World Journal of Gastroenterology

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DOI: 10.3748/wjg.v21.i4.1305

World J Gastroenterol 2015 January 28; 21(4): 1305-1314
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

META-ANALYSIS

Accuracy of urea breath test in *Helicobacter pylori* infection: Meta-analysis

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Received: March 11, 2014
Peer-review started: March 11, 2014
First decision: March 27, 2014
Revised: May 19, 2014
Accepted: June 14, 2014
Article in press: June 17, 2014
Published online: January 28, 2015

Abstract

AIM: To quantitatively summarize and appraise the available evidence of urea breath test (UBT) use to diagnose *Helicobacter pylori* (*H. pylori*) infection in patients with dyspepsia and provide pooled diagnostic accuracy measures.

METHODS: We searched MEDLINE, EMBASE, Cochrane library and other databases for studies addressing the value of UBT in the diagnosis of *H. pylori* infection. We included cross-sectional studies that evaluated the diagnostic accuracy of UBT in adult patients with dyspeptic symptoms. Risk of bias was assessed using QUADAS (Quality Assessment of Diagnostic Accuracy Studies)-2 tool. Diagnostic accuracy measures were pooled using the random-effects model. Subgroup analysis was conducted by UBT type (^{13}C *vs* ^{14}C) and by measurement technique (Infrared spectrometry *vs* Isotope Ratio Mass Spectrometry).

RESULTS: Out of 1380 studies identified, only 23 met the eligibility criteria. Fourteen studies (61%) evaluated ^{13}C UBT and 9 studies (39%) evaluated ^{14}C UBT. There was significant variation in the type of reference standard tests used across studies.Pooled sensitivity was 0.96 (95%CI: 0.95-0.97) andpooled specificity was 0.93 (95%CI: 0.91-0.94). Likelihood ratio for a positive test was 12 and for a negative test was 0.05 with an area under thecurve of 0.985. Meta-analyses were associated with a significant statistical heterogeneity that remained unexplained after subgroup analysis. The included studies had a moderate risk of bias.

CONCLUSION: UBT has high diagnostic accuracy for detecting *H. pylori* infection in patients with dyspepsia. The reliability of diagnostic meta-analytic estimates however is limited by significant heterogeneity.

Key words: *Helicobacter pylori*; Dyspepsia; Breath tests; Urea/analysis; Diagnosis; Sensitivity; Specificity; Gastritis; Positive predictive value; Negative predictive value

Core tip: Urea breath test (UBT) is a commonly used non-invasive test to diagnose *Helicobacter pylori* (*H. pylori*) infection in patients with dyspepsia. Multiple trials are available in literature, but they reported different diagnostic accuracy estimates. We conducted systemic review and meta-analysis to explore the available evidence and provide pooled diagnostic accuracy measures. Our meta-analysis showed that UBT has high diagnostic accuracy for detecting *H. pylori* infection in patients with dyspepsia. Given the potentially preventable diseases associated with chronic, untreated *H. pylori* infection, more widespread adoption of UBT testing may be indicated.

Ferwana M, Abdulmajeed I, Alhajiahmed A, Madani W, Firwana B, Hasan R, Altayar O, Limburg PJ, Murad MH, Knawy B. Accuracy of urea breath test in *Helicobacter pylori* infection: Meta-analysis. *World J Gastroenterol* 2015; 21(4): 1305-1314 Available from: URL: http://www.wjgnet.com/1007-9327/full/v21/i4/1305.htm DOI: http://dx.doi.org/10.3748/wjg.v21.i4.1305

INTRODUCTION

Helicobacter pylori (*H. pylori*) is a gram-negative bacterium found on the luminal surface of the gastric epithelium. It was first isolated by Warren and Marshall in 1983. It induces chronic inflammation of the underlying mucosa. The infection is usually contracted in the first few years of life and tends to persist indefinitely unless treated. At least 50% of the world's population is thought to carry *H. pylori*. The organism can survive in the acidic environment of the stomach partly owing to its remarkably high urease activity. Urease converts the urea present in gastric juice to alkaline ammonia and carbon dioxide[1].

Although the full spectrum of pathogenesis is currently unknown, *H. pylori* has been linked to a variety of upper gastrointestinal disorders. Reported symptoms of *H. pylori* infection are relatively non-specific, such as epigastric pain, postprandial fullness, bloating, nausea, and vomiting, along with signs of acid hypersecretion and delayed gastric emptying[2,3]. In addition, infection with *H. pylori* is linked to three important upper gastrointestinal diseases: duodenal or gastric ulcers, gastric cancer, and gastric mucosa-associated lymphoid-tissue lymphoma.

Many invasive and non-invasive methods can be used to diagnose *H. pylori* infection, including endoscopy with biopsy, serology for immunoglobulin titers, stool antigen analysis, and the urea breath test (UBT). Given the user-friendly, non-invasive features of UBT, this detection method may be preferred in many clinical settings. However, to date, the performance characteristics of UBT have been inconsistently described and remain incompletely defined.

UBT can play a useful role in the diagnostic evaluation of dyspeptic patients who have comorbidities that increase their risk of upper endoscopy, are intolerant to upper endoscopy, or have known or suspected gastric atrophy. Stool antigen testing can also be used to non-invasively detect active *H. pylori* infection, and the choice of diagnostic modality depends on factors such as cost, laboratory infrastructure, and concomitant use of medications such as proton pump inhibitors or antibiotics that may influence test results. Serum antibody test results can vary by geographic region, and may stay positive for a prolonged period following *H. pylori* eradication, thereby limiting the clinical utility for determining the presence or absence of current infection[4].

There are two UBTs available and gained Food and Drug Administration approval: ^{13}C and ^{14}C tests. Both tests are affordable and can provide real-time results. Some physicians may prefer the ^{13}C test as it is non-radioactive compared to ^{14}C which uses a radioactive isotope, especially in young children and pregnant women, though dose of radianis very minimal (about 1 microCi)[5]; the dose of radiation is the dose of ^{14}C-UBT with the mini dose equals to 1 microCi (37 kbq) which has a high diagnostic accuracy[6]. UBT is indicated to confirm *H. pylori* colonization and to monitor its eradication. Positive UBT indicates an active *H. pylori* infection which require treatment or further confirmation with invasive procedures. Initial treatment for *H. Pylori* consist of either triple, quadruple, or sequential therapy regimens, which all of them includes a proton pump inhibitor plus various antibiotic regimen; treatment periods generally varied from 7 to 14 d[4].

In this systematic review and meta-analysis, we aimed at summarizing data and appraising the relevant articles of UBT for diagnosis of *H. pylori* infection in dyspeptic patients and provide pooled diagnostic accuracy measures.

MATERIALS AND METHODS

Search and analysis methods, eligibility criteria, and the outcomes of interest were specified in advance in a protocol developed by study investigators.

Inclusion criteria

We included cross-sectional studies with consecutive patients that evaluated the diagnostic accuracy of UBT in adult patients with dyspeptic symptoms. We included articles that compare ^{13}C-UBT or ^{14}C-UBT

H. pylori test with a reference standard which is *H. pylori* (culture and/or histological examination) and/or not (serologic test either blood or stool).

We excluded studies that enrolled children or adolescents under 18 year of age, subjects who presented for reasons other than dyspeptic symptoms, bleeding peptic ulcer, complicated dyspeptic cases that need surgery, those who received previous therapy for *H. pylori* within the last 3 mo, or long term use of corticosteroids and immunosuppressant drugs and screening studies. Only articles presenting true positive, true negative, false positive and false negative data were included in the present study. Studies where data was missing and studies with high risk of bias were excluded.

UBT variants

There was no inclusion restriction on the type of UBT performed. Both ^{13}C and ^{14}C types where included. Studies where the UBT was performed through an invasive method were excluded.

Search strategy

A librarian searched electronic databases for published and in-press studies from 1990 (the date where UBT became available) through November 2013 including PubMed, EMBASE, LILACS and Cochrane databases. The search terms used were "*H. pylori*", "*Helicobacter pylori*", "*Helicobacter* infection", "gastritis", "dyspepsia", "breath test", "urea breath test", "UBT", "^{13}C-UBT" and "^{14}C-UBT" with its MeSH terms (Medical Subject Headings) and keywords. We used Boolean operator (OR) to combine synonyms and (AND) to combine the cases with tests. No language restriction was applied. Reference lists were also scanned.

Study and data selection

Two authors (MF, WM) screened titles and abstracts for inclusion criteria. Full text articles were retrieved for relevant articles. An abstraction format developed by authors that includes: study citation, author name and year of publication, patients' mean age and other baseline characteristics, UBT variant, gold standard used, time between the test and gold standard, description of the cases, and diagnostic study data (numbers of true positive, false positive, false negative, and true negative test results). Disagreement was resolved by consensus.

Quality assessment

Two reviewers (MF and IY) independently assessed the quality of the included studies using the QUADAS (Quality Assessment of Diagnostic Accuracy Studies)-2 instrument[7]. This tool is designed to assess the quality of primary diagnostic accuracy studies for inclusion in the systematic review. It consists of four key domains covering patient selection, index test, reference standard, and flow of patients through the study and timing of the index test(s) and reference standard. Each domain is assessed in terms of the risk of bias and the first three are also assessed in terms of concerns regarding applicability.

Risk of bias is judged as "low", "high", or "unclear". If all signaling questions for a domain are answered "yes" then risk of bias can be judged "low". If any signaling question is answered "no" this flags the potential for bias.

We considered low risk of bias in different domains as follows: Patient selection if non-complicated dyspeptic patients were enrolled in consecutively. Index test, where it was interpreted independent from the reference standard. Reference standard, when it correctly classifies *H. pylori* and non-*H. pylori*. Flow and time, the appropriate interval between index test and the reference standard is within 7 d, and breathing samples were collected within 30 min.

Meta-analysis

The meta-analysis was conducted using Meta-Disc 1.4[8]. Random effect model was followed in all analyses. The diagnostic accuracy measures used in the analysis were sensitivity, specificity, likelihood ratio for positive and negative test (LR+ and LR-), receiver operating characteristics (ROC) curve, and diagnostic odds ratio. We assessed heterogeneity using the I-squared statistic and *Q* test. Publication bias was conducted using the Deeks' funnel plot asymmetry test, with *P*-value < 0.05 for the slope coefficient indicating significant asymmetry[9].

Subgroup and sensitivity analyses

To explore the robustness of our results and evaluate for potential causes of heterogeneity, we conducted several a priori determined analyses. We tested the bivariate mixed effects regression model to determine if results were robust to the correlation between sensitivity and specificity. Bivariate analysis were conducted as implemented in STATA version 12.0 (StataCorp, College Station, TX, United States)[10].

We also conducted subgroup analyses based on the risk of bias in the included studies as it pertains to the various domains of QUADAS-2 tool (such as for the index test and the gold standard test). We evaluated if the type of UBT test (^{13}C *vs* ^{14}C) or measurement technique (isotope ration mass spectrometry *vs* infrared mass spectrometry) affected the pooled estimates. We conducted an interaction test for subgroup analyses as suggested by Altman and Bland[11] and there was no statistically significant difference to suggest a subgroup effect.

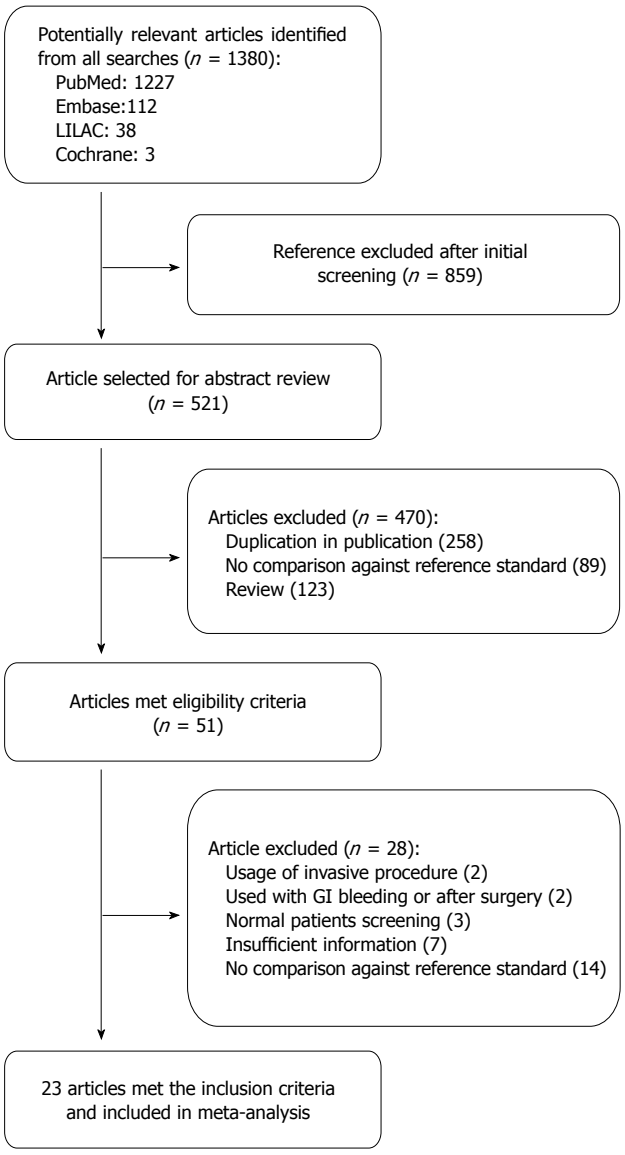


Figure 1 Study selection process.

RESULTS

Search results

The initial search yielded 1380 studies that were potentially relevant; of which, 23 studies that enrolled a total of 3999 participants were finally included. The study selection process is depicted in Figure 1 including causes of exclusion. More than 50% of quality assessment items articles have low risk of bias of all domains. The agreement between risk of bias assessment between reviewers were 70%, disagreement was resolved by discussion and consensus. Figure 2 visually summarizes the risk of biasin the included studies.

Characteristics of included studies

Table 1 shows the characteristics of all included studies. Of the 23 studies, 14 studies (61%) compared ^{13}C UBT with a reference standard, while 9 studies (39%) used ^{14}C UBT. The included studies were conducted in 16 countries, however all but one were published in English (Spanish)[12]. The mean age across studies was (40-59 year) and female gender distribution was (13%-74%).

There was variation (10 folds) in the type of reference standard tests used by different studies (Table 2). Seven studies (30.4%) used one reference standard starting with either histopathology or culture at first and only used subsequent tests if the first test was negative (histopathology in three studies[13-15], and culture in four studies[16-19]). Two studies (8.7%)[20,21] used histopathology or culture, nine studies (39.1%)[12,22-24] used two combined tests (histopathology and rapid urease test "RUT" in four studies, histopathology and serology in one study[25], histopathology and culture in one study[26], and any two tests in three studies[27-29]. Four studies (17.4%)[30-33] used three combined tests, and one study (4.3%)[3] used four combined tests as reference standard. Histopathology is the most common approach when combined tests were used. In three studies[3,27,31], UBT was part of combined reference standards.

Pooled estimate for UBT (Combined ^{13}C and ^{14}C)

UBT had high sensitivity and specificity 0.96 (95%CI: 0.95-0.97) and 0.93 (95%CI: 0.91-0.94); respectively. LR+ and LR- were 12.32 (95%CI: 8.38-18.1) and 0.05 (95%CI: 0.03-0.07) respectively. The AUC was 0.985. Forest plots are depicted in Figure 3. There was no evidence of publication bias (P > 0.05 using Deeks' asymmetry test).

Test of heterogeneity

Inconsistency between results for sensitivity and specificity among studies were 72.9% and 72% respectively with statistically significant Q test (P < 0.05). Heterogeneity could be explained by either clinical or methodological variation; the performed subgroup analyses could not explain the difference.

Subgroup analysis

^{13}C UBT *vs* ^{14}C UBT: Of the total studies recruited in this systematic review, 14 were conducted using ^{13}C UBT *vs* 9 using ^{14}C UBT (Table 3). Both versions of the test showed high performance against the Gold standard test without a significant difference. Figures are shown in online supplement materials (Figure 3). Interaction test for subgroup analyses as suggested by Altman and Bland[11] showed no statistically significant difference to suggest a subgroup effect (P = 0.87).

Use of infrared in UBT: Out of total 23 studies, 6 studies used infrared technique in measuring urea level. Both methods showed high performance against the gold standard test without a significant difference. Subgroup analysis based on the risk

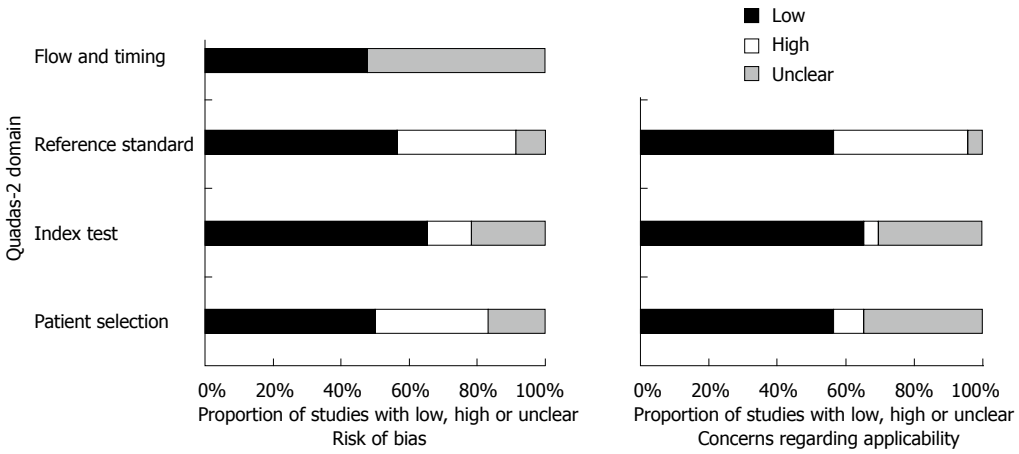


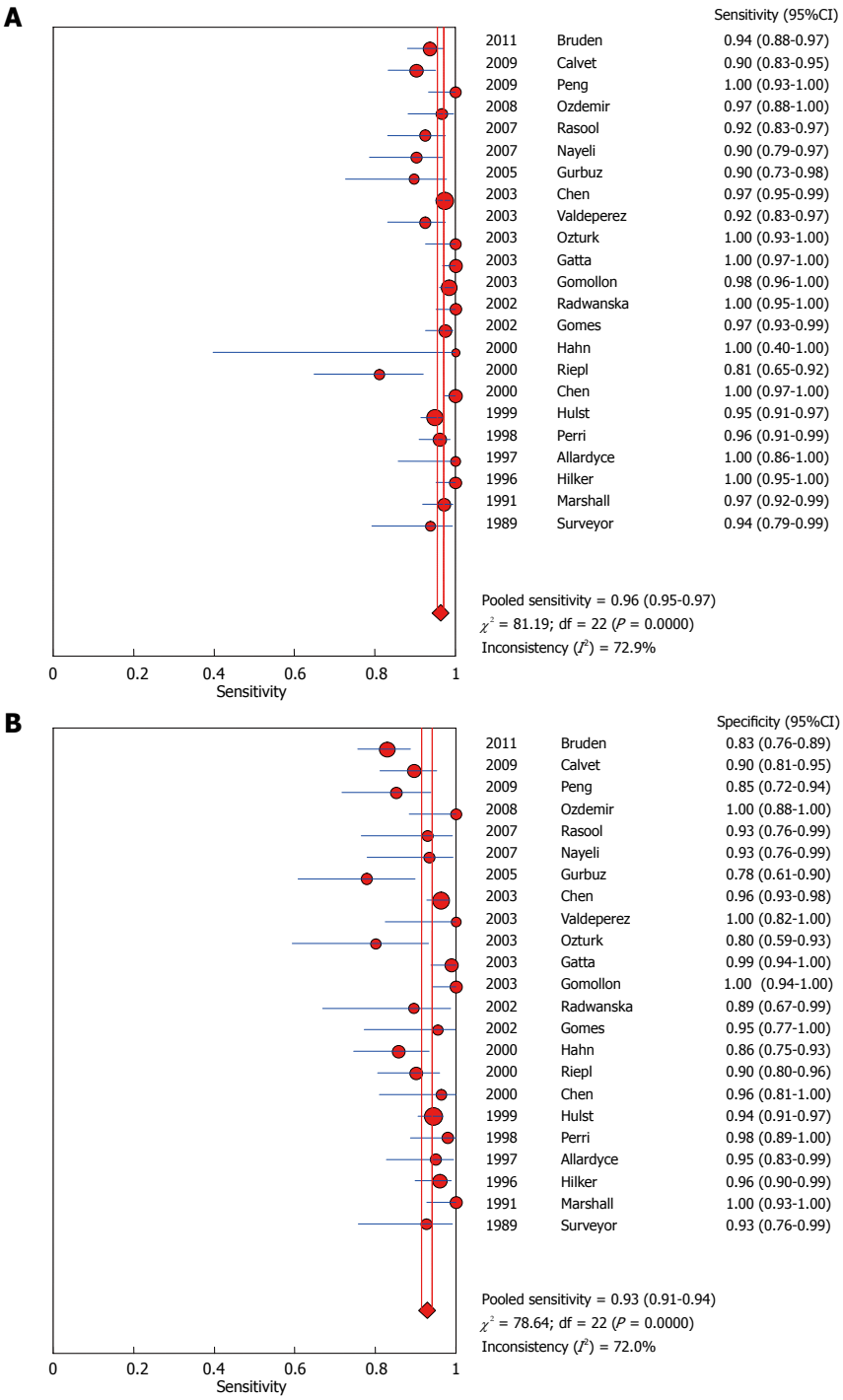
Figure 2 Risk of bias assessment.

Table 1 Baseline characteristics of the included studies

Ref.	Country	Year	No. of patients	Study design	UBT ($^{13}C/^{14}C$)	Infrared assisted	Reference standard	Mean age (mean ± SD)	Females	UBT threshold	Time
Allardyce *et al*[13]	New Zealand	1997	63	Cross-sectional	^{14}C	No	Histo or (Biopsy and rapid urea test)	56.5	26 41%	82% DPM	30 min and 60 min post ingestion
Bruden *et al*[16]	Estonia	2011	280	Cross-sectional	^{13}C	No	Culture or (Histo and RUT)	53.5	185 66%	≥ 5%	NA
Calvet *et al*[27]	Spain	2009	199	Cross-sectional	^{13}C	Yes	Any two positive (Histopathology, RUT, UBT, and fecal serology)	48.2 ± 14.2	107 53%	8.5%	20 min after drinking solution
Chen *et al*[29]	Taiwan	2003	586	Cross-sectional	^{13}C	Yes	Culture alone or RUT	45.7 ± 13.3	280 46.6%	≥ 2%	20 min after drinking solution
Chen *et al*[25]	Japan	2000	169	Cross-sectional	^{13}C	No	Combined (Histo and serology)	53.9 ± 15.7	68 40%	2.5%	20 min after normal respiration
Gatta *et al*[30]	Italy	2003	200	Cross-sectional	^{13}C	No	Combined (Histology and rapid urease) and/or culture	53 ± 13	113 56%	NA	30 min post ingestion
Gomes *et al*[22]	Brazil	2002	137	Cross-sectional	^{14}C	No	Combined (Histo and RUT)	46.7 ± 16.6	67 45%	1000-2000 CPM	30 min post ingestion
Gomollon *et al*[17]	Spain	2003	314	Cross-sectional	^{13}C	No	Culture and/or Combined (Histo and RUT)	54.1 ± 18	168 53.5%	≥ 5%	30 min post ingestion
Gurbuz *et al*[23]	Turkey	2005	65	Cross-sectional	^{14}C	No	Combind tests (Histo and RUT)	42.4 ± 15.5	46 67.7%	> 50 CPM	10 min after drinking solution
Hahn *et al*[31]	United States	2000	100	Cross-sectional	^{13}C	No	Combined (Histo, UBT and serology)	58.8 ± 14	9 13.4%	> 2.3%	30 min after administration
Hilker *et al*[14]	Germany	1996	174	Cross-sectional	^{13}C	No	Histo	46	106 60.9%	> 250	30 min after administration
van der Hulst *et al*[26]	Italy	1999	544	Cross-sectional	^{13}C	Yes	Histo and culture	46.5	379 62.7%	> 5%	30 min after administration
Marshall *et al*[32]	United States	1990	153	Cross-sectional	^{14}C	No	Combined (Culture, RUT and histo)	--	77 50%	> 6%	30 min after administration
Ortiz-Olvera Nayeli *et al*[18]	Mexico	2007	88	Cross-sectional	^{13}C	No	Culture and/or combined (Histo and RUT)	45 ± 15	49 55.6%	> 4.22%	30 min after administration
Ozdemir *et al*[28]	Turkey	2008	89	Cross-sectional	^{14}C	No	Combined; any 2 positive (RUT, PCR and histo)	45 ± 13	59 66%	> 25 CPM as Heliprobe	10 min after drinking solution
Oztürk *et al*[15]	Turkey	2003	75	Cross-sectional	^{14}C	No	Histology	41 ± 14	56 74.6%	100 DPM	NA
Peng *et al*[19]	Taiwan	2009	100	Cross-sectional	^{13}C	Yes	Culture or combind (Histo and RUT)	55	44 55%	4.8%	15 min after drinking solution
Perri *et al*[20]	Belgium	1998	172	Cross-sectional	^{13}C	No	Histo and/or culture	39.7 ± 14.1	81 47%	3.3%	Every 15 min for 1 h after ingestion of the urea solution

Kopański *et al*[3]	Poland	2002	92	Cross-sectional	^{14}C	No	Combined (Culture, serology, UBT and urine test for C-urea)	45.5	36	39%	> 5%	30 min after administration
Rasool *et al*[24]	Pakistan	2007	94	Cross-sectional	^{14}C	No	Two reference tests. Patient did both separately: (1) Histo; (2) RUT	40.8 ± 12.8	34	36%	> 50 CPM	After 10 min
Riepl *et al*[33]	Austria	2000	100	Cross-sectional	^{13}C	Yes	Combined 3 tests (Histo, UAT and culture)	51.6 ± 1.4	49	49%	> 4%	NA
Surveyor *et al*[21]	Australia	1989	63	Cross-sectional	^{14}C	No	Histo and/or culture	58.8 ± 14.5	30	47%	NA	Every 5 min for 30 min
Valdeperez *et al*[12]	Spain	2003	85	Cross-sectional	^{13}C	No	Histo and RUT	41.6	44	50.5%	NA	30 min after administration

Histo: Histopathology; RUT: Rapid urea test; UAT: Urea antigen; CLO: The CLOtest™ (Ballard Medical Products, Draper, UT, United States) was used for RUT; PCR: Polymerase chain reaction; NA: Not available; CPM: Counts per min; UBT: Urea breath test; DPM: Disintegrations per minute.



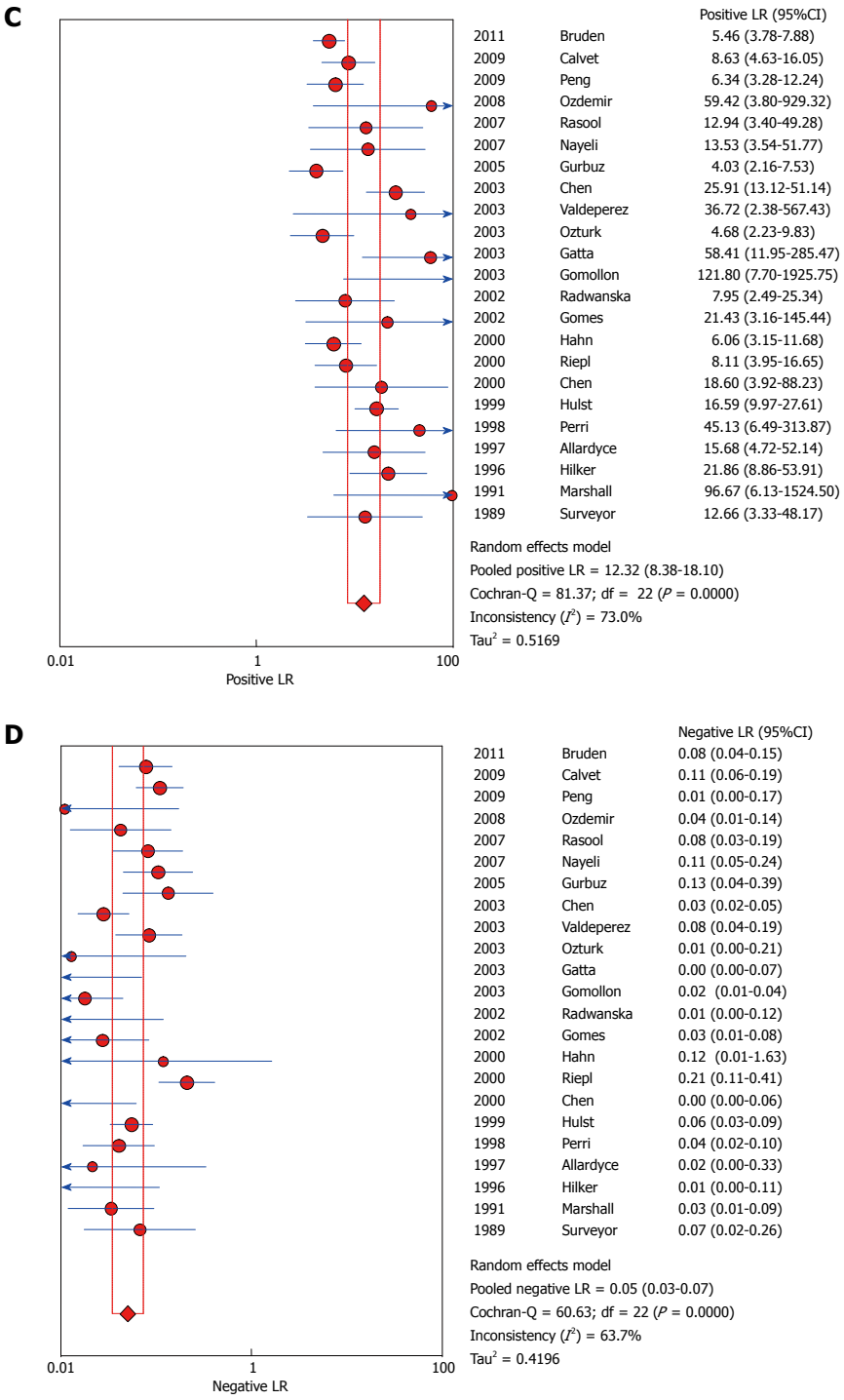


Figure 3 Pooled urea breath test result. A: Overall sensitivity; B: Overall specificity; C: Overall likelihood ratio for positive test; D: Overall likelihood ratio for negative test.

of bias. Figures are shown in online supplement materials (Figure 2).

There was no significant difference in diagnostic accuracy measures based on the risk of bias in terms of the key domains of patient selection, index test, reference standard, and flow of patients through the study and timing of the index test and reference standard. Interaction test for subgroup analyses showed no statistically significant difference to suggest a subgroup effect (P = 0.23).

Sensitivity analysis using bivariate model: Diagnostic accuracy measures were similar under the bivariate model and meta-analysis results appeared robust to the choice of model.

DISCUSSION

UBT is a noninvasive test for diagnosis of gastric *H. pylori* infection. Twenty-three studies for both UBT ^{13}C and ^{14}C for detection of *H. pylori* infection in

Table 2 Test values of included studies

Ref.	TP	FP	FN	TN	Total
Allardyce *et al*[13]	24	2	0	37	63
Bruden *et al*[16]	131	24	9	116	280
Calvet *et al*[27]	102	9	11	77	199
Chen *et al*[29]	361	8	10	205	584
Chen *et al*[25]	135	1	0	26	162
Gatta *et al*[30]	113	1	0	86	200
Gomes *et al*[22]	112	1	3	21	137
Gomollon *et al*[17]	249	0	4	61	314
Gurbuz *et al*[23]	26	8	3	28	65
Hahn *et al*[31]	4	9	0	54	67
Hilker *et al*[14]	76	4	0	94	174
van der Hulst *et al*[26] part 1	255	14	14	231	514
van der Hulst *et al*[26] part 2	161	3	12	72	248
Marshall *et al*[32]	101	0	3	49	153
Ortiz-Olvera Nayeli *et al*[18]	46	2	5	28	81
Ozdemir *et al*[28]	57	0	2	30	89
Oztürk *et al*[15]	48	5	0	20	73
Peng *et al*[19]	53	7	0	40	100
Perri *et al*[20]	121	1	5	46	173
Kopański *et al*[3]	75	2	0	17	94
Rasool *et al*[24]	61	2	5	26	94
Riepl *et al*[33]	30	7	7	63	107
Surveyor *et al*[21]	30	2	2	25	59
Valdeperez *et al*[12]	61	0	5	19	85

TP: True positive; FP: False positive; FN: False negative; TN: True negative.

adults were included. The result of the meta-analysis showed that the test performance was high and the test has significant discrimination power between those who have the infection and those who haven't.

The quality of this evidence is considered moderate due to the presence of heterogeneity, which may be explained by using different types of reference standards, timing between ingestion of the capsule and testand may be due to the variation in the methodological quality of the included studies It is very likely that the test performance is different across patients with varying pre-test risk although our analysis could not detect such difference. This analysis, focused on adults, shows similar diagnostic accuracy measures to those found in a different meta-analysis in children (sensitivity of 0.95 and specificity of 0.94 in children)[34].

In addition to the non-invasive nature of UBT, it offers the advantage of providing a comprehensive assessment that is not reliant upon the possible sampling error associated with endoscopic biopsy, due to patchy distribution of *H. pylori*[15]. Other limitations of the biopsy-based tests relate to their dependency on the pathologist skill and experience with studies documenting intern observer variability[35,36]. On the other hand, there are some limitations for UBT. For example, UBT results can be affected by exposure to *H. pylori* therapy such as, antibiotics, proton pump inhibitors or bismuth. It requires specialized equipment for carbon dioxide measurement and infrastructure to manage radioactive materials, and it is an expensive test.

Table 3 Subgroup analysis

Subgroup	No. of studies	Sensitivity	Specificity
UBT ^{13}C	14	0.96 (0.95-0.97)	0.94 (0.92-0.95)
UBT ^{14}C	9	0.97 (0.95-0.98)	0.91 (0.87-0.94)
Infrared assisted UBT	5	0.95 (0.93-0.96)	0.93 (0.91-0.95)
Infrared not assisted UBT	18	0.97 (0.96-0.98)	0.93 (0.91-0.95)

UBT: Urea breath test.

Strengths and limitations

The primary strength of this study relates to the search of electronic databases for relevant articles and the careful appraisal of study quality. The limitations mainly relate to dealing with aggregate data that limits our ability to provide estimates based on patient-level characteristics and pre-test risk level. Another significant limitation relates to heterogeneity that was unexplained despite multiple subgroup analyses. The observed heterogeneity can be attributed to several factors. The urease activity of the oral flora can affect the reading of the UBT; this can be accounted for by asking the patient to wash the mouth before conducting the test. Other authors suggested the use of Nasogastric tube. The cut off value and the time to take the reading after the meal ingestion was not clearly stated in many of the studies involved. The nature of the radioisotope meal and individual patient characteristics such as anthropometric measures, sex and age might have also contributed to within as well as between studies variability. All these factors could have contributed to the persistence of heterogeneity even after adjusting for UBT type (^{13}C *vs* ^{14}C) and technique of measurement (radioisotope mass spectrometry *vs* infrared spectrometry) in subgroup analysis.

In conclusion, UBT has high diagnostic accuracy for detecting *H. pylori* infection in patients with dyspepsia. Given the clinically significant, potentially preventable diseases associated with chronic, untreated *H. pylori* infection (such as gastric adenocarcinoma), more widespread adoption of UBT testing may be indicated to simultaneously improve public health and reduce treatment expense. The reliability of diagnostic meta-analytic estimates however is limited by significant heterogeneity, and the findings from this study should therefore be interpreted with appropriate caution.

COMMENTS

Background

Helicobacter pylori (*H. pylori*) is a gram-negative bacterium found on the luminal surface of the gastric epithelium and induces chronic inflammation of the underlying mucosa. The organism can survive in the acidic environment of the stomach partly owing to its remarkably high urease activity. Urease converts the urea present in gastric juice to alkaline ammonia and carbon dioxide. Urea

breath test (UBT) is a commonly used non-invasive test to diagnose *H. pylori* infection in patients with dyspepsia.

Research frontiers

There are two UBTs available and gained Food and Drug Administration approval: ^{13}C and ^{14}C tests. Both tests are affordable and can provide real-time results. UBT is indicated to confirm *H. pylori* colonization and to monitor its eradication.

Innovations and breakthroughs

Many invasive and non-invasive methods can be used to diagnose *H. pylori* infection, including endoscopy with biopsy, serology for immunoglobulin titers, stool antigen analysis, and the UBT. Given the user-friendly, non-invasive features of UBT, this detection method may be preferred in many clinical settings.

Applications

UBT can play a useful role in the diagnostic evaluation of dyspeptic patients who have comorbidities that increase their risk of upper endoscopy, are intolerant to upper endoscopy, or have known or suspected gastric atrophy. The study results suggest that UBT has high diagnostic accuracy for detecting *H. pylori* infection in patients with dyspepsia.

Peer review

This systematic review has been well performed; with a well expressed objective, precise criteria for the studies included and the relevant studies which have been selected for further evaluation. The quality of each included study has been properly evaluated. Its main drawback is the heterogeneity of the included studies; this, however, is not the fault of the authors of the meta-analysis.

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P- Reviewer: Cerwenka HR, Hara K, Hoff DAL **S- Editor**: Nan J
L- Editor: A **E- Editor**: Zhang DN

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ISSN 1007-9327
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