

Chronic Gastritis and *Helicobacter pylori* Burden in Women Previously Treated for Breast Cancer with Refractory Dyspepsia: A Retrospective Comparative Endoscopic Biopsy Study

BERKAN ACAR

berkanacar01@gmail.com

Giresun University

ALİ MUHTAROĞLU

Private Ada Tıp Hospital

ELİF YILMAZ

Private Umut Hospital

AHMET RECEP

Giresun University

GÖKHAN AYDIN

Giresun University

AHMET CUMHUR DÜLGER

Giresun University

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Abstract

Background

Persistent dyspepsia in women previously treated for breast cancer is often attributed to treatment-related or functional causes, but its gastric histopathological basis remains poorly defined. This study compared laboratory profiles and upper gastrointestinal biopsy findings in women previously treated for breast cancer and symptomatic women without breast cancer.

Methods

We retrospectively analysed 104 women who underwent upper gastrointestinal endoscopy for treatment-resistant dyspeptic symptoms: 43 women previously treated for breast cancer and 61 controls. Continuous variables are reported as median [interquartile range] and were compared using two-sided Mann-Whitney U tests. Histopathological biopsy scores were analysed as ordinal 0–3 outcomes and as binary indicators of any abnormality. Fisher's exact test was used for binary comparisons, and age-adjusted proportional-odds models were fitted for ordinal biopsy severity. False-discovery-rate adjustment was applied within laboratory and biopsy-outcome families.

Results

The groups were similar in age: 60.0 [53.0–66.5] versus 57.0 [48.0–70.0] years; $p = 0.646$. Albumin was lower in the breast cancer group after adjustment for multiple comparisons: 44.8 [42.0–46.1] versus 47.0 [43.6–50.0] g/L; $p = 0.001$; $q = 0.020$. Chronic inflammation was present in all patients in the breast cancer group compared with 75.4% of controls: risk difference, 24.6%; 95% CI, 12.4–36.7%; $p < 0.001$. The age-adjusted ordinal inflammation score was higher in the breast cancer group: adjusted OR, 5.62; 95% CI, 2.51–12.58; $q < 0.001$. *H. pylori* positivity was more frequent in the breast cancer group: 60.5% versus 26.2%; risk difference, 34.2%; 95% CI, 15.0–50.4%; $p < 0.001$, with higher age-adjusted density scores: adjusted OR, 7.83; 95% CI, 3.33–18.37; $q < 0.001$. Neutrophil activity, intestinal metaplasia, atrophy and dysplasia did not differ significantly after adjustment.

Conclusions

Women previously treated for breast cancer who underwent endoscopy for treatment-resistant dyspepsia showed higher chronic inflammation scores and greater *H. pylori* density than symptomatic controls. Persistent upper gastrointestinal symptoms in this population may therefore be associated with potentially treatable gastric pathology. These findings are hypothesis-generating and warrant prospective studies incorporating detailed oncological, hormonal and microbiome-related variables.

Background

Dyspepsia is one of the most common indications for upper gastrointestinal evaluation and encompasses persistent or recurrent symptoms centred on the epigastrium, including epigastric pain or burning, postprandial fullness, early satiety, nausea and bloating. Its aetiology is heterogeneous and may include peptic ulcer disease, gastro-oesophageal reflux disease, medication-related injury, biliary disorders, malignancy, *Helicobacter pylori* (*H. pylori*) infection and functional dyspepsia. Current guidelines therefore recommend a structured diagnostic approach based on symptom characteristics, alarm features, age and *H. pylori* status. In patients with persistent or treatment-resistant symptoms, upper gastrointestinal endoscopy with biopsy remains important because histopathological abnormalities may be present even when endoscopic findings are limited [1–3].

H. pylori remains a major cause of chronic gastritis and a well-established driver of gastric mucosal inflammation. Histopathological evaluation enables assessment of chronic inflammation, neutrophil activity, bacterial density, glandular atrophy, intestinal metaplasia and dysplasia, thereby providing clinically relevant information beyond symptom-based diagnosis alone [2, 3, 4]. Identification of *H. pylori*-associated gastritis is particularly important because eradication therapy may improve symptoms and reduce long-term gastric cancer risk in selected patients [2, 3].

Women treated for breast cancer frequently experience gastrointestinal symptoms during and after treatment. Although total mastectomy itself does not directly alter gastric anatomy or physiology, breast cancer management often includes chemotherapy, radiotherapy, endocrine therapy and multiple supportive medications that may affect gastrointestinal function. Previous studies have demonstrated high rates of nausea, vomiting, appetite loss, constipation, diarrhoea and other gastrointestinal symptoms during breast cancer treatment [5–9]. Furthermore, chemotherapy-related gastrointestinal toxicity has been associated with inflammatory pathways, nutritional impairment and alterations in the gut microbiome [8–12].

Recent evidence suggests that interactions between systemic inflammation, nutritional status and host–microbial factors may contribute to persistent gastrointestinal symptoms in cancer survivors. Alterations in intestinal microbiota composition have been reported during and after breast cancer treatment, and lower microbial diversity has been associated with greater gastrointestinal symptom burden [10–12, 16–19]. At the same time, *H. pylori* continues to be recognised as a major mediator of chronic gastric inflammation and mucosal injury through multiple inflammatory and cellular pathways [4, 13].

Despite the frequency of gastrointestinal complaints in breast cancer survivors, the histopathological basis of treatment-resistant dyspepsia in this population remains poorly defined. Most previous studies have focused on symptom burden, treatment-related toxicity or microbiome alterations rather than gastric biopsy findings. Consequently, it remains unclear whether women previously treated for breast cancer exhibit distinct gastric histopathological characteristics when compared with symptomatic women without breast cancer undergoing endoscopic evaluation for similar complaints.

Persistent gastrointestinal symptoms may negatively affect quality of life, nutritional status and survivorship outcomes in women treated for breast cancer. Better understanding of the histopathological basis of these symptoms may therefore have implications for supportive cancer care.

The present study was therefore designed to compare laboratory parameters and upper gastrointestinal histopathological findings between women who had undergone total mastectomy for breast cancer and subsequently presented with treatment-resistant dyspepsia and symptomatic female controls without breast cancer. Particular attention was given to chronic inflammation, *H. pylori* density, neutrophil activity, intestinal metaplasia, atrophy and dysplasia.

Methods

This retrospective comparative study was conducted at Giresun University Faculty of Medicine and included women who underwent upper gastrointestinal endoscopy for treatment-resistant dyspeptic symptoms between January 2022 and March 2026. The study was approved by the local ethics committee on 29 April 2026 with the approval number 29.04.2026/01. All patient data were reviewed after anonymisation and were analysed in accordance with the principles of the Declaration of Helsinki. Given the retrospective design and use of anonymised clinical data, the requirement for individual informed consent was waived by the ethics committee.

The study was designed to compare laboratory parameters and gastric biopsy findings between women previously treated for breast cancer and symptomatic women without breast cancer. The analysis was exploratory and observational; it was not intended to establish a causal relationship between breast cancer treatment and gastric mucosal pathology.

The study group consisted of women with histologically confirmed invasive ductal carcinoma of the breast who had undergone total mastectomy and subsequently underwent upper gastrointestinal endoscopy because of persistent dyspeptic symptoms. All patients in the study group had received adjuvant chemoradiotherapy as part of their oncological treatment pathway.

The control group consisted of women with no history of breast cancer who underwent upper gastrointestinal endoscopy during the same study period because of similar dyspeptic symptoms. Controls were selected from patients investigated for upper gastrointestinal complaints in routine clinical practice. Patients in the two groups were not individually matched; age was therefore assessed at baseline and included as an adjustment variable in the regression analyses.

Dyspepsia was defined clinically as persistent or recurrent upper gastrointestinal discomfort centred on the epigastrium, including epigastric pain or burning, postprandial fullness, early satiety, nausea, bloating or related upper abdominal symptoms. Symptoms were regarded as treatment-resistant when they persisted despite empirical medical treatment and were considered by the treating clinician to warrant endoscopic evaluation.

Patients were eligible if they were adult women, had undergone upper gastrointestinal endoscopy for dyspeptic symptoms, and had gastric biopsy results available. Patients with a documented history of *H. pylori* eradication treatment were excluded; no such history was identified in the final analytic cohort. Patients were also excluded when the available clinical, laboratory, or histopathological data were insufficient to reliably assign them to the study or control group. The final analytic cohort comprised 104 women, including 43 patients in the breast cancer/total mastectomy group and 61 controls.

Use of proton pump inhibitors and non-steroidal anti-inflammatory drugs was common in both groups, reflecting the treatment-resistant nature of the presenting symptoms. In routine clinical practice, patients were advised to discontinue proton pump inhibitors and non-steroidal anti-inflammatory drugs for ten days before endoscopy, whenever clinically appropriate. Because medication exposure was present in almost all patients and precise adherence to discontinuation advice could not be confirmed in all cases from the retrospective records, proton pump inhibitor and non-steroidal anti-inflammatory drug use were not included as comparative covariates in the primary statistical models.

All patients underwent upper gastrointestinal endoscopy as part of routine clinical care for persistent dyspeptic symptoms. Endoscopic examinations were performed by experienced endoscopists according to the local departmental protocol. The macroscopic appearance of the oesophagus, stomach and duodenum was assessed, and gastric mucosal biopsies were obtained for histopathological evaluation.

The department's standard gastric biopsy protocol consisted of biopsies from the antrum, incisura angularis and corpus. Where full mapping was performed, the sampling pattern followed the Updated Sydney approach: two biopsies from the antrum, one from the incisura angularis and two from the gastric corpus, with antrum/incisura and corpus specimens submitted in separately labelled containers when required by the pathology workflow. Any macroscopically suspicious lesion, focal ulceration, nodularity, mucosal irregularity or area of abnormal vascularity was biopsied separately at the discretion of the endoscopist.

Endoscopic biopsy specimens were fixed in formalin, embedded in paraffin and examined by the pathology department according to routine histopathological procedures. Haematoxylin and eosin staining was used for general mucosal assessment. *H. pylori* was assessed according to the department's standard protocol, using routine histology and modified Giemsa staining where indicated by local practice. Immunohistochemistry was reserved for equivocal cases or cases with persistent histological suspicion despite low organism density, according to the reporting pathologist's judgement.

The following histopathological variables were extracted from the biopsy reports: chronic inflammation, neutrophil activity, intestinal metaplasia, *H. pylori* density, glandular atrophy and dysplasia. Findings were recorded on an ordinal scale of 0–3, where 0 indicated the absence of the finding and higher scores indicated increasing severity or density. For statistical analysis, each biopsy variable was assessed both as an ordinal severity score and as a binary outcome indicating the presence of any abnormality (defined as a score > 0). For *H. pylori*, the final analysis was based on the histopathological density score reported in the pathology record. No patient had a documented previous history of *H. pylori* eradication therapy.

Demographic and laboratory data were extracted from the reviewed study database. Laboratory values recorded closest to the time of endoscopic assessment were used. The following variables were available for comparison between the study and control groups: age, leukocyte count, haemoglobin, haematocrit, mean corpuscular volume, platelet count, lymphocyte count or percentage, glucose, urea, creatinine, alanine aminotransferase, aspartate aminotransferase, albumin, sodium, potassium, calcium, C-reactive protein, prothrombin time and international normalised ratio. Laboratory units were checked and standardised before analysis.

Outcomes

The primary outcomes were the ordinal gastric biopsy scores for chronic inflammation, neutrophil activity, intestinal metaplasia, *H. pylori* density, atrophy and dysplasia. Secondary outcomes included the corresponding binary biopsy outcomes and routinely measured laboratory parameters.

The main purpose of the analysis was to determine whether women who had undergone total mastectomy for breast cancer and later presented with treatment-resistant dyspepsia showed a distinct laboratory or histopathological pattern compared with symptomatic women without breast cancer.

Statistical analysis

Continuous variables were inspected for distributional form and tested for normality using the Shapiro–Wilk test. Because most continuous variables were not normally distributed, data were summarised as median with interquartile range. Between-group comparisons for continuous variables were performed using two-sided Mann–Whitney U tests. Hodges–Lehmann median differences were calculated as the study group minus the control group, with 95% confidence intervals estimated by percentile bootstrap resampling using 4,000 iterations.

Histopathological biopsy scores were analysed as ordinal variables (0–3) and as binary indicators of any abnormality. Ordinal biopsy scores were compared between groups using two-sided Mann–Whitney U tests. Binary biopsy outcomes were compared using Fisher’s exact test. Risk differences were calculated as the study group minus the control group, with Newcombe–Wilson 95% confidence intervals.

Age-adjusted proportional-odds logistic regression models were fitted for ordinal biopsy outcomes when the outcome had sufficient variation across categories. These models included group allocation and age as covariates. Odds ratios greater than 1 indicated higher odds of a more severe histopathological score in the breast cancer/total mastectomy group. Dysplasia was not modelled because no dysplasia was detected in either group.

Multiplicity was handled using the Benjamini–Hochberg false-discovery-rate procedure. Adjustment was applied within clinically related families of comparisons: laboratory variables and biopsy outcomes. Two-sided p values below 0.05 were considered statistically significant, and false-discovery-rate-adjusted q values below 0.05 were interpreted as statistically robust within the corresponding outcome family.

Complete-case analysis was used for each variable. No imputation was undertaken. Because the sample size was determined by the number of eligible patients in the retrospective dataset, no formal a priori sample size calculation was performed.

All analyses were performed using Python 3.13.5 in 2026. The main packages used were pandas 2.2.3, NumPy 2.3.5, SciPy 1.17.0, statsmodels 0.14.6, Matplotlib 3.10.8 and openpyxl 3.1.5.

Results

The final analytic cohort included 104 women: 43 in the breast cancer/total mastectomy group and 61 in the control group. All patients contributed endoscopic biopsy data, and laboratory analyses were complete.

The groups were similar in age. Median age was 60.0 [53.0–66.5] years in the study group and 57.0 [48.0–70.0] years in the control group ($p = 0.646$; $q = 0.852$). Baseline laboratory results are summarised in Table 1. After false-discovery-rate adjustment, albumin was lower in the study group than in controls (44.8 [42.0–46.1] versus 47.0 [43.6–50.0] g/L; Hodges–Lehmann difference, -3.0 g/L; 95% CI, -4.5 to -1.3 ; $p = 0.001$; $q = 0.020$). No other laboratory variable met the prespecified $q < 0.05$ threshold.

Table 1
Baseline demographic and laboratory variables

Variable	Study group (n = 43)	Control group (n = 61)	Difference (95% CI)	p value	q value
Age, years	60.0 [53.0–66.5]	57.0 [48.0–70.0]	1.0 (-4.0 to 7.0)	0.646	0.852
Leukocyte count, $\times 10^3/\mu\text{L}$	6.00 [5.06–8.39]	6.70 [5.70–7.90]	-0.43 (-1.12 to 0.43)	0.218	0.533
Haemoglobin, g/dL	12.6 [11.9–13.4]	12.6 [11.7–14.0]	-0.1 (-0.7 to 0.5)	0.734	0.871
Haematocrit, %	39.1 [37.0–41.0]	38.3 [34.9–41.8]	0.4 (-1.3 to 2.1)	0.673	0.852
Mean corpuscular volume, fL	88.5 [83.5–91.4]	85.6 [81.2–87.9]	3.2 (0.7 to 5.5)	0.013	0.098
Platelet count, $\times 10^3/\mu\text{L}$	252.0 [200.0–286.5]	269.0 [218.0–308.0]	-16.0 (-44.0 to 11.0)	0.244	0.533
Lymphocyte count, $\times 10^3/\mu\text{L}$	1.80 [1.48–2.46]	2.00 [1.69–2.40]	-0.12 (-0.34 to 0.14)	0.325	0.618
Glucose, mg/dL	101.0 [93.5–120.5]	100.0 [90.0–108.0]	6.0 (-2.0 to 14.0)	0.151	0.478
Urea, mg/dL	28.2 [23.0–36.5]	28.0 [23.0–37.0]	0.0 (-4.0 to 4.0)	0.982	0.982
Creatinine, mg/dL	0.69 [0.65–0.78]	0.70 [0.60–0.80]	0.00 (-0.05 to 0.05)	0.957	0.982
Alanine aminotransferase, U/L	19.0 [13.0–25.2]	15.0 [11.0–19.0]	4.0 (0.4 to 7.0)	0.021	0.098
Aspartate aminotransferase, U/L	21.0 [17.5–24.0]	18.0 [16.0–21.0]	2.0 (0.0 to 4.0)	0.019	0.098
Albumin, g/L	44.8 [42.0–46.1]	47.0 [43.6–50.0]	-3.0 (-4.5 to -1.3)	0.001	0.020
Sodium, mmol/L	140.0 [138.5–143.0]	141.0 [140.0–141.0]	0.0 (-1.0 to 1.0)	0.481	0.831
Potassium, mmol/L	4.49 [4.20–4.72]	4.50 [4.10–4.80]	0.00 (-0.20 to 0.13)	0.837	0.936
Calcium, mg/dL	9.7 [9.4–9.9]	9.6 [9.3–9.9]	0.1 (-0.1 to 0.3)	0.252	0.533
C-reactive protein, mg/L	2.79 [1.73–4.89]	1.50 [0.70–3.90]	0.91 (0.10 to 1.76)	0.041	0.156
Prothrombin time, s	8.8 [8.6–10.7]	9.3 [8.7–10.6]	-0.1 (-0.5 to 0.3)	0.588	0.852

Variable	Study group (n = 43)	Control group (n = 61)	Difference (95% CI)	p value	q value
International normalised ratio	0.96 [0.92–1.03]	1.00 [0.90–1.00]	0.02 (-0.03 to 0.05)	0.535	0.848

Values are median [interquartile range]. The difference is the Hodges–Lehmann median difference, calculated as the study group minus the control group. Confidence intervals were estimated by percentile bootstrap resampling. p values are from two-sided Mann–Whitney U tests. q values are Benjamini–Hochberg false-discovery-rate-adjusted p values within the laboratory family.

Histopathological score distributions are shown in Table 2. Chronic inflammation scores differed between groups, with median scores of 2.0 [1.0–2.0] in the study group and 1.0 [1.0–1.0] in controls (ordinal p < 0.001; q < 0.001). *H. pylori* density scores also differed between groups, with median scores of 2.0 [0.0–3.0] and 0.0 [0.0–1.0], respectively (ordinal p < 0.001; q < 0.001). The distributions of chronic inflammation and *H. pylori* density are displayed in Figs. 1 and 2.

Table 2
Ordinal histopathological biopsy scores

Variable	Study median [IQR]	Control median [IQR]	Study score distribution 0/1/2/3	Control score distribution 0/1/2/3	Ordinal p value	Ordinal q value
Chronic inflammation	2.0 [1.0–2.0]	1.0 [1.0–1.0]	0/17/19/7	15/31/12/3	< 0.001	< 0.001
Neutrophil activity	0.0 [0.0–1.5]	0.0 [0.0–1.0]	22/10/7/4	42/8/8/3	0.087	0.173
Intestinal metaplasia	0.0 [0.0–0.0]	0.0 [0.0–0.0]	38/3/0/2	53/8/0/0	0.899	1.000
<i>H. pylori</i> density	2.0 [0.0–3.0]	0.0 [0.0–1.0]	17/3/10/13	45/16/0/0	< 0.001	< 0.001
Atrophy	0.0 [0.0–0.0]	0.0 [0.0–0.0]	41/2/0/0	57/4/0/0	0.689	1.000
Dysplasia	0.0 [0.0–0.0]	0.0 [0.0–0.0]	43/0/0/0	61/0/0/0	1.000	1.000

Scores are recorded on a 0–3 ordinal scale, where 0 denotes absence and higher values denote greater severity or density. p values are from two-sided Mann–Whitney U tests. q values are Benjamini–Hochberg false-discovery-rate-adjusted p values within the ordinal biopsy family.

[Figure 1 near here]

Figure 1. Distribution of chronic inflammation scores by group. Bars show the percentage of patients in each histopathological score category. Score 0 denotes absence; scores 1–3 denote increasing severity.

[Figure 2 near here]

Figure 2. Distribution of *H. pylori* density scores by group. Bars show the percentage of patients in each histopathological score category. Score 0 denotes no organisms detected; scores 1–3 denote increasing density.

The corresponding binary biopsy outcomes are presented in Table 3. Chronic inflammation was recorded in 43 of 43 patients in the study group and 46 of 61 controls (100.0% versus 75.4%; risk difference, 24.6%; 95% CI, 12.4 to 36.7; $p < 0.001$; $q = 0.002$). *H. pylori* was detected in 26 of 43 patients in the study group and 16 of 61 controls (60.5% versus 26.2%; risk difference, 34.2%; 95% CI, 15.0 to 50.4; $p < 0.001$; $q = 0.002$). Neutrophil activity, intestinal metaplasia, and atrophy did not differ after adjustment for multiplicity. Dysplasia was not recorded in either group.

Table 3
Binary histopathological outcomes

Variable	Study group	Control group	Risk difference (95% CI)	p value	q value
Chronic inflammation	43/43 (100.0%)	46/61 (75.4%)	24.6% (12.4 to 36.7)	< 0.001	0.002
Neutrophil activity	21/43 (48.8%)	19/61 (31.1%)	17.7% (-1.2 to 35.4)	0.101	0.202
Intestinal metaplasia	5/43 (11.6%)	8/61 (13.1%)	-1.5% (-14.0 to 12.8)	1.000	1.000
<i>H. pylori</i> density	26/43 (60.5%)	16/61 (26.2%)	34.2% (15.0 to 50.4)	< 0.001	0.002
Atrophy	2/43 (4.7%)	4/61 (6.6%)	-1.9% (-11.6 to 9.6)	1.000	1.000
Dysplasia	0/43 (0.0%)	0/61 (0.0%)	0.0% (-5.9 to 8.2)	1.000	1.000

Binary outcomes indicate any recorded finding, defined as a score greater than 0. Risk differences are the study group minus the control group. Confidence intervals are Newcombe–Wilson 95% confidence intervals. p values are from Fisher’s exact test. q values are Benjamini–Hochberg false-discovery-rate-adjusted p values within the binary biopsy family.

Age-adjusted proportional-odds models are shown in Table 4 and Fig. 3. In these models, the study group had higher odds of a greater chronic inflammation score (adjusted odds ratio, 5.62; 95% CI, 2.51 to 12.58; $p < 0.001$; $q < 0.001$) and a greater *H. pylori* density score (adjusted odds ratio, 7.83; 95% CI, 3.33 to 18.37; $p < 0.001$; $q < 0.001$). Age-adjusted models for neutrophil activity, intestinal metaplasia and

atrophy did not meet the false-discovery-rate-adjusted significance threshold. Dysplasia was not modelled because all scores were zero.

Table 4
Age-adjusted proportional-odds models for ordinal biopsy scores

Variable	N	Adjusted odds ratio (95% CI)	p value	q value
Chronic inflammation	104	5.62 (2.51 to 12.58)	< 0.001	< 0.001
Neutrophil activity	104	2.01 (0.92 to 4.40)	0.081	0.135
Intestinal metaplasia	104	0.95 (0.29 to 3.17)	0.936	0.936
<i>H. pylori</i> density	104	7.83 (3.33 to 18.37)	< 0.001	< 0.001
Atrophy	104	0.69 (0.12 to 3.98)	0.680	0.850
Dysplasia	104	Not estimable	—	—

Models included study group and age as covariates. Odds ratios greater than 1 indicate higher odds of a more severe ordinal score in the study group. Dysplasia was not estimable because all recorded scores were zero. q values are Benjamini–Hochberg false-discovery-rate-adjusted p values within the age-adjusted ordinal-model family.

[Fig. 3 near here]

Figure 3. Age-adjusted odds ratios from proportional-odds models for ordinal biopsy scores. Odds ratios are plotted on a logarithmic scale. Horizontal bars show 95% confidence intervals. The vertical reference line indicates an odds ratio of 1.

Discussion

The most clinically relevant finding of the present study was the markedly higher prevalence and density of *Helicobacter pylori* infection among breast cancer survivors who presented with treatment-resistant dyspepsia. In addition, these patients demonstrated significantly greater chronic gastric inflammation than symptomatic controls without breast cancer. Both findings remained significant after adjustment for age and correction for multiple comparisons, suggesting that the observed differences were robust and unlikely to be explained by chance alone. By contrast, no significant differences were identified in intestinal metaplasia, glandular atrophy, dysplasia or neutrophil activity. Taken together, these results indicate that the distinctive gastric biopsy pattern observed in the breast cancer group was driven primarily by increased *H. pylori* burden and chronic inflammatory activity rather than by advanced premalignant mucosal alterations.

From a clinical perspective, these findings are important because persistent dyspeptic symptoms in breast cancer survivors are often attributed to treatment-related adverse effects, functional

gastrointestinal disorders or psychosocial factors. The present results suggest that a substantial proportion of symptomatic patients may also harbour histologically demonstrable and potentially treatable gastric pathology, particularly *H. pylori*-associated chronic gastritis. Consequently, careful endoscopic evaluation and systematic histopathological assessment may provide clinically relevant information in selected breast cancer survivors with refractory upper gastrointestinal symptoms. Beyond symptom control, identification of potentially treatable gastric pathology may also have implications for nutritional status, quality of life and survivorship care in breast cancer patients.

The main value of these findings is that they move the discussion of dyspepsia in breast cancer survivors beyond symptoms alone. Persistent upper gastrointestinal complaints after cancer treatment are easily attributed to anxiety, medication exposure, functional dyspepsia, chemotherapy-related nausea or the broad burden of survivorship. Those explanations may be relevant, but the present data show that a biopsy-based diagnosis may reveal a measurable mucosal pattern. In this cohort, that pattern was not one of dysplasia or established premalignant change; it was driven by chronic inflammation and *H. pylori* density. This distinction is clinically important because *H. pylori*-associated gastritis is a treatable condition, whereas functional dyspepsia is usually managed through symptom control and longer-term follow-up.

The higher *H. pylori* burden in the study group is especially noteworthy. *H. pylori* remains one of the best-established causes of chronic gastritis, and recent reviews continue to emphasise its ability to drive chronic inflammation, epithelial injury, oxidative stress, DNA damage and multiple inflammatory signalling pathways in the gastric mucosa [4]. A 2025 review in Journal of Hematology & Oncology describes *H. pylori* as a major aetiological factor in gastric carcinogenesis and summarises mechanisms involving NF- κ B, STAT3, Hippo and Wnt/ β -catenin signalling, together with chronic inflammation and oxidative injury [13]. In the present study, however, the absence of significant differences in intestinal metaplasia, atrophy, or dysplasia suggests that the observed group difference should be interpreted as an inflammatory and microbial finding rather than as evidence of a more advanced precancerous gastric phenotype.

It is also important not to overstate the role of total mastectomy itself. Total mastectomy does not alter gastric anatomy, acid secretion, intestinal continuity or nutrient absorption. It is therefore unlikely to cause chronic gastritis through a direct surgical mechanism. The more plausible explanation lies in the wider treatment and survivorship context. Patients undergoing surgery for breast cancer are exposed to a sequence of physiological stresses: oncological treatment, systemic inflammation, altered nutritional intake, analgesics, antibiotics, proton pump inhibitors, non-steroidal anti-inflammatory drugs and, in many cases, changes in ovarian or endocrine function. These factors may not independently cause gastric disease, but they may lower the threshold at which an existing mucosal or microbial condition becomes symptomatic. Recent breast cancer literature supports this broader view. Gastrointestinal symptoms are common during chemotherapy, and inflammatory mediators have been linked to symptom trajectories in women receiving treatment for early-stage breast cancer. Arcos and colleagues reported that gastrointestinal symptoms in breast cancer patients undergoing chemotherapy negatively

affected quality of life and that baseline inflammatory markers, including interleukin-8, were associated with later gastrointestinal symptom progression [14]. Brown and colleagues have also discussed chemotherapy-induced inflammation as a systemic process that may involve the gut, liver and central nervous system rather than the gastrointestinal tract alone [15]. This is relevant to the present findings because dyspepsia after breast cancer treatment may arise from the meeting point of mucosal inflammation, systemic inflammatory tone and altered sensory processing.

The microbiome provides another biologically plausible bridge. Several recent studies have shown that breast cancer and its treatment may be associated with changes in intestinal microbial composition. Terrisse and colleagues reported that intestinal microbiota may influence both clinical outcome and side effects during early breast cancer treatment [16]. Aarnoutse and colleagues examined postmenopausal women with oestrogen receptor-positive breast cancer treated with neoadjuvant chemotherapy and explored associations between intestinal microbiota, toxicity and treatment response [17]. Wu and colleagues similarly reported longitudinal changes in the gut microbiome of breast cancer patients during the first year of chemotherapy [18]. These studies do not specifically address gastric *H. pylori* density, but they support the broader concept that breast cancer treatment may reshape host–microbial relationships. In that setting, a stronger *H. pylori* signal in symptomatic post-mastectomy patients is clinically plausible and deserves prospective evaluation.

The lower albumin concentration observed in the breast cancer group should be interpreted cautiously. Although the difference remained statistically significant after adjustment for multiple comparisons, albumin is a non-specific biomarker influenced by nutritional status, systemic inflammation, hepatic protein synthesis, hydration and overall physiological reserve. Therefore, the observed reduction in albumin cannot be regarded as a direct marker of gastric pathology. Instead, it may reflect differences in the overall clinical characteristics of the study population. Previous studies have demonstrated associations between cancer treatment, nutritional vulnerability, systemic inflammation and gastrointestinal symptom burden in breast cancer patients, which may contribute to variations in serum albumin levels. However, the present study was not designed to determine the underlying cause of the observed albumin difference, and causal inferences should therefore be avoided [12, 14, 15].

The mechanisms underlying the increased chronic inflammation and higher *Helicobacter pylori* density observed in the breast cancer group remain uncertain. Total mastectomy itself is unlikely to directly alter gastric anatomy or physiology. A more plausible explanation is that breast cancer survivorship represents a complex clinical context involving systemic treatment exposure, inflammatory activation, nutritional changes, medication use and potential alterations in host–microbial interactions [14–19]. Previous studies have demonstrated that chemotherapy and related oncological treatments may influence gastrointestinal symptoms, inflammatory pathways and gut microbiota composition in breast cancer patients [10–12, 14–19].

Recent experimental and translational studies have also suggested that oestrogen-responsive pathways, including G protein-coupled oestrogen receptor (GPER) signalling, may contribute to gastrointestinal

mucosal biology and inflammatory regulation [20–23]. In addition, growing interest has focused on the estrobolome and its potential role in host–microbial interactions during breast cancer treatment [24, 25]. However, the present study did not include hormonal analyses, receptor expression studies or microbiome profiling. Therefore, these mechanisms should be regarded as biologically plausible hypotheses rather than causal explanations for the observed histopathological findings.

Taken together, the current results support an association between breast cancer survivorship and increased chronic gastric inflammation and *H. pylori* burden in women with treatment-resistant dyspepsia, while the underlying biological pathways remain to be clarified in future prospective mechanistic studies.

Study strengths and limitations

The present study has several strengths. The comparison was made between two symptomatic groups undergoing endoscopy for similar clinical indications, rather than between symptomatic patients and healthy controls. The analysis was based on objective histopathological biopsy findings, and biopsy variables were evaluated both as ordinal severity scores and as binary clinical outcomes. In addition, age-adjusted proportional-odds models and false-discovery-rate correction were used to reduce the risk of overinterpreting chance findings.

Several limitations should also be stated clearly. First, the study was retrospective, and the sample size was modest. Second, the groups were not individually matched, and residual confounding remains possible despite age adjustment. Third, exposure to proton pump inhibitors and non-steroidal anti-inflammatory drugs was common, and adherence to pre-endoscopy discontinuation advice could not be verified in all patients. Fourth, several potentially important oncological and treatment-related variables were not available in sufficient detail for analysis, including chemotherapy regimen, cumulative chemotherapy exposure, endocrine therapy status, menopausal status, time interval between breast cancer treatment and endoscopic assessment, radiotherapy details, corticosteroid exposure and antibiotic exposure. Each of these factors may influence gastrointestinal symptoms, gastric mucosal inflammation, *H. pylori* detection, nutritional status or host–microbial interactions. Fifth, *H. pylori* status was based on histopathological assessment rather than a combined diagnostic strategy including urea breath testing, stool antigen testing or molecular resistance testing. Finally, the study did not include gastric immunohistochemistry for ER α , ER β or GPER, circulating oestradiol or gonadotrophin levels, gastric microbiome profiling or formal symptom-severity instruments. Therefore, residual confounding cannot be excluded, and the present findings should be interpreted as associative and hypothesis-generating rather than causal.

Conclusions

This study suggests an association between breast cancer survivorship and increased chronic gastric inflammation and *H. pylori* burden in women presenting with treatment-resistant dyspepsia. These

findings indicate that persistent upper gastrointestinal symptoms in breast cancer survivors may not be solely functional or treatment-related and may occasionally reflect potentially treatable gastric pathology. Greater recognition of this possibility may contribute to more individualised supportive care and survivorship management.

Future prospective studies should include detailed oncological variables, menopausal status, endocrine therapy, time since chemotherapy, medication exposure, validated dyspepsia scores and post-eradication symptom outcomes. Mechanistic studies may also evaluate gastric oestrogen-receptor signalling and host–microbial interactions, including GPER-related pathways and microbiome or estrobolome profiles, to clarify whether these factors contribute to gastric mucosal inflammation in breast cancer survivors.

Abbreviations

CI

confidence interval

CRP

C-reactive protein

FDR

false discovery rate

GPER

G protein-coupled oestrogen receptor

INR

international normalised ratio

IQR

interquartile range

NSAID

non-steroidal anti-inflammatory drug

OR

odds ratio

PPI

proton pump inhibitor

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the Ethics Committee of Giresun University Faculty of Medicine (Approval No. 29.04.2026/01). The requirement for individual informed consent was waived by the ethics committee because the study involved retrospective analysis of anonymised clinical data. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

BA conceptualised and supervised the study and critically reviewed the manuscript. AM designed the study, collected and processed the data, and drafted the manuscript. EY analysed and interpreted the data and reviewed the literature. AR collected and processed the data and reviewed the literature. GA and ACD contributed resources, and ACD provided study materials. All authors read and approved the final manuscript.

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Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available because of participant confidentiality but are available from the corresponding author on reasonable request, subject to applicable ethics committee and institutional requirements.

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Figures

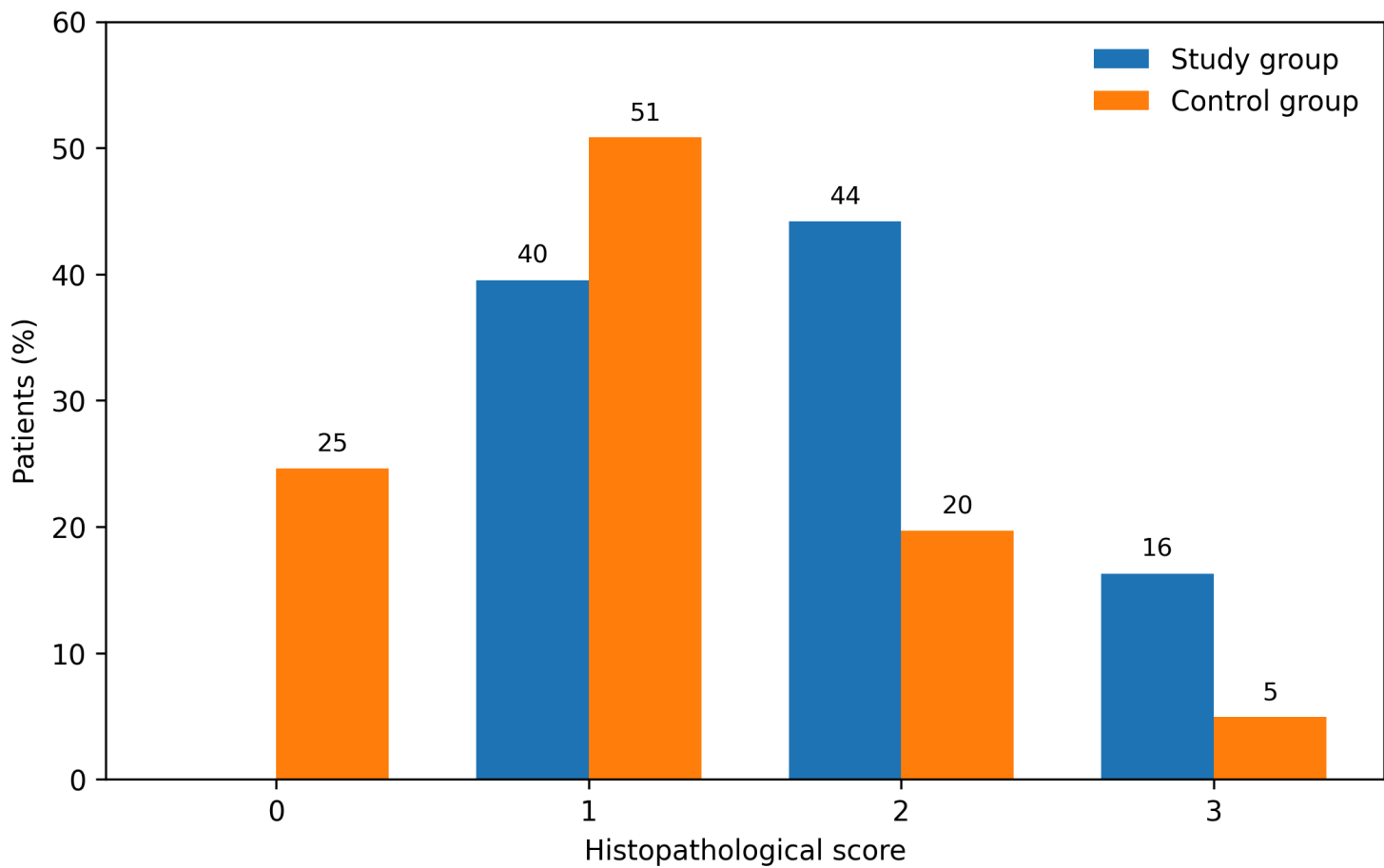


Figure 1

Distribution of chronic inflammation scores by group. Bars show the percentage of patients in each histopathological score category. Score 0 denotes absence; scores 1-3 denote increasing severity.

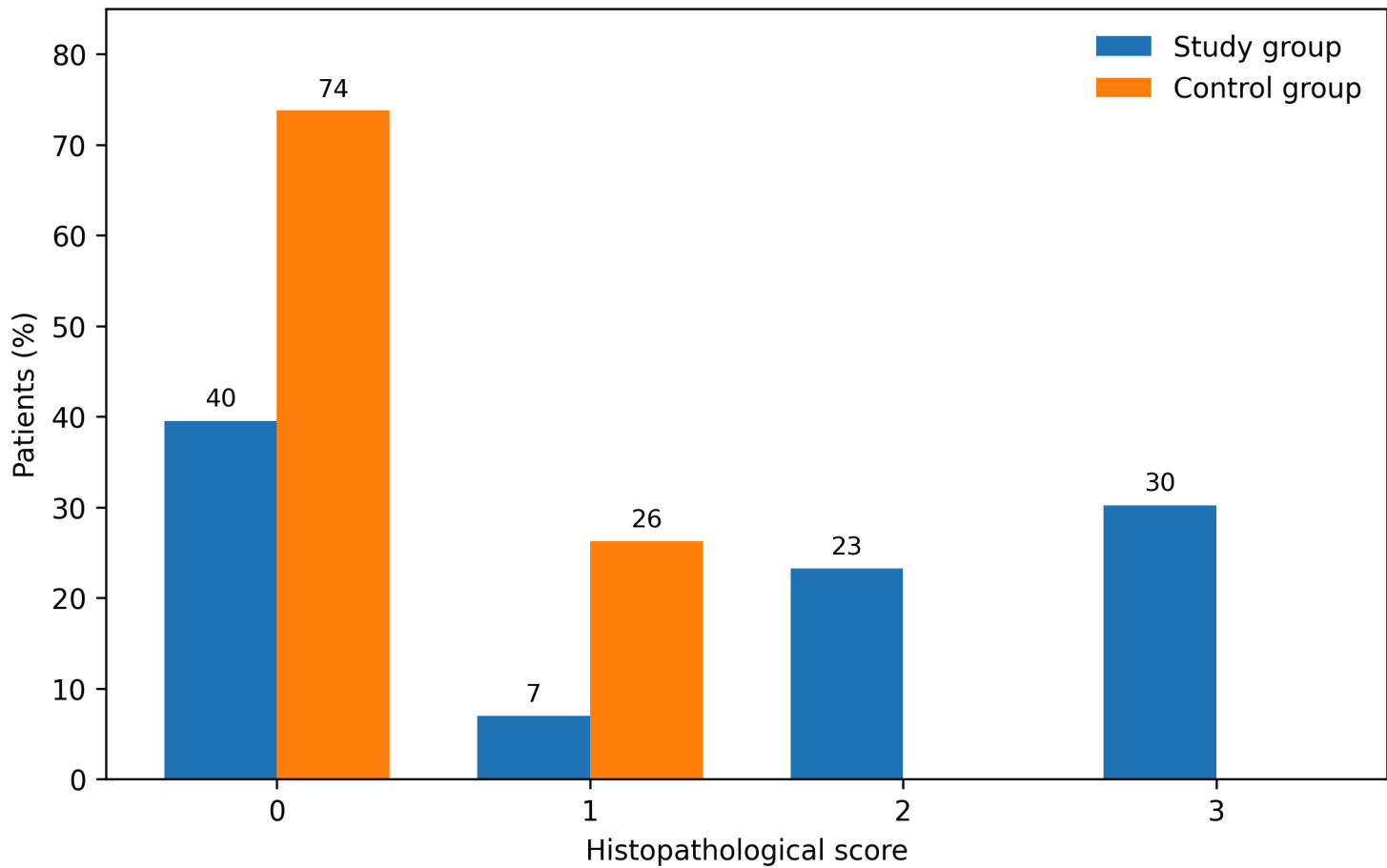


Figure 2

Distribution of *H. pylori* density scores by group. Bars show the percentage of patients in each histopathological score category. Score 0 denotes no organisms detected; scores 1-3 denote increasing density.

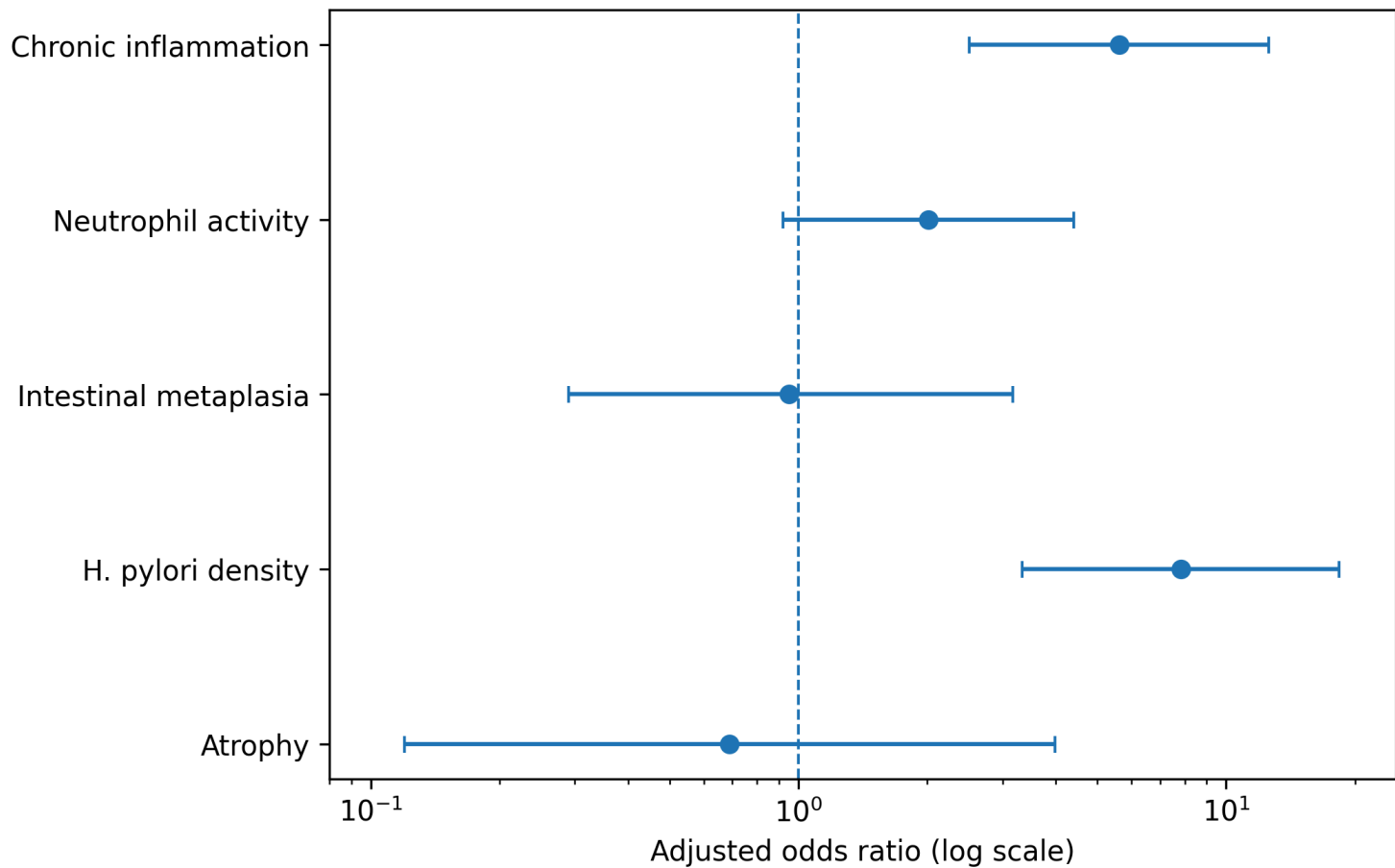


Figure 3

Age-adjusted odds ratios from proportional-odds models for ordinal biopsy scores. Odds ratios are plotted on a logarithmic scale. Horizontal bars show 95% confidence intervals. The vertical reference line indicates an odds ratio of 1.