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ORIGINAL ARTICLE

Retrospective Study

Ability of lactulose breath test results to accurately identify colorectal polyps through the measurement of small intestine bacterial overgrowth

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Abstract

BACKGROUND

While colorectal polyps are not cancerous, some types of polyps, known as adenomas, can develop into colorectal cancer over time. Polyps can often be found and removed by colonoscopy; however, this is an invasive and expensive test. Thus, there is a need for new methods of screening patients at high risk of developing polyps.

AIM

To identify a potential association between colorectal polyps and small intestine bacteria overgrowth (SIBO) or other relevant factors in a patient cohort with lactulose breath test (LBT) results.

METHODS

A total of 382 patients who had received an LBT were classified into polyp and non-polyp groups that were confirmed by colonoscopy and pathology. SIBO was diagnosed by measuring LBT-derived hydrogen (H) and methane (M) levels according to 2017 North American Consensus recommendations. Logistic regression was used to assess the ability of LBT to predict colorectal polyps. Intestinal barrier function damage (IBFD) was determined by blood assays.

RESULTS

H and M levels revealed that the prevalence of SIBO was significantly higher in the polyp group than in the non-polyp group (41% *vs* 23%, $P < 0.01$; 71% *vs* 59%, $P < 0.05$, respectively). Within 90 min of lactulose ingestion, the peak H values in the adenomatous and inflammatory/hyperplastic polyp patients were significantly higher than those in the non-polyp group ($P < 0.01$, and $P = 0.03$, respectively). In 227 patients with SIBO defined by combining H and M values, the rate of IBFD determined by blood lipopolysaccharide levels was significantly higher among patients with polyps than those without (15% *vs* 5%, $P < 0.05$). In regression analysis with age and gender adjustment, colorectal polyps were most accurately predicted with models using M peak values or combined H and M values limited by North American Consensus recommendations for SIBO. These models had a sensitivity of ≥ 0.67, a specificity of ≥ 0.64, and an accuracy of ≥ 0.66.

CONCLUSION

The current study made key associations among colorectal polyps, SIBO, and IBFD and demonstrated that LBT has moderate potential as an alternative noninvasive screening tool for colorectal polyps.

Key Words: Lactulose breath test; Colorectal polyp; Small intestine bacteria overgrowth; Intestinal barrier function; Retrospective study

Core Tip: As the lactulose breath test (LBT) is an indirect method of measuring bacteria in the digestive tract, it is primarily used to support small intestine bacteria overgrowth (SIBO) diagnosis but is implemented as a new method for screening colorectal polyps in this study. A total of 382 patients with LBT results were classified into polyp and non-polyp groups that were confirmed by colonoscopy and pathology. First, it applied the LBT for assessment of its utility as a noninvasive screening tool for colorectal polyps as well as for diagnosis of SIBO. Second, the results revealed certain key associations among colorectal polyps, SIBO and Intestinal barrier function damage (IBFD), such as SIBO was more prevalent in patients with colorectal polyp than those without polyp and IBFD was more susceptible in patients with colorectal polyp than those without polyp only when SIBO was evident. Third, in regression analysis with age and gender adjustment, colorectal polyp was best predicted by models using plain methane peak values or combined hydrogen and methane values limited by the North American Consensus for SIBO. One of the most important result was moderate potential of LBT as an alternative noninvasive screening tool for colorectal polyps.

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INTRODUCTION

Colorectal polyps are caused by colorectal mucosal proliferation that creates pedunculated or sessile outgrowths. They become more common as people age and are prevalent in individuals > 40 years of age[1,2]. While most polyps are benign, some can become cancerous and may even metastasize to other parts of the body[3]. Adenomatous polyps are known precursors of colon cancer but can be difficult to diagnose in their early stages. Moreover, most colorectal cancers develop from focal changes in benign polyps through a multistep process involving genetic, histological, morphological, and intestinal microbiome changes that accumulate over more than 10 years[4,5]. A long precancerous state provides an opportunity to screen for polyps and successfully prevent or treat any cancerous lesions that develop. Thus, new methods that can identify precancerous colorectal lesions can play an important role

in early-stage colorectal cancer treatment and prevention.

Several methods are used to screen for colorectal cancer, including fecal occult blood testing (FOBT), flexible sigmoidoscopy, and colonoscopy, each with its own merits and disadvantages. A pooled meta-analysis of randomized trials found that FOBT and flexible sigmoidoscopy screening reduced colorectal cancer mortality by 16% and 30%, respectively[6]. While colonoscopy is the best method for visualizing focal lesions and taking biopsies for diagnosis[7], it is invasive, costly, and can be uncomfortable, especially for asymptomatic participants with low compliance. Thus, colonoscopy may not suitable for primary screening of colorectal polyps and cancers. Despite the benefits of these modalities, there are overwhelming limitations, which highlight a need for more accurate, noninvasive screening tools for colorectal cancer and precancerous polyps.

The lactulose breath test (LBT) is an indirect method of measuring bacteria in the digestive tract. It uses equipment to determine the concentration in parts per million (ppm) of hydrogen (H) and methane (M) gas in the breath[8]. The LBT can indicate the approximate population size and location of the microbiome, as well as some information about the types of bacteria present. While jejunal aspiration culture remains the gold standard for diagnosing small intestine bacterial overgrowth (SIBO), LBT is widely used as a noninvasive method of diagnosing SIBO due to its safety, accessibility, and affordability. However, there is limited data on the association between SIBO and colorectal polyps.

SIBO is a condition in which the small bowel is colonized by excessive aerobic and anaerobic microbes that are normally present in the colon[9]. SIBO and intestinal microbiota are associated with several conditions, including Crohn's disease[10], irritable bowel syndrome (IBS)[11], functional gastrointestinal disorders (FGID)[12], nonalcoholic fatty liver disease[13], diabetes[14], and hepatic encephalopathy[15]. Recent studies have found a link between the gut microbiome and the pathogenesis of adenomatous polyps and colorectal cancer[16,17], offering a promising avenue for personalized prevention[18]. For example, higher numbers of some bacterial species are found in patients with adenomatous polyps than in those without[17]. The current study analyzed a patient cohort with LBT testing data to characterize potential associations among colorectal polyps, SIBO, and other relevant factors and assessed the use of LBT as a potential screening tool for colorectal polyps.

MATERIALS AND METHODS

Study subjects

Medical records from patients in registry database of The First Affiliated Hospital of Guangdong Pharmaceutical University who received an LBT for gastrointestinal symptoms from July 2017 to February 2019 were reviewed. A total of 382 patients (213 males and 169 females) were included in the study. The subjects ranged in age from 22 to 92 years (mean ± SD, 57 ± 14 years). All patients signed an informed consent prior to inclusion. The study was approved by the Ethics Committee of the First Affiliated Hospital of Guangdong Pharmaceutical University.

The patients were classified into a polyp group (n = 169) and a non-polyp group (n = 213). All colorectal polyps were diagnosed by colonoscopy and pathology. Patients with no polyps or other intestinal lesions identified by colonoscopy were included in the non-polyp group. Individuals with: (1) Acute intestinal infection; (2) antibiotic use within 4 wk before the test; (3) severe heart, lung, brain, and other diseases who are unable to tolerate colonoscopy; (4) susceptibility to hypoglycemia; and (5) age < 18 years were excluded from the study.

Blood assays to evaluate intestinal barrier function damage

Intestinal barrier function damage (IBFD) was assessed using the instruments and assay kits from Beijing Zhongsheng Jinyu Diagnostic Technology Co., Ltd. Blood samples were taken after 8 h of fasting and stored at 4 °C. Within 4 h, the blood samples were tested for diamine oxidase (DAO), D-lactate (D-lac), and lipopolysaccharide (LPS) concentration according to the manufacturer's instructions. Patients whose blood samples had values above the reference for DAO (10 U/L), D-lac (15 mg/L), and LPS (20 U/L) were defined as having IBFD.

Lactulose breath test

The LBT was completed using the Quintron Breath Tracker (SC model) to determine the concentration of H and M. Procedures were performed with common standards[9,19]. In brief, all patients fasted for 12 h and brushed their teeth prior to the test. Lactulose (10 g) in warm water was provided and breath samples were collected every 30 min for 150 min. No drink, food, or exercise was permitted during the test, but subjects were allowed to sleep.

Diagnosis of SIBO and prediction of colorectal polyps by LBT

Diagnosis of SIBO by LBT was made qualitatively according to the following definitions of a positive result recommended by the 2017 North American Consensus[19]: (1) A rise of > 20 ppm H within 90 min of substrate ingestion; and (2) ≥ 10 ppm methane. A patient was determined as having SIBO if either or

both standards were met.

LBT quantitative measurements were also used to predict the presence of colorectal polyps. The performance of prediction models was assessed with logistic regression supported by the R program, pROC. Each model was tested by 100-time repeated re-sampling to ensure its accuracy.

Statistical analyses

All data were tested for statistical differences using IBM SPSS software (v22.0). An ANOVA test was used to assess differences in measurements between groups, and a one-side Fisher Exact test was used to measure differences in frequency between one group and another. $P < 0.05$ was considered statistically significant.

RESULTS

Characteristics of patients and colorectal polyps

As shown in Table 1, patients in the polyp group were 9 years older than those in the non-polyp group (mean 62 *vs* 53 years, $P < 0.001$), and were more often male (64% *vs* 49%, $P < 0.01$). Colorectal polyps were least prevalent among patients 19-45 years of age (7%) and most common among those 61-92 years of age (55%). The polyp group also had a higher proportion of patients with constipation than the non-polyp group (22% *vs* 14%, $P < 0.05$), and more often had metabolic disorders, including diabetes (19% *vs* 10%, $P < 0.01$), hyperlipidemia (20% *vs* 13%, $P < 0.05$), and fatty liver/cirrhosis (41% *vs* 27%, $P < 0.01$), in addition to hypertension (38% *vs* 21%, $P < 0.001$). However, patients in the polyp group were less likely to have non-organic disorders, such as FGID (5% *vs* 13%, $P < 0.01$), IBS (8% *vs* 16%, $P < 0.05$) and gastroesophageal reflux disease (11% *vs* 16%, $P = 0.096$), than those in the non-polyp group.

Colonoscopy showed that the colorectal mucosa from 213 patients had a normal appearance, while colorectal polyps were found in 169 patients, including 81 with inflammatory/hyperplastic polyps, and 88 with adenomatous polyps. Polyp size was < 1.0 cm in 136 patients, 1.0-2.0 cm in 25 patients, and > 2.0 cm in eight patients. While 71 patients had single polyps, 98 patients had multiple polyps. In 114 patients, the polyps were found on the left side of the colon, including on the descending colon, sigmoid colon, and rectum, and in 55 patients, polyps were located on other parts of the colon.

Ability of LBT to detect SIBO and predict colorectal polyps

According to H, M measurements, alone or in combination, the prevalence of SIBO by LBT was all significantly higher in the polyp group than in the non-polyp group [H: 41% (70/169) *vs* 23% (49/213), $P < 0.001$; M: 71% (120/169) *vs* 59% (125/213), $P < 0.05$; combined: 80% (136/169) *vs* 67% (143/213), $P < 0.01$] (Table 2). Within 90 min of substrate ingestion, the peak values of hydrogen were significantly higher in patients with adenomatous or inflammatory/hyperplastic polyps than those in the non-polyp group ($P < 0.01$, and $P = 0.03$, respectively; Table 3). The peak values of methane were similar in all three groups ($P = 0.168$), and there was no significant difference in the number of patients with SIBO by polyp type ($P > 0.05$).

Associations between IBFD, SIBO, and colorectal polyps

A total of 311 of the 382 patients were evaluated for IBFD by blood assays, including measurements of DAO, D-lac, and LPS. Of these, 174 (56%) of the patients, including 82 in the polyp group (58%) and 92 in the non-polyp group (54%), were characterized as having potential IBFD using a combination of the three assays ($P > 0.05$) or each assay alone (all $P > 0.05$). Of the 311 patients, 227 were positive for SIBO using combined H and M measurements. Among patients with SIBO, the rate of IBFD using all three blood assays was marginally higher in the polyp group than in the non-polyp group (57% *vs* 48%, $P = 0.13$), but differed significantly when IBFD was defined using LPS alone (polyp = 15% *vs* non-polyp = 5%, $P < 0.05$; Figure 1). Among the remaining 84 patients without SIBO, there was no significant difference in the rate of IBFD between patients in the polyp and non-polyp groups using all three assays together or individually (all $P > 0.05$).

Prediction performance of LBT results for colorectal polyps

LBT was also assessed quantitatively for its prediction performance as a screening tool for colorectal polyps. Using different H and M cutoff values, 17 models were built using different subsets of the patient population (Table 4). Peak values in H and M were obtained during the tests and rise values were got from baseline subtracted peak values. To account for the effects of age and gender on the model performance, 7 of the 17 models with differences in the mean LBT value between the polyp and non-polyp groups ($P < 0.01$) were selected for further assessment (model # 1, 2, 4, 5, 11, 12 and 17; Table 4 and Figure 2A-G). Differences in the area under the receiver operating characteristic curve between age and gender-adjusted and unadjusted models were statistically significant (all $P < 0.01$). These models performed similarly well when age and gender were used as covariates, with almost all of them showing an accuracy of > 65% (Table 5). Models with a methane peak value with or without a ≥ 5

Table 1 Demographics and comorbidity of the study subjects, *n* (%)

	Overall (*N* = 382)	Polyps (*n* = 169)	Non-polyps (*n* = 213)	*P* value
Age, yr	57.0 ± 14.0	62.1 ± 11.7	53.0 ± 14.4	**0**
19-45	70 (18)	11 (7)	59 (28)	**0**
46-60	150 (39)	65 (38)	85 (40)	0.428
61-92	162 (43)	93 (55)	69 (32)	**0**
Male	213 (56)	108 (64)	105 (49)	**0.003**
Bilestone	34 (9)	18 (11)	16 (8)	0.187
Constipation	67 (18)	38 (22)	29 (14)	**0.017**
Diabetes	53 (14)	32 (19)	21 (10)	**0.008**
Fatty liver/cirrhosis	127 (33)	70 (41)	57 (27)	**0.002**
FGID	37 (10)	9 (5)	28 (13)	**0.007**
GERD	54 (14)	19 (11)	35 (16)	0.096
Hyperlipidemia	60 (16)	33 (20)	27 (13)	**0.046**
Hypertension	108 (28)	64 (38)	44 (21)	**0**
Hyperuricemia	42 (11)	20 (12)	22 (10)	0.38
IBS	49 (13)	14 (8)	35 (16)	**0.013**
PU	31 (8)	24 (14)	7 (3)	**0**

Values presented as mean ± SD, or *n* (%) of observations. *P* values were from one-side Fisher exact statistics, with bold font for those less than 0.05. FGID: Functional gastrointestinal disorders; GERD: Gastroesophageal reflux disease; IBS: Irritable bowel syndrome; PU: Peptic ulcer.

Table 2 Small intestine bacteria overgrowth distribution between polyp & non-polyp groups

SIBO (+)	Overall (*N* = 382)	Polyps (*n* = 169)	Non-polyps (*n* = 213)	*P* value
By methane	245 (64)	120 (71)	125 (59)	0.014[a]
By hydrogen 90 min	119 (31)	70 (41)	49 (23)	0.000[a]
By combined M and H	279 (73)	136 (80)	143 (67)	0.004[a]

[a]*P* < 0.05, polyps *vs* non-polyps.
SIBO: Small intestine bacteria overgrowth.

Table 3 The peak values of methane and hydrogen in inflammatory/hyperplastic polyp, adenomatous polyp and non-polyp groups

Peak values	Polyps (*n* = 169)	Non-polyps (*n* = 213)		*P* value
	Inflammatory/hyperplastic polyp	Adenomatous polyp		
Methane	208.2	197.86	182.52	0.168
Hydrogen within 90 min	209.53[b]	220.87[b]	172.51	0.001[a]

[a]*P* < 0.05 was considered to indicate a statistically significant difference between inflammatory/hyperplastic polyp, adenomatous polyp and non-polyp groups.
[b]*P* < 0.05 was considered to indicate a statistically significant difference between inflammatory/hyperplastic polyp and non-polyp groups or between adenomatous polyp and non-polyp groups. Univariate analysis was performed using the nonparametric tests (Kruskal-Wallis independent samples).

ppm cutoff (Figure 2A and D) and the model using the SIBO subpopulation (Figure 2G) performed best.

Table 4 Performance of prediction models for colorectal polyps

Model No.	Value cutoff (ppm) for subset	*N*	*n* (polyp/non-polyp)	Mean ppm (polyp)	Mean ppm (non-polyp)	Mean ppm (*P* value)	Sensitivity	Specificity	Accuracy
1	Methane peak value (not applied)	382	169/213	12.82	12.06	**0.074**[a]	0.427	0.578	0.511
2	Methane peak value (≥ 5)	359	160/199	13.34	12.66	**0.084**[a]	0.417	0.571	0.502
3	Methane peak value (≥ 10)	245	120/125	15.28	15.55	0.905	0.443	0.390	0.416
4	Hydrogen peak value (not applied)	380	169/211	52.34	45.48	**0.091**[a]	0.408	0.604	0.517
5	Hydrogen peak value (≥ 10)	310	140/170	62.05	55.24	**0.090**[a]	0.383	0.590	0.496
6	Hydrogen peak value (≥ 20)	259	125/134	67.85	66.02	0.776	0.400	0.439	0.421
7	Hydrogen rise value (not applied)	372	165/207	41.94	37.40	0.121	0.391	0.582	0.498
8	Hydrogen rise value (≥ 10)	280	130/150	52.12	49.93	0.406	0.380	0.477	0.432
9	Hydrogen rise value (≥ 20)	217	108/109	60.06	63.39	0.479	0.492	0.375	0.433
10	Hydrogen rise value (≥ 20 by 90 min)	119	70/49	47.74	50.10	0.929	0.460	0.323	0.403
11	Combined M peak & H peak (M ≥ 5 &/or H ≥ 10)	373	166/207	66.15	58.48	**0.068**[a]	0.412	0.615	0.525
12	Combined M peak & H peak (M ≥ 5 & H ≥ 10)	294	134/160	76.49	68.28	**0.055**[a]	0.391	0.607	0.508
13	Combined M peak & H risen (M ≥ 5 &/or H ≥ 10)	370	166/204	54.58	50.11	0.166	0.403	0.578	0.499
14	Combined M peak & H rise (M ≥ 5 & H ≥ 10)	267	124/143	66.54	62.50	0.239	0.379	0.530	0.460
15	Combined M peak & H peak (M ≥ 10 &/or H ≥ 20)	177	96/81	86.28	85.49	0.674	0.390	0.395	0.392
16	Combined M peak & H rise (M ≥ 10 & H ≥ 20)	149	84/65	77.32	83.17	0.723	0.522	0.346	0.445
17	Combined M peak & H rise (M ≥ 10 &/or H ≥ 20 by 90 min)	279	136/143	42.29	35.71	**0.008**[a]	0.382	0.702	0.546

[a]$P < 0.1$ for difference in mean value of lactulose breath test between polyp and non-polyp groups for further assessment.
Rise values are baseline-subtracted peak values during the tests. Bold *P* values indicate the 7 best models in further assessment. ppm: Parts per million.

DISCUSSION

Recent studies have shown that the gut microbiome is associated with certain gastrointestinal symptoms [12], colon polyps, and colorectal cancer[18,20]. However, little is known about the relationship between SIBO and colorectal polyps. The current study analyzed a patient cohort that had recently received LBT for uncertain gastrointestinal symptoms. The findings revealed certain key associations among colorectal polyps, SIBO, and IBFD while demonstrating that LBT had moderate potential as an alternative noninvasive screening tool for colorectal polyps. SIBO was more prevalent in patients with colorectal polyps than those without and IBFD was worse in patients with colorectal polyps than those without only when SIBO was evident.

SIBO is caused by gut microbiota dysregulation and is characterized by the excessive density and/or abnormal composition of bacteria in the small intestine. The current study was the first to demonstrate that patients with colorectal polyps had a higher prevalence of SIBO than those without, defined by methane and hydrogen test results alone or in combination. These findings suggest that SIBO may be a risk factor for colorectal polyps. While this study showed no difference in SIBO by polyp type, further investigation is needed to confirm this finding. The results also showed a higher rate of IBFD among patients with colorectal polyps than those without, however this was only true for patients with SIBO. This suggests that patients with polyps are more susceptible to IBFD when SIBO are present.

Table 5 Model performance with key parameters (area under the receiver operating characteristic curve, accuracy, sensitivity, and specificity)

Panel ID	AUC, % (95%CI)	Accuracy	Sensitivity	Specificity
a	71.6 (66.5-76.7)	0.659	0.666	0.653
b	71.4 (66.3-76.5)	0.642	0.663	0.625
c	72.0 (66.9-77.1)	0.650	0.669	0.634
d	71.7 (66.4-77.0)	0.663	0.679	0.651
e	72.9 (67.3-78.4)	0.651	0.677	0.629
f	72.6 (66.9-78.4)	0.650	0.683	0.622
g	71.7 (65.7-77.7)	0.658	0.673	0.643

AUC: Area under the curve.

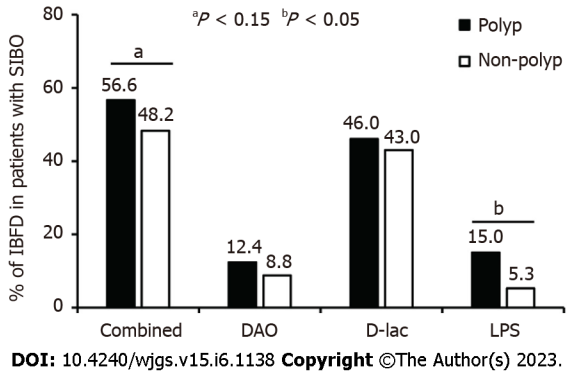

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Figure 1 Rate of intestinal barrier function damage in 227 small intestine bacteria overgrowth patients. [a]The rate of intestinal barrier function damage (IBFD) by 3 blood assays altogether was marginally higher in polyp group than that in non-polyp group, but no significance, $P = 0.13$. [b]It was significantly different between polyp group and non-polyp group when IBFD defined by lipopolysaccharide alone, $P < 0.05$. SIBO: Small intestine bacteria overgrowth; DAO: Diamine oxidase; LPS: Lipopolysaccharide.

The culture of small bowel aspirates is the gold standard for SIBO diagnosis, but this is an invasive method and it can be a challenge to culture gut flora[21,22]. As a result, noninvasive testing using LBT results is often used. While the diagnostic criteria for SIBO by LBT are not yet standardized, the 2017 North American Consensus guidelines used in this study can make the results comparable across studies with similar data and analysis. LBT is primarily used to support SIBO diagnosis but is implemented here as a new method for screening colorectal polyps. To our knowledge, this is the first study to use quantitative LBT measurements for prediction analysis. LBT had moderate potential as a screening tool to identify patients with polyps in the large intestine. The best fit models were greatly improved after adjusting for age and gender. It is worth noting that models that only included the peak methane values without filtering by cutoff values performed as well as the model with combined H and M values limited by North American Consensus guidelines (Figure 2H). This suggests that methane peak values were as useful as combined hydrogen and methane values in patients with SIBO when using LBT as a screening tool for colorectal polyps.

In this retrospective study, patients with colorectal polyps were about 9 years older and more often male than those without polyps. These findings are consistent with the characteristics of polyp development and support the results of prior studies. Most studies report that men have almost twice the prevalence of polyps as women[23,24], and this tends to increase with age[3]. In addition, comorbidity analysis showed that patients with colorectal polyps were more often complicated with metabolic disorders and less likely with non-organic abnormalities. This is consistent with recent studies indicating that metabolic syndrome is a high-risk factor for colorectal adenomatous polyps and cancer and should be included in colorectal cancer screening programs[25,26]. These findings suggest that metabolic disorders can be an inherent characteristic among certain patients with colorectal polyps.

The incidence of constipation was significantly higher in the polyp than non-polyp groups. Patients with constipation have prolonged oro-cecal transit time[27] and constipation can significantly increase the incidence of colorectal polyps[28]. However, colonoscopy for patients with constipation as the sole indication had fewer neoplastic lesions than for those undergoing routine screening colonoscopy[29].

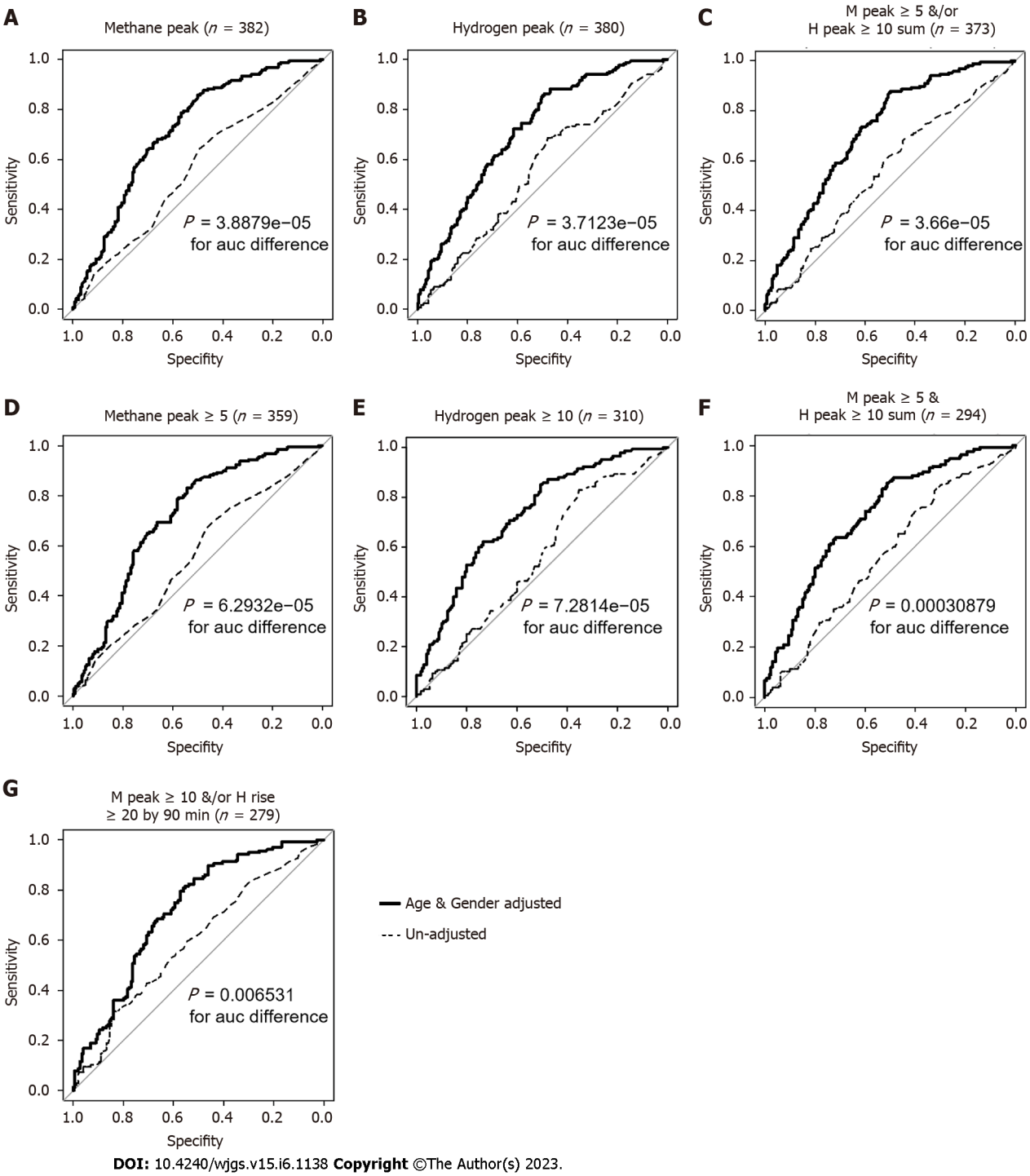

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Figure 2 The receiver operation characteristic curves for age and gender adjusted performance of prediction models. A-G: Each model is for a subset of patient population defined by the cutoffs and the size of the subpopulation showing at the top of each box.

Additional randomized controlled double-blind studies with a larger sample size are needed to confirm the findings of the present study.

CONCLUSION

The current study identified key associations among colorectal polyps, SIBO and IBFD while demonstrating the moderate potential of LBT as an alternative noninvasive screening tool for colorectal polyps. SIBO was more prevalent in patients with colorectal polyps than those without and IBFD was more severe in patients with colorectal polyp than those without only when SIBO has present. This study also found that colorectal polyps were more common in older individuals and men. Moreover,

patients with polyps tended to have metabolic disorders such as diabetes and hyperlipidemia and were less likely to have non-organic abnormalities such as functional gastrointestinal disease and IBS.

ARTICLE HIGHLIGHTS

Research background

Polyps can often be found and removed by colonoscopy; however, this is an invasive and expensive test. Due to its safety, accessibility, and affordability, the lactulose breath test (LBT) is widely used as a noninvasive method of diagnosing small intestine bacterial overgrowth (SIBO). SIBO suggests dysbiosis of the intestinal flora, which is associated with the pathogenesis of adenomatous polyps and colorectal cancer.

Research motivation

New methods that can identify precancerous colorectal lesions can play an important role in early-stage colorectal cancer treatment and prevention.

Research objectives

To identify a potential association between colorectal polyps and SIBO or other relevant factors in a patient cohort with LBT results.

Research methods

This retrospective analysis of data from a total of 382 patients who had received an LBT were collected. SIBO was diagnosed by measuring LBT-derived hydrogen (H) and methane (M) levels according to 2017 North American Consensus recommendations. Logistic regression was used to assess the ability of LBT to predict colorectal polyps. Intestinal barrier function damage (IBFD) was determined by blood assays.

Research results

H and M levels revealed that the prevalence of SIBO was significantly higher in the polyp group than in the non-polyp group (41% *vs* 23%; 71% *vs* 59%, respectively). Within 90 min of lactulose ingestion, the peak H values in the adenomatous and inflammatory/hyperplastic polyp patients were significantly higher than those in the non-polyp group. In regression analysis with age and gender adjustment, colorectal polyps were most accurately predicted with models using M peak values or combined H and M values limited by North American Consensus recommendations for SIBO. These models had a sensitivity of ≥ 0.67, a specificity of ≥ 0.64, and an accuracy of ≥ 0.66.

Research conclusions

The current study made key associations among colorectal polyps and SIBO and demonstrated that LBT has moderate potential as an alternative noninvasive screening tool for colorectal polyps.

Research perspectives

Due to its safety, accessibility, and affordability, the LBT has the potential to become one of the routine non-invasive screening methods for polyps and precancerous lesions. Furthermore, non-invasive tests such as fecal occult blood testing and LBT will help to improve the detection rate of precancerous lesions during colonoscopy screening.

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FOOTNOTES

Author contributions: Lan Li and Zhang XY have contributed equally to this work. Lan Li participated the study design and wrote the manuscript draft; Zhang XY conducted clinical data collections and participated the writing of the draft; Zhou HM and Qin Y performed lactulose breath test tests; Xie WR participated statistical analysis of the data; Ding WJ interpreted the lactulose breath test results; Yu JS participated the study design, performed the statistical analysis of the data, and edited the final version of the manuscript; He XX conceived the study concept and design, supervised all the work, provided the study funding, and reviewed the final version of the manuscript. All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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