

Successful endoscopic hemostasis compared to transarterial embolization in patients with colonic diverticular bleeding

Takashi Ueda,¹ Hideki Mori,² Tatsuya Sekiguchi,³ Yusuke Mishima,¹ Masaya Sano,¹ Erika Teramura,¹ Ryutaro Fujimoto,¹ Motoki Kaneko,¹ Hirohiko Nakae,¹ Mia Fujisawa,¹ Masashi Matsushima,¹ and Hidekazu Suzuki^{1,*}

¹Division of Gastroenterology and Hepatology, Department of Internal Medicine and ³Department of Diagnostic Radiology, Tokai University School of Medicine, Isehara, Kanagawa 259-1193, Japan

²Translational Research Center for Gastrointestinal Disorders (TARGID), University of Leuven, Leuven 3000, Belgium

(Received 4 September, 2021; Accepted 13 September, 2021; Released online in J-STAGE as advance publication 26 November, 2021)

Transarterial embolization (TAE) is performed in patients with colonic diverticular bleeding after difficult endoscopic hemostasis or rebleeding. A total of 375 patients with hematochezia at our hospital from 1 April 2016 to 31 March 2020 were retrospectively analysed. Firstly, we compared the group in which hemostasis was achieved by endoscopy alone with the group that eventually underwent TAE. Secondly, we compared the group in which hemostasis was achieved by endoscopy alone, with the group switched to TAE after endoscopic hemostasis failed. The group that eventually underwent TAE had a higher shock index and lower Alb and PT% than the endoscopic hemostasis group. The shock index was correlated with Alb and PT%. When the cut-off value for the shock index was defined as more than 0.740, an OR of 9.500, a positive predictive value (PPV) of 40.0%, a negative predictive value (NPV) of 93.4%, and an accuracy of 80.3% were obtained for predicting a switch to TAE treatment. The greatest risk for TAE was the presence of shock and extravasation on contrast-enhanced CT. A switch to TAE treatment was likely when the shock index was more than 0.740. TAE should be considered in cases with a high shock index and showing extravasation on contrast-enhanced CT.

Key Words: diverticular bleeding, TAE, shock index, extravasation on contrast-enhanced CT examination

Diverticular bleeding is one of the most common causes of acute lower gastrointestinal bleeding.⁽¹⁾ Due to an aging population, the number of diverticular bleeding cases has increased.⁽²⁾ Although in 70–80% of diverticular bleeding cases bleeding stops spontaneously and rarely causes shock,⁽³⁾ some cases are severe, requiring blood transfusions, colorectal resections, or causing death. Emergency hemostasis is often required for active bleeding. Hemostasis methods include endoscopic hemostasis, transarterial embolization (TAE), and surgery. Endoscopic hemostasis is the first choice of treatment for diagnosis and treatment.⁽⁴⁾ However, if endoscopic hemostasis is difficult, TAE and surgery are considered.⁽⁵⁾ Surgery is highly invasive, and TAE is at risk of postoperative intestinal necrosis and contrast-induced nephropathy. Currently, there is insufficient evidence regarding the criteria for TAE adaptation. Here, we conducted a study to compare patients who underwent an endoscopy and those who underwent TAE to determine which patients were eligible for TAE.

Materials and Methods

Study design and population. This was a retrospective, cross-sectional study. Data were extracted from the electronic medical records. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Research Ethics Committee (No. 20R-201; 10 September 2020). Patients hospitalised with hematochezia at our Hospital (tertiary emergency medical facility) from 1 April 2016 to 31 March 2020 were enrolled (Fig. 1). Diverticular bleeding was diagnosed using contrast-enhanced computed tomography (CT) and/or endoscopy. Cases with hematochezia due to causes other than diverticular bleeding were excluded. Patients diagnosed with diverticular bleeding and spontaneous bleeding were excluded from the analysis.

Treatment strategy. Patients included in this study underwent contrast-enhanced CT immediately upon arrival at the hospital, unless they had contraindications to contrast-enhanced CT examinations, such as contrast-enhanced allergies or a history of chronic kidney disease and asthma. Patients who could not undergo contrast-enhanced CT were subjected to simple CT examinations. Eligible patients underwent endoscopy within 24 h of their hospital visit (Fig. 1). An endoscope with a water jet function was used together with a transparent hood. By wearing a transparent tip hood, the bleeding area does not turn red. This means that it is easy to see the field of vision even when there is bleeding or when the diverticulum is in the approaching direction or between the folds, and it is possible to see accurately and quickly from the front.⁽⁶⁾ If bleeding had already stopped at the time of endoscopy, only observation was performed and excluded from this study as spontaneous hemostasis. Active bleeding, visible but not bleeding vessels or adherent clots were defined as signs of recent bleeding due to active diverticular bleeding (stigmata of recent haemorrhage: SRH).^(7,8)

During endoscopy, endoscopic hemostasis using clips was performed when SRH findings were observed (endoscopic clipping group). When the physician in charge judged that endoscopic hemostasis was difficult to achieve or when endoscopy itself appeared difficult to perform due to the patient's condition, TAE was chosen from the beginning without endoscopy (initial TAE group). In cases where endoscopic hemostasis was attempted but was unsuccessful, the treatment was switched to TAE. All cases in which TAE was finally performed were collec-

*To whom correspondence should be addressed.
E-mail: hsuzuki@tokai.ac.jp

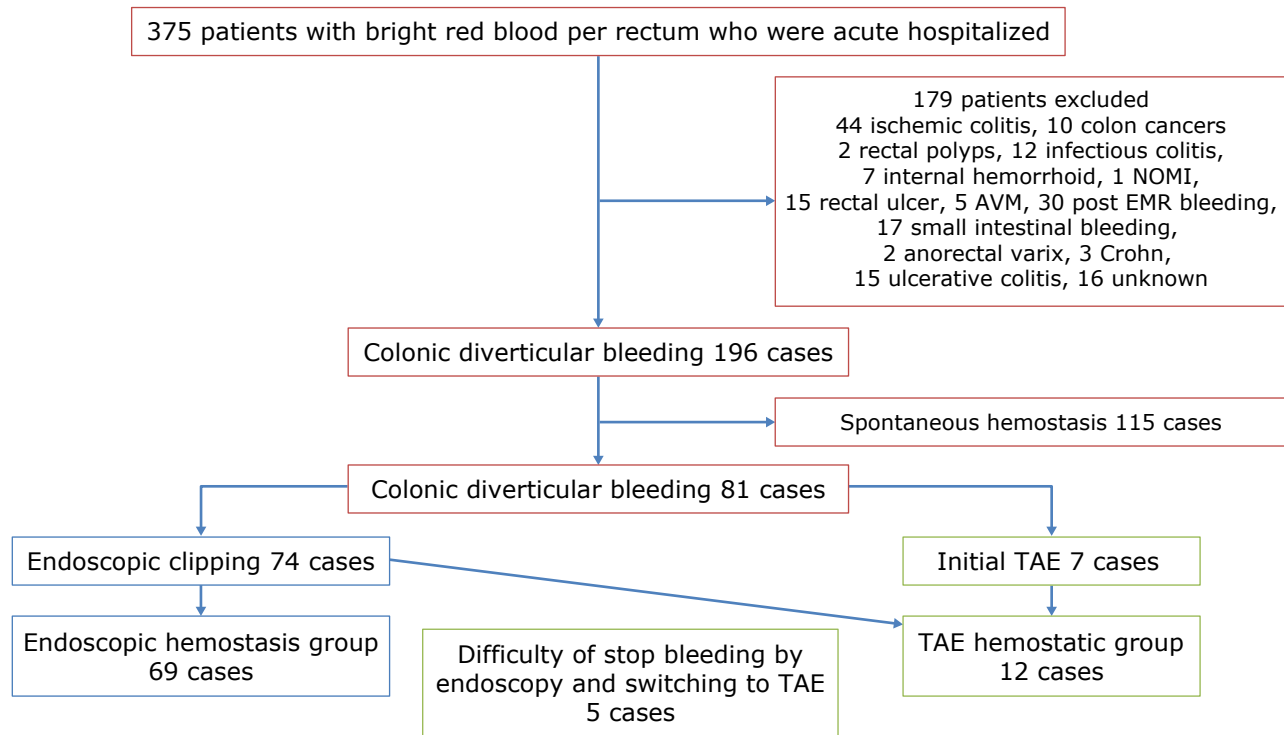


Fig. 1. Flow diagram of this study.

tively defined as the TAE hemostatic group. Patients in whom hemostasis was achieved by endoscopy were defined as the endoscopic hemostasis group.

Outcomes. This study consists of two analyses. Firstly, we compared the factors between the endoscopic hemostasis group and the TAE hemostasis group to investigate what kind of subjects ended up doing the TAE. Secondly, we compared the factors between the endoscopic hemostasis group and the group switched to TAE after endoscopic hemostasis failure to investigate which cases were difficult to achieve endoscopic hemostasis. These analyses were performed by examining electronic medical records for age, sex, drinking, smoking, medical history, shock index, bleeding site, blood sampling, time to TAE, complications, and extravasation on contrast-enhanced CT. The shock index was defined as the heart rate divided by the systolic blood pressure.

Statistics. A Fisher's exact test and Student's *t* test were used to assess the significance of the difference between the two groups, as appropriate. A univariate logistic regression analysis was used to evaluate factors associated with the selection of endoscopic hemostasis or TAE. Subsequently, multivariate logistic regression analysis was performed by adjusting for factors that showed a marginally significant association ($p < 0.1$) in the univariate analysis. Pearson's analysis was performed on the items that showed statistical significance. Using a receiver-operating characteristic (ROC) analysis, the best cut-off value was identified against the risks leading to TAE treatment. All statistical analyses were performed using IBM SPSS Statistics (IBM Corp., Armonk, NY). Statistical significance was defined at a *p* value of < 0.05 . Furthermore, *p* values between 0.05 and 0.1 were defined as marginally significant.

Results

Patient characteristics. A total of 375 patients were admitted to our hospital because of apparent hematochezia

(Fig. 1). Diverticular bleeding was diagnosed using contrast-enhanced CT and/or endoscopy. Of these, 179 patients were excluded due to ischaemic colitis ($n = 44$), colon cancer ($n = 10$), rectal polyps ($n = 2$), infectious colitis ($n = 12$), hemorrhoidal bleeding ($n = 7$), nonocclusive mesenteric ischaemia (NOMI) ($n = 1$), rectal ulcer ($n = 15$), arteriovenous malformation (AVM) ($n = 5$), post-endoscopic mucosal resection (EMR) bleeding ($n = 30$), small intestinal bleeding ($n = 17$), Crohn's disease ($n = 3$), ulcerative colitis ($n = 15$), anorectal varix ($n = 2$), and unknown causes ($n = 16$). Of these, 196 patients were diagnosed with diverticular bleeding, and spontaneous hemostasis was confirmed in these 115 patients. Twenty-three patients were diagnosed with diverticular bleeding by endoscopy, although contrast-enhanced CT could not be performed [asthma only ($n = 3$), CKD ($n = 15$), allergies ($n = 3$), and asthma and CKD ($n = 2$)]. Eventually, 81 patients with active colonic diverticular bleeding requiring endoscopic hemostasis or TAE treatment were analysed. Of the 81 cases, 74 were in the endoscopic clipping group, and seven were in the initial TAE group. Five patients in the endoscopic clipping group were re-allocated to the TAE group due to difficult endoscopic hemostasis. Finally, TAE stopped bleeding in a total of 12 patients, including these five patients and the initial TAE group (TAE hemostatic group). Sixty-nine patients in whom hemostasis was achieved by endoscopy alone were defined as the endoscopic hemostasis group. Eventually, the patients were mostly discharged, but two of the endoscopic hemostasis patients died in a condition different from endoscopic complications.

Risks leading to TAE treatment. Firstly, using the Student's *t* test and Fisher's exact test, we compared the factors between the endoscopic hemostasis and TAE hemostasis groups. There were significant differences in body mass index (BMI), Alb, extravasation by contrast-enhanced CT, and the shock index ($p = 0.040, 0.000, 0.000, 0.001$, respectively) (Table 1). When a univariate logistic analysis was performed for each factor, significant differences were found in the BMI [OR (odds ratio) 0.784; 95% confidence interval (CI) 0.621–0.989], Alb (OR 0.043;

Table 1. Clinical characteristics and risk of the group of endoscopic hemostasis and the group of TAE hemostasis

| | Endoscopic hemostasis | TAE hemostasis | <i>p</i> value | Univariate analysis OR (95% CI) | Multivariate analysis OR (95% CI) |
|--|-----------------------|----------------|--------------------|---------------------------------|-----------------------------------|
| Total number, <i>n</i> | 69 | 12 | | | |
| Age [years (mean ± SD)] | 71.87 ± 10.49 | 75.4 ± 11.5 | 0.296 [†] | 1.034 (0.971–1.101) | |
| Sex, <i>n</i> (%) male | 48 (69.6) | 10 (83.3) | 0.273 [‡] | 0.457 (0.092–2.27) | |
| Smoking, <i>n</i> (%) | 23 (33.3) | 6 (50.0) | 0.214 [‡] | 0.500 (0.145–1.723) | |
| Drinking, <i>n</i> (%) | 23 (33.3) | 4 (33.3) | 0.620 [‡] | 1.00 (0.272–3.671) | |
| BMI [kg/m ² (mean ± SD)] | 24.23 ± 4.48 | 21.4 ± 2.6 | 0.040 [†] | 0.784 (0.621–0.989) | 0.734 (0.513–1.053) |
| History of diverticular bleeding, <i>n</i> (%) | 21 (30.4) | 4 (33.3) | 0.542 [‡] | 0.875 (0.237–3.227) | |
| Medical history, <i>n</i> (%) | | | | | |
| Cerebral infarction | 8 (11.6) | 2 (16.7) | 0.457 [‡] | 0.656 (0.121–3.545) | |
| Heart disease | 22 (31.9) | 7 (58.3) | 0.077 [‡] | 0.334 (0.095–1.172) | |
| Hypertension | 40 (60.0) | 6 (50.0) | 0.607 [‡] | 1.379 (0.404–4.711) | |
| Hyperlipidemia | 17 (24.6) | 4 (33.3) | 0.346 [‡] | 0.615 (0.164–2.314) | |
| Diabetes | 16 (23.1) | 0 (0.0) | 0.335 [‡] | 0.604 (0.161–2.269) | |
| Asthma | 3 (4.3) | 0 (0.0) | 0.760 [‡] | N/A | |
| Kidney disease | 5 (7.2) | 0 (0.0) | 0.629 [‡] | N/A | |
| Contrast media allergy | 0 (0.0) | 0 (0.0) | N/A | N/A | |
| Drug, <i>n</i> (%) | | | | | |
| Antiplatelet | 12 (17.4) | 5 (41.7) | 0.070 [‡] | 0.295 (0.08–1.088) | |
| Anticoagulant | 16 (23.2) | 4 (33.3) | 0.335 [‡] | 0.604 (0.161–2.269) | |
| Blood test | | | | | |
| Hb [g/dl (mean ± SD)] | 11.32 ± 2.71 | 9.89 ± 2.70 | 0.099 [†] | 0.820 (0.646–1.040) | |
| PLT [$\times 10^4/\mu$ l (mean ± SD)] | 21.48 ± 6.77 | 23.29 ± 19.84 | 0.770 [†] | 1.016 (0.963–1.070) | |
| Alb [g/dl (mean ± SD)] | 3.66 ± 0.47 | 2.84 ± 0.55 | 0.000 [†] | 0.043 (0.008–0.217) | 0.057 (0.009–0.349) |
| PT% [% (mean ± SD)] | 84.72 ± 20.66 | 65.67 ± 28.94 | 0.056 [†] | 0.971 (0.948–0.994) | 0.974 (0.937–1.014) |
| Extravasation by contrast-enhanced CT, <i>n</i> (%) | 19 (31.7) | 12 (100) | 0.000 [†] | N/A | |
| The bleeding site is the right hemicolon, <i>n</i> (%) | 39 (56.5) | 9 (75.0) | 0.190 [†] | 0.433 (0.108–1.741) | |
| Shock index (mean ± SD) | 0.62 ± 0.20 | 0.84 ± 0.22 | 0.001 [†] | 44.812 (3.203–626.895) | 4.691 (0.149–147.544) |

Shock index measurement, blood test, and contrast-enhanced CT examination are performed immediately after the visit. TAE, transarterial embolization; BMI, body mass index; Hb, hemoglobin; Alb, albumin; PT%, prothrombin time%; CT, computed tomography; N/A, not applicable. [†]Student's *t* test; [‡]Fisher's exact test.

95% CI 0.008–0.217), PT% (OR 0.971; 95% CI 0.948–0.994), and shock index (OR 44.812; 95% CI 3.203–626.895). Alb was detected as an independent factor in the multivariate logistic analysis (OR 0.057; 95% CI 0.009–0.349) (Table 1). All 12 patients in the TAE hemostatic group had extravasation on contrast-enhanced CT, whereas only 31.7% of the endoscopic hemostasis group had this finding. Hence, extravasation on contrast-enhanced CT could not be analysed using a logistic regression analysis. A linear analysis was performed to investigate the relationship between the shock index, Alb, and PT%, which showed significant differences in the univariate analysis (Fig. 2A). In this model, Alb and PT% were correlated with the shock index ($r = -0.367$, $p = 0.001$; $r = -0.337$, $p = 0.002$, respectively). In addition, to investigate the relationship between anticoagulant medication and PT%, a Student's *t* test was performed (Fig. 2B). A significant increase in PT% was also observed in patients taking anticoagulants ($p = 0.001$). On the other hand, anticoagulants were not identified as risk factors for TAE treatment ($p = 0.335$, Table 1). These data suggest that the shock index, Alb, and PT%, which were detected as risks leading to TAE treatment, indicate a state of shock. ROC curves based on the shock index are shown in Fig. 3. When the cut-off value for the shock index was defined as more than 0.740, an OR of 9.500 (95% CI, 2.458–36.721), a positive predictive value (PPV) of 40.0%, a negative predictive value (NPV) of 93.4%, and an accuracy of 80.3% were obtained for predicting the occurrence of TAE treatment.

Risk of failure in endoscopic hemostasis. Using a Student's *t* test and Fisher's exact test, we compared the endoscopic hemostasis group, and the group switched to TAE due to endoscopic hemostasis failure. Alb, extravasation by contrast-enhanced CT, and the shock index showed significant differences ($p = 0.012$, 0.002, and 0.004, respectively) (Table 2). Using a univariate logistic analysis for each factor, significant differences were found in the antiplatelets (OR 0.140; 95% CI 0.021–0.933), Alb (OR 0.079; 95% CI 0.009–0.663), and shock index (OR 55.268; 95% CI 2.208–1,433.698). The background of the group who switched to TAE due to endoscopic hemostasis failure is shown in Table 3. From this table, three reasons for the difficulty in stopping bleeding. Firstly, multiple diverticula were observed in all cases, and it took time to identify the responsible diverticulum. Secondly, 80% of the patients had bleeding from the ascending colon and required deep insertion. Thirdly, 80% of the patients were taking antithrombotic drugs. These reasons suggest that it may be difficult to stop bleeding using the clip method.

Discussion

TAE achieves immediate hemostasis in 67%–98% of cases of diverticular bleeding with a rebleeding rate ranging from 12% to 50%.^(9–16) While TAE is an effective treatment, the risk of side effects such as intestinal ischaemia, intestinal perforation, lower extremity ischaemia, and contrast-induced nephropathy must be considered, and the selection criteria must be judged appropri-

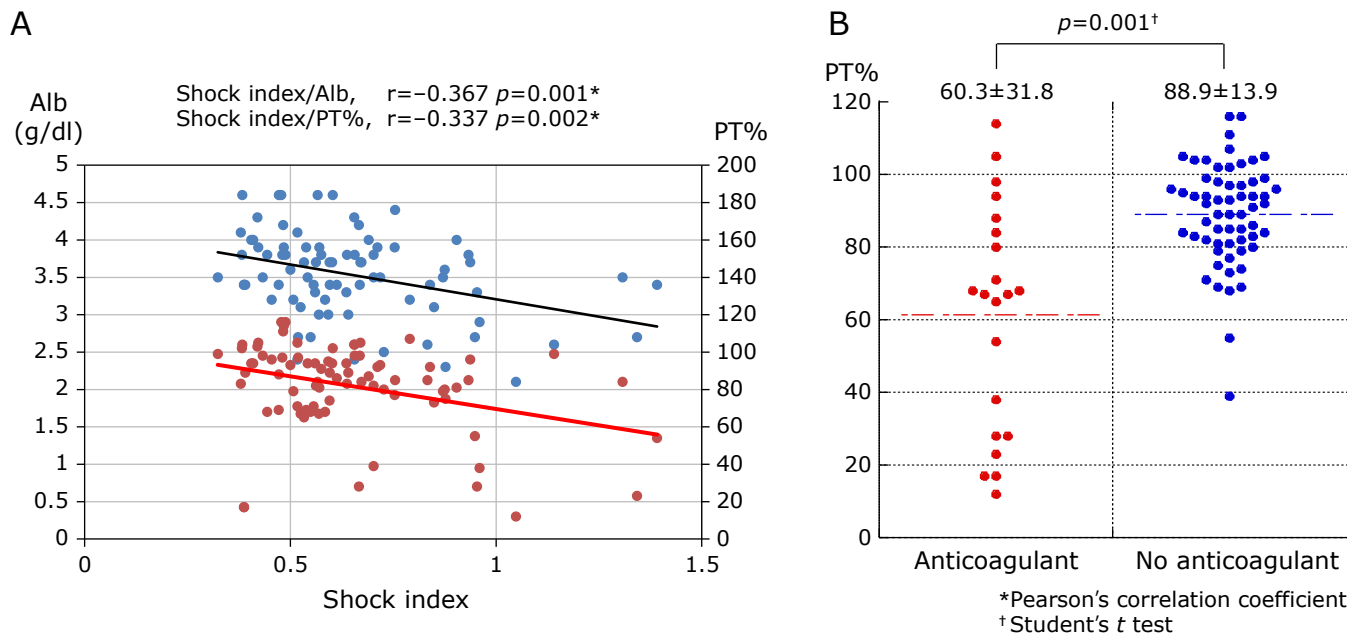


Fig. 2. (A) is showed a linear analysis to examine the relationship between Alb, PT%, and the shock index. (B) is showed that Kaleidagraph is used to show the correlation between anticoagulants and coagulants and PT%. PT% is significantly correlated with anticoagulants.

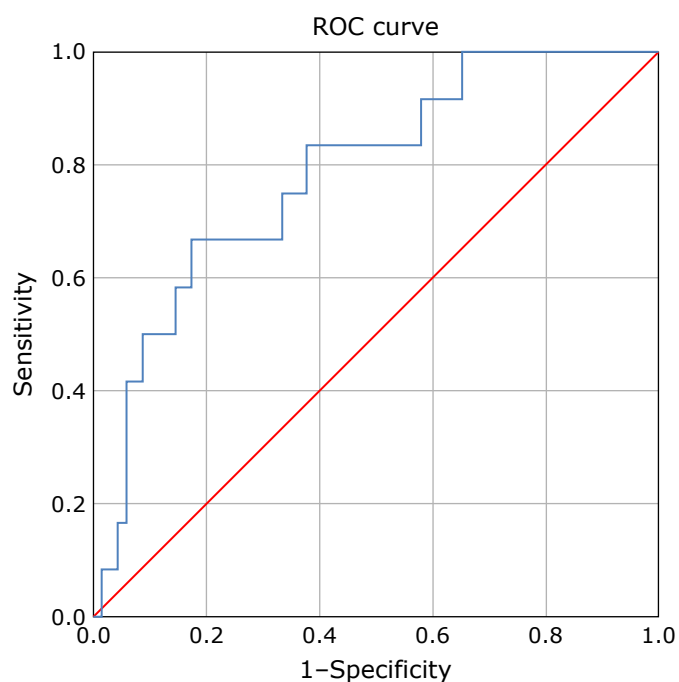


Fig. 3. This is showed ROC curves based on the shock index. When the cut-off value for the shock index was defined as more than 0.740, an OR of 9.500 (95% CI, 2.458 to 36.721), a positive predictive value (PPV) of 40.0%, a negative predictive value (NPV) of 93.4%, and an accuracy of 80.3% were obtained for predicting the occurrence of TAE treatment.

ately.⁽¹⁷⁻²¹⁾ The guidelines for colonic diverticular bleeding and colonic diverticulitis from the Japan Gastroenterological Association advocate that the indications for TAE are a large amount of bleeding, continuous bleeding and difficulty in stopping bleeding, recurrence of bleeding after endoscopic hemostasis,

and difficulty in identifying the bleeding site.⁽²²⁾ The American College of Gastroenterology guidelines also stated that because angiography relies on active bleeding and has the potential for serious complications, it should be reserved for patients with very brisk, ongoing bleeding.⁽²³⁾ However, no reports have examined the selection criteria for TAE based on specific evidence.

In this study, we first analysed the endoscopic hemostasis group and TAE hemostatic group and found that BMI, Alb, extravasation by contrast-enhanced CT, and the shock index are TAE risk factors. In the TAE hemostatic group, extravasation on contrast-enhanced CT examination was observed in all patients (Table 1). A univariate analysis revealed significant differences between these groups in Alb, PT%, and the shock index, and a multivariate analysis subsequently showed that Alb was an independent factor (Table 1). From these results, we performed a linear analysis to examine the relationship between Alb, PT%, and the shock index and found that Alb and PT% were strongly correlated with the shock index, indicating that a state of shock is causally related to the final hemostasis method (Fig. 2A). The results of the ROC analysis of the shock index and patients who ultimately required TAE showed that the NPV was 93.4% and the accuracy was 80.3% when the cut-off value of the shock index was set at 0.740 (Fig. 3). In other words, based on the results, this cut-off value could be used as a strong baseline to ensure the necessary backup of TAE specialists for TAE treatment.

In this study, PT% was significantly lower in the TAE hemostatic group, while the rate of anticoagulant medication was not significantly different between the TAE hemostatic group and endoscopic hemostasis group (Table 1). Although PT% was significantly correlated with anticoagulants (Fig. 2B), the fact that anticoagulant medication had no effect on the events that ultimately led to TAE suggests that the PT% identified as a risk factor for TAE in the logistic regression analysis can be interpreted as reflecting a state of shock rather than the effects of anticoagulants. As a cause of the drop in PT% during a state of shock, hypoperfusion leads to the activation of protein C with cleavage of activated factors V and VIII and the inhibition of plasminogen activator inhibitor 1 with subsequent hyper-

Table 2. Clinical characteristics and risk of the group of endoscopic hemostasis and the group of switched to TAE after endoscopic hemostasis failure

| | Endoscopic hemostasis | Switch to TAE after endoscopic hemostasis failure | <i>p</i> value | Univariate analysis OR (95% CI) | Multivariate analysis OR (95% CI) |
|--|-----------------------|---|--------------------|---------------------------------|-----------------------------------|
| Total number, <i>n</i> | 69 | 5 | | | |
| Age [years (mean ± SD)] | 71.87 ± 10.49 | 71.2 ± 4.26 | 0.889 [†] | 0.994 (0.910–1.085) | |
| Sex, <i>n</i> (%) male | 48 (69.6) | 5 (100) | 0.178 [‡] | N/A | |
| Smoking, <i>n</i> (%) | 23 (33.3) | 4 (80.0) | 0.056 [‡] | 0.125 (0.013–1.183) | |
| Drinking, <i>n</i> (%) | 23 (33.3) | 2 (40.0) | 0.553 [‡] | 0.750 (0.117–4.808) | |
| BMI [kg/m ² (mean ± SD)] | 24.23 ± 4.48 | 21.8 ± 2.31 | 0.241 [†] | 0.819 (0.589–1.137) | |
| History of diverticular bleeding, <i>n</i> (%) | 22 (31.9) | 3 (60.0) | 0.190 [‡] | 0.292 (0.045–1.876) | |
| Medical history, <i>n</i> (%) | | | | | |
| Cerebral infarction | 8 (11.6) | 2 (40.0) | 0.132 [‡] | 0.197 (0.028–1.362) | |
| Heart disease | 22 (31.9) | 2 (40.0) | 0.525 [‡] | 0.702 (0.109–4.508) | |
| Hypertension | 40 (60.0) | 3 (60.0) | 0.653 [‡] | 0.608 (0.404–4.711) | |
| Hyperlipidemia | 17 (24.6) | 1 (20.0) | 0.670 [‡] | 1.231 (0.128–11.816) | |
| Diabetes | 16 (23.1) | 2 (40.0) | 0.352 [‡] | 0.453 (0.069–2.951) | |
| Asthma | 3 (4.3) | 0 (0.0) | 0.808 [‡] | N/A | |
| Kidney disease | 5 (7.2) | 0 (0.0) | 0.698 [‡] | N/A | |
| Contrast media allergy | 0 (0.0) | 0 (0.0) | N/A | N/A | |
| Drug, <i>n</i> (%) | | | | | |
| Antiplatelet | 12 (17.4) | 3 (60.0) | 0.054 [‡] | 0.140 (0.021–0.933) | 0.094 (0.005–1.862) |
| Anticoagulant | 16 (23.2) | 2 (40.0) | 0.352 [‡] | 0.453 (0.069–2.951) | |
| Blood test | | | | | |
| Hb [g/dl (mean ± SD)] | 11.32 ± 2.71 | 10.2 ± 3.47 | 0.390 [†] | 0.862 (0.617–1.205) | |
| PLT [$\times 10^4/\mu\text{l}$ (mean ± SD)] | 21.48 ± 6.77 | 18.64 ± 5.68 | 0.369 [†] | 0.935 (0.808–1.081) | |
| Alb [g/dl (mean ± SD)] | 3.66 ± 0.47 | 3.08 ± 0.466 | 0.012 [†] | 0.079 (0.009–0.663) | 0.087 (0.007–1.062) |
| PT% [% (mean ± SD)] | 84.72 ± 20.66 | 69.0 ± 35.709 | 0.431 [†] | 0.976 (0.945–1.009) | |
| Extravasation by contrast-enhanced CT, <i>n</i> (%) | 19 (31.7) | 5 (100) | 0.002 [‡] | N/A | |
| The bleeding site is the right hemicolon, <i>n</i> (%) | 39 (56.5) | 4 (80.0) | 0.297 [‡] | 0.325 (0.035–3.060) | |
| Shock index (mean ± SD) | 0.62 ± 0.20 | 0.905 ± 0.257 | 0.004 [†] | 56.268 (2.208–1,433.698) | 28.972 (0.806–1,041.367) |

Shock index measurement, blood test, and contrast-enhanced CT examination are performed immediately after the visit. TAE, transarterial embolization; BMI, body mass Index; Hb, hemoglobin; Alb, albumin; PT%, prothrombin time%; CT, computed tomography; N/A, not applicable. [†]Student's *t* test; [‡]Fisher's exact test.

Table 3. Background of endoscopic hemostasis failure

| Case | Sex | Age | Areas with extravascular leakage by contrast-enhanced CT | Reasons of endoscopic hemostasis failure | Antithrombotics | Medical history |
|------|------|-----|--|--|------------------------|---------------------------|
| 1 | Male | 60s | A/C | Multiple diverticula Unable to draw a frontal view of the lesion | Warfarin | HT DM |
| 2 | Male | 70s | A/C | Multiple diverticula Unable to identify due to bleeding Difficult to add clips | Aspirin | HT CKD |
| 3 | Male | 60s | A/C | Multiple diverticula Difficult to add clips | Aspirin | HT |
| 4 | Male | 70s | S/C | Multiple diverticula Difficult to add clips | None | None |
| 5 | Male | 70s | A/C | Multiple diverticula Difficult to add clips | Warfarin Cilostazol | Cerebral infarction DM |

A/C, ascending colon; S/C, sigmoid colon; HT, hypertension; DM, diabetes mellitus; CKD, chronic kidney disease.

fibrinolysis. This results in the accompanying activation of protein C and subsequent inhibition of plasminogen activator inhibitor 1 with hyperfibrinolysis.⁽²⁴⁾

In the endoscopic hemostasis group, only 31.7% of patients had extravasation on contrast-enhanced CT examination. However, extravasation was observed in all cases in the TAE hemostasis group (*p* = 0.000, Table 1). Based on this result, even

if a patient is not in a state of shock at the time of admission, the possibility of transferring to TAE should always be considered if extravasation is observed on a contrast-enhanced CT scan. In contrast, TAE should not be performed in patients who do not have extravascular leakage because it causes a high rate of intestinal ischaemia.⁽²⁵⁾

In this study, a comparative analysis was also performed for

the group of patients who underwent successful endoscopic hemostasis (endoscopic hemostasis group) and the group of patients who failed endoscopic hemostasis and were switched to TAE. In this analysis, Alb, extravasation by contrast-enhanced CT, and the shock index were found to be risk factors for endoscopic hemostatic failure. This result is similar to the risk factors leading to TAE, but interestingly, this identified the antiplatelet agent as a factor with a marginally significant difference ($p = 0.054$, Table 2). Furthermore, based on the specific cases of endoscopic hemostatic failure shown in Table 3, we found that the reasons for switching to TAE due to difficulty in hemostasis by endoscopy were as follows: (1) when multiple diverticula were observed, (2) when deep insertion was required, (3) patients using antithrombotic drugs, and (4) patients in whom effective hemostasis could not be achieved with the first clip, and it was difficult to implant additional clips. In addition to the above, contrast medium extravasation was observed in all cases.

The advantage of endoscopy is that it allows for diagnosis by direct visualisation of the lesion. Furthermore, if SRH is detected, endoscopic hemostasis can be performed on the spot.⁽²⁶⁾ When considering the treatment strategy for diverticular haemorrhage, if endoscopic hemostasis with clips fails, it can be used as a landmark to select a vessel for TAE.⁽²⁷⁾ However, without bowel preparation before colonoscopy, bleeding and endoscopic hemostasis are difficult to observe. It is also important to note the possibility of aspiration of the intestinal cleansing agent in elderly patients. In a state of shock, there may be no time to take laxatives, making it difficult to perform endoscopy. On the other hand, TAE does not require pre-treatment, which can be advantageous, especially in elderly patients who have difficulty swallowing or patients in a state of shock. At the same time, we have to consider the risks of TAE, including intestinal ischemia, intestinal perforation, lower extremity ischaemia, and contrast-induced nephropathy.⁽¹⁹⁾ In addition to the findings from our study, it is important to understand these characteristics when

considering treatment strategies for diverticular bleeding.

There are several limitations to our study. Firstly, this study was conducted at a tertiary emergency medical facility. Therefore, more critically ill patients compared to the general population of patients with diverticular bleeding could have been enrolled. Secondly, no surgery or barium filling was performed in this cohort, meaning that other hemostasis methods could not be evaluated in this study.

Conclusion

The shock index is useful as an indicator of TAE in active diverticular bleeding. In addition, the transition to TAE should always be considered when extravasation images are observed on contrast-enhanced CT.

Abbreviations

| | |
|-----|----------------------------|
| A/C | ascending colon |
| Alb | albumin |
| BMI | body mass index |
| CKD | chronic kidney disease |
| CT | computed tomography |
| DM | diabetes mellitus |
| Hb | hemoglobin |
| HTI | hypertension |
| N/A | not applicable |
| PT% | prothrombin time% |
| S/C | sigmoid colon |
| TAE | transarterial embolization |

Conflict of Interest

No potential conflicts of interest were disclosed.

References

- Nagata N, Niikura R, Aoki T, *et al*. Lower GI bleeding risk of nonsteroidal anti-inflammatory drugs and antiplatelet drug use alone and the effect of combined therapy. *Gastrointest Endosc* 2014; **80**: 1124–1131.
- Wada M, Nishizawa T, Kato M, *et al*. Colonic diverticular bleeding and predictors of the length of hospitalization: an observational study. *J Gastroenterol Hepatol* 2019; **34**: 1351–1356.
- Tanaka Y, Motomura Y, Akahoshi K, *et al*. Predictive factors for colonic diverticular rebleeding: a retrospective analysis of the clinical and colonoscopic features of 111 patients. *Gut Liver* 2012; **6**: 334–338.
- Schwenk W. Endoscopy, angiography, surgery: diagnostic and therapeutic algorithms for diverticular bleeding. *Chirurg* 2019; **90**: 621–630. (in German)
- Strate LL, Gralnek IM. ACG Clinical Guideline: Management of Patients With Acute Lower Gastrointestinal Bleeding. *Am J Gastroenterol* 2016; **111**: 459–474.
- Cochran AA, Higgins GL 3rd, Strout TD. Intussusception in traditional pediatric, nontraditional pediatric, and adult patients. *Am J Emerg Med* 2011; **29**: 523–527.
- Foutch PG. Diverticular bleeding: are nonsteroidal anti-inflammatory drugs risk factors for hemorrhage and can colonoscopy predict outcome for patients? *Am J Gastroenterol* 1995; **90**: 1779–1784.
- Frossard JL, Spahr L, de Peyer R. Urgent colonoscopy for the diagnosis and treatment of severe diverticular hemorrhage. *N Engl J Med* 2000; **342**: 1610–1611.
- Yuhara H, Corley DA, Nakahara F, *et al*. Aspirin and non-aspirin NSAIDs increase risk of colonic diverticular bleeding: a systematic review and meta-analysis. *J Gastroenterol* 2014; **49**: 992–1000.
- Yamada A, Sugimoto T, Kondo S, *et al*. Assessment of the risk factors for colonic diverticular hemorrhage. *Dis Colon Rectum* 2008; **51**: 116–120.
- Tsuruoka N, Iwakiri R, Hara M, *et al*. NSAIDs are a significant risk factor for colonic diverticular hemorrhage in elder patients: evaluation by a case-control study. *J Gastroenterol Hepatol* 2011; **26**: 1047–1052.
- Okamoto T, Watabe H, Yamada A, Hirata Y, Yoshida H, Koike K. The association between arteriosclerosis related diseases and diverticular bleeding. *Int J Colorectal Dis* 2012; **27**: 1161–1166.
- Suzuki K, Uchiyama S, Imajyo K, *et al*. Risk factors for colonic diverticular hemorrhage: Japanese multicenter study. *Digestion* 2012; **85**: 261–265.
- Nagata N, Niikura R, Aoki T, *et al*. Colonic diverticular hemorrhage associated with the use of nonsteroidal anti-inflammatory drugs, low-dose aspirin, antiplatelet drugs, and dual therapy. *J Gastroenterol Hepatol* 2014; **29**: 1786–1793.
- Strate LL, Liu YL, Huang ES, Giovannucci EL, Chan AT. Use of aspirin or nonsteroidal anti-inflammatory drugs increases risk for diverticulitis and diverticular bleeding. *Gastroenterology* 2011; **140**: 1427–1433.
- Kvasnovsky CL, Papagrigoriadis S, Bjarnason I. Increased diverticular complications with nonsteroidal anti-inflammatory drugs and other medications: a systematic review and meta-analysis. *Colorectal Dis* 2014; **16**: O189–O196.
- Hur S, Jae HJ, Lee M, Kim HC, Chung JW. Safety and efficacy of transcatheter arterial embolization for lower gastrointestinal bleeding: a single-center experience with 112 patients. *J Vasc Interv Radiol* 2014; **25**: 10–19.
- Adusumilli S, Gosselink MP, Ctercteko G, *et al*. The efficacy of selective arterial embolization in the management of colonic bleeding. *Tech Coloproctol* 2014; **18**: 529–533.
- Maleux G, Roeflaer F, Heye S, *et al*. Long-term outcome of transcatheter embolotherapy for acute lower gastrointestinal hemorrhage. *Am J Gastroenterol* 2009; **104**: 2042–2046.
- Lipof T, Sardella WV, Bartus CM, Johnson KH, Vignati PV, Cohen JL. The efficacy and durability of super-selective embolization in the treatment of lower gastrointestinal bleeding. *Dis Colon Rectum* 2008; **51**: 301–305.
- Kodani M, Yata S, Ohuchi Y, Ihaya T, Kaminou T, Ogawa T. Safety and risk

- of superselective transcatheter arterial embolization for acute lower gastrointestinal hemorrhage with *n*-butyl cyanoacrylate: angiographic and colonoscopic evaluation. *J Vasc Interv Radiol* 2016; **27**: 824–830.
- 22 Nagata N, Ishii N, Manabe N, *et al*. Guidelines for Colonic Diverticular Bleeding and Colonic Diverticulitis: Japan Gastroenterological Association. *Digestion* 2019; **99 Suppl 1**: 1–26.
- 23 Strate LL, Gralnek IM. ACG Clinical Guideline: Management of Patients With Acute Lower Gastrointestinal Bleeding. *Am J Gastroenterol* 2016; **111**: 755.
- 24 Maegele M, Schöchl H, Cohen MJ. An update on the coagulopathy of trauma. *Shock* 2014; **41 Suppl 1**: 21–25.
- 25 Burgess AN, Evans PM. Lower gastrointestinal haemorrhage and superselective angiographic embolization. *ANZ J Surg* 2004; **74**: 635–638.
- 26 Wada M, Kato M, Hirai Y, *et al*. Initial management of colonic diverticular bleeding: observational study. *Digestion* 2018; **98**: 41–47.
- 27 Sato Y, Yasuda H, Nakamoto Y, *et al*. Risk factors of interventional radiology/surgery for colonic diverticular bleeding. *JGH Open* 2021; **5**: 343–349.



This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).
