Turk J Gastroenterol *2014; 25: 374-80*

Diagnostic and therapeutic efficacy of double-balloon endoscopy in patients with small intestinal diseases: Single-center experience in 513 procedures

SMALL BOWEL

Mesut Akarsu[1], Seda Akkaya Özdinç[1], Aygül Çeltik[2], Hale Akpınar[1]

[1]Department of Gastroenterology, Dokuz Eylül University Faculty of Medicine, İzmir, Turkey
[2]Department of Internal Medicine, Dokuz Eylül University Faculty of Medicine, İzmir, Turkey

Original Article

ABSTRACT

Background/Aims: Double-balloon endoscopy (DBE) is a technique that enables the evaluation and treatment of small intestinal diseases. The aim of the study was to evaluate the indications, therapeutic interventions, complications, and safety and to describe the experience with DBE in Turkish patients.

Materials and Methods: Four hundred twenty consecutive patients undergoing DBE were included in our study. Demographic features, indications, diagnostic findings, therapeutic interventions, complications, and technical aspects of the procedure were recorded. A total of 513 DBEs were carried out.

Results: In all, 420 patients underwent a total of 513 DBE procedures (369 (72%) oral and 144 (28%) anal). The most common clinical indications were obscure bleeding (26%), abdominal pain (25.2%), anemia (20%), chronic diarrhea (10.5%), and inflammatory bowel diseases (5.2%). A proper diagnosis was obtained or confirmed in 222 of 420 patients (52.3%). Ulcers/erosions (23.6%), vascular lesions (8.1%), and polyps/tumors (7.4%) represented the most common endoscopic findings. Perforation occurred in one patient as a complication after polypectomy. No major complications due to sedation occurred.

Conclusion: Double-balloon endoscopy is effective for the diagnosis and treatment of small intestinal diseases. Therapeutic interventions carried out by DBE seem to be useful and safe.

Keywords: Double-balloon endoscopy, small intestine, anemia, obscure bleeding, endoscopic treatment

INTRODUCTION

The small intestine is an important part of the gastrointestinal tract, since it harbors many diseases, like vascular malformations, tumors, polyps, and inflammatory diseases (1,2). The most popular nonsurgical endoscopic techniques are video capsule endoscopy and double-balloon endoscopy (DBE).

Double-balloon endoscopy is a method of endoscopy that enables visualization of the entire small intestine and allows tissue sampling and therapeutic interventions, like balloon dilatation, polypectomy, and mucosal resection (3-6). DBE is also superior to push enteroscopy, by which visualization of all the small intestine is impossible (7). The video capsule endoscopy also provides the visualization of the entire small intestine, but it is impossible to perform diagnostic or therapeutic interventions.

The present study describes the results of all patients who were examined by DBE since the introduction of this method in our endoscopy unit. The aim of the study was to retrospectively evaluate the indications, therapeutic interventions, complications, and safety of this technique.

MATERIALS AND METHODS

Between January 2006 and January 2013, 420 consecutive patients who underwent a total of 513 DBE because of suspected small intestinal disease were included. Demographic features, including age, gender, indication for enteroscopy, findings of prior gastrointestinal endoscopies, and radiological studies, including barium studies, computed tomography (CT), and angiography, where available were noted. For patients who were referred to our clinic for DBE after a diagnostic work-up in

Address for Correspondence: Mesut Akarsu, Department of Gastroenterology, Dokuz Eylül University Faculty of Medicine, İzmir, Turkey
E-mail: mesut.akarsu@deu.edu.tr
Received: 23.3.2013 **Accepted:** 22.10.2013

another hospital, re-examination with the same radiological or endoscopic method was impractical. The findings of the previous diagnostic work-up were recorded. The procedural details, including diagnostic findings and interventions, the length of advancement in centimeters, the way of approach, investigation time, reason for termination of DBE, and complications, were carefully recorded.

Written informed consent for the procedure and possible endoscopic interventions was obtained already from all cases after the endoscopist and anesthetist had explained the procedures and risks in detail.

Double-balloon endoscopy was performed using a Fujinon enteroscope (Fujinon EN-450T5, Fujinon Inc., Saitama, Japan), with a working length of 200 cm, outer diameter of 9.4 mm, and accessory channel of 2.8 mm.

The overtube has an outer diameter of 13.2 mm and a working length of 140 cm (2). The working channel allows introduction of a biopsy forceps, a snare, and an argon plasma catheter through the instrument. Two latex balloons, attached to the tip of the endoscope and to the overtube, are inflated and deflated by using the pump through an air channel in the endoscope. Inflation and deflation of the balloons alternatively cause advancement of the endoscope and overtube and pleating of the intestine onto the overtube. The latter facilitates insertion of the endoscope further and further through the intestine. The depth of endoscope insertion was calculated by the method described by May et al (8). The endoscope can be introduced via antegrade (oral) or retrograde (anal) approaches.

Patients underwent DBE via oral route after overnight fasting without any specific preparation. If the way of approach was anal, bowel cleansing with a standard colon lavage solution the day before the procedure and overnight fasting were required.

The way of approach was determined by the endoscopist according to the localization of the suspected lesion on the basis of clinical signs and symptoms and of radiological findings. Lesions estimated to be located in the upper two-thirds of the small intestine were initially examined by an oral approach. For lesions estimated to be in the lower one-third, the anal route was preferred initially. If no lesion was detected by one route, DBE was repeated via the other route if the indication required it. The intention to visualize the entire small intestine was required in some patients, especially in those with anemia and obscure bleeding, and was determined by the endoscopist according to the indication. If an appropriate diagnosis during the first procedure was not achieved or if all of the small intestine could not be visualized in one session, an india-ink tattoo was left as a landmark for another examination, and the next session was done via the alternative route. If a finding that was appropriate for the indication was detected, the procedure was terminated.

The indications for the termination of the procedure were patient intolerance, establishment of a diagnosis corresponding to the indication, completely effective treatment, failing to pass an obstruction, or moving forward along the small intestine.

All DBE examinations were performed by two experienced endoscopists. One nurse assisted the endoscopist in the operating room throughout the procedure. Another endoscopist assisted during therapeutic interventions.

The DBE was carried out with patients under conscious sedation, which was achieved by intravenous midazolam and propofol. The level of sedation and vital signs were followed by an anesthetist during the procedure. The patients were monitored by pulse oximetry, electrocardiography, and blood pressure.

Data were analyzed with Statistical Package of Social Science (SPSS), software version 11.0 (IBM Corporation, Armonk, New York) for Windows. Continuous variables were presented as mean±standard deviation (SD) and range (minimum-maximum). Categorical variables were presented as frequency and percentage.

RESULTS

Patients

A total of 513 DBE procedures (369 oral and 144 anal) were carried out in 420 patients. The mean age was 47.8±17.8 (range 7-88) years. There were 173 women and 247 men; 308 (245 patients via oral and 63 patients via anal approach) patients underwent a single procedure, 69 patients underwent both oral and anal procedures, and 43 patients underwent multiple procedures. Multiple procedures applied to 43 patients: 6 of them had two anal procedures, and 37 patients had two or more than two oral procedures. The demographic characteristics and clinical and radiological indications of the study group are presented in Table 1. The indications were evaluated in two major categories: the clinical indications that constituted the major complaints, laboratory findings, or established diseases and radiological/endoscopic indications that were detected during diagnostic evaluation. The most commonly seen clinical indications were abdominal pain, obscure bleeding, and anemia. Twenty-two patients had an established diagnosis of inflammatory bowel disease (IBD). All patients were known to have Crohn's disease except one patient who had Behçet's disease at the time of the DBE. Eleven had polyposis syndrome at the time of the DBE. Two patients who had hypoalbuminemia underwent DBE with a suspicion of protein-losing enteropathy. Intestinal lymphangiectasia was found only in one patient. DBE was performed in two patients to evaluate the small intestine for carcinoid tumors, but the endoscopic examinations were normal. Most of the radiologic/endoscopic indications were detected by computer tomography (CT) and upper and lower endoscopy. Thickened small bowel wall was the most common radiological finding. Angiodysplasia and terminal ileitis were

Table 1. Demographic characteristics of the patients and clinical and radiological indications

	n=420	%	Notes
Mean age (range)	47.8±17.8 years (7-88 years)		
Gender			
Male	247	58.8	
Female	173	41.2	
Clinical indications for DBE			
Obscure bleeding	109	26	
Abdominal pain	106	25.2	
Anemia	84	20	
Chronic Diarrhea	44	10.5	
Inflammatory bowel disease	22	5.2	Established Crohn's disease 12, Established Behçet's disease 1
Obstruction	20	4.8	
Polyposis	13	3.1	Established Peutz-Jegers syndrome 8, FAP 1, Cronkhite-Canada syndrome 2
Others	14	3.4	Established Celiac disease 2, Hypoalbuminemia 3, Searching for carcinoid tumor 2, Control after ileal resection 1 Oral hyperpigmentation 1
Nausea/vomiting	8	1.9	
Radiological/endoscopic indications for DBE			
Abnormal small intestinal barium graphy	33	7.8	Dilatation 5, mass 5, thickened bowel wall 12
Abnormal CT	133	31.6	Dilatation 16, mass 10, thickened bowel wall 78
Abnormal upper endoscopy	44	10.5	Tumor/polyp 4, polyposis 6, angiodysplasia 8
Abnormal lower endoscopy	58	13.8	Tumor/polyp 9, polyposis 7, angiodysplasia 11, terminal ileitis 17

frequent findings detected in the upper and lower endoscopy. In 9 patients whose upper or lower endoscopy revealed angiodysplasia and in 12 patients whose lower endoscopy revealed terminal ileitis, DBE was performed for further evaluation of the small intestine.

Technical aspects

Of 420 procedures, 245 (58.3%) were performed via the oral way and 63 (15%) were performed via the anal way. The mean duration of the procedures was 63.6±21.7 min. for the oral approach and 60.9±19.3 min. for the anal approach. A total of 17 (3.3%) procedures were terminated earlier than expected: 7 due to patient intolerance and 10 due to technical problems. Thirteen (2.5%) procedures were terminated secondary to obstruction (due to Crohn's disease in 4 of them, tumor in 2, due to ulcer in 3, and due to brid ileus in 4). The mean depth of examination was 249±108 cm (range 10-500 cm) for the oral approach and 110±76 cm (range 20-400 cm) for the anal approach.

Double-balloon endoscopy procedure was carried out intraoperatively in two patients who had intra-abdominal adhesions. One patient who had Peutz-Jegers syndrome underwent a procedure for polypectomy. The other patient had melena after hepaticojejunostomy operation, and bleeding at the level of the hepaticojejunostomy was detected by DBE.

It was impossible to reach the ileum in 22 (15.2%) of 144 anal procedures. In 7 procedures, ileocecal intubation was impossible. Patient intolerance (n=6) and inappropriate bowel cleansing (n=9) were the other causes. In other words, the small intestine was visualized successfully in 122 of 144 anal procedures.

Technical complications occurred in 5 oral and 5 anal procedures. Most were associated with the balloons of the endoscope. Seven complications resulted in the termination of the procedures earlier than expected. Perforation occurred in one patient with blue rubber bleb nevus syndrome (BRBNS) after polypectomy. No major complications secondary to sedation were observed.

Endoscopic diagnosis

Table 2 lists the endoscopic findings and the diagnosis of the patients. The procedure of DBE was unsuccessful in 13 of 420 patients due to patient intolerance (n=6) and inappropriate ileum intubation (n=7). As these patients were out of follow-up, it was impossible to re-examine these patients by DBE and to obtain a diagnosis. Endoscopic examination was normal in 180 patients. A proper diagnosis was established or confirmed in 222 of 420 patients (52.8%). Ulcers/erosions, polyps/tumors and vascular lesions were the most common endoscopic findings. Among patients diagnosed as having ulcers/erosions, 1 patient had collagenous ileocolitis, 1 had radiation ileitis, 2 patients had amyloidosis, and 3 patients had Meckel diverticulum. The malignant tumors diagnosed by DBE were gastrointestinal stromal tumors (n=4) (Figure 1), small intestinal cancer (n=9) (Figure 2), lymphoma (n=5), and angiosarcoma (n=1) (Figure 3). Parasitic diseases were detected in three patients by direct visualization of the parasites. DBE was carried out in 79 patients with iron deficiency anemia. Although the examination of the entire small intestine was achieved in 46.8% of the patients, a diagnosis was obtained in 28.5%. Ulcerations, erosions, and vascular lesions were among the most common endoscopic findings. The findings of 84 patients with obscure gastrointestinal bleeding were evaluated. It was possible to examine the entire small intestine in 59 (70.2%) patients. Lesions that could account for gastrointestinal bleeding were found in 42 (50%) of 84 patients. The most common findings were ulcerations, erosions, and vascular lesions, like the findings of patients with anemia.

Table 2. Endoscopic findings and diagnosis of the patients

	n=420	%	Notes
None	18	4.2	
Normal	180	42.8	
Polyps/Tumors	31	11.4	
Small intestinal cancer	9	2.1	
Gastrointestinal stromal tumor	4	1	
Lymphoma	5	1.2	
Others	5	1.7	Lipoma 2, angiosarcoma 1, inflammatory fibroid polyp 2
Vascular lesions	33	7.8	
Angiodysplasia	26	6.1	
Others	7	1.6	Osler-Weber-Rendu 4, jejunoileal varices 1
Ulcers/Erosions	94	22.3	
Ileitis, jejunitis or jejunoileitis	23	5.4	Ischemic 2, collagenous ileocolitis 1, radiation ileitis 1
Ulcer	18	4.2	
Crohn's	39	9.2	
Behçet disease	1	0.2	
Celiac disease	3	0.7	
Others	12	2.8	Duodenal erosion 7, amiloidosis 2, Meckel diverticulum 3
Obstruction	11	2.6	
Polyposis syndrome	14	3.3	Peutz-Jegers syndrome 8, follicular lymphoid hyperplasia 2, FAP 2, Cronkhite-Canada syndrome 2
Disease of stomach	22	5.2	Ulcers/erosions 13, angiodysplasia 4, polyp 2
Disease of colon	13	3.1	Angiodysplasia 5, ulcer/erosion 3, Dieulafoy's lesion 1, tumor 1, collagenous colitis 1

Twenty-two patients with a previously established diagnosis of IBD underwent DBE to evaluate the degree of activity and the extent of disease. All patients were known to have Crohn's disease, except one patient who had Behçet's disease at the time of the DBE. No pathological finding was detected in 6 of them, and they were recorded as having normal endoscopic findings. As an endoscopic finding, Crohn's disease was detected in 39 patients; 17 of these patients were diagnosed newly by DBE, and 17 of the 39 patients were those who had an established diagnosis of Crohn's disease at the time of the DBE.

Among 13 patients whose endoscopic findings were compatible with polyposis, 11 patients had an established diagnosis

Figure 1. Gastrointestinal stromal tumor detected in the jejunum.

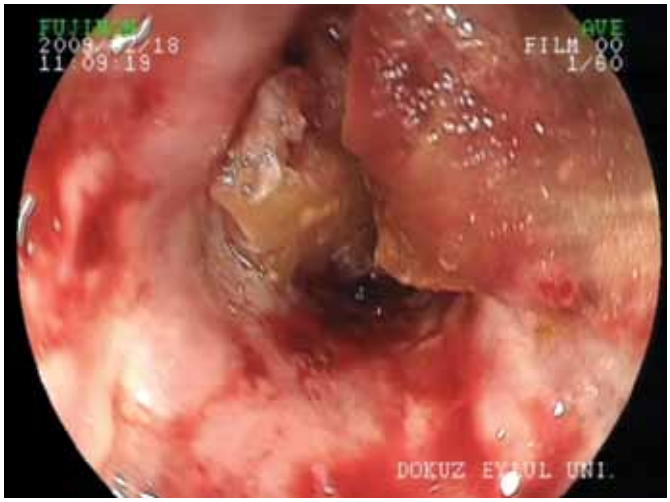

Figure 2. Adenocarcinoma detected in the third segment of the duodenum.

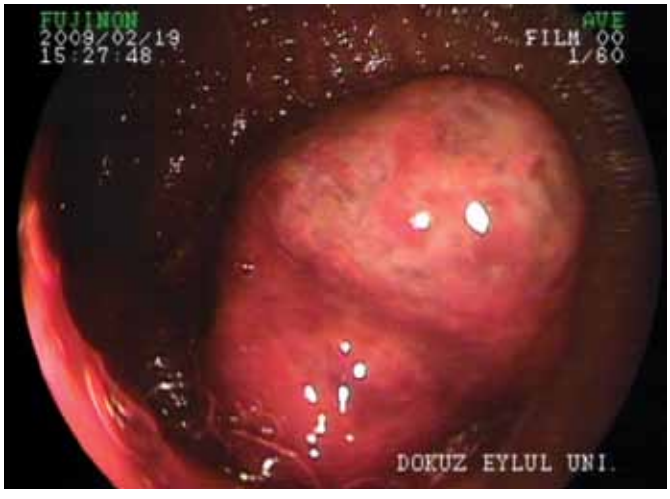

Figure 3. Endoscopic view of angiosarcoma in the jejunum.

of polyposis syndrome at the time of the procedure and underwent DBE, mainly for therapeutic purposes. Eight patients had Peutz-Jeghers syndrome (Figure 4), 2 had familial adenomatous polyposis, and 1 had Cronkhite-Canada syndrome. There was common variable immune deficiency syndrome

Original Article

Figure 4. Endoscopic view of one of the polyps in a patient with Peutz-Jegers syndrome who underwent multiple polypectomy procedures.

in 2 newly diagnosed patients, and they were diagnosed as lymphoid follicular hyperplasia. Multiple polyps in the duodenum and jejunum were detected in 1 patient who was referred for evaluation of chronic diarrhea. As he was out of follow-up, it was impossible to make a definite diagnosis in this patient, and he was recorded as having an undefined polyposis syndrome.

Therapeutic interventions

A total of 86 (20.4%) patients underwent a total of 420 therapeutic interventions, including argon plasma coagulation (APC) in 43 patients, polypectomy in 36 patients, dilatation in 2 patients, and sclerotherapy in 6 patients. The total numbers of APC, polypectomy, and sclerotherapy were 512, 231, and 6, respectively (Table 3). The most common indication for APC was angiodysplasia (43 patients). Angiodysplastic lesions were detected in the stomach in 1 patient and in the large intestine in another. APC was performed in 2 patients with Osler-Weber Rendu (OWR) and 1 patient with BRBNS for actively bleeding lesions. Multiple polypectomy interventions were performed in 11 patients with polyposis syndrome. After pathological evaluation of the polypectomy material, 1 patient was diagnosed as having a malignant tumor (angiosarcoma). Gastric and small intestinal benign polyps were detected in 5 patients, inflammatory fibroid polyp was detected in 1 patient, and lipoma was detected in 2 patients. The patient diagnosed as BRBNS had severe anemia that required blood transfusions 2-3 times a month; so, he underwent multiple snare polypectomy interventions of the vascular malformations to prevent anemia.

One major complication was observed due to therapeutic interventions. In a patient with BRBNS, perforation occurred after polypectomy. Three patients underwent APC after polypectomy to control bleeding. Sclerotherapy was performed in 2 patients after polypectomy and in 1 patient after biopsy to stop bleeding.

Table 3. Therapeutic interventions during double balloon endoscopy

		Examination route n=513		
		Oral n=369	Anal n=144	
	Number of the patients	Number of the interventions	Number of the interventions	Total number of the interventions
Argon plasma coagulation	43	408	104	512
Polypectomy	36	177	54	231
Dilatation	2	0	2	2
Sclerotherapy	6	6	0	6
Total	86*	591	160	751

*Some patients underwent multiple therapeutic interventions

DISCUSSION

In the study, 513 DBE procedures were performed in 420 patients. The most common clinical indications were obscure bleeding (26%), abdominal pain (25.2%), and anemia (20%). Thickened small bowel wall was the most common radiological indication. The most frequent findings in the upper and lower endoscopy were angiodysplasia and terminal ileitis. A proper diagnosis was established or confirmed in 222 of 420 patients (52.8%) by DBE. Ulcers/erosions (23.6%), vascular lesions (8.1%), and polyps/tumors (7.4%) were the most common endoscopic findings.

Three main indications for DBE were abdominal pain, obscure bleeding, and anemia, respectively. This finding was not compatible with previous studies. In most of the previous studies, nearly half of the indications were gastrointestinal bleeding, as the patients were not categorized as having anemia (9-12). But, in this study, patients with iron deficiency anemia were categorized separately. Only the patients with a history of bleeding were categorized in the obscure bleeding group. The percent of patients with anemia and obscure bleeding was 44.5%. This finding was similar with previous reports. Lahat et al. (13) categorized patients as having anemia and bleeding separately and found out that anemia was the main clinical indication in 46% of the patients.

The overall diagnostic yield of the study was 52.8%. The diagnostic yields of abdominal pain, obscure bleeding, and anemia-the most three common indications-were 22.6%, 25.7%, and 18.8%, respectively. The overall diagnostic yield of our study was similar to the reports of Kita et al. (10) and Heine et al. (12) but lower than that of two European studies (9-12). In these European studies, a diagnosis was obtained in 80% and 67% of the patients (9,11). The diagnostic yield for obscure bleeding was similar to previous studies but lower than that reported by Di Caro et al. (11) (12,14). As our hospital was a referral center, some patients were admitted only for DBE after a diagnostic

work-up, including a normal barium graphy, CT, and upper/lower endoscopy performed in another hospital. In 9 patients, a gastric or large intestinal lesion was detected, although their previous upper and lower endoscopic evaluations were found to be normal in another hospital. In fact, a small intestinal abnormality was detected in 60.7% of the patients with obscure bleeding. Among 44 patients with chronic diarrhea, 18 (40.9%) patients were found to have an endoscopic finding that might cause diarrhea. Among patients who had radiological findings irrespective of clinical indications, 50% had endoscopic findings appropriate with the previously detected radiological abnormalities. Heine et al. (12) found that DBE provided a diagnosis in 60% of the patients with radiological abnormalities.

Ulcers/erosions, polyps/tumors, and vascular lesions were the most common endoscopic findings. Crohn's disease was the most common finding among patients diagnosed as having ulcers/erosions. Twenty-two patients with an established diagnosis at the time of the DBE underwent the procedure, and 16 had an abnormal endoscopic evaluation. In the study, 2 patients who had abdominal pain or diarrhea were diagnosed as having IBD after DBE. The high incidence of Crohn's disease could be attributed to the intention to evaluate the entire gastrointestinal system for detection of the extent of disease in all patients with a suspicion of IBD. In a recent study, DBE was performed in 16 patients suspected having Crohn's disease to evaluate small intestines (15). İn 7 patients, there were abnormal endoscopic findings correlating with aphthous lesions and ileitis. Eleven patients were diagnosed with Crohn's disease, which was suspected clinically and radiologically. In our study, 15 of the 78 patients with a thickened small bowel wall shown by CT scan were diagnosed as having Crohn's disease by findings, like ileitis and ulcers in the terminal ileum. In 2 patients with a normal small bowel CT scan, macroscopic ulcers and clinical findings led to Crohn's disease. In another study, 44 Crohn's disease patients were evaluated by DBE. It is stated that DBE is superior to radiological methods about detecting lesions, like aphtous ulcers, small ulcers, and erosions in the ileum (16).

In concordance with previous studies, the most common finding in patients with obscure bleeding and anemia was angiodysplasia, and almost all of them were treated successfully with APC and sclerotherapy.

Double-balloon endoscopy is valuable for the diagnosis and regular surveillance of patients with polyposis syndrome. Polypectomy is an alternative to surgical removal of suspected polyps (12). Three patients were diagnosed as having polyposis syndrome. In our study, multiple polypectomy procedures were performed for polyps with a diameter more than 1 cm in 8 patients with polyposis syndrome. No major complication was seen after these procedures.

Therapeutic procedures were performed in 20.4% of the patients during 25.3% of the procedures. The number of patients who underwent the therapeutic intervention was lower than that reported previously. In most of the reported studies, 40%-45% of patients underwent interventions (9-11,13,17). Besides, the number of therapeutic interventions was very high in the presented study. This could be attributed to the high number of patients who needed multiple therapeutic interventions. In 8 patients with polyposis syndromes, 132 polypectomy procedures were performed during a total of 25 sessions. In 1 patient with BRBNS, 31 polypectomy procedures were performed in 3 sessions. Two patients with OWR disease underwent a total of 85 APCs in a total of 7 sessions. Perforation as a major complication occurred after therapeutic intervention in 1 patient. Our study demonstrated that DBE is a safe procedure, even after performance of multiple therapeutic interventions. Like our findings, major complications were very rarely reported in published previously series (11,12,17,18).

There are some limitations of this study. First, the accuracy and reliability of radiological and endoscopic findings may be low, because some patients were referred for DBE after radiological and endoscopic evaluation in another hospital. Second, it was impossible to perform another DBE in a minority of patients when an appropriate diagnosis was not obtained, as they were out of follow-up.

In conclusion, DBE is a valuable method for the evaluation of small intestinal diseases because of its good tolerability, high diagnostic yield, and therapeutic efficacy. It is worthwhile for the diagnosis, surveillance, and treatment of polyposis syndromes and syndromes characterized with vascular malformations. As shown in our report, it seems to be safe, even after performance of multiple therapeutic interventions.

Ethics Committee Approval: N/A.

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

Peer-review: Externally peer-reviewed.

Author contributions: Concept - M.A., H.A.; Design - M.A., H.A., S.A.O.; Supervision - M.A., H.A., S.A.O.; Resource - M.A., S.A.O., A.C.; Materials - M.A., S.A.O., A.C.; Data Collection&/or Processing - M.A., S.A.O., A.C.; Analysis&/or Interpretation - M.A., S.A.O., A.C.; Literature Search - M.A., S.A.O., A.C.; Writing - M.A., S.A.O., A.C.; Critical Reviews - M.A., S.A.O., H.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Pennazio M. Small-bowel endoscopy. Endoscopy 2008; 40: 835-42. [CrossRef]
2. Kita H, Yamamoto H. Double-balloon endoscopy for the diagnosis and treatment of small intestinal disease. Best Pract Res Clin Gastroenterol 2006; 20: 179-94. [CrossRef]
3. Yamamoto H, Sekine Y, Sato Y, et al. Total enteroscopy with a nonsurgical steerable double-balloon method. Gastrointest Endosc 2001; 53: 216-20. [CrossRef]

4. Yoshida N, Wakabayashi N, Nomura K, et al. Ileal mucosa-associated lymphoid tissue lymphoma showing several ulcer scars detected using double-balloon endoscopy. Endoscopy 2004; 36: 1022-4. **[CrossRef]**
5. Ohmiya N, Taguchi A, Shirai K, et al. Endoscopic resection of Peutz-Jeghers polyps throughout the small intestine at double-balloon enteroscopy without laparotomy. Gastrointest Endosc 2005; 61: 140-7. **[CrossRef]**
6. Kuno A, Yamamoto H, Kita H, et al. Double-balloon enteroscopy through a Roux-en-Y anastomosis for EMR of an early carcinoma in the afferent duodenal limb. Gastrointest Endosc 2004; 60: 1032-4. **[CrossRef]**
7. Pennazio M, Arrigoni A, Risio M, Spandre M, Rossini FP. Clinical evaluation of push-type enteroscopy. Endoscopy 1995; 27: 164-70. **[CrossRef]**
8. May A, Nachbar L, Schneider M, Neumann M, Ell C. Push-and-pull enteroscopy using the double-balloon technique: Method of assessing depth of insertion and training of the enteroscopy technique using the Erlangen Endo-Trainer. Endoscopy 2005; 37: 66-70. **[CrossRef]**
9. Monkemuller K, Weigt J, Treiber G, et al. Diagnostic and therapeutic impact of double-balloon enteroscopy. Endoscopy 2006; 38: 67-72. **[CrossRef]**
10. Kita H, Yamamoto H, Yano T, et al. Double balloon endoscopy in two hundred fifty cases for the diagnosis and treatment of small intestinal disorders. Inflammopharmacology 2007; 15: 74-7. **[CrossRef]**
11. Di Caro S, May A, Heine DG, et al. The European experience with double-balloon enteroscopy: indications, methodology, safety, and clinical impact. Gastrointest Endosc 2005; 62: 545-50. **[CrossRef]**
12. Heine GD, Hadithi M, Groenen et al. Double-balloon enteroscopy: Indications, diagnostic yield, and complications in a series of 275 patients with suspected small-bowel disease. Endoscopy 2006; 38: 42-8. **[CrossRef]**
13. Lahat A, Nadler M, Simon C, et al. Double balloon enteroscopy: A 2 year experience. Isr Med Assoc J 2009; 11: 456-9.
14. Yamamoto H, Kita H, Sunada K, et al. Clinical outcomes of double-balloon endoscopy for the diagnosis and treatment of small-intestinal diseases. Clin Gastroenterol Hepatol 2004; 2: 1010-6. **[CrossRef]**
15. Schulz C, Mönkemüller K, Salheiser M, Belluti M, Schütte K, Malterfertheiner P. Double-balloon enteroscopy in the diagnosis of suspected isolated Crohn's disease of the small bowel. Dig Endoscopy 2014 26: 236-42. **[CrossRef]**
16. Yukawa T, Yamagami H, Inagawa M, et al. Evaluation of deep small bowel involvement by double-balloon enteroscopy in Crohn's disease. Am J Gastroenterol 2006; 101: 1484-9. **[CrossRef]**
17. Cazzato IA, Cammarota G, Nista EC, et al. Diagnostic and therapeutic impact of double-balloon enteroscopy (DBE) in a series of 100 patients with suspected small bowel diseases. Dig Liver Dis 2007; 39: 483-7. **[CrossRef]**
18. Akahoshi K, Kubokawa M, Matsumoto M, et al. Double-balloon endoscopy in the diagnosis and management of GI tract diseases: Methodology, indications, safety, and clinical impact. World J Gastroenterol 2006; 12: 7654-9.