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Prediction models for recurrence in patients with small bowel bleeding

Ji Hyun Kim, Seung-Joo Nam

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Abstract

Obscure gastrointestinal bleeding (OGIB) has traditionally been defined as gastrointestinal bleeding whose source remains unidentified after bidirectional endoscopy. OGIB can present as overt bleeding or occult bleeding, and small bowel lesions are the most common causes. The small bowel can be evaluated using capsule endoscopy, device-assisted enteroscopy, computed tomography enterography, or magnetic resonance enterography. Once the cause of small-bowel bleeding is identified and targeted therapeutic intervention is completed, the patient can be managed with routine visits. However, diagnostic tests may produce negative results, and some patients with small bowel bleeding, regardless of diagnostic findings, may experience rebleeding. Predicting those at risk of rebleeding can help clinicians form individualized surveillance plans. Several studies have identified different factors associated with rebleeding, and a limited number of studies have attempted to create prediction models for recurrence. This article describes prediction models developed so far for identifying patients with OGIB who are at greater risk of rebleeding. These models may aid clinicians in forming tailored patient management and surveillance.

Key Words: Obscure gastrointestinal bleeding; Prediction model; Rebleeding; Small bowel bleeding; Video capsule endoscopy

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Core Tip: Some patients with small bowel bleeding, regardless of the diagnostic findings, may experience rebleeding. Predicting those at risk of rebleeding can help clinicians form individualized surveillance plans. This article describes prediction models developed so far for identifying patients with obscure gastrointestinal bleeding who are at greater risk of rebleeding. There are prediction models that can help identify patients with a greater risk of rebleeding.

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INTRODUCTION

Gastrointestinal (GI) bleeding is a common symptom in the emergency department and is associated with significant morbidity and mortality[1,2]. GI bleeding not identified upon initial esophago-gastroduodenoscopy (EGD), and colonoscopy has traditionally been known as obscure GI bleeding (OGIB), and many of these are caused by bleeding from small intestinal lesions[3,4]. OGIB can be divided into two groups as suggested by the American College of Gastroenterology guideline: Overt bleeding presenting with clinically evident bleeding as melena or hematochezia; and occult bleeding presenting as positive fecal occult blood test or anemia[3]. The small bowel can be evaluated using capsule endoscopy (CE), device-assisted enteroscopy (DAE), computed tomography enterography, or magnetic resonance enterography. CE is the preferred modality in suspected cases of small bowel bleeding because it is not invasive and allows direct visualization of the entire small bowel mucosa. The diagnostic yield is as high as 77%, which is superior to that of angiography; however, the diagnostic yield can vary depending on several factors[5]. Factors known to be associated with increased diagnostic yield include inpatient status, early CE (within 1 wk upon presentation of symptoms), large amount of overt bleeding requiring transfusion, hemoglobin < 10 g/dL, male sex, older age, and use of anti-coagulants[6-10]. Once the source of bleeding is identified and directed interventions are performed, approximately 50%-66% of patients have been reported to have no rebleeding during follow-up[11]. If bleeding lesions are not observed with initial CE, patients may be considered for re-evaluation with a second CE to increase the diagnostic yield if a decrease in hemoglobin of more than 4 g/dL is observed. However, studies and meta-analysis have reported that rebleeding rate in patients with negative CE is low compared to those on patients with positive CE[12-17]; moreover, experts suggest watchful waiting in such patients[18]. However, some discrepancies in rebleeding rates have been observed in different studies. Rebleeding in patients with positive CE results varies between 5.9% and 61.1%, and rebleeding in patients with negative CE results varies between 0% and 64.6%, suggesting that the results of CE alone may not be sufficient to predict outcomes in patients with OGIB [19-23]. In an attempt to identify patients who have a higher risk of rebleeding, different prediction models have been developed. This study reviews available prediction models, including Predicting Rebleeding in Small Bowel Bleeding (PRSBB) score, prediction model using 5 factors, Outcomes Registry for Better Informed Treatment (ORBIT) score, Ohmiya index, and Renal disease, Heart failure, Endoscopic findings, Major bleeding, Incomplete CE, Tobacco consumption, and Treatment by endoscopy (RHEMITT) score. A summary of the models is presented in Table 1.

RISK FACTORS FOR REBLEEDING

To date, there are conflicting results regarding rebleeding rates and associated factors from different studies; patients included in each study are heterogeneous and follow-up durations vary. Analysis on risk factors associated with rebleeding are also different among different studies. Some factors considered to be associated with rebleeding include overt bleeding, anticoagulation therapy, positive CE findings at initial assessment, age, gender, low serum hemoglobin, and accompanying conditions, such as liver cirrhosis and chronic kidney disease[17].

CE findings

Findings from CE can be classified into three types according to the Saurin classification; P0 lesions such as submucosal veins, diverticula without bleeding, or nodules without mucosa breaks have no bleeding potential; P1 lesions such as red spots and erosions have uncertain bleeding potential; and P2 lesions such as large ulcers, tumors, varices, and vascular lesions have high potential for bleeding[24]. Lorenceau-Savale *et al*[25] reported that a year follow-up of patients with P0 or P1 lesions showed no

Table 1 Prediction models for rebleeding in small bowel bleeding

Ref.	Prediction model	Variables	Rebleeding rate
Niikura <i>et al</i> [38], 2016	Prediction model using 5 factors	Female sex, liver cirrhosis, use of warfarin, overt bleeding, hemoglobin below 10 g/dL, positive CE findings	0% with 0 variable; 8.7% with 1 variable; 14.7% with 2 variables; 30.4% with 3 variables; 40.0% with 4 variables
Originally created by O'Brien <i>et al</i> [39], 2015; tested by Cúrdia Gonçalves <i>et al</i> [40], 2018	ORBIT score	Age ≥ 75 yr, hemoglobin (< 12 g/dL for women, < 13 g/dL for men), prior GI bleeding or intracranial hemorrhage, reduced kidney function (GFR < 60 mg/dL/1.73 m ²), use of antiplatelets	45% in low/intermediate risk group; 80% in high risk group; AUROC is 0.67 when cutoff value of 4
Uchida <i>et al</i> [37], 2018	PRSBB score	Age, sex, type of bleeding (occult or overt), transfusion requirement, cardiovascular disease, liver cirrhosis, CE findings, type of treatment	3.63% in low risk group; 12.8% in intermediate risk group; 23.4% in high risk group
Ohmiya <i>et al</i> [41], 2019	Ohmiya index	Angina pectoris, arrhythmia, congestive heart failure, chronic kidney disease, peripheral vascular disease, hemodialysis, valvular heart disease, hereditary vascular disease, portal hypertensive disease	33% in small bowel vascular disease predicted by score ≥ 2
de Sousa Magalhães <i>et al</i> [45], 2020	RHEMITT score	Renal disease (GFR mL/min), heart failure, endoscopic findings, major bleeding, incomplete CE, tobacco consumption, treatment by endoscopy	0.00% in low risk group; 25.4% in intermediate risk group; 63.8% in high risk group

AUROC: Area under the receiver operating characteristics curve; CE: Capsule endoscopy; GI: Gastrointestinal; GFR: Glomerular filtration rate; ORBIT: Outcomes Registry for Better Informed Treatment; PRSBB: Predicting Rebleeding in Small Bowel Bleeding; RHEMITT: Renal disease, Heart failure, Endoscopic findings, Major bleeding, Incomplete CE, Tobacco consumption, Treatment by endoscopy.

rebleeding, while a study by Koh *et al*[26] reported rebleeding in 23% of patients with P0 and P1 lesions within 6 mo after the initial presentation, and a prospective study by Laine *et al*[27] showed similar results, reporting rebleeding in 33% of patients with negative initial CE results. Yung *et al*[17] included 26 studies from eastern and western populations for meta-analysis on clinical outcome from small bowel bleeding with negative initial CE and reported that pooled rate of rebleeding after negative CE was 0.19 which is significantly lower than positive CE of 0.29 ($P < 0.001$). In another meta-analysis, Tziatzios *et al*[19] used 46 studies from different countries to analyze rebleeding rates. Similar to previous studies, they also reported that rebleeding rates were lower in negative CE than in positive CE (22% *vs* 28%). However, when data from eastern and western population were separately analyzed, similar findings were observed only in studies on eastern population and not in western population studies[19].

Occult and overt bleeding

Studies that compared overt and occult bleeding have also reported varying results. A study by Liu *et al*[28] reported that among 142 patients with OGIB, rebleeding was observed in 72 (50.7%) patients within 6 mo, and among them the initial presentation was overt bleeding in 70.4% compared to 29.6% of occult bleeding. Another study by Wetwittayakhleng *et al*[29] reported that during a follow-up duration of 26 mo, 35 patients (26.3%) had rebleeding where 60% had initial presentation as overt bleeding. Furthermore, a study by Kim *et al*[30] reported that 16 patients (26.7%) with negative CE had rebleeding within 36 mo, and among them, 81.3% had overt bleeding as the initial presenting symptom. In a study by Baba *et al*[31] 168 patients with small bowel bleeding were included, and patients were grouped into overt ongoing bleeding, overt previous bleeding, and occult bleeding groups. Multivariate analysis on rebleeding showed that overt previous bleeding (odds ratio = 3.68, $P = 0.01$), vascular lesions and chronic kidney disease, were risk factors associated with rebleeding. Other studies reported different results. A multicenter study by Kim *et al*[32] reported that no significant difference was observed between overt and occult bleeding in patients with rebleeding, and similar findings were also reported by Magalhães-Costa *et al*[33]. Some studies reported that overt bleeding was not a significant risk factor in rebleeding[28,30,33], while different studies have reported that overt bleeding is a significant risk factor for rebleeding[29,31,34]. Meta-analysis on initial mode of OGIB presentation showed that difference in the rebleeding rate after negative CE was not statistically significant[17], and the overall odds ratio did not differ between the two modes of presentation[19].

Therapeutic intervention

Once bleeding lesions are identified, DAE can be used for endoscopic hemostasis, such as argon plasma coagulation, or hemostatic clipping. Other specific treatments include surgery, angiographic hemostasis, discontinuation of anticoagulants and antiplatelets, and treatment targeted for specific lesions such as Crohn's disease. When bleeding lesion is not identified (negative CE), watchful waiting, blood transfusion, or iron supplementation are considered as nonspecific treatment. Some studies concluded

that receiving targeted therapeutic intervention did not have significant effects on rebleeding[32,35], while other studies reported that targeted specific therapeutic intervention lowered rebleeding rate[31, 34,36]. A meta-analysis by Yung *et al*[17] reported that specific treatment did not have significant effect on the risk of rebleeding, while Tziatzios *et al*[19] reported that in studies that enrolled patients with positive CE who received specific treatment, significantly lower risk of rebleeding were observed than that in cases without intervention. This suggests that if a bleeding lesion is identified from CE and specific treatment is done, it could lower the risk of rebleeding.

NOMOGRAM-BASED PREDICTION MODEL, THE 'PRSBB' SCORE

In a retrospective study by Uchida *et al*[37], 401 patients with small-bowel bleeding were included. Repeat EGD and colonoscopy were performed to identify possible missed lesions, and CE was performed using a PillCam SB. According to the CE findings, lesions were identified as normal (venous ectasia, mucosal erythema, small polyps without bleeding, isolated clots), non-vascular (active ulcer, diverticula, and small-bowel tumors), and vascular (angioectasia, Dieulafoy's lesion, varices, arteriovenous malformations, and active bleeding). For patients in good general condition who agreed to undergo further testing, double-balloon endoscopy was performed regardless of CE results to identify any missed small bowel lesions. The outcome was the occurrence of rebleeding, defined as hematochezia and melena in patients with overt bleeding, and anemia (a reduction in hemoglobin levels > 2 g/dL) in patients with occult bleeding. The least absolute shrinkage and selection operator (LASSO) plot was drawn using different factors including age, sex, comorbidities (diabetes, cardiovascular disease, chronic kidney disease, and liver cirrhosis), medication [anticoagulants and nonsteroidal non-steroidal anti-inflammatory drugs (NSAIDs)], type of small bowel bleeding (overt or occult), transfusion requirement, hemoglobin level, CE and enteroscopy findings, and type of treatment. According to the LASSO regression plot, eight factors were associated with rebleeding, which were age, sex, type of small bowel bleeding, transfusion requirement, history of cardiovascular disease, history of liver cirrhosis, CE findings, and type of treatment received. The weights and points for these factors were combined in the nomogram, and based on this nomogram, patients were grouped into different risk groups. The low-risk group represents < 10% rebleeding in 5 years, the intermediate group represents 10%-20% rebleeding, and the high-risk group represents > 20% rebleeding. When this nomogram was applied, cumulative rebleeding rate in the low, intermediate, and high risk groups were 3.63%, 12.8%, and 23.4%, respectively. This prediction model for rebleeding in small bowel bleeding (PRSBB), stratifies patients with small bowel bleeding into different risk groups so that clinicians can plan individualized follow-up strategies. However, there is a lack of data on the external validation of this model.

PREDICTION MODEL USING 5 FACTORS

Niikura *et al*[38] developed and reported a prediction model for rebleeding in OGIB cases. They gathered data on 320 patients from different centers in Japan who were identified as having OGIB on negative EGD and colonoscopy. Patients with upper GI bleeding (bleeding from lesions above ligament of Treitz) and lower GI bleeding (bleeding from lesions in colon and rectum) identified by repeated examinations were excluded from the study. At 3 and 6 mo after the initial diagnosis, patients were evaluated for rebleeding. The factors included in the analysis for rebleeding were age, sex, comorbidities (hypertension, dyslipidemia, diabetes, ischemic heart disease, cerebrovascular disease, heart failure, chronic kidney disease, liver cirrhosis, and chronic obstructive pulmonary disease), medications (low-dose aspirin, thienopyridines, anticoagulants, and NSAIDs), hemoglobin level, timing of CE, CE findings, and hemostatic interventions. Among them, female sex, history of liver cirrhosis, use of warfarin, overt bleeding, hemoglobin drop (less than 10 g/dL), and positive CE findings were associated with risk of rebleeding. Each risk factor was calculated to have equal weights in the prediction model; therefore, one point was assigned to each factor. Applying this prediction model showed that bleeding risk increased with increasing total score: 0 points, 0% rebleeding; 1 point, 8.7% rebleeding; 2 points, 14.7% bleeding; 3 points, 30.4% rebleeding; and 4 points, 40.0% rebleeding. The model showed a 73% prediction rate for rebleeding when applied to the collated retrospective data. Based on the results, the authors suggested that patients with 0 points did not need follow-up, patients with any of the five risk factors needed follow-up at 3-6 mo intervals for 1 year, and patients with more than four risk factors needed follow-up at 3-6 mo intervals for more than 1 year as they are at greater risk of rebleeding. Although this prediction model lacks external validation, it is simple, identifies patients with an increased risk of rebleeding, and suggests how to schedule follow-up visits.

ORBIT SCORE FOR THE PREDICTION OF REBLEEDING IN PATIENTS WITH SMALL BOWEL BLEEDING

In 2015, O'Brien *et al*[39] developed the ORBIT score, which assesses bleeding risk in patients with atrial fibrillation. Similar to HAS-BLED and HEMORR2HAGES scores, which were developed to identify patients at risk of bleeding who are administered long-term anticoagulants, ORBIT showed good prediction of major bleeding in patients with atrial fibrillation. It is a simple scoring system that uses five variables, with specific points assigned to each factor. One point is assigned for age ≥ 75 years, 2 points for hemoglobin (< 12 g/dL for women, < 13 g/dL for men) or hematocrit ($< 36\%$ for women, $< 40\%$ for men), 2 points for a history of prior GI bleeding or intracranial hemorrhage, 1 point for reduced kidney function (glomerular filtration rate < 60 mL/dL/1.73 m²), and 1 point for use of antiplatelets. A total of 0-2 points was considered as the low-risk group, 3 points as the intermediate-risk group, and > 4 points as the high-risk group. Cúrdia Gonçalves *et al*[40] used the ORBIT score to predict rebleeding in patients with small bowel bleeding. For evaluation, risk scores were grouped into low/intermediate risk (< 4 points) and high risk (≥ 4 points) groups. Using the data of 570 patients with suspected small bowel bleeding, 67 patients who were administered chronic anticoagulants were included in the final analysis, 41 patients were identified as the low/intermediate-risk group, and 26 patients were in the high-risk group. Analysis of the CE results showed that 16 patients in the low/intermediate-risk group (39.0%) had positive CE findings (P2 lesions representing high bleeding potential) and six patients in the high-risk group (23.1%) had positive CE findings that were not significantly different. During a mean follow-up duration of 35 mo, 15 patients (45.5%) in the low/intermediate-risk group had rebleeding, and 20 patients (80%) had rebleeding defined as symptomatic anemia, decrease in hemoglobin by more than 2 g/dL, need for transfusion, and overt GI bleeding. Rebleeding was significantly higher in the high-risk group than that in the low-risk group ($P = 0.003$). Using a cutoff value of 4, the area under the receiver operating characteristics curve (AUROC) was 0.67 (95% confidence interval: 0.53-0.79), sensitivity 57.1%; specificity, 78.3%; positive predictive value, 80.0%; and negative predictive value, 54.4%. This suggests a possible application of the ORBIT score for risk stratification in patients with atrial fibrillation. Ohmiya *et al*[41] applied the ORBIT score in 51 patients with small bowel bleeding and reported that 23% of 44 patients in the high-risk group showed rebleeding, while no rebleeding was observed in the low-risk group; however, only seven patients were included in the low-risk group, so the difference was not distinct between the two groups.

OHMIYA INDEX, PREDICTION MODEL USING COMORBIDITY INDEX

Among other risk factors for bleeding, comorbidities have been considered important factors that are associated with rebleeding. A study by Otani *et al*[34] reported that a Charlson comorbidity index (CCI) score ≥ 5 was associated with an increased risk of bleeding in OGIB. Harada *et al*[42] also reported that a CCI score ≥ 4 was associated with a risk of rebleeding in small-bowel vascular lesions. Specific comorbidities, such as chronic kidney disease and liver cirrhosis, have been associated with an increased risk of bleeding and have been adapted in some prediction models[37,38,40,43]. Using CCI, Ohmiya *et al*[41] created a new comorbidity index to identify patients with small bowel bleeding at greater risk of small bowel vascular diseases, such as angioectasia, Dieulafoy's lesion, arteriovenous malformation, and varix. Using data on the number and type of comorbidities from 404 patients with small bowel bleeding, they assigned a weighted index to significant comorbidities. A score of 1 was assigned to the presence of angina pectoris, arrhythmia, diabetes mellitus, congestive heart failure, and chronic kidney disease; a score of 2 was assigned to hemodialysis or peritoneal dialysis, peripheral vascular disease, and valvular heart disease; and a score of 3 was assigned to hereditary vascular diseases and portal hypertensive disease[44]. The combined score is the Ohmiya index. When applied to patients with small bowel bleeding, an index score of ≥ 2 identified small bowel vascular disease with 68% accuracy. In addition, patients with small bowel vascular disease were more prone to rebleeding than those with non-vascular disease (33% *vs* 15%, $P = 0.04$). Although more specifically designed to identify bleeding from vascular diseases of the small bowel, this score suggests the possible use of a comorbidity index to identify patients at higher risk of rebleeding.

RHEMITT SCORE

To create and validate a prediction model specifically aimed at identifying small bowel rebleeding after evaluation with CE, de Sousa Magalhães *et al*[45] developed the RHEMITT score in 2019. Using data gathered from 357 patients who underwent CE for the evaluation of small bowel bleeding, they analyzed demographic characteristics, medications, comorbidities, laboratory data, and CE findings in association with rebleeding, and then created a prediction score using seven variables. Renal disease (R), heart failure (H), endoscopic findings (E), major bleeding (M), incomplete CE (I), tobacco consumption

(T), and treatment using endoscopy (T) were assigned different scores, and the combined score created the RHEMITT score ranging from 0 to 18 points. Renal disease, defined as a glomerular filtration rate < 60 mL/min for more than 3 mo, was assigned a score of 3. Heart failure was defined as the presence of typical symptoms of reduced cardiac output and/or elevated cardiac pressure during rest or stress, which was assigned a score of 1. Endoscopic findings use the Saurin classification[24], where P1 lesions are assigned 2 points and P2 lesions are assigned 3 points. Major bleeding was defined as bleeding that causes a reduction in hemoglobin of ≥ 2 g/dL or requiring transfusion of 2 units of blood, and was given a score of 5. Incomplete CE was defined as failure to reach the colon during the recording time and was assigned a score of 2. Tobacco consumption was defined as active or former smokers and was assigned a score of 2. Finally, treatment by endoscopy was defined as hemostasis using coagulation with argon plasma coagulation or hemoclips and polypectomy with subsequent deep enteroscopy, which was assigned a score of 2. Based on the total score, 3 groups with different rebleeding risks were identified: 0-3 points indicated low risk (rebleeding rate, 0%), 4-10 points indicated intermediate risk (rebleeding rate, 25.4%), and 11-18 points indicated high risk (rebleeding rate, 63.8%). The AUROC was 0.843 (95% confidence interval: 0.801-0.885), showing good accuracy. Using this score, Silva *et al*[46] retrospectively analyzed the external validation in 166 patients with OGIB. Among them, five out of 86 (5.8%) patients in the low-risk group experienced rebleeding, 12 out of 64 (18.8%) patients in the intermediate-risk group had rebleeding, and six out of 10 (60.0%) patients in the high-risk group had rebleeding. Rebleeding rates were significantly different between each group, and the AUROC was 0.756, suggesting that the RHEMITT score accurately identified patients at a high risk of rebleeding. To evaluate the predictive accuracy, creators of the RHEMITT score tested accuracy with prospectively validation[47]. In the study, 162 patients with small bowel bleeding were included; 94 patients were grouped as low risk, 44 patients as intermediate risk, and 24 patients as high bleeding risk. A total of 30 patients experienced rebleeding; of these, 23 were in the high-risk group (95.8%), and no rebleeding was observed in the low-risk group. Five patients in the high-risk group experienced more than one rebleeding event, and high-risk patients were prone to bleeding within the first 6 mo. The study also suggested a surveillance protocol using the RHEMITT score; high-risk patients should be under strict surveillance using trimestral appointments with gastroenterology specialists and easy access to specialized hospital care as they are at risk of more than one bleeding event within 6 mo[47]. As previous studies were conducted in Europe, Boortalary *et al*[48] conducted external validation at a United States tertiary center. They retrospectively collected CE data from 361 patients and analyzed rebleeding using the RHEMITT score. Rebleeding was observed in 12/113 (10.6%) patients in the low risk group, 78/172 (45.3%) patients in the intermediate risk group, and 55/76 (72.4%) patients in the high risk group. The AUROC for rebleeding was 0.790 and the average time for rebleeding in the high-risk group was 7 mo. Unlike the other prediction models, the RHEMITT score showed promising results in external validation.

CONCLUSION

Patients with small bowel bleeding pose a challenge to clinicians, as rebleeding is observed even in patients with negative endoscopic findings on CE or DAE. Regular surveillance with follow-up visits are essential as rebleeding courses with increased morbidity; however, regular surveillance or referral to specialists for small bowel bleeding patients is not beneficial and problematic when there is limited health care resources. Therefore, there is a need for individualized surveillance strategies from simple watch-and-wait to regular short-interval follow-up, but no specific guidelines have been suggested. Scores assessing bleeding risks have been proposed and used in clinical practice, including HAS-BLED, HEMORR2HAGES, ORBIT, and ATRIA, which are widely used scores to identify patients at greater risk of bleeding, but they are scores created for specific population that predicts overall GI bleeding. Thus, the application of these scores to small bowel bleeding is limited. In addition, small bowel bleeding is more challenging to manage compared with upper GI bleeding or lower GI bleeding because it is not identified during initial examinations with EGD and colonoscopy.

Clinicians must consider various factors when stratifying patients with OGIB who are at risk of rebleeding. Identifying the source of bleeding is essential as it provides a treatment guide on which specific treatment intervention is needed. However, the diagnostic yield of CE can vary and isolated small bowel lesions can be missed if it is not captured during the limited amount of time the capsule passes, presence of bubbles or debris can reduce visibility and targeted observation is impossible as movement of capsule depends solely on peristaltic movement of the intestine. Once the lesion is identified, targeted treatment can be applied; moreover, studies have shown that appropriate intervention can reduce the risk of rebleeding[31,34,36,49]. Long term (more than 2 years) observational studies have shown that rebleeding can occur even in cases of negative CE; these findings suggests that negative CE does not imply the absence of a bleeding lesion. However, negative predict value of normal CE is high and studies have shown that rebleeding in patients with negative CE is lower compared to positive CE. Medications including steroids, NSAIDs, and anticoagulants are well known risk factors in overall GI bleeding and studies have shown that anticoagulants are also associated with risk of

rebleeding in OGIB[26,33,34].

Many studies from eastern and western countries have analyzed different factors associated with rebleeding; however, limited meta-analysis data and discrepancies between studies are challenges faced in creating generalized risk prediction model. As such, the authors of different prediction models described in this article used the pool of data from their centers, grouped patients into rebleeding and non-rebleeding, analyzed risk factors from that patient population, and created a prediction model that best identify high risk patients. With the exception of ORBIT score that was created to assess generalized bleeding risk, other scores were targeted specifically for patients with OGIB; moreover, the Ohmiya index only uses comorbidities as variables in prediction model. Other prediction models include CE findings or specific treatment interventions as part of variables which means that patients must undergo CE and DAE, which are required by some prediction models to identify patients at high risk of rebleeding. However, CE and DAE are not available in resource limited centers and primary physicians; hence, the ORBIT score or Ohmiya index may be used as an alternative measure. When available, the RHEMITT score, PRSBB score, and prediction model using 5 variables may be more appropriate for patients with OGIB; however, the lack of external validation for the PRSBB score and prediction model using 5 variables limits their generalized. This is why the RHEMITT score looks promising as high AUROC has also been validated in two other validation studies.

We described available prognostic prediction models for rebleeding in patients with small bowel bleeding that may aid clinicians in identifying at-risk patients and in forming surveillance strategies targeted for individual patients. Although some prognostic models require further prospective studies and external validation, future studies on larger and heterogeneous cohorts will provide effective scoring systems that will provide important guidance to clinicians in managing patients with small bowel bleeding.

FOOTNOTES

Author contributions: Kim JH and Nam SJ wrote the manuscript; and Nam SJ supervised the reported work.

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REFERENCES

- 1 Lanas A, García-Rodríguez LA, Polo-Tomás M, Ponce M, Alonso-Abreu I, Perez-Aisa MA, Perez-Gisbert J, Bujanda L, Castro M, Muñoz M, Rodrigo L, Calvet X, Del-Pino D, Garcia S. Time trends and impact of upper and lower gastrointestinal bleeding and perforation in clinical practice. *Am J Gastroenterol* 2009; **104**: 1633-1641 [PMID: 19574968 DOI: 10.1038/ajg.2009.164]
- 2 Mujtaba S, Chawla S, Massaad JF. Diagnosis and Management of Non-Variceal Gastrointestinal Hemorrhage: A Review of Current Guidelines and Future Perspectives. *J Clin Med* 2020; **9** [PMID: 32024301 DOI: 10.3390/jcm9020402]
- 3 Gerson LB, Fidler JL, Cave DR, Leighton JA. ACG Clinical Guideline: Diagnosis and Management of Small Bowel Bleeding. *Am J Gastroenterol* 2015; **110**: 1265-87; quiz 1288 [PMID: 26303132 DOI: 10.1038/ajg.2015.246]
- 4 Lau WY, Fan ST, Wong SH, Wong KP, Poon GP, Chu KW, Yip WC, Wong KK. Preoperative and intraoperative localisation of gastrointestinal bleeding of obscure origin. *Gut* 1987; **28**: 869-877 [PMID: 3498667 DOI: 10.1136/gut.28.7.869]
- 5 Saperas E, Dot J, Videla S, Alvarez-Castells A, Perez-Lafuente M, Armengol JR, Malagelada JR. Capsule endoscopy versus computed tomographic or standard angiography for the diagnosis of obscure gastrointestinal bleeding. *Am J Gastroenterol* 2007; **102**: 731-737 [PMID: 17397406 DOI: 10.1111/j.1572-0241.2007.01058.x]
- 6 Estévez E, González-Conde B, Vázquez-Iglesias JL, de Los Angeles Vázquez-Millán M, Pértiga S, Alonso PA, Clofent J, Santos E, Ulla JL, Sánchez E. Diagnostic yield and clinical outcomes after capsule endoscopy in 100 consecutive patients with obscure gastrointestinal bleeding. *Eur J Gastroenterol Hepatol* 2006; **18**: 881-888 [PMID: 16825907 DOI: 10.1097/00042737-200608000-00014]

- 7 **Lecleire S**, Iwanicki-Caron I, Di-Fiore A, Elie C, Alhameedi R, Ramirez S, Hervé S, Ben-Soussan E, Ducrotté P, Antonietti M. Yield and impact of emergency capsule enteroscopy in severe obscure-overt gastrointestinal bleeding. *Endoscopy* 2012; **44**: 337-342 [PMID: [22389234](#) DOI: [10.1055/s-0031-1291614](#)]
- 8 **Robinson CA**, Jackson C, Condon D, Gerson LB. Impact of inpatient status and gender on small-bowel capsule endoscopy findings. *Gastrointest Endosc* 2011; **74**: 1061-1066 [PMID: [21924720](#) DOI: [10.1016/j.gie.2011.07.019](#)]
- 9 **Sidhu R**, Sanders DS, Kapur K, Leeds JS, McAlindon ME. Factors predicting the diagnostic yield and intervention in obscure gastrointestinal bleeding investigated using capsule endoscopy. *J Gastrointest Liver Dis* 2009; **18**: 273-278 [PMID: [19795019](#)]
- 10 **Yamada A**, Watabe H, Kobayashi Y, Yamaji Y, Yoshida H, Koike K. Timing of capsule endoscopy influences the diagnosis and outcome in obscure-overt gastrointestinal bleeding. *Hepatogastroenterology* 2012; **59**: 676-679 [PMID: [22469708](#) DOI: [10.5754/hge12180](#)]
- 11 **Pennazio M**, Santucci R, Rondonotti E, Abbiati C, Beccari G, Rossini FP, De Franchis R. Outcome of patients with obscure gastrointestinal bleeding after capsule endoscopy: report of 100 consecutive cases. *Gastroenterology* 2004; **126**: 643-653 [PMID: [14988816](#) DOI: [10.1053/j.gastro.2003.11.057](#)]
- 12 **Lai LH**, Wong GL, Chow DK, Lau JY, Sung JJ, Leung WK. Long-term follow-up of patients with obscure gastrointestinal bleeding after negative capsule endoscopy. *Am J Gastroenterol* 2006; **101**: 1224-1228 [PMID: [16771942](#) DOI: [10.1111/j.1572-0241.2006.00565.x](#)]
- 13 **Iwamoto J**, Mizokami Y, Shimokobe K, Yara S, Murakami M, Kido K, Ito M, Hirayama T, Saito Y, Honda A, Ikegami T, Ohara T, Matsuzaki Y. The clinical outcome of capsule endoscopy in patients with obscure gastrointestinal bleeding. *Hepatogastroenterology* 2011; **58**: 301-305 [PMID: [21661386](#)]
- 14 **Mussetto A**, Fuccio L, Dari S, Gasperoni S, Cantoni F, Brancaccio ML, Triossi O, Casetti T. MiroCam capsule for obscure gastrointestinal bleeding: a prospective, single centre experience. *Dig Liver Dis* 2013; **45**: 124-128 [PMID: [22999594](#) DOI: [10.1016/j.dld.2012.08.016](#)]
- 15 **Katsinelos P**, Lazaraki G, Gkagkalis A, Gatopoulou A, Patsavela S, Varitimadis K, Mimidis K, Paroutoglou G, Koufokotsios A, Maris T, Terzoudis S, Gigi E, Chatzimavroudis G, Zavos C, Kountouras J. The role of capsule endoscopy in the evaluation and treatment of obscure-overt gastrointestinal bleeding during daily clinical practice: a prospective multicenter study. *Scand J Gastroenterol* 2014; **49**: 862-870 [PMID: [24940823](#) DOI: [10.3109/00365521.2014.889209](#)]
- 16 **Ormeci A**, Akyuz F, Baran B, Gokturk S, Ormeci T, Pinarbasi B, Soyer OM, Evirgen S, Akyuz U, Karaca C, Demir K, Kaymakoglu S, Besisik F. What is the impact of capsule endoscopy in the long term period? *World J Gastrointest Endosc* 2016; **8**: 344-348 [PMID: [27076873](#) DOI: [10.4253/wjge.v8.i7.344](#)]
- 17 **Yung DE**, Koulaouzidis A, Avni T, Kopylov U, Giannakou A, Rondonotti E, Pennazio M, Eliakim R, Toth E, Plevris JN. Clinical outcomes of negative small-bowel capsule endoscopy for small-bowel bleeding: a systematic review and meta-analysis. *Gastrointest Endosc* 2017; **85**: 305-317.e2 [PMID: [27594338](#) DOI: [10.1016/j.gie.2016.08.027](#)]
- 18 **Raju GS**, Gerson L, Das A, Lewis B; American Gastroenterological Association. American Gastroenterological Association (AGA) Institute medical position statement on obscure gastrointestinal bleeding. *Gastroenterology* 2007; **133**: 1694-1696 [PMID: [17983811](#) DOI: [10.1053/j.gastro.2007.06.008](#)]
- 19 **Tziatzios G**, Gkolfakis P, Hassan C, Toth E, Zullo A, Koulaouzidis A, Dimitriadis GD, Triantafyllou K. Meta-analysis shows similar re-bleeding rates among Western and Eastern populations after index video capsule endoscopy. *Dig Liver Dis* 2018; **50**: 226-239 [PMID: [29396130](#) DOI: [10.1016/j.dld.2017.12.031](#)]
- 20 **Apostolopoulos P**, Liatsos C, Gralnek IM, Kalantzis C, Giannakouloupoulou E, Alexandrakis G, Tsibouris P, Kalafatis E, Kalantzis N. Evaluation of capsule endoscopy in active, mild-to-moderate, overt, obscure GI bleeding. *Gastrointest Endosc* 2007; **66**: 1174-1181 [PMID: [18061718](#) DOI: [10.1016/j.gie.2007.06.058](#)]
- 21 **Delvaux M**, Fassler I, Gay G. Clinical usefulness of the endoscopic video capsule as the initial intestinal investigation in patients with obscure digestive bleeding: validation of a diagnostic strategy based on the patient outcome after 12 months. *Endoscopy* 2004; **36**: 1067-1073 [PMID: [15578296](#) DOI: [10.1055/s-2004-826034](#)]
- 22 **Rastogi A**, Schoen RE, Slivka A. Diagnostic yield and clinical outcomes of capsule endoscopy. *Gastrointest Endosc* 2004; **60**: 959-964 [PMID: [15605012](#) DOI: [10.1016/s0016-5107\(04\)02226-6](#)]
- 23 **Viazis N**, Papaxoinis K, Vlachogiannakos J, Efthymiou A, Theodoropoulos I, Karamanolis DG. Is there a role for second-look capsule endoscopy in patients with obscure GI bleeding after a nondiagnostic first test? *Gastrointest Endosc* 2009; **69**: 850-856 [PMID: [18950762](#) DOI: [10.1016/j.gie.2008.05.053](#)]
- 24 **Saurin JC**, Delvaux M, Gaudin JL, Fassler I, Villarejo J, Vahedi K, Bitoun A, Canard JM, Souquet JC, Ponchon T, Florent C, Gay G. Diagnostic value of endoscopic capsule in patients with obscure digestive bleeding: blinded comparison with video push-enteroscopy. *Endoscopy* 2003; **35**: 576-584 [PMID: [12822092](#) DOI: [10.1055/s-2003-40244](#)]
- 25 **Lorenceanu-Savale C**, Ben-Soussan E, Ramirez S, Antonietti M, Lerebours E, Ducrotté P. Outcome of patients with obscure gastrointestinal bleeding after negative capsule endoscopy: results of a one-year follow-up study. *Gastroenterol Clin Biol* 2010; **34**: 606-611 [PMID: [20822872](#) DOI: [10.1016/j.gcb.2010.06.009](#)]
- 26 **Koh SJ**, Im JP, Kim JW, Kim BG, Lee KL, Kim SG, Kim JS, Jung HC. Long-term outcome in patients with obscure gastrointestinal bleeding after negative capsule endoscopy. *World J Gastroenterol* 2013; **19**: 1632-1638 [PMID: [23539070](#) DOI: [10.3748/wjg.v19.i10.1632](#)]
- 27 **Laine L**, Sahota A, Shah A. Does capsule endoscopy improve outcomes in obscure gastrointestinal bleeding? Randomized trial versus dedicated small bowel radiography. *Gastroenterology* 2010; **138**: 1673-1680.e1; quiz e11 [PMID: [20138043](#) DOI: [10.1053/j.gastro.2010.01.047](#)]
- 28 **Liu B**, Liu S, Wen P, Wang S, Wang F, Gu X. Risk factors for rebleeding in patients with obscure gastrointestinal bleeding from southern China. *J Int Med Res* 2021; **49**: 3000605211028422 [PMID: [34605303](#) DOI: [10.1177/03000605211028422](#)]
- 29 **Wetwittayakhlang P**, Wonglhow J, Netinatsunton N, Chamroonkul N, Piratvisuth T. Re-bleeding and its predictors after capsule endoscopy in patients with obscure gastrointestinal bleeding in long-term follow-up. *BMC Gastroenterol* 2019; **19**: 216 [PMID: [31842770](#) DOI: [10.1186/s12876-019-1137-3](#)]

- 30 **Kim JB**, Ye BD, Song Y, Yang DH, Jung KW, Kim KJ, Byeon JS, Myung SJ, Yang SK, Kim JH. Frequency of rebleeding events in obscure gastrointestinal bleeding with negative capsule endoscopy. *J Gastroenterol Hepatol* 2013; **28**: 834-840 [PMID: 23425190 DOI: 10.1111/jgh.12145]
- 31 **Baba Y**, Kawano S, Kono Y, Inokuchi T, Kanzaki H, Iwamuro M, Harada K, Hiraoka S, Kawahara Y, Okada H. Clinical Characteristics and Risk Factors for Rebleeding in Patients with Obscure Gastrointestinal Bleeding. *Intern Med* 2020; **59**: 1345-1350 [PMID: 32023585 DOI: 10.2169/internalmedicine.3628-19]
- 32 **Kim Y**, Kim JH, Kang EA, Park SJ, Park JJ, Cheon JH, Kim TI, Park J, Jeon SR. Rebleeding Rate and Risk Factors for Rebleeding after Device-Assisted Enteroscopy in Patients with Obscure Gastrointestinal Bleeding: A KASID Multicenter Study. *Diagnostics (Basel)* 2022; **12** [PMID: 35454002 DOI: 10.3390/diagnostics12040954]
- 33 **Magalhães-Costa P**, Bispo M, Santos S, Couto G, Matos L, Chagas C. Re-bleeding events in patients with obscure gastrointestinal bleeding after negative capsule endoscopy. *World J Gastrointest Endosc* 2015; **7**: 403-410 [PMID: 25901220 DOI: 10.4253/wjge.v7.i4.403]
- 34 **Otani K**, Shimada S, Watanabe T, Nadatani Y, Higashimori A, Ominami M, Fukunaga S, Hosomi S, Kamata N, Tanaka F, Nagami Y, Taira K, Fujiwara Y. Long-term rebleeding rate and predictive factors of rebleeding after capsule endoscopy in patients with obscure GI bleeding. *Gastrointest Endosc* 2022; **96**: 956-969.e3 [PMID: 35850171 DOI: 10.1016/j.gie.2022.07.012]
- 35 **Hung HJ**, Chung CS, Tai CM, Chang CW, Tseng CM, Huang GS, Lin MC, Huang TY. Clinical characteristics and risk factors for rebleeding in uremic patients with obscure gastrointestinal bleeding undergoing deep enteroscopy: A multicenter retrospective study in Taiwan. *PLoS One* 2022; **17**: e0277434 [PMID: 36449459 DOI: 10.1371/journal.pone.0277434]
- 36 **Esaki M**, Matsumoto T, Yada S, Yanaru-Fujisawa R, Kudo T, Yanai S, Nakamura S, Iida M. Factors associated with the clinical impact of capsule endoscopy in patients with overt obscure gastrointestinal bleeding. *Dig Dis Sci* 2010; **55**: 2294-2301 [PMID: 19957038 DOI: 10.1007/s10620-009-1036-5]
- 37 **Uchida G**, Hirooka Y, Nakamura M, Watanabe O, Yamamura T, Matsushita M, Suhara H, Ishikawa T, Furukawa K, Funasaka K, Ohno E, Kawashima H, Miyahara R, Goto H. Nomogram-based prediction of rebleeding in small bowel bleeding patients: the 'PRSB' score. *Sci Rep* 2018; **8**: 6378 [PMID: 29686230 DOI: 10.1038/s41598-018-24868-0]
- 38 **Niikura R**, Yamada A, Nagata N, Kobayashi Y, Okamoto M, Mitsuno Y, Ogura K, Yoshida S, Shimbo T, Hirata Y, Koike K. New predictive model of rebleeding during follow-up of patients with obscure gastrointestinal bleeding: A multicenter cohort study. *J Gastroenterol Hepatol* 2016; **31**: 752-760 [PMID: 26487158 DOI: 10.1111/jgh.13201]
- 39 **O'Brien EC**, Simon DN, Thomas LE, Hylek EM, Gersh BJ, Ansell JE, Kowey PR, Mahaffey KW, Chang P, Fonarow GC, Pencina MJ, Piccini JP, Peterson ED. The ORBIT bleeding score: a simple bedside score to assess bleeding risk in atrial fibrillation. *Eur Heart J* 2015; **36**: 3258-3264 [PMID: 26424865 DOI: 10.1093/eurheartj/ehv476]
- 40 **Cúrdia Gonçalves T**, Arieira C, Monteiro S, Rosa B, Moreira MJ, Cotter J. ORBIT score: an useful predictor of small bowel rebleeding in patients under chronic anticoagulation. *Scand J Gastroenterol* 2018; **53**: 179-184 [PMID: 29216785 DOI: 10.1080/00365521.2017.1410568]
- 41 **Ohmiya N**, Nakamura M, Osaki H, Yamada H, Tahara T, Nagasaka M, Nakagawa Y, Shibata T, Tsukamoto T, Kuroda M. Development of a Comorbidity Index to Identify Patients With Small Bowel Bleeding at Risk for Rebleeding and Small Bowel Vascular Diseases. *Clin Gastroenterol Hepatol* 2019; **17**: 896-904.e4 [PMID: 30130626 DOI: 10.1016/j.cgh.2018.08.034]
- 42 **Harada A**, Torisu T, Fujioka S, Yoshida Y, Okamoto Y, Fuyuno Y, Hirano A, Umeno J, Torisu K, Moriyama T, Esaki M, Kitazono T. Risk of Rebleeding in Patients with Small Bowel Vascular Lesions. *Intern Med* 2021; **60**: 3663-3669 [PMID: 34120996 DOI: 10.2169/internalmedicine.6341-20]
- 43 **Pérez-Cuadrado Robles E**, Perrod G, Moreels TG, Zamora Nava LE, Blanco Velasco G, Esteban Delgado P, Samaha E, Hernández-Mondragón ÓV, Rahmi G, Cellier C. A comprehensive systematic review and meta-analysis of risk factors for rebleeding following device-assisted enteroscopy therapy of small-bowel vascular lesions. *Rev Esp Enferm Dig* 2020; **112**: 249-257 [PMID: 32193939 DOI: 10.17235/reed.2020.6802/2019]
- 44 **Ohmiya N**. Management of obscure gastrointestinal bleeding: Comparison of guidelines between Japan and other countries. *Dig Endosc* 2020; **32**: 204-218 [PMID: 31596970 DOI: 10.1111/den.13554]
- 45 **de Sousa Magalhães R**, Cúrdia Gonçalves T, Rosa B, Moreira MJ, Sousa-Pinto B, Cotter J. RHEMITT Score: Predicting the Risk of Rebleeding for Patients with Mid-Gastrointestinal Bleeding Submitted to Small Bowel Capsule Endoscopy. *Dig Dis* 2020; **38**: 299-309 [PMID: 31743910 DOI: 10.1159/000504385]
- 46 **Silva JC**, Pinho R, Ponte A, Rodrigues A, Ribeiro Gomes AC, Afeto E, Carvalho J. Predicting the risk of rebleeding after capsule endoscopy in obscure gastrointestinal bleeding - External validation of the RHEMITT Score. *Dig Dis* 2020 [PMID: 32640455 DOI: 10.1159/000509986]
- 47 **de Sousa Magalhães R**, Sousa-Pinto B, Boal Carvalho P, Rosa B, Moreira MJ, Cotter J. RHEMITT score: Predicting the risk of mid gastrointestinal rebleeding after small bowel capsule endoscopy: A prospective validation. *J Gastroenterol Hepatol* 2022; **37**: 310-318 [PMID: 34555864 DOI: 10.1111/jgh.15695]
- 48 **Boortalary T**, Erwin R, Dong M, Shinn B, Infantolino A, Tofani C. RHEMITT Score Predicts Rebleed After Capsule Endoscopy: First Validation at a U.S. Tertiary Care Center. *Dig Dis Sci* 2023; **68**: 187-192 [PMID: 35543830 DOI: 10.1007/s10620-022-07527-3]
- 49 **Endo H**, Matsushashi N, Inamori M, Akimoto K, Ohya T, Yanagawa T, Asayama M, Hisatomi K, Teratani T, Fujita K, Yoneda M, Nakajima A. Rebleeding rate after interventional therapy directed by capsule endoscopy in patients with obscure gastrointestinal bleeding. *BMC Gastroenterol* 2008; **8**: 12 [PMID: 18430253 DOI: 10.1186/1471-230X-8-12]



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