

Research Article

# Correlative Factors of Severity of Air Bubbles in the Large Intestine during Colonoscopy

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# **Abstract**

**Objectives** The condition of air bubbles in the large intestine is an influential factor for good quality of colonoscopy. However, the correlative factors of severity of air bubbles during colonoscopy in the large intestine are not established. Therefore, this study aimed to elucidate the correlative factors influencing the severity of air bubbles in the large intestine.

**Materials and Methods** A total of 314 examinees who underwent colonoscopy between August and September 2022 were enrolled (median age [range], 65 [18–88] years). Air bubbles were scored using the Colon Endoscopic Bubble Scale (CEBuS) and the clinical factors associated with the CEBuS scores, especially in the ileocecum, were analyzed.

**Results** In this study, 39.8% (125/314) of examinees harbored severe air bubbles in the ileocecum. Multiple linear regression analysis revealed that the CEBuS scores in the ileocecum were positively associated with the interval time from completion of bowel preparation to intubation of the cecum (p = 0.0016) and a history of cholecystectomy (p = 0.0198). Logistic regression analysis between no, mild, and moderate air bubbles group (n = 189) and severe air bubbles group (n = 125) also showed that severity was positively associated with the interval time from completion of bowel preparation to intubation of the cecum (p = 0.0332) and a history of cholecystectomy (p = 0.0095). **Conclusion** Interval time and history of cholecystectomy were associated with severity of air bubbles in the large intestine after bowel preparation.

#### **Keywords**

- ► colon
- colonoscopy
- ► colorectal polyp
- endoscopy

# Introduction

Colorectal cancer (CRC) is the third major cause of cancer and the second major cause of cancer death. The incidence and mortality of CRC are estimated to increase worldwide. CRC screening has the potential to reduce the mortality rate.<sup>3</sup> Colonoscopy and polypectomy significantly decrease the incidence and mortality of CRC.<sup>4,5</sup>

Bowel preparation prior to colonoscopy is indispensable. Its quality and visualization are related to the cecal

**DOI** https://doi.org/ 10.1055/s-0044-1779617. **ISSN** 0976-5042. © 2024. The Author(s).

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intubation rate,<sup>6</sup> cecal intubation time,<sup>6,7</sup> withdrawal time,<sup>6</sup> polyp detection rate (PDR),8 adenoma detection rate (ADR),9 and detection rate of sessile serrated lesion. 10 Adequate bowel preparation quality is required for high-quality colonoscopy. Previous studies demonstrated that clinical factors could cause inadequate bowel preparation. The predictors of inadequate bowel preparation were the American Society of Anesthesiologists-Physical Status (ASA-PS) score<sup>6</sup>; age; reported failure to follow preparation instructions; inpatient status; procedural indication of constipation; use of tricyclic antidepressants; use of opioids; male sex; and history of cirrhosis, stroke, or dementia. 11,12 However, air bubbles in the large intestine could be also an obstacle to visibility in colonoscopy and increase the risk of missed lesions, endoscopist fatigue, and flushing dose. 13-15 However, these studies focused on the influence of air bubbles on the quality and trouble of colonoscopy and the measures to reduce air bubbles during colonoscopy, not the risk factors of incidence and severity of air bubbles themselves. Clinical, procedural, timing, and medicinal factors affecting bowel bubble severity were not well identified.

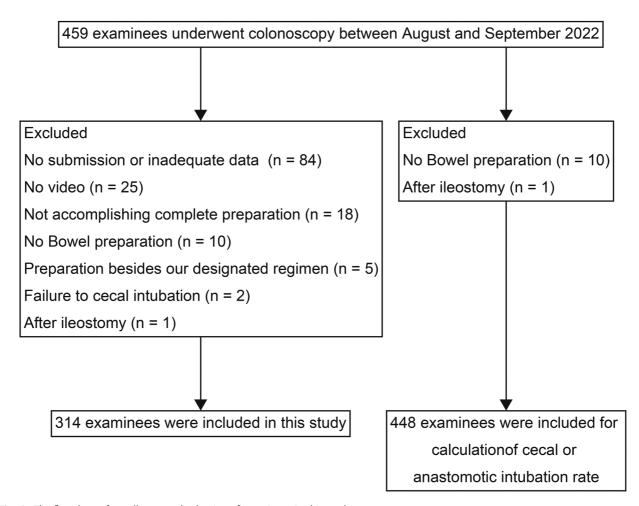
Therefore, this study aimed to elucidate the correlative factors of severity of air bubbles in the large intestine after bowel preparation.

## **Methods**

#### **Examinees**

This retrospective cohort study was conducted at a single institution. First, we recruited 459 examinees who underwent colonoscopy in an outpatient setting at the Medical Research Institute Kitano Hospital (Osaka, Japan) between August and September 2022. Clinical data were collected from their medical records, endoscopic videos, and endoscopic reports. We recorded almost all endoscopic videos from 2017, and that made it possible to collect the precise time from the videos.

The inclusion criteria of this study were as follows:  $\geq 18$  years of age, scheduled bowel preparation as mentioned in the bowel preparation section, successful total colonoscopy (the intubation of the cecum or anastomosis in case of ileocecal resection), and successful record of entire endoscopic videos. Examinees with colectomy (low anterior resection, n=8; right hemicolectomy, n=5; ileocolic resection, n=1; resection of the transverse, n=1; left hemicolectomy, n=1; sigmoid colectomy, n=1) were included except those with ileostomy (n=1). A flowchart of enrollment in this study is illustrated in ightharpoonup Fig. 1.



**Fig. 1** The flowchart of enrollment and selection of examinees in this study.

The exclusion criteria and the number of examinees excluded from this study were as follows: no submission or inadequate bowel preparation data (n = 84), no video (n = 25), not accomplishing complete bowel preparation (n = 18), no bowel preparation (n = 10), bowel preparation besides our designated regimen (i.e., Moviprep, Visiclear; n=5), failure to perform cecal intubation (n = 2), and after ileostomy (n = 1). A total of 314 examinees were enrolled in this study. Two examinees underwent colonoscopy with designated bowel preparation for observing only the lesion near the ileocecal valve. They were counted in all variables but excluded from the analysis of withdrawal time. Exceptionally, we included all examinees with designated bowel preparation and without ileostomy (n = 448) only when we calculated the cecal or anastomotic intubation rate as a clinical indicator.

#### **Bowel Preparation**

We generally instructed examinees to perform bowel preparation as follows. First, they were required to eat lowresidue diets 3 and 2 days before colonoscopy. They purchased and consumed the diet for colonoscopy (Clear Through; Kewpie, Tokyo, Japan) and were permitted to eat dinner the day before the colonoscopy. After dinner, 10 mL of 0.75% sodium picosulfate hydrate (Nichi-Iko Pharmaceutical Company, Toyama, Japan) and 24 mg of sennoside A/B calcium (Pfizer, New York City, New York, United States) were taken at 8 p.m. Second, the examinees began to take 2,000 mL of isotonic polyethylene glycol (PEG; NIFLEC; EA Pharma, Tokyo, Japan) at 7 a.m. Finally, colonoscopy was performed in the afternoon. Our bowel preparation method did not include simethicone. Only examinees who obeyed our designated bowel preparation method were included in this study, whereas we excluded those who required another isotonic PEG dose because of poor preparation.

The examinees were required to rate their stools in accordance with our instruction pamphlet. In our pamphlets, figures and figure legends of stool were illustrated and scored from 1 to 5 (-Supplementary Fig. S1, available in online version only). The examinees wrote the scores and timing in the pamphlets. We regarded 5 as complete bowel preparation. If the score did not reach 5 at the reserved time, colonoscopy was postponed and the examinees took another isotonic PEG dose. We retrieved the pamphlets and corrected the data regarding the first time a "5" was scored. No submission or inadequate data of bowel preparation pamphlets (n = 84) and colonoscopy that started before the examinees scored 5 (n = 18) were excluded from this study ( $\triangleright$  Fig. 1).

# **Evaluation of Air Bubbles and Bowel Preparation in the** Large Intestine

To assess air bubbles associated with bowel preparation in the large intestine, we adopted the Colon Endoscopic Bubble Scale (CEBuS), 16 which is thought to have good intra- and interobserver reliabilities (>Supplementary Fig. S2, available in online version only). The grade is defined as follows:

CEBuS-0 = No or minimal bubbles covering less than 5% of the surface not hampering mucosa visibility.

CEBuS-1 = Moderate number of bubbles covering between 5 and 50% of the surface, affecting mucosa visibility and requiring additional time for removal.

CEBuS-2 = Severe bubbling, covering more than 50% of the surface, obscuring mucosa visibility, and requiring additional time for removal.

We scored CEBuS in the ileocecum or anastomosis, transverse colon or splenic flexure, and rectum from the video when inserting the colonoscope because flushing and suctioning of fluid when withdrawing the colonoscope affected the assessment of CEBuS.

To assess bowel preparation as a whole, we adopted the Boston Bowel Preparation Scale (BBPS), <sup>17</sup> a well-validated scale for assessment of bowel preparation and considered to have high intra- and interobserver agreement. 17-19 The grade is defined as follows:

BBPS-0 = Unprepared colon segment with mucosa not seen due to solid stool that cannot be cleared.

BBPS-1 = Portion of mucosa of the colon segment seen, but other areas of the colon segment not well seen due to staining, residual stool, and/or opaque liquid.

BBPS-2 = Minor amount of residual staining, small fragments of stool, and/or opaque liquid, but mucosa of colon segment seen well.

BBPS-3 = Entire mucosa of colon segment seen well with no residual staining, small fragments of stool, or opaque liquid.

We scored the BBPS in the ileocecum or anastomosis, transverse colon or splenic flexure, and rectum. We assessed BBPS from the video when withdrawing the colonoscope because flushing and suctioning of fluid were needed to assess the accurate BBPS. Endoscopic videos were blinded, and CEBuS and BBPS were evaluated by six experts after learning the scales from the original articles. 16,17

The large intestine is a long organ, and it is difficult to express total situation of air bubbles. Because air bubbles in the ileocecum and ascending colon are more difficult to clear, we focused on CEBuS in the ileocecum or anastomosis when attempting to elucidate its correlative factors.

We validated the quality of colonoscopy based on the success rate of cecal or anastomotic intubation, <sup>20,21</sup> withdrawal time,<sup>20</sup> frequency of adverse events,<sup>20</sup> and PDR, an alternative index of ADR with a high degree of correlation,<sup>22,23</sup> asserted as clinical indicators.

## **Data Collection and Values**

The following variables were collected from medical records: age, sex, ASA-PS, body mass index (BMI), Eastern Cooperative Oncology Group-Performance Status (ECOG-PS), comorbidity, medication, history of abdominal surgery including colectomy and cholecystectomy, and history of abdominal radiotherapy. The following variables were collected from endoscopic records: cecal or anastomosis intubation, diverticulosis, polyp detection, and adverse events. The following variables were collected from endoscopic videos: CEBuS, BBPS, intubation time, withdrawal time, and the time interval of colonoscopy. We defined the time interval of colonoscopy as the gap between the time when examinees scored 5 first on the bowel preparation in the pamphlets and the time when colonoscopy reached the cecum or anastomosis.

#### **Statistics**

The Spearman's rank correlation coefficient was used to determine the correlation between continuous data of two groups. The Mann–Whitney U test was performed to compare the differences between the two independent groups. Single and multiple linear regression analyses were performed to predict the association between continuous or categorized explanatory variables and continuous objective variables. Logistic regression analysis was performed to predict the association of continuous or categorized explanatory variables with the binary group. For multivariate analysis, we included age, sex, ASA-PS, ECOG-PS, BMI, comorbidities, past history of operation including colectomy and cholecystectomy, past history of radiation, diverticulosis, medication, and the time interval of colonoscopy (minutes) as explanatory variables.

The Spearman's rank correlation coefficient and the Mann–Whitney U test were performed using GraphPad Prism (version 6.07 for Windows; GraphPad Software, San Diego, California, United States). Linear and logistic regression analyses were performed using EZR (version 1.51; Jichi Medical University, Saitama, Japan).<sup>24</sup> *p*-Values of <0.05 were considered statistically significant.

# **Study Approval**

Opt-out informed consent protocol was used for this study. This consent procedure was reviewed and approved by the Kitano Hospital (approval number [2209004], date of decision [September 14, 2022]). The study was conducted in accordance with the Declaration of Helsinki.

#### Results

## **Patient Characteristics**

The examinees' characteristics are summarized in **Fable 1**. The mean age (range) was 65 (18–88) years, and 179/314 (57.0%) patients were men. A total of 312 examinees (99.4%) maintained a good (0, 1) ECOG-PS. A total of 187 (59.6%) examinees had comorbidities. Eighty-seven (27.7%) examinees had undergone abdominal surgery before colonoscopy, including colectomy (n = 17 [5.4%]) and cholecystectomy (n = 17 [5.4%]).

## **Quality of Colonoscopy**

The clinical indicators of colonoscopy are listed in **Fable 2**. The bowel preparation adequacy rate (BBPS score  $\geq 6$ ) was 99.7% (313/314). The cecal or anastomosis intubation rate was 99.6% (447/449) during the research period. The mean withdrawal time was 13 (5–60) minutes. Furthermore, 99.4% (310/312) of the withdrawal times were  $\geq 6$  minutes, whereas 89.4% (279/312) were  $\geq 9$  minutes. In this study, the PDR was 52.9% (165/312). For the examinees with no polyps

**Table 1** Clinical characteristics of examinees

Examinees, n	314
Median age, y (range)	65 (88–18)
Sex (male/female), n	179/135
Median ASA-PS (range)	2 (1–3)
ASA-PS (0-2/3-4), n	220/94
Median ECOG-PS (range)	0 (0-2)
ECOG-PS (0-1/2-4), n	312/2
BMI (mean $\pm$ SD), kg/m <sup>2</sup>	23.3 ± 3.0
Comorbidity, n (%)	
Hypertension	109 (34.7)
Diabetes	61 (19.4)
Cardiovascular disease	40 (12.7)
Cerebrovascular disease	24 (7.6)
Renal disease	18 (5.7)
Liver disease	6 (1.9)
Dyslipidemia	77 (24.5)
Respiratory disease	18 (5.7)
Other malignancy	22 (7.0)
Having any comorbidities, n (%)	187 (59.6)
Having two or more comorbidities, n (%)	110 (35.0)
Abdominal operation, n (%)	87 (27.7)
Colectomy, n (%)	17 (5.4)
lleocecal resection, n (%)	2 (0.6)
Cholecystectomy, n (%)	17 (5.4)
Abdominal radiation, n (%)	3 (1.0)
Diverticulosis, n (%)	109 (34.7)
Medication, n (%)	
Antithrombotic drugs	52 (16.6)
Tricyclic antidepressants	0 (0.0)
Opioids	3 (1.0)
Proton pump inhibitors	72 (22.9)
Laxative	49 (15.6)

Abbreviations: ASA-PS, American Society of Anesthesiologists-Physical Status; BMI, body mass index; ECOG-PS, Eastern Cooperative Oncology Group-Performance Status; SD, standard deviation.

detected, the mean withdrawal time was 11 (5-33) minutes; 99.3% (146/147) of the withdrawal times were  $\geq 6$  minutes ( $\sim$  Supplementary Table S1, available in online version only). No adverse events were observed. The clinical indicators in this study met the optimal standards for colonoscopy  $^{25}$  and ensured that each colonoscopy was of high quality.

## Assessment of Air Bubbles in the Large Intestine

The results of the bowel bubble assessment are summarized in **- Table 3**. The median time interval of colonoscopy (range) was 237 (30–456) minutes. In addition, 6.7% (21/314), 23.9% (75/314), and 39.8% (125/314) of the examinees had a CEBuS

Table 2 Quality of colonoscopy

Median BBPS (range)	9 (5–9)
BBPS ≥ 6, <i>n</i> (%)	313/314 (99.7)
Cecal or anastomosis intubation rate, <i>n</i> (%)	446/448 (99.6)
Median withdrawal time (range), min	13 (5–60)
Withdrawal time $\geq$ 6 min, $n$ (%)	310/312 (99.4)
Withdrawal time $\geq$ 9 min, $n$ (%)	279/312 (89.4)
PDR, % (n)	52.9% (165/312)
Adverse event, n (%)	0/314 (0.0)

Abbreviations: BBPS, Boston Bowel Preparation Scale; PDR, polyp detection rate.

**Table 3** Assessment of air bubbles in the large intestine

Median time interval of colonoscopy (range), min	237 (30–456)
CEBuS	
Rectum, n (%)	
0	221 (70.4)
1	72 (22.9)
2	21 (6.7)
Transverse colon or splenic flexure, n (%)	
0	84 (26.8)
1	155 (49.4)
2	75 (23.9)
lleocecum or anastomosis, n (%)	
0	60 (19.1)
1	129 (41.1)
2	125 (39.8)

Abbreviation: CEBuS, Colon Endoscopic Bubble Scale.

of 2 in the rectum, transverse colon or splenic flexure, and ileocecum or anastomosis, respectively. The correlation coefficients of CEBuS at the three locations are shown in **Supplementary Table S2** (available in online version only). The correlation coefficient of the rectum and transverse colon or splenic flexure was 0.4433 (p < 0.0001), and that of the rectum and ileocecum or anastomosis was 0.3309 (p < 0.0001); however, that of the transverse colon or splenic flexure and ileocecum or anastomosis was 0.6658 (p < 0.0001).

CEBuS at the three locations were not significantly correlated with polyp detection (**Supplementary Table S3**, available in online version only).

# Correlative Factors for Air Bubbles in the Ileocecum or Anastomosis

We considered the CEBuS score a ranked variable and performed linear regression analysis. The single linear regression analysis showed that the time interval of colonoscopy was significantly correlated with the CEBuS score (p = 0.0004, **Fig. 2**). The results of the multiple linear

regression analysis are summarized in **\succTable 4**. The time interval of colonoscopy (p = 0.0016) and a history of cholecystectomy (p = 0.0198) were significantly correlated with the CEBuS score.

Since the difference between CEBuS-0 and CEBuS-1 is only 5% of bubbles covering the surface, we divided examinees into two groups: CEBuS-0 or 1 group (n = 189) and CEBuS-2 group (n = 125) in the ileocecum or anastomosis. We compared the CEBuS-2 group to the CEBuS-0 and CEBuS-1 groups. The results of the multivariate logistic regression analysis are summarized in **Table 5**. The time interval of colonoscopy (p = 0.033) and a history of cholecystectomy (p = 0.0095) were positively correlated with the CEBuS score.

We compared the 25% longer time interval of colonoscopy examinees and the 25% shorter time interval of colonoscopy examinees in terms of CEBuS at ileocecum in **Supplementary Table S4** (available in online version only). The analysis showed that a longer time interval of colonoscopy was significantly associated with a high CEBuS score (p = 0.0137).

Finally, we compared the examinees with less than 240-minute time interval of colonoscopy (<240-minute group) and those with more than 240 minutes (>240-minute group, **Table 6**). The analysis showed that <240-minute group scored lower CEBuS at the ileocecum or anastomosis than >240-minute group.

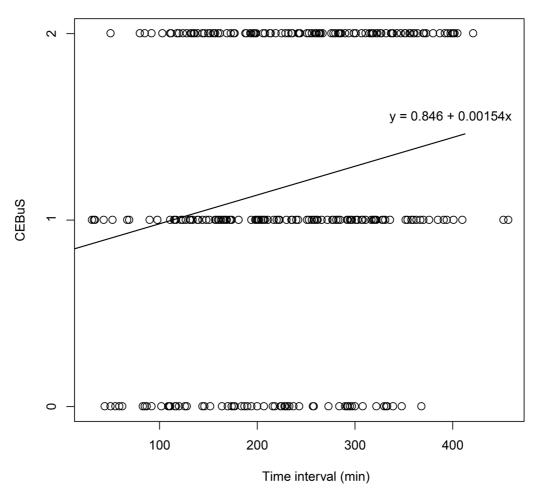
## **Discussion**

In this study, we confirmed that a longer time interval from the completion of bowel preparation to intubation is positively associated with the severity of air bubbles in the large intestine. Therefore, it is important to promptly perform colonoscopy if bowel preparation is completed.

The American Gastroenterological Association (AGA) stipulates preferred standards for colonoscopy screening. Accordingly, more than 95% of the BBPS scores should be  $\geq$ 6 points for aspirational quality of bowel preparation. In the present study, the median BBPS score was 9 points, and 99.7% of the examinations scored  $\geq$ 6 points. The results validated that bowel preparation was performed at an aspirational level. The standards of AGA also refer to the quality of colonoscopy. Aspirational cecal intubation rate is above 95% and withdrawal time is above 9 minutes, and optimal PDR is 30 to 40%. 22,26 In our study, cecal intubation rate was 99.6%, mean withdrawal time was 13 minutes, and PDR was 52.9%. Our study was also validated in terms of colonoscopy quality.

In the present study, we analyzed the correlation between the CEBuS score at three locations. The correlation of the rectum and transverse colon or splenic flexure, and that of the rectum and ileocecum or anastomosis were low.<sup>27</sup> However, that of the transverse colon or splenic flexure and ileocecum or anastomosis was moderate.<sup>27</sup> Therefore, it is difficult, but not impossible, to estimate the oral side CEBuS from the anal side CEBuS when the colonoscope is intubated.

We found that the time interval of colonoscopy is an important factor for good bubble condition during colonoscopy. One hypothesis is that air bubbles in the large intestine



**Fig. 2** The single linear regression analysis of CEBuS and the time interval between the time when examinees scored 5 on the preparation in the pamphlets and the time when colonoscopy reached the cecum or anastomosis. CEBuS, Colon Endoscopic Bubble Scale.

Table 4 Multiple linear regression analysis

	Coefficients (±Std. error)	<i>p</i> -Value
Age	$0.003340 \pm 0.003863$	0.3802
Sex	$-0.04166 \pm 0.09691$	0.6677
ASA-PS	$-0.1413 \pm 0.08877$	0.1127
ECOG-PS	$0.006209 \pm 0.1399$	0.9646
BMI	$-0.01588 \pm 0.01272$	0.2130
Hypertension	$0.06835 \pm 0.1161$	0.5568
Diabetes	$0.2271 \pm 0.1258$	0.0724
Cardiovascular disease	0.07227 ± 0.1647	0.6612
Cerebrovascular disease	$0.02798 \pm 0.2020$	0.8899
Renal disease	$-0.1433 \pm 0.2015$	0.4776
Liver disease	$-0.2346 \pm 0.3255$	0.4718
Dyslipidemia	$-0.1611 \pm 0.1162$	0.1668
Respiratory disease	$0.02578 \pm 0.2025$	0.8988
Other malignancy	$-0.06530 \pm 0.1852$	0.7247
Abdominal operation	$-0.05301 \pm 0.1207$	0.6610
Colectomy	$-0.2719 \pm 0.2118$	0.2003

Table 4 (Continued)

	Coefficients (±Std. error)	<i>p</i> -Value
Cholecystectomy	$0.5561 \pm 0.2371$	0.0198
Abdominal radiation	$0.3449 \pm 0.4600$	0.4541
Diverticulosis	$0.08932 \pm 0.1019$	0.3817
Antithrombotic drugs	0.08197 ± 0.1673	0.6247
Opioids	$-0.09589 \pm 0.4698$	0.8384
Proton pump inhibitors	$-0.09242 \pm 0.1198$	0.4413
Laxative	$0.01980 \pm 0.1336$	0.8823
Time interval	$0.001234 \pm 0.0005088$	0.0016
BBPS	$0.01309 \pm 0.1088$	0.9043

Abbreviations: ASA-PS, American Society of Anesthesiologists-Physical Status; BBPS, Boston Bowel Preparation Scale; BMI, body mass index; ECOG-PS, Eastern Cooperative Oncology Group-Performance Status.

are associated with bile secretion after bowel preparation. Bile is composed of bilirubin, fats, bile acids, and water. Bile is a natural detergent because bile salts contain both polar and nonpolar regions.<sup>28,29</sup> Therefore, bile can easily form

**Table 5** Logistic regression analysis

	Coefficients (±std. error)	Odds ratio (95% CI)	<i>p</i> -Value
Age	$0.0105 \pm 0.0115$	1.011 (0.9880-1.033)	0.3624
Sex	$0.0342 \pm 0.290$	1.035 (0.5850-1.830)	0.9064
ASA-PS	$-0.385 \pm 0.273$	0.6803 (0.3984–1.162)	0.1581
ECOG-PS	$0.0189 \pm 0.433$	1.019 (0.4363-2.380)	0.9653
BMI	$-0.0351 \pm 0.0392$	0.9655 (0.8940-1.043)	0.3711
Hypertension	0.116 ± 0.355	1.123 (0.5603–2.252)	0.7434
Diabetes	$0.703 \pm 0.391$	2.020 (0.9387-4.347)	0.0721
Cardiovascular disease	$0.209 \pm 0.518$	1.232 (0.4462–3.403)	0.6870
Cerebrovascular disease	$0.136 \pm 0.638$	1.146 (0.3281–4.000)	0.8313
Renal disease	$-0.692 \pm 0.673$	0.5004 (0.1337–1.873)	0.3039
Liver disease	$-0.251 \pm 0.992$	0.7778 (0.1113–5.437)	0.8001
Dyslipidemia	$-0.451 \pm 0.362$	0.6373 (0.3133–1.296)	0.2136
Respiratory disease	$-0.113 \pm 0.632$	0.8928 (0.2583-3.086)	0.8578
Other malignancy	$-0.334 \pm 0.575$	0.7160 (0.2318-2.212)	0.5615
Abdominal operation	$-0.0760 \pm 0.368$	0.9268 (0.4505–1.907)	0.8363
Colectomy	$-0.552 \pm 0.677$	0.5756 (0.1526–2.170)	0.4146
Cholecystectomy	$2.28 \pm 0.877$	9.735 (1.746–54.29)	0.0095
Abdominal radiation	$1.97 \pm 1.53$	7.184 (0.3590–143.7)	0.1971
Diverticulosis	$0.357 \pm 0.308$	1.430 (0.7820–2.613)	0.2456
Antithrombotic drugs	$0.00853 \pm 0.538$	1.009 (0.3511–2.897)	0.9874
Opioids	$-0.226 \pm 1.46$	0.7974 (0.04552–13.97)	0.8768
Proton pump inhibitors	$-0.495 \pm 0.375$	0.6094 (0.2921–1.271)	0.1866
Laxative	$-0.260 \pm 0.414$	0.7714 (0.3429–1.736)	0.5304
Time interval	$0.00329 \pm 0.00155$	1.003 (1.0003-1.0063)	0.0332
BBPS	$0.255 \pm 0.340$	1.290 (0.6623–2.513)	0.4541

Abbreviations: ASA-PS, American Society of Anesthesiologists-Physical Status; BBPS, Boston Bowel Preparation Scale; BMI, body mass index; CI, confidence interval; ECOG-PS, Eastern Cooperative Oncology Group-Performance Status.

Table 6 240-minute time interval and Colon Endoscopic Bubble Scale at the ileocecum or anastomosis

	0	1	2	Total
<240 min, n (%)	41 (25.9)	65 (41.1)	52 (32.9)	158 (100)
>240 min, n (%)	19 (12.2)	64 (41.0)	73 (46.8)	156 (100)
				p = 0.0013

bubbles, which are typically seen in the duodenum. Accordingly, our hypothesis is reinforced by the fact that postcholecystectomy is another correlative factor for severe air bubbles after bowel preparation. Postcholecystectomy, patients cannot store bile during fasting. Constant bile secretion toward the gastrointestinal tract occurs after the completion of bowel preparation. Therefore, it is important to start colonoscopy immediately after the completion of bowel preparation.

Previous reports also pointed out the importance of the time interval between completion of bowel preparation and colonoscopy.  $^{30,31}$  These previous reports showed that toolong intervals ( $\geq$ 6 hours or the day prior to the procedure) worsen the quality of bowel preparation. Bowel preparation quality was assessed using the Ottawa Bowel Preparation Scale score<sup>8</sup> or a unique score featuring liquid or solid material. These studies have focused on residual fluid, stool, mucus, and chyme. In our study, we confirmed that air bubbles were also affected by the interval time. In addition, our study suggested that within 240-minute intubation after completion of bowel preparation might be appropriate for PEG-based and simethicone-free regimen.

This study had some limitations. First, this was a retrospective single-center study. Second, we collected stool scores from the self-assessments of the examinees. The timing of a score of 5 in the pamphlets did not have objective reliability, even though the BBPS score in this study was excellent. Third, our method used only PEG as the bowel preparation drug and simethicone was not administered on the day of colonoscopy. Although PEG is a popular bowel preparation drug, it is also known as a nonionic detergent. Simethicone is a safe oral antifoaming drug, and previous reports have shown that simethicone-mixed preparation improves air bubbles and bowel preparation quality.<sup>32,33</sup> If another regimen was used or simethicone was added to the PEG regimen, the results might have been affected. Fourth, we could not collect the speed of PEG intake from the pamphlets. We could not investigate the association between the CEBuS score and the speed of PEG intake.

## **Conclusion**

In conclusion, here we analyzed the correlative factors of severity of air bubbles in the large intestine during colonoscopy. We found that the time interval of colonoscopy and cholecystectomy were correlative factors of severe bubbles. Therefore, it is important not to wait long before starting at the reserved time if the bowel preparation is accomplished.

#### **Authors' Contributions**

Conceptualization: T.Y., A.Y.; collection of data: K.I., S.O., Y.S., K.Tanaka, K.N.; data analysis: T.Y., A.Y., Y.M., K.O., R.I., Y.K., S.N., S.A., T.M., K.H., K.K., K.Takahashi, T.Kou, T.Katayama, S.Y.; writing-original draft: T.Y.

#### **Ethics Approval**

Opt-out informed consent protocol was used for this study. This consent procedure was reviewed and approved by Kitano Hospital (approval No. 2209004).

#### **Data Availability Statement**

The datasets generated and analyzed in the current study are available from the corresponding author on reasonable request.

# Funding

None.

#### Conflict of Interest

None declared.

## Acknowledgments

We truly appreciate the staff of the Minimally Invasive Center at the Medical Research Institute Kitano Hospital for safety colonoscopy and correction of data.

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