# Serum Gastrin Predicts Hydrogen-Producing Small Intestinal Bacterial Overgrowth in Patients With Abdominal Surgery: A Prospective Study

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OBJECTIVES: **Small intestinal bacterial overgrowth (SIBO) might be associated with a history of abdominal surgery. We aimed to evaluate the prevalence of SIBO and to investigate serum gastrin and pepsinogen as predictors of SIBO in patients with a history of hysterectomy, gastrectomy, or cholecystectomy.**

METHODS: **This prospective study surveyed 146 patients with a history of hysterectomy, gastrectomy, or cholecystectomy, and 30 healthy controls, who underwent a hydrogen ($H_2$)-methane ($CH_4$) glucose breath test (GBT) for SIBO. Serum pepsinogen I and II and gastrin levels were reviewed.**

RESULTS: **GBT positivity (+) was significantly higher in patients with histories of abdominal surgery than that in in controls (37.6% vs 13.3%, $P < 0.01$). Among GBT+ patients, 36.0% (18/50), 96.2% (25/26), and 17.1% (12/70) were in the hysterectomy, gastrectomy, and cholecystectomy groups, respectively. Among the GBT subtypes, 43.6% (24/55), 10.9% (6/55), and 45.5% (25/55) of patients were in the GBT($H_2$)+, GBT($CH_4$)+, and GBT(mixed)+ groups, respectively. The gastrectomy group had significantly more GBT+ or GBT($H_2$)+ patients than the other surgical groups. Gastrin levels were higher in GBT($H_2$)+ patients and lower in GBT($CH_4$)+ patients than those in GBT− patients. Previous gastrectomy and elevated gastrin levels were independent predictive factors of GBT($H_2$)+.**

DISCUSSION: **SIBO is not uncommon in patients with histories of abdominal surgeries, but it is more common in patients who have undergone gastrectomy. Serum gastrin level could be a serologic predictor of $H_2$-producing SIBO. The relationship between serum gastrin and SIBO requires further research.**

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## INTRODUCTION

An aging population and medical developments have led to an increase in the number of patients undergoing abdominal surgery (1). Many of these patients complain of abdominal discomfort that has no organic cause. Although several possibilities have been considered, small intestinal bacterial overgrowth (SIBO) has recently been considered to play a role (2–7).

SIBO is a disorder involving an increased number or alteration in the type of bacteria in the small intestine (8). The gut microbiota modulates important physiological processes, such as gastrointestinal motility and secretion, and maintains epithelial barrier integrity. Its role in the communication between the gut and the central nervous system might underlie its contribution to functional gastrointestinal symptoms (9–11). The etiologies of SIBO vary widely, from intestinal dysmotility to anatomical abnormalities, in addition to dysfunction of antibacterial mechanisms in the presence of low gastric acid secretory capacity. Patients with a history of abdominal surgery can be expected to have structural changes in the abdominal cavity, which might affect the gut microbiota and cause abdominal dysbiosis. Recently, gastrectomy, hysterectomy, and cholecystectomy have been considered to adversely affect the abnormal growth of small intestinal bacteria (2,4,6,7,12). However, most studies have analyzed retrospective data and have not able to determine the predictors of SIBO or its clinical considerations according to the type of surgery.

Serum pepsinogen (PG) and gastrin levels are useful indicators of the functional status of the gastric mucosa and acidity level (2–7). Moreover, serum gastrin is related to intestinal motor function (2–7). Because factors such as intestinal motility and gastric acid are involved in the occurrence of SIBO, serum PG and gastrin are likely to act as serologic test associated with SIBO;

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however, research on this is extremely rare. This study aimed to evaluate the prevalence of SIBO and serum PG or gastrin as possible predictors of SIBO in patients undergoing abdominal surgeries such as hysterectomy, gastrectomy, and cholecystectomy.

## METHODS

This study was approved by the Institutional Research Ethics Board of the Catholic University of Korea (VC15OISI0167) and adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from all patients.

### Study population

This prospective study was conducted at the Catholic University School of Medicine, St. Vincent's Hospital, from December 2015 to December 2017. We enrolled patients who had functional gastrointestinal symptoms and a history of gastrectomy, laparoscopic cholecystectomy, or hysterectomy but did not have evidence of surgical complications or sequelae (leakage, bleeding, adhesion, or perforation) and history of any other abdominal surgery. All patients were aged older than 18 years. Some patients underwent gastrectomy for peptic ulcer disease or early gastric cancer with no evidence of recurrence for at least 6 months of follow-up (12). Other patients underwent laparoscopic cholecystectomy due to acute cholecystitis at least 6 months before this study and had no evidence of remnant gallstones in the cystic duct or common bile duct based on blood chemistry tests and imaging studies (2). All women who underwent laparoscopic hysterectomy for myoma disease were followed-up with for 12 months (13,14).

Patients were excluded if they met any of the following criteria: history of diabetes mellitus, connective tissue disease, chronic pancreatitis, thyroid disease, liver disease, overlapping surgical history, use of antisecretory agents such as proton pump inhibitors or histamine $H_2$ receptor antagonists, use of antibiotics, probiotics, laxatives, bulking agents, prokinetics, narcotics, or antidiarrheal drugs within the previous 4 weeks; presence of gastrointestinal disease, renal insufficiency, major psychiatric disease, hearing impairment, masticatory dysfunction; or history of colonoscopy within the previous 3 months. Thirty historically healthy patients were enrolled as the control group, and their hydrogen ($H_2$) and methane ($CH_4$) glucose breath test (GBT) profiles were used to determine normal GBT values.

### Study design

All subjects underwent GBT, which entails $H_2$–$CH_4$ measurement. In addition, it was recommended that, on the day of the

**Table 1. Characteristics of the patients according to the types of abdominal surgery**

| | Hysterectomy (n = 50) | Gastrectomy (n = 26) | Cholecystectomy (n = 70) | *P* |
|---|---|---|---|---|
| Demographics | | | | |
| Age, yr | 56.86 ± 10.02 | 67.62 ± 8.79 | 59.40 ± 11.66 | <0.02 |
| T[a] | A | B | A | |
| Sex | | | | |
| Male | 0 (0.0) | 17 (65.4) | 25 (35.7) | <0.01 |
| Female | 50 (100.0) | 9 (34.6) | 45 (64.3) | |
| BMI, kg/m$^2$ | 24.32 ± 3.28 | 21.75 ± 3.00 | 24.25 ± 3.66 | 0.24 |
| GBT profiles | | | | |
| Total $H_2$, ppm | 237.22 ± 338.27 | 756.19 ± 614.87 | 167.94 ± 219.58 | <0.01 |
| T[a] | A | B | A | |
| Total $CH_4$, ppm | 162.14 ± 135.04 | 252.12 ± 90.15 | 154.19 ± 84.39 | <0.01 |
| T[a] | A | B | A | |
| Positive GBT | 18 (36.0) | 25 (96.2) | 12 (17.1) | <0.01 |
| $H_2$ | 11 (22.0) | 6 (23.1) | 7 (10.0) | <0.01 |
| $CH_4$ | 4 (8.0) | 1 (3.8) | 1 (1.4) | |
| Mixed | 3 (6.0) | 18 (69.2) | 4 (5.7) | |
| PG profiles[b] | | | | |
| PG I, ng/mL | 61.77 ± 50.66 | 23.04 ± 11.81 | 64.92 ± 39.61 | 0.13 |
| PG II, ng/mL | 14.49 ± 11.29 | 14.02 ± 8.41 | 19.44 ± 13.10 | 0.15 |
| Gastrin, pg/dL | 60.86 ± 107.22 | 22.00 ± 13.17 | 48.79 ± 39.54 | 0.48 |
| PG I/II ratio | 4.59 ± 1.58 | 1.64 ± 0.46 | 3.99 ± 2.07 | <0.01 |
| T[a] | A | B | A | |

Data are expressed as mean ± SD or n (%).
BMI, body mass index; $CH_4$, methane; GBT, glucose breath test; $H_2$, hydrogen; PG, pepsinogen.
[a]The same letters indicate nonsignificant differences between groups based on Tukey multiple comparison test.
[b]A total of 95 patients underwent tests for PG profiles with hysterectomy (n = 37), gastrectomy (n = 5), and cholecystectomy (n = 53).

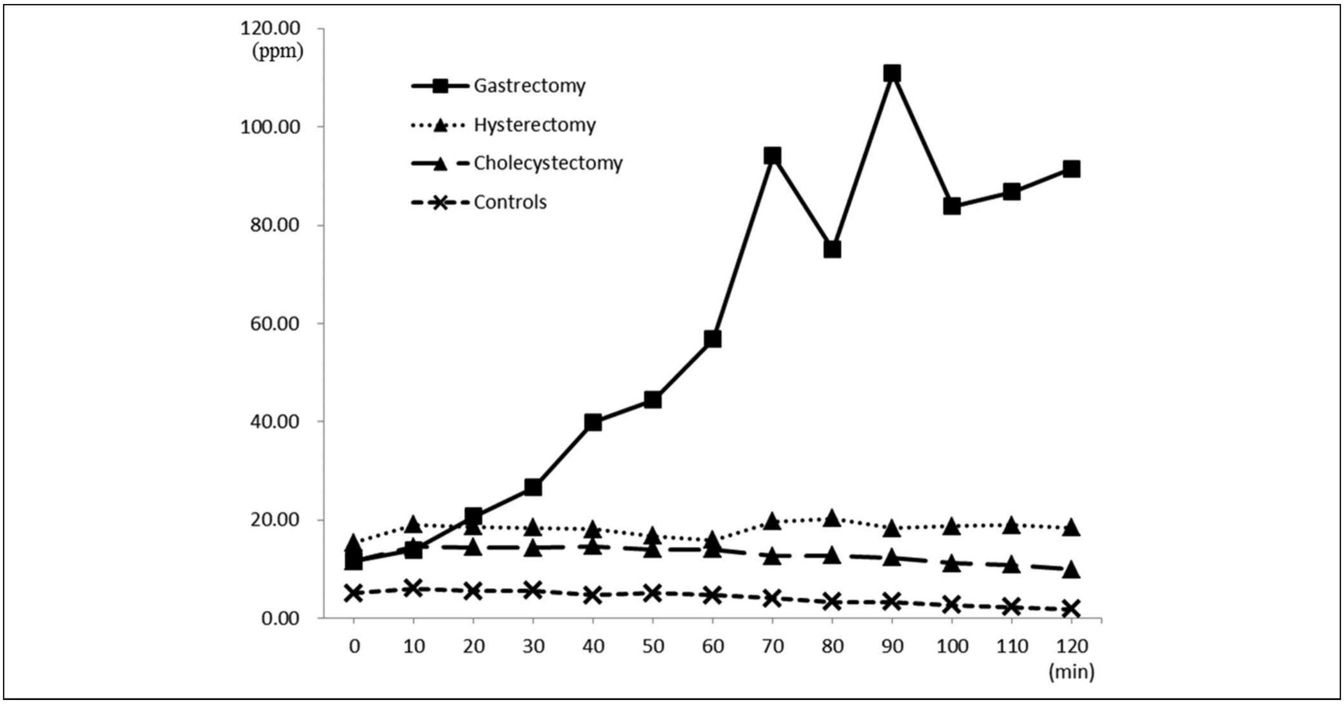


**Figure 1.** The profiles of glucose hydrogen breath test in controls and patients with history of gastrectomy, hysterectomy, and cholecystectomy.

GBT, the subjects undergo laboratory tests for fasting serum PG I and PG II and gastrin levels before the test.

### Glucose breath test

GBT was performed using a gas chromatography instrument (Breath Tracker SC; Quintron Instrument Company, Milwaukee, WI) after the patients underwent overnight fasting for at least 12 hours. The patients were advised to consume a low-residue, carbohydrate-restricted diet the day before the GBT. They were instructed to wash their mouths with 20 mL of 0.05% chlorhexidine 30 minutes before the test. Physical exercise and cigarette smoking were prohibited 2 hours before or during the test. The patients ingested 75 g of glucose dissolved in water (DIASOL-S SOLN; Taejoon Pharm, Seoul, Korea). A baseline end-expiratory breath sample was collected before ingesting the glucose solution. Additional breath samples were collected every 10 minutes for 2 hours, and $H_2$ and $CH_4$ levels were evaluated.

### Definition of SIBO

GBT positivity (GBT+) for $H_2$ [GBT($H_2$)+] or CH4 [GBT($CH_4$)+], indicating a diagnosis of SIBO, was defined as (i) an increase in breath $H_2$ level to ≥20 ppm above the baseline that occurred within the first 90 minutes or (ii) $CH_4$ level ≥10 ppm after ingesting the glucose solution (15). A patient with both GBT($H_2$)+ and GBT($CH_4$)+ status was classified as GBT(mixed)+.

### PG I, PG II, and gastrin

Fasting serum samples were acquired immediately before the GBT. The PG I and PG II levels were evaluated through a turbidimetric immunoassay using the Beckman Coulter AU5800 (Beckman Coulter, Brea, CA). Gastrin levels were measured with radioimmunoassay using the Immulite 2000 (Siemens Healthcare Diagnostics, Tarrytown, NY). Receiver operating characteristic curves of serum gastrin and total $H_2$ were used to determine cutoff values.

### Analysis

Baseline characteristics, including age, sex, body mass index, and serum PG and gastrin profiles, were surveyed. Total $H_2$ or $CH_4$ breath levels and positivity to GBT were determined during the GBT and at the established timepoints.

The GBT profiles of the enrolled patients with a history of abdominal surgery were compared with those of the historically healthy controls. All data were compared among the groups, including the 3 subtypes of surgical patients. For intergroup comparisons, categorical data were expressed as quantities and compared using the $\chi^2$ test or Fisher exact test. Continuous data were expressed as means ± SD and were analyzed using an independent *t* test or 1-way ANOVA and Tukey multiple comparison test as a post hoc analysis. Multiple stepwise logistic regression analysis was used to identify the independent factors associated with SIBO. Statistical analysis was performed using SPSS version 20.0 (SPSS, Chicago, IL). A $P$ value of $<0.05$ was considered statistically significant for all tests.

## RESULTS

### Study population

A total of 146 patients who underwent demographic assessment and GBT were enrolled in this study. The baseline characteristics are summarized in Table 1. The mean patient age was 60.0 ± 11.2 years, and 104 patients (71.2%) were women. Among them, 95 patients completed the routine laboratory tests for fasting PG and gastrin profiles on the day of the GBT.

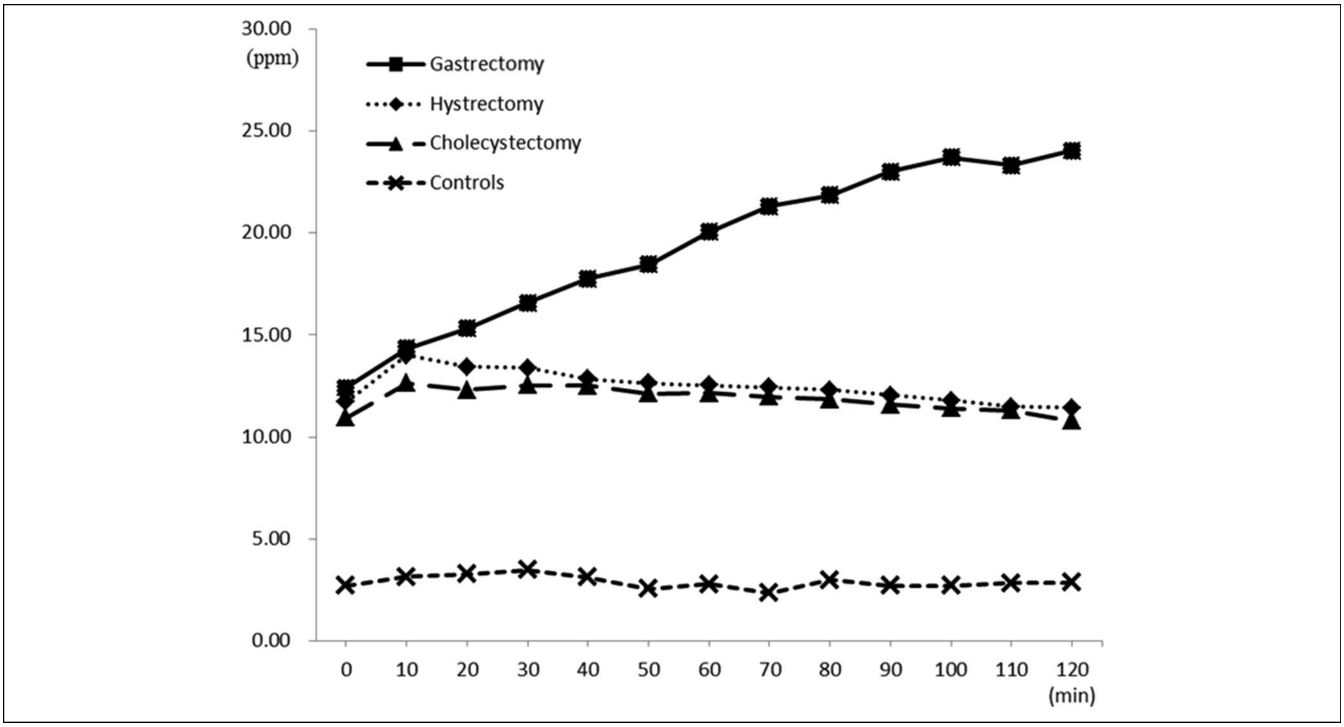


Figure 2. The profiles of glucose methane breath test in controls and patients with history of gastrectomy, hysterectomy, and cholecystectomy.

### Comparison of demographic, GBT, and PG and gastrin profiles among patients with a history of abdominal surgery and GBT results of healthy controls

The mean age was significantly high in gastrectomy patients. Male sex was predominant in patients who underwent gastrectomy, but female sex was predominant in patients who underwent cholecystectomy (Table 1). No significant difference in body mass index was observed among the surgical subjects. The prevalence of GBT+ among patients was 37.6% (55/146), which was significantly higher than the prevalence in the healthy controls (13.3%, 4/30) ($P < 0.01$). The distribution of GBT+ patients according to the type of abdominal surgery was as follows: 36.0% (18/50) in the hysterectomy group, 96.2% (25/26) in the gastrectomy group, and 17.1% (12/70) in the cholecystectomy group. Of the patients who underwent gastrectomy, 4, 5, and 17 patients received total, Billroth I (B-I), and B-II gastrectomy, respectively. Among them, only 1 patient with B-II showed negativity for GBT ($P = 0.76$).

The mean breath $H_2$ profiles at all timepoints of GBT were significantly higher in patients with a history of abdominal surgery than those in controls (Figure 1). The prevalence of GBT+ [GBT($H_2$)+ and GBT(mixed)+] and the total breath $H_2$ or $CH_4$ levels were significantly higher in patients who underwent gastrectomy than the values in those who underwent cholecystectomy or hysterectomy, whereas the PG I/PG II ratio was significantly lower (Table 1). The graph of breath $H_2$ profiles gradually increased with time during GBT in the gastrectomy group (Figure 2), and the hysterectomy and cholecystectomy groups showed similar trends (flat graph pattern). In the graph of breath $CH_4$ profiles, a relatively moderate upward curve in gastrectomy patients and a flat graph pattern in hysterectomy and cholecystectomy patients were observed with increasing baseline values (Figure 3).

### Characteristics of patients with a history of abdominal surgery according to positivity to GBT

Among the 55 GBT+ patients who had undergone abdominal surgery, 43.6% (24/55) were GBT($H_2$)+, 10.9% (6/55) were GBT($CH_4$)+, and 45.5% (25/55) were GBT(mixed)+ (Table 2). Among the abdominal surgery groups, no differences were observed between GBT+ and GBT− patients regarding sex and body mass index. GBT− patients were younger than GBT+ patients. The prevalence of GBT+ was significantly higher in the gastrectomy group than that in the hysterectomy and cholecystectomy groups. Significant differences were found in serum gastrin levels among patients who were GBT+ and GBT−. The gastrin levels showed a higher prevalence in the GBT($H_2$)+ subtype and a lower prevalence in the GBT($CH_4$)+ subtype than those in patients who were GBT−. No significant differences were found in PG I and PG II levels or the PG I/PG II ratios according to the subtype and presence of GBT positivity.

### Comparison of profiles according to serum gastrin cutoff value (29 pg/mL) in patients with a history of abdominal surgery

Based on the receiver operating characteristic curves of serum gastrin and breath $H_2$ levels, the optimal cutoff value of serum gastrin level was 29 pg/mL. PG I, PG II, GBT($H_2$)+, and female sex with a GBT+ status had higher significance or tendency in patients with gastrin levels $\geq$29 pg/mL (Table 3). The $H_2$ profiles of GBT at timepoints from 30 to 120 minutes were significantly higher in patients with gastrin levels $\geq$29 pg/mL than in those with $<$29 pg/mL, whereas no differences in $CH_4$ profiles were observed at any timepoints (Figure 3). No significant differences in demographic characteristics, surgery types, total breath levels, or PG I/PG II ratio were found about the cutoff gastrin level.

SMALL BOWEL

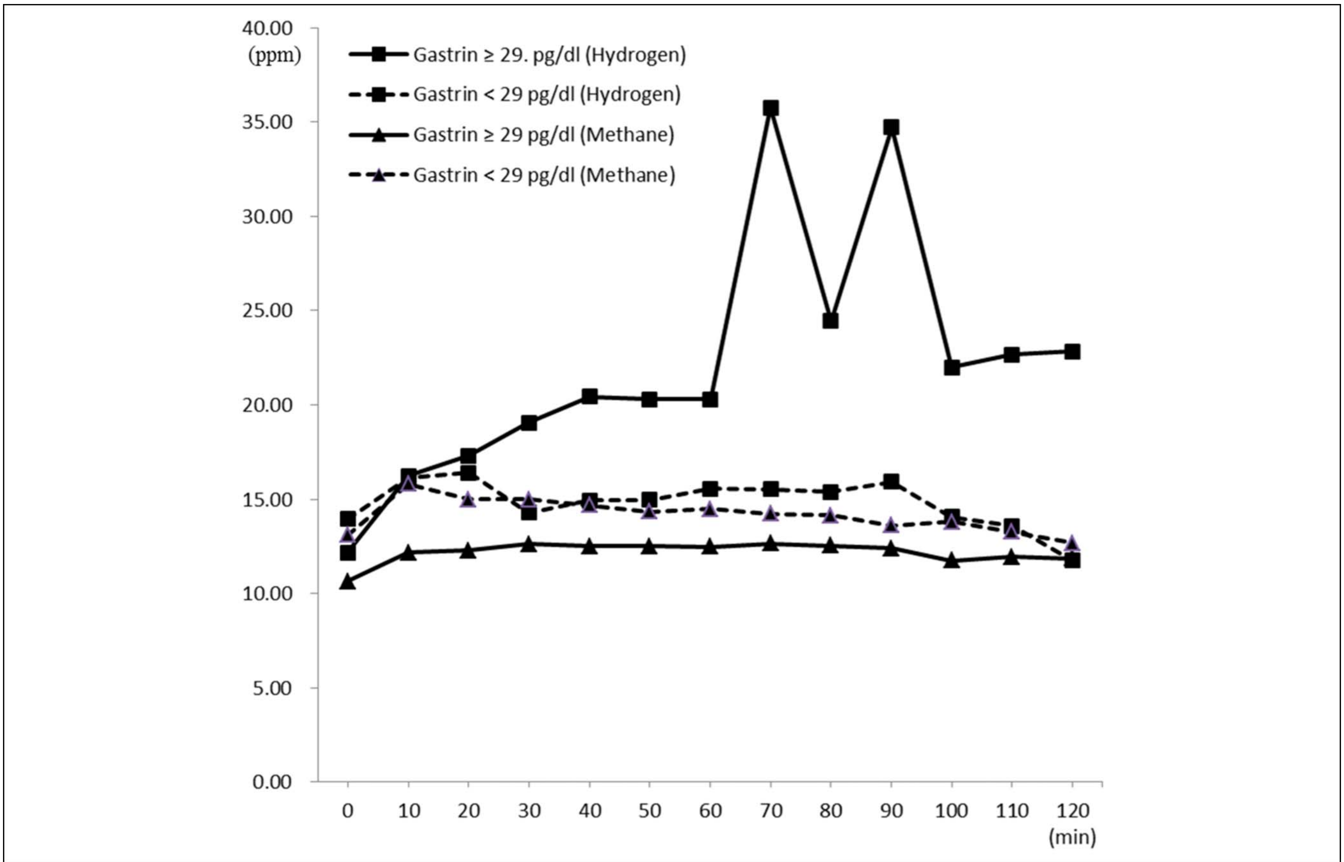


**Figure 3.** The profiles of glucose hydrogen–methane breath test according the cutoff value of serum gastrin, 29 pg/mL.

#### Predictive factors of positivity to GBT in patients with a history of abdominal surgery

The multivariable logistic regression analysis showed that previous gastrectomy and gastrin level ≥29 pg/mL were independent predictive factors of positivity for GBT or the GBT($H_2$)+ subtype among patients with a history of abdominal surgery (Table 4).

## DISCUSSION

This prospective cohort study demonstrated that using GBT to diagnose SIBO is not uncommon in patients with a history of hysterectomy, gastrectomy, or cholecystectomy. A GBT+ status was significantly more frequent in the gastrectomy group than in the other abdominal surgery groups, and an elevated level of serum gastrin might be a predictive factor of $H_2$-producing SIBO.

Abdominal surgery can cause postoperative pain, which is a unique entity with specific physiological and clinical features. High surgical rates have been reported in patients with gastrointestinal symptoms and functional gastrointestinal disorders, such as irritable bowel syndrome (16). Recently, SIBO has been suggested as one of the causes of these gastrointestinal symptoms. The suggested pathophysiologic mechanisms of SIBO in abdominal surgery include changes in anatomical features, such as adhesions after surgery, influx of substances in the intestine, or gastric acidity. In recent studies, a history of abdominal surgery has been correlated with a positive GBT (2–7).

The prevalence of SIBO is high in postcholecystectomy patients (2,4,17), although conflicting results have been reported (3). The absence of a gallbladder might alter the homeostasis of bile acid and intestinal motility or decrease the antimicrobial effect of bile acid (17–19). The prevalence of SIBO in patients without a gallbladder was 17.1% in this study, which was somewhat lower than that reported in previous retrospective studies (approximately 40%–50%) (3,13). This difference might be due to the prospective design of this study, along with its strict inclusion criteria. A recent prospective study also demonstrated a SIBO prevalence of 24.6% in the cholecystectomy group. Further prospective studies with a large number of patients are needed to evaluate the prevalence of SIBO using GBT. Some previous studies have suggested the possibility of an association between hysterectomy and irritable bowel syndrome (13,16), although few have examined whether hysterectomy is associated with SIBO. However, a retrospective study demonstrated that the overall GBT+ prevalence in patients with hysterectomy was 41.1% (4). The suggested pathophysiologic mechanism of SIBO might be impaired intestinal motility after a hysterectomy, which is a well-known major cause of adhesions in the small intestine (20). The high prevalence of SIBO in patients who have undergone gastrectomy has been reported, ranging from 15% to 83% (5–7,12). In this study, the prevalence of GBT+ in the gastrectomy group was significantly higher than that in the other 2 surgical groups, which was consistent with the results of another recent study (4). Some possible causes, such as malabsorption or anatomical changes, have been suggested; however, they remain inconclusive. Another likely mechanism is the imbalance of gastric acid (21). Gastric acid is one of the strongest protective factors against SIBO, and changes in existing gastric acid secretion could occur from structural changes caused by postoperative conditions. In this study, it was not possible to compare the difference in GBT+ for each type of gastrectomy because all but 1 patient who underwent gastrectomy showed positivity to GBT. Further

SMALL BOWEL

Table 2. The profiles according to the GBT status in patients with history of abdominal surgery

| | Positive GBT (n = 55) | | | | |
|---|---|---|---|---|---|
| | $H_2$ (n = 24) | $CH_4$ (n = 6) | Mixed (n = 25) | Negative GBT (n = 91) | *P* |
| Demographics | | | | | |
| Age, yr | 64.17 ± 10.97 | 57.50 ± 7.56 | 64.64 ± 10.84 | 57.78 ± 11.03 | <0.01 |
| Sex | | | | | |
| Male | 9 (37.5) | 1 (16.7) | 11 (44.0) | 21 (23.1) | 0.13 |
| Female | 15 (62.5) | 5 (83.3) | 14 (56.0) | 70 (76.9) | |
| BMI, kg/$m^2$ | 23.41 ± 3.95 | 24.91 ± 3.28 | 22.58 ± 3.55 | 24.21 ± 3.39 | 0.17 |
| Type of operation | | | | | |
| Hysterectomy | 11 (45.8) | 4 (66.7) | 3 (12.0) | 32 (35.2) | <0.01 |
| Gastrectomy | 6 (25.0) | 1 (16.7) | 18 (72.0) | 1 (1.1) | |
| Cholecystectomy | 7 (29.2) | 1 (16.7) | 4 (16.0) | 58 (63.7) | |
| PG profiles[a] | | | | | |
| PG I, ng/mL | 75.18 ± 52.80 | 37.35 ± 1.48 | 46.65 ± 60.56 | 61.37 ± 38.51 | 0.34 |
| PG II, ng/mL | 23.19 ± 15.61 | 8.55 ± 0.35 | 14.97 ± 6.75 | 24.21 ± 3.39 | 0.15 |
| Gastrin, pg/dL | 104.13 ± 156.70 | 16.50 ± 3.54 | 42.27 ± 29.10 | 42.18 ± 33.65 | 0.02 |
| PG I/II ratio | 3.72 ± 1.62 | 4.35 ± 0.35 | 3.49 ± 3.38 | 4.29 ± 1.71 | 0.51 |

Data are expressed as mean ± SD or n (%).
BMI, body mass index, CH4, methane; GBT, glucose breath test; $H_2$, hydrogen; PG, pepsinogen.
[a]A total of 95 patients underwent tests for PG profiles with GBT positive ($H_2$) (n = 16), $CH_4$ (n = 2), and mixed (n = 11) and GBT negative (n = 66).

prospective studies with a larger number of patients are needed to evaluate the prevalence of SIBO using GBT.

The prominent conditions that accompany SIBO are bacterial stasis due to impaired intestinal transit or dysfunction of protective mechanisms against enteric bacteria, such as gastric acid secretion. Few data have been reported on serologic indicators of SIBO. The strength of this study was the investigation of serologic profiles, such as PG and gastrin levels, in relation to GBT results. These results revealed that serum gastrin, rather than PG, seemed to be related to GBT+ status. Serum PG is known to be an indirect indicator of gastric acid secretion. However, it is also known to be affected by several other factors (22,23), such as *Helicobacter pylori* infection, age, or various gastrointestinal diseases including peptic ulcer, atrophic gastritis, and reflux esophagitis (24–26). The role of PG, depending on the interrelationship of these factors, remains uncertain. Gastrin, a peptide hormone that is primarily responsible for secreting hydrochloric acid into the stomach and enhancing gastric motility, is primarily released in response to vagal and gastrin-releasing peptide stimulation, secondary to ingestion of peptides and amino acids, gastric distention, and elevated stomach pH (27). Gastrin is present in the G-cells of the gastric antrum and duodenum. When low levels of gastric acid, which are indicative of a low PG profile, are secreted, serum gastrin or gastrin-releasing peptide increases, which promotes gastrointestinal motor function and regulates the intestinal peristaltic reflex pH (28,29), allowing the gastric acid function to remain intact. This study demonstrated that a GBT+ status, especially GBT($H_2$)+, is highly related to elevated gastrin levels. As shown in Figure 3, the flow curves of breath $H_2$ levels at most timepoints were significantly higher in patients with gastrin levels ≥29 pg/mL. Of interest, the GBT($CH_4$)+ group showed low gastrin levels. Although not statistically significant, the breath $CH_4$ level in the flow graph was lower in patients with gastrin levels ≥29 pg/mL. The reason why the gastrin levels showed contradictory results between the GBT($CH_4$)+ and GBT($H_2$)+ groups is unclear. We hypothesized that low gastrin levels could induce delayed intestinal transit, which has been reported to be related to the presence of $CH_4$-producing bacteria (30).

The multivariate analysis in this study indicated that serum gastrin levels and previous gastrectomy are independent predictors of positivity to GBT, particularly GBT($H_2$)+, among patients undergoing abdominal surgery. Patients with gastrectomy have both a loss of antibacterial effect and postoperative altered intestinal transit, which are representative risk factors of SIBO. Therefore, a higher morbidity of SIBO is expected in patients undergoing gastrectomy than in those who undergo a different abdominal surgery. Elevated serum gastrin levels could reflect the altered status of intestinal motility and gastric acidity, which has been the main suggestion for the pathogenesis of intestinal bacteria. However, serum gastrin level was not independently associated with the GBT($CH_4$) status, which could be attributed to the small number of enrolled GBT($CH_4$)+ patients. Most of those in the GBT+ group were GBT(mixed)+ and GBT($H_2$)+, accounting for 45.5% and 43.6%, respectively. Further studies with a larger number of $CH_4$ excretors are warranted.

The strength of this study is that it was well-designed than previous prospective studies. This study demonstrated that gastrectomy is a strong risk factor of SIBO. An additional advantage of this study was the investigation of serum PG profiles and gastrin levels. We found that, rather than the PG profile, serum gastrin level was correlated with GBT($H_2$)+ status.

This study had several limitations. First, we used historical controls. However, the positivity for GBT in controls has already been validated in our previous studies (5–7,12). Second, it should be considered that this study was conducted in Korea, which has a prevalence of *Helicobacter pylori* of more than 40%. *H. pylori* infection affects the secretion of gastric acid and ginsenosides, such as gastrin, so more research needs

Table 3. The profiles according to the cutoff value with 29 pg/dL of serum gastrin in patients with history of abdominal surgery

| | Gastrin, pg/dL (n = 95) | | |
|---|---|---|---|
| | ≥29 (n = 52) | <29 (n = 43) | *P* |
| Demographics | | | |
| Age, yr | 61.10 ± 11.72 | 57.88 ± 10.08 | 0.16 |
| Sex | | | |
| Male | 9 (17.3) | 14 (32.6) | 0.08 |
| Female | 42 (82.9) | 29 (67.4) | |
| BMI, kg/m$^2$ | 24.44 ± 4.21 | 23.90 ± 3.37 | 0.51 |
| Type of operation | | | |
| Hysterectomy | 19 (36.5) | 18 (41.9) | |
| Gastrectomy | 2 (3.8) | 3 (7.0) | 0.63 |
| Cholecystectomy | 31 (59.6) | 22 (51.2) | |
| GBT profiles | | | |
| Total $H_2$, ppm | 288.19 ± 474.81 | 192.40 ± 248.54 | 0.21 |
| Total $CH_4$, ppm | 158.33 ± 86.03 | 184.12 ± 156.71 | 0.31 |
| Positive GBT | 20 (38.5) | 9 (20.9) | 0.06 |
| $H_2$ | 13 (25.0) | 3 (7.0) | 0.04 |
| $CH_4$ | 0 (0) | 2 (4.7) | |
| Mixed | 7 (13.5) | 4 (9.3) | |
| PG profiles[a] | | | |
| PG I, ng/mL | 71.67 ± 52.41 | 48.89 ± 26.06 | <0.01 |
| PG II, ng/mL | 20.68 ± 13.73 | 13.05 ± 8.99 | <0.01 |
| Gastrin, pg/dL | 79.09 ± 90.67 | 19.49 ± 5.13 | <0.01 |
| PG I/II ratio | 4.01 ± 2.25 | 4.21 ± 1.49 | 0.62 |

Data are expressed as mean ± SD or n (%).
BMI, body mass index; $CH_4$, methane; GBT, glucose breath test; $H_2$, hydrogen; PG, pepsinogen.
[a]A total of 95 patients undergoing tests for PG profiles were included.

to be conducted to verify similar results in regions with low rates of *H. pylori* infection. Another limitation was the incomplete analysis of data on serum gastrin and PG levels in the enrolled patients. Because serum PG profiles were surveyed from regular follow-up data, we could not use some information for reasons such as patient refusal of blood tests or failure to perform the tests on the same day as the GBT. A cautious process for future studies is needed. However, all data were collected consecutively and prospectively using the same standard approach.

There was a possibility that a high gastrin level improved motility and caused rapid small bowel transit, which would give a false positive diagnosis. A glucose substrate was used for the breath test to evaluate the SIBO. GBT can detect only proximal bacteria because glucose is completely absorbed in the proximal small bowel. There are some advantages to the use of glucose. During the lactulose breath test, it is difficult to distinguish SIBO from colonic bacteria in cases of rapid intestinal transit (31,32). Breath tests using glucose over lactulose because the substrate have lower rates of false positivity and are superior for diagnosing SIBO (33,34). Figure 1 shows that the double peak curve was well-formed in the test results at around 90 minutes in gastrectomy patients. Therefore, the diagnostic cutoff value of GBT seemed to be appropriate.

Table 4. Multivariate analysis for the predicting independent factors of the positivity to GBT in patients with abdominal surgery[a]

| | OR | 95% CI | *P* |
|---|---|---|---|
| Positive GBT | | | |
| Gastrectomy status | 14.09 | 1.15–172.21 | 0.04 |
| Gastrin (≥29 pg/dL) | 3.09 | 1.06–8.99 | 0.04 |
| PG I/II ratio | 0.90 | 0.68–1.19 | 0.48 |
| Positive GBT ($H_2$) | | | |
| Gastrectomy status | 19.15 | 1.452–252.55 | 0.03 |
| Gastrin (≥29 pg/dL) | 4.56 | 1.42–14.59 | 0.01 |
| PG I/II ratio | 0.87 | 0.65–1.18 | 0.38 |
| Positive GBT ($CH_4$) | | | |
| Hysterectomy status | 0.73 | 0.15–3.51 | 0.69 |
| Gastrin (≥29 pg/dL) | 0.83 | 0.18–3.84 | 0.82 |
| PG I/II ratio | 0.1.1 | 0.75–1.50 | 0.75 |

$CH_4$, methane; CI, confidence interval; GBT, glucose breath test; $H_2$, hydrogen; OR, odds ratio; PG, pepsinogen.
[a]A total of 95 patients undergoing tests for PG profiles were included.

In conclusion, patients with a history of abdominal surgery should consider the occurrence of SIBO because it is found in a significant portion of them. SIBO is more common in patients with a history of gastrectomy than that in patients with a history of other abdominal surgeries. Further studies are needed to fully understand the clinical role of SIBO in patients with abdominal surgical history and to demonstrate the precise role of gastrin according to SIBO subtypes.

## CONFLICTS OF INTEREST

**Guarantor of the article:** Chang Nyol Paik, MD, PhD.
**Specific author contributions:** Study planning and concept: C-.N.P. Analysis of data and drafting of the manuscript: Y-.J.K. Statistical analysis: I.H.C., D.B.K. and J.M.L. Acquisition of data: Y-.J.K., C-.N.P., and I.H.C. Supervision and critical revision of the manuscript for important intellectual content: I.H.C., D.B.K. and J.M.L. All authors have approved the final revision.
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## Study Highlights

### WHAT IS KNOWN

✓ Small intestinal bacterial overgrowth (SIBO) might be considered a possible cause of abdominal discomfort after surgery.

### WHAT IS NEW HERE

✓ SIBO is common in patients who had undergone abdominal surgery.

### TRANSLATIONAL IMPACT

✓ SIBO is frequently observed in patients who had undergone gastrectomy, and the serum gastrin levels could be a useful serologic test, however, more research is warranted.

SMALL BOWEL

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