Early experience with double balloon enteroscopy: a leap forward for the gastroenterologist

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ABSTRACT

Introduction: Double balloon enteroscopy (DBE) is a novel procedure that allows complete visualisation, biopsy and treatment of small intestinal disorders. We describe our early experience with the use of DBE, evaluating the indications, diagnostic rates and complications. A secondary aim of the study was to compare the findings from DBE with wireless capsule endoscopy (WCE).

Methods: Retrospective study of patients referred to the Department of Gastroenterology and Hepathology at the Singapore General Hospital for evaluation of suspected small bowel diseases between February 2005 and May 2006 was done. A total of 34 procedures were conducted on 30 patients. A standardised data collection form was used.

Results: DBE was carried out via the oral approach (19 patients), anal approach (eight patients), and both approaches (three patients). Mean age was 53 (range 16–79) years. 12 procedures (35.3 percent) had one endoscopist and 22 (64.7 percent) procedures had two. The overall diagnostic input from DBE was 73.3 percent (22 of 30 patients). A positive diagnosis was achieved in 19 patients: jejunal gastrointestinal stromal tumour (GIST) (one), jejunal sarcoma (one), jejunal adenocarcinoma (one), duodenal adenocarcinoma (one), malignant lymphangioma (one), eosinophilic enteritis (one), pseudomembranous ileitis (one), tuberculous ileitis (one), jejunitis/ileitis (seven), lymphangiectasia attributed to relapsed Non-Hodgkins lymphoma (one), combination of angiodysplastic lesions and apthous jejunal/ileal lesions (one), and focal villous atrophy (two). Small intestinal pathology was excluded in three patients with abnormal computed tomography (CT) findings. Endoscopy time for antegrade DBE was 46.1 (+/- 20.1) minutes and for retrograde DBE was 70.8 (+/- 11.0) minutes. The findings of WCE correlated with DBE findings in nine of 12 (75 percent) patients. Apart from the first three DBE procedures, all subsequent cases were performed without fluoroscopy. When stratified into antegrade and retrograde DBEs respectively, procedural duration, sedative use and diagnostic yield were comparable for one and two endoscopist DBEs. No complications were recorded.

Conclusion: Our early experience with DBE shows it to be safe and effective in imaging the small intestine, and it may soon become a standard mode of investigation for the gastroenterologist.

Keywords: double balloon enteroscopy, obscure gastrointestinal bleeding, small intestinal disorders, wireless capsule endoscopy

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INTRODUCTION

Double balloon enteroscopy (DBE) is a new diagnostic and therapeutic modality originally described by Yamamoto et al in 2001[1] that allows high resolution visualisation, diagnostic and therapeutic interventions in all segments of the small intestine. Developments in endoscopy have provided us with new instruments for non-surgical evaluation of the small intestine which is an anatomically-challenging area of the gastrointestinal tract to study, in view of its remoteness from the mouth and anus. The availability of wireless capsule endoscopy (WCE) which was approved by the United States Food and

Drug Administration (FDA) in August 2001 represented a significant breakthrough in small bowel imaging[2], but its use has largely been limited by the inability to perform conventional endoscopic as well as therapeutic interventions[3]. Nevertheless, WCE remains clinically useful in identifying small bowel pathology as it is non-invasive and avoids the need for sedation; maintaining its important role in the gastroenterologist's armamentarium for the workup of small intestinal disorders.

At present, the main indications for DBE are the investigation of obscure gastrointestinal (GI) bleeding and inflammatory bowel diseases, evaluation of suspected small-bowel diarrhoea, chronic abdominal pain, abnormal radiological studies, removal of small bowel polyps, confirmation and treatment of angiodysplasia, assessing Roux-en-Y anastomoses and evaluation of abnormal WCE findings. Peptic ulcer disease remains the leading cause of upper GI bleeding[4], while diverticulosis and angiodysplasia are the predominant causes of lower GI bleeding[5]. Up to 5% of patients presenting with GI bleeding have an obscure course, defined as bleeding for which a definitive GI source has yet to be identified despite standard initial endoscopic and radiological evaluation of at least six months[6]. The aetiology of obscure GI bleeding is diverse, including vascular malformations, tumours, diverticuli, polyps and Crohn's disease. Patients with obscure GI bleeding may present with either frank bleeding (obscure-overt bleeding) or guaiac-positive stools in the presence of iron deficiency anaemia (obscure-occult bleeding).

In the evaluation of obscure GI bleeding, multiple investigations may be done without localising the bleeding source. Prior to the advent of DBE, conventional diagnostic modalities for the investigation of small intestinal diseases included: (a) conventional barium follow-through with a diagnostic yield of 0–20%[7]; (b) angiography with a diagnostic yield of 40–60%, which although allowing for therapeutic intervention, requires active bleeding at 3–5 ml/min during the study time[8]; and (c) technetium (Tc) 99m-labelled red blood cell scintigraphy with a diagnostic yield of 20–40% but requires active bleeding of 0.1–0.5 ml/min[9].

Traditional forms of push enteroscopy using either standard colonoscopies (160 cm) or specifically-designed small intestinal endoscopes (200–270 cm) yielded diagnostic rates of 30% to 50%[10–12], while Sonde enteroscopy which has a longer instrument length (270–400 cm) and traverses the small intestine by peristalsis, achieved diagnostic rates between 23% and 33%[13,14] but did not gain wide acceptance in view of the lack of therapeutic capability and poor luminal visualisation. Intraoperative endoscopy, while allowing for immediate surgical intervention, is by far the most invasive of all investigations. The advent of WCE and DBE in 2001 provided the gastroenterologist with new tools for direct visualisation of the small intestine, but unlike WCE, DBE allows for air insufflation, tissue rinsing, biopsy samples and therapeutic interventions.

This paper describes our pilot experience with the first 30 patients who underwent DBE at the Singapore General Hospital between February 2005 and May 2006. We retrospectively evaluated the clinical indications, diagnostic yield and clinical outcome. Comparisons were made between procedures requiring one and two endoscopists in diagnostic yields, endoscopy time, complication rates and sedation required. A secondary aim of the study was to compare the diagnostic yield of WCE with that obtained from DBE. This was done in 12 of 30 patients who had undergone a prior WCE before DBE.

METHODS

This was a retrospective study of patients who were evaluated for small bowel diseases by two senior consultant gastroenterologists at the Department of Gastroenterology and Hepatology at the Singapore General Hospital between February 2005 and May 2006. The patients were being investigated for obscure GI bleeding, unexplained diarrhoea, suspected inflammatory bowel disease, clarification of abnormal radiological investigations and/or abnormal WCE findings. Patients provided written informed consent after the endoscopist provided a detailed explanation of DBE.

DBE was carried out using the Fujinon system (FN450-T5/20, Fujinon Corporation, Saitama, Japan) in the Endoscopy Unit. Details of the system, described in detail elsewhere[15–17], consisted of the endoscope (length 200 cm, outer diameter 8.5 mm, working channel diameter 2.2 mm) and a flexible overtube (length 145 cm, outer diameter 12.2 mm) which were both provided with soft latex balloons connected through a built-in air route to a controlled pump system. The working channel allowed a biopsy forceps, a snare and a thin argon plasma catheter to be advanced through the endoscope. Advancement or withdrawal of the scope was achieved by deflating (-45 mmHg) or inflating (+45 mmHg) the balloons, respectively.

The endoscope was introduced by the antegrade (oral) and/or retrograde (anal) approach, and was carried out under conscious sedation. Before endoscopic insertion, the overtube was slid over the endoscope from the tip with both balloons deflated. When both balloons reached the duodenum from the oral approach or the caecum from the anal approach, the balloon attached to the overtube was inflated to keep the tube in position, while the endoscope was advanced as much as possible. Following this, the balloon of the endoscope was inflated, while the balloon of the outer tube was deflated. The outer

tube was then advanced towards the endoscope tip. When the distal end of the overtube reached the endoscope tip, the overtube balloon was inflated to secure its position within the intestine. Gentle withdrawal of both outer tube and endoscope (with both balloons inflated) allowed for pleating of the intestine on the outer tube, in the process shortening the intestine and preventing looping.

In a two-endoscopist DBE, the first endoscopist controlled and manoeuvered the enteroscope while the second endoscopist was responsible for advancement and withdrawal of the outer tube and control of the balloons. Where DBE was performed by one endoscopist and an assistant (trained endoscopy nurse), we referred to this procedure as a one-endoscopist DBE. In such cases, the single endoscopist assumed primary responsibility for all procedures, including control of the enteroscope, advancement and/or withdrawal of the outer tube and enteroscope in an alternating manner and control of the balloons. The assistant helped the endoscopist by holding onto the outer tube during advancement or withdrawal of the enteroscope. For all lesions detected during DBE, biopsy specimens were obtained and the lesion treated appropriately.

The clinical presentation and the results of prior diagnostic workup were used to aid our decision in the route of DBE. The intention of DBE is to inspect as much of the small intestine via either the antegrade or retrograde approach, within the limits of patient tolerability, safety and diagnostic yield. All patients were required to fast overnight for eight hours prior to DBE. In patients undergoing DBE via the retrograde approach, bowel preparation was the same as for colonoscopy, with patients prescribed standard colon lavage solution (Polyethylene-Glycol) and a clear liquid diet one day before procedure. Fluoroscopical guidance was used only in our first three cases. All procedures were performed using conscious sedation with a combination of dormicum and fentanyl/pethidine, with close monitoring of pulse oximetry, blood pressure and pulse rate during and after the procedure. Patients were monitored continuously during DBE and for up to two hours after completion in the endoscopy suite. The decision to perform an alternate examination after the antegrade or retrograde routes depended on the findings from initial DBE, and was usually conducted at least 24 hours after the initial procedure.

We evaluated the indications, diagnostic yield, procedural duration, sedation required and any major complications arising from DBE, further stratified by procedures with one and two endoscopists. Complications arising from DBE that have previously been reported in overseas series[17,18] including bleeding and perforation, were actively looked out for. We defined a negative yield of DBE when no additional information was obtained from either antegrade and/or retrograde DBE, or the failure to establish a definitive diagnosis necessitating more invasive procedures.

A secondary aim of our retrospective study was to compare our findings from DBE with the results of capsule endoscopy in 12 patients who had undergone both procedures. Capsule endoscopy has been developed as a method for examining the small intestine. Technical description of the Pill Cam endoscopic capsule (Given Imaging, Yogneam Israel) are available elsewhere[19,20]. Following an overnight fast, patients were admitted to the endoscopy centre for placement of the recording device. After swallowing the M2A capsule, recording began. The capsule transmitted continuous video images to the recorder for eight hours. Patients were allowed clear feeds and soft diet two hours and four hours, respectively, after swallowing the capsule. Patients returned the recording system eight hours after the beginning of the study and the transmitted video images were downloaded onto a computer (using the Rapid® programme).

Recordings from the patients were analysed by one of the two same gastroenterologists who were involved in performing DBE. After the study, patients were instructed to observe for spontaneous passage of the capsule in the stools. The potentially most serious adverse event after WCE is capsule non-excretion requiring surgical intervention that occurred in 0.75% of patients (seven of 934 patients) in Barkin's series; all of whom had localised pathology[21]. With only one report of temporary capsule holdup in a small bowel diverticlum[22] reported in case series so far, the risk of capsule endoscopy in patients with small bowel diverticular disease was regarded as being theoretical only[23]. Nevertheless, the American Society for Gastrointestinal Endoscopy (ASGE) recommends a small bowel series prior to capsule endoscopy to exclude adhesive or inflammatory obstruction[24]. Although there have been reports of capsule endoscopy being used in patients with cardiac pacemakers or defibrillators[25,26] without causing any interference, current recommendations regard the presence of such cardiac devices as a contraindication to capsule endoscopy[24]. A word of caution with magnetic resonance (MR) imaging after capsule endoscopy: patients should not undergo MR imaging unless they have passed out the capsule; should there be any doubt of retained capsule, an abdominal radiograph can easily be performed[24].

A standardised data collection form was used. Data extracted for analysis included patient demographics, results of prior investigations (endoscopies, radiological imaging and WCE if applicable), indications for DBE, duration of procedure and sedation administered, use of fluoroscopy, as well as clinical outcome. Descriptive statistics were calculated for patient demographics and clinical parameters, using means, range and standard deviation. Results are presented as a mean ± standard

Table I. Demographical and clinical characteristics of 30 patients who underwent DBE.

	No. of patients	%
Mean age (range in years)	53.2 (16–79)	
Gender: Female	10	33.3
Male	20	66.7
Indications for DBE		
Obscure GI bleeding	18	60.0
Iron deficiency anaemia	2	6.7
Abnormal CT findings	3	10.0
CD assessment	1	3.3
Chronic diarrhoea	1	3.3
Chronic abdominal pain	2	6.7
Persistent vomiting	1	3.3
Hypoalbuminaemia	1	3.3
Abnormal barium studies	1	3.3

GI: gastrointestinal; PR: per rectal; CT: computed tomography; CD: Crohn's disease

deviation for continuous data and as a percentage for categorical data. In view of the small patient numbers, comparison of data for one and two operator procedures was by the nonparametric Mann-Whitney test, while chi-square test was used for comparison of categorical data. A p-value < 0.05 was considered to be statistically significant. All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 10.0 (Chicago, IL, USA).

RESULTS

Singapore General Hospital performed its first DBE in February 2005 using the Fujinon system. Between February 2005 and May 2006, 30 patients (10 females, 20 males; mean age 53.2 ± 15.9 years, age range 16–79 years) with suspected small bowel diseases previously documented by abnormal radiological imaging or WCE, or after negative upper and/or lower endoscopy underwent 34 procedures by our department. The demographics and clinical indications are illustrated in Table I. In our cohort, 29 of 30 patients had all their investigations conducted at our centre, except for patient no. 30 who was referred from an overseas centre after having undergone several investigative procedures including two normal gastroscopies, one colonoscopy showing angiodysplasia in the terminal ileum treated with argon plasma coagulation; and capsule endoscopy showing suspicious angiodysplastic lesions in the small intestine. 26 of 30 patients had previously undergone at least one gastroscopy and colonoscopy prior to DBE. In four patients, DBE was performed without a prior gastroscopy and colonoscopy for the following indications: clarification of abnormal small intestinal thickening seen on abdominal computed tomography (CT) in two patients; evaluation of extent of small intestinal involvement in one patient with terminal ileal Crohn's disease diagnosed on prior colonoscopy, and investigation of chronic dyspepsia in one patient with a normal gastroscopy.

A total of 34 DBE procedures were carried out on 30 patients. 27 patients underwent a single procedure (antegrade 19, retrograde eight), two patients had both antegrade and retrograde DBE performed, and one patient underwent a total of three DBEs (antegrade one, retrograde two). A mean dose of 5.6 mg of dormicum (range 2.5–14.0) and 78.7 mg of fentanyl (range 50–150) was used for conscious sedation in all but one patient who received a combination of 6 mg of dormicum and 50 mg of pethidine. The mean examination times for antegrade and retrograde approaches were 46.1 (± 20.1) minutes and 70.8 (± 11.0) minutes, respectively. The median follow-up period was 5.2 (0.5–74.2) months. When stratified into antegrade and retrograde DBEs respectively, duration of procedure and amount of sedation required for one endoscopist DBE was comparable to two. The clinical findings and outcome of DBE are illustrated in Table II. No complications were recorded. DBE was tolerated in all patients.

The indications for DBE in our cohort are illustrated in Table I. Of the 30 patients in our series, we obtained a diagnostic yield from DBE in 20 patients and excluded small bowel disease in three patients. Small intestinal lesions were detected in 20 of 30 patients; in 14 of 18 patients who were evaluated for obscure GI bleeding (seven erosions/benign small intestinal ulcerations, one patient with both angiodysplastic lesions and apthous jejunal/ileal lesions, one pseudomembranous ileitis, one tuberculous ileitis, one jejunal sarcoma, one duodenal adenocarcinoma, one malignant retroperitoneal lymphangioma with invasion into duodenum, one jejunal gastrointestinal stromal tumour [GIST]); in one of two patients with iron deficiency anaemia (attributed to jejunal adenocarcinoma); in one patient with chronic diarrhoea (eosinophilic enteritis); in one patient previously treated for non-Hodgkin lymphoma presenting with hypoalbuminaemia (jejunal lymphangiectasia from relapsed non-Hodgkin lymphoma); in one patient presenting with recurrent vomiting post-Bilroth II gastrectomy (remnant gastric carcinoma); assessment of extent of Crohn's disease in one patient (partial villous atrophy involving upper jejunum) and clarification of abnormal small bowel series in one patient (focal jejunal villous atrophy).

Suspected pathology of the small bowel was excluded in all three patients who had abnormal jejunal

Table II. Summary of patients and results of DBE.

Case	Age (years)/ gender	Indications	Findings	Histopathology	Outcome
1	74/M	Obscure GI bleeding	Jejunal circumferential ulcer	High grade sarcoma	Surgery
2	47/M	Obscure GI bleeding	Ileal ulcers	Ileitis	Avoidance of NSAIDs
3	63/M	Obscure GI bleeding	Normal	ND	Expectant
4	49/M	Obscure GI bleeding	Jejunal polyp	Jejunal GIST	Surgery
5	16/M	Obscure GI bleeding	Ulcerated polyp in jejunum with contact bleeding	Retroperitoneal lymphangioma	Surgery
6	38/M	Obscure GI bleeding	Ileal erosions	Ileitis	Avoidance of NSAIDs
7	69/M	Obscure GI bleeding	Normal	ND	Expectant
8	45/F	Obscure GI bleeding	Ileal ulcers	Pseudomembranous ileitis	Medical therapy (metronidazole)
9	72/M	Chronic diarrhoea	Jejunal erosions, apthous ulcers in ileum	Eosinophilic enteritis	Medical therapy (steroids)
10	60/M	Iron deficiency anaemia	Circumferential ulcerated jejunal tumour	Jejunal adenocarcinoma	Surgery
11	39/M	Crohn's disease assessment	Jejunal villous blunting	Partial villous atrophy	Medical therapy (prednisolone, mesalazine)
12	50/M	Previous history of Non Hodgkin's Lymphoma (NHL) presenting with hypoalbuminaemia	Jejunal villous blunting	Villous atrophy and lymphangiectasis, -relapsed NHL	Medical therapy (chemotherapy)
13	58/M	Obscure GI bleeding	Erythematous ileal ulcers	Tuberculosis ileum	Medical therapy (Anti-TB therapy)
14	77/M	Persistent vomiting, previous Bilroth II gastrectomy	Anastomotic site ulcer (efferent limb)	Remnant gastric carcinoma	Surgery (completion gastrectomy)
15	34/M	Obscure GI bleeding	Jejunal erosions	Jejunitis	Avoidance of NSAIDs
16	74/F	Obscure GI bleeding	Erythema in jejunum/ileum	Jejunitis/ileitis	Surgery(resection of spurting dieulafoy lesion in jejunum)
17	49/F	Clarification of abnormal small intestinal thickening reported on CT scan	Normal	Random biopsies normal	Expectant
18	57/F	Obscure GI bleeding	Jejunal erosions/apthous ulcers	Jejunitis	Avoidance of NSAIDs
19	27/M	Obscure GI bleeding	Jejunal erosions	Jejunitis	Avoidance of NSAIDs
20	49/F	Clarification of abnormal mucosal irregularity reported on barium follow through	Villous blunting jejunum	Focal villous atrophy	Expectant
21	54/M	Obscure GI bleeding	Ileal erosions	Ileitis	Expectant
22	51/M	Obscure GI bleeding	Duodenal bulb pseudo-diverticulum and erosions	Duodenitis	Expectant
23	45/M	Clarification of abnormal small intestinal thickening reported on CT scan	Normal	Random biopsies normal	Discharged
24	69/M	Clarification of abnormal jejunal thickening reported on CT scan	Normal	Random biopsies normal	Discharged
25	41/F	Chronic abdominal pain	Normal	Random biopsies normal	Expectant
26	74/F	Iron deficiency anaemia	Normal	Random biopsies normal	Expectant
27	55/M	Obscure GI bleeding	Tumour in D3/D4	Duodenal adenocarcinoma	Palliative chemotherapy/ radiotherapy
28	51/F	Obscure GI bleeding	Jejunal and ileal angiodysplasias, apthous ulcers jejunum	Jejunitis/ileitis	Expectant
29	32/F	Chronic abdominal pain	Normal	Random biopsies normal	Expectant
30	79/F	Obscure GI bleeding	Jejunal apthous ulcers, vascular malformation in ascending colon	Jejunitis, angiodysplasia ascending colon	APC to angiodysplastic lesions

F: female; m: male; CT: computed tomography; NSAIDs: non-steroidal anti-inflammatory drugs; GIST: gastrointestinal stroma tumour; D3/D4: third and fourth parts of duodenum; GI: gastrointestinal; APC: argon plasma coagulation; ND: not done.

thickening reported on abdominal CT. These patients had normal antegrade DBE findings and normal histological findings on random biopsies. Although a positive diagnosis of remnant gastric carcinoma was diagnosed from DBE in one patient (patient no. 14) who had a previous Bilroth 2 gastrectomy, this case was excluded from the overall diagnostic yield. This case involved a 77-year-old Chinese man who had a significant past history of a Bilroth II partial gastrectomy performed in 1969. He had remained well post-surgery up to his presentation to our hospital in October 2005. The initial gastroscopy showed irregular nodularity at the anastomotic site of the efferent limb, for which multiple biopsies revealed intestinal metaplasia. In view of on-going symptoms of persistent vomiting and the negative biopsy from earlier gastroscopy, we proceded to perform antegrade DBE. The afferent limb was normal; findings from the efferent limb showed multiple areas of erythema and superficial ulcerations at the anastomotic site, causing a relative stenosis at the opening of the efferent loop. Biopsies revealed adenocarcinoma, and the patient subsequently underwent completion gastrectomy for remnant gastric cancer. As the endoscopic abnormalities detected in this case were within reach of a gastroscope, we did not include this case in our diagnostic yield. Hence, our overall diagnostic yield was in 22 of 30 patients (73.3%).

As a result of DBE findings, specific medical therapy administered to patients included the use of oral metronidazole for pseudomembranous ileitis (one patient) (Fig. 1); prednisolone for eosinophilic enteritis (one patient) (Fig. 2); anti-tuberculous treatment for tuberculous ileitis (one patient); chemotherapy for relapsed non-Hodgkin's lymphoma (one patient); and combined chemotherapy and radiotherapy for one patient with metastatic duodenal adenocarcinoma. In one patient with angiodysplastic lesions in the ascending colon, argon plasma coagulation (APC) was applied to the colonic lesions via retrograde DBE. Data on the natural history and treatment of non-steroidal anti-inflammatory drug (NSAID)-induced enteropathy are scant. Recognition of the cause of enteropathy and cessation of the offending agent are the mainstay of therapy[27]. All patients with small intestinal erosions and/or ulcers were advised complete abstinence from NSAIDs.

Biopsy of small intestinal lesions identified on DBE allowed for a specific pre-operative diagnosis in five patients who underwent surgery for the following indications: jejunal sarcoma (one patient), jejunal adenocarcinoma (one patient) (Fig. 3), malignant lymph-angioma (one patient), resection of gastrointestinal stromal tumour in the jejunum (one patient) and completion gastrectomy for remnant gastric cancer (one patient). A summary of DBE findings and the clinical outcome is illustrated in Table II. Double balloon enteroscopy was non-diagnostic in seven patients: in four of 18 patients evaluated for obscure GI bleeding; in one of two patients with chronic iron deficiency anaemia; and in both patients evaluated for chronic abdominal pain. There was one patient with a missed diagnosis in our cohort. This case involved a 74-year-old Chinese woman with end-stage renal failure who had undergone multiple

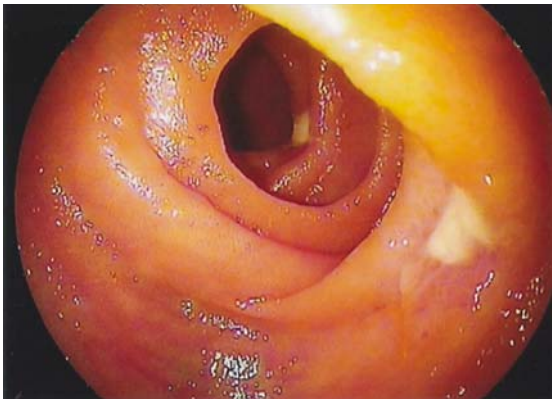

Fig. 1 Double balloon enteroscopic photograph of ileal ulcers (histology revealed pseudomembranous ileitis).

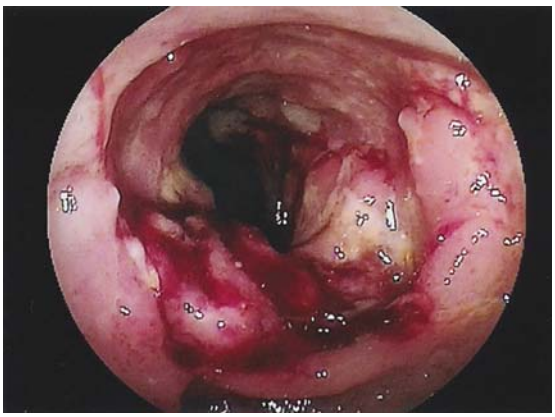

Fig. 2 Double balloon enteroscopic photograph of tuberculous ileitis.

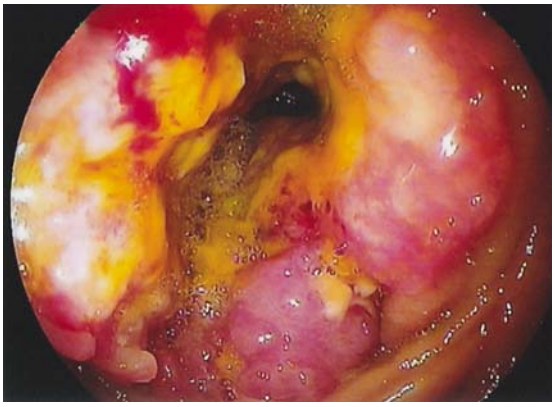

Fig.3 Double balloon enteroscopic photograph of jejunal adenocarcinoma.

Table III. Comparison of one-endoscopist vs two-endoscopist DBEs.

	One operator	Two operators	p-value
No. of procedures	12	22	–
Diagnostic yield	75%	63.6%	0.705 (NS)*
Duration (oral) Mean±SD (minutes)	43.5 ± 19.4	48.3 ± 21.1	0.456(NS)†
Duration (rectal) Mean±SD (minutes)	67.5 ± 10.6	71.5 ± 11.6	0.758(NS)†
Dormicum dose (oral) Mean±SD (mg)	5.1 ±1.9	6.8 ± 3.3	0.314(NS)†
Dormicum dose (rectal) Mean±SD (mg)	5.3 ± 2.5	4.8 ± 1.4	0.758 (NS)†
Fentanyl dose (oral) Mean±SD (mg)	70.0 ±35.0	81.3 ±32.2	0.628 (NS)†
Fentanyl dose (rectal) Mean±SD (mg)	75.0 ±35.4	84.9 ± 33.7	0.909 (NS)†

* Chi-square test, † Mann-Whitney test

gastroscopies and colonoscopies for obscure GI bleeding. Retrograde DBE showed erythemous areas in the ileum and distal jejunum. In view of ongoing bleeding (manifest as falling haemoglobin levels and malaena), a diagnostic laparotomy and intraoperative on-table enteroscopy was performed. Intraoperatively, a spurting Dieulafoy lesion in the proximal jejunum 60 cm from the duodenal-jejunal junction was identified and resected.

With reference to patient no. 14 (a 77-year-old Chinese man with a previous Bilroth II gastrectomy presenting with recurrent vomiting), a repeat gastroscopy could possibly have led to a diagnosis of remnant gastric carcinoma. However, the reasons for proceeding onto antegrade DBE were two-fold: clarification of abnormal findings from prior gastroscopy (which showed irregular mucosal thickening at the anastomotic site) and in the process, allowing for repeat biopsy samples to be obtained, as well as the opportunity to examine a much greater portion of the efferent anastomotic limb. However, the presence of mucosal oedema and ulcerations at the anastomotic site of the efferent limb resulting in relative stenosis precluded us from achieving the latter aim. It is likely that sampling error from the initial gastroscopy resulted in a negative initial biopsy, and a positive biopsy could have been obtained from repeating a gastroscopy. Hence, this case was excluded from the overall diagnostic yield.

Patient no. 30 was a 79-year-old Chinese woman who was referred from an overseas centre for evaluation of obscure occult GI bleeding. She had presented with malaena for which she had undergone a series of investigations at her referral centre. These included a normal gastroscopy, colonoscopy showing multiple angiodysplastic lesions in the terminal ileum treated with argon plasma coagulation, mesenteric angiogram and deployment of a mini-coil for bleeding from a distal jejunal lesion and a capsule endoscopy showing multiple angiodysplastic lesions in the small intestine with mild oozing. Taking into account the prior extensive work-up and findings, a retrograde DBE followed by an antegrade DBE were performed. Contrary to the earlier reports from her referral centre, no angiodysplastic lesions were seen in the jejunum and ileum on retrograde DBE. However, angiodysplastic lesions with areas of oozing were instead seen in the upper descending colon. These were treated with APC. Non bleeding jejunal apthous ulcers were seen on antegrade DBE. Although the angiodysplastic lesions in the right ascending colon were easily within reach of a normal colonoscopy, DBE allowed us to evaluate and clarify the extent and severity of the previously reported small intestinal lesions.

No major complications related to patient sedation or to the DBE procedure were encountered. The major complications which we were on the look-out for include bleeding, perforation or need for hospital admission. None of these were encountered in our series. Similarly, WCE was well tolerated in our patients, with spontaneous elimination of the capsule in the stools reported in all 12 patients. When stratified into one and two endoscopist DBEs, there were no significant differences with regard to duration of procedure, amount of sedation required and diagnostic yield. Table III illustrates the comparison between one and two endoscopist DBEs, further stratified by route of DBE.

Capsule endoscopy was uncomplicated in our patients. Comparison of WCE with DBE findings is shown in Table IV. Apart from patient no. 30 who was referred from an overseas centre with abnormal WCE findings, the remaining 11 patients had their capsule endoscopies read by either one of the two same senior gastroenterologists who were involved in performing DBE. Of these 11 cases, a positive correlation with DBE was seen in nine cases (seven patients with similar positive findings on WCE and DBE, one patient with normal findings on both

Table IV. Comparison of WCE with DBE findings in 12 patients.

Case	Age(years)/ gender	Indications	WCE findings	DBE findings	Final diagnosis
1	74/M	Obscure GI bleeding	Bleeding ulcer mid jejunum	Circumferential ulcer mid jejunum	Jejunal sarcoma
6	38/M	Obscure GI bleeding	Ileal erosions	Ileal erosions	Ileitis
7	69/M	Obscure GI bleeding	No bleeding noted from small intestine; blood seen in caecum	Retrograde approach up to proximal ileum, no small intestinal abnormalities seen. Bleeding source from presumptive caecal diverticuli (seen on colonoscopy)	Caecal diverticuli
8	45/F	Obscure GI bleeding	Ileal ulcers	Ileal ulcers	Pseudomembranous ileitis
9	72/M	Chronic diarrhoea	Jejunal erosions with ulcers in ileum	Jejunal erosions, non bleeding apthous ulcers in ileum	Eosinophilic enteritis
10	60/M	Iron deficiency anaemia	Jejunal erosions with mild oozing	Circumferential ulcerated tumour extending for 12 cm in proximal-mid jejunum	Jejunal adenocarcinoma
13	58/M	Obscure GI bleeding	Ileal ulcers with oozing	Erythematous ulcers ileum	Ileal TB
18	57/F	Obscure GI bleeding	Erosions in jejunum	Jejunal erosions/apthous ulsers	Jejunitis
19	27/M	Obscure GI bleeding	Normal	Erosions in jejunum	Jejunitis
25	41/F	Chronic abdominal pain	Normal	Normal	No pathology detected
28	51/F	Obscure GI bleeding	Telangiectasic spots in jejunum/ileum	Jejunal and ileal angiodysplasia and apthous ulcers	Small intestinal angiodysplasia and apthous ulcers
30	79/F	Obscure GI bleeding	Multiple angiodysplastic lesions in small intestine	Antegrade DBE: apthous ulcers upper jejunum; Retrograde DBE: normal findings in small intestine up to distal jejunum, presence of angiodysplasia in ascending colon	Angiodysplasia colon

WCE: wireless capsule endoscopy; DBE: double balloon enteroscopy; GI: gastrointestinal; TB: tuberculosis

WCE and DBE, and one patient with bleeding localised to the caecum). Two patients had a mistaken diagnosis from WCE (one patient who had jejunal erosions identified on WCE was diagnosed with jejunal adenocarcinoma following DBE; one patient with a normal WCE was found to have multiple jejunal erosions on subsequent DBE). In patient no. 30 who had undergone extensive workup for obscure GI bleeding (including a capsule endoscopy which had reported multiple angiodysplastic lesions in the small intestine), antigrade and retrograde DBE detected apthous ulcers in the upper jejunum and angiodysplastic lesions that were localised to the ascending colon. While the DBE and WCE findings in patient no. 30 did not correlate, it was not included in our comparison data as WCE had been performed by her referral centre. Hence, the overall diagnostic accuracy rate of WCE in the 11 cases performed at our centre was nine of 11 (82%).

DISCUSSION

Obscure GI bleeding has traditionally been a tremendous diagnostic and therapeutic challenge for the gastroenterologist[28]. In the evaluation of patients with chronic gastrointestinal bleeding, the traditional method of intraoperative enteroscopy has a high diagnostic yield[29], but is often impractical in view of its invasive nature. The diagnostic and therapeutic role of DBE in the evaluation of small intestinal disorders and its non-invasive nature represent significant advances made in the field of gastrointestinal endoscopy. Favourable results have been reported from Japanese and Western series[15,17,18,30,31]. In our experience, the overall diagnostic yield of 73.3% was comparable to published series. Our detection rates, procedural duration and sedative dosages required were comparable for both one and two endoscopist DBEs. DBE was safe and conducted in the endoscopy suite

using conscious sedation with conventional drugs which are already in existing use. Apart from the first three procedures where fluoroscopical guidance was used, the remaining 31 procedures were conducted without fluoroscopy. While fluoroscopy is useful in negotiating bends and visualising intestinal loops, its disadvantages include the need for additional equipment and radiation exposure. As our experience with DBE increased, our diagnostic yield and safety profile were not compromised by the avoidance of fluoroscopy.

DBE has previously been reported to allow endoscopic examination of the entire small bowel[17,18], a process referred to as panenteroscopy. This is achieved by a combination of both the antegrade (oral) and retrograde (rectal) approach. In rare situations, panenteroscopy can be achieved via a single (oral or rectal) approach. Panenteroscopy is demonstrated by India ink injection at the most distal site during antegrade (or retrograde) DBE and by successful advancement of the enteroscope to the tattooed area during the opposite approach. Panenteroscopy using only a single approach was successful in two out of 178 patients from Yamamoto et al's[17] series and in two out of 137 patients from May et al's[18] series, where the authors successfully reached the caecum via a single (antegrade) approach. Conversely, panenteroscopy using a combination of both antegrade and retrograde approaches was achieved in 86% in Yamamoto et al's series[17] but much lower rates were reported in May et al's series[18] at 45%, and unsuccessful in the Kaffes et al's[30] series.

Panenteroscopy using a single or double approach was not successful in our series. The initial chosen approach we adopted was either antegrade (oral) or retrograde (anal) based on the presumptive source of bleeding and from results of WCE (if available). In our experience, the culprit lesion was identified in 19 of 21 patients via a single approach. Taking into account the experiences from both May et al's[18] and Kaffes et al's[30] series where lower success rates of panenteroscopy were achieved, we restricted dual approach DBEs to patients in whom a strong clinical suspicion of small intestinal pathology persisted in the face of negative investigative findings. However, we were unable to achieve total enteroscopy in them. Nevertheless, our diagnostic yield from partial DBE remained favourable. Apart from one patient in our series who had a Dieulafoy's lesion diagnosed only after surgical exploration, the remaining patients had a high diagnostic yield from partial DBE and remained well on follow-up for a median period of 5.2 months. Hence, the clinical utility of total enteroscopy is uncertain.

Bleeding and perforation are well-reported complications of any endoscopical procedure. Few major complications arising from DBE have been reported in the literature. In the Yamamoto series[17], there were two complications reported out of 178 cases. In the first case, DBE was performed for post-chemotherapeutic evaluation of a patient with malignant lymphoma of the small intestine. Following a laparotomy which showed multiple perforations in regions of the small intestine with lymphomatous infiltration, including areas that had not been within the reach of DBE, the authors concluded that spontaneous chemotherapy induced small intestinal perforation was the most likely cause. In the second case, a patient who was diagnosed with small intestinal Crohn's disease on DBE developed post-procedural abdominal pain and fever which was treated conservatively with gut rest and intravenous antibiotics.

In similar large studies by May et al[18] and Di Caro et al[31], no major complications were reported. A word of caution with this procedure is to avoid further insertion of the endoscope across a fragile small intestinal lesion, such as an acute ulcer in view of the risk of perforation[17]. Similar to any endoscopical procedure, minor complications encountered by patients may include throat discomfort, abdominal distension or fever. DBE should always be conducted in an endoscopy unit with the patients under close monitoring both during and after procedure, in view of the need for sedation with its attendant risks such as aspiration pneumonia or respiratory compromise.

The limitations of DBE include: (a) long procedural time; (b) patient discomfort and increased need for sedation; and (c) need for additional endoscopy staff, either by two endoscopists or one endoscopist with the assistance of a trained endoscopy nurse. Although no major adverse complications were encountered in our series, namely bleeding, perforation or the need for hospital admission after DBE, the lack of a systematic analysis of all possible major and/or minor complications represents a limitation in our study findings. Nevertheless, the referring physician should be cautious of potential complications that may arise from DBE. The minor complications of antegrade and retrograde DBE are similar to gastroscopy and colonoscopy respectively. These include throat discomfort, abdominal distension, mucosal trauma and transient fever.

Lesions responsible for obscure GI bleeding may actually be within the reach of a normal gastroscopy or colonoscopy but are only evident after further investigations[32,33]. Sampling error was the most likely reason for the failure to obtain a diagnosis of remnant gastric carcinoma in patient no.14 (a 77-year-old Chinese man with a previous Bilroth II gastrectomy presenting with recurrent vomiting). DBE allowed for the chance to obtain repeat biopsy specimens in addition to evaluating a longer segment of the efferent gastrojejunal anastomotic limb. Among the newer diagnostic tools, wireless capsule endoscopy is another promising non-invasive procedure. Unfortunately, missed detection rates of up to 36% have

been reported with wireless capsule endoscopy[20]. The results obtained from WCE served a key determinant factor in our approach taken for DBE. In 11 capsule endoscopies which were performed in our centre, the findings of WCE correlated with DBE in nine.

While both DBE and WCE represent significant breakthroughs in small bowel imaging, one should be aware of the inherent advantages and disadvantages of either procedure. While WCE is a purely diagnostic method which allows for an evaluation of the entire length of the small bowel in a physiological state without the need for sedation, its visibility is limited for the following reasons: (a) inability to obtain a circumferential view of the small intestine; and (b) inability to perform routine endoscopical procedures such as flushing and air insufflation and histological sampling[20]. Conversely, the ability for direct visualisation, biopsy of suspicious lesions and the therapeutic potential of DBE are key advantages over WCE.

Although our positive detection rates from DBE were comparable to larger series published[15,17,18,30,31], an important caveat is the selection bias that existed in our patients who underwent DBE. As 40% of our patients had a capsule endoscopy done prior to DBE, a potential selection bias may have accounted for the high diagnostic rates from DBE. In view of the inherent selection bias associated with new technology, novel diagnostic tests have the potential to create falsely high results. Nevertheless, DBE is a new technology that is fast gaining popularity in overseas centres and its role in the evaluation of small intestinal disorders, particularly obscure GI bleeding is likely to surpass traditional radiological investigations.

As expertise increases, both DBE and WCE are likely to become more widely accepted and utilised in the diagnostic work-up and management of patients with small intestinal disorders, and the importance of such new technologies should not be underappreciated. Both WCE and DBE are new procedures and hence do not feature in traditional diagnostic algorithms in the management of small intestinal lesions. While it is well established that conventional diagnostic tests have limited yield, it is still uncertain whether such traditional tests should precede WCE and/or DBE. Furthermore, the role and timing of WCE in patients who are schelduled for DBE is also unclear. Hence, it is prudent for the clinician to access each case individually and decide on the most appropriate course of action for the patient.

Whether DBE will eventually surpass traditional diagnostic modalities or even the more recent WCE remains to be proven in the years to come. A limitation of our study was the small patient numbers. More studies are awaited comparing the relative merits of these two novel procedures which represent revolutionary advances in small bowel imaging. The future ahead remains challenging for the practising gastroenterologist, as we scale the heights of endoscopy.

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