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Alteration of Heart Rate Variability in People With Bowel Preparation Before Colonoscopy

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Abstract: In current health examination setting, people frequently undergo heart rate variability (HRV) analysis and colonoscopy on the same day. However, it remains unclear whether the bowel preparation before colonoscopy affects HRV. This study aimed to evaluate the association between HRV and bowel preparation.

We conducted a cross-sectional observational study of 1755 people from January 2012 to December 2013 in Taipei, Taiwan. The participants, aged 45 to 65 years, received health examinations that included a physical examination, blood tests, and an HRV analysis. Among these people, 1099 additionally received a colonoscopy on the same day and underwent bowel preparation 1 day before the colonoscopy. The association between HRV and bowel preparation was derived by a multivariable linear regression with adjusted confounding factors.

Bowel preparation was associated with a lower standard deviation of the normal-to-normal intervals (SDNN), the root mean square of the successive differences (RMSSD), low-frequency power (LF), and high-frequency power (HF) (all $P < 0.0001$). After adjusting confounding factors, bowel preparation remained correlated with lower SDNN, RMSSD, LF, and HF (all $P < 0.0001$). Higher serum phosphorus and lower serum potassium levels were noted in the bowel preparation group ($P < 0.0001$), and an association between lower HRV and higher serum phosphorus and lower serum potassium levels was only noted in the bowel preparation group.

Bowel preparation was significantly associated with lower HRV. The underlying mechanism may be related to an electrolyte imbalance. Cautions may be needed when interpreting HRV reports for people receiving bowel preparations before colonoscopy.

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Abbreviations: BMI = body mass index, CKD = chronic kidney disease, DBP = diastolic blood pressure, HD = hemodialysis, HDL = high-density lipoprotein, HF = high-frequency component of spectral HRV, HRV = heart rate variability, LDL = low-density lipoprotein, LF = low-frequency component of spectral HRV, LF/HF = ratio of low-frequency and high frequency components of spectral HRV, RMSSD = root mean square of successive differences, SBP = systolic blood pressure, SDNN = standard deviation of all normal to normal intervals, TG = triglyceride.

INTRODUCTION

Heart rate variability (HRV) is the variation in the time interval between heartbeats, and an HRV assessment is used for examining the interaction between the sympathetic and parasympathetic nervous systems. Because of the convenience and noninvasiveness of the examination, HRV analysis is widely applied in healthcare settings and provides indices of autonomic function. Measurement of HRV includes a time domain and a frequency domain, which generally represent the autonomic nervous activity and balance, respectively.[1] HRV is reported to be related to age,[2] gender,[3,4] obesity,[5] hypertension,[6,7] diabetes,[8,9] and hyperlipidemia.[10,11] A decreased HRV reflects an imbalance of the autonomic system and is an important predictor for poor prognosis in patients with heart disease[12,13] and in the general population[14] and in a medical preparation before surgery.[15–17] HRV may also be influenced by alterations in respiration,[18] smoking habits,[19] and the circadian rhythm[20] and should be performed under a careful procedural protocol to minimize artifacts and achieve more reliable results.

Colonoscopy is considered to be the standard procedure in the diagnosis and treatment of colonic diseases and is commonly administered worldwide. Adequate bowel preparation is essential for optimal performance and visualization of mucosal lesions and details, contributing to the success of a colonoscopy.[21] Currently available options for colorectal cleansing include polyethylene glycol solution and sodium phosphate. Patients undergoing bowel preparation may experience gastrointestinal discomfort associated with nausea, vomiting, perianal irritation, dizziness, weakness, fatigue, thirst, and headache.[22,23] These pharmacological effects in healthy individuals generally do not cause severe complications and subside quickly.

In a modern health examination setting, participants frequently undergo colonoscopy and HRV analysis on the same day. However, information regarding whether bowel preparation before colonoscopy affects HRV is lacking. If bowel cleansing affects HRV, the derived HRV result might reveal an acute status rather than the basal status, possibly resulting in misinterpretation of the autonomic nervous condition. This study aimed to understand the effect of bowel preparation on HRV.

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METHODS

Participants

A total of 1755 participants, aged 45 to 65 years submitted to health check-ups at a medical center in Taipei City from January 2012 to December 2013. We retrospectively retrieved participants' profiles from the health check-up database and conducted a cross-sectional observational study. This study was approved by the Institutional Review Board of the Tri-Service General Hospital, National Defense Medical Center (TSGHIRB103-05-106). All of the participants received health examinations, which included a physical examination, biochemical analysis, and HRV examination. Among these participants, 1099 received a colonoscopy and 656 did not (the control group). Bowel preparation before colonoscopy included oral administration of 2 bottles (45 ml each) of oral sodium phosphate, 12 hours apart, 1 day before the health examination.

This study analyzed the data on the participants' demographic characteristics (age and gender), weight (kg) and height (cm), body mass index (BMI; kg/m^2), waist circumference (cm), systolic blood pressure (SBP; mm Hg) and diastolic blood pressure (DBP; mm Hg) and biochemical values, including triglyceride (TG; mg/dl), high-density lipoprotein (HDL; mg/dl), low-density lipoprotein (LDL; mg/dl), fasting plasma glucose (mg/dl), sodium (mmol/L), potassium (mmol/L), calcium (mmol/L), phosphorus (mmol/L), blood urea nitrogen (mg/dl), and creatinine (mg/dl). Participants with a fasting blood glucose level above 126 mg/dl were considered to be diabetic.

HRV Evaluation

HRV was assessed using a measuring system (SA-3000P; Medicore Co., Ltd, Korea) to acquire, store, and process electrocardiography (ECG) signals for 5 minutes.[24] The participants were examined in a seated position in a quiet and dark room with a regular temperature (22–24°C), and the ECG recording was performed in the morning (8:00 AM–12:00 noon) to minimize the diurnal fluctuation. The time and frequency domains were calculated automatically. For the time domain, standard deviation of all normal to normal intervals (SDNN, ms), and root mean square of successive differences (RMSSD, ms) were measured. For the frequency domains, low-frequency component of spectral HRV (LF, 0.04–0.15 Hz, ms^2), high-frequency component of spectral HRV (HF, 0.15–0.4 Hz, ms^2), and LF/HF ratio were measured using the Fast Fourier Transform system. HF reflects the vagal modulation of the sinus node, and LF represents the sympathetic modulation or a combination of the sympathetic and vagal influences. The LF/HF ratio is considered to reflect the sympathovagal influence on the heart rate control.[1,25,26] The time and frequency domain parameters were natural log-transformed to correct the skewed distribution. The absolute and log-transformed HRV values were both presented in the results.

Statistical Analysis

The data were analyzed with PASW, 18.0, statistical software for Windows. The results were expressed as the mean ± SD. The statistical significance of the differences between the respective groups was evaluated using Student *t* test for the continuous data and Pearson χ^2 test for the categorical variables. The association between HRV and bowel preparation was derived by a multivariable linear regression with adjusted factors, including age, gender, diabetes mellitus, BMI, SBP, TG, and HDL. The correlation between HRV parameters and electrolyte changes was assessed using Pearson partial analysis. A P-value < 0.05 was considered statistically significant.

RESULTS

The characteristics of the participants are listed in Table 1. In comparison to participants without bowel preparation (control group), participants with bowel preparation showed few differences in clinical or demographic data but higher serum levels of TG and phosphorus as well as lower levels of HDL cholesterol and potassium.

The HRV parameters of both groups are provided in Table 2. The bowel preparation group showed significantly lower SDNN, RMSSD, LF, and HF results; however, there was no difference between groups in the LF/HF ratio. Based on the LF/HF ratio, the subjects were further classified into low (<0.5), normal (0.5–2), and high groups (>2), although no differences were observed between participants with and without bowel preparation ($\chi^2 = 0.334$, $P = 0.84$).

To determine the effect of bowel preparation on HRV parameters, we used a multiple linear regression model that included potentially confounding factors (age, BMI, gender, diabetes mellitus, SBP, TG, and HDL). As shown in Table 3, bowel preparation was significantly associated with lower SDNN, RMSSD, LF, and HF values and no difference in the LF/HF ratio.

Pearson partial correlation coefficients between the HRV parameters and the electrolyte changes in the bowel preparation group are shown in Table 4. The serum phosphorus and potassium levels were significantly correlated with the HRV,

TABLE 1. Demographic and Clinical Data of Participants

	Bowel Preparation		
	N	Y	*P*
Male, %	393 (59.9%)	632 (57.5)	0.323
Age, y	53.2 ± 5.4	54.7 ± 5.6	<0.001
Height, cm	166.6 ± 9.0	164.4 ± 9.3	<0.001
Weight, cm	67.6 ± 14.0	66.3 ± 13.2	0.067
BMI, kg/m^2	24.2 ± 3.8	24.3 ± 3.7	0.294
Waist circumference, cm	81.3 ± 10.5	82.9 ± 10.8	0.003
SBP, mm Hg	118.6 ± 18.0	121.1 ± 18.8	0.007
DBP, mm Hg	75.9 ± 11.5	77.9 ± 11.7	0.001
Total cholesterol, mg/dL	189.3 ± 36.1	193.2 ± 36.4	0.026
TG, mg/dL	117.6 ± 81.1	142.2 ± 80.1	<0.001
HDL, mg/dL	55.0 ± 15.0	50.9 ± 15.3	<0.001
LDL, mg/dL	122.2 ± 34.2	125.0 ± 33.3	0.128
Fasting sugar, mg/dL	93.4 ± 21.4	96.8 ± 21.4	0.001
BUN, mg/dL	13.2 ± 4.3	12.1 ± 3.8	<0.001
Cre, mg/dL	0.86 ± 0.22	0.82 ± 0.20	0.002
Total Ca, mmol/L	9.27 ± 0.37	8.86 ± 0.39	<0.001
P, mmol/L	3.60 ± 0.72	5.71 ± 1.51	<0.001
Na, mmol/L	140.73 ± 1.99	142.95 ± 2.22	<0.001
K, mmol/L	4.05 ± 0.33	3.49 ± 0.34	<0.001

Data presented as mean ± standard deviation. BMI = body mass index; BUN = blood urea nitrogen; Ca = calcium; Cre = creatinine; DBP = diastolic blood pressure; HDL = high-density lipoprotein; K = potassium; LDL = low-density lipoprotein; Na = sodium; P = phosphorus; SBP = systolic blood pressure; TG = triglyceride.

TABLE 2. Comparison of Heart Rate Variability Between Participants With and Without Bowel Preparation

	Bowel Preparation		
	N	Y	*P*
SDNN, ms	46.25 ± 21.95	39.60 ± 21.09	<0.001
RMSSD, ms	34.03 ± 21.24	29.08 ± 20.61	<0.001
LF, ms^2	553.18 ± 741.20	391.77 ± 632.36	<0.001
HF, ms^2	356.10 ± 424.00	239.24 ± 316.61	<0.001
LF/HF	2.24 ± 3.23	2.33 ± 3.05	0.564
ln SDNN, ms	3.73 ± 0.46	3.57 ± 0.46	<0.001
ln RMSSD, ms	3.37 ± 0.56	3.20 ± 0.57	<0.001
ln LF, ms^2	5.63 ± 1.23	5.23 ± 1.24	<0.001
ln HF, ms^2	5.34 ± 1.08	4.91 ± 1.10	<0.001
ln LF/HF	0.29 ± 1.00	0.32 ± 1.03	0.569

Each spectral HRV component was presented as both absolute and natural log-transformed (ln) values. Data presented as mean ± standard deviation. HF = high-frequency component of spectral HRV; HRV = heart rate variability; LF/HF = ratio of low-frequency and high-frequency components of spectral HRV; LF = low-frequency component of spectral HRV; RMSSD = root mean square of successive differences; SDNN = standard deviation of all normal to normal intervals.

although this relationship was not noted in the control group (data not shown).

DISCUSSION

The major finding of this study is that bowel preparation before colonoscopy was significantly associated with decreased HRV, including lower SDNN, RMSSD, LF, and HF values. The relationship between bowel preparation and HRV was verified using multiple linear regression analysis after adjusting for potentially confounding factors. The association between HRV and changes in serum phosphorus and potassium levels was only demonstrated in the bowel preparation group.

TABLE 3. Factor-Adjusted Associations Between Bowel Preparation and Heart Rate Variability

	Bowel Preparation			
	β	SE	CI	*P*
SDNN, ms	−4.348	2.162	−8.588 to −0.107	0.044
RMSSD, ms	−2.618	2.126	−6.788 to 1.552	0.218
LF, ms^2	−168.101	68.070	−301.607 to −34.594	0.014
HF, ms^2	−80.414	37.157	−153.290 to −7.538	0.031
LF/HF	0.150	0.317	−0.472 to 0.772	0.636
ln SDNN, ms	−0.123	0.022	−0.168 to −0.080	<0.001
ln RMSSD, ms	−0.132	0.028	−0.187 to −0.077	<0.001
ln LF, ms^2	−0.260	0.060	−0.378 to −0.142	<0.001
ln HF, ms^2	−0.351	0.054	−0.456 to −0.245	<0.001
ln LF/HF	0.060	0.050	−0.037 to 0.158	0.224

Each spectral HRV component was presented as both absolute and natural log-transformed (ln) values. Factors (age, gender, diabetes mellitus, body mass index, systolic blood pressure, triglycerides, and high-density lipoprotein–cholesterol) were included in the same regression model. β = parameter estimate indicating the change in spectral HRV components caused by one unit of change in the explaining variable; CI = confidence interval; HF = high-frequency component of spectral HRV; HRV = Heart rate variability; LF/HF = ratio of low-frequency and high-frequency components of spectral HRV; LF = low-frequency component of spectral HRV; RMSSD = root mean square of successive differences; SDNN = standard deviation of all normal to normal intervals; SE = standard error.

TABLE 4. Pearson's Partial Correlation Between Heart Rate Variability Parameters and Electrolytes in Bowel Preparation Group

	P, mmol/L		K, mmol/L		Ca, mmol/L	
	CC	*P*	CC	*P*	CC	*P*
SDNN, ms	−0.053	0.085	0.065	0.034	0.039	0.203
RMSSD, ms	−0.071	0.021	0.041	0.183	−0.008	0.782
LF, ms^2	−0.022	0.466	0.056	0.067	0.031	0.309
HF, ms^2	−0.085	0.006	0.019	0.529	−0.025	0.417
LF/HF	0.010	0.754	0.089	0.003	0.014	0.639
ln SDNN, ms	−0.086	0.005	0.076	0.013	0.030	0.324
ln RMSSD, ms	−0.106	<0.001	0.028	0.358	−0.030	0.325
ln LF, ms^2	−0.060	0.048	0.092	0.003	−0.005	0.870
ln HF, ms^2	−0.120	<0.001	−0.009	0.770	−0.034	0.266
ln LF/HF	0.054	0.075	0.126	<0.001	0.030	0.332

Each spectral HRV component was presented as both absolute and natural log-transformed (ln) values. Ca = calcium; CC = correlation coefficient; HF = high-frequency component of spectral HRV; HRV = heart rate variability; K = potassium; LF/HF = ratio of low-frequency and high-frequency components of spectral HRV; LF = low-frequency component of spectral HRV; P = phosphorus; RMSSD = root mean square of successive differences; SDNN = standard deviation of all normal to normal intervals.

One serious concern raised in our study is that HRV data acquired using the current health examination protocol might not reflect the basal status; instead, these data might reflect an acute condition in people who undergo bowel preparation before colonoscopy. The details of the mechanisms by which bowel preparation affects HRV remain unclear, although an electrolyte imbalance may play an important role.

Studies investigating the relationship between serum electrolytes and HRV are rare. Most available research in this field has focused on the relationship between HRV and serum electrolytes in particular pathological conditions, such as chronic kidney disease (CKD).[27–29] Using a multivariable linear regression model, Drawz et al[28] demonstrated that elevated serum phosphorus was associated with lower SDNN and RMSSD in patients with CKD. In addition, elevated serum phosphorus has been reported to be associated with a lower LF/HF ratio.[29] Wen et al studied the relationship between a rapid change in the serum phosphorus level and HRV in 23 CKD patients before and after hemodialysis (HD). A significant decrease in serum phosphorus was noted after HD, with no significant correlation between the serum phosphorus level and HRV.[27] In our study, rapid elevation of the serum phosphorus level was noted in the bowel preparation group, and an association between the serum phosphorus level and HRV was noted in the bowel preparation group; this association was not observed in the control group. The mechanism by which an acute change in the serum phosphorus level interacts with HRV remains unclear.

Hill et al reported that patients developing hypokalemia after bowel preparation were predisposed to cellular potassium depletion. Decreased serum potassium is negatively correlated

with the basal intracellular potassium concentration,[30] and a loss of serum potassium lowers the threshold for cell depolariration, increases the QT variation, induces cardiac arrhythmia[31] and, theoretically, affects the HRV. Several studies have examined the effects of rapidly altered levels of serum potassium on HRV in CKD patients before and after HD,[27,32] and the results revealed that decreased serum potassium after HD showed no significant correlation with HRV. Lutfi[33] evaluated the effects of electrolyte concentrations on HRV in apparently healthy subjects, and these data revealed no significant correlations between the potassium level and the HRV indices. In our study, the serum potassium level was decreased in the bowel preparation group, and the relationship between the serum potassium level and HRV was only noted in the bowel preparation group, implicating a possible role of serum potassium in mediating HRV. Probable explanations for the discrepancy in the results of the relationship between serum potassium and HRV include variability between study groups (eg, CKD patients)[27,32] and different study designs (eg, without a rapid change of serum potassium).[33] In addition, the level of serum potassium might not accurately reflect the intracellular potassium levels,[34] although the measurement of intracellular potassium levels is technically difficult.

Physical or psychiatric stress can result from bowel preparation-related adverse events, including abdominal pain, abdominal fullness, nausea, vomiting, perianal irritation, dizziness, weakness, fatigue, thirst, and headache.[22,23] Individuals under stress theoretically precipitate activation of the sympathetic nervous system and depression of the parasympathetic nervous system, and different types of stress might exert different HRV changes. Previous reports have shown that physiological (eg, exercise) and pathological stress (eg, sepsis) results in decreased SDNN; however, a diminished LF/HF ratio was only noted with exercise.[35] In addition, psychological stress is correlated with increased LF, decreased HF, and/or an increased LF/HF ratio.[36,37] Work stress has been reported to correlate with decreased SDNN, LF, and HF.[38] It is supposed that stress might play an important role in mediating the effect of the bowel preparation on HRV. Further studies are needed to investigate the association between bowel preparation-related stress and HRV.

The strengths of this study include the large sample size and extensive baseline assessment. The important contribution of our study is the demonstration that bowel preparation might affect HRV. To our knowledge, this study is the first to investigate the role of bowel preparation and rapid changes of electrolytes in relation to HRV in a relatively healthy population.

There are several limitations to this study. First, we could not determine when bowel preparation begins to affect HRV, when bowel preparation exerts the greatest effect on HRV or when HRV returns to normal. We did not investigate the heart rhythm behavior during colonoscopy and whether there are more ventricular or supraventricular arrhythmias in the bowel preparation group of participants compared to the control group. We also had insufficient data to determine whether other dosages or regimens of bowel preparation exhibit similar HRV responses. Second, the stress effect of bowel preparation might affect HRV; however, we did not perform an objective assessment of the quantification of stress. Third, there are many factors that possibly mediate HRV that were not analyzed in our study, including the past medical history and cardiovascular medication history of each participant. Fourth, this work is an observational study, which limits our ability to assess causality; thus, longitudinal studies and repeated measurements are needed.

In conclusion, bowel preparation before colonoscopy was associated with lower HRV, and the underlying mechanism for the alteration of the cardiovascular autonomic nervous system after bowel preparation might be related to an electrolyte imbalance. HRV data derived using the current health examination protocol might not reflect the basal status; rather, these data might reflect an acute condition in participants who undergo bowel preparation before colonoscopy. Additional studies to elucidate the role of bowel preparation in HRV are required, and caution may be necessary for interpreting HRV reports in people having undergone bowel preparation.

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