









Regular arrangement of collecting venules as a predictor of *Helicobacter pylori* absence using white-light endoscopy: a multicenter prospective study outside Asia

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Abstract

Background and aims: Endoscopic assessment of the regular arrangement of collecting venules (RAC) is a simple and reliable tool for predicting the absence of *Helicobacter pylori* (*H. pylori*) infection in the stomach, particularly in Asian populations. While initial studies in Western countries have yielded similar findings, RAC assessment has not yet been widely adopted in these settings. This study aims to evaluate the diagnostic accuracy of RAC in determining *H. pylori* status in a non-Asian population.

Methods: This prospective, multicenter study was conducted in 12 hospitals across non-Asian countries. Patients with no history of *H. pylori* infection or eradication were included, regardless of proton pump inhibitor (PPI) use. All participants underwent high-definition upper endoscopy without magnification or virtual chromoendoscopy. Endoscopists were trained using a 20-image test to identify the RAC pattern. *H. pylori* status was determined by histology and/or immunohistochemistry.

Results: A total of 648 patients were included, with an *H. pylori* infection prevalence of 34.7%. The RAC+ pattern was observed in 31.5% of patients, with no significant differences between those receiving PPI treatment and those who were not ($p=0.55$). Absence of pathological endoscopic findings was significantly associated with a RAC+ pattern ($p=0.01$). The sensitivity and negative predictive value (NPV) of RAC+ for ruling out *H. pylori* infection were 0.97 (95% CI: 0.94–0.99), reaching 1.00 when discordant images were reviewed by a blinded expert endoscopist. No significant differences in sensitivity or NPV were found between PPI users and non-users, or between regions with high and low *H. pylori* prevalence.

Conclusion: The presence of the RAC pattern along the minor gastric curvature, as assessed with white-light endoscopy, accurately identifies patients without *H. pylori* infection in non-Asian countries, regardless of PPI use.

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Plain language summary

A simple blood-vessel pattern seen during a routine stomach endoscopy can almost always rule out infection with *Helicobacter pylori*: findings from 648 patients examined at 12 Western hospitals

Helicobacter pylori (*H. pylori*) is a bacteria that can infect the stomach and is linked to various gastrointestinal problems. Detecting whether a person has this infection can be challenging. A specific pattern observed during a stomach examination called the “Regular Arrangement of Collecting Venules” (RAC) can help predict the absence of *H. pylori*. Earlier work in Asian hospitals showed that when RAC is visible, *H. pylori* infection is very unlikely—but Western endoscopists have rarely used this sign. This international study involved 648 patients from 12 hospitals in non-Asian countries. None of the participants had a known history of *H. pylori* infection or treatment. The patients underwent a stomach examination using high-definition endoscopy to look for the RAC pattern. Endoscopists were trained to recognize the RAC pattern before the study. Results showed that the RAC pattern was present in about 31.5% of patients. Notably, there was no difference between patients who were using acid-reducing medication (PPIs) and those who were not. Additionally, patients with the RAC pattern were less likely to show signs of gastric lesions. The ability of the RAC pattern to correctly indicate the absence of *H. pylori* was very high (97%), and in some cases, it reached 100% when reviewed by an expert. These findings suggest that using white-light endoscopy to look for the RAC pattern is a reliable way to identify patients who do not have *H. pylori*, even in Western clinical practice and regardless of medication use.

Keywords: gastric mucosa, *Helicobacter pylori*, regular arrangement of collecting venules, white light endoscopy

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Background

Helicobacter pylori (*H. pylori*) is the main risk factor for gastric cancer worldwide.^{1–3} Its eradication and the early detection of preneoplastic conditions are the essential strategies in the primary and secondary prevention of gastric cancer.⁴

Recent advances in endoscopic technology have significantly improved the ability to observe the gastric mucosa, even in the absence of magnifying endoscopy. A variety of endoscopic findings have been correlated with the presence of *H. pylori* infection.^{5–7} Among these findings, the regular arrangement of collecting venules (RAC) is particularly noteworthy, demonstrating high reliability with sensitivity and negative predictive value (NPV) exceeding 90% for identifying *H. pylori*-negative mucosa.^{8–11}

Although many of these studies were conducted in Asia using magnifying endoscopy,¹² recent

research performed in Europe utilizing high-definition (HD) endoscopes without magnification reported a sensitivity and NPV of around 100%.^{6,7,13} These preliminary findings are unsurprising because the gastric mucosal micro-anatomy observed endoscopically is comparable in Asian and Western populations. What remains largely unexplored, however, is the reliability of RAC assessment as a routine diagnostic surrogate for *H. pylori* infection in everyday Western practice—its reproducibility and diagnostic accuracy have yet to be rigorously quantified. Moreover, RAC evaluation is rarely performed outside Asia and is still absent from Western guidelines for high-quality endoscopy.

A significant challenge in the diagnosis of *H. pylori* is the use of proton pump inhibitors (PPI), which can lead to the bacteria migrating to more proximal stomach regions and a reduction in colonization density.^{14,15} PPIs are known to cause

false-negative results when biopsies are taken from the antrum and may also alter the appearance of the gastric mucosa and the RAC pattern. Therefore, discontinuing PPIs at least 2 weeks before testing for *H. pylori* is standard practice,^{14,16} and all studies examining the RAC pattern have excluded patients actively using PPIs. However, up to 36% of elderly patients are on PPIs at the time of endoscopy in routine clinical settings,^{17,18} underscoring the importance of developing a reliable diagnostic method for *H. pylori* infection in these circumstances.

The objectives of this study were to evaluate the value of RAC as a real-time diagnostic method to rule out *H. pylori* infection in routine clinical practice and the impact of PPI usage on the performance of RAC in non-Asian countries with different prevalence of *H. pylori* infection.

Methods

Study design and population

A multicenter prospective study was carried out across 12 hospitals (11 in Europe and one in South Africa). The study included consecutive patients undergoing non-urgent diagnostic esophagogastroduodenoscopy (EGD) for any clinical indication using HD white-light endoscopes without magnification from December 2021 to March 2024. Exclusion criteria were defined as follows: patients under 18 years of age; recent antibiotic use (within 14 days before the procedure); history of *H. pylori* eradication; intake of nonsteroidal anti-inflammatory drugs (NSAIDs), aspirin, antithrombotic, or oral anticoagulants (OAC); history of portal hypertension, lymphoma involving mucosa-associated lymphoid tissue (MALT) or previous gastric surgery; refusal to participate in the study. Patients on PPIs were not excluded from the study.

The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.¹⁹ The study protocol was approved by the Ethics Committee at the Hospital Clinic of Barcelona (HCB/2021/0898) and all the participating centers. Patients gave informed consent that included the use of pictures.

Endoscopic procedures and endoscopists

All EGDs were performed using HD endoscopes (Olympus, Tokyo, Japan; Fujifilm, Tokyo, Japan;

and SonoScape Medical, Shenzhen, China) without the use of magnification were conducted by 17 different endoscopists. Following the routine examination of the esophagus, stomach, and duodenum, a detailed inspection of the distal part of the lesser curvature near the incisura angularis was performed using white light and appropriate gastric insufflation.²⁰ The presence of a regular or irregular arrangement of collecting venules was evaluated in real time. The RAC sign originally described in 2002 was defined under conventional white-light endoscopy. Since then, virtually all studies—whether in pediatric or adult populations and with or without magnification—have likewise relied on white light, with only a single report having explored its assessment using narrow-band imaging (NBI).^{6–13,21} We therefore elected to retain white-light endoscopy without magnification as the primary detection method, both to maintain continuity with the existing body of research and to facilitate implementation in everyday clinical practice. Electronic chromoendoscopy was, of course, available during the procedures for the detection of additional signs related to chronic gastritis or preneoplastic lesions and could be used at the discretion of the endoscopist whenever additional mucosal evaluation was deemed necessary. If minute red points were visible consistently and uniformly, the finding was considered RAC positive (RAC+) (Figure 1(a)). If the finding was absent or displayed a patchy distribution, it was categorized as RAC negative (RAC-) (Figure 1(b) and (c)).²¹ For each patient, the most representative image that was used for the assessment of RAC was anonymized and stored. Any discordant cases classified as RAC+ but confirmed to have *H. pylori* infection were blindly reviewed, along with other RAC+ and RAC- cases, by an experienced endoscopist familiar with the RAC pattern. To standardize RAC interpretation, a training session was conducted using cases not included in the study. A set of 20 images illustrating both positive and negative RAC cases was presented to the participant endoscopists remotely.

Recording data

Personal data (sex, age, and PPI use) and endoscopic findings (such as erosive gastritis, gastric ulcers, gastric adenoma, gastric cancer, and signs of atrophic gastritis or intestinal metaplasia) were recorded. We did not consider recording the endoscopic severity of gastritis or intestinal metaplasia, and we only stored the pictures taken for

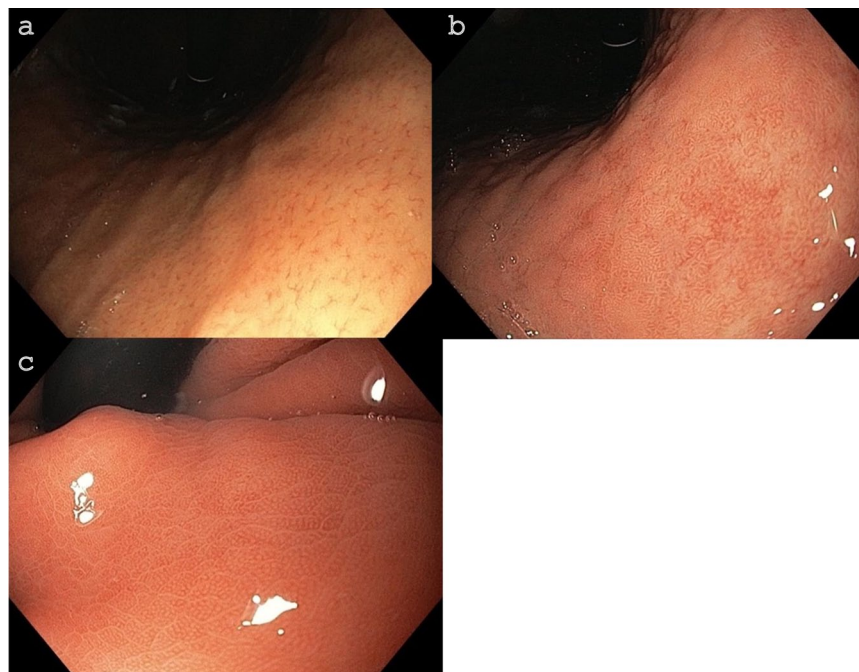


Figure 1. Examples of RAC. RAC+ pattern: minute, starfish-like red points are visibly distributed regularly and homogeneously in the lower part of the lesser curvature (a). Examples of RAC-patterns include inflammatory changes in the lesser curvature without visible collecting venules (b, c). RAC, Regular Arrangement of Collecting Venules.

the evaluation of RAC. In the training session, we only standardized RAC interpretation, and each endoscopist evaluated the presence of atrophy or intestinal metaplasia based on their own experience.

H. pylori infection status was determined by gastric biopsies following the updated Sydney protocol. An immunohistochemical (IHC) study was systematically performed in patients with PPI intake and a negative histologic study for *H. pylori*. Study data and images were collected and managed using Research Electronic Data Capture (REDCap) tools hosted at the Spanish Gastroenterology Association (AEG).

Statistical methods for data analysis

Sample size calculation. The estimated prevalence of *H. pylori* in Europe varies significantly (it is less than 20% in Northern Europe and exceeds 30% in Mediterranean countries).²² Assuming a prevalence of 20%, a minimum sample size of 488 patients was calculated to retain 415 analyzable subjects (including 98 true *H. pylori*-positive cases) and maintain 80% power to show that the sensitivity is at least 90% with the lower bound of

the one-sided 95% confidence interval not dropping below 80%. The trial was initially launched at 10 centers, each assigned a recruitment target of 50 patients. After two additional centers were added, the per-center quota was deliberately maintained to preserve uniform enrollment goals, which proportionally increased the overall sample size.

Quantitative data are presented as medians and interquartile ranges (IQR) or as means and standard deviation (SD), depending on the distribution, while qualitative data are shown as proportions. Categorical variables were compared using the chi-squared test, and continuous variables were analyzed using the *t*-test. A *p*-value of less than 0.05 was considered statistically significant. The sensitivity, specificity, positive predictive value (PPV), NPV, and accuracy of RAC in diagnosing *H. pylori*-negative patients, with a 95% confidence interval (CI), were calculated using standard formulas. Multiple logistic regression analysis was performed to identify predictor factors of RAC+ pattern and *H. pylori* infection. Candidate variables for inclusion in the model were those achieving a *p*-value ≤ 0.1 in the univariate analysis. Odds ratios (ORs) and associated

95% CIs were used to quantify the level of association. All statistical analyses were conducted using SPSS version 26 (IBM SPSS Inc., Chicago, IL, USA).

Results

Study participants and baseline characteristics

A total of 648 patients were included in 12 centers, with an average age of 52 years (IQR: 40–63) and 363 (56%) were female. One hundred and seventy-three (26.7%) patients were on active treatment with PPIs. Significant endoscopic abnormalities (erosive gastritis, gastric ulcer, gastric adenoma, gastric cancer, and signs of atrophic gastritis or intestinal metaplasia) were found in 180 (27.7%) patients, including six cases of gastric cancer. The baseline characteristics of the patients are detailed in Table 1. *H. pylori* infection was confirmed in 225 (34.7%) patients with a high variability among countries (median 28%). Only two out of 131 patients taking PPIs and testing negative for *H. pylori* in histopathology were found positive using the IHC test.

RAC pattern and H. pylori infection

Two hundred and four patients (31.5%) had a RAC+ pattern; 198 (97.1%) of these patients were free from *H. pylori* infection according to mucosal biopsy and IHC results (Figure 2). Conversely, the absence of RAC was associated with *H. pylori* infection in 49.1% (218 out of 444 cases). Six out of the 225 (2.7%) patients with confirmed *H. pylori* infection exhibited a RAC+ pattern. This finding resulted in an NPV and sensitivity of 97.1% (95% CI: 95–100) and 97.3% (95% CI: 94–100), respectively. When analyzing the diagnostic performance of the RAC pattern in patients treated with PPIs, no statistically significant differences were found regarding sensitivity, specificity and NPV, whereas PPV was lower in patients under PPI (Table 2).

All six discordant cases involved adults aged 42–58 years (four women, two men) recruited from different centers. None had received oral anticoagulants, NSAIDs or antibiotics within the preceding 4 weeks, and two had taken proton pump inhibitors during the 2 weeks before endoscopy, and—although collecting venules were visible—their distribution was uneven or patchy. After independent reassessment by an expert endoscopist, all six patients who had been labeled

Table 1. Baseline characteristics of the included individuals (N=648).

Age, median, years (IQR)	52 (40–63)
Gender, women, N (%)	363 (56)
On treatment with PPI, N (%)	173 (26.7)
Prevalence of <i>H. pylori</i> infection, N (%)	225 (34.7)
RAC+ pattern, N (%)	204 (31.5)
Under PPI, N (%)	51 (29.5)
Not under PPI, N (%)	153 (32.2)
Significant endoscopic findings (%)	180 (27.7)
Erosive gastritis, N (%)	70 (10.8)
Benign gastric ulcer, N (%)	13 (2)
Atrophic gastritis, N (%)	43 (6.6)
Intestinal metaplasia, N (%)	42 (6.5)
Gastric adenoma, N (%)	6 (0.9)
Gastric cancer, N (%)	6 (0.9)

IQR, interquartile range; PPI, proton pump inhibitor; RAC, Regular Arrangement of Collecting Venules.

RAC positive yet tested positive for *H. pylori* were re-classified as RAC negative, resulting in 100% sensitivity and negative predictive value. The six discordant cases (initial RAC+, *H. pylori*+) are illustrated in Figure 3.

We also analyzed the sensitivity and NPV of the RAC+ pattern based on the region and prevalence of *H. pylori*, and both were better in low-prevalence areas, although there were no statistically significant differences.

Predictor factors of RAC+ and H. pylori infection

The presence of any pathological finding on EGD (erosive gastritis, gastric ulcer, gastric adenoma, gastric cancer, or optical signs of atrophic gastritis or intestinal metaplasia) was associated with the absence of RAC+ pattern (OR 0.23; 0.14–0.38) and the presence of *H. pylori* infection (OR 1.6; 1.12–2.28). On the other hand, patients under PPI had a lower prevalence of *H. pylori* infection (OR 0.53; 0.35–0.78). Histology identified 43 patients with atrophic gastritis and 42 with intestinal metaplasia. In this dataset, the “atrophic

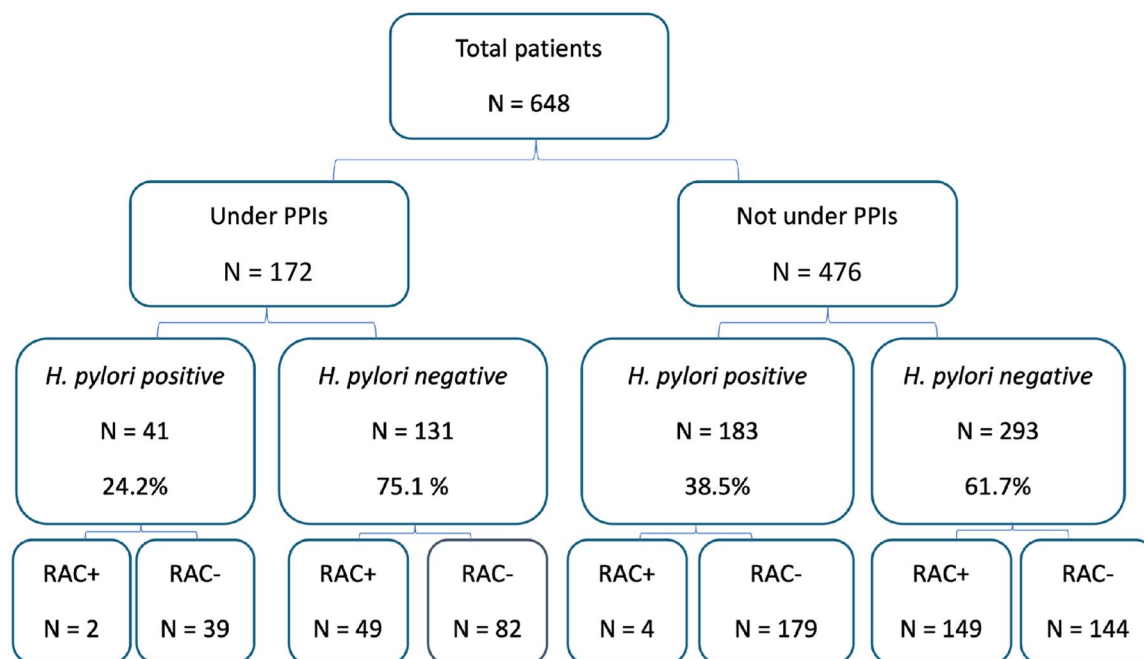


Figure 2. Flow-chart of the study.

Table 2. Performance characteristics of RAC to detect *H. pylori* infection globally depending on the use or not of PPI.

Diagnostic parameter	Total N = 648 (95% CI)	PPI use N = 173 (95% CI)	No PPI use N = 475 (95% CI)
Sensitivity	0.97 [0.94–0.99]	0.95 [0.89–0.99]	0.98 [0.93–0.99]
Specificity	0.46 [0.41–0.51]	0.37 [0.29–0.47]	0.51 [0.45–0.57]
Positive predictive value	0.49 [0.45–0.51]	0.33 [0.25–0.41]	0.55 [0.49–0.61]
Negative predictive value	0.97 [0.94–0.99]	0.96 [0.86–0.99]	0.97 [0.91–0.99]

PPI, proton pump inhibitor; RAC, Regular Arrangement of Collecting Venules.

gastritis” group, by definition, showed no evidence of intestinal metaplasia, whereas the “intestinal-metaplasia” group could exhibit concomitant atrophy. Among patients with atrophic gastritis, the RAC pattern was negative in 93.3% and positive in 6.7%. Likewise, in the intestinal-metaplasia group, 90.5% were RAC negative and 9.5% were initially scored RAC positive. All these findings are summarized in Table 3.

Discussion

This study confirms the reliability and clinical applicability of RAC after brief training using only HD white-light endoscopy without

magnification in a non-Asian cohort, irrespective of PPI use and *H. pylori* prevalence. We employed conventional white-light endoscopy without optical magnification to streamline implementation during routine diagnostic gastroscopies; nonetheless, ongoing technological advances and wider availability of modalities such as virtual chromoendoscopy and high-magnification endoscopy may further enhance RAC detection as well as other normal structures, such as crypt openings or subepithelial capillary network.²³

Training for endoscopic assessment of *H. pylori* is predominantly conducted in Asian regions where magnifying endoscopy is widely available. In the

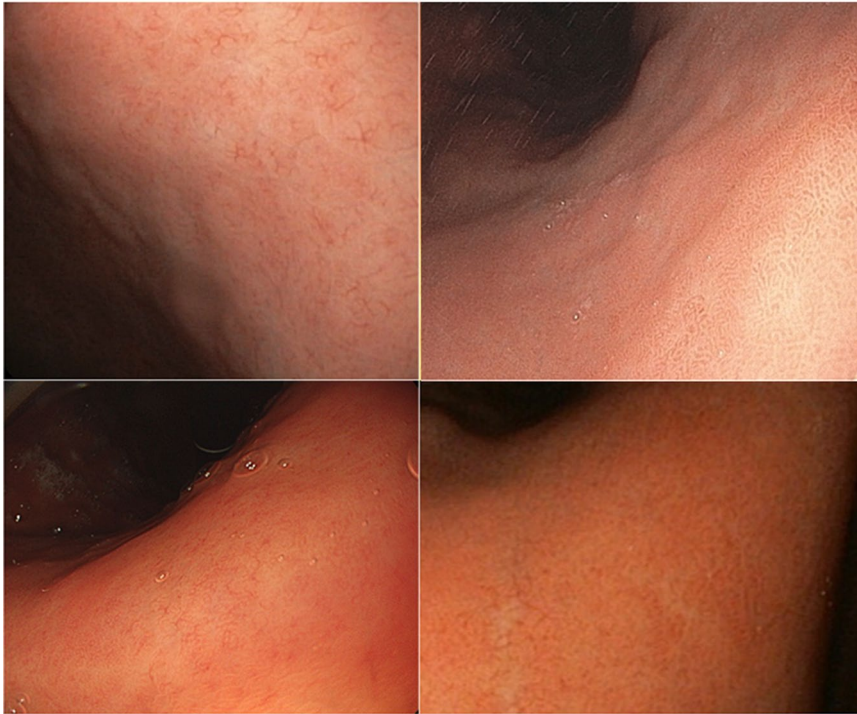


Figure 3. Examples of discordant cases (RAC+, *H. pylori*+).
RAC, Regular Arrangement of Collecting Venules.

research conducted by Watanabe *et al.*,²⁴ novice endoscopists with less than 500 EGDs were trained systematically over 2 years during routine clinical practice. At the conclusion of their training, 11 specific endoscopic features indicative of *H. pylori* infection were re-evaluated. RAC showed the highest inter-observer agreement (0.58), which improved to 0.81 by the end of the training. Our study demonstrated that, following brief training provided to all endoscopists, the RAC pattern serves as a reliable predictor for excluding *H. pylori* infection, with a sensitivity and NPV of approximately 97%, rising to 100% when independently reviewed by another blinded experienced endoscopist.

While RAC serves as a valuable marker for real-time identification of *H. pylori*-negative normal gastric mucosa, its clinical application outside Asia remains limited. Although there are some studies in the European population that demonstrate a high reliability to rule out *H. pylori* infection,^{6,7} most western endoscopists are unaware of its existence. With this multicenter study, we aimed to involve as many endoscopists from different countries as possible to disseminate the use of the RAC sign as widely as possible.

Diagnosing *H. pylori*-related gastritis, atrophy, and/or metaplasia based on endoscopic observations is critically important but can be challenging in non-Asian countries due to inconsistent adherence to guideline recommendations for biopsy sampling.^{25,26} Real-time endoscopic suspicion of *H. pylori* infection may improve patient management by suggesting more detailed evaluations, such as magnification or virtual chromoendoscopy, as well as biopsies for antimicrobial susceptibility testing. Conversely, in cases of normal gastric mucosa that test negative for *H. pylori*, this approach could reduce the necessity for biopsies.²⁵⁻²⁸

A previous study by our group reported that using RAC with only white-light endoscopy achieved a 100% NPV for excluding *H. pylori* infection.⁶ However, similar to other studies, patients taking PPI were excluded due to the potential negative impact of these drugs on infection diagnosis.¹⁴ In the current study, we observed no significant differences in RAC+ prevalence between patients on PPIs (30% vs 32.2%, p 0.55), with comparable sensitivity and NPV. Furthermore, we demonstrated that the RAC pattern performs exceptionally well in both high and low *H. pylori* prevalence regions, with comparable sensitivity and NPV.

Table 3. Predictor factors of RAC+ and *H. pylori* infection.

Clinical and endoscopic characteristics	RAC pattern				<i>H. pylori</i> infection			
	+	-	p-Value (univariate)	OR (multivariate)	+	-	p-Value (univariate)	OR (multivariate)
Age, years (median and IQR)	47 (34–60)	53 (41–65)	0.01	—	50 (35–63)	52 (40–64)	0.22	—
Sex, female vs male (%)	31.3/31.4	68.4/68.6	0.99	—	35.5/33.8	64.5/66.2	0.65	—
PPI use vs not (%)	30/32.2	70/67.8	0.55	—	24.3/38.3	75.7/61.7	0.01	0.53 (0.35–0.78)
Endoscopic findings* (any) vs not, (%)	11.7/60.9	88.3/39.1	0.01	0.23 (0.14–0.38)	74 (41.1)	106 (58.9)	0.01	1.6 (1.12–2.28)
Atrophy (%)	6.7	93.3	<0.01	0.14 (0.04–0.47)	—	—	—	—
Intestinal metaplasia (%)	9.5	90.5	<0.01	0.21 (0.08–0.61)	—	—	—	—
<i>H. pylori</i> infection (%)	2.7	97.3	<0.01	0.04 (0.02–0.08)	—	—	—	—

*Erosive gastritis, gastric ulcer, gastric adenoma, gastric cancer, atrophic gastritis or intestinal metaplasia. IQR, interquartile range; PPI, proton pump inhibitor; RAC, Regular Arrangement of Collecting Venules.

Although the effectiveness of RAC has been noted to diminish with age due to age-associated inflammatory changes in the gastric mucosa,^{20,21,29,30} we did not find differences in our study. Contrarily, we observed that the presence of significant endoscopic findings, such as erosive or preneoplastic lesions, was significantly associated with the presence of *H. pylori* infection and the disappearance of the RAC pattern. The exclusion of individuals taking drugs with a well-known gastroerosive effect, such as aspirin, NSAIDs, or OACs, may have contributed to this association.

This study has several notable strengths. It represents a multicenter cohort including 11 hospitals from European countries and 1 hospital from South Africa, encompassing over 600 patients. To the best of our knowledge, this is the first multicenter international study to assess the performance of the RAC pattern in non-Asian countries, irrespective of PPI use. In addition, photodocumentation of the RAC pattern was conducted in all cases and subsequently reviewed by an independent external endoscopist blinded to the results, further enhancing the consistency of our conclusions.

The limitation of the study is that including patients actively taking PPIs may result in some false negatives for *H. pylori* due to bacterial migration to the more proximal stomach areas and decreased bacterial load.^{16,31} To mitigate this, biopsies were taken

from both the antrum and corpus, and IHC testing was performed on all PPI-using patients with *H. pylori*-negative hematoxylin and eosin (H&E) biopsies. IHC staining offers greater sensitivity and specificity than H&E, especially beneficial in cases with PPI use, which can cause atypical cell forms or mucus in H&E samples.^{32,33} Although additional tests could have been employed to increase diagnostic yield, our approach yielded similar *H. pylori* prevalence rates regardless of PPI use.

Conclusion

In summary, the use of white-light HD endoscopy to diagnose *H. pylori* based on the arrangement of gastric collecting venules is a simple and highly reproducible technique, consistent across different examiners and applicable in regions with varying *H. pylori* prevalence, including patients on PPIs. Our findings support the integration of RAC as a real-time diagnostic tool for confirming *H. pylori*-negative status in Western clinical settings, potentially eliminating the need for biopsies when RAC+ is observed.

Declarations

Ethics approval and consent to participate

The reporting of this study conforms to the Strengthening the Reporting of Observational

Studies in Epidemiology (STROBE) statement. The study protocol received approval from the institutional Ethics Committee at the Hospital Clinic of Barcelona (Registration Number HCB/2021/0898) and was conducted following the Declaration of Helsinki guidelines (current version; Fortaleza, Brazil, October 2013) and in accordance with the protocol and with the legal requirements established by Law 14/2007 of July 3, on Biomedical Research. The ClinicalTrials.gov identifier of the study was NCT05046990. All the co-authors had access to the study data and reviewed and approved the final manuscript. Written informed consent was obtained from each participant.

Consent for publication

Consent for publication was included in the informed consent.

Author contributions

Rodrigo Garcés-Duran: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Writing – original draft; Writing – review & editing.

Joan Llach: Formal analysis; Investigation; Methodology; Writing – original draft; Writing – review & editing.

Pedro Delgado-Guillena: Investigation.

Riccardo Vasapolli: Investigation.

Gertjan Rasschaert: Investigation.

Liv Vandermeulen: Investigation.

Jan Bornschein: Investigation.

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Masa Cavlina Sevo: Investigation.

Stefano Realdon: Investigation.

Ivan Lyutakov: Investigation.

Alanna Ebigbo: Investigation.

Innocent Francis: Investigation.

Romanas Zyklus: Investigation.

Tadas Urbonas: Investigation.

Stefania Maiero: Investigation.

Mirjana Kalauz: Investigation.

Henry Córdova: Validation.

Leticia Moreira: Validation.

Gloria Fernández-Esparrach: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Supervision; Validation; Writing – review & editing.

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Competing interests


The authors declare that there is no conflict of interest.

Availability of data and materials

All data are available from the corresponding author upon reasonable request (mgfern@clinic.cat)

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References

1. Banks M, Graham D, Jansen M, et al. British Society of Gastroenterology guidelines on the diagnosis and management of patients at risk of gastric adenocarcinoma. *Gut* 2019; 1545–1575.
2. Gawron AJ, Shah SC, Altayar O, et al. AGA technical review on gastric intestinal

- metaplasia-natural history and clinical outcomes. *Gastroenterology* 2020; 158(3): 705–731.e5.
3. Saumoy M, Schneider Y, Shen N, et al. Cost effectiveness of gastric cancer screening according to race and ethnicity. *Gastroenterology* 2018; 155(3): 648–660.
 4. Pimentel-Nunes P. Management of epithelial precancerous conditions and lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter and Microbiota Study Group (EHMSG), European Society of Pathology (ESP), and Socied. *Endoscopy* 2019; 51(4): 365–388.
 5. Cho J-H, Chang YW, Jang JY, et al. Close observation of gastric mucosal pattern by standard endoscopy can predict *Helicobacter pylori* infection status. *J Gastroenterol Hepatol* 2013; 28(2): 279–284.
 6. Garcés-Durán R, García-Rodríguez A, Córdova H, et al. Association between a regular arrangement of collecting venules and absence of *Helicobacter pylori* infection in a European population. *Gastrointest Endosc* 2019; 90(3): 461–466.
 7. Garcés-Durán R, Galdín-Ferreya M, Delgado-Guillena PG, et al. Diagnosis of *Helicobacter pylori* infection by the arrangement of collecting venules using white light endoscopy: evaluation of interobserver agreement. *Dig Dis* 2021; 39(6): 661–668.
 8. Suzuki H, Marshall B and Warren R. *Helicobacter pylori*. Tokyo: Springer Japan, 2016. 1–267.
 9. Katake Y, Ichikawa K, Fujio C, et al. Irregular arrangement of collecting venules (IRAC) provides a critical endoscopic insight in *Helicobacter pylori*-induced gastritis: a secondary publication. *Biomed Rep* 2013; 1(1): 23–27.
 10. Yan S, Wu S, Chen C, et al. Mucosal patterns of *Helicobacter pylori*-related gastritis without atrophy in the gastric corpus using standard endoscopy. *World J Gastroenterol* 2010; 16(4): 496–500.
 11. Mao T, Wang Y, Yin F, et al. Association of endoscopic features of gastric mucosa with *Helicobacter pylori* infection in Chinese patients. *Gastroenterol Res Pract* 2016; 2016: 6539639.
 12. Toyoshima O, Nishizawa T and Koike K. Endoscopic Kyoto classification of *Helicobacter pylori* infection and gastric cancer risk diagnosis. *World J Gastroenterol* 2020; 26(5): 466–477.
 13. Li L, Jing J, Gao H, et al. Regular arrangement of collecting venules under endoscopy for predicting a *Helicobacter pylori*-negative stomach: a systematic review and meta-analysis. *Gastroenterol Hepatol* 2021; 44(4): 286–292.
 14. El-Zimaity H, Serra S, Szentgyorgyi E, et al. Gastric biopsies: the gap between evidence-based medicine and daily practice in the management of gastric *Helicobacter pylori* infection. *Can J Gastroenterol* 2013; 27(10): e25–e30.
 15. Logan RPH, Walker MM, Misiewicz JJ, et al. Changes in the intragastric distribution of *Helicobacter pylori* during treatment with omeprazole. *Gut* 1995; 36(1): 12–16.
 16. Malfertheiner P, Megraud F, Rokkas T, et al. Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report. *Gut* 2022; 71(9): 1724–1762.
 17. Pottegård A, Broe A, Hallas J, et al. Use of proton-pump inhibitors among adults: a Danish nationwide drug utilization study. *Therap Adv Gastroenterol* 2016; 9(5): 671–678.
 18. Hálfðánarson Ó, Pottegård A, Björnsson ES, et al. Proton-pump inhibitors among adults: a nationwide drug-utilization study. *Therap Adv Gastroenterol* 2018; 11: 1–11.
 19. von Elm E, Altman DG, Egger M, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *PLoS Med* 2007; 4(10): e296.
 20. Nakayama Y, Horiuchi A, Kumagai T, et al. Discrimination of normal gastric mucosa from *Helicobacter pylori* gastritis using standard endoscopes and a single observation site: studies in children and young adults. *Helicobacter* 2004; 9(2): 95–99.
 21. Hidaka N, Nakayama Y, Horiuchi A, et al. Endoscopic identification of *Helicobacter pylori* gastritis in children. *Dig Endosc* 2010; 22(2): 90–94.
 22. Chen YC, Malfertheiner P, Yu HT, et al. Global prevalence of *Helicobacter pylori* infection and incidence of gastric cancer between 1980 and 2022. *Gastroenterology* 2024; 166(4): 605–619.
 23. Kurtcehajic A, Zerem E, Bokun T, et al. Could near focus endoscopy, narrow-band imaging, and acetic acid improve the visualization of microscopic features of stomach mucosa? *World J Gastrointest Endosc* 2024; 16(3): 157–167.
 24. Watanabe K, Nagata N, Shimbo T, et al. Accuracy of endoscopic diagnosis of *Helicobacter pylori* infection according to level of endoscopic experience and the effect of training. *BMC Gastroenterol* 2013; 13(1): 128.

25. Delgado-Guillena PG, Morales-Alvarado VJ, Elosua-González A, et al. Gastroenterologists' attitudes on the detection and management of gastric premalignant conditions: results of a nationwide survey in Spain. *Eur J Cancer Prev* 2021; 30(6): 431–436.
26. Bornschein J, Tran-Nguyen T, Fernandez-Esparrach G, et al. Biopsy sampling in upper gastrointestinal endoscopy - a survey from ten tertiary referral centres across Europe. *Dig Dis* 2021; 39(3): 179–189.
27. Matrakool L, Tongtawee T, Bartpho T, et al. Improved detection of *Helicobacter pylori* infection and premalignant gastric mucosa using conventional white light source gastroscopy. *Asian Pac J Cancer Prev* 2016; 17(4): 2099–2103.
28. Robles-Medranda C, Valero M, Puga-Tejada M, et al. High-definition optical magnification with digital chromoendoscopy detects gastric mucosal changes in dyspeptic-patients. *World J Gastrointest Endosc* 2020; 12(1): 23–32.
29. Alaboudy A, Elbahrawy A, Matsumoto S, et al. Regular arrangement of collecting venules: does patient age affect its accuracy? *World J Gastrointest Endosc* 2011; 3(6): 118–123.
30. Machado RS, Viriato A, Kawakami E, et al. The regular arrangement of collecting venules pattern evaluated by standard endoscope and the absence of antrum nodularity are highly indicative of *Helicobacter pylori* uninfected gastric mucosa. *Dig Liver Dis* 2008; 40(1): 68–72.
31. Negovan A, Iancu M, Mocan S, et al. *Eur J Intern Med* 2018; 50: e31–e32.
32. Loharamtaweethong K and Puripat N. Comparison of immunohistochemistry and conventional stains for helicobacter pylori detection in gastric biopsies of patients receiving proton pump inhibitors. *J Heal Sci Med Res* 2020; 38(4): 321–330.
33. Lee JY and Kim N. Diagnosis of helicobacter pylori by invasive test: histology. *Ann Transl Med* 2015; 3(1): 1–8.

Appendix

Acronyms and abbreviations

AEG	Spanish Gastroenterology Association
CI	Confidence Interval
EGD	Esophagogastroduodenoscopy
H. pylori	Helicobacter pylori
H&E	Hematoxylin and Eosin
HD	High definition
IHC	Immunohistochemistry
IQR	Interquartile ranges
MALT	Mucosa-associated lymphoid tissue
N	Total Number
NPV	Negative predictive value
NSAIDs	Nonsteroidal anti-inflammatory drugs
OAC	Oral anticoagulants
OR	Odds ratio
PPI	Proton Pump Inhibitors
PPV	Positive predictive value
RAC	Regular arrangement of collecting venules
RAC+	Regular arrangement of collecting venules positive
RAC–	Regular arrangement of collecting venules negative
REDCap	Research Electronic Data Capture
SD	Standard deviation
Se	Sensitivity
Sp	Specificity

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