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Efficacy of urgent colonoscopy for colonic diverticular bleeding: A propensity score-matched analysis using a nationwide database in Japan

Rintaro Moroi,* Kunio Tarasawa,† Hisashi Shiga,* Kota Yano,* Yusuke Shimoyama,* Masatake Kuroha,* Yoichi Kakuta,* Kiyohide Fushimi,‡ Kenji Fujimori,† Yoshitaka Kinouchi* and Atsushi Masamune*

*Division of Gastroenterology, Department of Internal Medicine, †Department of Health Administration and Policy, Tohoku University Graduate School of Medicine, Sendai, and ‡Department of Health Policy and Informatics, Tokyo Medical and Dental University Graduate School of Medicine, Bunkyo, Japan

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Correspondence
Dr Rintaro Moroi, Division of Gastroenterology, Tohoku University Hospital, 1-1, Seiryo, Aoba-ku, Sendai, Miyagi 980-8574, Japan.
Email: rinta@med.tohoku.ac.jp

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Abstract

Background and Aim: Although colonic diverticular bleeding (CDB) is considered to have good prognosis with conservative therapy, some cases are severe. The efficacy of urgent colonoscopy for CDB and clinical factors affecting CDB prognosis are unclear. This study aimed to evaluate the efficacy of urgent colonoscopy for CDB and identify risk factors for unfavorable events, including in-hospital death during admission, owing to CDB.

Methods: We collected CDB patients' data using the Diagnosis Procedure Combination database system. We divided eligible patients into urgent and elective colonoscopy groups using propensity score matching and compared endoscopic hemostasis and in-hospital death rates and length of hospital stay. We also conducted logistic regression analysis to identify clinical factors affecting CBD clinical events, including in-hospital death, a relatively rare CDB complication.

Results: Urgent colonoscopy reduced the in-hospital death rate (0.35% *vs* 0.58%, $P = 0.033$) and increased the endoscopic hemostasis rate (3.0% *vs* 1.7%, $P < 0.0001$) compared with elective colonoscopy. Length of hospitalization was shorter in the urgent than in the elective colonoscopy group (8 *vs* 9 days, $P < 0.0001$). Multivariate analysis also revealed that urgent colonoscopy reduced in-hospital death (odds ratio = 0.67, 95% confidence interval: 0.46–0.97, $P = 0.036$) and increased endoscopic hemostasis (odds ratio = 1.84, 95% confidence interval: 1.53–2.22, $P < 0.0001$).

Conclusion: Urgent colonoscopy for CDB may facilitate identification of the bleeding site and reduce in-hospital death. The necessity and appropriate timing of urgent colonoscopy should be considered based on patients' condition.

Introduction

Colonic diverticular bleeding (CDB) is one of the most common causes of lower gastrointestinal bleeding (LGB) in clinical practice, accounting for approximately 30% of LGB cases.[1–4] Although CDB is considered to have good prognosis with conservative therapy,[5] some cases are severe, requiring blood transfusion and invasive treatments, such as endoscopic hemostasis, radiological intervention, and surgical bowel resection. Furthermore, in most serious cases, death can ensue.[2,6] Risk factors for such unfavorable events are unclear.

We usually conduct urgent endoscopy to detect the cause of LGB and perform hemostasis if possible. However, the bleeding point is sometimes difficult to detect, and the appropriate timing of endoscopy for CDB is unknown. Moreover, the efficacy of urgent endoscopy for LGB, particularly CDB, is controversial. One single-center retrospective observational study reported that urgent colonoscopy for CDB could shorten the length of hospitalization.[7] However, several randomized control trials have reported controversial results regarding the efficacy of urgent colonoscopy for LGB.[8–11] However, these studies contained a small number of patients and included various types of LGB, rather than being limited to CDB. Therefore, a large-scale study investigating the efficacy of urgent colonoscopy for CDB is necessary.

The Diagnosis Procedure Combination (DPC) is a national database of hospitalizations in Japan.[12] This database contains data of

a large number of patients and is useful for studying rare diseases and complications, as compared with conventional studies, including randomized control trials. The DPC also contains the data of a large number of patients with CDB.

Thus, this study aimed to evaluate the efficacy of urgent colonoscopy for CDB and identify risk factors of unfavorable events, such as in-hospital death owing to CDB, using the DPC database.

Methods

Diagnosis Procedure Combination system. The DPC database, which has been introduced since 2003, is a medical claims database of admissions to acute-care hospitals in Japan. The DPC system was adopted at 1730 hospitals in 2018 and covers approximately 83% of the acute-care beds in Japan.[13] The DPC database contains patients' demographics, diagnosis, main disease triggering admission, comorbidities at admission, complications after admission, medications, surgeries, procedures (including endoscopic hemostasis, blood transfusion, and radiological intervention), and condition at discharge.[2,12,14] The physicians input patients' diagnosis into the DPC database according to *International Classification of Diseases*, Tenth Revision. The DPC database has been used for various clinical studies, including those of LGB,[2] and its diagnostic validity is recognized.[12]

Patients. This study included patients with CDB who were admitted to DPC-participating hospitals from April 2016 through March 2019. CDB was identified using the *International Classification of Diseases*, Tenth Revision code K573 and a DPC diagnosis containing the phrase "colonic diverticular bleeding." Entries of CDB suspicious cases containing the word "suspicious" were excluded. We subsequently also excluded patients who did not undergo colonoscopy during their hospital stay.

Data collection. We collected the following data on patient and clinical characteristics, procedures, and condition at discharge from the DPC database: age, sex, body mass index (BMI), smoking habit, Charlson comorbidity index,[15] prescription of anti-coagulant or anti-platelet drugs, bowel preparation for colonoscopy, hospital type (academic hospital or not), colonoscopy including endoscopic hemostasis, red blood cell transfusion, radiological intervention, surgical bowel resection, and in-hospital death.

Data analysis. We classified the eligible patients into five categories according to their age (≤49, 50–59, 60–69, 70–79, ≥80 years) and into three categories according to BMI (underweight, <18.5 kg/m^2; normal range, 18.5–24.9 kg/m^2; and overweight, >25.0 kg/m^2) based on the World Health Organization classification.[16] The eligible patients were also divided into two groups according to the date of first endoscopy after admission, as follows: urgent colonoscopy group (days 1 or 2) and elective colonoscopy group (from day 3 onward). The DPC database does not include the time of admission; only the date of admission was recorded. Therefore, we defined a colonoscopy conducted on day 1 or day 2 after admission as urgent endoscopy.

We conducted propensity score-matched analysis to compare the efficacy of urgent colonoscopy with that of elective colonoscopy. We used the following variables for propensity score matching: sex, age categories, and BMI categories as described above, comorbidity (heart failure, cerebrovascular disease, respiratory disease, liver disease, diabetes with chronic complications, and renal disease), smoking habit, bowel preparation, prescription of anti-coagulant or anti-platelet drugs, and hospital type (academic hospital or not). We subsequently compared the rates of endoscopic hemostasis, in-hospital death, red blood cell transfusion, and surgery between the urgent and elective colonoscopy groups, using chi-square tests; and the length of hospital stay and the medical costs of hospital stay, using Wilcoxon's signed-rank test. We also performed a multivariate analysis using logistic regression analysis with the data before propensity score matching to identify clinical factors that affect in-hospital death and endoscopic hemostasis. The threshold for statistical significance was $P < 0.05$. All analyses were performed using JMP Pro14 (SAS Institute, Tokyo, Japan) software.

Ethics. The study protocol was reviewed and approved by the Ethics Committee Tohoku University Graduate School of Medicine (2019-1-415). Owing to the anonymous nature of the data, informed consent was waived for the approval.

Results

Patient characteristics. We finally included 26 999 eligible cases, of whom 17 698 were assigned to the urgent colonoscopy group and the remaining 9301 to the elective colonoscopy group. After propensity score matching, 8694 pairs of patients were selected. The *C*-statistic was 0.59. The characteristics of the study population are summarized in Table 1. The characteristics of both groups were similar after propensity score matching.

Comparison of clinical event rates between urgent and elective colonoscopy after propensity score matching. The relationship between colonoscopy type and clinical events is summarized in Table 2. The rate of endoscopic hemostasis was higher in the urgent colonoscopy group than in the elective colonoscopy group (3.0% *vs* 1.7%, $P < 0.0001$). The rate of in-hospital death was conversely lower in the urgent colonoscopy group than in the elective colonoscopy group (0.35% *vs* 0.58%, $P = 0.033$). The urgent colonoscopy group also had a lower radiological intervention rate in the urgent colonoscopy group ($P < 0.0001$), whereas there were no differences in red blood cell transfusion and surgery rates.

Length of hospital stay and medical costs. The median hospital stay of the urgent colonoscopy group and the elective colonoscopy group was 8 and 9 days, respectively (Table 2). The length of hospital stay in the urgent colonoscopy group was shorter than that in the elective colonoscopy group ($P < 0.0001$). The median medical costs of hospital stay of the urgent colonoscopy group and the elective colonoscopy group were 365 805 and 406 000 JPY, respectively (Table 2). The medical costs of

Table 1 Comparison of clinical characteristics of study population between before and after propensity score matching

	Before propensity score matching Total *n* = 26 999			After propensity score matching Total *n* = 17 388			
	Urgent colonoscopy *n* = 17 698	Elective colonoscopy *n* = 9301	*P* value	Urgent colonoscopy *n* = 8694	Elective colonoscopy *n* = 8694	*P* value	Standardized difference
Sex (male/female)	11 024/6674	5618/3683	**0.002**	5268/3426	5287/3407	0.99	0.0045
Age (mean ± SD), years	73.8 ± 12.0	74.5 ± 11.7	<**0.0001**	74.4 ± 11.8	74.4 ± 11.7	0.83	0
Age categories							
≥ 80 years	6572	3691		3464	3420		
70–79 years	5472	2863		2645	2693		
60–69 years	3327	1641		1527	1537		
50–59 years	1540	766		728	719		
≤ 49 years	787	340		330	325		
Body mass index (mean ± SD), kg/m^2	23.5 ± 4.5	23.3 ± 3.7	**0.006**	23.5 ± 4.9	23.3 ± 3.7	0.23	0.046
BMI categories							
Overweight (> 25.0 kg/m^2)	5035	2534		2518	2533		
Normal range (18.5–24.9 kg/m^2)	10 088	5441		5487	5441		
Under weight (< 18.5 kg/m^2)	1319	722		691	722		
Comorbidity							
Heart failure	915	513	0.22	463	479	0.61	0.0081
Cerebrovascular disease	1382	763	0.26	704	712	0.85	0.0033
Respiratory disease	551	301	0.58	250	286	0.12	0.024
Liver disease	346	224	**0.016**	183	204	0.30	0.016
Diabetes with chronic complications	364	192	0.96	141	183	**0.021**	0.036
Renal disease	807	432	0.76	377	408	0.27	0.017
Smoking (yes/no)	7292/10 406	3677/5624	**0.008**	3385/5309	3425/5269	0.54	0.0094
Bowel preparation (yes/no)	13 485/4213	8256/1045	<**0.0001**	947/7747	948/7746	1.00	0.042
Prescription of anti-coagulant or anti-platelet drugs (yes/no)	3809/13 889	2032/7269	0.54	1895/6799	1892/6802	0.97	0.00084
Academic hospital (yes/no)	1791/15 907	723/8578	<**0.0001**	678/8016	684/8010	0.88	0.0026

The use of bold emphasis means statistical significant difference.

Table 2 Comparison of clinical event rates and hospital stay between urgent and elective colonoscopy groups

Clinical events	After propensity score matching Total (*n* = 17 386)		
	Urgent colonoscopy (*n* = 8693)	Elective colonoscopy (*n* = 8693)	*P* value
Endoscopic hemostasis, *n* (%)	263 (3.0%)	146 (1.7%)	<**0.0001**[†]
In-hospital death, *n* (%)	30 (0.35%)	50 (0.58%)	**0.033**[†]
Red blood cell transfusion, *n* (%)	3135 (36.0%)	3066 (35.3%)	0.39[†]
Radiological intervention, *n* (%)	37 (0.43%)	81 (0.93%)	<**0.0001**[†]
Surgery, *n* (%)	64 (0.74%)	73 (0.84%)	0.49[†]
Median days of hospital stay (interquartile range), days	8 (6.0–11.0)	9 (7.0–13.0)	<**0.0001**[‡]
Median medical costs of hospital stay (interquartile range), JPY	365 805 (265 893–521 488)	406 000 (309 110–574 939)	<**0.0001**[‡]

The use of bold emphasis means statistical significant difference.
[†]Chi-square test.
[‡]Wilcoxon signed-rank test.

hospital stay in the urgent colonoscopy group were lower than those in the elective colonoscopy group ($P < 0.0001$).

Multivariate analysis for in-hospital death before propensity score matching. The results of the multivariate analysis for in-hospital death are summarized in Table 3. On multivariate analysis, urgent colonoscopy (odds ratio [OR] = 0.67, 95% confidence interval [CI]: 0.46–0.97, $P = 0.036$), red blood cell transfusion (OR = 4.98, 95% CI: 3.18–7.81, $P < 0.0001$), heart failure (OR = 2.49, 95% CI: 1.55–4.00, $P = 0.0002$), liver disease (OR = 2.75, 95%

Table 3 Multivariate analysis[†] of the association among clinical factors and in-hospital death

Clinical factors	Number of patients (before propensity score matching)	In-hospital death		
		Odds ratio	95% CI	*P* value
Colonoscopy	Urgent: 17 698	**0.67**	**0.46–0.97**	**0.036**
	Elective: 9301	1		
Surgery	Yes: 209	2.34	076–6.56	0.14
	No: 26 790	1		
Red blood cell transfusion	Yes: 9788	**4.98**	**3.18–7.81**	**<0.0001**
	No: 17 211	1		
Radiological intervention	Yes: 187	1.63	0.37–7.18	0.52
	No: 26 812	1		
Heart failure	Yes: 1428	**2.49**	**1.55–4.00**	**0.0002**
	No: 25 571	1		
Cerebrovascular disease	Yes: 2145	0.81	0.41-1.57	0.52
	No: 24 854	1		
Respiratory disease	Yes: 852	1.73	0.79–3.78	0.17
	No: 26 147	1		
Liver disease	Yes: 570	**2.75**	**1.24–6.09**	**0.013**
	No: 26 429	1		
Diabetes with chronic complication	Yes: 556	1.72	0.72–4.10	0.22
	No: 26 443	1		
Renal disease	Yes: 1239	**2.66**	**1.66–4.26**	**<0.0001**
	No: 25 660	1		
Body mass index	Over weight: 7569	**0.47**	**0.26–0.85**	**0.013**
	Normal range: 15 529	1		
	Underweight: 2041	**2.56**	**1.69–3.87**	**<0.0001**
Sex	Male: 16 642	1		**0.0034**
	Female: 10 357	**0.54**	**0.36–0.82**	
Age	≥ 80 years: 10 262	1		
	70–79 years: 8335	**0.54**	**0.35–0.84**	**0.0068**
	60–69 years: 4968	**0.39**	**0.20–0.76**	**0.0051**
	50–59 years: 2306	**0.28**	**0.087–0.91**	**0.034**
	≤ 49 years: 1127	0.19	0.026–1.40	0.10
Smoking	Yes: 10 968	0.80	0.53–1.20	0.28
	No: 16 030	1		
Bowel preparation	Yes: 21 741	**0.30**	**0.21–0.43**	**<0.0001**
	No: 5257	1		
Prescription of anti-coagulant or anti-platelet drugs	Yes: 5840	0.67	0.43–1.05	0.080
	No: 21 158	1		
Academic hospital	Yes: 2514	**0.39**	**0.16–0.98**	**0.046**
	No: 24 485	1		

The use of bold emphasis means statistical significant difference.
[†]Logistic regression analysis.

CI: 1.24–6.09, $P = 0.013$), renal disease (OR = 2.66, 95% CI: 1.66–4.26, $P < 0.0001$), BMI categories (lower BMI), sex (male), age categories (advanced age), bowel preparation prior to colonoscopy (OR = 0.30, 95% CI: 0.21–0.43, $P < 0.0001$), and academic hospital (OR = 0.39, 95% CI: 0.16–0.98, $P = 0.046$) were identified as the clinical factors that affected in-hospital death.

Multivariate analysis for endoscopic hemostasis before propensity score matching. The results of multivariate analysis for endoscopic hemostasis are summarized in Table 4. On multivariate analysis, urgent endoscopy (OR = 1.84, 95% CI: 1.53–2.22, $P < 0.0001$), renal disease (OR = 1.50, 95% CI: 1.11–2.02, $P = 0.0077$), female sex (OR = 0.80, 95% CI: 0.67–0.96, $P = 0.016$), bowel preparation prior to colonoscopy (OR = 0.64, 95% CI: 0.54–0.77, $P < 0.0001$), and academic hospital (OR = 1.53, 95% CI: 1.23–1.91, $P = 0.0002$) were identified as the clinical factors that affected endoscopic hemostasis.

Discussion

We here investigated the efficacy of urgent colonoscopy for CDB and analyzed the clinical factors that affect the clinical course of CDB using a nationwide database in Japan. Our propensity score-matched analysis showed that urgent colonoscopy reduced the mortality rate owing to CDB and increased the rate of performing endoscopic hemostasis. The length of hospitalization was shorter in the urgent colonoscopy group than in the elective colonoscopy group. Multivariate analysis using the data before

Table 4 Multivariate analysis[†] of the association among clinical factors and endoscopic hemostasis

Clinical factors	Number of patients (before propensity score matching)	Endoscopic hemostasis		
		Odds ratio	95% CI	*P* value
Colonoscopy	Urgent: 17 698	**1.84**	**1.53–2.22**	**<0.0001**
	Elective: 9301	1		
Heart failure	Yes: 1428	1.22	0.90–1.66	0.20
	No: 25 571	1		
Cerebrovascular disease	Yes: 2145	0.91	0.68–1.22	0.53
	No: 24 854	1		
Respiratory disease	Yes: 852	0.88	0.56–1.39	0.59
	No: 26 147	1		
Liver disease	Yes: 570	0.89	0.51–1.55	0.68
	No: 26 429	1		
Diabetes with chronic complication	Yes: 556	1.28	0.82–2.02	0.28
	No: 26 443	1		
Renal disease	Yes: 1239	**1.50**	**1.11–2.02**	**0.0077**
	No: 25 660	1		
Body mass index	Over weight: 7569	0.88	0.74–1.05	0.16
	Normal range: 15 529	1		
	underweight: 2041	1.15	0.88–1.51	0.30
Sex	Male: 16 642	1		**0.016**
	Female: 10 357	**0.80**	**0.67–0.96**	
Age	≥ 80 years: 10 262	1		
	70–79 years: 8335	1.06	0.88–1.28	0.50
	60–69 years: 4968	0.97	0.78–1.23	0.84
	50–59 years: 2306	0.81	0.58–1.13	0.22
	≤ 49 years	1.41	0.99–2.02	0.059
Smoking	Yes: 10 968	1.02	0.86–1.20	0.82
	No: 16 030	1		
Bowel preparation	Yes: 21 741	**0.64**	**0.54–0.77**	**<0.0001**
	No: 5257	1		
Prescription of anti-coagulant or anti-platelet drugs	Yes: 5840	1.19	0.99–1.44	0.063
	No: 21 158	1		
Academic hospital	Yes: 2514	**1.53**	**1.23–1.91**	**0.0002**
	No: 24 485	1		

The use of bold emphasis means statistical significant difference.
[†]Logistic regression analysis.

propensity score matching also revealed a similar tendency. Moreover, our study showed several other clinical factors that affected the clinical course of CDB.

Although numerous studies have investigated LGB, the number of studies researching CDB is small. However, CDB is the most common cause of LGB.[17] Thus, investigating the efficacy of urgent colonoscopy for the rate of CDB-related unfavorable event, including in-hospital death, and clinical factors that affect the clinical course of CDB is necessary to treat LGB.

According to previous studies, the efficacy of urgent colonoscopy for CDB was controversial. One retrospective study reported that urgent colonoscopy shortened the length of admission for CDB.[7] Similar randomized control trial studies, which targeted LGB rather than CDB, reported inconsistent results regarding the efficacy of urgent colonoscopy in terms of the length of hospital stay, blood transfusion, re-bleeding, and surgery.[9–11] Another study, which was based on propensity matching score analysis using a regional database in Japan, reported that urgent colonoscopy for LGB made it possible to perform endoscopic hemostasis and shorten the length of hospitalization.[18] However, it also reported that urgent colonoscopy for LGB did not reduce mortality.[18] This discrepancy among studies might be because of the relatively small number of patients included in each study.

Our study, which included a large number of patients, showed the efficacy of urgent colonoscopy for CBD. The chi-square test after propensity score matching and multivariate analysis before propensity score matching revealed that urgent colonoscopy reduced in-hospital death. To the best of our knowledge, no previous study had reported an association between urgent colonoscopy and in-hospital death. Although CDB typically has a relatively good prognosis,[4,5,17] some cases have a fatal course. However, the rate of mortality in CDB is very low. In our cohort, the mortality rate owing to CDB was only 0.51%, which was similar to previous findings.[2,9,11,18] This may have had an impact on the lack of evidence in previous, smaller-scale studies regarding the efficacy of urgent colonoscopy in reducing mortality cases.

Our study also showed that urgent colonoscopy and bowel preparation affected performance of endoscopic hemostasis. Although

urgent colonoscopy is useful for identification of the bleeding site, leading to increased endoscopic hemostasis, bowel preparation decreased the possibility of endoscopic hemostasis. However, multivariate analysis showed that bowel preparation was able to reduce the morality rate in CDB. There seems to be some discrepancy between in-hospital death and endoscopic hemostasis in terms of bowel preparation. We hypothesized that patients who could undergo bowel preparation generally were in a good condition, which contributed to decreased mortality cases. Previous reports showed opposite results about the efficacy of bowel preparation.[19,20] The necessity of bowel preparation before urgent colonoscopy was unclear in our study. Bowel preparation might wash away coagula attached to a diverticulum, which make it difficult to detect bleeding points in CDB cases. Our results indicated that urgent colonoscopy without bowel preparation might increase the detection rate of the bleeding point in CDB, even though the endoscopist may have difficulty in the colonoscopy owing to the amount of coagula and stool present. Nevertheless, urgent colonoscopy could lead to performance of endoscopic hemostasis, which may help to reduce mortality. Thus, the necessity and appropriate timing of urgent colonoscopy should be considered based on the patient's condition.

Our study revealed a shorter length of hospitalization in the urgent colonoscopy group, which was consistent with the findings of previous reports.[7,19,21] This may only reflect that urgent colonoscopy allows physicians to recognize patients' condition and decide on the therapeutic strategy, which contributes to an earlier discharge from hospital. However, as described above, urgent colonoscopy could facilitate early endoscopic hemostasis, which could contribute to shortening the length of hospital stay. The medical costs of hospital stay were also lower in the urgent colonoscopy group compared with the elective colonoscopy group. This result might reflect that shorter length of hospital stay contribute to the lower medical costs in the urgent colonoscopy group.

According to multivariate analysis, other clinical factors, such as red blood cell transfusion, heart failure, liver disease, renal disease, underweight, male sex, and advanced age, were identified as risk factors for mortality. It is plausible that patients who require red blood cell transfusion or have an advanced age have a higher risk of mortality and complications (heart failure, liver disease, and renal disease). Although the reason for the higher risk of mortality in men and in underweight cases is unclear, a previous study also found that advanced age is a risk factor for mortality.[2] The multivariate analysis also revealed that academic hospital was related to decreased in-hospital death and increased endoscopic hemostasis. This result indicates that high volume centers such as academic hospital, which can provide intensive therapies, have an advantage for treating CDB.

This study had several limitations. First, the DPC database does not record the time of admission; it includes only the date of admission. Thus, we defined colonoscopy on day 1 or day 2 as urgent colonoscopies. Other studies have defined urgent colonoscopy as a colonoscopy conducted within 24 h after admission.[22] Therefore, we cannot simply compare this study with other studies. Second, the DPC database does not contain details of the patients' condition, such as endoscopic findings, laboratory data, and computed tomography findings. Therefore, we could not evaluate the severity of the patients' condition precisely. Third, the DPC-participating hospitals were typically acute-care and relatively large-volume hospitals. Therefore, data from the DPC did not necessarily reflect all patients. Fourth, the *C*-statistics of the propensity score matching was 0.59 (<0.6). Although the patients' backgrounds before propensity score matching seemed to be different, differences in their sex, age, and BMI were not particularly large, which may account for the low *C*-statistics. The standardized differences after propensity score matching were also <0.1 in all factors. Therefore, we consider that the propensity score matching was conducted properly. Nevertheless, the efficacy of urgent colonoscopy was recognized in both the chi-square test after propensity score matching and in the multivariate analysis before propensity score matching. Although there were several limitations, the DPC database allowed us to collect and handle data from a large number of patients, which is useful for establishing hypothesis and for future study design.

In conclusion, urgent colonoscopy for CDB might lead to identification of the bleeding site and reducing in-hospital death. The necessity and appropriate timing of urgent colonoscopy should be established based on the patient's condition. Although the mortality rate owing to CDB is very low, the DPC database was useful for analyzing such a rare complication.

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