

Peripheral blood inflammation indices versus age in predicting gastritis histopathology: A cross-sectional study

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Abstract

Objective: We evaluated a comprehensive panel of hematological inflammation indices in relation to histopathological features of gastritis and benchmarked them against age.

Materials and Methods: In this single-center, retrospective, cross-sectional study, 254 adults who underwent upper gastrointestinal endoscopy with gastric biopsy between June and December 2025 were analyzed. Conventional cellular ratios, composite inflammation indices, C-reactive protein- and nutrition-based measures, and exploratory immature granulocyte-based indices were computed from the pre-procedural hemogram. The primary endpoint was active inflammation; secondary endpoints were chronic inflammation, *Helicobacter pylori*, atrophy, and intestinal metaplasia. Discrimination was assessed by receiver operating characteristic analysis with DeLong comparison, multivariable logistic regression, and five-fold cross-validation; Benjamini-Hochberg correction was applied for multiple testing.

Results: Active inflammation was present in 100 patients (39.4%) and corresponded almost entirely to *Helicobacter pylori*-associated chronic active gastritis (kappa 0.98). No index differed with respect to any histopathological endpoint, nor did any distinguish gastritis subtypes. After correction, age was the only variable independently associated with active inflammation (an odds ratio of 0.65 per standard deviation, 95% confidence interval 0.50-0.86; $p = 0.002$). Age discriminated active inflammation better than each other index (area under the curve 0.631 versus 0.51-0.55), and this difference was statistically significant for all comparisons except for the systemic immune-inflammation index (DeLong $p = 0.096$). Adding the blood panel to age reduced the cross-validated discrimination from 0.632 to 0.594.

Conclusions: Peripheral hematological inflammatory indices did not reflect the histopathological status of the gastric mucosa. The only discriminating variable was age, which reflected the natural history of gastric disease rather than a systemic inflammatory signal.

Keywords: age factors, biomarkers, blood cell count, gastritis, *Helicobacter pylori*, neutrophils

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INTRODUCTION

Gastritis is less a single disease than a convergence of distinct histopathological processes that may coexist in varying combinations within the same mucosa: chronic mononuclear inflammation, active neutrophilic inflammation, glandular atrophy and intestinal metaplasia (IM) (1). Their recognition and grading are based almost entirely on the histopathological examination of biopsies obtained during upper gastrointestinal (GI) endoscopy. The Updated Sydney System provides a semiquantitative framework for the severity and activity of inflammation, while the atrophy- and metaplasia-based OLGA (Operative Link on Gastritis Assessment) and OLGIM (Operative Link on Gastric Intestinal Metaplasia Assessment) staging systems translate these findings into a graded estimate of gastric cancer risk (2).

The principal driver of chronic gastritis is *Helicobacter pylori* (*H. pylori*), the recognized initiator of the Correa cascade, in which chronic active gastritis progresses over years through atrophy and IM toward dysplasia and adenocarcinoma. Within this sequence, active inflammation is the component most directly tied to an acute inflammatory response: defined by neutrophilic infiltration of the gastric mucosa, it is, of all the histopathological components, the one most plausibly mirrored by neutrophil-based systemic markers (3). Reactive gastritis (more accurately termed chemical gastropathy) stands in deliberate contrast. Arising from nonsteroidal anti-inflammatory drugs (NSAIDs), bile reflux or alcohol, it is characterized by foveolar hyperplasia with conspicuously sparse inflammation and is separated from chronic active gastritis by both pathogenesis and management (1). That two of the most common patterns encountered on a gastric biopsy should differ so fundamentally in their inflammatory content raises the clinically meaningful question of whether peripheral blood can distinguish between them.

Histopathology remains the diagnostic reference standard, yet it is invasive, costly, prone to sampling error, subject to interobserver variability and ill-suited to repeated assessment or population-level screening (2). These limitations have sustained a long search for

non-invasive surrogates of the mucosal state, of which serum pepsinogens, gastrin-17 and their combination with *H. pylori* serology are the most extensively studied (4). Against this backdrop, indices derived from the complete blood count have attracted particular interest, for they are inexpensive, universally available, and do not require tests beyond those already performed in nearly every patient presenting for endoscopy.

The biological rationale for these indices is straightforward. Systemic inflammation tends to raise neutrophil and platelet counts while depressing lymphocytes, and ratios that capture this shift are held to quantify the intensity of the inflammatory response in peripheral blood (5). The neutrophil-to-lymphocyte ratio (NLR), the platelet-to-lymphocyte ratio (PLR) and the systemic immune-inflammation index (SII), which integrates all three lineages, are the most widely applied; more recent composites such as the pan-immune-inflammation value (PIV) and the systemic inflammation response index (SIRI) extend the concept by incorporating the monocyte compartment (6). Across oncology, cardiovascular disease, and inflammatory bowel disease, these markers have shown prognostic and, less consistently, diagnostic value.

In gastroenterology, however, their evaluation has been unduly narrow. Most studies have examined the indices against the binary presence of *H. pylori*, and even here the literature is discordant: some reporting that NLR, PLR or SII track infection or its severity, others finding no such association (7). Related work has explored these ratios in gastric adenocarcinoma and in peptic ulcer and dyspepsia, but a common limitation persists: the histopathological components of gastritis are rarely dissected individually, and clinically divergent subtypes (*H. pylori*-associated chronic active gastritis versus chemically mediated reactive gastritis) are seldom set against one another (8,9). The implicit and largely untested assumption underlying this entire body of work is that a localized mucosal process leaves a faithful signature in the systemic circulation.

We sought to interrogate that assumption directly. In adults undergoing upper GI endoscopy with gastric biopsy, we examined the relationship between pre-

procedural hematological inflammation indices and the individual histopathological features of gastritis, with active (neutrophilic) inflammation as the primary endpoint and chronic inflammation, *H. pylori*, atrophy, and IM as secondary endpoints. We further investigated whether these indices could discriminate chronic active from reactive gastritis and, crucially, benchmarked their performance against age, a readily obtainable clinical variable, to determine not only whether the indices carry information about the gastric mucosa but also whether they provide information beyond that available from simpler measures.

MATERIALS AND METHODS

Study design and setting

This single-center, retrospective, cross-sectional observational study was conducted in the endoscopy unit of the Department of General Surgery at Bolu Abant İzzet Baysal University Faculty of Medicine Hospital. Consecutive adult patients who underwent upper GI endoscopy with gastric biopsy between 22 June 2025 and 22 December 2025 were identified through the hospital information management system and the electronic medical records. The study was approved by the Bolu Abant İzzet Baysal University Clinical Research Ethics Committee (approval date [07/04/2026], number [2026/159]) and conducted in accordance with the principles of the Declaration of Helsinki; given its the retrospective design, the requirement for written informed consent was waived.

Participants

Patients were eligible if they were 18 years of age or older, had undergone gastric biopsy at the time of upper GI endoscopy with an available histopathological report, and had a complete blood count obtained within seven days of the endoscopic procedure. When more than one hemogram was available, the result closest to the procedure was used; when a patient had undergone more than one endoscopy, only the first was analyzed. Patients were excluded because of missing or insufficient clinical, laboratory, or histopathological data; clinical or laboratory evidence of active infection; a history of malignancy; a known hematological disorder; ongoing immunosuppressive therapy or

systemic corticosteroid use; presentation with acute GI bleeding; or any concurrent condition expected to perturb the systemic inflammatory response. After these criteria were applied, 254 patients constituted the final study population.

Data collection and laboratory variables

Demographic data (age, sex) and pre-procedural laboratory parameters were recorded systematically. The components of the complete blood count included white blood cell count (WBC), neutrophil count, lymphocyte count, monocyte count, platelet count, hemoglobin, red cell distribution width (RDW), and immature granulocyte percentage (IG%) with its absolute count (IG#). Biochemical parameters included C-reactive protein (CRP), serum albumin, urea, and creatinine. CRP values reported by the analyzer as being below the assay threshold were entered using the actual numerical results retrieved from the laboratory information system, rather than imputed substitutes, thereby preserving the continuity of the distribution for the CRP-derived indices.

Histopathological evaluation

Histopathological assessment was based on the reported biopsy findings, graded according to the Updated Sydney System (2). Chronic inflammation, active inflammation (neutrophilic activity), atrophy, IM, and *Helicobacter pylori* (*H. pylori*) were recorded dichotomously as present or absent. Active inflammation was defined by the presence of neutrophilic infiltration of the gastric mucosa. Reported diagnoses were used to classify patients into gastritis subtypes (chronic active gastritis, chronic inactive gastritis, and reactive gastritis) for comparison among subtypes.

Hematological inflammation indices

Indices were computed from the pre-procedural hemogram according to established definitions (5,6): NLR, PLR, the monocyte-to-lymphocyte ratio (MLR; monocyte/lymphocyte), SII, SIRI and PIV. To capture the inflammation–nutrition axis, we derived the CRP-to-lymphocyte ratio (CLR), the CRP-to-albumin ratio (CAR), the prognostic nutritional index (PNI; albumin

+ 5 × lymphocyte), and the hemoglobin–albumin–lymphocyte–platelet (HALP) score. Finally, recognizing that immature granulocytes index emergency granulopoiesis (a plausible systemic correlate of mucosal neutrophilic activity), we constructed and evaluated a set of exploratory composite indices incorporating IG% and IG#. Cell counts were expressed as absolute values ($\times 10^3/\mu\text{L}$) in the index formulas; the resulting composite indices (e.g., SII, SIRI, PIV) are dimensionless. Because this exploratory panel multiplied the number of statistical comparisons, all analyses were subjected to formal correction for multiple testing, as detailed below.

Outcomes

The primary endpoint was histopathological evidence of active inflammation. Secondary endpoints were chronic inflammation, *H. pylori*, atrophy, and IM. A prespecified secondary objective was to determine the discriminatory value of the indices in distinguishing between the chronic active and reactive gastritis subtypes.

Statistical analysis

The distribution of continuous variables was examined with the Shapiro–Wilk test and by inspection of histograms. Because most variables departed from normality, they were summarized as medians (interquartile ranges) and compared with the Mann–Whitney U test for binary outcomes and the Kruskal–Wallis test for comparisons across the three subtypes. Categorical variables are presented as counts and percentages and compared using the chi-square test or Fisher’s exact test; agreement between active inflammation and *H. pylori* status was quantified using Cohen’s κ coefficient. The discriminatory performance of each variable for the primary endpoint was assessed by the area under the receiver operating characteristic curve (AUC), and the AUCs for age and the inflammation indices were compared using the DeLong method. Variables associated with an endpoint in univariable testing, together with age and sex, were entered into multivariable binary logistic regression

models, and continuous predictors were standardized to permit comparison of effect estimates. To address the inflation of type I error arising from the breadth of the index panel and the number of endpoints, p-values were adjusted using the Benjamini–Hochberg false discovery rate procedure, and adjusted significance was reported alongside nominal values. The internal validity of the predictive comparison was further examined using five-fold cross-validated AUC. A two-sided p value below 0.05 was considered statistically significant. All statistical analyses were performed in Python (version 3.12; Python Software Foundation), using the SciPy and stats models libraries for hypothesis testing and regression modeling, and the scikit-learn library for receiver operating characteristic analysis and cross-validation. The DeLong test for comparing correlated areas under the curve and the Benjamini–Hochberg false discovery rate correction were implemented in this environment.

RESULTS

Cohort characteristics and the primary endpoint

Of the 254 patients analyzed, 100(39.4%) had histopathologically confirmed active inflammation and 154(60.6%) did not. The median age of the cohort was 58 years (interquartile range [IQR] 49–68) and 115 patients (45.3%) were men. Chronic inflammation was present in 212 patients (83.5%), IM in 49(19.3%), and atrophy in 13 (5.1%). *H. pylori* was identified in 102(40.2%). The distribution of pre-procedural laboratory parameters and derived indices according to active inflammation status is presented in Table 1.

A defining feature of the cohort emerged at the outset. Active inflammation and *H. pylori* status effectively constituted the same variable: every patient with active inflammation was *H. pylori*-positive (100%), whereas only 2 of 154 patients without active inflammation (1.3%) harbored the organism, yielding almost perfect agreement (Cohen κ = 0.98). All patients with active inflammation also showed chronic inflammation. Active inflammation, corresponded in practice, to *H. pylori*-associated chronic active gastritis.

Table 1. Demographic, laboratory, and hematological index values by active inflammation status.

Variable	All (n = 254)	Active (+) (n = 100)	Active (-) (n = 154)	p
Age, years	58.0 (49.0–68.0)	56.0 (45.0–62.2)	61.5 (51.2–70.0)	<0.001
Male, n (%)	115 (45.3)	47 (47.0)	68 (44.2)	0.752
WBC, $\times 10^3/\mu\text{L}$	7.2 (5.9–8.7)	7.4 (6.2–8.7)	7.1 (5.8–8.6)	0.187
Neutrophil, $\times 10^3/\mu\text{L}$	4.2 (3.1–5.3)	4.3 (3.4–5.4)	4.0 (3.0–5.3)	0.133
Lymphocyte, $\times 10^3/\mu\text{L}$	2.2 (1.8–2.8)	2.2 (1.8–2.8)	2.1 (1.8–2.8)	0.484
Monocyte, $\times 10^3/\mu\text{L}$	0.6 (0.5–0.7)	0.6 (0.5–0.7)	0.6 (0.5–0.7)	0.735
Platelet, $\times 10^3/\mu\text{L}$	250.5 (208.0–294.8)	258.5 (227.3–304.3)	244.0 (201.0–286.5)	0.038
Hemoglobin, g/dL	14.0 (13.0–15.2)	14.1 (13.1–15.4)	14.0 (12.9–15.2)	0.640
RDW, %	13.2 (12.7–14.0)	13.1 (12.7–13.7)	13.3 (12.7–14.2)	0.026
IG, %	0.3 (0.2–0.4)	0.3 (0.2–0.4)	0.3 (0.2–0.4)	0.497
IG#, $\times 10^3/\mu\text{L}$	0.02 (0.01–0.03)	0.02 (0.01–0.03)	0.02 (0.01–0.03)	0.200
CRP, mg/L	3.2 (1.5–6.2)	3.5 (1.5–6.0)	3.1 (1.5–6.5)	0.899
Albumin, g/L	46.0 (44.0–48.0)	47.0 (44.0–48.0)	46.0 (44.0–48.0)	0.367
Urea, mg/dL	31.0 (25.0–37.0)	28.5 (23.0–36.2)	32.0 (25.2–38.0)	0.065
Creatinine, mg/dL	0.81 (0.67–0.95)	0.79 (0.66–0.91)	0.83 (0.68–0.98)	0.108
NLR	1.78 (1.37–2.56)	1.93 (1.38–2.55)	1.74 (1.36–2.56)	0.651
PLR	111.7 (86.6–147.9)	116.3 (90.3–148.1)	107.5 (86.0–147.3)	0.413
MLR	0.24 (0.20–0.33)	0.23 (0.20–0.29)	0.25 (0.20–0.34)	0.220
SII	452.8 (320.7–660.5)	493.6 (340.8–686.1)	425.2 (305.1–632.7)	0.187
SIRI	1.03 (0.72–1.53)	0.99 (0.71–1.44)	1.03 (0.75–1.63)	0.873
PIV	248.3 (156.9–426.6)	255.1 (170.2–424.6)	246.4 (150.4–428.7)	0.429
CLR	1.33 (0.77–2.72)	1.35 (0.76–2.57)	1.33 (0.77–2.90)	0.739
CAR	0.07 (0.03–0.14)	0.08 (0.03–0.14)	0.07 (0.03–0.14)	0.872
PNI	57.5 (54.2–60.8)	58.0 (55.0–60.8)	57.3 (53.6–60.7)	0.261
HALP	5.63 (4.15–7.89)	5.45 (4.12–7.80)	6.08 (4.17–8.07)	0.533

Data are median (IQR) unless otherwise stated. Mann-Whitney U test for continuous variables; chi square test for sex. Abbreviations: IQR, interquartile range; WBC, white blood cell; RDW, red cell distribution width; IG, immature granulocyte; IG#, absolute immature granulocyte count; CRP, C-reactive protein; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; PIV, pan-immune-inflammation value; CLR, CRP-to-lymphocyte ratio; CAR, CRP-to-albumin ratio; PNI, prognostic nutritional index; HALP, hemoglobin-albumin-lymphocyte-platelet score.

Hematological indices and active inflammation

None of the composite hematological inflammation indices differed between patients with and without active inflammation (Table 1). NLR ($p = 0.651$), PLR ($p = 0.413$), SII ($p = 0.187$), SIRI ($p = 0.873$), PIV ($p = 0.429$), MLR ($p = 0.220$), CLR ($p = 0.739$), CAR ($p = 0.872$), PNI ($p = 0.261$) and HALP ($p = 0.533$) were all statistically indistinguishable across the two groups. Among the individual parameters, only age

($p < 0.001$), platelet count ($p = 0.038$) and RDW ($p = 0.026$) reached nominal significance. After correction for multiple testing across the full panel using the Benjamini-Hochberg false discovery rate, age was the only variable to retain significance (adjusted $p = 0.011$); the associations for platelet count and RDW did not survive correction (adjusted $p = 0.32$ for both), suggesting that they are probable artifacts of multiple comparisons.

Table 2. Discriminatory performance for active inflammation and DeLong comparison against age.

Variable	AUC	DeLong p (vs. age)
Age	0.631	—
SII	0.549	0.096
PLR	0.530	0.044
PIV	0.529	0.044
NLR	0.517	0.028
CLR	0.512	0.014
CAR	0.506	0.010

DeLong test comparing the AUC of each index against that of age. Abbreviations: AUC, area under the receiver operating characteristic curve; SII, systemic immune-inflammation index; PLR, platelet-to-lymphocyte ratio; PIV, pan-immune-inflammation value; NLR, neutrophil-to-lymphocyte ratio; CLR, C-reactive protein-to-lymphocyte ratio; CAR, C-reactive protein-to-albumin ratio.

The exploratory composite indices incorporating immature granulocytes, constructed on the rationale that emergency granulopoiesis might mirror mucosal neutrophilic activity, also showed no association with active inflammation and did not survive correction for any endpoint (all adjusted $p > 0.05$).

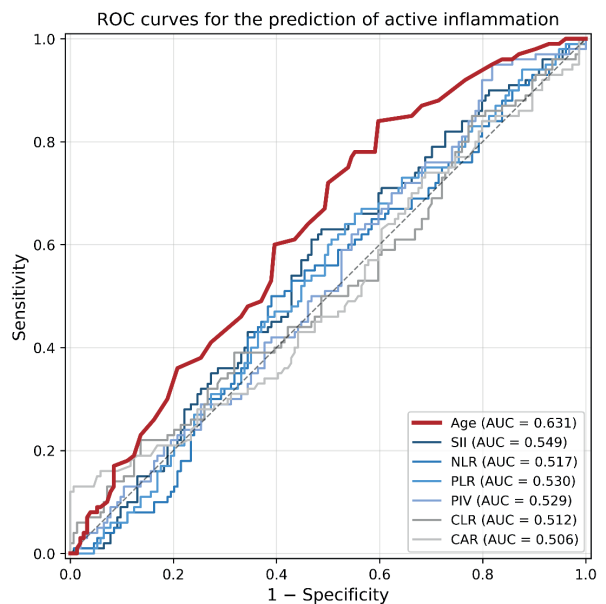
Discriminatory performance: age versus the indices

Receiver operating characteristic (ROC) analysis reinforced this pattern (Table 2). Age discriminated active inflammation with an area under the curve (AUC) of 0.631; this value is modest in absolute terms, but the highest of any variable examined. Each composite index performed at or near chance level: SII = 0.549, PLR = 0.530, PIV = 0.529, NLR = 0.517, CLR = 0.512, CAR = 0.506. Receiver operating characteristic analysis was limited to these six indices; MLR, SIRI, PNI, and HALP showed no differences between groups in comparison testing (Table 1) and were not modeled further. Formal comparison using the DeLong test showed that age significantly outperformed NLR ($p = 0.028$), PLR ($p = 0.044$), PIV ($p = 0.044$), CLR ($p = 0.014$), and CAR ($p = 0.010$); it was numerically superior to SII ($p = 0.096$). Receiver operating characteristic analysis was performed on the six indices most frequently reported in the gastritis literature (SII, PLR, PIV, NLR, CLR, and CAR). MLR, SIRI, PNI, and HALP were evaluated by group comparisons only. The ROC curves illustrate

this divergence: the age curve rose well above the reference diagonal, whereas every composite index tracked it closely (Figure 1).

Multivariable modeling

In a multivariable logistic regression model for active inflammation that included age, sex, platelet count, NLR, SII, and CRP (with continuous predictors standardized), age was the only independent predictor (odds ratio [OR] 0.65 per standard deviation, 95% confidence interval [CI] 0.50–0.86; $p = 0.002$). None of the hematological variables retained any association after adjustment (platelet OR 1.21, $p = 0.515$; NLR OR 0.93, $p = 0.881$; SII OR 1.02, $p = 0.964$; CRP OR 1.13, $p = 0.363$). The inverse direction of the age estimate indicates that active inflammation was characteristic of younger rather than older patients.

**Figure 1.** Receiver operating characteristic (ROC) curves for the prediction of histopathological active inflammation.

Age (red) yielded the highest discrimination (AUC = 0.631), significantly exceeding NLR, PLR, PIV, CLR and CAR (DeLong $p < 0.05$) and numerically exceeding SII. All composite indices clustered near the diagonal (AUC 0.51–0.55).

NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; PIV, pan immune-inflammation value; CLR, C-reactive protein-to-lymphocyte ratio; CAR, C-reactive protein-to-albumin ratio.

The incremental value of the blood panel was evaluated using five-fold cross-validation. Age alone achieved a cross-validated AUC of 0.632; adding the entire hematological panel did not improve discrimination; rather, it degraded out-of-sample performance to an AUC of 0.594, consistent with the addition of noise rather than signal.

Secondary endpoints and gastritis subtypes

For the remaining histopathological endpoints, the indices were similarly uninformative. Chronic inflammation was associated only with modestly higher neutrophil count (median 4.3 vs. $3.7 \times 10^3/\mu\text{L}$; $p = 0.021$) and WBC count (7.4 vs. $6.3 \times 10^3/\mu\text{L}$; $p = 0.025$) in univariable analysis, neither of which remained significant after adjustment for age. No index discriminated *H. pylori* beyond what was already captured by age, and none was associated with atrophy or IM (all $p > 0.05$); the small number of atrophy cases ($n = 13$) precluded robust modeling of that endpoint.

The three diagnostic subtypes (chronic active gastritis [$n = 100$], chronic inactive gastritis [$n = 104$], and reactive gastritis [$n = 50$]) differed in age but not in any hematological index (Table 3). Patients with chronic active gastritis were younger (median 56 years, IQR 45–62) than those with reactive gastritis (median

61 years, IQR 51–70) or chronic inactive gastritis (median 61.5 years, IQR 52.8–70.0; Kruskal–Wallis $p = 0.002$; chronic active vs. reactive $p = 0.019$). Across all composite indices, the Kruskal–Wallis test was not significant, indicating that systemic inflammatory markers did not distinguish between the clinically and pathogenetically divergent chronic active and reactive subtypes.

DISCUSSION

In a cohort of 254 patients examined using a panel ranging from conventional ratios to newer composite and purpose-built indices, no hematological inflammation markers reflected the histopathological state of the gastric mucosa. None of the following could be distinguished by NLR, PLR, SII, SIRI, PIV, or any of the CRP- and nutrition-based indices: active or chronic inflammation; *H. pylori* infection; atrophy; IM; or any diagnostic subtype. The single variable that carried reproducible information about the mucosa was age, and it did so modestly but consistently better than the indices designed for the that purpose. The central message is, therefore, not that we failed to find the right index, but that peripheral blood, at least in the setting of chronic gastritis, does not appear to transcribe what is happening at the mucosal surface.

Table 3. Age and representative indices across gastritis subtypes.

Variable	Chronic active (n = 100)	Reactive (n = 50)	Chronic inactive (n = 104)	p
Age, years	56.0 (45.0–62.2)	61.0 (51.0–70.0)	61.5 (52.8–70.0)	0.002
NLR	1.93 (1.38–2.55)	1.70 (1.37–2.66)	1.74 (1.36–2.53)	0.877
PLR	116.2 (90.3–148.1)	102.1 (86.8–145.4)	109.2 (85.1–148.7)	0.712
MLR	0.23 (0.20–0.29)	0.26 (0.21–0.33)	0.24 (0.20–0.36)	0.468
SII	493.6 (340.8–686.1)	403.9 (314.0–577.7)	436.4 (304.5–662.7)	0.316
SIRI	0.99 (0.71–1.44)	0.99 (0.73–1.60)	1.05 (0.75–1.64)	0.820
PIV	255.1 (170.2–424.6)	223.5 (150.4–389.1)	259.6 (155.1–437.3)	0.542
CLR	1.35 (0.76–2.57)	1.01 (0.77–2.49)	1.38 (0.82–3.56)	0.590
CAR	0.08 (0.03–0.14)	0.05 (0.03–0.13)	0.07 (0.03–0.14)	0.559
PNI	58.0 (55.0–60.8)	57.1 (54.1–60.6)	57.5 (53.2–60.7)	0.527
HALP	5.45 (4.12–7.80)	6.26 (4.51–7.97)	6.08 (4.02–8.11)	0.712

Data are median (IQR). Kruskal–Wallis test. Abbreviations: IQR, interquartile range; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; PIV, pan-immune-inflammation value; CLR, C-reactive protein-to-lymphocyte ratio; CAR, C-reactive protein-to-albumin ratio; PNI, prognostic nutritional index; HALP, hemoglobin–albumin–lymphocyte–platelet score.

This conclusion runs counter to the literature that is itself far less unanimous than its volume suggests. Studies relating hematological indices to *H. pylori* infection have produced contradictory results; the discordance extends even to the direction of the association. Guclu and Agan, for instance, found that NLR was significantly lower, not higher, in *H. pylori*-positive patients, with no accompanying difference in mean platelet volume (10). Erman, in a large retrospective cohort of dyspeptic patients with biopsy-confirmed *H. pylori* status, found no significant difference in either NLR or PLR between infected and uninfected groups (11). When the broader discordance of the field is taken into account, our findings are less an outlier than a clarification: where most studies have reported one significant marker among many and built a claim upon it, a comprehensively tested panel subjected to correction for multiple comparisons reveals that the underlying signal is, for practical purposes, absent (7).

That these indices succeed elsewhere but fail here is instructive rather than contradictory. In gastric adenocarcinoma, inflammatory ratios retain prognostic value and the same is true across numerous malignancies and inflammatory states (12). The distinction lies in the biology being interrogated. A tumor represents a sustained, high-volume systemic stimulus: necrosis, cytokine release, and a measurable shift in the circulating leukocyte pool. Mucosal gastritis, even in its active neutrophilic form, is a spatially confined process in which neutrophils are recruited locally to the epithelium; the amount of inflammatory traffic it generates is simply too small and too compartmentalized to register against the noise of peripheral blood. The indices are not invalid; they are being asked to detect a signal below their resolution.

The one finding that did emerge (the younger age of patients with active, *H. pylori*-associated gastritis) is best understood not as a biomarker but as a cross-sectional glimpse of the Correa cascade (3). The natural history of gastric disease is age-dependent: *H. pylori*-associated active inflammation predominates earlier and as the mucosa progresses toward atrophy and metaplasia the organism is frequently lost from a hostile, hypochlorhidric environment, so that

detectable infection paradoxically declines with age while atrophic and metaplastic changes accumulate (13). This age-stratified drift is well documented, with atrophy and OLGA stage rising in older cohorts and with the atrophy–metaplasia axis defining the trajectory toward neoplasia (14,15). Our data recapitulate this sequence in a contemporary surgical-endoscopic population. The clinical corollary is sobering for the index hypothesis: the limited discriminatory power for detecting active inflammation is captured by date of birth, and the blood adds nothing to it.

Perhaps the most pointed result concerns the immature granulocytes. We had reasoned that emergency granulopoiesis (the bone marrow's release of immature neutrophil precursors) might be the systemic event most likely to reflect mucosal neutrophilic activity, and we constructed several indices around it. Yet, immature granulocytes, whether raw or combined, were inert. The explanation is consistent with their established biology: immature granulocytes rise in response to substantial systemic infection, sepsis and major tissue injury, conditions categorically different in scale from the focal recruitment of neutrophils to gastric pits (16,17). In our view, the fact that even this most mechanistically plausible candidate failed constitutes the strongest single piece of evidence for compartmentalization: local mucosal and systemic compartments behaved independently.

Several features lend our null result more weight than is customary. The panel was deliberately broad, so that a true association would have had many opportunities to appear; the Benjamini–Hochberg correction guarded against the multiple-comparison artifacts that pervade this literature; the DeLong comparison established that age was statistically superior to all indices except SII, for which the advantage was only numerical; and fivefold cross-validation confirmed that adding the blood panel to age degraded, rather than improved, out-of-sample discrimination. Importantly, the dataset was not inert (it detected the age signal clearly), so the absence of an index effect cannot be dismissed as being due to insensitivity of the method.

These observations have practical implications. Hematological inflammation indices are inexpensive and reflexively ordered, and there is a temptation to

read mucosal significance into them. Our data counsel against this: a normal or elevated NLR or SII does not reliably indicate the presence of gastritis, its activity, *H. pylori* status or subtype, and should not influence the decision to biopsy or the interpretation of mucosal disease.

Study limitations

This study has several limitations. Its retrospective, single-center, cross-sectional design cannot establish temporal or causal relationships. Clinical confounders relevant to reactive gastropathy (nonsteroidal anti-inflammatory drug use, proton pump inhibitor use, and bile reflux exposure) were not systematically recorded, which may have blurred the characterization of that subtype. The near-perfect collinearity between active inflammation and *H. pylori* ($\kappa = 0.98$) means that, although listed as separate endpoints, they essentially interrogate a single biological entity. Atrophy was infrequent ($n = 13$), precluding robust modeling of that endpoint. All blood counts and index values derived from a single hematology analyzer may not be directly transferable across platforms. Finally, these findings are hypothesis-clarifying rather than definitive and await confirmation in prospective, multicenter cohorts.

These findings carry three practical implications. Clinically, hematological inflammation indices should not be read as surrogates for mucosal disease: in a patient with dyspeptic symptoms, a raised NLR or SII conveys nothing about the presence or activity of gastritis, its *H. pylori* status, or its subtype, and endoscopy with biopsy remains irreplaceable for that purpose. Methodologically, the discordance between our null result and the positive associations reported elsewhere illustrates how readily an uncorrected panel of correlated indices generates significant findings. Studies in this field should report the full panel tested, apply corrections for multiple comparisons, and benchmark any candidate marker against simple demographic variables before claiming discriminatory value. For future research, prospective designs incorporating OLGA and OLGIM staging would allow the question to be reframed in terms of cumulative mucosal damage rather than a binary histopathological label; serial measurement before and after eradication

therapy could test whether a dynamic change carries information that a single cross-sectional value does not; and direct comparison with mucosa-specific serological markers such as pepsinogen I and II would clarify whether the failure of peripheral indices reflects the limitations of the blood count itself or the compartmentalization of mucosal inflammation more broadly.

CONCLUSION

Across a broad, rigorously analyzed panel of hematological indices of inflammation, none reflected the histopathological state of the gastric mucosa: neither active nor chronic inflammation, nor *H. pylori* infection, nor atrophy, nor metaplasia, nor gastritis subtype. The only variable carrying reproducible discriminatory information was age, an expression of the age-dependent natural history of gastric disease rather than a systemic inflammatory signal, and one that the entire blood panel failed to improve upon. For the assessment of gastritis, the periphery is a poor mirror of the mucosa: a complete blood count—regardless of how its components are combined—is no substitute for histopathological examination. Whether any peripheral signature can capture localized mucosal inflammation remains an open question for prospective multicenter studies.

Ethical approval

This study has been approved by the Clinical Research Ethics Committee of Bolu Abant İzzet Baysal University (approval date 07.04.2026, number 2026/159). Owing to the retrospective design of the study, the requirement for written informed consent was waived by the ethics committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Author contribution

Concept: MFK; Design: MFK; Data Collection or Processing: MFK, FB; Analysis or Interpretation: MFK; Literature Search: FB; Writing: MFK, FB. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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