Use of the NOBLADS Score to Predict Endoscopic Treatment in Patients with Colonic Diverticular Bleeding by Age Stratification

Ayaka Takasu¹, Takashi Ikeya¹, Yasutoshi Shiratorî¹, Zhehao Dai², Takaaki Yoshimoto¹, Kazuki Yamamoto¹, Takeshi Okamoto¹, Shuhei Okuyama¹, Koichi Takagi¹ and Katsuyuki Fukuda¹

Abstract:
Objective  A high NOBLADS score reflecting the severity of lower gastrointestinal bleeding contributes to the identification of stigmata of recent hemorrhage (SRH) in colonic diverticular bleeding (CDB). The burden of colonoscopy is particularly high in elderly patients; therefore, we investigated the utility of the NOBLADS score for managing CDB by age stratification. The NOBLADS score performance in SRH prediction was estimated by the area under the receiver operating characteristic calculation and a multiple logistic regression model.

Methods  This was a single-center, retrospective cohort study. Patients who underwent initial colonoscopy with CDB between April 2008 and December 2019 were divided into a young group (<65 years old) and an elderly group (≥65 years old). We further categorized patients according to colonoscopy findings as SRH-positive, with successful endoscopic hemostasis performance, and SRH-negative, with suspected CDB. The main outcome measure was successful SRH identification.

Results  Four-hundred and seventeen CDB patients were included, of whom 250 (60.0%) were elderly. There were 72 (43.1%) SRH-positive patients in the young group and 94 (37.6%) in the elderly group. The areas under the receiver operating characteristic curves of the NOBLADS score predicting SRH identification were 0.76, 0.71, and 0.81 for all ages, young patients, and elderly patients, respectively. A multiple logistic regression analysis showed that SRH identification was significantly associated with NOBLADS scores in both groups. Eighty-one patients (32.4%) scored ≥4 in the elderly group, and 60 of those were SRH-positive (74.1%). All 27 patients (10.8%) who scored ≥4 with extravasation on computed tomography were found to have SRH.

Conclusion  The NOBLADS score is useful for predicting SRH identification, especially in elderly patients.

Key words: NOBLADS score, colonic diverticular bleeding

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Introduction

Colonic diverticular bleeding (CDB) is the most common cause of acute lower gastrointestinal bleeding (AL-GIB) (1, 2). In approximately 75% of CDB cases, the responsible diverticulum cannot be identified despite endoscopic procedures, and bleeding ceases spontaneously (3, 4). However, some CDB cases develop severe bleeding, which can be life-threatening (4, 5).

The diagnosis of CDB is made through the detection of stigmata of recent hemorrhage (SRH) such as active bleed-
ing (AB), adherent clot (AC), and non-bleeding visible vessels (NBVV) (6). The identification of SRH enables endoscopic treatment, such as endoscopic band ligation (EBL) or endoscopic clips (EC) (6). However, the SRH identification rate is low because of the large and complex surface area of the colon and the multitude of diverticula present (7, 8).

Recently, the NOBLADS score was developed as a scoring system to predict the prognosis of ALGIB (9). This is composed of the following eight factors: use of non-steroid anti-inflammatory drugs; absence of diarrhea; absence of abdominal tenderness; systolic blood pressure ≤100 mmHg; use of antiplatelet therapy, except aspirin; albumin <3 g/dL; Charlson Comorbidity Index ≥2; and presence of syncope. A NOBLADS score ≥4 points reportedly predicts a high risk of a poor prognosis.

We previously reported that a high NOBLADS score prior to endoscopy contributes to the identification of SRH (10). This study examined all age groups and did not take age differences into account. However, the incidence and mortality of CDB is higher in elderly patients than in younger ones (11-13). Furthermore, in clinical practice, it is speculated that colonoscopy should be performed for elderly patients because the burden, including preparation, is higher than for young patients. Therefore, the relationship between CDB and the NOBLADS score should be considered for different age groups.

The present study investigated the usefulness of the NOBLADS score in CDB by age stratification.

### Materials and Methods

#### Study design and patients

The protocol of this study was approved by the institutional research board of St. Luke’s International Hospital (20-R079). This retrospective cohort study included patients with ALGIB who were admitted to St. Luke’s International Hospital, a tertiary referral center in Tokyo, Japan, between April 2008 and December 2020.

A total of 1,002 patients with ALGIB underwent colonoscopy during the study period. We excluded patients whose ALGIB was documented during hospitalization for other reasons or whose causes of bleeding were other than CDB (colorectal cancer, post-polypectomy bleeding, inflammatory bowel disease, ischemic colitis, other colitis, rectal ulcer, vascular ectasia, hemorrhoid, or rectal varices).

#### The diagnosis of CDB

All patients with ALGIB, except those with renal dysfunction or contrast medium allergy, underwent contrast-enhanced computed tomography (CT). For the remaining patients, the decision to perform plain CT was left to the physicians’ discretion.

Colonoscopy was performed with a water-jet scope (PCF-Q260AZI, PCF-Q260JH, PCF-H290L, or GIF-Q260J; Olympus Medical Systems, Tokyo, Japan) with a soft hood (D 201-12704; Olympus Medical Systems) attached after bowel preparation using polyethylene glycol, unless the patient was hemodynamically unstable. Colonoscopy was performed by expert or nonexpert endoscopists under supervision. Expert endoscopists were defined as institutional teaching staff of St. Luke’s International Hospital who were also board-certified members of the Japanese Society of Gastroenterology and had performed more than 5,000 routine colonoscopies. Nonexpert endoscopists were not board-certified but had performed more than 500 routine colonoscopies before performing endoscopic hemostasis. The most frequently performed initial therapy for CDB was EC with Hemoclips (HX-600-090 L, HX-600-135, HX-610-090 L, or HX-610-135; Olympus Optical, Tokyo, Japan) from January 2008 to May 2009, and EBL with a band ligator device (MD-48710 EVL Device or MD-48912B EBL Device; Sumitomo Bake-lite, Tokyo, Japan) from June 2009 to December 2019.

#### Data collection and definition

The following data were obtained from patient medical records: age; sex; comorbidities; use of nonsteroidal anti-inflammatory drugs and antithrombotic agents; symptoms; vital signs upon initial visit; albumin level; CT status and results; colonoscopic findings, including whether or not SRH was identified and the location of diverticula with SRH; and endoscopic procedures (EC and/or EBL). Elderly patients were defined as those ≥65 years old. As for the location of diverticula, cases in the cecum, ascending colon, hepatic flexure, transverse colon, or splenic flexure were defined as in the right-sided colon, and those in the descending or sigmoid colon or rectum were defined as in the left-sided colon. SRH included AB, AC, and NBVV (6). Definite CDB was defined as CDB with SRH, and presumptive CDB was defined as ALGIB with diverticula and no other major colonic lesions or evidence of SRH (6).

We retrospectively calculated the NOBLADS score for each patient based on the data collected at the initial visit. The NOBLADS score comprises the use of non-steroid anti-inflammatory drugs; absence of diarrhea; absence of abdominal tenderness; systolic blood pressure ≤100 mmHg; use of antiplatelet therapy, except aspirin; albumin <3 g/dL; Charlson Comorbidity Index ≥2; and presence of syncope, with 1 point assigned for each item.

#### Statistical analyses

Primary statistical analyses were performed using the IBM SPSS Statistics 24.0 software program (IBM, Armonk, USA) and R 4.0.0 (R Foundation, Vienna, Austria). We compared the baseline characteristics between two groups (young, <65 years old and elderly, ≥65 years old) using the Mann-Whitney U test and the chi-square test for continuous and categorical variables, respectively. A receiver operating characteristic (ROC) curve was generated, and the area under the curve (AUC) and 95% confidence interval (CI) were calculated to determine the best discriminating level of the NOBLADS score to identify SRH. In addition, the sensitiv-
ity, specificity, and positive and negative predictive values were calculated. The NOBLADS score and other clinically significant factors, such as gender, colonoscopy time (early or not), preparation, and findings of CT extravasation, were included in the multivariate logistic regression model. The covariates were selected based on a previous report (8).

A multivariate logistic regression analysis was performed to adjust for potential confounders and to calculate odds ratios (ORs) and 95% CIs for SRH identification among young and elderly patients. Simple and multivariate Cox proportional hazards regression analyses were performed to evaluate hazard ratios (HRs) with their 95% CIs for each possible predictor. All p values were two-sided. A p value <0.05 was considered statistically significant.

Results

Patient characteristics

We recruited 1,002 patients who presented with ALGB, 585 of whom were subsequently excluded. A total of 417 patients were finally included, and 167 (40.0%) were young, while 250 (60.0%) were elderly. There were 72 (43.1%) SRH-positive patients in the young group and 94 (37.6%) in the elderly group (Fig. 1). The baseline characteristics of the 417 patients are described in Table 1. SRH-positive patients presented with more frequent syncope, a lower systolic blood pressure, and higher NOBLADS scores than SRH-negative patients.

Endoscopic findings in the SRH-positive group

Endoscopic findings in the SRH-positive group are reported in Table 2. Most of the treated diverticula were located on the right side, including the cecum and ascending and transverse colon, among both young and elderly individuals. AB was the most common SRH.

NOBLADS score

The median NOBLADS score (interquartile range) was 3 (2-4) and 3 (2-3) in the young and elderly groups, respectively. Distributions of NOBLADS scores were similar in both young and elderly individuals, as shown in Fig. 2. The AUC of the NOBLADS score for predicting SRH identification was 0.76 (95% CI, 0.72-0.80) in the entire population and 0.71 (95% CI, 0.64-0.78) and 0.81 (95% CI, 0.76-0.86) in young and elderly individuals, respectively (Fig. 3).

We determined the optimal cut-off for endoscopic treatment in each group by reviewing the sensitivity, specificity, positive predictive value, and negative predictive value of each score, as shown in Table 3. The optimal cut-off was 4 points for the elderly and 3 points for the young group. A total of 81 patients (32.4%) in the elderly group scored ≥4, and 60 of those were SRH-positive (74.1%). A total of 76 patients (30.4%) in the elderly group scored <3, and 70 of those were SRH-negative (92.1%). Of the 102 young patients with a NOBLADS score of ≥3, a total of 59 (57.8%) were SRH-positive. In the multivariate analysis, the NOBLADS score and extravasation on CT were independent factors for successful SRH identification, and the NOBLADS score tended to have a better predictive performance in the elderly than in the young (Table 4). The SRH identification rate tended to be higher in each subgroup stratified by age and NOBLADS score, which was significant in elderly patients with a NOBLADS score ≥4 points (Fig. 4).

Discussion

This study demonstrated that a higher NOBLADS score was associated with the identification of SRH, particularly
Table 1. Patient Characteristics.

|                      | Young (n=167) | Elderly (n=250) | p value |
|----------------------|--------------|----------------|--------|
| **SRH (+)** | **SRH (-)** | **SRH (+)** | **SRH (-)** |
| Age (years) | 55 (49-59) | 55 (50-62) | 0.77 | 76 (71-83) | 77 (71-84) | 0.70 |
| Male gender | 67 (93.1) | 85 (89.5) | 0.59 | 67 (71.3) | 102 (65.4) | 0.40 |
| Vital sign | | | | | |
| Systolic blood pressure ≤100 mmHg | 26 (36.1) | 20 (21.1) | 0.04 | 21 (22.3) | 7 (4.5) | <0.001 |
| Heart rate >100/min | 24 (33.3) | 24 (25.3) | 0.30 | 23 (24.5) | 27 (17.3) | 0.19 |
| Symptoms | | | | | |
| Absence of diarrhea | 71 (98.6) | 91 (95.8) | 0.39 | 73 (77.7) | 104 (66.7) | 0.08 |
| Absence of abdominal tenderness | 72 (100) | 92 (96.8) | 0.26 | 91 (96.8) | 146 (93.6) | 0.38 |
| Presence of syncope | 35 (48.6) | 19 (20.0) | <0.001 | 20 (21.3) | 8 (5.1) | <0.001 |
| Albumin <3 g/dL | 0 (0) | 3 (3.2) | 0.26 | 15 (16.0) | 9 (5.8) | 0.01 |
| Hypertension | 33 (45.8) | 45 (47.4) | 0.88 | 73 (77.7) | 104 (66.7) | 0.08 |
| Diabetes mellitus | 14 (19.4) | 19 (20.0) | 1.00 | 25 (26.6) | 30 (19.2) | 0.21 |
| Dyslipidemia | 18 (25.0) | 28 (29.5) | 0.60 | 34 (36.2) | 54 (34.0) | 0.78 |
| Chronic kidney disease | 2 (2.8) | 6 (6.3) | 0.47 | 25 (26.6) | 26 (16.7) | 0.07 |
| Dialysis | 1 (1.4) | 2 (2.1) | 1.00 | 7 (7.4) | 0 (0) | 0.001 |
| Cerebrovascular disease | 2 (2.8) | 3 (3.2) | 1.00 | 20 (21.3) | 23 (14.7) | 0.23 |
| Ischemic heart disease | 5 (6.9) | 10 (10.5) | 0.59 | 25 (26.6) | 29 (18.6) | 0.15 |
| Past history of CDB | 13 (18.1) | 20 (21.1) | 0.70 | 18 (19.1) | 39 (25.0) | 0.35 |
| Charlson comorbidity index | 0 (0-1) | 0 (0-1) | 0.96 | 2 (1-3) | 1 (0-2) | 0.95 |
| Medication | | | | | |
| NSAIDs | 5 (6.9) | 3 (3.2) | 0.29 | 14 (14.9) | 16 (10.3) | 0.32 |
| Antiplatelet (nonaspirin) agents | 7 (9.7) | 5 (5.3) | 0.37 | 14 (14.9) | 14 (9.0) | 0.16 |
| Low-dose aspirin | 6 (8.3) | 17 (17.9) | 0.11 | 38 (40.4) | 51 (32.7) | 0.22 |
| Anticoagulants | 3 (4.2) | 7 (7.4) | 0.62 | 17 (18.1) | 23 (14.7) | 0.48 |
| CT | | | | | |
| No CT | 3 (4.2) | 5 (5.3) | 0.92 | 5 (5.3) | 17 (10.8) | 0.23 |
| Plain CT | 4 (5.6) | 6 (6.3) | 0.96 | 9 (9.6) | 19 (12.1) | |
| Contrast CT | 65 (90.3) | 84 (88.4) | 0.84 | 80 (85.1) | 120 (76.9) | |
| Contrast extravasation on CT † | 12 (17.6) | 9 (10.7) | 0.24 | 37 (46.2) | 22 (18.3) | <0.001 |
| Preparation | 6 (8.3) | 86 (90.5) | 0.46 | 81 (86.2) | 139 (89.1) | 0.55 |
| Colonoscopy within 24 h | 55 (76.4) | 71 (74.7) | 0.86 | 76 (80.9) | 119 (76.3) | 0.43 |
| NOBLADS score | 3 (3-4) | 2 (2-3) | <0.001 | 4 (3-4) | 3 (2-3) | <0.001 |

Results are presented as median (interquartile range) or number (%), unless noted otherwise. CDB: colonic diverticular bleeding, NSAIDs: nonsteroidal anti-inflammatory drugs, CT: computed tomography.

†Percentage presented is calculated with the denominator being the number of patients who had taken contrast CT.

Table 2. Endoscopic Findings in SRH-positive Group.

|                      | Young (n=72) | Elderly (n=94) | p value |
|----------------------|--------------|----------------|--------|
| **SRH** | | | |
| Location of the treated diverticular, n (%) | | | |
| Right side | 54 (75.0) | 65 (69.1) | 0.407 |
| Left side | 18 (25.0) | 29 (30.9) | |
| Stigmata of recent hemorrhage, n (%) | | | |
| Active bleeding (AB) | 28 (38.9) | 40 (42.6) | 0.575 |
| Nonbleeding visible vessel (NBV) | 21 (29.2) | 29 (30.9) | |
| Adherent clot (AC) | 23 (31.9) | 25 (26.6) | |

SRH: stigmata of recent hemorrhage.

in elderly patients. Higher NOBLADS scores, when combined with positive extravasation on contrast CT, further increased the positive predictive value for SRH identification, particularly in elderly patients. Another major finding of this study is that the cut-off values for the NOBLADS score for identifying SRH differed between the young and elderly patients at 3 and 4 points, respectively. To our knowledge, this is the first attempt to provide evidence concerning the use-
fulness of the NOBLADS score in endoscopic hemostasis for CDB, taking age into consideration.

We previously reported that a high NOBLADS score before colonoscopy and extravasation on CT contribute to increased SRH identification rates (10). However, in clinical practice, a scoring system for elderly ALGIB patients is required to assist in the decision to perform colonoscopy, given the huge burden and increased comorbidities within this group. Besides suggesting that young and elderly patients had different cut-off values for the NOBLADS score to identify SRH, our results suggest that the NOBLADS score to predict SRH might be more useful in elderly patients than in young patients. This may be due to the items included in the NOBLADS score, as elderly patients with high NOBLADS scores may have more comorbidities, such as hypoalbuminemia; present with a higher disease score; and take more medication, such as antithrombotic agents. In contrast, in young patients with high scores, score items such as syncope, blood pressure, and pulse rate may reflect transient or variable conditions, as represented by the vagal reflex. We therefore believe that the NOBLADS score can identify severe cases more efficiently in elderly patients than in younger ones.

Many scoring systems for ALGIB have been reported (9, 14-16); most include outcomes of length of hospital stay and blood transfusion, but none have endoscopic

Figure 2. The distributions of NOBLADS scores in the young and elderly groups.

Figure 3. The receiver operating characteristics curves of the NOBLADS score for predicting SRH identification, along with the AUC in all ages, as well as the young and elderly groups. AUC: area under the curve, SRH: stigmata recent hemorrhage, CI: confidence interval.
Table 3. Each Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value Using NOBLADS Score.

| Cut-off | Sensitivity | Specificity | PPV | NPV | Sensitivity | Specificity | PPV | NPV |
|---------|-------------|-------------|-----|-----|-------------|-------------|-----|-----|
|         | Young (n=167) |            |     |     | Elderly (n=250) |            |     |     |
| 0       | 1.00        | 0.00        | 0.57 | -   | 1.00        | 0.00        | 0.38 | -   |
| 1       | 1.00        | 0.00        | 0.57 | -   | 1.00        | 0.00        | 0.38 | -   |
| 2       | 1.00        | 0.03        | 0.44 | 1.00| 1.00        | 0.05        | 0.39 | 1.00|
| 3       | 0.82        | 0.55        | 0.58 | 0.80| 0.94        | 0.45        | 0.51 | 0.92|
| 4       | 0.35        | 0.87        | 0.68 | 0.64| 0.64        | 0.87        | 0.74 | 0.80|
| 5       | 0.07        | 0.98        | 0.71 | 0.58| 0.20        | 0.97        | 0.79 | 0.67|
| 6       | 0.00        | 1.00        | 0.06 | 1.00| 0.06        | 1.00        | 1.00 | 0.64|
| 7       | 0.00        | 1.00        | 0.01 | 1.00| 0.01        | 1.00        | 1.00 | 0.63|
| 8       | 0.00        | 1.00        | 0.00 | 1.00| 0.00        | 1.00        | 1.00 | 0.62|

PPV: positive predictive value, NPV: negative predictive value.

Table 4. Univariate and Multivariate Analysis Comparing Risk Factors SRH Identification between Young and Elderly.

|                  | Young (Crude OR 95% CI) | p value | Adjusted OR 95% CI | p value | Elderly (Crude OR 95% CI) | p value | Adjusted OR 95% CI | p value |
|------------------|-------------------------|---------|--------------------|---------|--------------------------|---------|--------------------|---------|
| NOBLADS score≥3  | 5.49 (2.73-11.68)       | <0.001  | 6.72 (3.05-14.79)  | <0.001  | 11.34 (6.18-21.57)       | 2x10^-14| 6.74 (2.2-17.55)  | <0.001  |
| Male             | 1.58 (0.51-4.83)        | 0.43    | 1.74 (0.51-5.92)   | 0.37    | 1.31 (0.75-2.92)         | 0.34    | 1.75 (0.53-6.39)  | 0.37    |
| Colonoscopy within 24h | 1.09 (0.54-2.23)      | 0.81    | 1.10 (0.50-2.41)   | 0.82    | 1.31 (0.70-2.47)         | 0.40    | 1.09 (0.50-2.42)  | 0.83    |
| Preparation      | 0.65 (0.25-1.69)        | 0.38    | 1.00 (0.25-2.88)   | 0.99    | 0.76 (0.35-1.65)         | 0.49    | 1.00 (0.34-2.90)  | 1.00    |
| CT findings      |                         |         |                    |         |                          |         |                    |         |
| No extravasation on CT | 1.89 (0.75-4.93)      | 0.18    | 3.62 (1.23-11.50)  | 0.023   | 3.83 (2.04-7.34)         | <0.001  | 3.59 (1.72-7.66)  | <0.001  |
| Extravasation on CT| 0.90 (0.31-2.44)       | 0.84    | 0.83 (0.27-2.45)   | 0.74    | 0.88 (0.42-1.78)         | 0.74    | 0.81 (0.34-1.83)  | 0.061   |

CT: computed tomography, SRH: stigmata of recent hemorrhage, OR: odds ratio, CI: confidence interval.

NOBLADS score, gender, colonoscopy time (early or not), preparation, and findings of CT extravasation, were included in the multivariate logistic regression model.

Table 3: The table shows the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for different cut-off values of the NOBLADS score in young and elderly patients. The NOBLADS score is used to predict the presence of stigmata of recent hemorrhage (SRH) in patients with Cushing’s disease (CDB). The table includes the cut-off values, sensitivity, specificity, PPV, and NPV for each group.

Table 4: The table presents the results of univariate and multivariate analysis comparing risk factors for SRH identification between young and elderly patients. The analysis includes variables such as NOBLADS score, gender, colonoscopy time, preparation, and CT findings. The table also includes the odds ratios and confidence intervals for these variables. The results indicate that the NOBLADS score is a predictor of SRH identification.
Figure 4. SRH identification rate when stratified by the presence of extravasation on CT, NOBLADS score, and age, among patients who underwent contrast-enhanced CT. CT: computed tomography, SRH: stigmata of recent hemorrhage

BLADS score ≥4, and those with extravasation on contrast CT are also recommended to undergo colonoscopy. Patients with a NOBLADS score <3 can be managed conservatively, with caution.

Several limitations associated with the present study warrant mention. First, this was a retrospective observational study from a single center and could not avoid unknown confounding factors. Second, bleeding sources in presumptive CDB cases might not be colonic diverticula, which can cause information bias. Third, routine CT may be an unusual practice in many hospitals. Finally, it has been reported in previous studies that colonoscopy preceded by CT offers a high SRH identification rate; therefore, because almost all patients underwent CT in our study, information bias cannot be denied.

In conclusion, the NOBLADS score was useful for predicting SRH identification, especially in elderly patients. The optimal cut-off value for the NOBLADS score differed between young and old patients (3 and 4, respectively).

The authors state that they have no Conflict of Interest (COI).

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