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**Long-term outcome in patients with obscure gastrointestinal bleeding after negatice capsule endoscopy**

Koh SJ *et al*. Outcome in patients with OGIB after negative CE

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**Abstract**

**AIM:** To investigate the long-term outcome in patients with obscure gastrointestinal bleeding (OGIB) after negative capsule endoscopy (CE) and to identify risk factors for rebleeding.

**METHODS:** A total of 113 consecutive patients underwent CE for OGIB from May 2003 to June 2010 at Seoul National University Hospital. Ninety-five patients (84.1%) with a subsequent follow-up after CE of at least 6 mo were enrolled in this study. Follow-up data were obtained from the patients’ medical records. The CE images were reviewed by two board-certified gastroenterologists and consensus diagnosis was used in all cases. The primary outcome measure was the detection of rebleeding after CE, and factors associated with rebleeding were evaluated using multivariate analysis.

**RESULTS**: Of the 95 enrolled patients (median age 61, range 17–85 years), 62 patients (65.3%) were male. The median duration of follow-up was 23.7 mo (range 6.0–89.4). Seventy-three patients (76.8%) underwent CE for obscure-overt bleeding. Complete examination of the small bowel was achieved in 77 cases (81.1%). Significant lesions were found in 38 patients (40.0%). The overall rebleeding rate was 28.4%. The rebleeding rate was higher in patients with positive CE (36.8%) than in those with negative CE (22.8%). However, there was no significant difference in cumulative rebleeding rates between the two groups (log rank test; *P* = 0.205). Anti-coagulation after CE examination was an independent risk factor for rebleeding (hazard ratio, 5.019; 95%CI, 1.560–16.145; *P* = 0.007), regardless of CE results.

**CONCLUSION:** Patients with OGIB and negative CE have a potential risk of rebleeding. Therefore, close observation is required and alternative modalities should be considered in clinically suspicious cases.

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**Key words:** Capsule endoscopy; Gastrointestinal Hemorrhage; Risk factors; Prognosis; Enteroscopy

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**INTRODUCTION**

Obscure gastrointestinal bleeding (OGIB) represent about 5% of all gastrointestinal (GI) hemorrhage and is defined as recurrent or persistent bleeding or iron deficiency anemia from a GI tract origin with negative evaluation results from upper and lower endoscopies[[1](#_ENREF_1),[2](#_ENREF_2)]. It has been reported that small-bowel hemorrhage is the most common cause for OGIB[[3](#_ENREF_3)]. However, the difficulty in establishing a diagnosis in patients suspected to have small-bowel hemorrhage has made assessment of OGIB problematic, and a diagnosis of OGIB is often delayed. Recently, there have been advances in the identification of small-bowel hemorrhage using capsule endoscopy (CE) or balloon-assisted endoscopy.

CE is useful in the detection of the cause of small-bowel hemorrhage, and CE has a higher diagnostic yield than other diagnostic modalities[[4-7](#_ENREF_4)]. In addition, CE has advantages over balloon-assisted endoscopy, in that CE allows observation of the whole small bowel and identification of the bleeding focuses[[8](#_ENREF_8)]. Furthermore, CE allows non-invasive viewing of the whole small-bowel mucosa. Most investigators, therefore, agree that CE should be the initial form of investigation for OGIB[[3](#_ENREF_3)].

Several studies have evaluated the clinical implications of negative CE results over the long-term. However, there are contradictory findings regarding long-term outcome in patients with OGIB and negative CE results[[9-11](#_ENREF_9)]. In addition, most of these studies comprise relatively small number of patients and have short-term follow-up durations. Furthermore, it has been reported that significant small-bowel pathology may be missed during CE examinations, but can be subsequently diagnosed using alternative diagnostic tools including double-balloon enteroscopy[[12](#_ENREF_12),[13](#_ENREF_13)]. On the basis of these results, establishment of long-term clinical outcomes in patients with OGIB and negative CE remains unknown. The aim of this study was to investigate the long-term outcomes in patients with OGIB and a negative CE result and to identify the risk factors that are associated with rebleeding.

**MATERIALS AND METHODS**

***Patients and study design***

Between May 2003 and June 2010, a total of 113 consecutive patients at Seoul National University Hospital that had OGIB underwent CE to identify the cause of bleeding. Of those, long-term follow-up (more than 6 mo) data were available for 95 (84.1%) patients. OGIB was defined as either obscure-overt (presented as melena or hematochezia) or obscure-occult (iron-deficiency anemia with or without positive fecal occult blood) GI bleeding. Patient enrollment required one or more nondiagnostic esophagogastroduodenoscopy and colonoscopy examinations prior to CE examination. Clinical information and follow-up data were obtained from the patients’ medical records; the data included age, sex, comorbidities, anti-coagulation use, aspirin use, nonsteroidal anti-inflammatory drug (NSAID) use, hemoglobin value, and type of treatment for bleeding. This study was approved by the Institutional Review Board of Seoul National University Hospital.

***Capsule endoscopy and outcome measurement***

CE was performed with the PillCam™ SB (Given Imaging, Yoqneam, Israel) or the MiroCam® (IntroMedic, Seoul, Korea) capsule endoscopy systems. After a 12 h fasting, the CE was taken by the patients. According to our unit’s protocol, bowel preparation was not performed. Patients were allowed to drink water 2 h after swallowing CE and to have a light meal 4 h later. The recorder was stopped at about 8 or 12 h after swallowing the PillCam SB and the MiroCam, respectively. Patients were advised to keep away from magnetic exposure until capsule excretion.

The CE images were reviewed by two board-certified gastroenterologists; consensus diagnosis was used in all cases. Inter-observer agreement was higher than 95%. The videos were read at a speed of 15 frames per second.

According to standard practice guideline, CE findings were categorized into three lesions types: lesions considered to have a high potential for OGIB (P2); lesions regarded as having uncertain bleeding potential (P1); and lesions having no bleeding potential (P0)[[14](#_ENREF_14),[15](#_ENREF_15)]. An abnormal CE finding was classified as a P2 lesion when it was possible to explain the OGIB. Positive studies were defined as examinations that identified one or more P2 lesions, whereas those that identified only P1 or no abnormal lesions were regarded as negative results. Further evaluations such as abdominal computed tomography (CT), small bowel follow-through, bleeding scan, or conventional angiography were performed in patients with persistent overt GI bleeding. However, because it was only introduced in our institution at September 2009, balloon-assist endoscopy was only performed in 4 patients who had positive CE findings. Patients who showed minor OGIB without recurrence were carefully observed without further evaluations.

Each patient’s subsequent management was decided according to their CE results and clinical conditions. Specific treatment was performed in patients with identifiable causes on CE or with persistent overt bleeding; treatments, which included endoscopic, angiographic or surgical hemostasis, discontinuation of anti-coagulation treatment, NSAIDs, aspirin, or other antiplatelet agents, steroids for patients with Crohn’s disease, and anti-tuberculosis medication for patients with tuberculosis enterocolitis. Red blood cell (RBC) transfusion, iron supplement or watchful waiting, which were classified as non-specific treatments, were performed in patients with negative CE after minor OGIB.

The primary outcome measure was the detection of rebleeding after CE. Rebleeding was defined as evidence of GI bleeding at least 30 d after the initial bleeding. Evidence of GI bleeding was defined as overt bleeding (melena or hematochezia) or a fall in hemoglobin value of 2 g/dL or more compared with the baseline value and in the absence of other causes of decline in hemoglobin level[[10](#_ENREF_10)]. Secondary outcome measures were the rate of transfusion and subsequent hospitalization after CE.

***Statistical analysis***

Univariate analyses were performed using Student’s *t*-test for continuous variables and the chi*-*square or Fisher’s exact tests for categorical variables. A Kaplan-Meier curve with a log rank test was used to analyze the cumulative rebleeding rates. Multivariate analysis was done by using the Cox proportional hazards model to identify the risk factors associated with rebleeding. Statistical significance was determined using a *P* value < 0.05. All analyses were carried out by using the software package SPSS for Windows version 12.0 (SPSS Inc, Chicago, IL, United States).

**RESULTS**

***Patient characteristics***

Ninety-five patients who had undergone CE and subsequent followed-up for more than 6 mo within the defined period were studied. The baseline characteristics of the patients are summarized in Table 1. The median age was 61.0 (range 17 to 85) years and 62 patients (65.3%) were men. Seventy-three (76.8%) underwent CE for obscure-overt GI bleeding. Complete small-bowel visualization was achieved in 77 patients (81.1%). The median follow-up period was 23.7 (range 6.0 to 89.4) mo after CE. The majority of patients had undergone additional diagnostic workups, which included abdominal CT (61.1%, 58/95), small bowel follow-through (21.1%, 20/95), RBC scan (14.7%, 14/95), and conventional angiography (9.5%, 9/95).

***Capsule endoscopy findings***

The details of the CE results are summarized in Table 2. Thirty-eight (40.0%) had a significant abnormality that showed as one or more P2 lesions. These included erosion or ulcer (21.1%, 8/38), angiodysplasia (26.3%, 10/38), inflammatory bowel disease including tuberculosis enteritis (23.7%, 9/38), small-bowel tumors (5.3%, 2/38), and active bleeding of unknown origin (23.7%, 9/38). There was no significant difference in the prevalence of positive findings according to the initial manifestation (*P* = 0.921), with 29 of 73 patients with overt GI bleeding showing a positive CE result (39.7%) compared to 9 of 22 patients with occult bleeding showing a positive CE result (40.5%).

***Clinical course and management after capsule endoscopy***

Of the 38 patients with positive CE results, 24 received specific treatments. Conservative management such as iron replacement, watchful waiting, or blood transfusion was performed in 14 patients. Of the 10 patients with angiodysplasia, argon plasma coagulation (APC) was performed in 3 patients. The rebleeding rate was higher in patients treated with APC (66.7%, 2/3) than those undergoing conservative management (28.6%, 2/7). In 8 patients with small-bowel ulcer or erosion, one patient with multiple ulcers was considered to have involvement of myeloproliferative disease, which was treated with systemic chemotherapy. Five patients discontinued NSAID use. Two patients with small-bowel tumor underwent surgical resection; their tumors were histologically diagnosed as GI stromal tumor and an inflammatory fibroid polyp, respectively. Of the 9 patients classified as members of the inflammatory bowel disease (IBD) group, including Crohn’s disease and tuberculosis enterocolitis, all were treated with steroid or anti-tuberculosis medication. Of the 4 patients who had active bleeding without identifiable cause, one was treated with explorative laparotomy and diagnosed as radiation enterocolitis. One patient was confirmed with Crohn’s disease after performing balloon-assisted endoscopy. One patient was also confirmed with early stage Crohn’s disease that involved terminal ileum and cecum after performing colonoscopy and biopsy. Finally, one patient was diagnosed with angiodysplasia of duodenum and treated with APC.

Of the 51 patients with negative CE, rebleeding was identified in 12 patients. Among 12 patients who rebled, 9 patients underwent additional evaluations due to recurrent overt GI bleeding. The evaluation included abdominal CT, small bowel follow-through, RBC scan, Meckel’s scan, and explorative laparotomy. Despite these examinations, the focus of significant bleeding was not detected in 6 patients. However, significant small-bowel lesions were detected in 3 patients. In one of those, a bleeding diverticulum arising from distal ileum was identified on CT angiography and treated with angiographic embolization. In another, an ulcer was identified in distal ileum using small bowel follow through. That lesion was confirmed with extranodal marginal zone lymphoma after explorative laparotomy. In the last case, jejunal angiodysplasia was identified as the focus of the recurrent bleeding through explorative laparotomy with intraoperative enteroscopy. The remaining 3 patients who showed recurrent occult bleeding and had negative CE result received symptomatic treatments including iron replacement.

***Subsequent risk for rebleeding and long-term outcome in patients with OGIB***

The rebleeding rates in the CE results are summarized in Table 2. Of the 95 patients, 27 (28.4%) showed one or more rebleeding events during their follow-up periods. The median time to rebleeding was 10.0 (range 1.0–25.0) mo. The rebleeding rate in patients with positive and negative CE was 36.8% and 22.8%, respectively. There was no statistical difference in rebleeding between those two groups (*P* = 0.205, log rank test; Figure 1). In addition, there was no significant difference in the cumulative rebleeding rates between P1 and P0 lesion groups (*p* = 0.711, log rank test). Subsequent hospitalizations for bleeding were required in 5 patients (13.2%) in the CE positive group compared to 7 patients (12.3%) in the CE negative group (*p* = 1.000). Subsequent blood transfusions were given in 3 (7.9%) *vs* 6 (10.5%) patients, respectively (*P* = 1.000).

On the basis of multivariable analysis *via* the Cox proportional hazards analysis, anti-coagulation therapy was independently associated with an increased risk of rebleeding (HR, 5.019; 95% CI, 1.560–16.145; *P* = 0.007). However, negative CE and specific treatment were not associated with a decreased risk of rebleeding (Table 3). To identify the risk factors of rebleeding in patients with negative CE, we performed subgroup analysis. Anti-coagulation therapy was identified as an independent risk factor for rebleeding in patients with negative CE (hazard ratio, 7.069; 95% confidential interval, 1.942-29.809; *P* = 0.004).

**DISCUSSION**

CE is a safe and effective tool in evaluating small-bowel disease. It is generally accepted as the first diagnostic choice for patients with OGIB[[3](#_ENREF_3)]. It provides a higher diagnostic yield compared to other modalities because of its improved visualization. However, there are several limitations of CE reported in evaluations of small-bowel pathology. These include a limited visual field of the bowel lumen, poor bowel preparation, inadequate luminal distension, rapid passage around the proximal small bowel, and incomplete study of the cecum[[16](#_ENREF_16),[17](#_ENREF_17)]. Therefore, it is plausible that CE can miss significant lesions; a risk which could translate into poor prognosis in patients with OGIB in the long-term. Although there have been many reports determining the clinical impact of negative CE, the long-term risk of recurrent bleeding in patients with OGIB after negative CE remains controversial. According to a prospective analysis comparing CE with intraoperative endoscopy as the standard of reference, the negative predictive values (NPV) for CE was 86%[[18](#_ENREF_18)]. Delvaux *et al*[[19](#_ENREF_19)]in a 12 mo follow-up study reported that the NPV was 100% in patients with normal findings on CE. In addition, several studies have reported that patients with OGIB and negative CE results have very low rebleeding rates[[9](#_ENREF_9),[10](#_ENREF_10),[20](#_ENREF_20),[21](#_ENREF_21)]. Therefore, it has been generally accepted that a negative CE result predicts a favorable prognosis in patients with OGIB. However, a well-designed prospective study reported that the rebleeding rate during 1-year follow-up was 33% in patients with normal CE findings[[22](#_ENREF_22)]. Moreover, a retrospective study demonstrated that there was no significant difference in the cumulative rebleeding rates between patients with positive CE and those with negative CE[[11](#_ENREF_11)]. The present study demonstrates that the overall rebleeding rates in patients with positive and negative CE results during the minimum 6 mo follow-up period were 36.8% and 22.8%, respectively. There was no significant difference in the cumulative rebleeding rates between those two groups. In addition, multivariable analysis showed that CE results were not associated with a risk of rebleeding. Therefore, our results indicate that the risk for recurrent bleeding is considerable, even if patients with OGIB have a negative CE result.

According to the current recommendations for OGIB from the American Gastroenterological Association, subsequent intervention directed by CE findings is recommended in patients with a positive CE result. Moreover, further diagnostic testing can be deferred in patients with a negative CE, and balloon-assisted endoscopy is considered only in patients with a high suspicion of small-bowel pathology. However, little information is available on the duration of follow-up. The duration of follow-up in previous studies, which found very low rebleeding rates was only 12 mo[[19](#_ENREF_19),[21](#_ENREF_21)]. However, increased rebleeding rates have been reported with the longer follow-up periods in recent studies[[9](#_ENREF_9),[10](#_ENREF_10)]. In the present study, approximately 50% of the patients showed a first rebleeding episode more than one year after the initial bleeding, while the maximum time to rebleeding was 24 mo after a negative CE result. Moreover, Park *et al*[[11](#_ENREF_11)] reported a rebleeding rate of 35.7% during a 32 mo follow-up. On the basis of these results, a close follow-up duration of at least 2 years is needed in patients with OGIB, even if patients have a negative CE finding (Table 4).

CE can improve the diagnostic yield in patients with OGIB, but it remains uncertain whether CE improves clinical outcomes. A recent, prospective, randomized control trial demonstrated that a substantial improvement in diagnostic yield with the use of CE did not lead to improved outcome in patients with OGIB[[22](#_ENREF_22)]. In addition, a recent study showed that positive CE results are not predictive of a favorable outcome in patients with iron deficiency anemia[[23](#_ENREF_23)]. On that basis, treatment directed by CE may not improve long-term outcome in patients with OGIB. In contrast, Park *et al*[[11](#_ENREF_11)] demonstrated that specific treatments decrease long-term rebleeding after CE, suggesting that vigorous investigation to detect the bleeding focus could definitely reduce the rebleeding. In addition to this, Delvaux *et al*[[19](#_ENREF_19)] also showed that only one patient among 18 patients who were treated lesions directed by CE relapsed during 1-year follow-up. In the present study, a significant proportion (63.2%) of patients with positive CEs had specific treatments. Higher rebleeding rate was found in patients with angiodysplasia and IBD, while patients with tumors exhibited no rebleeding after surgical intervention. There was no significant difference in the cumulative rebleeding rates regardless of specific treatment. In addition, multivariate analysis showed that specific treatment did not reduce the risk of rebleeding. These results suggest that CE plays a limited role in clinical outcome among patients with OGIB. However, these results should be interpreted with caution because out data retrospectively obtained from a single tertiary referral hospital. Outcomes in patients with OGIB are likely attributable to various etiologies and to the severity of initial presentation. Moreover, the natural history of the etiologies such as angiodysplasia remains unclear. Therefore, prospective, well-designed, long-term follow-up studies that include the various etiologies of OGIB are required to determine whether diagnostic testing with CE will translate into a significant improvement in the management and outcome in patients with OGIB.

Recently, no clear guidelines exist for evaluating patients with a negative initial CE. The management of these patients with OGIB still remains elusive. However, patients having evidence of ongoing or recurrent OGIB need further investigation. The options include repeating upper and lower endoscopies, CE, double-balloon endoscopy (DBE), radiologic or nuclear medicine scans, and intraoperative enteroscopy[[24](#_ENREF_24)]. In a recent study, patients with negative CE in the first test would benefit from a second-look CE if the bleeding presentation changes from occult to overt or if the hemoglobin value drops ≥ 4 g/dL[[25](#_ENREF_25)]. In addition to this, DBE could be useful in evaluating patients with a negative CE because it has a diagnostic yield similar to that of CE[[26](#_ENREF_26)]. Furthermore, it has great advantage in providing histologic confirmation and simultaneous treatment[[27](#_ENREF_27)]. Therefore, well-designed prospective studies are required to improve the management in OGIB patients with a nondiagnostic CE test.

Our study has a few limitations. First, our study is limited by its use of the data obtained from a single tertiary referral hospital and by its retrospective study design. Second, balloon-assisted endoscopy was not performed in most of the patients. Therefore, the possibility exists that a less-invasive approach might lead to higher rebleeding rates in both groups. Finally, it is possible that some lesions may be missed because our data included uncompleted CE results.

In conclusion, patients with OGIB and negative CE have a potential risk of rebleeding. Therefore, close observation is needed even in patients with negative CE and alternative modalities should be considered in clinically suspicious cases.

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**COMMENTS**

***Background***

Obscure gastrointestinal bleeding represent about 5% of all gastrointestinal hemorrhage and is defined as recurrent or persistent bleeding or iron deficiency anemia from a gastrointestinal tract origin with negative evaluation results from upper and lower endoscopies. Capsule endoscopy is useful in the detection of the cause of small-bowel hemorrhage, and capsule endoscopy has a higher diagnostic yield than other diagnostic modalities.

***Research frontiers***

Wireless capsule endoscopy is considered a first-line investigation in patients with obscure gastrointestinal bleeding. However, a significant portion of patients with obscure gastrointestinal bleeding have nondiagnostic capsule endoscopy results. Although there have many studies investigating diagnostic yield of capsule endoscopy, little information is available about long-term outcome in patients after negative capsule endoscopy. In addition, it remains uncertain whether treatment directed by capsule endoscopy lead to improve long-term outcome in patients with obscure gastrointestinal hemorrhage.

***Innovations and breakthroughs***

This study showed that the rebleeding rate in patients with obscure gastrointestinal bleeding after negative capsule endoscopy results was substantial. Treatment directed by capsule endoscopy did not reduce the risk of rebleeding.

***Applications***

The study showed that negative capsule endoscopy does not predict favorable outcome, which suggest that close observation for rebleeding are warranted.

***Peer review***

In this manuscript, authors have reported that patients with obscure gastrointestinal bleeding and negative capsule endoscopy have a potential risk of rebleeding. Treatments directed by capsule endoscopy were not associated with the decreased risk of rebleeding. The data provided in this study contribute to understanding of long-term outcome in patients with obscure gastrointestinal hemorrhage.

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**P-Reviewers** Figueiredo P, Velayos B **S-Editor** Wen LL  **L-Editor**  **E-Editor**



**Figure 1 Cumulative rebleeding rates according to the initial capsule endoscopy results.**

**Table 1 Clinical characteristics of the patients with obscure gastrointestinal bleeding**

|  |  |
| --- | --- |
| **Characteristics** | **Total (*n* = 95)** |
| Age (yr), median (range)  | 61.0 (17-85) |
| Male, *n*  | 62 (65.3%) |
| Obscure-overt bleeding, *n* | 73 (76.8%) |
| Complete small-bowel visualization, *n*  | 77 (81.1 %) |
| Comorbidity, *n* | 43 (45.3%) |
| Hb concentration at the time of the procedure, g/dL, mean ± SD | 8.3 ± 2.0 |
| Need for transfusion before CE, *n*  | 50 (52.6%) |
| Diagnostic yield, *n*  | 38 (40.0%) |
| Follow-up duration (month), median (range) | 23.7 (6.0-89.4) |
| > 12-month follow-up, *n*  | 73 (76.8%) |
| Aspirin use, *n*  | 23 (24.2%) |
| Other antiplatelet agent, *n*  | 13 (13.7%) |
| Anticoagulation, *n*  | 8 (8.4%) |
| NSAIDs, *n*  | 10 (10.5%) |

CE: Capsule endoscopy; Hb: Hemoglobin; NSAIDs: Nonsteroidal anti-inflammatory drugs.

**Table 2 Capsule endoscopy results of the 95 patients with obscure gastrointestinal bleeding and rebreeding rates (%)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Findings** | **Total (*n* = 95)** | **Specific treatment,** ***n***  | **Rebleeding,**  ***n***  |
| **P2 lesion** | 38  | 24 (63.2) | 14 (36.8) |
|  Ulcer or erosion | 8  | 6 (75.0) | 3 (37.5) |
| Tumor | 2  | 2 (100) | 0 (0) |
|  Angiodysplasia | 10  | 3 (30.0) | 4 (40.0) |
|  Bleeding from unknown focus | 9  | 4 (44.4) | 4 (44.4) |
|  IBD including tuberculosis enteritis | 9  | 9 (100) | 3 (33.3) |
| **P1 lesion** | 6  | 0 (0) | 1 (16.7) |
|  Erosion | 2  | 0 (0) | 1 (50.0) |
|  Nonbleeding polyp  | 2  | 0 (0) | 0 (0) |
|  Lymphangiectasia | 2  | 0 (0) | 0 (0) |
| **P0 lesion** | 51  | 3 (5.9) | 12 (23.5) |
| **Total**  | 95 | 27 (28.4) | 27 (28.4) |

IBD: Inflammatory bowel disease.

**Table 3 Risk factors for rebleeding in patients with obscure gastrointestinal bleeding**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variables** | **Hazard ratio** | **95% CI** | ***P* value** |
| Male Age > 50 yrHb < 8 g/dLTransfusion before CEComorbidityAspirin useAnticoagulation use NSAIDs use Obscure-overt bleedingSpecific treatment Positive CE | 2.082 | 0.882-4.910 | 0.094 |
| 0.980 | 0.328-2.922 | 0.971 |
| 0.861 | 0.365-2.029 | 0.732 |
| 1.719 | 0.674-4.382 | 0.257 |
| 1.619 | 0.661-3.969 | 0.292 |
| 1.020 | 0.357-2.914 | 0.970 |
| 5.019 | 1.560-16.145 | 0.007 |
| 1.153 | 0.314-4.232 | 0.830 |
| 1.143 | 0.382-3.416 | 0.811 |
| 1.123 | 0.368-3.422 | 0.839 |
| 1.564 | 0.561-4.355 | 0.392 |

Hb: Hemoglobin; CE: Capsule endoscopy; NSAIDs: Nonsteroidal anti-inflammatory drugs.

**Table 4 Follow-up duration and rebreeding rates in patients with obscure gastrointestinal bleeding after negative capsule endoscopy**

|  |  |  |  |
| --- | --- | --- | --- |
| **Study**  | **Number of enrolled cases** | **Follow-up duration (mo)** | **Rebleeding rates after negative capsule endoscopy (%)** |
| Lorenceau-Savale *et al*[[21](#_ENREF_21)] | 35 | 12 | 0 |
| Delvaux *et al*[[19](#_ENREF_19)] | 44 | 12 | 0 |
| Lai *et al*[[9](#_ENREF_9)] | 49 | 12 | 6 |
| Macdonald *et al*[[10](#_ENREF_10)] | 49 | 17 | 11 |
| Koh *et al*1 | 51 | 23 | 23 |
| Park *et al*[[11](#_ENREF_11)] | 51 | 32 | 36 |

1Current study.