Double Balloon Enteroscopy in a North American Setting: A Large Single Center 5-year Experience

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Background/Aims: Double balloon enteroscopy (DBE) allows both diagnosis and therapeutic maneuvers in the small bowel. Its use was pioneered in Europe and Asia but there remains a relative paucity of literature from North America. Our aim in this study was to determine diagnostic and therapeutic yield in a North American setting. **Methods:** A five-year retrospective analysis of all patients undergoing DBE at a single tertiary care North American hospital was performed. **Results:** Four-hundred fifty-seven procedures, 265 antegrade and 192 retrograde, were performed on 335 patients. The most common indications were obscure gastrointestinal bleeding, small bowel obstruction, and suspected masses and mucosal abnormalities. Total enteroscopy was achieved in 19 of the 89 patients who had both antegrade and retrograde procedures. Overall diagnostic yield in the determination of cause of symptoms or previous imaging was 52%. The most common causes of obscure bleeding were small bowel ulcers (10%), vascular lesions (25%) and neoplasms (10%). The most common causes of small bowel obstruction were strictures, some of which underwent dilation. Other therapeutic interventions included polypectomy, retrieval of retained capsules, stent retrievals and percutaneous enteral jejunostomy tube placement. Overall complication rates were very low (0.6%) and included medication reaction (n=1), scope dysfunction (n=1) and perforation (n=1). **Conclusions:** DBE can be performed safely and with good diagnostic yield in a single referral center in North America. (*Intest Res* 2013;11:34-40)

Key Words: Intestinal neoplasms; Gastrointestinal hemorrhage; Double balloon enteroscopy; Capsule endoscopy

INTRODUCTION

Prior to the advent of double balloon enteroscopy (DBE) in 2001, small bowel enteroscopy was significantly limited in its reach for deep small bowel lesions. While visualization of the entire small bowel was radically improved by the development of video capsule endoscopy (VCE), therapeutic maneuvers and tissue acquisition were constrained by the use of intraoperative endoscopy or push enteroscopy. While intraoperative endoscopy carries a substantial cost and rate of complications, push enteroscopy was also suboptimal given its limited reach and inability to provide complete endoscopic interrogation of the small bowel. With DBE, total en-

teroscopy can be achieved without the need for laparotomy, usually with a bidirectional approach, and both tissue acquisition and therapy, including polypectomy, stricture dilation and cauterization, can be performed.¹ Complication rates are reportedly low, and learning curves appear to indicate rapid proficiency.^{2,3}

Pioneered in Japan and Europe, there are few North American studies of the utility and safety of DBE in the evaluation of small bowel disease. In this study, we present an overview of a five-year experience in DBE performed at a single North American center. The aim of the study was to determine the indications, diagnostic accuracy and complication rates of DBE in a tertiary/quaternary hospital setting.

METHODS

1. Recruitment

Between January 2007 and December 2011, a total of 374

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patients underwent a total of 501 DBE. Demographic, clinical, procedural, and outcome data were collected retrospectively. Among them, a total of 335 patients with clinically suspected or documented small bowel diseases were analyzed. Patients who underwent DBE for device-assisted endoscopic retrograde cholangiopancreatography (ERCP) were excluded. The study was approved by the institutional review board (IRB 11157).

2. Enteroscopic Examinations

All examinations were performed using the DBE (Fujinon EN-450T5; Fujinon Inc., Saitama, Japan) with a working channel of 2.8 mm using alternating push and pull and inflation and deflation of an overtube balloon and a scope-tip balloon as described previously.⁴

All procedures were performed by 5 experienced endoscopists. Fluoroscopy was used in some patients depending upon the preference of the endoscopists. The choice of approach was determined by endoscopist, according to suspected location of lesions, based on clinical findings and/or the results of the previous investigations. The oral route (antegrade) was chosen for those suspected to have a jejunal lesion, whereas the retrograde approach was initially selected when ileal lesions were suspected. Antegrade procedures were done under general anesthesia by an anesthesia provider, while retrograde DBE was generally performed with patients under conscious sedation. Colon cleansing was required prior to retrograde DBE but not prior to antegrade DBE.

Total procedure time was defined as the period from the insertion to withdrawal of the enteroscopy. When the unidirectional DBE route did not yield diagnosis, the opposite route was generally used for the second investigation. The deepest point of insertion during the initial DBE was marked with submucosal injection of 2-3 mL of india ink. Total enteroscopy was confirmed when india ink injected at the point of deepest insertion could be identified by DBE in the opposite direction or if the ileocecal valve was reached from the antegrade route. Enteroscopic examination was sometimes but not always discontinued when the lesion was found or no further progress was possible. Total enteroscopy rate was calculated as the ratio of patients with complete small bowel visualization either by a single DBE examination or with both retrograde and antegrade DBE, as documented by visualization of the previously placed tattoo on the second examination.

Therapeutic interventions were defined as polypectomy, balloon dilation of stricture, foreign body removal, and hemostasis procedures, such as argon plasma coagulation (APC), heater probe and/or clip. Polypectomy was performed in standard fashion. Balloon dilation of strictures was performed using through-the-scope balloons (CRE; Boston Scientific Inc, Natick, MA, USA). Fluoroscopy and wire guid-

ance were used at the discretion of the endoscopist. Foreign body removal was performed with Roth net devices (US Endoscopy, Mentor, OH, USA). APC was performed using 1.5 mm or 2.3 mm probes and the ERBE device (ERBE USA Inc., Marietta, GA, USA) at settings per discretion of the endoscopist. Hemostatic clips (Resolution[®] clips; Boston Scientific Inc., Natick, MA, USA) were sometimes altered slightly for use with the DBE. The outer sheaths were removed to allow passage through the channel. Patients were monitored for complications during the procedure and for at least 2 hours after recovery.

3. Definitions and Analysis

Indications for DBE were categorized as follows: 1) obscure gastrointestinal bleeding (OGIB); 2) suspected small bowel obstruction; 3) suspected neoplastic lesions (benign or malignant tumors) or mucosal abnormalities and 4) symptoms/signs only or 5) therapeutic (foreign body retrieval or percutaneous enteral jejunostomy [PEJ] tube). OGIB was described as occult or overt bleeding of unknown origin including melena, hematochezia, and/or iron deficiency anemia. Small bowel obstruction was defined as the presence of abdominal pain, nausea, vomiting and/or other symptoms or imaging supporting obstruction of the small bowel. Any clinical symptoms, such as abdominal pain, diarrhea, weight loss, and other gastrointestinal complaints without radiological images and VCE not included in the previous categories were defined as indications of symptoms/signs only.

Findings explaining the patients' symptoms and the abnormalities seen on the previous investigations and resulted in a change in the management were considered positive findings. The detection rate was defined as the ratio of patients with positive findings over all patients since some of the patients underwent more than one procedure. The positive findings were categorized as: vascular lesions (including arteriovenous malformations [AVMs], varices); inflammatory lesions (including CD, erythema, erosions, ulcers); neoplastic lesions (benign or malignant tumors, including polyps); diverticula; and others (any positive findings not included in the previous categories). Findings from VCE pre-dating the DBE examinations were recorded but not independently verified for this study. VCE examinations in patients were performed at our institution and at outside institutions.

4. Study Endpoints

The primary outcome measure was to determine the endoscopic findings and clinical outcomes of DBE/therapy and complications during and after procedure.

5. Statistical Analysis

Descriptive statistics were calculated using SPSS for pa-

tient data and clinical parameters, with means, range, and standard deviation. VCE and DBE findings were divided into seven categories and compared. Agreement between modalities was adjusted for chance and calculated using the kappa statistic (STATA 12, College Station, TX, USA).⁵

RESULTS

During the study period, a total of 457 DBE examinations were performed in 335 patients (Table 1). The patients' mean age was 61 years (range 15-93 years); there were 172 men and 163 women. One-hundred eighty-eight patients (56%) had previous abdominal and/or pelvic surgery, including small bowel resection in 39, colonic resection in 29, gastric surgery in 22, and ileocolonic surgery in 4. Of the 457 procedures, 265 (57.8%) were performed by the antegrade approach, 192 (41.9%) by the retrograde approach, and one by

an ileostomy. In total, 89 patients (26.4%) were examined both antegrade and retrograde approaches; 17 patients received a third procedure, and 1 patient a fourth. Total enteroscopy was achieved in 19 of the 89 patients (21%), in whom both approaches were performed. In another patient who had small bowel resection, total enteroscopy was accomplished with only antegrade approach.

Antegrade procedures were done under general anesthesia in 87% of the patients and retrograde procedures were performed under conscious sedation in 72%. The mean procedure time was 61±20 minutes for overall procedures, 64±22 minutes for the antegrade approach, 58±18 minutes for retrograde approach, and there was no significant difference between two approaches ($P>0.05$).

1. Indications

The most common indication was OGIB, accounting for 225 of the 335 patients (67%) (Table 2). Forty-nine (14%) patients underwent DBE for suspected small bowel obstruction and 23 (7%) had suspected small bowel neoplastic lesions. DBE was performed for suspected small bowel mucosal disease (CD, celiac disease, refractory sprue, ulcerative jejunitis, etc.) in 24 patients (11%). In 3 patients (1%), DBE was performed to retrieve biliary stents (2) and esophageal stent (1) in the small bowel and in one patient for placement of a percutaneous jejunostomy. In 10 patients, DBE was performed for symptomatology or imaging findings not otherwise specified.

2. Findings

Of the 335 patients, 178 (53%) had abnormalities in the small bowel, which were significant enough to explain symptoms or abnormal findings on the previous investigations and 153 (46%) had normal examination (Table 3). In addition, 4 patients had abnormal findings on DBEs, such small polyps and some mucosal changes, but not thought to be associated with the indication. Positive findings were found in 74

Table 1. Baseline Characteristic of Patients

Characteristic	Data
Patients (n)	335
Procedures (n)	457
Age (yr)	61±17
Gender (male/female)	172/163
Previous surgery	188 (56)
Previous capsule endoscopy	234 (70)
Known diseases	30 (9)
Inflammatory bowel disease	17
Celiac disease	7
Peutz-Jeghers syndrome	3
Familial adenomatous polyposis	1
Gardner's syndrome	1
Cowden's disease	1

Values are presented as n, mean±SD, or n (%).

Table 2. Indications and Detection Rates

Indication	Patient, n (%)	Procedure, n	Rate of detection, %
OGIB	225 (67)	323	56
Small bowel obstruction	49 (14)	63	47
Suspected mucosal abnormalities, or neoplastic lesions	47 (14)	56	33
Symptoms/signs	10 (3)	11	10
Stent retrieval/PEJ	4 (1)	4	NA
Total	335 (99)	457	52

OGIB, obscure gastrointestinal bleeding; PEJ, percutaneous enteral jejunostomy tube; NA, not available.

Nota bene: rate of detection calculated as number of positive findings correlating with cause of OGIB, obstruction, suspected abnormality or symptoms.

Table 3. Positive Findings in 335 Patients with Suspected Small Bowel Diseases

Finding	Patient (n)
Vascular abnormalities	59
Ulcerations and/or erosions	32
Neoplastic lesions	34
Small bowel strictures	25
Diverticulosis	12
Inflammatory lesions	12
Multiple venous blebs	4
Nonspecific findings	4

patients by the antegrade procedure (42%), in 46 patients the retrograde procedure (27%), and in 54 (31%) patients who underwent both approaches. In patients who underwent bidirectional DBEs, positive findings were found by antegrade DBE in 20 of the 55 patients (36%), by retrograde DBE in 15 patients (27%), and in both approaches in 20 patients (36%).

A total of 222 (66%) patients had VCE prior to DBE; 192 patients had abnormal findings and 30 had a normal examination. Of the 192 patients, a DBE showed abnormal findings in 108 patients and normal in 84 patients. Findings for both DBE and VCE were categorized as follows: 1) normal 2) vascular lesion 3) ulcer 4) mass 5) stricture 6) blood 7) other. Findings from capsule studies were compared with findings from DBE by means of kappa value calculations. Unweighted kappa value was found to be 0.12 with a *P*-value of <0.0001.

3. Obscure Gastrointestinal Bleeding

Of the 225 patients with OGIB, 140 (62%) had overt bleeding (melena, *n*=131; hematochezia, *n*=9) and 85 patients (38%) had occult bleeding (positive hemoccult test, *n*=16; anemia, *n*=69). One-hundred eighty-four patients had VCE prior to DBE, 154 of which had findings suggestive of a possible underlying pathology.

In total, 323 procedures were performed, with 76 patients undergoing multiple DBEs (34%). Bidirectional DBE was performed in 69 patients (31%). Findings consistent with the source of bleeding were identified in 123 patients (54%). In 22 of those patients, the findings were within the reach of standard colonoscopies and endoscopies and included: gastric antral ectasia, Cameron's lesions, gastric and colonic AVM's, and severe duodenitis or gastritis. In addition, there were 7 patients with findings in both the small bowel and in the colon/proximal gastrointestinal tract. Findings in the entire group included small bowel ulcers in 23 (10%) patients, vascular lesions in 57 (25%), neoplasms in 23 (10%), diverticulae in 6 (3%) and strictures in 5 (2%). Of the vascular lesions, AVMs were the most commonly identified vascular lesions (*n*=46; 81%), followed by Dieulafoy's lesions, venous blebs

and hemangiomas. Identified neoplastic lesions included carcinoids, adenomas, malignant melanoma, gastrointestinal stromal tumors (GISTs), and lymphoma.

Treatment of potentially bleeding lesions was performed in 67 (30%) patients. Most commonly this involved use of APC (83%) but endoscopic clips and heater probe were also used. Polypectomy was performed in 8 patients.

4. Small Bowel Obstruction

Forty-nine patients underwent DBE for recurrent small bowel obstruction or obstructive symptoms with imaging consistent with small bowel obstruction. Seven patients had a pre-existing diagnosis of CD. Fourteen patients in total had identifiable strictures and 6 of those patients underwent balloon dilation for the strictures. In addition, 6 patients had retained capsules, 3 of which were successfully retrieved. Other findings included ulcerations (*n*=4) and adhesion/extrinsic compression (*n*=5) and diverticulosis (*n*=4).

5. Suspected Small Bowel Tumors and Mucosal Abnormalities

Forty-seven underwent DBE for suspected small bowel neoplastic lesions or suspected mucosal abnormalities on previous examination. Ulcers were found in three patients, one of whom had ulcerative jejunoileitis and one of whom had CD. Various other mucosal abnormalities were found in 9 patients and included mucosal nodularity, apthae, scalloping and edema. Six patients had known polyposis syndromes: Peutz-Jeghers (*n*=3), familial adenomatous polyposis/Gardner's (*n*=2) and Cowden's disease (*n*=1). Polyps and masses were found in 9 patients in whom a small bowel tumor was suspected. This compares to the entire cohort of patients, in whom 31 lesions were found, including 6 neuroendocrine tumors, one adenoma, two adenocarcinomas, 4 lymphomas, one GIST and one leiomyoma.

6. Therapeutic Interventions

A total of 113 therapeutic interventions were performed in 84 patients. The most common therapeutic procedure was APC and performed in 65 patients (19% of total number of patients). These included coagulation of vascular lesions in 56, ablation of small polyps in 4, and control of bleeding in 5. Other interventions were polypectomies in 14 patients, dilation of small bowel strictures in 9 patients, and injection therapy at bleeding sites in 5. Hemoclips were used in 13 patients to control of bleeding, to treat an ulcer and/or to prevent perforation after polypectomy. Removal of capsule was successful in 3 of the 6 patients who had retained capsule and stent removal was successful in one of the 3 patients. In addition, one patient underwent PEJ placement successfully.

In 3 patients, DBE was performed to retrieve biliary stents

Fig. 1. Complications of double balloon enteroscopy. Perforation occurred during a procedure involving balloon dilation of a stricture. The stricture prior to balloon dilation is shown (A). Balloon dilation is shown (B) and the perforation is immediately evident after balloon deflation (C, D).

(2) and esophageal stent (1) in the small bowel. In all three cases, foreign body removal was successful. In addition, in 3 of 6 retained capsules were retrieved as noted above.

7. Complications

In total, 3 complications (0.6%) occurred as a result of the procedures: medication reaction (n=1), scope dysfunction (n=1) and perforation (n=1) (Fig. 1A-D). No late bleeding complications occurred as a result of the procedure. The medication reaction involved a paradoxical reaction to sedatives. The procedure was stopped prematurely. The perforation occurred during balloon dilation of a stricture in the ileum. The complication was recognized immediately, and the patient required an uneventful surgical repair. Scope malfunction occurred in one procedure and scope tip deflection was no longer possible. The procedure was terminated. No acute pancreatitis occurred in this series of patients. No complications related to polypectomy were reported. There were no known complications secondary to general anesthesia.

DISCUSSION

Direct small bowel imaging has changed radically in the

past ten years. The availability of wireless VCE, single balloon enteroscopy, DBE and spiral overtube assisted enteroscopy have allowed for marked improvement in the investigation of suspected small bowel disease. DBE was first described in 2001 but global utilization of the technology has grown slowly, particularly in North America. To date, all large multi-center and single center studies have originated from Europe and Asia (Table 4).^{1,4,6-12} The current study represents one of the largest single center studies of DBE for the evaluation of suspected small bowel disease.

In our cohort, the most common indication for DBE was OGIB. Bidirectional enteroscopy was most commonly performed in this subgroup, but total enteroscopy rates were relatively low at 21%, comparable to some studies, but lower than in other recent studies. Shishido,¹³ for example, reports a total enteroscopy rate of 48%, but rates of bleeding source location are similar (48% vs. 54% in our cohort). The exact reasons for the highly variable rates of total enteroscopy are unclear, however, it is possible that the use of fluoroscopy in the Shishido paper aided in deeper intubation. Therapy was performed in 30%. Clinical outcomes of therapy were beyond the scope of this paper.

Given a lack of gold standard, overall accuracy between DBE and capsule cannot be compared. Our comparison of

Table 4. Comparison of Current Study Compared to Previous Studies of Obscure Gastrointestinal Bleeding from Europe and Asia

Author	Year	Country	Patient (n)	Procedure (n)	Diagnostic yield (%)	Therapy (%)	Complication rate (%)
Current study	2012	USA	335	457	52.0	24.7	0.6
Chen ⁶	2010	China	75	84	58.7	NA	NA
Maaser ⁷	2010	Germany	NA	545	39.7	31.1	0.9
Lin ⁸	2009	Taiwan	90	113	75.6	85.3	0.9
May ¹	2007	Germany	353	635	75.0	67.0	3.2
Zhong ⁹	2007	China	378	378	65.3	84.2	NA
Manabe ¹⁰	2006	Japan	31	31	74.2	67.7	0
Sun ¹¹	2006	China	152	191	75.7	NA	15.1
Di Caro ¹²	2005	Italy	62	89	80.0	41.9	0
Yamamoto ⁴	2004	Japan	123	178	76.0	12.3	1.1

NA, not available.

DBE to VCE demonstrated very low correlation in findings ($\kappa=0.12$). This is a lower level of correlation than those found in ($\kappa=0.46$) other studies of OGIB.¹⁴ There are several possible explanations for this. Firstly, several of the capsule studies we report were performed at outside centers and could not be independently verified in this study. Secondly, results of DBE and VCE were categorized by findings rather than dividing the cases into “abnormal or normal”. If analyzed in a binary fashion, this would not take into consideration that abnormal findings may have been different on VCE than what was found during DBE. For example, in several cases, “blood” seen on VCE may or may not have been correlated with the actual source of bleeding found on DBE. By our analysis, these would have not have been considered correlative. Nonetheless, in many cases, the DBE allowed for treatment, biopsy or tattooing of the lesion where the capsule findings may have been non-specific as to the exact nature of the bleeding source. In addition, DBE facilitated the retrieval of three retained capsules in the current series. Ultimately, given the relatively non-invasive nature of VCE, the two modalities will likely remain complementary in the evaluation of potential small bowel pathology.

The overall rate of small bowel tumor diagnosis was 9% in our patient cohort, over half of which were malignant. This compares to other studies in Asia and Europe, where overall diagnosis rates were between 8.8% and 17.4%.¹⁵⁻¹⁷ Our rate may be falsely elevated however, due to the inclusion of patients with known polyposis syndromes (n=5). Biopsies were usually taken when polypectomy was not feasible and sites were additionally marked with submucosal tattoo. Diagnosis was obtained in 58% but failed in other cases due to negative biopsies, submucosal location or obstructive strictures.

Complication rates in this study were extremely low and comparable to other large published series.^{18,19} Our perforation rate was 0.2% and was due to dilation associated with the DBE rather than due to the DBE itself (Fig. 1). The rate of

perforation secondary to dilation was therefore 11%. Interestingly, we did not have complications associated with polypectomy, including post-polypectomy bleeding or perforation.

Limitations of this study were largely dependent on its retrospective nature. Initial evaluations including endoscopy, colonoscopy and VCE were often performed at outside institutions and were not repeated at our institution prior to DBE. The long-term clinical impact of DBE was not assessed and outside of the scope of this paper. In addition, as we are a referral center servicing five states, it is possible that complications may have gone unrecognized if patients presented to their local referring institution for management rather than at our center. Rates of findings were affected by referral bias, detection bias due to prior studies and by the presence of pre-existing diseases (CD, polyposis syndromes, etc.).

In conclusion, we have shown that DBE performed at a single referral center in the United States appears to have similar rates of findings and complication rates as centers in Europe and Asia.

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