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# Predicting Inadequate Bowel Preparation When Using Sodium Picosulfate plus Magnesium Citrate for Colonoscopy: Development and Validation of a Prediction Score

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**Keywords**
Bowel cleansing effect · Bowel preparation · Colonoscopy · Patient acceptability · Sodium picosulfate plus magnesium citrate

**Abstract**
***Introduction:*** Sodium picosulfate plus magnesium citrate is a bowel preparation agent with high patient acceptability. However, it is unclear which patients are more likely to have inadequate bowel preparation when using this agent. This study aimed to identify the risk factors for inadequate bowel preparation when using sodium picosulfate plus magnesium citrate for colonoscopy and to develop a scoring model to predict which patients will have inadequate bowel preparation. ***Methods:*** A total of 350 Japanese patients were enrolled from June 2021 to April 2022. Data on patient background, details of colonoscopy, and satisfaction assessment questionnaire results were prospectively collected. The scoring model for inadequate bowel preparation was developed based on multiple logistic regression analyses, and its performance was internally validated using bootstrapping. ***Results:*** Adequate bowel preparation was obtained in 295 patients (84.3%); 335 (95.7%) were able to ingest the drug without difficulty. The scoring model consisted of five independent risk factors and points of risk scores were assigned to each one as follows: American Society of Anesthesiologists physical status III (1 point), diabetes comorbidities (5 points), use of laxatives (4 points), no defecation once in a day (2 points), and drug use for mental disorder (6 points). The C-statistics of the scoring system for inadequate bowel preparation was 0.75. ***Discussion:*** We identified five risk factors for inadequate bowel preparation when using sodium picosulfate plus magnesium citrate regimen and developed a scoring model for inadequate bowel preparation with satisfactory discrimination and calibration.



## Introduction

According to worldwide epidemiological studies, colorectal cancer is the third most common cancer and the second most common cause of cancer-related deaths [1]. This trend follows in Japan also, where colorectal cancer is ranked first in the frequency of occurrence and second in the number of cancer-related deaths [2]. In order to reduce colorectal cancer-related deaths, early detection and treatment are necessary [3, 4]; therefore, the demand for colonoscopy is increasing. In the Japanese colorectal cancer screening program, fecal

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occult blood tests (FOBT) are recommended for people over 40 years of age. However, it has been reported that only 69.7% of patients with a positive FOBT undergo subsequent colonoscopy [5]. In a questionnaire survey of patients with positive FOBT who did not undergo colonoscopy, 8% of patients cited difficulty taking bowel preparation agents as the reason for not undergoing colonoscopy [6]. In order to further increase the number of patients undergoing colonoscopy, a bowel cleansing method that is both effective and acceptable to patients is desirable.

Sodium picosulfate plus magnesium citrate (SP + MC) (PICOPREP; Nippon-Chemiphar Ltd., Tokyo, Japan) has been commercially available in Japan since 2016. SP + MC has the following features: (i) orange flavor, (ii) it requires a lower dose of the drug solution compared to the conventional agents, and (iii) drinking any kind of liquid is acceptable after taking the drug solution, as long as it is clear (e.g., tea, gas water, sports drink, clear apple juice, or clear soup with no solids) [7]. Other bowel preparation agents do not have these features; thus, SP + MC is expected to have greater patient acceptability. In a meta-analysis comparing SP + MC and polyethylene glycol (PEG), SP + MC had significantly higher preparation completion rates than PEG, and the proportion of patients willing to repeat the same bowel preparation was significantly higher in the SP + MC group [8]. However, no significant differences were observed in the bowel cleansing effect of these two agents, and the effect direction showed a trend in favor of PEG [8]. These results indicate that SP + MC has a significantly higher patient acceptability than PEG; however, its bowel cleansing efficacy is slightly inferior to that of PEG. Therefore, we thought that by using SP + MC to avoid patients who tend to have inadequate bowel preparation with SP+MC, colonoscopy could be achieved with both satisfactory bowel cleansing and high patient acceptability. Although there have been several studies investigating the risk factors for inadequate bowel preparation with various agents [9, 10], none have focused on SP + MC. This study aimed to identify the risk factors for inadequate bowel preparation in Japanese patients when using SP + MC for colonoscopy and to develop a scoring model to predict the patients with inadequate bowel preparation.

## Materials and Methods

*Study Design*

We conducted a two-center prospective cohort study at a hospital and a clinic in Japan. We prospectively enrolled patients from June 2021 to February 2022. Opt-out methods of obtaining consent were used, and all patients provided informed consent in this study. The study protocol was approved by the Ethics Committee at Kobe University Hospital (Approval No. B210008-1). This study was performed in accordance with the ethical standards of the Declaration of Helsinki in 1964 and its later amendments.

*Patients*

Patients who met the following inclusion criteria were included consecutively: (i) those who required colonoscopy (except for emergency cases) and (ii) Japanese and over 20 years of age. The exclusion criteria included the following: patients who had (i) severe renal dysfunction (creatinine clearance <30 mL/min), (ii) severe hepatic failure (Child-Pugh score C or higher), (iii) severe heart failure (New York Heart Association class III or IV), (iv) poorly controlled hypertension (systolic blood pressure ≥170 mm Hg, diastolic blood pressure ≥100 mm Hg), (v) prior bowel resection, (vi) suspected bowel obstruction or perforation, and (vii) failed to consume the bowel preparation agent as directed. Data on patient background, details of colonoscopy, and satisfaction assessment questionnaire results were systematically collected. Drugs for mental disorders included anxiolytics, antipsychotics, and antidepressants; however, sleeping drugs or antiepileptic drugs were not included.

*Sample Size*

We considered it necessary to perform a multivariate analysis with at least five factors in 50 patients with inadequate bowel preparation to clarify the associated risk factors. In previous reports, the percentage of patients who achieved adequate bowel preparation with an SP + MC regimen was reported to be 75.7–97.7% [11–17]. We assumed the percentage of patients who undergo colonoscopy with inadequate bowel preparation to be 15% and calculated that the total number of patients needed to be 333. Assuming that there would be a few ineligible patients, the final number of patients to be enrolled in this study was set as 350.

*Bowel Preparation Method*

The medical staff and physicians instructed the patients on the proper use of bowel preparation methods. The patient was instructed to avoid high fiber vegetables, indigestible foods, and seaweed for 2 days prior to the colonoscopy. One sachet of PICOPREP (sodium picosulfate 10 mg, magnesium oxide 3.5 g, and citric acid 12 g) was dissolved in 150 mL water and was administered at 8:00 p.m. on the day before the colonoscopy, followed by at least 1.25 L of clear liquid within the following 2.5 h. Two tablets of sennoside A and B calcium (12 mg) were taken before bedtime. On the day of the colonoscopy, one sachet of PICOPREPP was dissolved in 150 mL water and administered 5 h before the colonoscopy, followed by 750 mL of clear liquid within the following 1.5 h. No additional laxative medications or enemas were administered immediately before the colonoscopy.

*Outcome Measures*

The primary aim of this study was to identify the risk factors that lead to inadequate bowel preparation in patients who undergo colonoscopy. The bowel cleansing quality was assessed by three expert endoscopists using the Boston Bowel Preparation Scale (BBPS). The BBPS is a four-point scoring system that applies to each of the three segments of the colon (right-side colon, including the cecum and ascending colon; transverse colon, including the

**Table 1.** Baseline characteristics of patients and colonoscopy-related parameters ($n$ = 350)

| | |
|---|---|
| Baseline characteristics of patients | |
| Age (mean±SD), years | 59.9±15.4 |
| Gender, *n* (%) | |
| Men/women | 175 (50.0)/175 (50.0) |
| BMI (mean±SD), kg/m$^2$ | 22.5±3.5 |
| Outpatient/inpatient, *n* (%) | 335 (95.7)/15 (4.3) |
| ASA-PS, *n* (%) | |
| 1/2/3 | 190 (54.3)/157 (44.9)/3 (0.9) |
| Colonoscopy indication, *n* (%) | |
| Screening/surveillance | 149 (42.6) |
| Abdominal symptoms/blood loss/anemia | 114 (32.6) |
| Positive FOBT | 50 (14.3) |
| Inflammatory bowel disease | 32 (9.1) |
| Others | 5 (1.4) |
| Comorbidities, *n* (%) | |
| Neurological disease | 3 (0.9) |
| Diabetes | 28 (8.0) |
| Inflammatory bowel disease | 25 (7.1) |
| History of abdominal surgery, *n* (%) | 110 (31.4) |
| Use of laxatives | |
| None/one kind/more than two kinds | 295 (84.3)/45 (12.9)/10 (2.9) |
| Defecation habit | |
| Daily/once in every 2–3 days/or more | 265 (75.7)/70 (20.0)/15 (4.3) |
| Use of drugs for mental disorder, *n* (%) | 24 (6.9) |
| Colonoscopy-related parameters | |
| Cecum intubation time (mean±SD), min | 5.4±3.5 |
| Adenoma detection rate, % | 54.9 |
| Colorectal cancer, *n* (%) | 19 (5.4) |
| Colonoscopy-related adverse events, *n* (%) | |
| Mucosal injury | 1 (0.3) |
| Bowel preparation agent-related adverse events, *n* (%) | |
| Nausea | 10 (2.9) |
| Abdominal pain | 5 (1.4) |
| Dizziness | 1 (0.3) |
| Palpitation | 1 (0.3) |

SD, standard deviation; ASA-PS, American Society of Anesthesiologists physical status.

hepatic and splenic flexures; and left-side colon, including the descending colon, sigmoid colon, and rectum) [18]. The classifications are defined as follows: 0 – unprepared colon segment with invisible mucosa due to the presence of solid stool that could not be cleared; 1 – a portion of the colon mucosa is visible; however, other areas of the colon segment are not clearly visible because of staining, residual stool, and/or opaque liquid; 2 – a minor amount of residual staining, small fragments of stool, and/or opaque liquid are present; however, the colon mucosa is clearly visible; and 3 – the entire mucosa of the colon segment is clearly visible, with no residual staining, small fragments of stool, or opaque liquid. The BBPS score of 0–3 for each colon segment was totaled to give an overall score ranging from 0 to 9. Inadequate preparation was defined as a total BBPS score <6 or a score <2 for any individual segment [12]. Adequate preparation was defined as a total BBPS score ≥6 or a score ≥2 for adequate preparation of any individual segment. Excellent bowel preparation was defined as a total BBPS score of 9. The secondary endpoints were the frequency of patients with inadequate bowel preparation, adenoma detection rate, adverse events, cecal intubation time, and patient satisfaction.

*Statistical Analyses*

The continuous variables and categorical variables were presented as mean ± standard deviation and as percentages, respectively. The continuous variables were compared using the Student's $t$ test (normally distributed data) or Wilcoxon rank-sum test (skewed data). The categorical variables were compared using the Fisher's exact test. A Friedman test, which is the nonparametric equivalent of a one-way repeated measures analysis of variance, was carried out to examine the difference in the BBPS within all the colon segments. Post hoc analyses with Wilcoxon signed-rank tests using a Bonferroni method were carried out to examine the differences between the BBPS scores in the colon segments.

Factors with significant (<0.05) or marginally significant (<0.1) $p$ values in the univariate analysis were selected as the final risk factors. Multivariable logistic regression analysis was used to determine the weight of the final risk factors associated with inadequate bowel preparation. We developed a scoring system by assigning a weight to each risk factor based on the β coefficients of the final logistic regression model and calculated the estimated risk for inadequate bowel preparation according to the total scores [19]. Considering the internal validation of the risk-scoring system, bootstrap resampling was begun by fitting the risk-scoring system in a bootstrap sample of 350 subjects, which was drawn with replacement from the original sample. Averages and the 95% confidence intervals (CI) of performance measures were taken with over 2,000 repetitions (Rpackage "rms," "boot," "DescTools"). The discriminative ability was quantified with concordance statistics ($c$-statistics). A calibration was quantified with the slope, and the intercept was calculated through linear regression. The overall performance was quantified with the Brier score, calculated as the mean squared distance between the observed outcomes and the prediction.

## Results

*Baseline Characteristics of the Patients*

A total of 350 Japanese patients were enrolled in this study from June 2021 to April 2022. All patients underwent total colonoscopy and answered the satisfaction assessment questionnaire. The demographic and clinical characteristics of the 350 patients are summarized in Table 1.

*Colonoscopy and Bowel Preparation*

The mean cecum intubation time for colonoscopy was 5.4 ± 3.5 min and the mean adenoma detection rate was

**Table 2.** Efficacy of bowel cleansing based on Boston scale ($n = 350$)

| | |
|---|---|
| Total colon (numerical), mean±SD | 7.4±1.8 |
| Total colon (categorical), *n* (%) | |
| Score 0–3 | 15 (4.3) |
| Score 4–6 | 80 (22.9) |
| Score 7–9 | 255 (72.9) |
| Adequate bowel preparation, *n* (%) | 295 (84.3) |
| Excellent bowel preparation, *n* (%) | 113 (32.3) |
| Right-side colon (numerical), mean±SD | 2.2±0.7 |
| Right-side colon (categorical), *n* (%) | |
| Score 0 | 2 (0.6) |
| Score 1 | 44 (12.6) |
| Score 2 | 181 (51.7) |
| Score 3 | 123 (35.1) |
| Transverse colon (numerical), mean±SD | 2.6±0.6 |
| Transverse colon (categorical), *n* (%) | |
| Score 0 | 1 (0.3) |
| Score 1 | 24 (6.9) |
| Score 2 | 84 (24.0) |
| Score 3 | 241 (68.9) |
| Left-side colon (numerical), mean±SD | 2.6±0.7 |
| Left-side colon (categorical), *n* (%) | |
| Score 0 | 7 (2.0) |
| Score 1 | 25 (7.1) |
| Score 2 | 86 (24.6) |
| Score 3 | 232 (66.3) |

SD, standard deviation.

**Table 3.** Convenience and satisfaction with PICOPREP medication ($n = 350$)

| | |
|---|---|
| Were you able to perform the bowel preparation as instructed?, *n* (%) | |
| Yes | 344 (98.3) |
| No | 6 (1.8) |
| How easy or difficult was it to consume the PICOPREP medication?, *n* (%) | |
| Very easy | 80 (22.9) |
| Easy | 204 (58.3) |
| Tolerable | 51 (14.6) |
| Difficult | 15 (4.3) |
| Very difficult | 0 (0) |
| How was the taste of the PICOPREP medication?, *n* (%) | |
| Very good | 85 (24.3) |
| Good | 167 (47.7) |
| Tolerable | 83 (23.7) |
| Bad | 15 (4.3) |
| Very bad | 0 (0) |
| How was the amount of the PICOPREP medication?, *n* (%) | |
| No problem | 347 (99.1) |
| Large | 3 (0.9) |
| Very large | 0 (0) |
| Would you ask your doctor for the PICOPREP medication if you need another colonoscopy in the future?, *n* (%) | |
| Yes | 305 (87.1) |
| No | 45 (12.9) |

54.9%. Colorectal cancer was detected in 19 patients (5.4%) (Table 1).

The average point of bowel cleansing efficacy in total colon based on the BBPS was 7.4 ± 1.8. Adequate and excellent bowel preparations were obtained in 295 (84.3%) and 113 patients (32.3%), respectively. Compared to those of the other colon sections, the right-side colon had the lowest BBPS score (Friedman test: $p < 0.0001$, Wilcoxon signed-rank test: Bonferroni adjusted $p$ value <0.0001 for right-transverse; <0.0001 for right-left; 0.032 for transverse-left) (Table 2).

*Satisfaction Assessment Questionnaire*

Three hundred and forty-four patients (98.5%) were able to perform the bowel preparation as instructed: 6 patients who could consume the bowel preparation agent but were unable to take any additional fluids were included in the analysis. Three hundred and thirty-five patients (95.7%) were able to ingest the bowel preparation without difficulty, and 305 patients (87.1%) stated that they would choose this bowel preparation agent again for future colonoscopies (Table 3).

*Comparison of Patients with Adequate and Inadequate Bowel Preparation*

Table 4 shows the comparison of patients with adequate and inadequate bowel preparation. The proportion of diabetes comorbidities was significantly higher in patients with inadequate bowel preparation than in those with adequate bowel preparation ($p < 0.0001$). The proportion of laxative use was significantly higher in patients with inadequate bowel preparation ($p < 0.0001$). Defecation habits were significantly worse in patients with inadequate bowel preparation ($p = 0.0065$). The proportion of use of drugs for mental disorders was significantly higher in patients with inadequate bowel preparation ($p < 0.0001$).

*Development of a Risk-Scoring System for Predicting Inadequate Bowel Preparation in Patients Who Undergo Colonoscopy*

The univariate analysis identified several significant predictive factors for inadequate bowel preparation, including American Society of Anesthesiologists physical status (ASA-PS) class III, diabetes comorbidities, use of laxatives, defecation habit of less than once in every 2–3

**Table 4.** Comparison of patients with adequate and inadequate bowel preparation

| | Adequate bowel preparation (*n* = 295) | Inadequate bowel preparation (*n* = 55) | *p* value |
|---|---|---|---|
| Age (mean±SD), years | 59.5±15.5 | 62.8±14.6 | 0.31 |
| Gender, *n* (%) (men/women) | 146 (49.5)/149 (50.5) | 29 (52.7)/26 (47.3) | 0.65 |
| BMI (mean±SD), kg/m$^2$ | 22.5±3.5 | 22.9±3.8 | 0.45 |
| Outpatient/inpatient, *n* (%) | 283 (95.9)/12 (40.1) | 52 (94.5)/3 (5.5) | 0.73 |
| ASA-PS, *n* (%) (1/2/3) | 161 (54.6)/133 (45.1)/1 (0.3) | 29 (52.7)/24 (43.6)/2 (3.6) | 0.05 |
| Comorbidities | | | |
| Neurological disease, *n* (%) | 3 (1.0) | 0 (0) | 0.45 |
| Diabetes, *n* (%) | 16 (5.4) | 12 (21.8) | <0.0001 |
| Inflammatory bowel disease, *n* (%) | 19 (6.4) | 6 (10.9) | 0.23 |
| History of abdominal surgery, *n* (%) | 89 (30.2) | 21 (38.1) | 0.24 |
| Use of laxatives, *n* (%) | | | |
| (None/one kind/more than 2 kinds) | 259 (87.8)/32 (10.8)/4 (1.4) | 36 (65.5)/13 (23.6)/6 (10.9) | <0.0001 |
| Defecation habit, *n* (%) | | | |
| (Daily/once every 2–3 days/or more) | 231 (78.3)/55 (18.6)/9 (3.1) | 34 (61.8)/15 (27.3)/6 (10.9) | 0.0065 |
| Use of drugs for mental disorders, *n* (%) | 12 (4.1) | 12 (21.8) | <0.0001 |

**Table 5.** The univariable analyses for patients with inadequate bowel preparation

| | OR | 95% CI | *p* value |
|---|---|---|---|
| Age (≥75 years/<75 years) | 1.53 | 0.76–2.94 | 0.23 |
| Gender (men/women) | 1.14 | 0.64–2.04 | 0.66 |
| BMI (≥25/<25) | 1.30 | 0.62–2.58 | 0.47 |
| Outpatient/inpatient | 0.80 | 0.24–3.57 | 0.74 |
| ASA-PS (3/1 or 2) | 11.1 | 1.05–241.1 | 0.046 |
| Comorbidities | | | |
| Neurological disease | | | |
| (Yes/no) | NA | NA | NA |
| Diabetes | | | |
| (Yes/no) | 4.87 | 2.12–10.96 | 0.0003 |
| Inflammatory bowel disease | | | |
| (Yes/no) | 1.78 | 0.62–4.45 | 0.24 |
| History of abdominal surgery | | | |
| (Yes/no) | 1.43 | 0.78–2.58 | 0.25 |
| Use of laxatives | | | |
| (Yes/no) | 3.80 | 1.95–7.29 | 0.0001 |
| Defecation habit (Once in every | | | |
| 2–3 days or more/daily) | 2.23 | 1.20–4.08 | 0.012 |
| Use of drugs for mental disorders | | | |
| (Yes/no) | 6.58 | 2.76–15.74 | <0.0001 |

BMI, body mass index; ASA-PS, American Society of Anesthesiologists physical status; OR, odds ratio; CI, confidence interval.

days, and use of drugs for mental disorders (Table 5). The multivariate analysis revealed five independent risk predictors for inadequate bowel preparation: ASA-PS class III (OR, 1.34; 95% CI, 0.75–40.51; $p = 0.84$), diabetes comorbidities (OR, 4.42; 95% CI, 1.64–11.42; $p = 0.0024$), use of laxatives (OR, 6.14; 95% CI, 1.73–7.62; $p = 0.00058$), no defecation once in a day (OR, 1.64; 95% CI, 0.61–3.22; $p = 0.16$), and the use of drugs for mental disorders (OR, 6.14; 95% CI, 2.30–16.19; $p = 0.0023$) (Table 6).

The points attributed to the five risk factors were as follows: ASA-PS class III (1 point), diabetes comorbidities (5 points), use of laxatives (4 points), no defecation once a day (2 points), and use of drugs for mental disorders (6 points) (Table 6). The total risk scores ranged from 0 to 15, and Table 7 shows the estimated risk for inadequate bowel preparation for each score.

*Internal Validation of the Risk-Scoring System*

Our scoring model showed satisfactory discriminatory performance among the 2,000 bootstrap internal samples (bootstrap-corrected area under the receiver-operating characteristic curve, 0.75; 95% CI, 0.68–0.82). In terms of calibration, the slope and intercept were 1.03 (95% CI, 0.71–1.40) and −0.045 (95% CI, −0.54 to 0.73), respectively. The Brier score was 0.11 (95% CI, 0.09–0.13).

## Discussion

Adequate bowel preparation is essential for optimal colonoscopy. However, from the patient's point of view, a bowel preparation agent that is easy to ingest and less burdensome is desirable. If a bowel preparation method

**Table 6.** Factors associated with inadequate bowel preparation

| Risk factors | Multivariate analysis | | | |
|---|---|---|---|---|
| | OR (95% CI) | β coefficient | *p* value | point assigned |
| Intercept | 0.084 (0.051–0.13) | −2.48 | | |
| ASA-PS | | | | |
| 1 or 2 | Reference | | | |
| 3 | 1.34 (0.75–40.51) | 0.30 | 0.84 | 1 |
| Diabetes | | | | |
| No | Reference | | | |
| Yes | 4.42 (1.64–11.42) | 1.49 | 0.0024 | 5 |
| Use of laxatives | | | | |
| No | Reference | | | |
| Yes | 6.14 (1.73–7.62) | 1.29 | 0.00058 | 4 |
| Defecation habit | | | | |
| Daily | Reference | | | |
| Nondaily | 1.64 (0.61–3.22) | 0.49 | 0.16 | 2 |
| Use of drugs for mental disorders | | | | |
| No | Reference | | | |
| Yes | 6.14 (2.30–16.19) | 1.81 | 0.00023 | 6 |

ASA-PS, American Society of Anesthesiologists physical status; OR, odds ratio; CI, confidence interval.

**Table 7.** Risk for patients with inadequate bowel preparation

| Risk points, *N* | Estimated risk, % | Observed no. of inadequate bowel preparation, *n*/*N* (%) |
|---|---|---|
| 0 | 7.7 | 13/207 (6.3) |
| 1 | 10.1 | NA |
| 2 | 13.2 | 8/48 (16.7) |
| 3 | 16.9 | NA |
| 4 | 21.5 | 9/25 (36.0) |
| 5 | 26.9 | 3/15 (20.0) |
| 6 | 33.1 | 11/37 (29.7) |
| 7 | 40.0 | 3/5 (60.0) |
| 8 | 47.3 | 2/4 (50.0) |
| 9 | 54.6 | NA |
| 10 | 61.8 | 0/1 (0) |
| 11 | 68.5 | 0/2 (0) |
| 12 | 74.6 | 0/1 (0) |
| 13 | 79.8 | NA |
| 14 | 84.1 | 1/2 (50.0) |
| 15 | 87.7 | 3/3 (100) |
| 16 | 90.5 | 0/0 (0) |
| 17 | 92.8 | 0/0 (0) |
| 18 | 94.5 | 0/0 (0) |

with sufficient bowel cleansing efficacy and high patient acceptability can be developed, the number of patients able to undergo colonoscopy may increase. This is the first study to develop a scoring model to predict inadequate bowel preparation when using the SP + MC regimen for colonoscopy. In this study, 95.7% of patients were able to ingest SP + MC without any difficulty, and five clinical risk factors that led to inadequate bowel preparation were identified, including ASA-PS class III, diabetes comorbidities, use of laxatives, no defecation once in a day, and use of drugs for mental disorders. Based on these risk factors, we developed a scoring model that can easily be used in clinical practice, to predict inadequate bowel preparation in colonoscopy. Our scoring model could predict the degree of risk and calculate the estimated risk of inadequate bowel preparation in colonoscopy with satisfactory discrimination and calibration.

This study revealed the five clinical factors, including ASA-PS class III, diabetes comorbidities, use of laxatives, defecation habit of less than once in every 2–3 days, and use of drugs for mental disorders that were independent risk factors for inadequate bowel preparation. Several previous studies have reported independent risk factors for inadequate bowel preparation. Factors that are associated with inadequate bowel preparation fall into two categories: factors related to reduced gastrointestinal motility, and those related to medication compliance. Factors related to medication compliance include health awareness, educational level, illiteracy, marital status, appointment waiting time, and the indication for colonoscopy [20–23]. We did not include such factors in our model because our intention was to develop a clinically

useful predictive model that would identify patients who would benefit more from the SP + MC regimen. Our study included information that was readily available from a medical interview conducted prior to colonoscopy to assess the candidate factors. These five factors have been reported in previous studies, and all were associated with reduced gastrointestinal motility. The ASA score has been reported to be a risk factor for inadequate bowel preparation because it reflects the patient's clinical condition and is a surrogate for patient age, physical condition, obesity, medications, and comorbidities [10]. It has been reported that gastrointestinal motility is reduced in diabetic patients, which leads to delayed transit time and constipation symptoms [24]. Bowel cleansing using the PEG agent showed less effectiveness in diabetic patients than in nondiabetic patients, regardless of insulin use, diabetic control, or diabetic neuropathy [25]. Through their anticholinergic effects, several drugs used for mental disorders have been associated with constipation and altered bowel motility. Other studies have shown that tricyclic antidepressants, a class of drugs commonly used for mental disorders, are risk factors for inadequate bowel preparation and tend to have a stronger effect on bowel preparation than other factors [10]. Male sex, older age, and history of abdominal surgery have also been reported to be associated with inadequate bowel preparation; however, these factors were not found to be significant in our study. It is difficult to directly address the causes of these differences; however, the differences in agent, higher oral compliance due to higher patient acceptability, and racial differences might have caused these differences.

Our scoring model for prediction of inadequate bowel preparation showed satisfactory discrimination and calibration. Of the five factors, diabetes comorbidity, laxative use, and use of medications for mental disorders had a greater impact on the cleansing effect. Although any one factor increased the risk of inadequate bowel preparation, when the score exceeded 3 points, the estimated risk of inadequate bowel preparation also exceeded 15.7% in this study. The percentage of inadequate preparation of bowel preparation agents containing PEG was previously reported to be 71.3–93.5% [26], and we considered an estimated risk of over 85% to be acceptable. Therefore, we suggest using the SP + MC regimen for patients with a score of 2 or less and a regimen other than SP + MC for patients with a score of 3 or more. In this study, 255 patients (72.9%) with a score of 2 or less were recommended SP + MC, which is a considerable proportion. For patients with a score of 3 or higher, individual and institution-specific regimen modifications should be made, for example, lengthening the duration of dietary restriction, switching to alternative agents, or adding other laxatives, such as PEG, picosulfate sodium hydrate, or senna.

There are some limitations to the present study. First, we did not evaluate the cleansing efficacy of SP + MC alone, since the SP + MC regimen used in this study was combined with sennosides. Changing the laxative used in combination with SP + MC might be more effective in producing a desirable effect. Second, although this study was validated using bootstrapping based on prospectively collected data, external validation with prospective data is necessary in future.

In conclusion, we identified five risk factors for inadequate bowel preparation in Japanese patients when using an SP + MC regimen. We developed a scoring model with satisfactory discrimination and calibration to predict patients with inadequate bowel preparation. We believe that this scoring model could contribute to achieving colonoscopy with both high cleansing efficacy and patient acceptability through the effective use of SP + MC, which has high patient acceptability.

## Statement of Ethics

The study protocol was approved by the Ethics Committee at Kobe University Hospital (Approval No. B210008-1). The Ethics Committee waivered the need for written informed consent because the study used data from routine medical care and the only additional information was a questionnaire. Therefore, consent was obtained using the opt-out method.

## Conflict of Interest Statement

The authors declare that they have no conflict interest.


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## Author Contributions

Norihiro Okamoto and Shinwa Tanaka conceived the idea of the study. Hirofumi Abe developed the statistical analysis plan and conducted statistical analyses. Haruka Miyazaki, Tatsuya Nakai, Kauhiro Tsuda, Hiroya Sakaguchi, Tetsuya Yoshizaki, and Nobuaki Ikezawa contributed to the interpretation of the results. Norihiro Okamoto and Shinwa Tanaka drafted the original manu-

script. Jun Inoue, Makoto Ooi, and Yuzo Kodama supervised the conduct of this study. All the authors reviewed the manuscript draft and revised it critically on intellectual content. All the authors approved the final version of the manuscript to be published.

## Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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