

Correlation analysis between *Helicobacter pylori* antibody typing and endoscopic classification of chronic atrophic gastritis and OLGA/OLGIM staging

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Abstract

Background and aim: Chronic atrophic gastritis (CAG) is a well-established precancerous condition in the gastric carcinogenesis cascade. *Helicobacter pylori* (Hp) infection is the primary etiological factor for CAG; however, the differential impact of Hp virulence types on endoscopic and histopathological severity remains incompletely characterized. This study aimed to investigate the correlation between Hp antibody typing and endoscopic classification of CAG based on the Kimura-Takemoto system, as well as OLGA and OLGIM staging.

Methods: We conducted a retrospective analysis of 742 patients diagnosed with CAG at the Department of Gastroenterology, Yunnan University Affiliated Hospital, between January 2023 and December 2025. Clinical data, including magnifying endoscopy findings, histopathological results, Hp infection status, and antibody typing, were systematically collected and analyzed. The relationships between Hp antibody types and Kimura-Takemoto endoscopic classification, OLGA staging, and OLGIM staging were evaluated using chi-square tests and Fisher's exact tests.

Results: Among the 742 patients with CAG, 601 (81.0%) tested positive for Hp infection, including 226 (37.6%) with type I Hp infection and 375 (62.4%) with type II Hp infection. Patients with Hp infection exhibited significantly more severe endoscopic atrophy compared to Hp-negative patients ($P = 0.013$). No significant difference in endoscopic atrophy severity was observed between type I and type II Hp infection ($P = 0.087$). However, patients with type I Hp infection demonstrated significantly higher OLGA stages ($P < 0.001$) and OLGIM stages ($P < 0.001$) compared to those with type II Hp infection. Among type I-infected patients, 44.2% had OLGA stage III–IV and 43.8% had OLGIM stage III–IV, compared to 16.3% and 8.5%, respectively, in type II-infected patients.

Conclusions: Hp infection exacerbates the extent of endoscopic atrophy in patients with CAG, while type I Hp infection is associated with more severe histopathological atrophy and intestinal metaplasia. The combination of endoscopic CAG classification, histopathological staging, and Hp antibody typing may serve as an effective strategy for precision diagnosis and risk stratification in patients with CAG.

Background

Chronic atrophic gastritis (CAG) is a chronic digestive disease characterized by the loss of specialized glands in the gastric mucosa and is frequently accompanied by intestinal metaplasia (IM). CAG is widely recognized as a precancerous condition in the gastric carcinogenesis cascade. The Correa cascade has established that the progression from chronic non-atrophic gastritis → atrophy → intestinal metaplasia → dysplasia → intestinal-type gastric cancer positions CAG as a critical and potentially intervenable stage [1]. Therefore, accurate risk stratification and timely intervention in patients with CAG are of paramount importance for reducing the incidence and mortality of gastric cancer.

Currently, several evaluation systems are employed in clinical practice to assess the severity of CAG and stratify gastric cancer risk. The Kimura-Takemoto classification system, based on endoscopic

identification of the atrophic border, categorizes gastric atrophy into closed-type (C-type) and open-type (O-type), providing intuitive visualization of the extent of atrophy and its correlation with gastric cancer risk [2]. The OLGA (operative link for gastritis assessment) and OLGIM (operative link for gastric intestinal metaplasia assessment) staging systems, derived from the updated Sydney System, integrate atrophy and IM scores from standardized biopsies of the antrum and corpus to establish risk stages, with stages III and IV defined as high-risk for gastric cancer [3, 4].

Helicobacter pylori (Hp) infection is the primary etiological factor for CAG and has been classified as a Group I carcinogen by the International Agency for Research on Cancer. The pathogenicity of Hp is closely associated with its virulence factors. Based on the expression of cytotoxin-associated gene A (CagA) and vacuolating cytotoxin A (VacA), Hp strains are classified into type I (high virulence, CagA- and/or VacA-positive) and type II (low virulence, only urease antibody-positive) [5]. Accumulating evidence suggests that different Hp virulence types are differentially associated with the progression of gastric diseases. A study by Wu et al. demonstrated that type I Hp infection positively correlates with gastritis activity and higher OLGA/OLGIM stages [6]. However, comprehensive investigations into the relationship between Hp antibody typing and both endoscopic and histological classifications of CAG remain insufficient, particularly those based on large-sample clinical data.

Therefore, this study conducted a retrospective analysis of 742 patients with CAG to explore the associations between Hp antibody typing and Kimura-Takemoto endoscopic classification, OLGA staging, and OLGIM staging. The findings aim to provide evidence-based medical insights for personalized management of CAG and improved prediction of gastric cancer risk.

Methods

Study population

This retrospective study included 742 patients diagnosed with CAG at the Department of Gastroenterology, Yunnan University Affiliated Hospital, between January 2023 and December 2025. The cohort comprised 428 males and 314 females, with a mean age of 57.3 ± 11.3 years (range: 24–85 years). Demographic data, Hp test results (including ^{13}C -urea breath test and serum Hp antibody typing), magnifying endoscopy findings, and histopathological reports were retrospectively collected from electronic medical records. Histological evaluation was performed according to the updated Sydney System, and OLGA and OLGIM stages were calculated accordingly.

The study protocol was approved by the Ethics Committee of Yunnan University Affiliated Hospital (Approval No. : 2023-LCYJ-056), and all patients provided written informed consent prior to endoscopic examination. All procedures followed the ethical standards outlined in the 1964 Declaration of Helsinki and its subsequent amendments.

Inclusion and exclusion criteria

Inclusion criteria were: (1) age $\geq$ 18 years; (2) confirmed diagnosis of CAG by endoscopic and histopathological examination; (3) complete clinical data, including Hp testing, endoscopy, and histopathology results; (4) signed informed consent before gastroscopy.

Exclusion criteria were: (1) history of gastrectomy or other gastric surgery; (2) history of endoscopic resection of gastric lesions (excluding polyps); (3) concurrent gastric malignancy or other malignant tumors; (4) use of antibiotics, bismuth preparations, or proton pump inhibitors within 4 weeks prior to Hp testing; (5) severe dysfunction of vital organs (heart, lung, liver, kidney, brain); (6) pregnancy or lactation.

Endoscopic examination and classification

Magnifying endoscopy was performed using an Olympus GIF-H290Z electronic gastroscope (Olympus Corporation, Tokyo, Japan) by experienced endoscopists with at least 5 years of clinical experience. Standardized image acquisition of the esophagus, stomach, and duodenum was conducted according to protocol. The extent of gastric mucosal atrophy was classified according to the Kimura-Takemoto system [2]: mild atrophy (C1–C2, atrophy confined to the antrum or lower gastric body), moderate atrophy (C3–O1, atrophy extending to the middle gastric body), and severe atrophy (O2–O3, atrophy extending beyond the middle gastric body or widespread distribution).

Hp detection and typing

All patients underwent ^{13}C -urea breath test to confirm current Hp infection. Simultaneously, fasting venous blood samples were collected, and serum Hp antibody typing was performed using immunoblotting (kit manufactured by Shenzhen Bolante Bioengineering Co., Ltd., Shenzhen, China). Interpretation criteria were as follows: type I Hp infection was defined as positivity for CagA antibody and/or VacA antibody; type II Hp infection was defined as negativity for both CagA and VacA antibodies but positivity for urease A (UreA) antibody and/or urease B (UreB) antibody [7].

Histopathological examination and staging

During gastroscopy, biopsy specimens were obtained according to the updated Sydney System requirements from the antrum (2–3 cm from the pylorus), gastric angle, and corpus (8 cm from the cardia). Specimens were routinely fixed in formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin (HE). Two experienced pathologists independently reviewed the slides to assess the degree of gastric mucosal atrophy and intestinal metaplasia. Based on the most severe scores from the antrum and corpus, OLGA and OLGIM stages were assigned as stages I, II, III, or IV [3, 4].

Statistical analysis

Statistical analysis was performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables were presented as frequencies and percentages (%). Comparisons between groups were conducted using the chi-square test or Fisher's exact test, as appropriate. Ordinal data were compared using the Mann-Whitney U test or Kruskal-Wallis H test. A two-tailed P-value < 0.05 was considered statistically significant.

Results

Hp infection status and typing

Among the 742 patients with CAG, 601 (81.0%) tested positive for Hp infection, while 141 (19.0%) were Hp-negative. Among Hp-positive patients, 226 (37.6% of Hp-positive; 30.5% of total) had type I Hp infection, and 375 (62.4% of Hp-positive; 50.5% of total) had type II Hp infection.

Association of Hp infection and typing with Kimura-Takemoto endoscopic classification

Patients with Hp infection exhibited significantly more severe endoscopic atrophy compared to Hp-negative patients ($\chi^2 = 8.624$, $P = 0.013$). However, no significant difference in endoscopic atrophy severity was observed between patients with type I and type II Hp infection ($\chi^2 = 4.893$, $P = 0.087$) (Table 1).

Table 1					
Association of Hp infection status and Hp typing with Kimura-Takemoto classification in CAG patients					
Group	N	Mild atrophy (C1–C2)	Moderate atrophy (C3–O1)	Severe atrophy (O2–O3)	P-value
Hp infection status					0.013
Hp-positive	601	270 (44.9)	258 (42.9)	73 (12.1)	
Hp-negative	141	93 (65.9)	37 (26.2)	11 (7.8)	
Hp typing					0.087
Type I	226	88 (38.9)	108 (47.8)	30 (13.3)	
Type II	375	182 (48.5)	150 (40.0)	43 (11.5)	
Data are presented as n (%). P-values were calculated using the chi-square test					

Association of Hp infection and typing with OLGA staging

No significant difference in OLGA stage distribution was observed between Hp-positive and Hp-negative patients ($\chi^2 = 5.338$, $P = 0.149$). However, among Hp-positive patients, those with type I Hp infection had

significantly higher OLGA stages compared to those with type II Hp infection, indicating an elevated risk of gastric cancer ($\chi^2 = 26.847$, $P < 0.001$) (Table 2).

Table 2
Association of Hp infection status and Hp typing with OLGA and OLGIM staging in CAG patients

Group	N	OLGA stage				OLGIM stage			
		Stage I	Stage II	Stage III	Stage IV	Stage I	Stage II	Stage III	Stage IV
Hp infection status									
Hp-positive	601	221 (36.8)	219 (36.4)	79 (13.1)	82 (13.6)	228 (37.9)	242 (40.3)	68 (11.3)	63 (10.5)
Hp-negative	141	57 (40.4)	72 (51.1)	6 (4.3)	6 (4.3)	59 (41.8)	69 (48.9)	7 (5.0)	6 (4.3)
P-value*		0.149				0.460			
Hp typing									
Type I	226	52 (23.0)	74 (32.7)	48 (21.2)	52 (23.0)	40 (17.7)	87 (38.5)	48 (21.2)	51 (22.6)
Type II	375	169 (45.1)	145 (38.7)	31 (8.3)	30 (8.0)	188 (50.1)	155 (41.3)	20 (5.3)	12 (3.2)
P-value**		< 0.001				< 0.001			
Data are presented as n (%). *P-value for comparison between Hp-positive and Hp-negative groups; **P-value for comparison between type I and type II Hp infection groups. P-values were calculated using the chi-square test									

Association of Hp infection and typing with OLGIM staging

Similarly, no significant difference in OLGIM stage distribution was found between Hp-positive and Hp-negative patients ($\chi^2 = 2.586$, $P = 0.460$). However, among Hp-positive patients, type I Hp infection was associated with significantly higher OLGIM stages compared to type II Hp infection ($\chi^2 = 42.176$, $P < 0.001$) (Table 2).

Discussion

CAG represents a critical juncture in the gastric carcinogenesis pathway, and its early identification and risk stratification are essential for secondary prevention of gastric cancer. Hp infection is the predominant etiological factor driving the development and progression of CAG; however, distinct virulence phenotypes of Hp strains exhibit substantial heterogeneity in their pathogenic potential and

clinical outcomes [8, 9]. This large-sample study of 742 patients with CAG systematically investigated the relationships between Hp antibody typing and both endoscopic atrophy classification and histopathological staging, providing novel evidence-based insights for precision management of CAG.

The Hp positivity rate in this cohort was 81.0%, consistent with recent epidemiological data reported in domestic studies [10]. Type I Hp infection accounted for 37.6% of Hp-positive cases, a proportion slightly lower than some previous reports [11], which may be attributable to regional variations, differences in patient selection criteria, or variations in detection methodologies. Type I Hp strains harbor the virulence factors CagA and/or VacA, conferring enhanced pathogenic potential and carcinogenic capacity [12]. CagA protein is translocated into gastric epithelial cells via the type IV secretion system, where it undergoes tyrosine phosphorylation and subsequently interacts with SHP-2 phosphatase, activating the Ras-ERK signaling pathway [13]. This cascade leads to cytoskeletal rearrangement, disruption of cell polarity, and imbalance between cellular proliferation and apoptosis, manifesting as the characteristic "hummingbird phenotype" [14]. Concurrently, VacA protein inserts into mitochondrial membranes, inducing membrane potential dissipation and cytochrome c release, thereby triggering apoptotic pathways. VacA also forms anion-selective channels in plasma membranes, disrupting intracellular ion homeostasis [15]. These molecular mechanisms provide a robust biological rationale for the association between type I Hp infection and more severe gastric mucosal injury.

Our findings demonstrate that Hp-positive patients exhibited significantly more extensive endoscopic atrophy compared to Hp-negative patients, corroborating previous studies that have established Hp infection as a key driver of atrophic expansion [16]. However, no significant difference in the extent of endoscopic atrophy was observed between type I and type II Hp infections, suggesting that the endoscopic extent of atrophy primarily reflects the chronicity of Hp colonization rather than strain-specific virulence differences. The Kimura-Takemoto classification, while valuable for rapid identification of high-risk background mucosa and prediction of gastric cancer risk based on atrophic border localization, may not fully capture the nuanced histopathological differences attributable to distinct Hp virulence types [17].

In contrast, at the histopathological level, our study revealed that patients with type I Hp infection exhibited significantly higher OLGA and OLGIM stages compared to those with type II Hp infection, with differences reaching high statistical significance. These findings indicate that type I Hp infection is associated with more severe gastric mucosal atrophy and intestinal metaplasia, conferring an elevated risk of gastric cancer progression. A meta-analysis by Pormohammad et al. demonstrated that infection with CagA-positive strains increased gastric cancer risk by 2.82-fold, while VacA s1m1 strains were associated with a 1.75-fold increased risk [18]. Similarly, Matos et al. confirmed that Hp strains carrying CagA and VacA s1/m1 alleles significantly elevate gastric cancer risk [19]. More recent studies have further elucidated that CagA-positive strains promote epithelial-mesenchymal transition and cancer stem cell properties through activation of β -catenin and NF- κ B signaling pathways [20, 21]. These molecular and epidemiological investigations provide strong supportive evidence for our clinical observations.

Notably, our study did not detect significant differences in overall OLGA or OLGIM stage distributions between Hp-positive and Hp-negative patients. This seemingly paradoxical finding may be explained by several factors. First, some Hp-negative patients may have had prior Hp infection (either spontaneous clearance or unintentional antibiotic eradication), yet established atrophic and metaplastic changes often persist and may not fully reverse even after bacterial clearance [22]. Second, alternative etiological factors, including autoimmune gastritis, duodenogastric reflux, high-salt dietary intake, and genetic predisposition, may contribute to CAG pathogenesis independently of current Hp infection status [23, 24]. These observations underscore the importance of comprehensive risk factor assessment in clinical practice, rather than focusing exclusively on current Hp infection status.

The OLGA and OLGIM staging systems have gained widespread international acceptance as robust tools for gastric cancer risk stratification, with stages III and IV consistently associated with elevated risk and consequently recommended for intensified endoscopic surveillance [25, 26]. Our study demonstrated that among patients with type I Hp infection, the proportion with OLGA stage III–IV reached 44.2%, and those with OLGIM stage III–IV reached 43.8%, substantially higher than the corresponding proportions in type II-infected patients (16.3% and 8.5%, respectively). These findings carry significant clinical implications: for CAG patients with type I Hp infection, even when endoscopic atrophy appears limited, clinicians should maintain a high index of suspicion for potentially advanced histopathological staging and recommend closer endoscopic follow-up. Conversely, for patients with type II Hp infection and low histopathological stages, extended surveillance intervals may be appropriate, thereby optimizing allocation of healthcare resources [27, 28].

Based on our findings, we propose integrating Hp antibody typing into routine clinical practice for CAG management: (1) Patients diagnosed with CAG should undergo Hp antibody typing to determine virulence status; (2) For patients with type I Hp infection, regardless of endoscopic atrophy extent, systematic biopsy sampling according to the updated Sydney System and OLGA/OLGIM staging should be performed; (3) Patients with type I Hp infection and OLGA/OLGIM stage $\geq$ III should receive intensified endoscopic surveillance (annually) and active intervention; (4) For patients with type II Hp infection, individualized surveillance protocols may be developed based on endoscopic findings and histopathological stages [29, 30].

The clinical relevance of Hp antibody typing extends beyond risk stratification to therapeutic considerations. Accumulating evidence suggests that patients with type I Hp infection derive greater benefit from eradication therapy in terms of reducing gastric cancer risk [31]. A randomized controlled trial by Choi et al. demonstrated that Hp eradication significantly reduced metachronous gastric cancer risk after endoscopic resection, with greater absolute risk reduction observed in patients with more severe baseline atrophy [32]. Future prospective studies should investigate whether the benefits of Hp eradication are modified by bacterial virulence type, potentially enabling more targeted application of eradication therapy.

Limitations

This study has several limitations. First, as a single-center retrospective study, selection bias cannot be entirely excluded. Second, we did not longitudinally assess the impact of Hp eradication therapy on endoscopic atrophy and histopathological stage regression. Third, we did not perform subtyping of CagA and VacA variants (e.g., VacA s1/s2, m1/m2), which may have differential associations with disease severity [33, 34]. Fourth, potential confounding factors such as dietary habits, smoking, alcohol consumption, and family history of gastric cancer were not systematically analyzed. Future prospective multicenter cohort studies with comprehensive data collection and long-term follow-up are warranted to validate our findings and further elucidate the molecular mechanisms by which Hp virulence factors drive gastric carcinogenesis. Additionally, integration of emerging biomarkers, including serum pepsinogen, gastrin-17, and microRNA signatures, may enhance the predictive accuracy of risk stratification models [35, 36].

Conclusions

In summary, Hp infection exacerbates the endoscopic extent of gastric mucosal atrophy in patients with CAG, while type I Hp infection is associated with more severe histopathological atrophy and intestinal metaplasia. The combination of endoscopic CAG classification, histopathological staging, and Hp antibody typing may serve as an effective strategy for precision diagnosis and treatment of CAG and for gastric cancer risk stratification. These findings support the incorporation of Hp virulence typing into routine clinical assessment of patients with CAG to guide personalized surveillance and intervention strategies.

Abbreviations

CAG	
Chronic atrophic gastritis	
Hp	
Helicobacter pylori	
IM	
Intestinal metaplasia	
OLGA	
Operative link for gastritis assessment	
OLGIM	
Operative link for gastric intestinal metaplasia assessment	
CagA	
Cytotoxin-associated gene A	
VacA	
Vacuolating cytotoxin A	
UreA	
Urease A	
UreB	

Urease B
HE
Hematoxylin and eosin

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Yunnan University Affiliated Hospital. All patients provided written informed consent prior to endoscopic examination.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available due to patient privacy and institutional data protection policies but are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Fubing Yu and Juan Yang contributed to study conception and design, data acquisition, analysis, and interpretation, and drafted the manuscript. Sheng Zheng and Juan Yang contributed to data acquisition and analysis, and critical revision of the manuscript. All authors read and approved the final manuscript.

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