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Development and validation of a new scoring system to determine the necessity of small-bowel endoscopy in obscure gastrointestinal bleeding

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ABSTRACT

Background: Small bowel capsule endoscopy (SBCE) is the recommended first-line procedure for obscure gastrointestinal bleeding (OGIB). However, a method for predicting the necessity of subsequent double-balloon endoscopy (DBE) has not been established.
Aims: We aimed to develop a new scoring system that predicts the necessity of DBE in OGIB.
Methods: A retrospective study was performed in 330 patients who underwent SBCE for OGIB at Nagoya University Hospital. The enrolled patients were randomly assigned to either a development or a validation dataset. The former was used to construct a prediction scoring system to assess the necessity of DBE using independent predictors selected by logistic regression. The diagnostic yield of the prediction model was assessed using the validation dataset.
Results: Multivariate logistic regression analysis of the development dataset identified OGIB type, blood transfusion, and SBCE findings as independent predictors of the necessity of DBE. A prediction score gave an area under the receiver operating characteristics curve of 0.77. The sensitivity, specificity, positive predictive value, and negative predictive value at a cutoff ≥2.5 points were 72.5%, 74.6%, 72.6%, and 74.5%, respectively.
Conclusion: Our scoring system may aid clinicians in deciding when to recommend DBE for patients with OGIB.

1. Introduction

Small bowel capsule endoscopy (SBCE) and double-balloon endoscopy (DBE) are excellent tools for the diagnosis and treatment of obscure gastrointestinal bleeding (OGIB). The diagnostic yields of SBCE and DBE are similar [1]; further, SBCE allows painless endoscopic imaging of the entire small bowel [2] and shows localization of lesions before DBE [3]. The rebleeding rate after a normal capsule examination is very low, and conservative management is appropriate in these patients [4]. Since SBCE has a high negative predictive value (NPV), an SBCE-guided DBE approach has been developed to avoid DBE in patients with low pretest probability for small bowel findings [5]. In addition, SBCE increases the diagnostic and therapeutic yields of DBE [6]. Therefore, several guidelines for the management of small bowel bleeding recommend SBCE as the first-line procedure for diagnosis [7–9].

Although SBCE may be a useful screening tool before DBE in patients with OGIB, it can neither obtain tissue for histology nor provide endoscopic therapy. In addition, the administration of SBCE and interpretation of capsule images are time-consuming, particularly in cases of massive bleeding. SBCE also presents a risk of capsule retention. DBE enables endoscopic procedures such as tis-

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sue sampling and hemostasis. OGIB patients occasionally require detailed diagnosis followed by rapid treatment by DBE. However, complications such as post-procedure abdominal pain, pancreatitis, bleeding, and small bowel perforation have been associated with the procedure [7]. Furthermore, some lesions, such as small lymphangioma, do not require endoscopic procedures and are reportedly difficult to detect with DBE, even though it is the gold standard diagnostic tool [10].

Although DBE is not always necessary in OGIB patients with positive SBCE findings, a method for predicting the necessity of DBE has not been established. The purpose of this study was to develop a new and simple numerical scoring system that predicts which OGIB patients require DBE on the basis of clinical profiles, laboratory findings, and SBCE results.

2. Materials and methods

2.1. Study population

Of 1139 patients who underwent SBCE at Nagoya University Hospital between June 2004 and December 2015, 386 patients with OGIB were selected. OGIB was defined as overt bleeding or recurrent occult fecal bleeding with iron deficiency anemia of unknown origin, as determined by both conventional esophagogastroduodenoscopy and colonoscopy [11]. Fifty-six patients with lesions outside the small bowel were excluded. Therefore, we retrospectively collected data for 330 referral patients by reviewing their medical records and conducting telephone interviews.

Patients with OGIB were classified as having ongoing overt bleeding (bleeding documented within 48 h of SBCE administration), previous overt bleeding (last episode of bleeding occurring >48 h before SBCE), or occult bleeding (anemia with a positive fecal occult blood test). Patients with overt rebleeding were defined as having hematochezia, melena, and hematemesis. Patients with occult rebleeding were defined as having progressive anemia (drop in hemoglobin of >2 g/dL) [12].

2.2. SBCE procedure

Patients were examined using the PillCam SB (SB, SB2, or SB3; Medtronic Japan Co., Ltd, Tokyo, Japan), which measures 26×11 mm and is propelled by peristalsis. The technical procedures and evaluations of capsule images have been described previously [1]. Patients who experienced incomplete SBCE or complete SBCE with poor small bowel visibility underwent DBE without a second SBCE, and their SBCE findings were evaluated within the range observed with SBCE.

2.3. DBE procedures

Our DBE system (Fujifilm Co., Ltd, Tokyo, Japan) consisted of a video endoscope with an inner diameter biopsy channel of 2.8 mm (EN-450T5) or 3.2 mm (EN-580T), a flexible overtube, and a balloon controller. Details of the insertion method have been described elsewhere [13]. An oral or anal approach for the first examination was selected on the basis of medical history or SBCE results, such as transit time and lesion localization. The cutoff values used for route selection for DBE equated to half of the small bowel transit time in the SBCE complete examination [14]. Further, the localization map in the workstation, a computer system, was used to interpret SBCE images to estimate small bowel location [15]. The preparation for both approaches has been described previously [1]. Patients enrolled in the database were always advised to undergo DBE due to the possibility of false-negative findings with SBCE. Patients were only followed-up with SBCE if they refused to undergo DBE or if they were in very poor general condition. Patients with positive SBCE and negative first examination with DBE received a second DBE with the opposite approach.

2.4. Data analysis

We used a split-sample approach to develop and validate the new scoring system for predicting the necessity of DBE. Enrolled patients were randomly divided into two datasets at a ratio of 2:1 [16,17]. The development dataset was used to develop our predictive scoring model, which was subsequently tested on the validation dataset. Patients in the development dataset were classified as DBE necessary or DBE unnecessary. The DBE-necessary group included patients in whom (1) the SBCE diagnosis differed from the DBE diagnosis, (2) the SBCE diagnosis was confirmed histologically or morphologically by DBE, (3) the final diagnosis could be confirmed only by SBCE but DBE procedures such as hemostasis or tattooing were required, and (4) rebleeding occurred within six months when DBE was not performed. The DBE-unnecessary group included patients in whom (1) the final diagnosis could be confirmed only by SBCE and no DBE procedures were required, (2) rebleeding did not occur within six months after SBCE when DBE was not performed, and (3) no lesion was detected with DBE.

The gold standard in this study was a diagnosis made with DBE. When only SBCE was performed, the final diagnosis was made on the basis of the SBCE result and a six-month follow-up of the clinical course. SBCE findings that explained patient symptoms and resulted in a change in therapeutic management were considered diagnostically positive. SBCE findings included bleeding sources such as vascular lesions (angiodysplasia, arteriovenous malformation, and active bleeding), erosion, tumors, ulcers, and others (e.g., parasitic disease, diverticula).

2.5. Statistical analysis

All analyses were performed with the SPSS statistical software package, version 23 (SPSS Japan, Tokyo). Categorical variables were presented as percentages and were compared with the chi-square test. Numerical variables were summarized as medians. The nonparametric Mann–Whitney U test was used when appropriate for between-group comparisons. For all analyses, a two-sided P value <0.05 indicated statistical significance.

Univariate analysis was performed to determine whether baseline characteristics differed between the DBE-necessary and DBE-unnecessary groups. The lowest blood hemoglobin level was chosen for analysis. To identify the independent predictors of necessary DBE, we constructed multivariate logistic regression models using the variables selected by the univariate analysis.

Multivariate logistic regression analysis was performed using stepwise logistic regression with forward selection and backward elimination. A P value <0.05 was required for entry into the model, and a P value >0.05 resulted in elimination. Results were expressed as odds ratios with 95% confidence intervals (CIs). The discriminatory capacity of the model was assessed using the area under the receiver operating characteristics (ROC) curve. The goodness of fit of the regression model was tested with the Hosmer–Lemeshow test, for which a P value >0.05 indicated a lack of deviation between the model and the observed event rate [18].

To enhance the usefulness of our risk stratification for use in clinical settings, we created a simple scoring model based on the logistic coefficients for each of the multivariable predictors of the necessity of DBE. We rounded the logistic coefficients to the nearest integer and assigned them as points to indicate the presence of each covariate. The sum of all points was calculated as the DBE score for each patient.

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