

Randomized Controlled Trial

Effect of posture on ¹³C-urea breath test in partial gastrectomy patients

Shu-Ming Yin, Fan Zhang, Dong-Mei Shi, Ping Xiang, Li Xiao, Yi-Qin Huang, Gan-Sheng Zhang, Zhi-Jun Bao

Shu-Ming Yin, Fan Zhang, Dong-Mei Shi, Ping Xiang, Li Xiao, Yi-Qin Huang, Gan-Sheng Zhang, Zhi-Jun Bao, Division of Gastroenterology, Huadong Hospital, Shanghai Medical College of Fudan University, Shanghai 200040, China

Author contributions: Yin SM and Zhang F contributed equally to this work; Yin SM and Zhang F designed the research, analyzed the data and wrote the manuscript; Shi DM, Xiang P, Xiao L, Huang YQ and Zhang GS performed the research; Bao ZJ designed the research and integrated the sections.

Supported by The Guidance Project of Science and Technology Commission of Shanghai Municipality, No. 134119a1700; the Appropriate Project of Shanghai Municipal Health Bureau, No. 2013SY049; Shanghai Key Laboratory of Clinical Geriatric Medicine, No. 13DZ2260700; and the Scientific Research Projects of Shanghai Municipal Health Bureau, No. 20134377.

Institutional review board statement: The study was reviewed and approved by the Medical Ethics Committee of Huadong Hospital Affiliated to Fudan University.

Clinical trial registration statement: This study is registered at <http://www.chictr.org.cn/listbycreator.aspx>. The registration identification number is ChiCTR-ICQ-15006798.

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Conflict-of-interest statement: We certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

[licenses/by-nc/4.0/](http://creativecommons.org/licenses/by-nc/4.0/)

Correspondence to: Dr. Zhi-Jun Bao, Division of Gastroenterology, Huadong Hospital, Shanghai Medical College of Fudan University, No. 221 West Yan'an Road, Shanghai 200040, China. xinyi8681@sina.com
Telephone: +86-21-62487221
Fax: +86-21-62490486

Received: April 19, 2015
Peer-review started: April 21, 2015
First decision: July 10, 2015
Revised: August 3, 2015
Accepted: September 30, 2015
Article in press: September 30, 2015
Published online: December 7, 2015

Abstract

AIM: To investigate whether posture affects the accuracy of ¹³C-urea breath test (¹³C-UBT) for *Helicobacter pylori* (*H. pylori*) detection in partial gastrectomy patients.

METHODS: We studied 156 consecutive residual stomach patients, including 76 with *H. pylori* infection (infection group) and 80 without *H. pylori* infection (control group). *H. pylori* infection was confirmed if both the rapid urease test and histology were positive during gastroscopy. The two groups were divided into four subgroups according to patients' posture during the ¹³C-UBT: subgroup A, sitting position; subgroup B, supine position; subgroup C, right lateral recumbent position; and subgroup D, left lateral recumbent position. Each subject underwent the following modified ¹³C-UBT: 75 mg of ¹³C-urea (powder) in 100 mL of citric acid solution was administered, and a mouth wash was performed immediately; breath samples were then collected at baseline and at 5-min intervals up to 30 min while the position was maintained. Seven breath

samples were collected for each subject. The cutoff value was 2.0‰.

RESULTS: The mean delta over baseline (DOB) values in the subgroups of the infection group were similar at 5 min ($P > 0.05$) and significantly higher than those in the corresponding control subgroups at all time points ($P < 0.01$). In the infection group, the mean DOB values in subgroup A were higher than those in other subgroups within 10 min and peaked at the 10-min point ($12.4‰ \pm 2.4‰$). The values in subgroups B and C both reached their peaks at 15 min (B, $13.9‰ \pm 1.5‰$; C, $12.2‰ \pm 1.7‰$) and then decreased gradually until the 30-min point. In subgroup D, the value peaked at 20 min ($14.7‰ \pm 1.7‰$). Significant differences were found between the values in subgroups D and B at both 25 min ($t = 2.093$, $P = 0.043$) and 30 min ($t = 2.141$, $P = 0.039$). At 30 min, the value in subgroup D was also significantly different from those in subgroups A and C (D *vs* C: $t = 6.325$, $P = 0.000$; D *vs* A: $t = 5.912$, $P = 0.000$). The mean DOB values of subjects with Billroth I anastomosis were higher than those of subjects with Billroth II anastomosis irrespectively of the detection time and posture ($P > 0.05$).

CONCLUSION: Utilization of the left lateral recumbent position during the procedure and when collecting the last breath sample may improve the diagnostic accuracy of the ¹³C-UBT in partial gastrectomy patients.

Key words: *Helicobacter pylori*; ¹³C-urea breath test; Gastrectomy; Position

© The Author(s) 2015. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The efficiency of the ¹³C-urea breath test in the diagnosis of *Helicobacter pylori* (*H. pylori*) infection in patients after gastrectomy is still controversial. Many factors may affect the diagnostic accuracy, and posture is especially important. We suggest that residual stomach patients should be kept in the horizontal position on the left side during the procedure and when collecting the last breath sample in order to improve the accuracy of detection of *H. pylori* infection.

Yin SM, Zhang F, Shi DM, Xiang P, Xiao L, Huang YQ, Zhang GS, Bao ZJ. Effect of posture on ¹³C-urea breath test in partial gastrectomy patients. *World J Gastroenterol* 2015; 21(45): 12888-12895 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v21/i45/12888.htm> DOI: <http://dx.doi.org/10.3748/wjg.v21.i45.12888>

INTRODUCTION

Helicobacter pylori (*H. pylori*), a spiral gram-negative bacterium, can colonize epithelial cells of the gastric mucosa under micro-aerobic growth condition. *H. pylori*

infection leads to multiple gastric disorders, including chronic active gastritis, ulcer, adenocarcinoma, and mucosa-associated lymphoid tissue lymphoma^[1-3]. It has also been considered one of the factors inducing residual gastric mucosa carcinogenesis in postoperative patients with early-stage gastric carcinoma^[4]. Therefore, it is crucial to accurately detect whether *H. pylori* is present in patients who underwent partial gastrectomy.

Due to the lack of specific clinical manifestations, *H. pylori* detection in residual stomach relies on additional examinations. Although the ¹³C-urea breath test (¹³C-UBT), a noninvasive diagnostic method for *H. pylori* infection, is inferior to bacterial culture and histological examinations^[5], it represents a fast, safe, and reliable technology which is able to accurately determine *H. pylori* infection in an intact stomach. Accordingly, it has been widely used in the general population^[6,7]. However, a standardized international protocol defining specific steps, detection methods, and the cutoff value for the ¹³C-UBT is currently lacking. In addition, ¹³C-UBT diagnosis is limited by some factors, such as fasting and mouth washing, dose and dosage form of ¹³C-urea (tablet, capsule, or powder), presence of test meal, time of breath sample collection and storage, and cutoff values^[5,8-10]. Since the bacterial load is lower and emptying of the stomach is faster in residual stomach subjects, there are some disputes on the efficiency of the ¹³C-UBT in gastrectomy patients^[5,11-15]. In particular, the influence of posture on the results of the ¹³C-UBT in detecting *H. pylori* infection in partial gastrectomy patients has been a focus of attention. In the existing reports on the ¹³C-UBT diagnosis and treatment for *H. pylori* infection in such patients, researchers from different countries utilized the conventional ¹³C-UBT protocol for the general population^[7,16,17]. Gastric remnant subjects were kept in the sitting position when breath samples were collected, and they usually maintained this position between the collections^[14,18]. Only a few studies included the horizontal supine position^[15] or the horizontal position on the left side^[11,12]. Although Togashi *et al*^[9] have performed a preliminary study of different positions (left-lateral horizontal, sitting, or supine position), which position is more suitable for gastrectomy subjects is not yet fully addressed.

The purpose of the present study was to assess whether the position of partial gastrectomy patients during the test affects the diagnostic accuracy of ¹³C-UBT for *H. pylori* infection. We attempted to develop a convenient as well as reliable means for *H. pylori* detection and follow-up after eradication therapy in patients who underwent partial gastrectomy.

MATERIALS AND METHODS

Subjects

The infection group consisted of 76 patients with partial gastrectomy who visited Huadong Hospital Affiliated

Table 1 Characteristics of the patients in the infection and control groups

	Infection group				P value	Control group				Statistic	P value
	A (n = 19)	B (n = 19)	C (n = 19)	D (n = 19)		A (n = 20)	B (n = 20)	C (n = 20)	D (n = 20)		
Age (yr)	59.9 ± 11.2	63.1 ± 9.2	66.1 ± 10.9	66.0 ± 12.5	F = 1.341	58.7 ± 12.1	62.0 ± 8.5	65.2 ± 10.7	61.7 ± 14.1	F = 1.081	0.362
Sex (M:F)	12:7	14:5	14:5	13:6	$\chi^2 = 0.686$	15:5	14:6	15:5	13:7	$\chi^2 = 0.671$	0.880
Indication for gastrectomy					$\chi^2 = 0.452$					$\chi^2 = 0.251$	0.969
Peptic ulcer	7	8	6	7	-	5	6	5	6	-	-
Early-stage gastric cancer	12	11	13	12	-	15	14	15	14	-	-
Reconstructive procedure					-					-	-
B- I	11	11	11	11	-	10	10	10	10	-	-
B- II	8	8	8	8	-	10	10	10	10	-	-
Interval (yr)	8.9 ± 5.9	7.4 ± 5.1	7.3 ± 3.9	7.9 ± 4.9	F = 0.429	8.6 ± 6.0	7.6 ± 5.8	7.8 ± 5.0	8.4 ± 4.6	F = 0.150	0.929

to Fudan University from November 2012 to March 2015. *H. pylori* infection was confirmed by histopathological examination. The following inclusion criteria were used: the time interval after the subtotal gastrectomy was at least 1 year; the surgical procedure was distal gastrectomy with Billroth I or II (B- I or B- II) anastomosis; the indication for surgery included benign peptic ulcer or early gastric cancer; endoscopy, histological examination, and rapid urease test (RUT) were performed before and after the operation.

The control group contained 80 patients who underwent partial gastrectomy during the same period, met the inclusion criteria, and were *H. pylori*-negative based on histological examination. Patient characteristics such as age, sex, disease etiology, reconstruction method, and postoperative course in the control group were matched to those in the infected group.

In both groups, the subjects were divided into four subgroups according to their posture after ¹³C-urea administration: subgroup A, sitting position; subgroup B, supine position on a bed; subgroup C, horizontal position on the right side; as well as subgroup D, horizontal position on the left side. The patients were assigned randomly to A, B, C, or D subgroup according to their reconstruction method. The following exclusion criteria were used: *H. pylori* eradication therapy prior to the present study; treatment with antibiotics, proton pump inhibitors, H₂-receptor antagonists, or bismuth salts within 1 mo before the study; absence of endoscopic examination, RUT, pre- and post-operative histological detection for *H. pylori*; presence of test contraindications; distal gastrectomy without B- I or B- II anastomosis; and previous gastrointestinal surgery history. The subjects were excluded if they fulfilled any of the above criteria.

The research protocol was approved by the Ethical Committee of Huadong Hospital Affiliated to Fudan University. All individuals provided written informed consent. The characteristics of the patients in the infection and control groups are shown in Table 1.

¹³C-UBT procedure

Modified ¹³C-UBT test was conducted in each participant within a week after the endoscopy. Overnight fasting was required before the test. In the following morning, breath samples were taken at baseline (T₀) and at 5-min intervals up to 30 min (T₅, T₁₀, T₁₅, T₂₀, T₂₅, and T₃₀) after an oral administration of ¹³C-labelled urea powder (75 mg/100 mL citric acid solution; AltaChem Pharma Ltd., Canada) and an immediate mouth wash to remove the residual compound. The first breath sample was taken in the sitting position. The patients were then placed in the positions according to their subgroups and maintained them for 30 min while the rest of the breath samples were collected. These gas samples were collected separately for analysis of the ¹³CO₂/¹²CO₂ ratio (Δ¹³CO₂, ‰) with an isotope mass spectrometer (IRIS 3, Frankfurt, Germany), which was normalized using a standard gas sample. The analysis was performed by Wagner Analysen Technik GmbH (Bremen, Germany). Differences between the values at T₅, T₁₀, T₁₅, T₂₀, T₂₅, and T₃₀ and those at T₀ were presented as delta over baseline (DOB, Δδ, ‰). Based on the related reports^[5,11,12] and our previous study of 194 samples^[19], the cutoff value for this diagnostic test was defined as 2.0‰. Subjects with a DOB > 2.0‰ were considered *H. pylori*-positive,

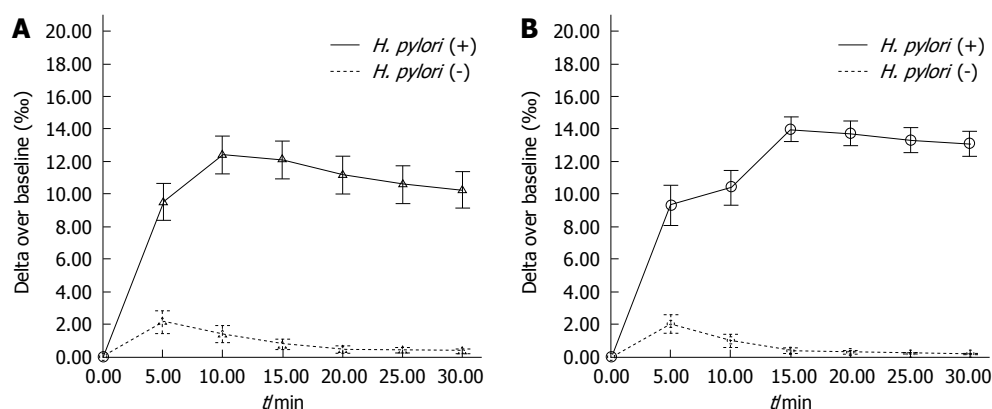


Figure 1 Mean delta over baseline values for the *Helicobacter pylori*-positive or -negative subjects in the sitting position at each time point. A: Subgroup A; B: Subgroup B.

whereas those with a DOB < 2.0‰ were considered *H. pylori*-negative.

Reference standard for *H. pylori* infection diagnosis

Four gastric mucosa biopsy samples were collected separately from the greater curvature of the mid-to-high body as well as the gastric side of the anastomotic stoma, in that order (2 samples from each position), during endoscopy for RUT and histological examination. A positive RUT result was defined as a color alteration from yellow to red during a 24-h period. In most patients, this color change occurred within 120 min. For histological examinations such as hematoxylin and eosin (HE) or Giemsa staining, curved rods were used to identify *H. pylori* in a sectioned specimen. The result of the histological examination was considered positive if *H. pylori* was detected at any site. Only patients with positive RUT and positive histological test were defined as the ones with *H. pylori* infection^[1]. Conversely, a patient was considered uninfected when both tests were negative. If inconsistent results were obtained between the RUT and histological test, the corresponding patients were excluded. All biopsy specimens were assessed by a single pathologist who was blinded to the results of endoscopic examinations and UBT for *H. pylori*.

Cancer staging system

We used the cancer staging system from the American Joint Committee on Cancer (AJCC) Cancer Staging Manual (version 7th)^[20].

Statistical analysis

Statistical Product and Service Solutions (SPSS) software (version 16.0) was used in this study for all statistical analyses. Continuous variables are expressed as mean \pm SD and analyzed by Student's *t* test, one-way analysis of variance or Wilcoxon's rank-sum test. Classified variables were analyzed by χ^2 test or Fisher's exact test. *P* values < 0.05 were defined as statistical significance.

RESULTS

The patients in the infection group (76 subjects) and control group (80 subjects) were divided into four subgroups: A, B, C, and D. As a result, there were 19 infected patients (B- I, 11 subjects; B- II, 8 subjects) and 20 uninfected patients (B- I, 10 subjects; B- II, 10 subjects) in each subgroup. No statistically significant differences were found in age, sex, indications for gastrectomy, or postoperative course between the subgroups within the infection group and the control group (*P* > 0.05). The subjects in the infection and control groups were placed in the sitting position, supine position, and right or left lateral recumbent position according to their subgroups. Significantly higher DOB values for each subgroup in the infection group were detected compared with the control group at T₅ and thereafter regardless of the patients' posture (*P* < 0.01). No borderline or false-negative results were found in any position and at any time point in the infection group. In the control group, no borderline or false-positive results were found in any position at T₁₀, T₁₅, T₂₀, T₂₅, or T₃₀. The mean DOB values for the four subgroups of each group are plotted in Figures 1 and 2.

According to the DOB value curves in the infection group (Figure 3), the mean DOB values in the subgroups were similar at T₅ (*F* = 0.421, *P* = 0.738). The mean values in subgroup A were higher than in other subgroups within the first 10 min. At T₁₀, the mean DOB value was 12.4‰ \pm 2.4‰, exceeding the mean DOB value in subgroup D (11.2‰ \pm 2.1‰, *t* = 1.617, *P* = 0.115) and being significantly higher than those in subgroups B (10.4‰ \pm 2.4‰, *t* = 2.634, *P* = 0.012) and C (9.9‰ \pm 1.6‰, *t* = 3.811, *P* = 0.001). The values in subgroups B and C both reached their peaks (B: 13.9‰ \pm 1.5‰, C: 12.2‰ \pm 1.7‰) at T₁₅ and then both decreased gradually until 30 min. In subgroup D, the value peaked (14.7‰ \pm 1.7‰) at T₂₀ and was significantly higher than those at T₅, T₁₀, and T₁₅ (*F* = 30.628, *P* = 0.000) but did not differ

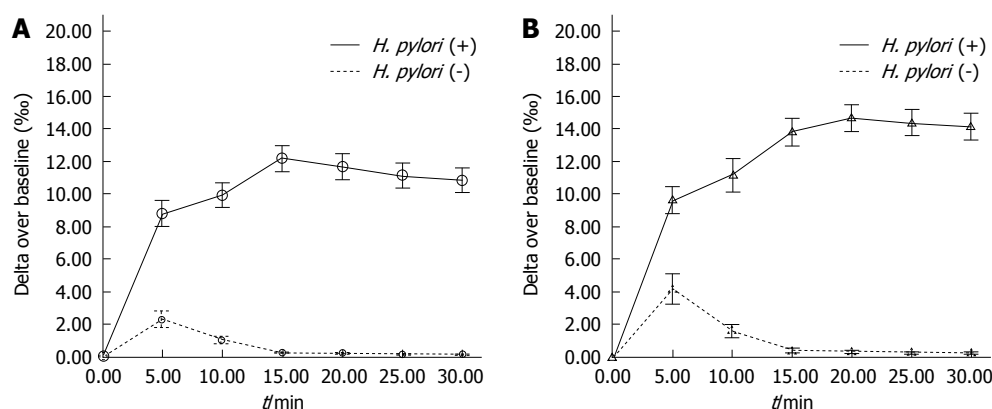


Figure 2 Mean delta over baseline values for the *Helicobacter pylori*-positive or -negative subjects in the right (A)/left (B) lateral recumbent position at each time point. A: Subgroup C; B: Subgroup D.

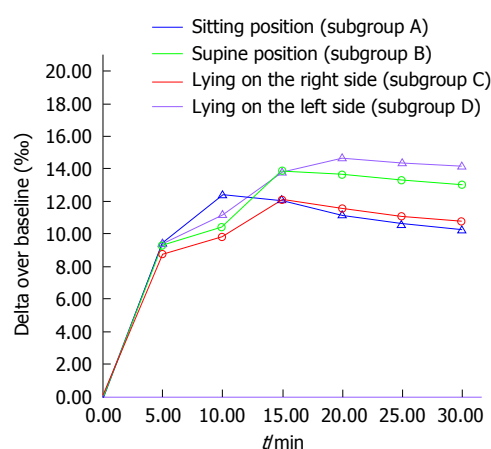


Figure 3 Mean delta over baseline value curves in the four subgroups of the infection group.

significantly from those at T_{25} and T_{30} ($F = 0.396$, $P = 0.675$). At T_{20} , no statistically significant values were determined ($t = 1.812$, $P = 0.078$) between the subgroups D and B ($13.7\text{‰} \pm 1.60\text{‰}$), but significant differences were observed between the values in these two subgroups at both T_{25} (D: $14.4\text{‰} \pm 1.69\text{‰}$, B: $13.3\text{‰} \pm 1.60\text{‰}$, $t = 2.093$, $P = 0.043$) and T_{30} (D: $14.2\text{‰} \pm 1.7\text{‰}$, B: $13.1\text{‰} \pm 1.6\text{‰}$, $t = 2.141$, $P = 0.039$). At T_{30} , the value in subgroup D was also significantly different from those in subgroups A ($10.3\text{‰} \pm 2.3\text{‰}$, $t = 5.912$, $P = 0.000$) and C ($10.8\text{‰} \pm 1.6\text{‰}$, $t = 6.325$, $P = 0.000$).

In the infection group, the mean DOB values of the subjects with B- I anastomosis were higher than those of the subjects with B- II anastomosis irrespectively of the time point and position. However, these differences (except at T_5 , T_{10} , and T_{15} in subgroup D) were not statistically significant ($P > 0.05$). Table 2 shows the reconstructive procedure and mean DOB values for the subjects in the infection group.

DISCUSSION

The ^{13}C -UBT is an internationally recognized gold

standard for *H. pylori* infection detection and anti-*H. pylori* drug efficacy monitoring^[2]. It has been widely recommended, even for children, gravidas, and the elderly^[7]. However, the application of ^{13}C -UBT in diagnosing *H. pylori* infection in partial gastrectomy patients remains controversial. In spite of the fact that the gastric remnant is not suitable for colonization by *H. pylori* and its survival, the bacteria can still be transmitted *via* fecal-oral, gastric-oral, oral-oral, and other ways. Gisbert *et al*^[5] concluded that the ^{13}C -UBT was not suitable for gastric remnant patients who underwent Billroth gastrectomy as the ingested ^{13}C -urea passed through the stomach faster and entered the duodenum (B- I) and small intestine (B- II) more easily, which would definitely impact the diagnostic accuracy. However, other reports^[9,11,12] showed that, with a proper procedure and an appropriate cutoff value, the ^{13}C -UBT was a reliable detection method in patients after gastrectomy.

Miwa *et al*^[21] investigated the effect of different positions (supine position and sitting position) and of changing the position by rolling during the period after ^{13}C -urea injection on the diagnostic performance of the ^{13}C -UBT for *H. pylori* infection in infected patients with intact stomach. The study revealed that posture affected the DOB values at T_5 and T_{10} but did not affect the results at the 15-min, 20-min, and later time points. Compared with the intact stomach, the anatomy, pH, motility, and distribution of *H. pylori* in the residual stomach are considerably altered, which makes the posture during the ^{13}C -UBT an important clinical factor. Therefore, we conducted this study to determine the optimal posture for residual stomach subjects.

Our study showed that the DOB values in the control group were lower compared with the infection group at all time points, and the first positive results appeared at T_5 , which might be due to the presence of urease-positive organisms in the oral cavity early in the procedure. The study by Lee *et al*^[8] proved that the effect of oral bacteria was most remarkable at T_5 and T_{10} , decreased at T_{15} , and was weakest at T_{30} .

Table 2 The reconstructive procedure and mean delta over baseline values (‰) for the subjects in the infection group

Subgroup	Time	DOB (B- I)	DOB (B- II)	t value	P value
A	T ₅	9.67 ± 1.79	9.30 ± 3.00	0.314	0.760
	T ₁₀	12.57 ± 1.92	12.18 ± 3.06	0.324	0.752
	T ₁₅	12.28 ± 1.95	11.89 ± 3.08	0.319	0.756
	T ₂₀	11.50 ± 1.93	10.80 ± 2.94	0.588	0.568
	T ₂₅	10.91 ± 1.90	10.20 ± 2.98	0.592	0.566
B	T ₃₀	10.58 ± 1.88	9.86 ± 2.93	0.609	0.555
	T ₅	9.74 ± 2.33	8.74 ± 2.85	0.841	0.412
	T ₁₀	10.69 ± 2.11	10.01 ± 2.60	0.628	0.538
	T ₁₅	14.20 ± 1.56	13.56 ± 1.56	0.880	0.391
	T ₂₀	13.99 ± 1.59	13.35 ± 1.62	0.861	0.401
C	T ₂₅	13.57 ± 1.60	12.91 ± 1.62	0.885	0.389
	T ₃₀	13.34 ± 1.56	12.69 ± 1.59	0.890	0.386
	T ₅	8.96 ± 1.69	8.69 ± 1.71	0.344	0.735
	T ₁₀	10.03 ± 1.53	9.81 ± 1.67	0.288	0.777
	T ₁₅	12.33 ± 1.74	12.05 ± 1.73	0.347	0.733
D	T ₂₀	11.79 ± 1.69	11.50 ± 1.72	0.364	0.720
	T ₂₅	11.26 ± 1.62	10.99 ± 1.69	0.352	0.729
	T ₃₀	10.95 ± 1.62	10.72 ± 1.62	0.295	0.771
	T ₅	10.21 ± 1.54	8.39 ± 2.18	2.136	0.048
	T ₁₀	12.12 ± 1.57	9.98 ± 2.56	2.446	0.026
	T ₁₅	14.51 ± 1.39	12.91 ± 1.76	2.213	0.041
	T ₂₀	15.32 ± 1.37	13.83 ± 1.82	2.049	0.056
	T ₂₅	15.04 ± 1.38	13.56 ± 1.77	2.057	0.055
	T ₃₀	14.84 ± 1.37	13.33 ± 1.82	2.068	0.054

DOB: Delta over baseline.

However, Togashi *et al.*^[9] found that oral organisms could affect the final results in residual stomach subjects. Therefore, we suggest that a thorough cleaning of the oral cavity with a mouth wash is important in residual stomach patients after ¹³C-urea administration, especially if the powder form is used.

Based on comparing the different subgroups of the infection group, we found that the posture in the period after the first measurement affected the results to some degree. The DOB values peaked at a different point in each subgroup, with those in the sitting position subgroup reaching the maximum at the earliest point (T₁₀) and those in the left lateral recumbent position peaking at the latest point (T₂₀). Although the DOB values in all subgroups were similar at T₅, they differed substantially thereafter. Thus, the DOB values in the subgroups diverged at T₁₀, suggesting that they may be affected by the posture early in the test, except for the component caused by the presence of residual organisms in the oral cavity. Furthermore, during the late stage (especially at T₂₀ and thereafter), the DOB values were mainly affected by the posture. As the gastric antrum, the most common site of colonization by *H. pylori*, is removed during the operation, the *H. pylori* infection rate in patients after B- I or B- II gastrectomy is reduced by about 50%^[22]. Park *et al.*^[23] reported *H. pylori* infection rates of 70.8% (B-I) and 45.9% (B- II). From the viewpoint of pathophysiology, gastric emptying is faster in the absence of the gastric antrum, and the clearance of ¹³C-urea is further accelerated in the sitting position

by the gravity force. Together, these factors reduce the time of exposure of the gastric mucosa to ¹³C-urea, leading to a significant decrease in DOB values during the late stage of the test. This is the main reason of the low diagnostic accuracy of the ¹³C-UBT in residual stomach patients. A test meal, such as citric acid solution, commonly used in the routine ¹³C-UBT to prolong gastric emptying and improve the diagnostic accuracy for *H. pylori* infection is ineffective in partial gastrectomy subjects^[15]. The time dependence of the DOB values in the right lateral recumbent position group, which was also affected by gastric anatomy and motility, was similar to that in the sitting position group. In the left lateral recumbent position, ¹³C-urea clearance was delayed, which allowed better access of the substrate to *H. pylori* urease, resulting in the DOB values peaking at a later time point (T₂₀) and remaining relatively stable during the late stage of the test. The DOB values in subgroup D at T₂₅ and T₃₀ were higher than those in the remaining three subgroups. For clinical convenience^[16,24] and to avoid the influence of intestinal bacteria during the late stage, we did not collect breath samples beyond 30 min. Urita *et al.*^[24] suggested that the routine ¹³C-UBT should be conducted for at least 20 min to diagnose *H. pylori* infection. Combined with our findings, the duration of 30 or 25 min with the subject positioned horizontally on the left side during the procedure might be optimal for residual stomach patients.

Based on the effect of posture on DOB values, we conclude that the patients' posture during breath samples collection could also influence final results. To balance the accuracy and convenience, we recommend that residual stomach patients are placed in the sitting position when collecting the first sample and in the left lateral recumbent position thereafter, including when collecting the last sample.

We found no significant differences in DOB values between the groups with different reconstruction methods (B- I and B- II), indicating that the anastomosis type does not affect the diagnostic value of ¹³C-UBT, which is consistent with the study of Togashi *et al.*^[9]. The differences in DOB values between the subjects with B- I and B- II anastomoses at T₅, T₁₀, and T₁₅ in infection subgroup D suggest that the late stage of the test (T₂₀ and thereafter) may be optimal for avoiding the effect of the operation type. Moreover, the left lateral recumbent position during the ¹³C-UBT procedure was most suitable for the B- I and B- II subjects. In this study, we selected subjects with B-I and B- II gastrectomy to simplify the analysis and to be able to use universal conditions during the test, and other operative methods will require further research.

As the *H. pylori* load is lower and gastric emptying is faster after the operation, the CO₂ concentration in breath samples may be insufficient to detect positive results, and the cutoff value for the ¹³C-UBT in residual stomach subjects should be lower than that in the

general population^[1,5,12]. Therefore, the cutoff value in this study was reduced from 3.5‰ to 2‰. According to the literature^[9], the sensitivity of the ¹³C-UBT for gastric mucosa *H. pylori* detection is 82.2%-96.3%, and the specificity is 94.6%-100%. Based on the comparison with the results of histological examinations, Kubota *et al.*^[11] found that the most appropriate cutoff value in residual stomach subjects was 2.0‰ as determined using a receiver operating characteristic curve. Under these conditions, high sensitivity (96.3%), specificity (100%), and accuracy (97.1%) were achieved. Our previous study^[19] found that, when the cutoff value was 2.0‰, the ¹³C-UBT had a high sensitivity (88.6%) and specificity (94.9%), and its accuracy (92.6%) was similar to that of the invasive test method (histological examination, 93.5%), with good consistency between the two approaches (Kappa = 0.84). Accordingly, the 2.0‰ cutoff value is more suitable for residual stomach subjects than the conventional value of 3.5‰.

Gisbert *et al.*^[25] suggested that values in the 2.0‰-5.0‰ range represented borderline results. We did not observe such borderline results in the present study. We suggest that a reexamination by the ¹³C-UBT or other tests should be performed to verify the results for residual stomach patients whose DOB values are within the above-mentioned range, and special attention should be paid in cases with DOB values around 5‰.

In conclusion, unlike in the general population, posture can influence the diagnostic accuracy of the ¹³C-UBT in residual stomach subjects, especially during the late stage of the test (20 min and thereafter). We suggest that the mouth should be washed after ¹³C-urea solution administration and that a cutoff value of 2.0‰ and the horizontal position on the left side should be used during the procedure (whose optimal time is 30 or 25 min) and when collecting the last breath sample. The modified ¹³C-UBT may be a simple, safe, and effective method for diagnosing *H. pylori* infection and for long-term follow-up after eradication therapy in residual stomach subjects.

COMMENTS

Background

Accurate detection of the presence of *Helicobacter pylori* (*H. pylori*) in patients with partial gastrectomy is of crucial importance. The efficiency of the ¹³C-urea breath test (¹³C-UBT) in the diagnosis of *H. pylori* infection in patients after gastrectomy is still controversial.

Research frontiers

Many factors may affect the diagnostic accuracy, and posture is especially important.

Innovations and breakthroughs

Unlike in the general population, posture may affect the diagnostic accuracy of the ¹³C-UBT in residual stomach subjects, especially during the late stage of the test (20 min and thereafter). Utilization of the left lateral recumbent position during the procedure and when collecting the last breath sample may improve

the diagnostic accuracy of the ¹³C-UBT in partial gastrectomy patients.

Applications

The modified ¹³C-UBT may be a simple, safe, and effective method for diagnosing *H. pylori* infection and for long-term follow-up after eradication therapy in residual stomach subjects.

Peer-review

This manuscript is interesting to me. Authors meticulously designed four subgroups in *H. pylori* infection and control patients with different postures for demonstrating the significance of outcome of ¹³C-urea breath test. The data analysis is confident and exact. I think authors need amend some information of outcome of ¹³C-urea breath test in the same patient with four different postures, which can provide the more trustful results.

REFERENCES

- 1 Malfertheiner P, Megraud F, O'Morain C, Bazzoli F, El-Omar E, Graham D, Hunt R, Rokkas T, Vakil N, Kuipers EJ. Current concepts in the management of *Helicobacter pylori* infection: the Maastricht III Consensus Report. *Gut* 2007; **56**: 772-781 [PMID: 17170018 DOI: 10.1136/gut.2006.101634]
- 2 Chey WD, Wong BC. American College of Gastroenterology guideline on the management of *Helicobacter pylori* infection. *Am J Gastroenterol* 2007; **102**: 1808-1825 [PMID: 17608775 DOI: 10.1111/j.1572-0241.2007.01393.x]
- 3 Tian XY, Zhu H, Zhao J, She Q, Zhang GX. Diagnostic performance of urea breath test, rapid urea test, and histology for *Helicobacter pylori* infection in patients with partial gastrectomy: a meta-analysis. *J Clin Gastroenterol* 2012; **46**: 285-292 [PMID: 22392025 DOI: 10.1097/MCG.0b013e318249c4cd]
- 4 Sinning C, Schaefer N, Standop J, Hirner A, Wolff M. Gastric stump carcinoma - epidemiology and current concepts in pathogenesis and treatment. *Eur J Surg Oncol* 2007; **33**: 133-139 [PMID: 17071041 DOI: 10.1016/j.ejso.2006.09.006]
- 5 Gisbert JP, Pajares JM. ¹³C-urea breath test in the management of *Helicobacter pylori* infection. *Dig Liver Dis* 2005; **37**: 899-906 [PMID: 16280266 DOI: 10.1016/j.dld.2005.09.006]
- 6 Braden B, Lembcke B, Kuker W, Caspary WF. ¹³C-breath tests: current state of the art and future directions. *Dig Liver Dis* 2007; **39**: 795-805 [PMID: 17652042 DOI: 10.1016/j.dld.2007.06.012]
- 7 Campuzano-Maya G. An optimized ¹³C-urea breath test for the diagnosis of *H. pylori* infection. *World J Gastroenterol* 2007; **13**: 5454-5464 [PMID: 17907288 DOI: 10.3748/wjg.v13.i41.5454]
- 8 Lee TH, Yang JC, Lee SC, Farn SS, Wang TH. Effect of mouth washing on the. *J Gastroenterol Hepatol* 2001; **16**: 261-263 [PMID: 11339415 DOI: 10.1046/j.1440-1746.2001.02437.x]
- 9 Togashi A, Matsukura N, Kato S, Masuda G, Ohkawa K, Tokunaga A, Yamada N, Tajiri T. Simple and accurate (¹³C)-urea breath test for detection of *Helicobacter pylori* in the remnant stomach after surgery. *J Gastroenterol* 2006; **41**: 127-132 [PMID: 16568371 DOI: 10.1007/s00535-005-1731-8]
- 10 Colaiocco Ferrante L, Papponetti M, Marcuccitti J, Neri M, Festi D. ¹³C-urea breath test for *Helicobacter pylori* infection: stability of samples over time. *Scand J Gastroenterol* 1999; **34**: 942-943 [PMID: 10522617]
- 11 Kubota K, Shimoyama S, Shimizu N, Noguchi C, Mafune K, Kaminishi M, Tange T. Studies of ¹³C-urea breath test for diagnosis of *Helicobacter pylori* infection in patients after partial gastrectomy. *Digestion* 2002; **65**: 82-86 [PMID: 12021481 DOI: 10.1159/000057709]
- 12 Kubota K, Hiki N, Shimizu N, Shimoyama S, Noguchi C, Tange T, Mafune K, Kaminishi M. Utility of [¹³C] urea breath test for *Helicobacter pylori* detection in partial gastrectomy patients. *Dig Dis Sci* 2003; **48**: 2135-2138 [PMID: 14705818 DOI: 10.1023/B:DDAS.000004516.45529.ee]
- 13 Adamopoulos AB, Stergiou GS, Sakizlis GN, Tiniakos DG, Nasothimiou EG, Sioutis DK, Achimastos AD. Diagnostic value of rapid urease test and urea breath test for *Helicobacter pylori*

- detection in patients with Billroth II gastrectomy: a prospective controlled trial. *Dig Liver Dis* 2009; **41**: 4-8 [PMID: 18606579 DOI: 10.1016/j.dld.2008.05.010]
- 14 **Schilling D**, Jakobs R, Peitz U, Sulliga M, Stolte M, Riemann J, Labenz J. Diagnostic accuracy of (13)C-urea breath test in the diagnosis of Helicobacter pylori infection in patients with partial gastric resection due to peptic ulcer disease: a prospective multicenter study. *Digestion* 2001; **63**: 8-13 [PMID: 11173894 DOI: 10.1159/000051866]
 - 15 **Sheu BS**, Lee SC, Lin PW, Wang ST, Chang YC, Yang HB, Chuang CH, Lin XZ. Carbon urea breath test is not as accurate as endoscopy to detect Helicobacter pylori after gastrectomy. *Gastrointest Endosc* 2000; **51**: 670-675 [PMID: 10840298 DOI: 10.1067/mge.2000.105719]
 - 16 **Ohara S**, Kato M, Asaka M, Toyota T. Studies of 13C-urea breath test for diagnosis of Helicobacter pylori infection in Japan. *J Gastroenterol* 1998; **33**: 6-13 [PMID: 9497214 DOI: 10.1007/PL00009968]
 - 17 **Logan RP**, Polson RJ, Misiewicz JJ, Rao G, Karim NQ, Newell D, Johnson P, Wadsworth J, Walker MM, Baron JH. Simplified single sample 13Carbon urea breath test for Helicobacter pylori: comparison with histology, culture, and ELISA serology. *Gut* 1991; **32**: 1461-1464 [PMID: 1773948 DOI: 10.1136/gut.32.12.1461]
 - 18 **Kwon YH**, Kim N, Lee JY, Choi YJ, Yoon K, Yoon H, Shin CM, Park YS, Lee DH. The diagnostic validity of the (13)c-urea breath test in the gastrectomized patients: single tertiary center retrospective cohort study. *J Cancer Prev* 2014; **19**: 309-317 [PMID: 25574466 DOI: 10.15430/JCP.2014.19.4.309]
 - 19 **Yin SM**, Zhang GS, Xiang P, Xiao L, Huang YQ, Chen J, Bao ZJ, Yu XF. Application value of 13C-urea breath test in the diagnosis of Helicobacter pylori infection in gastric remnant. *Zhongguo Xiaohua Zazhi* 2012; **32**: 669-673 [DOI: 10.3760/cma.j.issn.0254-1432.2012.10.005]
 - 20 **Edge SB**, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. *Ann Surg Oncol* 2010; **17**: 1471-1474 [PMID: 20180029 DOI: 10.1245/s10434-010-0985-4]
 - 21 **Miwa H**, Murai T, Ohkura R, Kawabe M, Tanaka H, Ogihara T, Watanabe S, Sato N. Effect of fasting subjects' posture on 13C-urea breath test for detection of Helicobacter pylori infection. *Helicobacter* 1997; **2**: 82-85 [PMID: 9432333]
 - 22 **Danesh J**, Appleby P, Peto R. How often does surgery for peptic ulceration eradicate Helicobacter pylori? Systematic review of 36 studies. *BMJ* 1998; **316**: 746-747 [PMID: 9529411]
 - 23 **Park S**, Chun HJ. Helicobacter pylori infection following partial gastrectomy for gastric cancer. *World J Gastroenterol* 2014; **20**: 2765-2770 [PMID: 24659869 DOI: 10.3748/wjg.v20.i11.2765]
 - 24 **Urita Y**, Hike K, Torii N, Kikuchi Y, Kanda E, Kurakata H, Sasajima M, Miki K. Breath sample collection through the nostril reduces false-positive results of 13C-urea breath test for the diagnosis of helicobacter pylori infection. *Dig Liver Dis* 2004; **36**: 661-665 [PMID: 15506664 DOI: 10.1016/j.dld.2004.06.008]
 - 25 **Gisbert JP**, Olivares D, Jimenez I, Pajares JM. Long-term follow-up of 13C-urea breath test results after Helicobacter pylori eradication: frequency and significance of borderline delta13CO2 values. *Aliment Pharmacol Ther* 2006; **23**: 275-280 [PMID: 16393307 DOI: 10.1111/j.1365-2036.2006.02741.x]

P- Reviewer: Bener A **S- Editor:** Yu J **L- Editor:** Wang TQ
E- Editor: Wang CH





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>



ISSN 1007-9327

