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The Association between Diverticular Rebleeding and Early-Morning Blood Pressure and Surge: A Prospective Observational Trial

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Keywords
Pre-awaking surge · Diverticular rebleeding · 24-h blood pressure · Hypertension

Abstract
Introduction: Colonic diverticular bleeding is the major cause of lower gastrointestinal bleeding. Hypertension is a major risk factor for diverticular rebleeding. Direct evidence of an association between actual 24-h blood pressure (BP) and rebleeding is lacking. Therefore, we analyzed the association between 24-h BP and diverticular rebleeding. ***Methods:*** We performed a prospective observational cohort trial involving hospitalized patients with colonic diverticular bleeding. We performed 24-h BP measurements (ambulatory BP monitoring [ABPM]) in the patients. The primary outcome was diverticular rebleeding. We evaluated the 24-h BP difference and the morning and pre-awaking BP surge between rebleeding and non-rebleeding patients. Morning BP surge was defined as early-morning systolic BP minus the lowest night systolic BP >45 mm Hg (highest quartile of morning BP surge). The pre-awaking BP surge was defined as the difference between morning BP and pre-awaking BP. ***Results:*** Of 47 patients, 17 were excluded, leaving 30 who underwent ABPM. Of the 30 patients, 4 (13.33%) had rebleeding. The mean 24-h systolic and diastolic BP were 125.05 and 76.19 mm Hg in rebleeding patients and 129.98 and 81.77 mm Hg in non-rebleeding patients, respectively. Systolic BP at 5:00 (difference −23.53 mm Hg, p = 0.031) and 11:30 (difference −31.48 mm Hg, p = 0.006) was significantly lower in rebleeding patients than in non-rebleeding patients. Diastolic BP at 2:30 (difference −17.75 mm Hg, p = 0.023) and 5:00 (difference −16.12 mm Hg, p = 0.043) was significantly lower in rebleeding patients than in non-rebleeding patients. A morning surge was observed in one rebleeding patient and no non-rebleeding patients. The pre-awaking surge was significantly higher in rebleeding patients (28.44 mm Hg) than in non-rebleeding patients (9.30 mm Hg) (p = 0.015). ***Conclusion:*** Lower BP in the early-morning and a higher pre-awaking surge were risk factors for diverticular rebleeding. A 24-h ABPM can identify these BP findings and reduce the risk of rebleeding by enabling interventions in patients with diverticular bleeding.

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Introduction

Colonic diverticular bleeding is one of the most common severe lower gastrointestinal bleeding events requiring hospitalization, transfusion, and hemostatic interventions [1, 2]. Rebleeding is the most important clinical issue in colonic diverticular bleeding patients. In observational studies, hypertension- and arteriosclerosis-related factors were associated with the risk of rebleeding [3–6]. However, these studies analyzed the association between hypertension drug use and rebleeding but did not measure blood pressure (BP) or its association with rebleeding.

Colonic diverticular bleeding and rebleeding often occur at night or in the early morning. Thus, 24-h BP monitoring can be used to evaluate the association between hypertension and rebleeding in patients with colonic diverticular bleeding. Ambulatory BP monitoring (ABPM) has been used in studies of cardiovascular diseases [7–13] and cerebrovascular diseases [14]. ABPM can also evaluate the 24-h BP-related circadian rhythm and morning BP surge, which are significantly associated with cardiovascular events [7–13]. We hypothesized that this 24-h BP-related circadian rhythm could be applicable to colonic diverticular bleeding in hypertension patients.

We performed a prospective ABPM trial involving colonic diverticular bleeding patients with 1-year follow-up data to evaluate the association between 24-h BP and rebleeding events. Furthermore, we evaluated the association between 24-h BP-related circadian rhythm and colonic diverticular rebleeding.

Methods

Patients

Outpatients aged 20–84 years who presented with hematochezia requiring hospitalization were eligible. The inclusion criteria were (1) diagnosis of colonic diverticular bleeding, defined as diverticulosis with active bleeding, visible vessels, or blood clot or without other reasons for bloody stool [15] by colonoscopy and (2) requirement of hypertension drug therapy or a systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg.

The exclusion criteria were upper gastrointestinal bleeding, other lower gastrointestinal bleeding, pregnancy, acute cardiovascular and cerebrovascular diseases, malignant diseases, colectomy for hemostasis, vasculitis, Raynaud's syndrome, or hemodialysis patients with a blood shunt on both arms. Eligible patients were interviewed by the investigators to collect information about medications and the current statuses of smoking and regular alcohol use.

Trial Design, Colonic Diverticular Bleeding Treatment, ABPM Examination, and Follow-Up

Colonoscopies were performed using an electronic video endoscope (Olympus Optical, Tokyo, Japan or Fujifilm Corporation, Tokyo, Japan) after administration of 2–4 L oral bowel preparation solution. Patients diagnosed with recent colonic diverticular bleeding were treated by endoscopic hemostasis. Endoscopic findings, including definitive/presumptive colonic diverticular bleeding, were immediately recorded after examination. Definitive colonic diverticula bleeding was defined as positive stigmata recent of hemorrhage colonic diverticular bleeding. Stigmata recent of hemorrhage included active bleeding, a visible vessel, or an adherent clot [16]. Endoscopic hemostasis methods were decided by each endoscopist. The decision to continue or discontinue antithrombotic agents was performed by the attending physicians. Patients with a hemoglobin level <7 g/dL on admission received blood transfusions. After resolution of colonic diverticular bleeding, the patients underwent ABPM examinations.

We performed ABPM examinations using a noninvasive, portable device (Omron, HEM-7051®, 217AGBZX00002000). Systolic and diastolic BP and heart rate were measured every 30 min for 24 h, including the day (0900–2100 h) and night (0100–0600 h). During the examination, patients were only allowed to perform normal activities necessary for life. Data were automatically recorded on a portable device and immediately transferred to a software package. Colonic diverticular rebleeding was monitored at 3-month intervals for 1 year after initial colonic diverticular bleeding.

Outcomes

The primary outcome was colonic diverticular rebleeding, defined as significant fresh blood loss after initial colonoscopy with any of the following: (i) identification of blood pooling on further colonoscopy; (ii) diverticulosis with active bleeding, visible vessels, or blood clot or without any other reasons for blood stool. We evaluated the 24-h BP difference between rebleeding and non-rebleeding patients. The 24-h BP was calculated from the mean 24-h systolic and diastolic BP and the systolic and diastolic BP at each time point. We also evaluated BP circadian rhythm type, morning BP surge, pre-awaking BP surge, sleep BP, awake BP, evening BP, lowest BP, pre-awaking BP, and morning BP. BP circadian rhythm type was evaluated as 100 × (1 − average sleep time BP ÷ average wake time BP); >20% was defined as the extreme dipper type; 10–20% as the dipper type; 0–10% as the non-dipper type; <0% as the riser type. Morning BP surge was defined as early-morning systolic BP minus the lowest night systolic BP >45 mm Hg (highest quartile of the morning BP surge) (Fig. 1).

Statistical Analysis

The mean 24-h BP was compared between rebleeding and non-rebleeding patients using the Wilcoxon rank sum test. Data on circadian BP rhythm and morning and pre-awaking BP surges were compared between rebleeding and non-rebleeding patients using the χ^2 test. Sleep BP, awake BP, evening BP, lowest BP, pre-awaking BP, and morning BP were also compared between rebleeding and non-rebleeding patients using the Wilcoxon rank sum test. A p value of <0.05 was considered significant. All statistical analyses were performed using SAS software (ver. 9.4; SAS Institute, Cary, NC, USA).

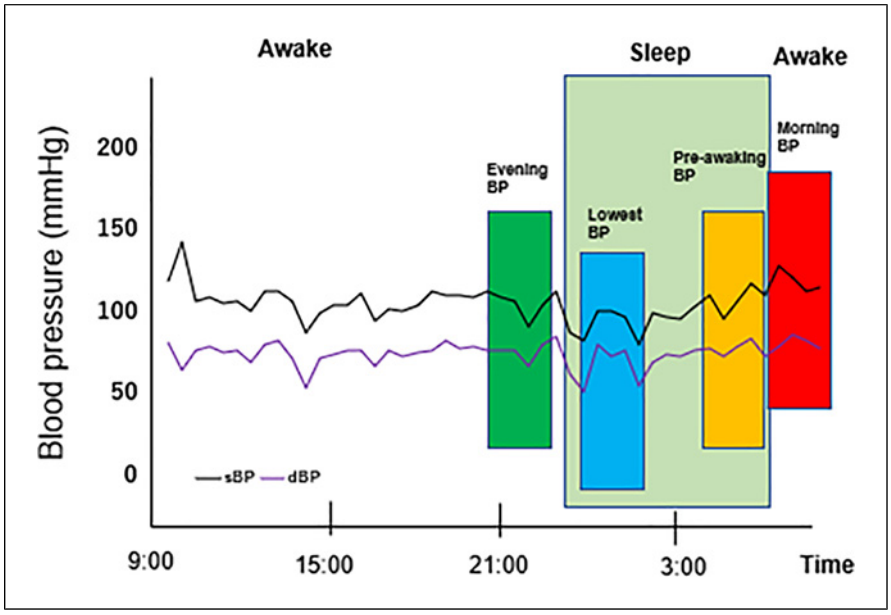

Fig. 1. Definition of 24-h ABPM: data of case no. 1. Sleep-through surge = morning SBP – lowest SBP. Morning surge: sleep-through surge >45–55 mm Hg. Pre-awaking surge = morning SBP – pre-awake SBP. Sleep time SBP reduction rate = 100 × (1 – average sleep time SBP/average wake time BP). Extreme dipper: >20%, dipper: 10–20%, non-dipper: 0–10%, riser: <0%.

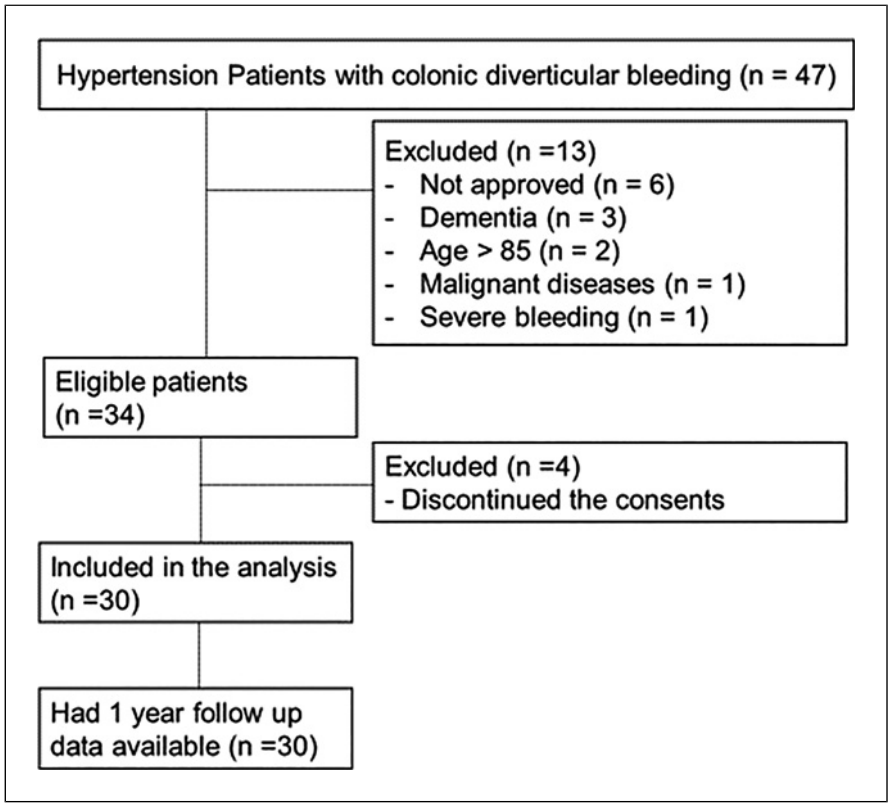

Fig. 2. Patient flow.

Results

Of 47 patients enrolled from 2013 to 2015, 17 were excluded, leaving 30 who underwent ABPM (Fig. 2). Of the 30 patients who underwent ABPMs, 26 had hypertension comorbidities and were using antihypertensive drugs, and 4 patients had a systolic BP >140 mm Hg during hospitalization for colonic

Table 1. Baseline characteristics (N = 30)

Variables	Rebleeding (n = 4)	Non-rebleeding (n = 26)	p value
Sex, male	3 (75.00)	16 (61.54)	1.000
Mean age, years	65.00±8.12	70.38±9.51	0.233
Mean body mass index	26.70±7.82	23.07±3.10	0.562
Current smoking	3 (75.00)	7 (26.92)	0.095
Regular alcohol use	1 (25.00)	6 (23.08)	1.000
Diverticular bleeding history	3 (75.00)	11 (42.31)	0.316
Comorbidities			
Ischemic heart disease	1 (25.00)	7 (26.92)	1.000
Chronic obstructive pulmonary disease	0 (0.00)	0 (0.00)	1.000
Peripheral vascular disease	2 (50.00)	0 (0.00)	**0.014**
Liver cirrhosis	0 (0.00)	1 (3.85)	1.000
Diabetes mellitus	2 (50.00)	5 (19.23)	0.225
Chronic heart failure	0 (0.00)	1 (3.85)	1.000
Stroke	0 (0.00)	4 (15.38)	1.000
Dementia	0 (0.00)	1 (3.85)	1.000
Collagen diseases	0 (0.00)	2 (7.69)	
Chronic kidney disease	0 (0.00)	7 (26.92)	0.548
Dyslipidemia	1 (25.00)	11 (42.31)	0.632
Hyper uric acid	0 (0.00)	1 (7.69)	1.000
Acquired immunodeficiency syndrome	0 (0.00)	0 (0.00)	1.000
Medications			
Antihypertensive drug*	2 (50.00)	20 (76.92)	0.284
Calcium receptor blocker	0 (0.00)	14 (53.85)	0.103
ARB/ACEI	2 (50.00)	10 (38.46)	1.000
B blocker	0 (0.00)	7 (23.33)	0.548
The number of antihypertensive drugs			
Non/single/double/triple	2/2/0/0	6/10/8/2	0.65
NSAIDs	1 (25.00)	3 (11.54)	0.455
Antiplatelet drugs	1 (25.00)	10 (38.46)	1.000
Anticoagulation drugs	0 (0.00)	4 (15.38)	1.000
Steroid	0 (0.00)	4 (15.38)	1.000
Sleeping drug	0 (0.00)	3 (11.54)	1.000
Laboratory data on admission			
Mean hemoglobin, g/dL	10.63±0.48	10.78±2.09	1.000
Mean hematocrit	31.50±1.00	32.92±6.00	0.756
Endoscopic findings			
Definitive/presumptive bleeding	1/3	5/22	0.538
Stigmata recent of hemorrhage (active/nonactive)	1/0	2/3	0.612
Treatment/management			
Endoscopic hemostasis (clipping)	1 (25.00)	4 (15.38)	0.538
Transfusion	0 (0.00)	8 (30.77)	0.550
Management of antithrombotic agents			
Continuation	1 (25.00)	4 (15.38)	0.500
Discontinuation with heparin bridge	0 (0.00)	1 (7.69)	
Discontinuation without heparin bridge	0 (0.00)	6 (23.08)	

Definitive colonic diverticula bleeding was defined as positive stigmata recent of hemorrhage colonic diverticular bleeding. Stigmata recent of hemorrhage included active bleeding, a visible vessel, or an adherent clot. Percentages are shown in parentheses. ± shows standard deviation; bold shows $p < 0.05$. *Duplicated allowed.

diverticular bleeding. The baseline characteristics are shown in Table 1. The diverticular type was on the left side in 6 patients, on the right side in 8 patients, and bilaterally in 16 patients. Eight patients received transfusions, and five underwent endoscopic hemostasis.

Table 2. Association between 24-h BP and colonic diverticula rebleeding

Outcome	Rebleeding patients (n = 4)	Non-rebleeding patients (n = 26)	Mean difference of systolic BP between rebleeding and non-rebleeding groups	p value
Mean 24-h systolic BP	125.0	129.1	−4.08 (−7.54 to −0.63)	**0.021**
Systolic BP				
Time point				
00:00	104.5	128.2	−23.66 (−49.68 to 2.36)	0.107
00:30	122.0	120.7	1.28 (−30.61 to 33.17)	0.591
01:00	119.0	117.7	1.16 (−27.74 to 30.06)	0.635
01:30	125.3	122.2	3.05 (−28.01 to 34.11)	0.975
02:00	101.7	121.3	−19.60 (−51.54 to 12.33)	0.252
02:30	99.67	118.1	−18.41 (−42.41 to 5.58)	0.069
03:00	113.8	122.4	−8.63 (−32.88 to 15.61)	0.562
03:30	104.7	122.1	−17.41 (−40.53 to 5.70)	0.119
04:00	121.7	121.4	0.23 (−24.48 to 24.93)	0.824
04:30	118.3	123.4	−5.07(-30.32 to 20.19)	0.710
05:00	102.8	126.3	−23.53 (−49.13 to 2.07)	**0.031**
05:30	120.0	127.2	−7.15 (−31.75 to 17.45)	0.562
06:00	125.5	127.2	−1.70 (−27.28 to 23.88)	0.874
06:30	124.0	130.5	−6.52 (−29.95 to 16.90)	0.467
07:00	129.0	132.8	−3.80 (−27.39 to 19.79)	0.752
07:30	130.5	137.5	−6.96 (−31.67 to 17.75)	0.533
08:00	132.5	135.5	−3.00 (−28.21 to 22.21)	0.818
08:30	142.3	140.1	2.13 (−21.34 to 25.60)	1.000
09:00	134.8	138.6	−3.81 (−30.62 to 23.00)	0.849
09:30	131.0	140.5	−9.45 (−47.34 to 28.44)	0.732
10:00	121.7	141.0	−19.29 (−44.41 to 5.83)	0.127
10:30	129.0	129.4	−0.41 (−25.07 to 24.25)	0.749
11:00	123.0	134.3	−11.32 (−33.61 to 10.97)	0.296
11:30	107.3	138.7	−31.48 (−51.31 to −11.65)	**0.010**
12:00	122.8	130.8	−8.10 (−29.03 to 12.84)	0.376
12:30	124.3	124.0	0.25 (−33.49 to 33.99)	0.855
13:00	134.5	129.5	5.04 (−18.07 to 28.14)	0.691
13:30	125.5	127.4	−1.93 (−27.39 to 12.54)	0.855
14:00	130.3	122.6	7.65 (−18.20 to 33.50)	0.527
14:30	131.0	125.6	5.36 (−15.09 to 25.81)	0.507
15:00	136.5	127.5	9.02 (−14.14 to 32.18)	0.608
15:30	127.0	129.9	−2.92 (−21.93 to 16.09)	0.635
16:00	127.8	131.4	−3.65 (−25.25 to 17.95)	0.825
16:30	132.0	133.6	−1.61(−23.23 to 20.00)	1.000
17:00	129.1	135.0	5.92 (−17.19 to 29.03)	0.647
17:30	126.8	134.3	−7.57 (−30.31 to 15.17)	0.752
18:00	124.5	134.1	−9.58 (−31.82 to 12.66)	0.486
18:30	140.8	133.8	6.90 (−16.32 to 30.13)	0.393
19:00	127.3	134.3	−7.06 (−30.00 to 15.88)	0.522
19:30	138.8	133.1	5.63 (−19.00 to 30.26)	0.752
20:00	123.3	130.3	−7.06 (−28.63 to 14.52)	0.604
20:30	132.0	125.2	6.81 (−17.18 to 30.80)	0.647
21:00	134.5	129.0	5.46 (−20.00 to 30.92)	0.507
21:30	130.8	131.3	−0.54 (−27.70 to 26.62)	0.922
22:00	125.8	129.1	−3.33 (−26.72 to 20.06)	0.825
22:30	124.0	129.9	−5.88 (−25.39 to 13.63)	0.527
23:00	122.3	125.4	−31.15 (−27.07 to 20.77)	0.658
23:30	124.0	123.8	0.20 (−26.64 to 27.04)	0.327

Table 2 (continued)

Outcome	Rebleeding patients (n = 4)	Non-rebleeding patients (n = 26)	Mean difference of systolic BP between rebleeding and non-rebleeding groups	p value
Mean diastolic BP	76.2	81.2	−5.03 (−7.30 to 2.75)	**<0.001**
Diastolic BP				
Time point				
00:00	62.3	79.1	−16.87 (−33.16 to −0.58)	0.106
00:30	76.0	74.0	1.96 (−14.68 to 18.60)	1.000
01:00	68.3	77.8	−9.50 (−30.12 to 11.10)	0.375
01:30	72.3	76.0	−3.79 (−16.70 to 9.11)	0.506
02:00	60.3	73.6	−13.28 (−32.36 to 5.80)	0.068
02:30	59.3	77.1	−17.75 (−35.67 to 0.18)	**0.023**
03:00	74.0	78.1	−4.08 (−22.04 to 13.89)	0.410
03:30	61.7	76.5	−14.81 (−28.78 to −0.84)	0.094
04:00	71.3	76.3	−4.95 (−19.33 to 9.44)	0.552
04:30	68.3	80.2	−11.91 (−26.94 to 3.13)	0.094
05:00	65.0	81.1	−16.12 (−31.96 to −0.27)	**0.043**
05:30	68.0	79.3	−11.35 (−24.97 to 2.28)	0.189
06:00	81.8	81.4	0.31 (−12.86 to 13.48)	0.975
06:30	75.0	81.4	−6.36 (−21.71 to 8.99)	0.569
07:00	75.0	85.7	−10.72 (−25.71 to 4.27)	0.217
07:30	81.8	85.5	−3.75 (−19.49 to 11.99)	0.410
08:00	81.3	87.5	−6.21 (−26.72 to 14.31)	0.250
08:30	90.5	89.4	1.14 (−13.38 to 15.66)	0.924
09:00	80.8	83.8	−3.01 (−24.80 to 18.78)	0.752
09:30	69.0	79.9	−11.85 (−43.83 to 20.13)	0.331
10:00	74.3	84.7	−10.41 (−29.20 to 8.39)	0.172
10:30	83.0	85.5	−2.55 (−21.55 to 16.46)	0.749
11:00	79.0	79.3	−0.32 (−20.72 to 20.08)	1.000
11:30	73.3	84.2	−10.98 (−27.82 to 5.86)	0.246
12:00	79.8	83.3	−3.52 (−21.73 to 14.69)	0.669
12:30	78.8	79.5	−0.75 (−16.44 to 14.94)	0.647
13:00	80.8	84.1	−3.37 (−19.73 to 12.99)	0.760
13:30	76.5	78.7	−2.15 (−18.67 to 14.06)	0.482
14:00	70.8	77.6	−6.81 (−22.24 to 8.62)	0.526
14:30	81.0	81.1	−0.08 (−14.94 to 14.78)	0.950
15:00	82.0	79.3	2.65 (−10.63 to 15.94)	0.657
15:30	78.8	81.9	−3.13 (−17.48 to 11.22)	0.613
16:00	77.3	83.3	−6.03 (−22.82 to 10.76)	0.548
16:30	79.5	85.2	−5.69 (−22.76 to 11.38)	0.502
17:00	81.0	82.5	−1.46 (−12.80 to 9.88)	0.760
17:30	79.8	79.8	−0.09 (−13.82 to 13.64)	0.924
18:00	79.5	85.5	−6.02 (−20.57 to 8.53)	0.194
18:30	84.5	83.3	1.15 (−15.03 to 17.34)	1.000
19:00	84.0	83.8	0.15 (−16.92 to 17.22)	0.783
19:30	82.0	81.6	0.40 (−13.35 to 14.15)	0.704
20:00	79.3	82.7	−3.48 (−19.37 to 12.41)	0.604
20:30	76.8	78.0	−1.21 (−16.53 to 14.10)	0.669
21:00	83.5	82.3	1.18 (−16.12 to 18.48)	0.752
21:30	79.0	83.8	−4.83 (−23.11 to 13.45)	0.449
22:00	78.0	81.8	−3.80 (21.23 to 13.63)	0.375
22:30	73.5	83.0	−9.54 (−22.54 to 3.46)	0.128
23:00	67.8	81.0	−12.21 (−27.48 to 3.06)	0.194
23:30	72.8	78.7	−5.93 (−20.26 to 8.40)	0.704

95% CIs are in parentheses. Bold shows $p < 0.05$. BP, blood pressure.

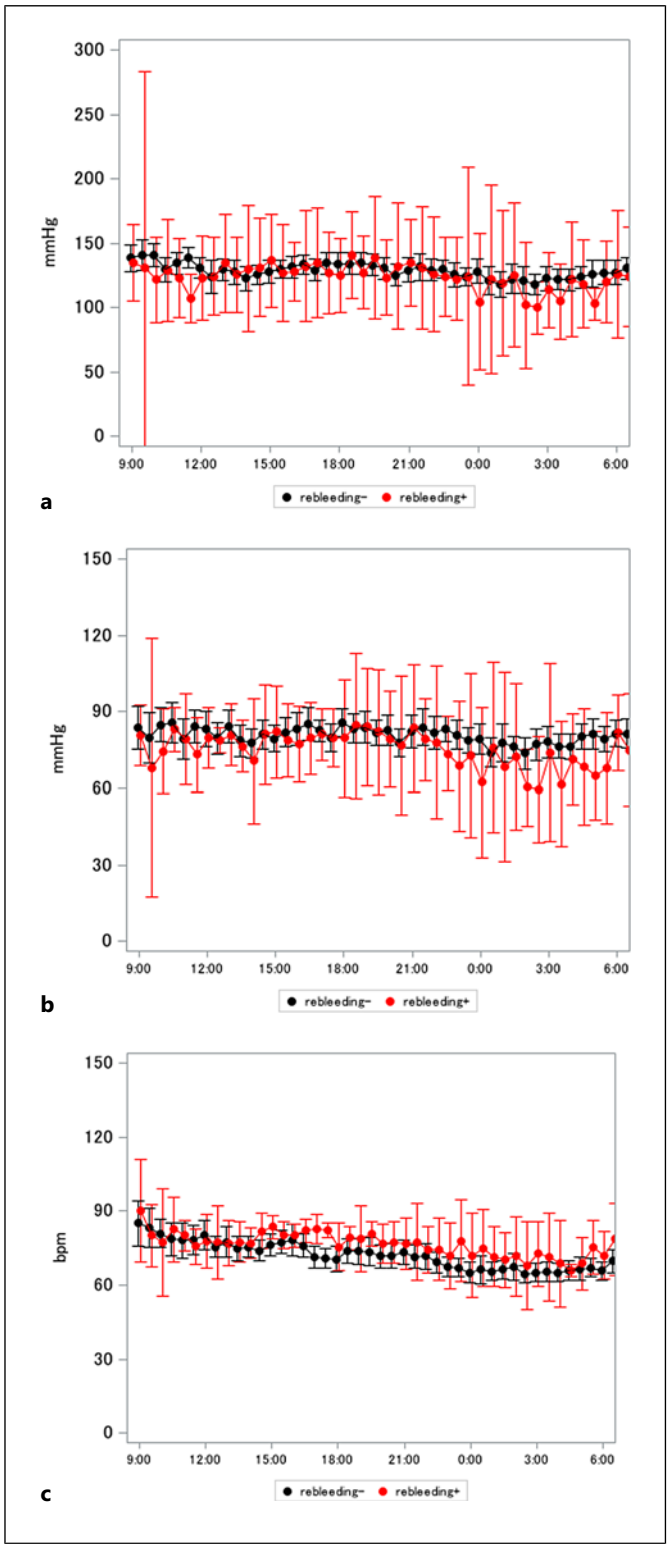

Fig. 3. 24-h BP at each time point: systolic BP (**a**), diastolic BP (**b**), and heart rate (**c**).

24-h BP

Of the 30 patients who underwent APBMs, 4 patients (13.33%) occurred rebleeding. Antihypertensive drugs were used by 2 rebleeding patients and 20 non-rebleeding patients. The mean 24-h systolic and diastolic BP were 125.0 and 76.2 mm Hg in rebleeding patients and 129.1 and 81.2 mm Hg in non-rebleeding patients, respectively. Systolic and diastolic BPs at the various time points are shown in Table 2 and Figure 3. The systolic BP at 5:00 (difference −23.53 mm Hg, 95% confidence interval [CI] −49.13 to 2.07, p = 0.031) and 11:30 (difference −31.48 mm Hg, 95% CI −51.31 to −11.65, p = 0.006) was significantly lower in rebleeding patients than in non-rebleeding patients. The diastolic BP at 2:30 (difference −17.75 mm Hg, 95% CI −35.67 to 0.18, p = 0.023) and 5:00 (difference −16.12 mm Hg, 95% CI −31.97 to −0.27, p = 0.043) was significantly lower in rebleeding patients than in non-rebleeding patients.

24-h BP-Related Circadian Rhythm

Regarding circadian BP rhythm, 1 and 2 rebleeding and non-rebleeding patients had the extreme dipper type, 2 and 11 rebleeding and non-rebleeding patients the dipper type, 1 and 9 rebleeding and non-rebleeding patients the non-dipper type, and 0 and 4 rebleeding and non-rebleeding patients the riser type, respectively. There was no significant association between the circadian BP rhythm type and rebleeding occurrence. Morning surge occurred in one rebleeding patient and in no non-rebleeding patient. The mean pre-awaking diastolic BP was significantly lower in rebleeding patients (64.31 mm Hg) than in non-rebleeding patients (78.20 mm Hg). The pre-awaking surge was significantly higher in rebleeding patients (28.44 mm Hg) than in non-rebleeding patients (9.30 mm Hg) (p = 0.015). No significant difference in sleep BP, awake BP, evening BP, lowest BP, pre-awaking BP, or morning BP was observed between the rebleeding and non-rebleeding patients (Table 3).

Discussion

The systolic and diastolic BPs in the early morning were significantly lower in rebleeding patients than in non-rebleeding patients. Additionally, the pre-awaking surge was higher in rebleeding patients than in non-rebleeding patients.

Approximately 70% of patients with acute lower gastrointestinal bleeding experience bleeding events

Table 3. Associations between 24-h BP-related circadian rhythm and colonic diverticular bleeding

Outcomes	Rebleeding patients (n = 4)	Non-rebleeding patients (n = 26)	p value
BP circadian rhythm type			
Extreme dipper/dipper/non-dipper/riser	1/2/1/0	2/11/9/4	0.616
Morning surge >45 mm Hg	1 (25.00)	0 (0.00)	0.133
Pre-awaking surge	28.44±9.98	9.30±28.44	**0.015**
Mean sleep BP			
Systolic BP	112.62±16.82	122.32±17.73	0.344
Diastolic BP	69.03±14.47	78.81±14.93	0.152
Mean awake BP			
Systolic BP	131.34±19.15	133.28±15.44	0.737
Diastolic BP	80.00±8.26	83.13±9.61	0.410
Mean evening BP			
Systolic BP	134.50±28.88	132.38±18.04	0.879
Diastolic BP	78.06±6.79	84.38±12.83	0.212
Mean night lowest BP			
Systolic BP	103.56±13.78	113.20±17.47	0.170
Diastolic BP	64.31±12.36	79.07±37.87	0.286
Mean pre-awaking BP			
Systolic BP	105.94±12.50	123.45±19.34	0.059
Diastolic BP	64.31±8.44	78.20±12.32	**0.024**
Mean morning BP			
Systolic BP	134.38±17.05	132.75±19.97	0.807
Diastolic BP	83.00±5.88	86.67±12.07	0.329

± shows standard deviation. Bold shows $p < 0.05$. BP, blood pressure.

after medical care, including early morning and midnight [16]. However, whether BP and its changes are associated with the risk of colonic diverticular rebleeding is unknown. In this study, colonic diverticular rebleeding patients had lower systolic and diastolic BP in the early morning, which may have contributed to the pre-awaking and morning surges (rapid BP changes of almost 20 mm Hg) and resulted in colonic diverticular rebleeding. Morning and pre-awaking surges are risk factors for cardiovascular events and stroke [7–9]. A rapid change in BP in the morning may lead to vessel burden, thrombosis, and rupture. In addition, BP surge could contribute to the progression of arteriosclerosis and alter arterial elasticity, increasing the risk of vessel rupture.

Our findings and prior reports suggest that optimal BP management of pre-awaking surge and lower BP in early morning may reduce the risk of colonic diverticular bleeding. 24-h ABPM is needed to evaluate whether antihypertensive treatments can control BP in the early morning and reduce the morning and pre-awaking surges. If patients with a history of colonic diverticular bleeding do not achieve an appropriate BP, physicians need to confirm their compliance with antihypertensive medication regimens. The timing of administration of antihypertensive drugs is important. Observational studies [17, 18] and a clinical trial [19] have shown that evening administration of antihypertensive medications reduces BP in early morning and prevents cardiovascular events. In this study, half of the rebleeding patients used antihypertensive medications in the morning. A change in the evening administration of antihypertensives might reduce the risk of colonic diverticular rebleeding.

In this study, we analyzed the association between 24-h BP and the risk of diverticular rebleeding for only hypertension patients because of ethical reasons. Therefore, the impact of BP change on diverticular rebleeding in patients without hypertension is unknown. However, rapid BP alteration, including pre-awaking surge within the normal range of BP, might be a risk factor for diverticular rebleeding even for patients without hypertension. Further studies are needed to elucidate these associations in the future.

This study has several strengths. It is the first prospective observational study of the association between 24-h BP and the risk of colonic diverticular rebleeding. A low BP in early morning and a higher pre-awaking BP surge were associated with a higher risk of colonic diverticular rebleeding. This study has

the limitations of a very small sample size and a single-center design, which limited the generalizability of the findings.

Conclusion

In conclusion, a lower BP in early morning and pre-awaking surge are risk factors for colonic diverticular rebleeding. Twenty-four-hour ABPM can identify these BP findings and thereby enable administration of anti-hypertensives in a timely manner to patients with colonic diverticular bleeding.

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Statement of Ethics

This trial obtained written informed consent. This trial was approved by the Institutional Review Board of the University of Tokyo (registration no. 10393-(2)).

Conflict of Interest Statement

The authors declare that they have no conflicts of interest.

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Author Contributions

Ryota Niikura and Atsuo Yamada conceptualized the trial design. Junya Arai, Ryota Niikura, and Atsuo Yamada collected the data. Junya Arai and Ryota Niikura analyzed the data. Junya Arai and Ryota Niikura drafted the manuscript. Atsuo Yamada, Tomonori Aoki, Nobumi Suzuki, Yosuke Tsuji, Yoku Hayakawa, Takashi Kawai, and Mitsuhiro Fujishiro contributed to manuscript editing. All the authors approved the final version of the manuscript.

Data Availability Statement

Data are not publicly available due to ethical reasons. Further inquiries can be directed to the corresponding author.

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