Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.8761-21
Intern Med 61: 2247-2253, 2022
http://internmed.jp

【 ORIGINAL ARTICLE 】

Construction of a Model for Predicting the Severity of Diverticular Bleeding in an Elderly Population

Tomoyuki Okada[1], Tsuyoshi Mikamo[1], Ayana Nakashima[1], Atsushi Yanagitani[1], Kiwamu Tanaka[1] and Hajime Isomoto[2]

Abstract:

Objective To identify the risk factors for severe diverticular bleeding in an elderly population.

Methods Using a comprehensive computerized hospital database, severe and non-severe diverticular bleeding cases were compared for 19 factors: the age, sex, body mass index, comorbid conditions (hypertension, cardiovascular disease, cerebrovascular disease, and chronic renal failure, including those undergoing dialysis), history of diverticular bleeding, use of low-dose aspirin, use of antiplatelet agent besides aspirin, use of anticoagulant agent, use of prednisolone, use of non-steroidal anti-inflammatory drugs, use of cyclooxygenase-2 selective inhibitors, changes in vital signs, hypoalbuminemia, bilateral diverticula, identification of bleeding lesion, and rebleeding. Severe bleeding was defined as the need for blood transfusion, emergency surgery, or vascular embolization.

Patients A total of 258 patients were admitted for lower gastrointestinal bleeding between August 2010 and July 2020, among whom 120 patients over 65 years old diagnosed with diverticular bleeding were included in this study.

Results Fifty-one patients (43%) had severe diverticular bleeding. Independent risk factors for severe diverticular bleeding were as follows: change in vital signs [odds ratio (OR), 5.23; 95% confidence interval (CI), 1.9-14.4; p=0.0014], hypoalbuminemia (OR, 12.3; 95% CI, 1.97-77.3; p=0.0073), bilateral diverticula (OR, 3.47; 95% CI, 1.33-9.02; p=0.011), and rebleeding (OR, 5.92; 95% CI, 2.21-15.8; p<0.001). The area under the receiver operating characteristic curve was 0.79 after cross validation.

Conclusion Severe diverticular bleeding in elderly population may be predicted by changes in their vital signs, hypoalbuminemia, bilateral diverticula, and rebleeding.

Key words: diverticular bleeding, severity, elderly population

(Intern Med 61: 2247-2253, 2022)
(DOI: 10.2169/internalmedicine.8761-21)

Introduction

Diverticular bleeding is a common cause of lower gastrointestinal hemorrhaging. In a cohort study conducted in the United Kingdom, 26.4% of 2,528 cases of lower gastrointestinal bleeding were diagnosed with diverticular bleeding (1). Among gastrointestinal bleeding cases in the elderly population, 16% were identified as diverticular bleeding (2). In a cohort study conducted in Japan, the incidence of diverticular bleeding increased from 2003 to 2011 and is expected to continue increasing for decades to come (3). Furthermore, the number of elderly diverticular bleeding cases is increasing yearly and may increase further in the future with the aging of the population (4).

Diverticular bleeding occasionally causes rebleeding or severe bleeding and sometimes requires blood transfusion or emergency surgery (5, 6). In a retrospective review, 5.2% of 1,112 patients with lower gastrointestinal bleeding were readmitted, and more than half of them had diverticular bleeding (7). Lee et al. reported that 23 of 99 diverticular bleeding cases were classified as severe bleeding, 14 required massive transfusion, and 7 required emergency surgery (6). Some rebleeding cases result in mortality (8); therefore, pre-

[1]Tottori Prefectural Central Hospital, Japan and [2]Division of Medicine and Clinical Science, Faculty of Medicine, Tottori University, Japan
Received: October 1, 2021; Accepted: November 29, 2021; Advance Publication by J-STAGE: January 13, 2022
Correspondence to Dr. Tomoyuki Okada, tomoyuki19880123@yahoo.co.jp

dicting the severity of diverticular bleeding is important.

Non-steroidal anti-inflammatory drugs (NSAIDs), hypertension, and bilateral diverticula have been reported as risk factors for diverticular bleeding (9, 10), and NSAIDs and a high body mass index (BMI) have been reported as risk factors for recurrence (9, 11). In addition, right colon diverticulosis, NSAIDs, being a woman, and warfarin have been reported as risk factors for severe diverticular bleeding requiring transfusion and/or surgery (12, 13).

As mentioned above, there have been several reports on risk factors for diverticular bleeding; however, few studies have examined diverticular bleeding in an elderly population (2, 8). Furthermore, no studies have developed a model for predicting the severity of diverticular bleeding in an elderly population.

Therefore, we constructed a model for predicting the severity of diverticular bleeding in an elderly population in the present study.

Materials and Methods

Patients

Patients over 65 years old who presented to Tottori Prefectural Central Hospital (Tottori, Japan) with lower intestinal bleeding between August 2010 and July 2020 were eligible for inclusion in the study. Patients were excluded if any indication of upper gastrointestinal tract or small intestinal bleeding became evident. Patients were also excluded if there was an unclear source of bleeding or bleeding originated from the large intestine other than diverticular bleeding. Diverticular bleeding was diagnosed based on the appearance of hematochezia, identification of diverticula by computed tomography (CT) or endoscopy, and absence of other hemorrhagic disorders in the gastrointestinal tract. Endoscopic treatment, such as clipping, was performed when the bleeding source was identified by endoscopy. Upper gastrointestinal endoscopy or capsule endoscopy was performed in patients with suspected upper gastrointestinal or small bowel bleeding. A total of 258 patients were admitted for lower gastrointestinal bleeding, 120 of whom were diagnosed with diverticular bleeding.

This study was approved by the Institutional Review Board of Prefectural Central Hospital (Tottori, Japan; approval number: 2020-86) and performed in accordance with the principles of the Declaration of Helsinki (14). Informed consent was obtained by way of an opt-out option on our website.

Data collection

Data were collected using standardized instruments. Observations, laboratory results, radiology and endoscopy reports, blood product transfusion requirements, and operation notes were obtained from a comprehensive computerized hospital database.

Predictive variables

Using the relevant literature and clinical experience as a reference, 19 predictors were selected: age (65-79 and ≤80 years old) (8); sex; BMI ≥25 kg/m^2; comorbid conditions (hypertension, cardiovascular disease, cerebrovascular disease, and chronic renal failure, including those undergoing dialysis) (13); history of diverticular bleeding; use of low-dose aspirin (1, 15); use of antiplatelet agents besides aspirin; use of anticoagulant agents; use of prednisolone; use of NSAIDs, which were considered individually, whether it was a cyclooxygenase-2 (COX-2) selective inhibitor or not (4, 12); changes in vital signs (systolic blood pressure ≤100 mmHg, heart rate ≥100 bpm); hypoalbuminemia (serum albumin ≤3.0 g/dL) (16); bilateral diverticula, i.e. diverticula on both the right and left hemicolons (10); identification of a bleeding lesion (11); and rebleeding. The identification of a bleeding lesion was determined based on the verification of the diverticulum with continuous bleeding or stigmata of recent bleeding by endoscopy. Furthermore, cases of verified diverticulum with extravasation of contrast medium by CT were also defined. Rebleeding was defined as the continuous appearance of fresh hematochezia during the first 24 hours or recurrent bleeding after initial colonoscopy during hospitalization.

Outcome criteria

Severe diverticular bleeding was the outcome in this study, defined as a case requiring more than 2 units of blood transfusion, vascular embolization, or emergency colectomy. Blood transfusion was administered when the level of hemoglobin dropped below 7.0 g/dL upon arrival (16), significant bleeding or rebleeding expected to alter the vital signs was observed, or the hemoglobin level decreased to <10 g/dL within several days due to bleeding or rebleeding. Patients who were refractory to endoscopic treatment underwent vascular embolization or emergency surgery.

Statistical analyses

Using the χ^2 test or Fisher's exact test, a univariate analysis was performed. Predictors with a p value <0.05 were considered potential candidates for inclusion in the multivariate analysis. A total of 51 events were sufficient to obtain a score with 5 candidate variables to perform a multivariable logistic regression analysis, which required at least 10 events for each included independent variable. These variables were thus entered into the multivariable model using a logistic regression analysis via the backward elimination method. Predictors with p values <0.05 were selected for the final model. The variance inflation factor (VIF) was used to check for multicollinearity, and variables with a VIF >10 were removed from the model. The goodness-of-fit of the model was evaluated using the likelihood ratio test. A scoring system for predicting severe diverticular bleeding was constructed based on variables that were significant in the multivariate analysis. To evaluate the predictive perform-

Table 1. Clinical Features and Characteristics among Participants.

Total	120
Age, mean (SD)	79 (7.9)
Age ≥80, n (%)	65 (54)
Males/females, n	77/43
BMI, mean	19.8
BMI ≥25, n(%)	25 (21)
Comorbidity, n (%)	
HT	81 (68)
HD	52 (43)
CVD	30 (25)
CRF	35 (29)
Undergoing dialysis	2 (2)
History of DB	30 (25)
Medication use, n (%)	
LDA	34 (28)
APA besides LDA	25 (21)
OAC	25 (21)
PSL	4 (3)
NSAIDs	13 (11)
COX-2 inhibitor	12 (10)
Change of VS	36 (30)
Hypoalbuminemia	13 (11)
Bilateral diverticula	67 (26)
Identification of BL	35 (29)
Rebleeding	41 (34)

BMI: body mass, HT: hypertension, HD: heart disease, CVD: cerebrovascular disease, CRF: chronic renal failure, DB: diverticular bleeding, LDA: low dose aspirin, APA: antiplatelet agent, OAC: oral anticoagulant agent, PSL: prednisolone, NSAIDs: non-steroidal anti-inflammatory drugs, Cox-2: cycloxygenase-2, VS: vital signs, BL: bleeding lesion

Table 2. Clinical Features and Characteristics in Severe Diverticulum Bleeding*.

Total	51
Transfusion	
RBC transfusion, n (%)	49 (96)
Mean RBC units (range)	6.8 (2-22)
Colonoscopy, n (%)	51 (100)
Identification of BL, n (%)	20 (39)
Interventional radiography	
Vascular embolization, n (%)	1 (2.0)
Surgery, n (%)	10 (20)

RBC: red blood cell, BL: bleeding lesion

*Severe diverticular bleeding was defined as the case that required more than 2 units of blood transfusion or required vascular embolization or emergency surgery.

ance of the model, discrimination was measured using the area under the receiver operating characteristic curve (ROC-AUC). To examine the degree of overfitting of the prediction model to the development sample, 10-fold cross validation was performed (17). The predictive ability of the cross-validated scores was examined by comparing the area under the curve with that obtained from the naïve prediction scores.

All statistical analyses were performed using the EZR software program (18).

Results

Patients

The clinical features and characteristics of the 120 patients are shown in Table 1. The mean age was 79 (range, 65-97) years old, and 43 patients were women. The mean BMI was 19.8 kg/m^2. Thirty patients had a history of diverticular bleeding. Hypertension was the most common comorbidity (81/120). Thirty-four patients were taking low-dose aspirin, 25 were taking antiplatelet agents besides aspirin, and 25 were taking anticoagulants. Twenty-five patients were taking NSAIDs, 12 of whom were taking COX-2 selective inhibitors. Four patients were taking prednisolone (PSL). Thirty-six patients exhibited changes in vital signs during the observation period (HR>100 bpm/BP<100 mmHg/HR>100 bpm, and BP<100 mmHg=7/17/12). Thirteen patients had hypoalbuminemia, 67 bilateral diverticula, 25 left-sided diverticula, and 28 right-sided diverticula. The definite source of bleeding was identified in 34 patients, among whom 29 sources were identified by colonoscopy, 2 by CT, and 3 by both colonoscopy and CT. Forty-one patients experienced rebleeding.

Severe diverticular bleeding

Of the 120 patients, 51 experienced severe diverticular bleeding (Table 2). Of these patients, 40 received blood transfusion, 2 underwent emergency surgery, 1 underwent both blood transfusion and vascular embolization, and 8 underwent both blood transfusion and emergency surgery. The average number of transfusions was 6.8 units (range, 2-22 units). All patients with severe diverticular bleeding underwent colonoscopy, and the definite source of bleeding was identified in 20 of them. There were no deaths directly associated with diverticular bleeding.

To establish predictive factors, we compared two groups of patients with or without severe diverticular bleeding (Table 3). In severe cases, a univariate analysis revealed significant differences in the following factors: changes in vital signs ($p<0.001$), hypoalbuminemia ($p=0.0019$), bilateral diverticula ($p=0.0057$), identification of bleeding lesion ($p=0.0047$), and rebleeding ($p<0.001$). A multivariable logistic regression analysis revealed changes in vital signs [odds ratio (OR), 5.23; 95% confidence interval (CI), 1.9-14.4; $p=0.0014$], hypoalbuminemia (OR, 12.3; 95% CI, 1.97-77.3; $p=0.0073$), bilateral diverticula (OR, 3.47; 95% CI, 1.33-9.02; $p=0.011$), and rebleeding (OR, 5.92; 95% CI, 2.21-15.8; $p<0.001$) as independent risk factors for severe diverticular bleeding (Table 4). None of the VIFs attained a value of 10,

Table 3. Comparison between Patients with Severe DB and Without*.

	Patients without severe DB (n=69)	Patients with severe DB (n=51)	Unadjusted OR (95% CI)	p value
Age, mean	78.4	79.1		0.669
Age ≥80	35	30	1.38 (0.62-3.07)	0.459
Males/females	46/23	31/20	1.28 (0.56-2.92)	0.565
BMI	22.6	21.4		0.105
BMI ≥25	17	8	0.57 (0.19-1.56)	0.263
Comorbidity				
HT	48	33	0.80 (0.35-1.87)	0.694
HD	26	26	1.71(0.77-3.82)	0.192
CVD	18	12	0.87 (0.34-2.18)	0.832
CRF	17	18	1.66 (0.70-3.98)	0.228
Undergoing dialysis	1	1	Reference	1
History of DB	14	16	1.79 (0.72-4.50)	0.203
Medication use				
LDA	17	17	1.52 (0.64-3.67)	0.313
APA besides LDA	12	13	1.62 (0.61-4.35)	0.363
OAC	14	11	1.08 (0.40-2.87)	1
PSL	3	1	Reference	0.636
NSAIDs	5	8	2.36 (0.63-9.83)	0.234
Cox-2 inhibitor	6	6	1.40 (0.35-5.60)	0.760
Change of VS	10	26	6.03 (2.40-16.3)	<0.001
Hypoalbuminemia	2	11	9.05 (1.84-88.3)	<0.01
Bilateral Diverticula	31	36	2.91 (1.28-6.85)	<0.01
Identification of BL	13	22	3.23 (1.34-8.11)	<0.01
Rebleeding	12	29	6.15 (2.53-15.8)	<0.001

DB: diverticulum bleeding, OR: odds ratio, CI: confidence interval, BMI: body mass, HT: hypertension, HD: heart disease, CVD: cerebrovascular disease, CRF: chronic renal failure, LDA: low dose aspirin, APA: antiplatelet agent, OAC: oral anticoagulant agent, PSL: prednisolone, NSAIDs: non-steroidal anti-inflammatory drugs, Cox-2: cycloxygenase-2. VS: vital signs, BL: bleeding lesion

* OR, 95% CI and p values were determined using Fisher's exact test or t test.

Table 4. Independent Risk Factors for Severe Diverticulum Bleeding*.

Predictor	OR (95% CI)	VIF	p value
Change of VS	5.23 (1.90-14.4)	1.05	<0.01
Hypoalbuminemia	12.3 (1.97-77.3)	1.05	<0.01
Bilateral Diverticula	3.47 (1.33-9.02)	1.08	0.011
Rebleeding	5.92 (2.21-15.8)	1.17	<0.001

OR: odds ratio, CI: confidence interval, VIF: variance inflation factor, VS: vital signs

* OR, 95% CI and p values were determined using multivariable logistic regression analysis.

and there was no collinearity in the model. The likelihood ratio test confirmed the model to be a good fit (p<0.001). Each factor was assigned 1 point. Among patients with 0, 1, 2, 3, and 4 points, the rates of severe diverticular bleeding were 7.69%, 26.9%, 87.0%, 76.5%, and 100%, respectively, and there was a positive correlation between the scores and rates of severe diverticular bleeding using Spearman's rank correlation test (rs=0.59, p<0.001, Fig. 1).

An ROC analysis revealed that when the cut-off value was set at 2 points using Youden's index, the sensitivity, specificity, positive likelihood ratio, and AUC value were 68.6%, 89.9%, 6.79, and 0.83, respectively (Fig. 2). On determining the presence or absence of severity using the four variables, the AUC was 0.82 (range, 0.69-0.97) for naïve prediction and 0.79 (range, 0.61-0.97) after cross validation.

Discussion

Some reports have described the risk factors for diverticular bleeding. Kinjo et al. reported that obese men (BMI≥25) developed diverticular bleeding more frequently than non-obese men (4). The use of NSAIDs and anticoagulants, including aspirin, has also been reported as a risk factor for diverticular bleeding (4, 9, 19).

In addition, Tsuruoka et al. (9) reported that hypertension and hyperlipidemia were risk factors in patients younger than 65 years old, a finding contrary to that in the elderly population. However, the risk factors for the onset and development of severe bleeding may vary. Lee et al. (6) re-

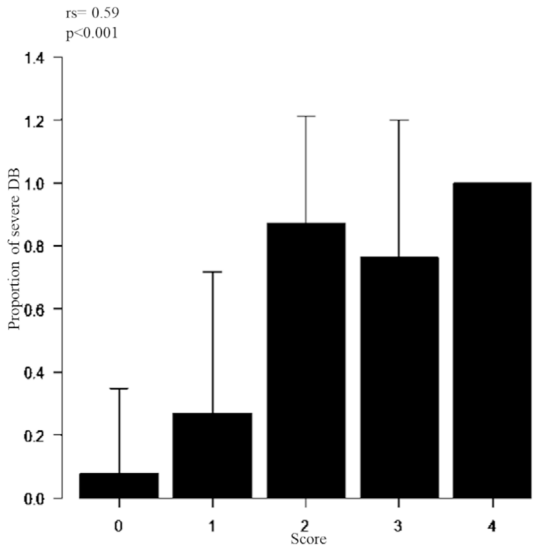

Figure 1. Prevalence of severe diverticular bleeding based on score (n=120). Spearman's rank correlation test was used to determine the correlation coefficient and p value. DB: diverticular bleeding

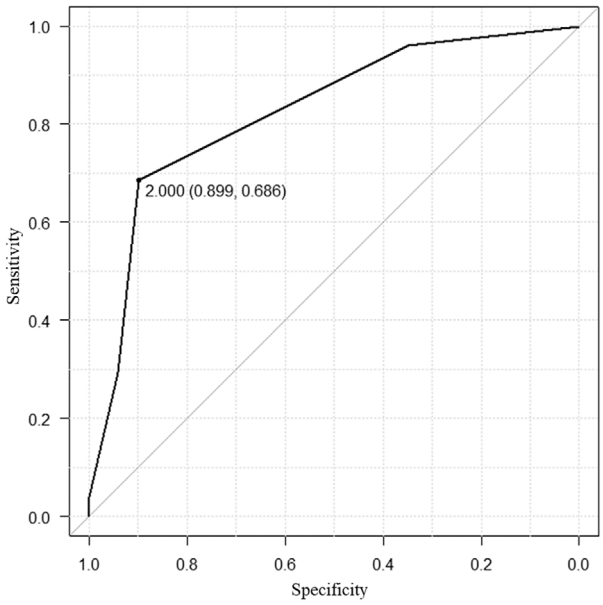

Figure 2. Receiver operating characteristics curve (ROC) for our scoring system of severe diverticular bleeding. The optimal cut-off value was set at 2 points based on Youden's index. The positive likelihood ratio was 6.79 at the cut-off value, and the area under the receiver operating characteristic curve (ROC-AUC) was 0.83.

ported that taking any blood pressure medications and low initial hemoglobin levels were associated with severe diverticular bleeding, and Gilshtein et al. (5) reported that neither anticoagulant nor antiaggregation treatments were associated with an increased risk of recurrent hemorrhaging, including that requiring surgery. This study also demonstrated that risk factors, such as being a man, obesity, using NSAIDs and anticoagulants, and a history of diverticular bleeding, were not significant predictors of severe diverticular bleeding, so the risk factors for the onset and development of severe bleeding need to be considered individually.

Several reports have indicated that changes in vital signs are a risk factor for severe diverticular bleeding (6, 15, 16). Changes in vital signs are also associated with the severity of upper gastrointestinal bleeding (UGIB), and the shock index, which is calculated based on the heart rate and blood pressure (20), can identify patients likely to require blood transfusion (21). Although few data reports have described lower gastrointestinal bleeding (LGIB) using the shock index, the National Confidential Enquiry into Patient Outcome and Death report, which included LGIB, found that changes in vital signs were associated with mortality (22). Changes in vital signs include decreased blood pressure and increased heart rate associated with the need for blood transfusion (23, 24), which potentially indicates massive blood loss. In this study, changes in vital signs were also identified as a predictor of severity, so diverticular bleeding involving changes in vital signs should be carefully evaluated.

Several studies have revealed that hypoalbuminemia is associated with the severity of UGIB (25, 26). Furthermore, hypoalbuminemia is related to low hemoglobin levels in patients with UGIB (27). Fukuda et al. reported that hypoalbuminemia was associated with mortality (28). Hypoalbuminemia causes the effective intravascular volume to leak into the interstitial space, which induces a hypovolemic state (29, 30). Blood loss due to diverticular bleeding and hypoalbuminemia cause a reduction in the effective circulating volume, resulting in the need for blood transfusion. In addition, the serum albumin level is associated with wound healing (31), so hypoalbuminemia may delay healing of diverticular bleeding, resulting in exacerbation.

Strate et al. reported that continuous bleeding per the rectum is correlated with severe bleeding (15). Jensen et al. reported that 9 of 17 patients treated medically for diverticular bleeding experienced recurrent or persistent bleeding; all of them required blood transfusion, and 6 of them required emergency surgery (32). Continuous bleeding or recurrent bleeding increased the amount of bleeding, resulting in severe diverticular bleeding. Therefore, patients who experienced rebleeding required blood transfusion, vascular embolization, or emergency surgery.

Regarding the location of the diverticular bleeding, right colon diverticular bleeding reportedly tends to be severe, requiring surgery (5, 12, 33). Right-sided diverticula are often larger than left-sided diverticula; hence, the vasa recta of right-sided diverticula are more often exposed to harmful factors that can cause injury (33, 34). In addition, the extent of right-sided diverticular bleeding is often greater than that from the left side due to the thinner intestinal wall (33, 34). However, Aytac et al. reported that patients frequently experienced rebleeding of left-sided colon diverticula, and most of them required surgical interventions (35). Having bilateral diverticula is reportedly a potential risk factor for both left and right diverticular bleeding; therefore, the presence of bilateral diverticula may be associated with aggravation.

There have been no reports describing the relationship between the number of colorectal diverticula and severity of diverticular bleeding; however, greater numbers of diverticula may increase the risk of injury to the vasa recta, resulting in the occurrence of severe diverticular bleeding.

Several limitations associated with the present study warrant mention. First, the study was retrospective; therefore, it was incomplete and inaccurate compared to prospective studies. Furthermore, this was a single-institution study with a small number of cases. As such, although the results were statistically cross-validated, an external-validity evaluation is required. Finally, some cases in which diverticula were not identified as the source of bleeding were included in this study; we therefore cannot discuss the relationship between the location of the bleeding source and severity.

In conclusion, this study demonstrated that changes in vital signs, hypoalbuminemia, bilateral diverticula, and rebleeding were risk factors for severe diverticular bleeding, with cut-off, sensitivity, specificity, and positive likelihood ratio values of 2 points, 68.6%, 89.9%, and 6.79, respectively. Using these factors as indicators, it may be possible to predict the severity of diverticular bleeding in an elderly population.

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

References

1. Oakland K, Guy R, Uberoi R, et al. Acute lower GI bleeding in the UK: patient characteristics, interventions and outcomes in the first nationwide audit. Gut **67**: 654-662, 2018.
2. Geyer M, Stamenic I, Bühler H, Bertschinger P. Epidemiology of gastrointestinal bleeding in the GI bleeding in the elderly. Praxis (Bern 1994) **95**: 757-765, 2006.
3. Nagata N, Niikura R, Aoki T, et al. Increase in colonic diverticulosis and diverticular hemorrhaging in an aging society: lessons from a 9-year colonoscopic study of 28,192 patients in Japan. Int J Colorectal Dis **29**: 379-385, 2014.
4. Kinjo K, Masui T, Hisabe T, et al. Increase in colonic diverticular hemorrhaging and confounding factors. World J Gastrointest Pharmacol Ther **7**: 440-446, 2016.
5. Gilshtein H, Kluger Y, Khoury A, Issa N, Khoury W. Massive and recurrent diverticular hemorrhaging, risk factors and treatment. Int J Surg **33**: 136-139, 2016.
6. Lee KK, Shah SM, Moser MA. Risk factors predictive of severe diverticular hemorrhaging. Int J Surg **9**: 83-85, 2011.
7. Gayer C, Chino A, Lucas C, Yamasaki T, Edelman AD, Sugawa C. Acute lower gastrointestinal bleeding in 1,112 patients admitted to an urban emergency medical center. Surgery **146**: 600-607, 2009.
8. Lorenzo D, Gallois C, Lahmek P, et al.; Groupe des Hémorragies Digestives Basses de l'ANGH (Association Nationale des Hépato-Gastroentérologues des Hôpitaux Généraux). Middle-term mortality and re-bleeding after initial diverticular bleeding: a nationwide study of 365 mostly elderly French patients. United Eur Gastroenterol **5**: 119-127, 2017.
9. Tsuruoka N, Iwakiri R, Hara M, et al. NSAIDs are a significant risk factors for colonic diverticular hemorrhaging in elder patients: evaluation by a case-control study. J Gastroenterol Hepatol **26**: 1047-1052, 2011.
10. Suzuki K, Uchiyama S, Imajyo K, et al. Risk factors for colonic diverticular hemorrhaging: Japanese multicenter study. Digestion **85**: 261-265, 2012.
11. 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 **6**: 334-338, 2012.
12. Kinjo K, Matsui T, Hisabe T, et al. Risk factors for severity of colonic diverticular hemorrhaging. Intest Res **16**: 458-466, 2018.
13. Nagata N, Niikura R, Aoki T, et al. Risk factors for adverse in-hospital outcomes in acute colonic diverticular hemorrhaging. World J Gastroenterol **21**: 10697-10703, 2015.
14. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA **310**: 2191-2194, 2013.
15. Strate LL, Orav EJ, Syngal S. Early predictors of severity in acute lower intestinal tract bleeding. Arch Intern Med **163**: 838-843, 2003.
16. Aoki T, Nagata N, Simbo T, et al. Development and validation of a risk scoring system for severe acute lower gastrointestinal bleeding. Clin Gastroenterol Hepatol **14**: 1562-1570.e2, 2016.
17. Efron B, Tibshirani R. Statistical data analysis in the computer age. Science **253**: 390-395, 1991.
18. Kanda Y. Investigation of the freely-available easy-to-use software "EZR" (Easy R) for medical statistics. Bone Marrow Transplant **48**: 452-458, 2013.
19. Yamada A, Sugimoto T, Kondo S, et al. Assessment of risk factors for colonic diverticular hemorrhaging. Dis Colon Rectum **51**: 116-120, 2008.
20. Olaussen A, Blackburn T, Mitra B, Fitzgerald M. Review article: shock index for prediction of critical bleeding post-trauma: a systematic review. Emerg Med Australas **26**: 223-228, 2014.
21. Rassameehiran S, Teerakanok J, Suchartlikiwong S, Nugent K. Utility of the shock index for risk stratification in patients with acute upper gastrointestinal bleeding. South Med J **110**: 738-743, 2017.
22. National Confidential Enquiry into Patient Outcomes and Death. Time to get control? National Confidential Enquiry into Patient Outcomes and Death. 2015 [Internet]. Available from: http://www.ncepod.org.uk
23. Rau CS, Wu SC, Kuo SCH, et al. Prediction of massive transfusion in trauma patients with shock index, and age shock index. Int J Environ Res Public Health **13**: 683, 2016.
24. Sohn CH, Kim WY, Kim SR, et al. An increase in initial shock index is associated with the requirement for massive transfusion in emergency department patients with primary postpartum hemorrhaging. Shock **40**: 101-105, 2013.
25. Tung CF, Chow WK, Chang CS, Peng Y, Hu WH. The prevalence and significance of hypoalbuminemia in non-variceal upper gastrointestinal bleeding. Hepatogastroenterology **54**: 1153-1156, 2007.
26. Saltzman JR, Tabak YP, Hyett BH, Sun X, Travis AC, Johannes RS. A simple risk score accurately predicts in-hospital mortality, length of stay, and cost in acute upper GI bleeding. Gastrointest Endosc **74**: 1215-1224, 2011.
27. Cheng HC, Yang EH, Wu CT, et al. Hypoalbuminemia is a predictor of mortality and rebleeding in peptic ulcer bleeding under proton pump inhibitor use. J Formos Med Assoc **117**: 316-325, 2018.
28. Fukuda S, Shimodaira Y, Watanabe K, et al. Risks for rebleeding and in-hospital mortality after gastrointestinal bleeding in a tertiary referral center in Japan. Digestion **101**: 31-37, 2020.
29. Valdespino-Trejo A, Orea-Tejeda A, Castillo-Martinez L, et al. Low albumin levels and high impedance ratio as risk factors for worsening kidney function during hospitalization of decompensated heart failure patients. Exp Clin Cardiol **18**: 113-117, 2013.
30. Kim K, Seo H, Chin JH, Son HJ, Hwang JH, Kim YK. Preoperative hypoalbuminemia and anemia as predictors of transfusion in radical nephrectomy for renal cell carcinoma: a retrospective

study. BMC Anesthesiol **15**: 103, 2015.

31. Chu CC, Yuan TL, Jeng KJ, et al. Risk factors for delayed perineal wound healing and its impact on prolonged hospital stay after abdominoperineal resection. World J Surg Oncol **17**: 226, 2019.

32. Jansen DM, Machicado GA, Jutabha R, Kovacs TO. Urgent colonoscopy for the diagnosis and treatment of severe diverticular hemorrhaging. N Engl J Med **342**: 78-82, 2000.

33. Wong SK, Ho YH, Leong AP, Seow-Choen F. Clinical behavior of complicated right-sided and left-sided diverticulosis. Dis Colon Rectum **40**: 344-348, 1997.

34. Meyers MA, Alonso DR, Bear JW. Pathogenesis of massively bleeding colonic diverticulosis: new observations. AJR Am J Roentgenol **127**: 901-908, 1976.

35. Aytac E, Stocchi L, Gorgun E, Ozuner G. Risk of recurrence and long-term outcomes after colonic diverticular bleeding. Int J Colorectal Dis **29**: 373-378, 2014.