% for the postoperative anastomotic site. There were no statistically significant differences in the rate of scope passage among the different dilation sites.

Long-Term Outcome

In the long term, the surgery-free rate was 76.7% for the overall intestinal tract, 85.7% for the large intestine, 73.3% for the small intestine, and 75.0% for the anastomotic site (Figures 2, 3). The surgery rate after EBD was significantly higher for anastomotic lesions. There were no statistically significant differences in the surgery-free rate among the different dilation sites. When related factors were examined in terms of the presence/absence of surgery, the CD activity index at the time of EBD implementation was significantly higher in patients who underwent surgery (Table 2).

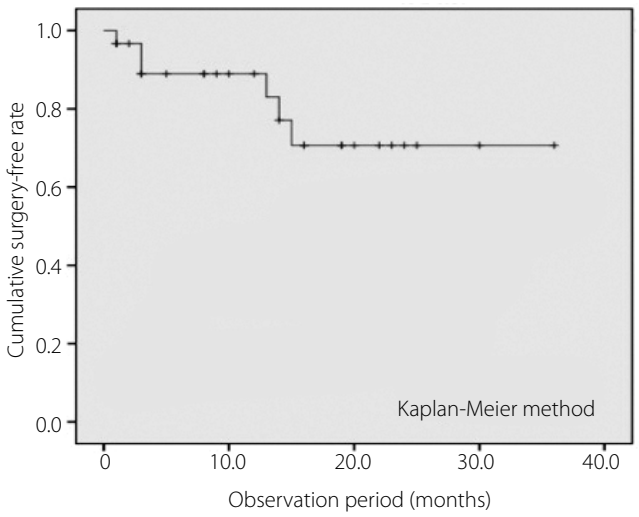

Figure 2. Cumulative surgery-free rate. The cumulative surgery free rate was 76.7% at 3 years after EBD, based on observations over 13.4±9.8 months after EBD

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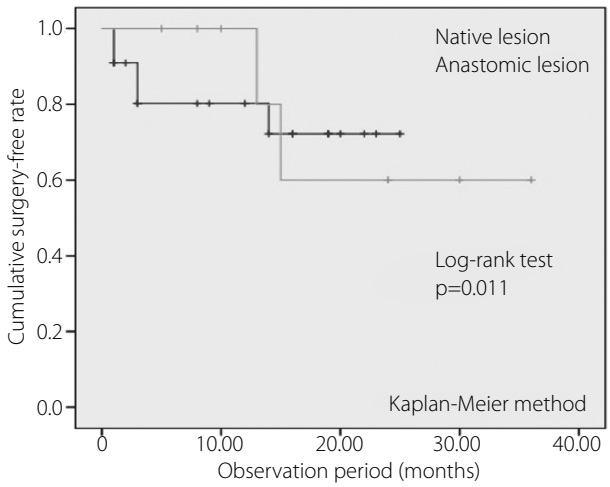

Figure 3. Comparison of cumulative surgery-free rates between native and anastomotic lesions

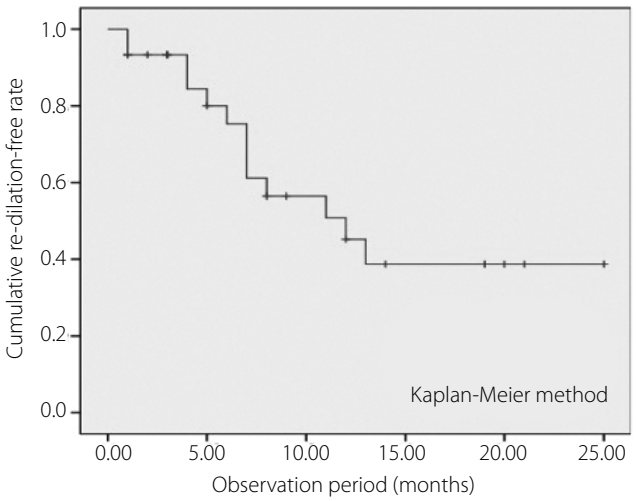

Figure 4. Cumulative re-dilation-free rate. The re-dilation rate after EBD was 50% at 1 year

Table 2. Comparison of dilation: with versus without operation

	With operation	Without operation	p
No. of patients	7	23	
Gender (Male:Female)	4:3	17:6	0.343
Age (years)	37.9±8.6	36.6±11.6	0.788
Disease duration (months)	141.1±147.8	165.8±96.0	0.605
History of surgery (present)	4	14	0.597
Disease type (small intestine: small/ large intestine: large intestine)	1:6:0	3:16:4	
Stenosis			
Site of stenosis (non-surgical site: anastomotic site)	5:2	17:6	0.623
Large intestine:small intestine: anastomotic site	1:4:2	6:11:6	
Length of stenosis (mm)	23.8±16.4	18.8±10.5	0.691
Treatment			
Anti-TNF α antibody	4	18	0.261
Adrenocortical steroid	2	1	0.128
Immunomodulator	3	16	0.429
Elemental diet therapy	6	16	0.377
Before EBD			
CDAI	213.6±164.3	106.4±58.4	0.012
CRP (mg/dL)	2.5±4.2	0.8±1.4	0.638
TP (g/dL)	6.9±1.1	7.1±0.6	0.386
Alb (g/dL)	3.4±1.0	3.9±0.5	0.088
ESR (mm/1hr)	36.9±28.0	18.0±16.6	0.059
Endoscope insertion (oral:anal)	0:7	1:22	0.767
Maximum balloon diameter (mm)	14.1±2.5	14.0±1.5	0.739
Scope passage (yes)	6	21	0.564

CDAI at the time of EBD was significantly higher in patients who underwent surgery after EBD.

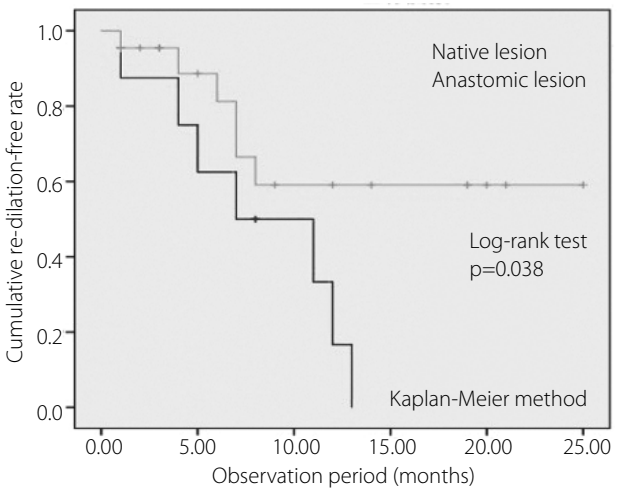

Figure 5. Comparison of cumulative re-dilation-free rates between native and anastomotic lesions. The re-dilation rate after EBD was significantly higher for anastomotic lesions. During the observation period, 87.5% of the anastomotic lesions required re-dilation

The rate of re-dilation was 46.7%, and the observation time until re-dilation was 6.6±3.6 months (Figure 4). EBD was re-implemented in about half of the patients. Among patients who underwent repeat EBD, the intervals of re-implementation of EBD were determined by the doctor in charge when there were no symptoms. In patients deemed to require EBD re-implementation, EBD was often performed at the anastomotic site, and the length of the stenosis was significantly greater than those patients not requiring additional EBD (Figure 5, Table 3).

Inflammation of the Distal Intestinal Tract

The stenotic portion of the distal intestinal tract could be observed after EBD in 27 patients, and inflammation in the distal intestinal tract was found in 18 of these patients. Among these 18 patients, the treatment was actually changed in 11 (61.1%), the intensification of treatment was not possible in 4 (22.2%), and a treatment change was unnecessary in 3 (16.7%) because mucosal inflammation was endoscopically mild. When related factors, including the rate of scope passage and the surgery-free rate,

Table 3. Comparison of dilation: with versus without re-dilation

Re-dilation	Yes	No	p
No. of patients	13	17	
Gender (Male:Female)	11:2	10:7	0.130
Age (years)	35.5±9.5	37.9±11.4	0.567
Disease duration (months)	202.1±118.4	127.9±82.0	0.061
History of surgery (present)	11	10	0.130
Disease type (small intestine:small/ large intestine:large intestine)	2:9:2	2:12:3	
Stenosis			
Site of stenosis (non-surgical site: anastomotic site)	6:7	16:1	
Large intestine:small intestine: anastomotic site	3:3:7	4:12:1	
Length of stenosis (mm)	25.4±9.9	16.0±11.6	0.016
Treatment			
Anti-TNF α antibody	10	12	0.515
Adrenocortical steroid	2	1	0.397
Immunomodulator	9	10	0.485
Elemental diet therapy	11	11	0.212
Before EBD			
CDAI	137.5±125.9	126.7±73.4	0.818
CRP (mg/dL)	1.4±2.9	1.0±1.7	0.784
TP (g/dL)	6.9±0.8	7.2±0.7	0.867
Alb (g/dL)	3.8±0.7	3.9±0.6	0.632
ESR (mm/1hr)	20.0±22.3	24.2±18.9	0.544
Endoscope insertion (oral:anal)	1:12	0:17	0.433
Maximum balloon diameter (mm)	13.8±1.9	14.3±1.5	0.965
Scope passage (yes)	12	15	0.603
Surgery (yes)	3	4	0.660

Anastomotic lesions were more frequent, and the length of the stenosis was significantly greater in patients with re-dilation than in those without re-dilation.

Table 4. Inflammation of distal intestinal tract

Inflammation of distal intestinal tract	Present	Absent	p
No. of patients	18	9	
Gender (Male:Female)	12:6	6:3	0.672
Age (years)	35.3±9.1	38.8±13.9	0.458
Disease duration (months)	140.9±82.7	176.8±116.8	0.385
History of surgery (present)	9	6	0.343
Duration of hospital stay (days)	19.2±20.8	10.1±8.1	0.198
Disease type (small intestine:small/ large intestine:large intestine)	2:12:4	1:7:1	
Stenosis			
Site of stenosis (non-surgical site: anastomotic site)	14:4	7:2	0.695
Large intestine:small intestine: anastomotic site	5:9:4	2:5:2	
Length of stenosis (mm)	20.8±12.6	19.0±9.7	0.976
Treatment			
Anti-TNFα antibody	12	7	0.450
Adrenocortical steroid	2	0	0.407
Immunomodulator	9	7	0.167
Elemental diet therapy	13	6	0.550
Before EBD			
CDAI	155.0±116.5	96.3±51.1	0.136
CRP (mg/dL)	1.8±2.8	0.2±0.2	0.121
TP (g/dL)	7.2±0.8	7.0±0.6	0.553
Alb (g/dL)	3.7±0.7	4.1±0.5	0.,113
ESR (mm/1hr)	27.5±24.2	14.8±10.1	0.455
Endoscope insertion (oral:anal)	0:18	1:8	0.333
Maximum balloon diameter (mm)	14.1±1.8	14.3±1.8	0.628
Re-dilation (yes)	7	5	0.393
Surgery (yes)	6	0	0.063

were examined in terms of the presence/absence of inflammation in the distal intestinal tract, there were no statistically significant differences in the background factors, pretreatment blood data, or the surgery-free rate. Of the 18 patients, surgery was performed in 6 who had inflammation in the distal intestinal tract, whereas none of the 9 patients without inflammation in the distal intestinal tract underwent surgery (Table 4). Factors necessitating surgery included the insufficient improvement in stenotic symptoms after EBD, the failure of remission maintenance due to secondary ineffectiveness of anti-TNFα antibody products, and the presence of multiple stenoses or ulcers in first-onset cases.

Differences Among Scope Types

The rate of scope passage, the surgery-free rate, and related factors were analyzed in terms of whether the scope used was a small bowel endoscope or a conventional endoscope (Table 5). Among the background factors, the serum albumin level before EBD was significantly lower in patients who underwent small bowel endoscopy.

Safety Profile

As a complication of EBD, portal emphysema due to excessive CO_2 gas insufflation occurred in one patient, but the patient responded promptly to conservative treatment. There were no serious complications such as gastrointestinal perforation or massive bleeding. In terms of mild complications, slight bleeding occurred in all patients, fever in one, vomiting in 2, and abdominal pain in 3, but all responded well to conservative treatment.

Table 5. Comparison of scopes

	Small bowel endoscope	Conventional endoscope	p
No. of patients	13	17	
Gender (Male:Female)	7:6	14:3	0.099
Age (years)	37.2±12.8	36.6±8.7	0.907
Disease duration (months)	136.7±114.4	177.9±95.4	0.307
History of surgery (present)	7:6	11:6	0.547
Disease type (small intestine:small/large intestine:large intestine)	4:9:0	0:12:5	
Stenosis			
Site of stenosis (non-surgical site: anastomotic site)	10:3	12:5	0.515
Large intestine:small intestine: anastomotic site	1:9:3	6:6:5	
Length of stenosis (mm)	18.8±11.5	20.8±12.1	0.678
Treatment			
Anti-TNFα antibody	8	14	0.579
Adrenocortical steroid	1	2	0.603
Immunomodulator	7	12	0.287
Elemental diet therapy	10	12	0.515
Before EBD			
CDAI	133.8±69.9	129.6±117.6	0.490
CRP (mg/dL)	1.2±1.9	1.2±2.6	0.784
TP (g/dL)	6.8±0.7	7.3±0.7	0.061
Alb (g/dL)	3.6±0.5	4.0±0.7	0.038
ESR (mm/1hr)	26.4±19.5	19.4±20.9	0.187
Endoscope insertion (oral:anal)	1:12	0:17	0.433
Maximum balloon diameter (mm)	14.9±1.3	13.4±1.7	0.030
Scope passage (yes)	12	15	0.603
Surgery (yes)	4	3	0.340

In patients who underwent EBD with a small bowel endoscope, EBD was often performed for lesions in the small intestine or at the anastomotic site, and the serum albumin level was significantly lower.

DISCUSSION

Crohn's disease is a chronic inflammatory bowel disease involving the entire gastrointestinal tract, and it is complicated by stenosis and fistulation, resulting in decreased QOL due to repeated operations. EBD is an alternative to surgery in CD cases with intestinal stenosis. The use of EBD for the stenotic lesions of CD has been reported since the 1990s, with the procedure being conducted using an upper gastrointestinal endoscope or colonoscope mainly for the stenosis in the upper gastrointestinal tract, in the large intestine, or at the anastomotic site (17-25). In recent years, along with the advancements in small bowel endoscopy, EBD has been employed for lesions in the small intestine (26). However, most investigations of EBD have been small-scale cohort studies, and the safety and long-term usefulness of EBD have not yet been adequately examined (27-30).

Definitions of the short-term outcomes of EBD have varied among previous studies, with some relying on the technical success, while others basing their results on the disappearance of the stenotic symptoms after EBD. The technical success rate of EBD reportedly ranges from 71% to 100%, and the rate of disappearance of the clinical symptoms ranges from 53% to 100% (27-31). In this study, one of our aims was the observation of the distal intestinal tract during EBD, and the short-term outcomes of EBD were defined as the scope passage after technically successful EBD. A previous study demonstrated the rate of scope passage to be 73.8% (32), and we obtained a similar rate of scope passage after EBD, in this study. As it is often difficult to control or hold the scope in cases with lesions in the small intestine or at the anastomotic site, the rate of scope passage was expected to be low in our cases. However, the therapeutic outcomes were equivalent, regardless of the site of the stenosis, demonstrating that EBD outcomes do not vary according to the site of dilation.

With regard to long-term outcomes, the surgery-free rate for the entire patient group was 76.7%. The rate of reoperation due to relapse at the anastomotic site is reportedly 25% at 4 years, such that the surgery-free rate in patients with lesions at the anastomotic site was predicted to be lower than that in patients with lesions at other sites. However, there were no statistically significant differences in the surgery-free rate among different lesion sites, indicating that EBD is equally effective at all stenotic sites (9-13). In this study, patients without stenotic symptoms were included as subjects, and the maximum observation period after EBD was only 3 years. Therefore, the cumulative surgery-free rate was approximately 70% at 3 years, similar to the results of previous studies (17-25,32). The cumulative rate of surgery in CD reportedly ranges from 46% to 62% at 5 years and from 61% to 75% at 10 years. As the cumulative surgery rate after EBD is considered to remain low, it can reasonably be suggested that EBD for stenotic lesions allows the postponement or even avoidance of surgery, regardless of whether or not stenotic symptoms are present (9-13).

It has been reported that symptom relapse occurs in 22–31% of patients after EBD, and that re-dilation may be required to avoid surgery (27-30). In this study, repeat EBD was required in 46.7% of the patients. The rate of re-dilation was particularly high at the anastomotic site, presumably because the relapse of CD is more likely to occur in this area. In addition, the stenotic portion was significantly longer in patients who underwent re-dilation than in those who did not. Considering that previous studies also showed a higher rate of EBD failure in patients with longer stenotic portions, the mucosal inflammation was speculated to be severe in cases with long stenotic portions, leading to the insufficient efficacy of EBD (30). An important premise for the success of EBD is that the local inflammation is

well controlled. Patients with stenosis at the anastomotic site or with a long stenotic portion are at a high risk for restenosis. Therefore, in these patients, considering the possible need for re-dilation, it is important to conduct periodic surveillance after EBD and to determine the optimal timing of re-dilation. Further investigation is necessary for establishing the most appropriate interval until re-dilation.

Mucosal healing has recently become a treatment target. Not only has the dilation of the stenotic portion but also a detailed evaluation of the mucosa by EBD allowed an accurate evaluation of the CD status. In this study, the distal intestinal tract could be observed after EBD in 27 patients. In 9 of these patients, EBD made accurate inflammation evaluation possible because the inflammation was limited to the intestinal tract distal to the stenosis. In actuality, an intensified treatment had to be considered in most patients who had inflammation in the intestinal tract distal to the stenosis. In addition, only patients with inflammation in the distal intestinal tract underwent surgery during the observation period, whereas none of the patients free from inflammation in the distal intestinal tract required surgery. Our results suggest that the observation of the distal intestinal tract by EBD would be useful in cases in which reconsideration of the therapeutic strategy is deemed necessary, in addition to providing information that facilitates decision-making about surgical treatment. We can reasonably speculate that future studies involving larger numbers of subjects might yield a statistically significant difference. Further accumulation of evidence is thus awaited.

Recent advancements in small bowel endoscopy have allowed the implementation of EBD for the stenotic lesions of the small intestine (27-30). The serum albumin level before EBD was significantly lower in patients in whom the small bowel endoscope had been used. When lesions are present in the small intestine, a chronic state of malnutrition is induced by malabsorption. The lower serum albumin level observed in this study might have been a reflection of such malnutrition. There was no statistically significant difference in the rate of scope passage or the surgery-free rate between the two types of scopes employed. Although EBD using a small bowel endoscope is associated with the technical difficulty during insertion or when holding the scope, this endoscope achieves EBD implementation with results equivalent to those of the conventional endoscope, even in cases with stenotic lesions in the small intestine. However, currently, small bowel endoscopy is not a common treatment, with the rates of its use varying among different countries and regions. Therefore, further spread of this procedure is desirable.

The serious complications of EBD include perforation and bleeding. The incidence of perforation is reportedly 0–9%, and this complication accounts for 5–25% of all cases with serious complications (17-25,27-30,33). In this study, portal emphysema developed in one patient (34); this complication was apparently attributable to the excessive CO_2 gas insufflation at the time of scope insertion, in addition to a pre-existing tendency for intestinal gas retention. Although the examination was discontinued in consideration of safety, conservative treatment achieved prompt improvement in the patient. None of our cases experienced serious complications, such as perforation or bleeding requiring blood transfusion, with the results being very similar to those of previous studies.

According to etiology, stenosis associated with CD is classified into the inflammatory and fibrotic forms. Inflammatory stenosis requires the intensification of medical treatment or EBD, and fibrotic stenosis is considered to be a good indication for EBD. Although these two types of stenoses have not been clearly differentiated by means of endoscopic findings, magnetic resonance imaging can reportedly differentiate between the inflammatory and fibrotic forms of stenosis (35). If the differentiation between the inflammatory and fibrotic forms of stenosis becomes more accurate and feasible in the future, it will be easier to further investigate the indications for EBD.

The results of this study demonstrate that EBD is associated with favorable short-term and long-term outcomes and a high level of safety, that EBD performed with a small bowel endoscope provides therapeutic results equivalent to those of the conventional endoscope, and finally, that the observation of the distal intestinal tract by EBD influences the decision-making for therapeutic strategies. Our observations also suggest that EBD may allow the postponement or even avoidance of surgery. Thus, EBD is useful not only for intestinal dilation but also for evaluating mucosal healing, serving as an effective alternative treatment for intestinal stenotic lesions in CD.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Dokkyo Medical University.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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REFERENCES

1. Yanai H, Hanauer SB. Assessing response and loss of response to biological therapies in IBD. Am J Gastroenterol 2011; 106: 685-98. [CrossRef]
2. Hanauer SB, Feagan BG, Lichtenstein GR, et al. Maintenance infliximab for Crohn's disease : the ACCENT I randomised trial. Lancet 2002; 359: 1541-9. [CrossRef]

3. Sands BE, Anderson FH, Bernstein CN, et al. Infliximab maintenance therapy for fistulizing Crohn's disease. New Engl J Med 2004; 350: 876-85. **[CrossRef]**
4. Rutgeerts P, Van Assche G, Vermeire S. Optimizing anti TNF treatment in inflammatory bowel disease. Gastroenterology 2004; 126: 1593-610. **[CrossRef]**
5. Ford AC, Sandborn WJ, Khan KJ, Hanauer SB, Talley NJ, Moayyedi P. Efficacy of biological therapies in inflammatory bowel disease : systematic review and meta-analysis. Am J Gastroenterol 2011; 106: 644-60. **[CrossRef]**
6. Hanauer SB, Sandborn WJ, Rutgeerts P, et al. Human anti-tumor necrosis factor monoclonal antibody (adalimumab) in Crohn's disease : the CLASSIC-I trial. Gastroenterology 2006; 130: 323-33. **[CrossRef]**
7. Sandborn WJ, Rutgeerts P, Enns R, et al. Adalimumab induction therapy for Crohn disease previously treated with infliximab : a randomized trial. Ann Intern Med 2007; 146: 829-38. **[CrossRef]**
8. Colombel JF, Sandborn WJ, Rutgeerts P, et al. Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease : the CHARM trial. Gastroenterology 2007; 132: 52-65. **[CrossRef]**
9. Van Assche G, Geboes K, Rutgeerts P. Medical therapy for Crohn's disease strictures. Inflamm Bowel Dis 2004; 10: 55-60. **[CrossRef]**
10. Futami K, Arima S. Role of strictureplasty in surgical treatment of Crohn's disease. J Gastroenterol 2005; 40 (Suppl 16): 35-9. **[CrossRef]**
11. Dietz DW, Laureti S, Strong SA, et al. Safety and longterm efficacy of strictureplasty in 314 patients with obstructing small bowel Crohn's disease. J Am Coll Surgeons 2001; 192: 330-8. **[CrossRef]**
12. De Cruz P, Kamm MA, Prideaux L, Allen PB, Desmond PV. Postoperative recurrent luminal Crohn's disease: a systematic review. Inflamm Bowel Dis 2012; 18: 758-77. **[CrossRef]**
13. Rutgeerts P. Protagonist et al. Crohn's disease recurrence can be prevented after ileal resection. Gut 2002; 51: 152-3. **[CrossRef]**
14. Wibmer AG, Kroesen AJ, Gröne J, Buhr HJ, Ritz JP. Comparison of strictureplasty and endoscopic balloon dilation for stricturing Crohn's disease–review of the literature. Int J Colorectal Dis 2010; 25: 1149-57. **[CrossRef]**
15. Yamamoto T. Factors affecting recurrence after surgery for Crohn's disease. World J Gastroentero 2005; 11: 3971-9. **[CrossRef]**
16. Koltun WA. Long-term value of endoscopic dilation for Crohn's strictures. Gut 2010; 59: 288. **[CrossRef]**
17. Blomberg B, Rolny P, Jamerot G. Endoscopic treatment of anastomotic strictures in Crohn's disease. Endoscopy 1991; 23: 195-8. **[CrossRef]**
18. Couckuyt H, Gevers AM, Coremans G, Hiele M, Rutgeerts P. Efficacy and safety of hydrostatic balloon dilation of ileocolonic Crohn's strictures:A prospective longterm analysis. Gut 1995; 36: 577-80. **[CrossRef]**
19. Matsui T, Ikeda K, Tsuda S, et al. Long-term outcome of endoscopic balloon dilation in obstructive gastrointestinal Crohn's disease: A prospective long-term study. Diagn Ther Endosc 2000; 6: 67-75. **[CrossRef]**
20. Singh VV, Draganov P, Valentine J. Efficacy and safety of endoscopic balloon dilation of symptomatic upper and lower gastrointestinal Crohn's disease strictures. J Clin Gastroenterol 2005; 39: 284-90. **[CrossRef]**
21. Nomura E, Takagi S, Kikuchi T, et al. Efficacy and safety of endoscopic balloon dilation for Crohn's disease. Dis Colon Rectum 2006; 49: S59-67. **[CrossRef]**
22. Ferlitsch A, Reinisch W, Püspök A, et al. Safety and efficacy of endoscopic balloon dilation for treatment of Crohn's disease strictures. Endoscopy 2006; 38: 483-7. **[CrossRef]**
23. Thienpont C, D'Hoore A, Vermeire S, et al. Long-term outcome of endoscopic dilation in patients with Crohn's disease is not affected by disease activity or medical therapy. Gut 2010; 59: 320-4. **[CrossRef]**
24. Mueller T, Rieder B, Bechtner G, Pfeiffer A. The response of Crohn's strictures to endoscopic balloon dilation. Aliment Pharmacol Ther 2010; 31: 634-9. **[CrossRef]**
25. Scimeca D, Mocciaro F, Cottone M, et al. Efficacy and safety of endoscopic balloon dilation of symptomatic intestinal Crohn's disease strictures. Digest Liver Dis 2011; 43: 121-5. **[CrossRef]**
26. Yamamoto H, Kita H, Sunada K, et al. Clinical outcomes of double-balloon endoscopy for the diagnosis and treatment of small intestinal disease. Clin Gastroenterol 2004; 2: 1010-6. **[CrossRef]**
27. Fukumoto A, Tanaka S, Yamamoto H, et al. Diagnosis and treatment of small-bowel stricture by double balloon endoscopy. Gastrointest Endosc 2007; 66: S108-12. **[CrossRef]**
28. Ohmiya N, Arakawa D, Nakamura M, et al. Small-bowel obstruction: Diagnostic comparison between double-balloon endoscopy and fluoroscopic enteroclysis, and the outcome of enteroscopic treatment. Gastrointest Endosc 2009; 69: 84-93. **[CrossRef]**
29. Despott EJ, Gupta A, Burling D, et al. Effective dilation of small-bowel strictures by double-balloon enteroscopy in patients with symptomatic Crohn's disease (with video). Gastrointest Endosc 2009; 70: 1030-6. **[CrossRef]**
30. Hirai F, Beppu T, Sou S, Seki T, Yao K, Matsui T. Endoscopic balloon dilation using double-balloon endoscopy is a useful and safe treatment for small intestinal strictures in Crohn's disease. Digest Endosc 2010; 22: 200-4. **[CrossRef]**
31. Hassan C, Zullo A, De Francesco V, et al. Systematic review: Endoscopic dilation in Crohn's disease. Aliment Pharmacol Ther 2007; 26: 1457-64. **[CrossRef]**
32. Hirai F, Beppu T, Takatsu N, et al. Long-term outcome of endoscopic balloon dilation for small bowel strictures in patients with Crohn's disease. Digest Endosc 2014; 26: 545-51. **[CrossRef]**
33. Thienpont C, D'Hoore A, Vermeire S, et al. Long-term outcome of endoscopic dilatation in patients with Crohn's disease is not affected by disease activity or medical therapy. Gut 2010; 59: 320-4. **[CrossRef]**
34. Takahashi F, Tominaga K, Hiraishi H. Hepatic portal venous gas caused by endoscopic ballon dilatation for Crohn's stenosis. Clin Gastroenterol Hepatol 2016; 16: S1542-3565.
35. Rimola J, Palanell N, Rodriguez S, et al. Characterization of Inflammation and Fibrosis in Crohn's Disease Lesions by Magnetic Resonance Imaging. Am J Gastroenterol 2015; 110: 432-40. **[CrossRef]**