

# Diagnosis of Obscure Gastrointestinal Bleeding: Capsule Endoscopy or Double Balloon Enteroscopy?

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**How to cite this paper:** Prasad, G.S., Yu, Q., Pu, C.B. and Mulmi, S.S. (2018) Diagnosis of Obscure Gastrointestinal Bleeding: Capsule Endoscopy or Double Balloon Enteroscopy? *Open Journal of Gastroenterology*, 8, 79-85.

<https://doi.org/10.4236/ojgas.2018.83008>

**Received:** January 16, 2018

**Accepted:** March 16, 2018

**Published:** March 19, 2018

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## Abstract

The development of capsule endoscopy (CE) and double balloon enteroscopy (DBE) has significantly enhanced the visualization of the small bowel. CE and DBE have proven to be the choice of investigation for the diagnosis of small bowel disease and is an evident indication for obscure gastrointestinal bleeding (OGIB). CE or DBE respectively are frequent option of professionals for the diagnosis of obscure gastrointestinal bleeding. The purpose of this review is to provide an overview of studies focused on patients with obscure gastrointestinal bleeding with previous CE and/or DBE intervention. Studies show that CE and DBE have similar diagnostic yields for obscure gastrointestinal bleeding. Although with few chances for false negative results, most researches showed good concordance between CE and DBE. However due to its non-invasiveness, safety, patient tolerability and ability to view the entire small bowel, CE can be recommended as a first choice of investigation. DBE, despite being more invasive, is a necessary second choice, which has both diagnostic and therapeutic value, although skilled endoscopist and sedation are required and complications like bleeding, perforation, pancreatitis etc. may occur.

## Keywords

Obscure Gastrointestinal Bleeding, Capsule Endoscopy, Double Balloon Enteroscopy

## 1. Introduction

Obscure gastrointestinal bleeding (OGIB) is defined as persistent or recurrent gastrointestinal bleeding after initial negative evaluation including upper ga-

strointestinal endoscopy and colonoscopy. Patients with OGIB usually present with recurrent or unexplained iron deficiency anemia and, or positive fecal occult blood test. On the basis of presence and absence of clinically evident bleeding, it is categorized into overt and occult. OGIB is perceived as one of the difficult problems to diagnose and treat. Amid all GI bleedings OGIB accounts for about 5%, among which more than 80% originating from the small bowel and rest from the lesions that were missed by conventional endoscopes, either because of intermittent bleeding or truly missed lesions [1] [2] [3]. Previously the conventional endoscopes available were not much effective as it did not provide complete visualization of small bowel [2] [3]. Therefore, small bowel was considered a black box due to its length and complex anatomy. Diagnostic efficacy and reliability of conservative techniques, including radio contrast studies, computed tomography (CT), magnetic resonance imaging (MRI), digital subtraction angiography (DSA), radionuclide imaging were not satisfactory for diseases of the small intestine which aid very little contribution in the diagnosis and treatment of OGIB [4] [5] [6]. The development of capsule endoscopy (CE) and double-balloon enteroscopy (DBE) in 2001, revolutionized the visualization of small bowel [7] [8]. The accurate diagnosis and treatment of small bowel disease then had drastically improved [8] [9]. The dilemma for which diagnostic tool to be considered as a first line for OGIB has always been a subject of interest. Multiple studies each focusing CE and DBE as a primary diagnostic tool has been conducted.

The non-invasiveness, better tolerance, and handiness of Capsule Endoscopy proves as first choice of diagnostic modality in OGIB, but it lacks the ability to obtain biopsy specimens and perform therapeutic interventions as polypectomy and electro-cauterization. Other cons of CE are that the observation of CE cannot be repeated or paused for the confirmation, we cannot control the direction and speed of movement, the images are transient and random, the quality of the image provided by CE is easily affected by the cleanliness of intestinal canal and the motility of GI tract and in addition, there is a risk of capsule retention although the incidence is quite low (1.5% - 5%) [10] [11]. With the upcoming new technologies, there are recent advancements of capsule endoscopy. Control over the CE movement, equipping therapeutic or tissue biopsy function show a promising future, although these technologies are premature and still on research [12]. If the lesion in the small bowel is detected with CE, the gastroenterologists still has to consider other forms of interventions such as DBE to determine the definite site of lesion and for the therapeutic interventions if required [12].

DBE is more challenging, invasive procedure requiring sedation. But with spectrum of performances as, mucosal biopsy, argon plasma coagulation, polypectomy and balloon dilation at a single intervention exhibit great therapeutic value. It requires special training and skills to perform DBE with reported range of 0.8% - 4% complications such as small bowel perforation, ileus, and pancreatitis [13] [14] [15]. It also does not allow complete small bowel visualization on single examination making it necessary for a proper selection of route, which is

either oral (antegrade) or anal (retrograde) beforehand. CE is an effective measure applied before DBE for route selection. Therefore these two examinations are considered to complement each other.

## 2. Methods and Search Strategy

Analysis of multiple studies from Pub Med, Elsevier, Springer, Scopus, Science direct, Wiley and other multidisciplinary databases were conducted. The terminologies focusing obscure gastrointestinal bleeding, capsule endoscopy, double balloon enteroscopy and their combination were used. Whereas publications on capsule endoscopy and double balloon enteroscopy were prioritized.

## 3. Diagnostic Yield of CE and DBE

Although a few number of Comparative studies and meta-analysis in OGIB concerning CE and DBE has been performed previously. Multiple studies showed that the diagnostic rate of DBE in OGIB within the range of 43% - 75% [16] [17]. Whereas diagnostic yield of CE in OGIB was reported to be 38% - 83% [18]. A study from Arakawa *et al.* showed the overall diagnostic yield of CE (54%) and DBE (64%), which was not much significantly different. This study suggests, the initial selection of CE for lesion detection followed by DBE for management of after disease detection in most OGIB cases [17]. Another meta-analysis by Teshima *et al.* also estimated that overall diagnostic yield of CE was 62% (95% confidence interval 47.3 - 76.1) and for DBE was 56% (95% CI 48.9 - 62.1), with an odds ratio (OR) of 1.39 (95% CI 0.88 - 2.20;  $P = 0.16$ ) for CE compared with DBE. This study also showed that the yield for DBE done after a previously positive CE was 75.0% (95% CI 60.1 - 90.0). The OR for confirmation of diagnosis with DBE after a positive CE compared with DBE in all patients was 1.79 (95% CI 1.09 - 2.96;  $P = 0.02$ ). On the contrary, the diagnostic yield for DBE after a previously negative CE was only 27.5% (95% CI 16.7 - 37.8). Thus they concluded that the diagnostic yield of DBE after positive CE results was significantly higher, while the diagnostic yield of CE and DBE performed individually was similar [19]. Another meta-analysis by Pasha *et al.* included 11 studies which included total of 397 patients; and showed the collective overall yield for CE and DBE was 60% and 57%, respectively [9]. In a systemic review by Liao *et al.*, performed in 2010, which involved 22,840 cases of CE from 227 studies, OGIB was the most common indication (66.0%), and the pooled diagnostic yield for OGIB was 60.5% [20].

As explained by these studies, the most frequent diagnosis was angiodysplasias, followed by tumors and ulcerations/erosions. Most studies concluded that the DBE has confirmed the findings of CE in the majority of cases. These studies revealed that the diagnostic yield of CE varied between 38% and 83% and DBE varied between 43% and 75%.

## 4. Concordance between CE and DBE

In most studies comparing diagnostic yield of CE and DBE, DBE has been con-

sidered for the confirmation of the findings after positive CE results in most cases. The concordance between findings of CE with those of DBE varied between 29% and 92% (**Table 1**). However, many studies showed that both DBE and CE give rise to false negative results. Several allusions missed by CE were later detected by DBE and vice versa. Lesions most commonly missed by CE but identified by DBE included angiodysplasias [24] [25] [27] [28], ulcers [21] [25] [28] small bowel diverticula [24] [26] [28] gastrointestinal stromal tumor (GIST) [24] [25], malignant lymphoma [24], leiomyosarcoma [24], enteric tuberculosis [24], varices [25] and colorectal cancer [26]. Arakawa *et al* performed studies in total of 162 patients with OGIB, among them 74 underwent both CE and DBE, and had 11 DBE positive cases where CE finding was normal. Likewise, few lesions which were found by CE, were not confirmed by subsequent DBE [17].

### 5. Factors Influencing Diagnostic Yield of CE and DBE

The rate of procedure completion is one of the important clinical factors affecting diagnostic yield. CE non-invasively examines the entire small bowel without patient discomfort and with the completion rate up to 90%. However, completion of DBE has been reported along 16% - 86% [8] [29]. The reasons influencing lower and variable completion rates of DBE are considered to be their complicated manipulation which often requires skillful endoscopist to visualize the entire small bowel. Furthermore, if the endoscopist performing DBE found the bleeding source might affect their decision to proceed. Chen *et al.* also concluded that diagnostic yield in OGIB varies according to the insertion approaches. The diagnostic yield of CE was significantly higher than that of DBE when the combination of oral (antegrade) and anal (retrograde) approaches was not used (62% vs. 50%,  $P = 0.02$ ). However, the diagnostic yield of DBE performed (combine antegrade and retrograde approach) was significantly higher than that of CE (87% vs. 46%,  $P = 0.004$ ) [30]. Therefore, the comparison of diagnostic yield between CE and DBE cannot be simply defined and an evaluation of results and its significance are not always interpretable.

**Table 1.** Overview of other studies performed for the diagnostic yields on capsule endoscopy (CE) and double balloon enteroscopy (DBE) in obscure gastrointestinal bleeding (OGIB).

Author (Reference)	n	Age (mean)	Diagnostic Yield CE (%)	Diagnostic Yield DBE (%)	Concordance (%)
Kaffes [21]	60	62	83	75	65
Kameda [22]	32	62	72	66	50
Matsumoto [23]	13	48	38	46	92
Fujimori [24]	45	60	40	50	89
Ohmiya [25]	74	-	50	53	73
Nakamura [26]	32	59	59	43	29

Note: (-) Indicates missing data.

## 6. Which One to Choose?

Many studies comparing the diagnostic yield between CE and DBE suggested that non-invasiveness, tolerance, similar diagnostic yield compared to DBE, high negative predictive value and very few complications of CE makes it an initial diagnostic choice in OGIB. DBE in spite of its invasiveness and more complicated procedure, should be considered as a second-line modality for OGIB patients with initial positive CE examination with necessary tissue biopsy or intervention. Many studies performed in recent years showed that CE is superior to other diagnostic modalities such as conventional endoscopy, angiography, DBE and enterocolysis for OGIB.

## 7. Conclusion

With the recent advances on Capsule Endoscopy (CE) and Double Balloon Enteroscopy (DBE), the visualization of the small bowel has enhanced exponentially. Although they complement each other with similar diagnostic yield, the noninvasive CE is recommended prior to DBE in OGIB exploration. CE also serves as a guide for insertion route enhancing subsequent DBE yield. Therefore, DBE interventions are preferred if further explorations are required. Although there is no direct provision of long term clinical outcomes, the noninvasive CE is vital for patient selection who requires further invasive interventions (DBE). CE also identifies low recurrent bleeding risks allowing physicians to consider conservative management. The benefits above positions CE as the first line diagnostic tool followed by DBE for further intervention if required.

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