



# Enteroscopy in Crohn's Disease: Are There Any Changes in Role or Outcomes Over Time? A KASID Multicenter Study

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**Background/Aims:** Although balloon-assisted enteroscopy (BAE) enables endoscopic visualization of small bowel (SB) involvement in Crohn's disease (CD), there is no data on the changes in outcomes over time. We therefore investigated the changes in BAE use on CD patients over different time periods in terms of its role and clinical outcomes.

**Methods:** We used a multicenter enteroscopy database to identify CD patients with SB involvement who underwent BAE (131 procedures, 116 patients). We compared BAE-related factors and outcomes between the first period (70 procedures, 60 patients) and the second period (61 procedures, 56 patients). The specific cutoff point for dividing the two periods was 2007, when BAE guidelines were introduced.

**Results:** Initial diagnosis of SB involvement in CD was the most common indication for BAE during each period (50.0% vs 31.1%,  $p=0.034$ ). The largest change was in the number of BAE uses for stricture evaluation and/or treatment, which increased significantly in the latter period (2.9% vs 21.3%,  $p=0.002$ ). The diagnostic yield in patients with suspected CD was 90.7% in the first period and 95.0% in the second ( $p=0.695$ ). More endoscopic interventions were performed in the second period than in the first (5.1% vs 17.6%,  $p=0.041$ ). Enteroscopic success rates were high throughout (100% in the first period vs 80.0% in the second period,  $p>0.999$ ). In the first and second periods, therapeutic plans were adjusted in 62.7% and 61.4% of patients, respectively.

**Conclusions:** The overall clinical indications, outcomes, and effectiveness of BAE were constant over time in CD patients with SB involvement, with the exception that the frequency of enteroscopic intervention increased remarkably. (*Gut Liver* 2021;15:375-382)

**Key Words:** Balloon-assisted enteroscopy; Crohn disease; Small bowel; Time; Outcome

## INTRODUCTION

The incidence and prevalence of inflammatory bowel disease, including Crohn's disease (CD) and ulcerative colitis, has been increasing in Asian countries.<sup>1-3</sup> CD is a chronic inflammatory bowel disease characterized by its

relapsing course and its involvement of the entire gastrointestinal tract. Although small bowel (SB) involvement is common in patients with CD, it is relatively difficult to access with conventional endoscopy.<sup>4</sup> The introduction of balloon-assisted enteroscopy (BAE) and of capsule endoscopy (CE) have drastically changed the diagnostic

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approach and therapeutic decision making of CD with SB involvement. The role of CE includes ensuring early diagnosis of CD with SB involvement, making differential diagnoses, evaluating unexplained symptoms, extent of inflammation, disease activity and mucosal healing, or recurrence in CD patients.<sup>5-8</sup> Unlike CE, BAE can be performed on patients with stenosis of the SB and further aids in differential diagnosis by obtaining tissue specimen.<sup>9,10</sup>

According to a study on double-balloon enteroscopy (DBE) in suspected CD (sCD) cases, SB involvement was found in 60% and therapeutic adjustments were initiated in 75% of patients.<sup>11</sup> Another study of CD patients with strictures reported that the technical success rate was 80% with the avoidance of surgery rate of 60%. The authors therefore suggested that DBE was an effective diagnostic and therapeutic method in patients with CD-associated SB strictures.<sup>12</sup>

However, these studies have only focused on diagnostic yield, therapeutic result or technical aspects for relatively short periods. There has been no studies evaluating these parameters over long periods of time. We aim to evaluate the influence of cumulated knowledge and experience on BAE-related outcomes in CD patients with SB involvement. Therefore, our study investigated the changes in the indications and clinical outcomes of BAE use between different time periods.

## MATERIALS AND METHODS

### 1. Study design and patients

We retrospectively analyzed the records from the enteroscopy multicenter database of CD patients with SB involvement who underwent BAE between January 2004 and February 2013. Patients who had medication histories such as nonsteroidal anti-inflammatory drugs, anticoagulant, or antiplatelet agent use were excluded. From 1,057 procedures (on 990 patients), a total of 131 (116 patients) met the inclusion criteria and were enrolled in this study. We then categorized them into two periods, the first (January 2004 to December 2007) and the second (January 2008 to February 2013). Only one of the enrolled patients received BAE in both time periods. The specific cutoff point was chosen with the assumption that more knowledge and experience of BAE would have been accumulated during the second time point after the introduction of BAE guidelines in 2008.<sup>13</sup> Data collection and analysis were approved by the institutional review board of each facility. Due to the retrospective nature of this study, patients' informed consent to participate was waived in accordance with the institutional review board. All authors had access to the study

data and had reviewed and approved the final manuscript.

### 2. BAE procedure

Procedures were performed using the commercially available DBE system (EN450P5/20, T5/20; Fujinon Inc, Saitama, Japan) or the single-balloon enteroscopy system (Olympus Optical Co., Ltd., Tokyo, Japan). For BAE with an oral approach, patients received nil-by-mouth for at least 8 hours before the procedure. For BAE with an anal approach, patients were prepared for colonoscopy using at least 2 L polyethylene glycol–electrolyte lavage solution the day before the procedure, which was the accepted protocol at that time. BAE procedures were performed on patients under monitored anesthesia care with a fluoroscopy unit. All BAE procedures were performed under sedation administered by the endoscopists following the sedation protocol of each center. The procedures were divided into expert and non-expert groups based on the endoscopists' learning curve, where a cutoff was defined as 30 cases based on previous study.<sup>14</sup>

### 3. Definitions

Diagnosis of CD was confirmed based on clinical symptoms and a combination of endoscopic, histological, radiological, and/or biochemical investigations.<sup>15</sup> Early CD was defined as a disease duration of less than 2 years.<sup>16</sup> Phenotypes were classified according to the Montreal classification.<sup>17</sup> Disease location was classified into four groups: (1) L1 (ileal), (2) L2 (colonic), (3) L3 (ileocolonic), and (4) L4 (isolated upper disease). Disease behavior was classified into three groups: (1) B1 (non-stricturing, non-penetrating), (2) B2 (stricturing), and (3) B3 (penetrating). Extent of CD was classified into extensive (CD affecting a >100 cm area irrespective of the location) and localized (CD affecting a <30 cm area).<sup>15</sup> The endoscopic activity of CD was graded as follows: (1) grade 0 (no activity: normal villous pattern); (2) grade 1 (mild activity: mucosal edema and erythema, and/or presence of small ulcerative lesions in combination with normal mucosa); (3) grade 2 (moderate activity: presence of larger ulcerative lesions in combination with normal mucosa); (4) grade 3 (severe activity: presence of larger ulcerative lesions with absence of normal mucosa); (5) grade 4 (strictures with or without activity of CD, to be or not to be passed by the endoscope).<sup>11</sup>

### 4. Measurement factors

We evaluated the changes of indications, enteroscopic findings, diagnostic yield, treatment, and clinical impact over the indicated study period. Indications for BAE were classified into seven groups, as adopted from a previous study:<sup>18</sup> (1) initial diagnosis, (2) evaluation of cause for

obscure gastrointestinal bleeding (OGIB), (3) differential diagnosis, (4) evaluation and/or treatment of strictures, (5) evaluation of disease extent or activity, (6) to identify complications or malignancy, and (7) evaluation of postoperative recurrence. Initial diagnosis was defined as performance of BAE in sCD patients based on guidelines.<sup>13</sup> OGIB was defined as recurrent and persistent visible bleeding or anemia from an unknown origin that fail to be identified with upper and lower endoscopy. Although OGIB as initial presentation of CD without other gastrointestinal symptoms is uncommon, it could not be negligible. Therefore, we analyzed OGIB separately as indications of BAE. Differential diagnosis was defined as BAE use to differentiate CD when tuberculosis or other inflammatory diseases were concurrently observed in other examination findings prior to BAE. The enteroscopic finding most commonly used to diagnose CD is the presence of more than three ulcerations in the absence of nonsteroidal anti-inflammatory drugs, or aphthae or erosive lesions (>10) with continuous or segment-like distribution, or circumferential ulceration and stenosis on BAE.<sup>19,20</sup> Enteroscopic findings included in our study were as follows: (1) longitudinal ulcer, (2) aphthous ulcer, (3) variable ulcer, (4) cobblestone appear-

ance, (5) stricture, (6) inflammatory polyp, (7) scar change, and (8) fistula. The diagnostic yield was defined based on enteroscopic findings of sCD patients. As previously mentioned, all these factors were compared between the first and second periods of the study.

## 5. Statistical analysis

Statistical analyses were performed using SPSS version 18.0 (SPSS Inc, Chicago, IL, USA). All continuous variables were compared using a two-tailed Student t-test. All categorical variables were compared using Fisher exact test. A p-value of <0.05 was used as the cutoff for statistical significance.

## RESULTS

### 1. Baseline characteristics

A total of 131 procedures (on 116 patients) were divided based on the two periods, with 70 procedures (on 60 patients) in the first period and 61 procedures (on 56 patients) in the second period. The mean age of patients was 36.4 years and 81% were male. There were no significant

**Table 1.** Baseline Characteristics

| Variable                           | All          | First period | Second period | p-value |
|------------------------------------|--------------|--------------|---------------|---------|
| No. patients/No. procedure         | 116/131      | 60/70        | 56/61         |         |
| Age, yr                            | 36.4±14.4    | 34.7±11.9    | 38.3±16.7     | 0.176   |
| Male sex                           | 94 (81.0)    | 47 (79.7)    | 47 (82.5)     | 0.814   |
| Disease duration                   |              |              |               | 0.012   |
| <2 yr                              | 119 (90.8)   | 68 (97.1)    | 51 (83.6)     |         |
| ≥2 yr                              | 12 (9.2)     | 2 (2.9)      | 10 (16.4)     |         |
| History of abdominal surgery       | 18 (15.5)    | 9 (15.3)     | 9 (15.8)      | 0.937   |
| Medication at BAE                  |              |              |               | 0.384   |
| No                                 | 40 (32.5)    | 22 (34.4)    | 18 (30.5)     |         |
| 5-ASA                              | 38 (30.9)    | 23 (35.9)    | 15 (25.4)     |         |
| Steroid                            | 2 (1.6)      | 1 (1.6)      | 1 (1.7)       |         |
| Thiopurine                         | 2 (1.6)      | 2 (3.1)      | 0             |         |
| Biologics                          | 2 (1.6)      | 0            | 2 (3.4)       |         |
| 5-ASA+thiopurine                   | 17 (13.8)    | 9 (14.1)     | 8 (13.6)      |         |
| 5-ASA+steroid                      | 14 (11.4)    | 4 (6.3)      | 10 (16.9)     |         |
| 5-ASA+thiopurine+steroid           | 7 (5.7)      | 3 (4.7)      | 4 (6.8)       |         |
| 5-ASA+thiopurine+steroid+biologics | 1 (0.8)      | 0            | 1 (1.7)       |         |
| Laboratory test                    |              |              |               |         |
| Hemoglobin, mg/dL                  | 11.4±2.5     | 11.2±2.3     | 11.6±2.8      | 0.418   |
| ESR, mm/hr                         | 24.5±23.0    | 18.9±30.1    | 30.1±28.6     | 0.026   |
| CRP, mg/dL                         | 4.6±15.5     | 1.9±5.9      | 7.0±20.3      | 0.118   |
| Albumin, mg/dL                     | 3.6±0.7      | 3.5±0.8      | 3.6±0.6       | 0.322   |
| Diagnosis by other modalities      |              |              |               |         |
| Capsule endoscopy                  | 21/22 (95.5) | 7/7 (100)    | 14/15 (93.9)  | 0.523   |
| Abdominal CT                       | 65/99 (65.7) | 28/49 (57.1) | 37/50 (74.0)  | 0.164   |
| SBFT                               | 49/68 (72.1) | 31/43 (72.1) | 18/25 (72.0)  | 0.774   |

Data are presented as mean±SD or number (%).

BAE, balloon-assisted enteroscopy; ASA, aminosalicic acid; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; CT, computed tomography; SBFT, small bowel follow through.

differences with regards to age and sex between patients of both periods. In the first period, patients with the disease of <2 years were of a significantly higher percentage than those in the second period (97.1% vs 83.6%,  $p=0.012$ ). No significant differences were observed with regards to history of abdominal surgery or medication. However, the rate of patients who received biologics was very small (3/116) because a high proportion of patients were at early CD (90.8%) and also restricted by health insurance policy during the study period.<sup>21</sup> Mean erythrocyte sedimentation rate was statistically higher in the second period than in the first period ( $18.9\pm 30.1$  mm/hr vs  $30.1\pm 28.6$  mm/hr,  $p=0.026$ ). Among patients who underwent other modalities including CE, abdominal computed tomography or SB follow-through, diagnostic yield was not statistically different. Table 1 summarizes the baseline characteristics of patients undergoing BAE.

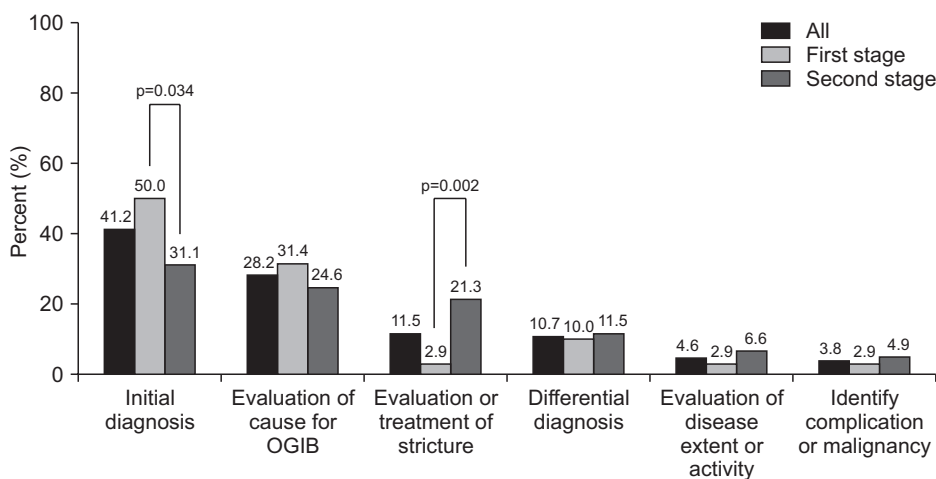
## 2. Indications and procedure-related data

Initial diagnosis of SB involvement of CD was the most

common indication for BAE during each period (50.0% vs 31.1%,  $p=0.034$ ), followed by evaluation of cause for OGIB and evaluation and/or treatment of strictures. Evaluation and/or treatment of strictures increased significantly in the second period as compared with the first (2.9% vs 21.3%,  $p=0.002$ ) (Fig. 1). Almost all procedures used DBE in both periods. No significant differences between periods were observed with regards to endoscopists' experience with BAE, mean total procedure time and time elapsed to deepest point (Table 2). No major complications such as perforation or pancreatitis were observed.

## 3. Enteroscopic findings and diagnostic yield

Throughout the study period, the locations of CD were as follows: L4 (71.6%), L1+L4 (17.2%), L2+L4 (8.6%), and L3+L4 (2.6%). The occurrence of CD activity of grades 1, 2, 3, and 4 were 37.3%, 50.0%, 0%, and 15.5%, respectively. The most common disease behavior was B1 (55.2%) and extended CD was detected in 81.9% of cases. CD location, activity, behavior and extent were not significantly



**Fig. 1.** Balloon-assisted enteroscopy (BAE) indications. Initial diagnosis was the most common indication for BAE during each period (50.0% vs 31.1%,  $p=0.034$ ), followed by evaluation of the cause of obscure gastrointestinal bleeding (OGIB) and evaluation and/or treatment of strictures. Evaluation and/or treatment of strictures as an indication was significantly more common in the second period than in the first (2.9% vs 21.3%,  $p=0.002$ ).

**Table 2.** Balloon-Assisted Enteroscopy Related Data

| Variable                            | All             | First period    | Second period   | p-value |
|-------------------------------------|-----------------|-----------------|-----------------|---------|
| Type of enteroscopy                 |                 |                 |                 | 0.098   |
| DBE                                 | 128 (97.7)      | 70 (100)        | 58 (95.1)       |         |
| SBE                                 | 3 (2.3)         | 0               | 3 (4.9)         |         |
| Experience of BAE                   |                 |                 |                 | 0.144   |
| Expert ( $\geq 30$ procedures)      | 101 (77.1)      | 50 (71.4)       | 51 (83.6)       |         |
| Non-expert (<30 procedures)         | 30 (22.9)       | 20 (28.6)       | 10 (16.4)       |         |
| Total procedure time (min)          | 78.7 $\pm$ 43.7 | 79.8 $\pm$ 43.9 | 77.5 $\pm$ 43.9 | 0.795   |
| Time elapsed to deepest point (min) | 50.2 $\pm$ 31.9 | 48.9 $\pm$ 22.8 | 51.6 $\pm$ 40.5 | 0.727   |
| Route                               |                 |                 |                 | 0.718   |
| Oral                                | 50 (38.8)       | 25 (36.8)       | 25 (41.0)       |         |
| Anal                                | 79 (61.2)       | 43 (63.2)       | 36 (59.0)       |         |
| Major complications                 | 0               | 0               | 0               |         |

Data are presented as number (%) or mean $\pm$ SD.

DBE, double-balloon enteroscopy; SBE, single-balloon enteroscopy; BAE, balloon-assisted enteroscopy.

different between both periods. Longitudinal ulcers were the most common finding for both study periods (40.7% vs 26.3%), followed by aphthous ulcers (23.7% vs 26.3%) and strictures (10.2% vs 12.3%), but these did not show significant differences (Table 3). The diagnostic yield of BAE obtained by combining the results of other modalities in sCD patients was 90.7% in the first period and 95.0% in the second with no significant differences between both ( $p=0.695$ ).

#### 4. Therapeutic data and clinical impact

Experience with BAE was not significantly different between both periods. In each, therapeutic data including the number of enteroscopic therapy, enteroscopic success rate and therapeutic plan adjustments were also not significantly different between expert and non-expert groups.

Throughout the study period, 11.2% (13/116) required endoscopic therapies including balloon dilatation, clipping and CE removal, with the rate of endoscopic therapy performed in the second period being significantly more than that in the first period (5.1% vs 17.6%,  $p=0.041$ ).

Among them, three patients received additional surgery-segmental resection of SB: two patients continued to have obstructive symptoms which were not relieved after balloon dilatation, and one patient required resection due to CE retention within a stenotic lesion. Enteroscopic success rate was high throughout the study period (100% vs 80.0%,  $p>0.999$ ). The need for addition of medication was slightly, but insignificantly higher in the first period than in the second (62.7% vs 58.7%), the same goes to the need for therapeutic adjustments (62.7% and 61.4%). Table 4 shows the therapeutic data and clinical impact.

## DISCUSSION

The present study is a revisit of our previous study that also looked at the changes of DBE parameters over time.<sup>22</sup> Previous limitations, such as the single-center and single-operator approach, were mitigated.

Approximately 10% to 30% of CD cases involved solitary SB,<sup>15</sup> while involvement of both SB and colon

**Table 3.** Disease Phenotypes and Enteroscopic Findings

| Variable                                  | All       | First period | Second period | p-value |
|---|-----------|--------------|---------------|---------|
| Location                                  |           |              |               | 0.493   |
| L4  | 83 (71.6) | 39 (66.1)    | 44 (72.2)     |         |
| L1+L4                                     | 20 (17.2) | 11 (18.6)    | 9 (15.8)      |         |
| L2+L4                                     | 10 (8.6)  | 7 (11.9)     | 3 (5.3)       |         |
| L3+L4                                     | 3 (2.6)   | 2 (3.4)      | 1 (1.8)       |         |
| Behavior                                  |           |              |               | 0.530   |
| B1  | 64 (55.2) | 16 (27.1)    | 21 (36.8)     |         |
| B2  | 37 (31.9) | 16 (27.1)    | 21 (36.8)     |         |
| B3  | 15 (12.9) | 8 (13.6)     | 7 (12.3)      |         |
| Endoscopic activity                       |           |              |               | 0.516   |
| Grade 1                                   | 40 (37.3) | 22 (27.3)    | 18 (31.6)     |         |
| Grade 2                                   | 58 (50.0) | 30 (50.8)    | 28 (49.1)     |         |
| Grade 3                                   | 0         | 0            | 0             |         |
| Grade 4                                   | 18 (15.5) | 7 (11.9)     | 11 (19.3)     |         |
| Extension                                 |           |              |               | 0.475   |
| Localized                                 | 21 (18.1) | 9 (15.3)     | 12 (21.1)     |         |
| Extended                                  | 95 (81.9) | 50 (84.7)    | 45 (78.9)     |         |
| Enteroscopic findings                     |           |              |               | 0.746   |
| Longitudinal ulcer                        | 39 (33.6) | 24 (40.7)    | 15 (26.3)     |         |
| Aphthous ulcer                            | 29 (25.0) | 14 (23.7)    | 15 (26.3)     |         |
| Stricture                                 | 13 (11.2) | 6 (10.2)     | 7 (12.3)      |         |
| Variable ulcer                            | 12 (10.3) | 4 (6.8)      | 8 (14.0)      |         |
| Longitudinal ulcer+aphthous ulcer         | 7 (6.0)   | 3 (5.1)      | 4 (7.0)       |         |
| Longitudinal ulcer+cobblestone appearance | 6 (5.2)   | 4 (6.8)      | 2 (3.5)       |         |
| Longitudinal ulcer+stricture              | 1 (0.9)   | 0            | 1 (1.8)       |         |
| Cobblestone appearance                    | 2 (1.7)   | 1 (1.7)      | 1 (1.8)       |         |
| Scar change                               | 2 (1.7)   | 1 (1.7)      | 1 (1.8)       |         |
| Aphthous ulcer+stricture                  | 1 (0.9)   | 0            | 1 (1.8)       |         |
| Aphthous ulcer+cobblestone appearance     | 1 (0.9)   | 0            | 1 (1.8)       |         |
| Inflammatory polyp+fistula                | 1 (0.9)   | 1 (1.7)      | 0             |         |

Data are presented as number (%).

**Table 4.** Therapeutic Data and Clinical Impact

| Variable                    | All           | First period | Second period | p-value |
|-----------------------------|---------------|--------------|---------------|---------|
| Surgery                     | 6 (5.2)       | 5 (8.5)      | 1 (1.8)       | 0.207   |
| Medical treatment           | 97 (83.6)     | 51 (86.4)    | 46 (80.7)     | 0.835   |
| Maintain                    | 38 (39.2)     | 19 (37.3)    | 19 (41.3)     |         |
| Add                         | 59 (60.8)     | 32 (62.7)    | 27 (58.7)     |         |
| Enteroscopic therapy        | 13 (11.2)     | 3 (5.1)      | 10 (17.6)     | 0.041   |
| Balloon dilatation          | 8 (61.5)      | 1 (33.3)     | 7 (70.0)      |         |
| Clipping                    | 2 (15.4)      | 1 (33.3)     | 1 (10.0)      |         |
| Capsule endoscopy removal   | 3 (23.1)      | 1 (33.3)     | 2 (20.0)      |         |
| Enteroscopic success rate   | 11/13 (84.6)  | 3/3 (100.0)  | 8/10 (80.0)   | >0.999  |
| Therapeutic plan adjustment | 72/116 (62.1) | 37/59 (62.7) | 35/57 (61.4)  | >0.999  |

Data are presented as number (%).

surpassed this with reports of up to 67% case.<sup>23</sup> In a population-based cohort study and a single-center study, SB involvement at diagnosis was associated with stricturing or penetrating complications.<sup>24,25</sup> It is also relatively difficult to access the SB using conventional endoscopy and insertion through the terminal ileum is not always achieved with colonoscopy.<sup>13</sup> Therefore, BAE has been preferred in the diagnosis of CD involving the SB.

In this study, the most common indications for BAE were comparable to those reported in a previous study: diagnosis (43.2%), OGIB (27.0%), and stenosis (18.9%).<sup>26</sup> Interestingly, significantly more patients from the first period than the second had early CD (lasting <2 years), although the reason for this is unclear. When BAE was performed, majority of the enrolled patients (81.9%) was first diagnosed with CD. This implies that BAE, regardless of clinical indication, was more often performed on newly-diagnosed sCD patients rather than on patients with established diagnosis of CD.

To avoid re-operations, assessment of endoscopic activity in the SB is important. According to a previous study, endoscopic recurrence was revealed in majority of postoperative CD patients.<sup>27</sup> In another study, lesions on the SB and/or anastomosis sites were detected in 94.7% of patients 1 year after operation, and biologics were started in a considerable number of patients (73.3%) based on single-balloon enteroscopy findings.<sup>28</sup> Although BAE has been indicated to evaluate SB involvement and to establish postoperative therapeutic plans,<sup>28</sup> no BAE indication for the evaluation of postoperative recurrence was present in our study. This may have implied that BAE is difficult for postoperative use and that our research is limited by insufficient coverage of the study period.

Endoscopic findings and procedure-related data and diagnostic yield, as well as the most common indication, did not change during the entire study period. There is presently no standardized endoscopic criteria for diagnosing CD.<sup>29</sup> In this study, endoscopic findings varied from typical

endoscopic features in CD such as longitudinal ulcers and cobblestone appearances to early or minor findings such as aphthous and small ulcers.

In terms of procedure-related outcomes, there were three cases of capsule retention related to SB strictures. Our results therefore support that BAE is useful in detecting SB involvement without concerns of capsule retention in the SB.<sup>30</sup>

The diagnostic yield of BAE has been reported in 22% to 70% of sCD patients.<sup>26,31-33</sup> Although the diagnostic yield of BAE were not significantly different between both periods, it showed a higher diagnostic yield of 92.6% than that reported in our previous study.<sup>22</sup> This is possibly due to the fact that a significant number of sCD patients underwent BAE for biopsy or definite diagnosis based on abnormal findings through other imaging modalities. However, this study showed that evaluation and/or treatment of strictures increased significantly in the second period (2.9% vs 21.3%,  $p=0.002$ ) compared with the first. As a result of this influence, more endoscopic interventions were performed in the second period (5.7% vs 16.4%,  $p=0.048$ ) than in the first.

More endoscopic therapy including balloon dilatation, clipping, and CE removal were performed in the second period than in the first, and this was a statistically significant difference (5.1% vs 17.6%,  $p=0.041$ ). Enteroscopic success rate was high, achieving more than 80% throughout the study. This result was comparable to that of DBE reported as 80% in a previous study of 19 CD patients with 13 strictures.<sup>12</sup> This study also showed that adjustment of therapeutic plans based on BAE results was initiated in more than 60% of CD patients with SB involvement. This is in line with a multicenter retrospective study that included 98 DBE procedures (81 patients), who reported that DBE influenced therapeutic managements in 79% of patients.<sup>34</sup> Although our result was relatively lower than that of the recent study, therapeutic plans in both periods were adjusted in nearly two-thirds of all patients (62.7% vs 61.4%,

$p > 0.999$ ). This suggests that BAE may play an important role in therapeutic decision making such as adjustment of medical treatment, surgical consultation, and endoscopic therapeutic intervention.<sup>10</sup>

This study had several potential limitations. Firstly, we switched from the enteroscopy multicenter database registry to a novel web-based registry by the Small Intestine Research Group of the Korean Association for the Study of Intestinal Diseases in October 2015, and as the records were not merged, our records on patients in the second study period might be incomplete as it has disregarded those from the Small Intestine Research Group. Secondly, there might have been a patient selection bias because only CD patients who underwent BAE in tertiary referral centers were included. We believed that BAE, being an invasive procedure, would require physicians of expertise who would most likely be based in tertiary centers. Thirdly, although each BAE indications had subtle differences, indications such as initial diagnosis, assessing OGIB and treatment strategy could be overlapped, despite our efforts to analyze them as objectively as possible. Since this study included only CD patients, percentage of differential diagnosis as an indication could be influenced by patients with other kinds of diseases who received BAE. Lastly, due to the lack of long-term follow-up data, further analysis regarding the clinical outcomes could not be performed. Nevertheless, this study has value by showing the changes in procedure indications and clinical outcomes of BAE on CD patients with SB involvement over time. Based on our results, it is suggested that BAE has not been commonly used for follow-up assessment of CD activity. However, it has been considered a relatively safe and effective therapeutic tool before surgery.

In conclusion, the overall clinical indications, outcomes and usefulness of BAE did not change over time in CD patients with SB involvement, except for the frequency of enteroscopic interventions which has remarkably increased.

## CONFLICTS OF INTEREST

S.J.P. and J.P.I. are editorial board members of the journal but did not involve in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

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Conceptualization, critical revision of the manuscript for important intellectual content and study supervision: D.K.C. Drafting of the manuscript, methodology, and statistical analysis: S.R.J. Acquisition of data; analysis and interpretation of data: J.O.K., J.S.B., D.H.Y., B.M.K., H.J.G., H.J.J., S.J.P., E.R.K., S.N.H., J.P.I., S.E.K., J.S.K., C.S.E. Approval of final manuscript: all authors.

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