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Age- and Sex-Related Endoscopic Gastric Changes in Patients with Ischemic Heart Disease: A Cross-Sectional Study

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Research Article

Keywords: ischemic heart disease, gastric hyperemia, atrophic gastritis, endoscopy, gastrointestinal pathology

Posted Date: July 25th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9956373/v1

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Additional Declarations: No competing interests reported.

Abstract

Ischemic heart disease (IHD) is associated with systemic vascular dysfunction, chronic inflammation, and tissue hypoxia, which may contribute to upper gastrointestinal mucosal injury. However, the relationship between IHD duration and specific endoscopic gastric abnormalities remains insufficiently explored.

Aim: To evaluate the association between IHD duration and upper gastrointestinal endoscopic findings after adjustment for age and sex.

Methods: This retrospective cross-sectional study included 2,924 patients with IHD who underwent upper gastrointestinal endoscopy. Patients were stratified according to disease duration (≤1 year and >1 year). Endoscopic findings included gastric atrophy, hyperemia, hyperplasia, and esophagitis. Multivariable logistic regression was used to estimate adjusted odds ratios (OR) with 95% confidence intervals (CI).

Results: Gastric hyperemia was significantly associated with IHD duration (OR = 1.79, 95% CI: 1.05–3.05, p = 0.033). No significant associations were observed for gastric atrophy, hyperplasia, or esophagitis. Age was a strong independent predictor of gastric atrophy, hyperplasia, and esophagitis (p < 0.001). Female sex was inversely associated with gastric hyperemia (OR = 0.48, 95% CI: 0.31–0.73, p = 0.001).

Conclusion: IHD duration is independently associated only with gastric hyperemia, whereas age is the dominant determinant of most gastric mucosal changes. These findings highlight the importance of age-related gastrointestinal vulnerability in patients with IHD.

Introduction

Ischemic heart disease remains one of the leading causes of morbidity and mortality worldwide and is frequently associated with systemic vascular dysfunction, endothelial impairment, chronic inflammation, and tissue hypoxia [1,2,10]. Gastrointestinal manifestations, particularly inflammatory and erosive lesions of the stomach and duodenum, are increasingly recognized in patients with cardiovascular disease [4,8].

Autonomic and neurohumoral dysregulation accompanying chronic coronary syndromes may aggravate gastric mucosal injury through alterations in microcirculation, inflammatory signaling, and mucosal defense mechanisms [4,5]. Furthermore, age-related deterioration of gastric mucosal integrity may increase susceptibility to endoscopic abnormalities in patients with IHD [6,7]. However, the independent effect of IHD duration on specific endoscopic gastric abnormalities remains insufficiently studied, particularly after adjustment for age and sex.

Therefore, this study aimed to evaluate the association between IHD duration and upper gastrointestinal endoscopic findings using multivariable logistic regression.

The purpose of research: to assess the association between the duration of ischemic heart disease and upper gastrointestinal endoscopic changes while accounting for the effects of age and sex.

Material and Methods

This retrospective cross-sectional study included 2,924 patients diagnosed with ischemic heart disease who underwent upper gastrointestinal endoscopy at the Republican Specialized Scientific and Practical Medical Center of Cardiology between January 2017 and December 2018.

Patients were divided into two groups according to disease duration: ≤1 year and >1 year.

Upper gastrointestinal endoscopy was performed using FUJINON 2500 and PENTAX 5000 (Japan) systems following standard diagnostic protocols. Gastric atrophy, hyperemia, hyperplasia, and esophagitis were evaluated.

Continuous variables were expressed as mean ± standard deviation. Group comparisons were performed using Student's t-test, while categorical variables were analyzed using Pearson's chi-square test.

Multivariable logistic regression analysis was used to determine independent associations between IHD duration, age, sex, and endoscopic findings. Results were reported as OR with 95% CI. Statistical significance was defined as $p < 0.05$. All analyses were performed using STATA version 15.0.

RESULTS

The study included 2,924 patients with ischemic heart disease, of whom 414 (14.2%) had a disease duration of ≤ 1 year and 2,510 (85.8%) had a duration of > 1 year. Patients with longer disease duration were significantly older than those with disease duration ≤ 1 year (61.65 vs. 54.14 years, $t = -16.10$, $p < 0.001$). In addition, sex distribution differed significantly between the groups. Female patients accounted for a greater proportion of the > 1-year group compared with the ≤ 1-year group (36.6% vs. 20.8%, $\chi^2 = 39.53$, $p < 0.001$) (Table 1).

Table 1
Baseline Characteristics of Patients According to IHD Duration

Variable	≤ 1 year (n = 414)	> 1 year (n = 2510)	Test statistic	p-value
Age, years (mean)	54.14	61.65	t = -16.10	< 0.001
Male, n (%)	328 (79.2)	1591 (63.4)	$\chi^2 = 39.53$	< 0.001
Female, n (%)	86 (20.8)	919 (36.6)		

Logistic Regression Analysis of Gastric Atrophy

The independent association between ischemic heart disease (IHD) duration, age, sex, and the presence of gastric atrophy was assessed using multivariable logistic regression (Table 2).

Table 2
Multivariable Logistic Regression of Gastric Atrophy

Variable	OR	Std. Error	z-value	p-value	95% CI
IHD duration (≤ 1 vs > 1 year)	1.06	0.38	0.15	0.881	0.52–2.16
Age (per year)	1.15	0.013	12.43	< 0.001	1.13–1.18
Sex (female vs male)	1.19	0.22	0.97	0.33	0.84–1.70
Intercept	–	–	–15.12	< 0.001	–

The results indicated that age was a strong and statistically significant predictor of gastric atrophy (OR = 1.15 per year increase, 95% CI: 1.128–1.180, $p < 0.001$). In contrast, neither IHD duration (≤ 1 year vs > 1 year; OR = 1.056, 95% CI: 0.518–2.155, $p = 0.881$) nor sex (OR = 1.194, 95% CI: 0.836–1.704, $p = 0.33$) showed a statistically significant independent association with gastric atrophy.

The model showed a pseudo R-squared of 0.168, indicating a moderate goodness-of-fit. The likelihood ratio chi-square test confirmed that the model was statistically significant overall ($\chi^2 = 194.10$, $p < 0.001$). These findings suggest that age, rather than IHD duration or sex, is the primary factor associated with the presence of gastric atrophy in patients with IHD.

Prevalence and Logistic Regression Analysis of Gastric Hyperemia

The prevalence of gastric hyperemia differed significantly according to the duration of ischemic heart disease (IHD) (Table 3). Among patients with an IHD duration of ≤ 1 year (n = 414), 21 (5.1%) had hyperemia, whereas among patients with IHD duration > 1 year (n = 2,510), 72 (2.9%) had hyperemia. Pearson's chi-square test confirmed a statistically significant association between IHD duration and the presence of hyperemia ($\chi^2 = 5.61$, $p = 0.018$). Multivariable logistic regression was conducted to evaluate independent associations between IHD duration, age, sex, and hyperemia (Table 3).

Table 3
Multivariable Logistic Regression Analysis of Factors Associated with Gastric Hyperemia.

Variable	Adjusted OR	95% CI	z-value	p-value
IHD duration (> 1 year vs ≤ 1 year)	1.79	1.05–3.05	2.13	0.033
Age (per 1-year increase)	1.02	1.00–1.04	1.59	0.112
Female sex (vs male)	0.48	0.31–0.73	-3.39	0.001

Adjusted for age, sex, and IHD duration. OR > 1 indicates increased odds of gastric hyperemia, whereas OR < 1 indicates decreased odds.

The analysis showed that:

- IHD duration was significantly associated with hyperemia; patients with longer IHD duration had higher odds of hyperemia (OR = 1.79, 95% CI: 1.05–3.05, p = 0.033).
- Sex was also a significant predictor, with female patients showing lower odds of hyperemia compared to male patients (OR = 0.48, 95% CI: 0.31–0.73, p < 0.001).
- Age was not a significant predictor in this model (OR = 1.02, 95% CI: 0.996–1.044, p = 0.112).

The logistic regression model was statistically significant overall (likelihood ratio $\chi^2 = 17.34$, p = 0.001), but the pseudo R^2 was low (0.021), indicating that additional factors may influence the presence of hyperemia.

Although the crude prevalence of gastric hyperemia was lower in patients with longer IHD duration (2.9% vs. 5.1%), multivariable adjustment for age and sex revealed a significant positive association between prolonged IHD duration and gastric hyperemia, suggesting confounding by demographic factors. This finding suggests the presence of confounding effects related to demographic characteristics.

Prevalence and Multivariable Analysis of Gastric Hyperplasia

The prevalence of gastric hyperplasia was low in the study population and did not differ significantly according to the duration of ischemic heart disease (IHD) (Table 4).

Table 4
Multivariable Logistic Regression Analysis of Gastric Hyperplasia.

Variable	Adjusted OR	95% CI	z-value	p-value
IHD duration (> 1 year vs ≤ 1 year)	1.45	0.51–4.17	0.70	0.486
Age (per 1-year increase)	1.04	1.01–1.08	2.55	0.011
Sex (female vs male)	0.86	0.47–1.56	-0.51	0.613

n = 2,924; LR χ² = 8.37; p = 0.039; Pseudo R² = 0.017; AIC = 505.64; BIC = 529.56.

Hyperplasia was observed in 4 patients (1.0%) in the ≤ 1 year group and in 46 patients (1.8%) in the > 1 year group. Pearson's chi-square test showed no statistically significant association between IHD duration and gastric hyperplasia (χ² = 1.59, p = 0.208).

In multivariable logistic regression analysis, IHD duration was not significantly associated with gastric hyperplasia after adjustment for age and sex (OR = 1.45, 95% CI: 0.51–4.17, p = 0.486). However, age was identified as a significant independent predictor, with each additional year of age increasing the odds of gastric hyperplasia (OR = 1.04, 95% CI: 1.01–1.08, p = 0.011). Sex was not significantly associated with hyperplasia (OR = 0.86, 95% CI: 0.47–1.56, p = 0.613).

The overall model was statistically significant (χ² = 8.37, p = 0.039), although the explanatory power was low (Pseudo R² = 0.017), indicating that other unmeasured factors likely contribute to the development of gastric hyperplasia.

Prevalence and Multivariable Analysis of Esophagitis

The prevalence of esophagitis was common in the study population and showed a borderline association with the duration of ischemic heart disease (IHD) (Table 5).

Table 5
Multivariable Logistic Regression Analysis of Esophagitis.

Variable	Adjusted OR	95% CI	z-value	p-value
IHD duration (> 1 year vs ≤ 1 year)	1.16	0.85–1.57	0.94	0.346
Age (per 1-year increase)	1.02	1.01–1.03	3.66	< 0.001
Sex (female vs male)	0.90	0.73–1.10	-1.02	0.308

Model statistics

n = 2,924; LR χ² = 17.51; p = 0.001; Pseudo R² = 0.006; AIC = 2703.29; BIC = 2727.21.

Esophagitis was observed in 59 patients (14.3%) in the ≤ 1 year group and in 453 patients (18.0%) in the > 1 year group. However, Pearson's chi-square test indicated that this difference did not reach statistical significance (χ² = 3.55, p = 0.060).

In multivariable logistic regression analysis, IHD duration was not independently associated with esophagitis after adjustment for age and sex (OR = 1.16, 95% CI: 0.85–1.57, p = 0.346). In contrast, age was significantly associated with esophagitis, with each additional year increasing the odds of the condition (OR = 1.02, 95% CI: 1.01–1.03, p < 0.001). Sex was not a significant predictor (OR = 0.90, 95% CI: 0.73–1.10, p = 0.308) (Fig. 1).

The overall model was statistically significant ($\chi^2 = 17.51$, $p = 0.001$), although the explanatory power was low (Pseudo $R^2 = 0.006$), suggesting that additional clinical factors contribute to the development of esophagitis in IHD patients.

DISCUSSION

This cross-sectional study investigated the association between IHD duration and upper gastrointestinal endoscopic changes while adjusting for age and sex in a large cohort of 2,924 patients. The findings indicate that age is a consistent predictor of gastric mucosal changes, including atrophy, hyperplasia, and esophagitis, whereas IHD duration is independently associated only with gastric hyperemia.

The strong association between age and multiple gastric abnormalities observed in this study aligns with previous evidence demonstrating that aging contributes to progressive deterioration of gastric mucosal integrity, impaired epithelial regeneration, reduced mucosal blood flow, and increased oxidative stress [6, 7, 8, 13]. These processes explain the increased prevalence of atrophy and other structural abnormalities among older patients.

Gastric hyperemia was the only endoscopic finding significantly associated with longer IHD duration. Chronic coronary disease is characterized by persistent systemic inflammation, endothelial dysfunction, and impaired vascular homeostasis, all of which may influence gastric microcirculation and mucosal perfusion [2, 4, 10]. Prolonged exposure to these mechanisms may contribute to increased vascular permeability and inflammatory activity within the gastric mucosa [4, 10].

The absence of significant associations between IHD duration and gastric atrophy, hyperplasia, or esophagitis suggests that these abnormalities may be predominantly driven by aging and other gastrointestinal risk factors rather than by the duration of cardiovascular disease itself [6, 7, 9]. Helicobacter pylori infection is a well-known cofactor for chronic gastritis and gastric atrophy [3, 8, 15].

The inverse association between female sex and gastric hyperemia may reflect sex-related biological differences in vascular and inflammatory responses. Estrogen exerts protective effects on endothelial function and mucosal perfusion, potentially reducing susceptibility to gastric mucosal injury [11, 14].

Despite the significant associations identified, the relatively low pseudo-R^2 values indicate that additional factors contribute to the development of endoscopic abnormalities, including H. pylori infection, antiplatelet therapy, NSAID use, smoking, alcohol consumption, dietary habits, and comorbid metabolic disorders [3, 5, 8, 12].

Strengths and Limitations. The major strengths of this study include a large sample size, standardized endoscopic assessment, and adjustment for key confounders such as age and sex. However, the study is limited by its cross-sectional design, which precludes causal inference. Additionally, important clinical variables such as Helicobacter pylori status, antiplatelet therapy, anticoagulant use, proton-pump inhibitor treatment, and lifestyle factors were not included in the analysis. Finally, the relatively low

pseudo R^2 values suggest that unmeasured confounders may contribute to the observed associations. Furthermore, the study was based on data collected between 2017 and 2018, which may limit the direct applicability of the findings to current clinical practice. However, the large sample size and standardized endoscopic assessment provide valuable epidemiological information regarding gastrointestinal manifestations in patients with IHD.

Conclusion

age is the primary determinant of upper gastrointestinal endoscopic abnormalities in patients with IHD, while prolonged IHD is independently associated with gastric hyperemia. Female sex appears to confer partial protection against hyperemia. These findings highlight the importance of age- and sex-specific risk assessment in the gastroenterological management of patients with ischemic heart disease. Further longitudinal studies are warranted to clarify the causal pathways and to identify modifiable risk factors for gastrointestinal pathology in this population.

Declarations

Funding

The authors received no external funding for this study.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This retrospective cross-sectional study was approved by the Ethics Committee of the Republican Specialized Scientific and Practical Medical Center of Cardiology (RSSPMC of Cardiology), Uzbekistan (Protocol No. 11, June 22, 2026). The Committee confirmed that the study was based on retrospectively collected anonymized clinical and endoscopic data obtained during routine medical practice between January 2017 and December 2018. Because the study involved only anonymized retrospective data and no additional patient contact or intervention, the Ethics Committee approved a waiver of additional informed consent. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Consent to participate

All patients had provided consent for medical examination and treatment during routine clinical care. The present study involved retrospective analysis of anonymized records, and no additional contact with patients was performed.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author contributions

Shukrullo Kodirov conceived the study, performed the statistical analyses, interpreted the data, and prepared the first draft of the manuscript.

Lola Daminova supervised the study and approved the final version of the manuscript.

Maqsud Sabirov contributed to the study design, data interpretation, and manuscript revision.

Kamola Daminova participated in data collection and data verification.

Nasiba Muhitdinova participated in data collection and conducted the literature review.

Burxon Munnavarov contributed to the development of the methodology and critically revised the manuscript.

Akmal Zaripov contributed to endoscopic data acquisition and manuscript editing.

All authors read and approved the final manuscript.

Acknowledgements

The authors would like to thank the staff of the Republican Specialized Scientific and Practical Medical Center of Cardiology for their support during data collection.

References

1. Virani SS, Alonso A, Aparicio HJ, et al. Heart disease and stroke statistics—2024 update: a report from the American Heart Association. Circulation. 2024;149:e347–e913. doi:10.1161/CIR.0000000000001144
2. European Society of Cardiology. 2024 ESC guidelines for the management of chronic coronary syndromes. Eur Heart J. 2024;45:3415–3537. doi:10.1093/eurheartj/ehaa1040.
3. Malfertheiner P, Megraud F, Rokkas T, et al. Management of Helicobacter pylori infection: the Maastricht VI/Florence Consensus Report. Gut. 2022;71:1724–1762. doi:10.1136/gutjnl-2022-327745.

4. Sung JJY, Kuipers EJ. Gastrointestinal mucosal injury and cardiovascular disease: emerging clinical evidence. Nat Rev Gastroenterol Hepatol. 2021;18:559–572. doi:10.1038/s41575-021-00448-9.
5. Kaplan RC, Frishman WH. Chronic inflammation and ischemic heart disease: mechanisms and clinical implications. Cardiol Rev. 2021;29:257–266. doi:10.1097/CRD.0000000000000367.
6. Shichijo S, Hirata Y. Endoscopic diagnosis of gastric atrophy and intestinal metaplasia: current evidence and future perspectives. Dig Endosc. 2022;34:700–713. doi:10.1111/den.14112.
7. Yamamoto K, Kato M. Aging-associated changes in gastric mucosa and upper gastrointestinal diseases. J Gastroenterol Hepatol. 2023;38:181–189. doi:10.1111/jgh.16123.
8. Eusebi LH, Rugge M, et al. Gastritis: epidemiology, pathophysiology and clinical management. Nat Rev Gastroenterol Hepatol. 2020;17:675–689. doi:10.1038/s41575-020-0333-1.
9. Kahrilas PJ, Boeckxstaens G. Gastroesophageal reflux disease and esophagitis: advances in pathogenesis and management. Lancet Gastroenterol Hepatol. 2023;8:454–466. doi:10.1016/S2468-1253(23)00041-5.
10. Libby P. The changing landscape of atherosclerosis and inflammation in cardiovascular disease. J Am Coll Cardiol. 2021;78:2081–2101. doi:10.1016/j.jacc.2021.09.005
11. Fedorova OV, et al. Impact of cardiovascular disease on gastrointestinal mucosal perfusion: a systematic review. J Clin Med. 2022;11:5012. doi:10.3390/jcm11175012 .
12. Lanza FL, Chan FK, Quigley EM. Guidelines for prevention of NSAID-related ulcer complications. Am J Gastroenterol. 2020;115:1129–1145. doi:10.14309/ajg.0000000000000582.
13. Jensen MD, et al. Endoscopic evaluation of upper gastrointestinal lesions in patients with cardiovascular disease. Dig Dis Sci. 2021;66:1456–1465. doi:10.1007/s10620-020-06669-4.
14. Kato S, et al. Sex differences in gastric mucosal injury and protective mechanisms: a clinical review. Neurogastroenterol Motil. 2021;33:e14172. doi:10.1111/nmo.14172.
15. Suzuki H, et al. Role of chronic inflammation and oxidative stress in gastric mucosal vulnerability in cardiovascular disease. Antioxidants (Basel). 2020;9:1212. doi:10.3390/antiox9121212.

Figures

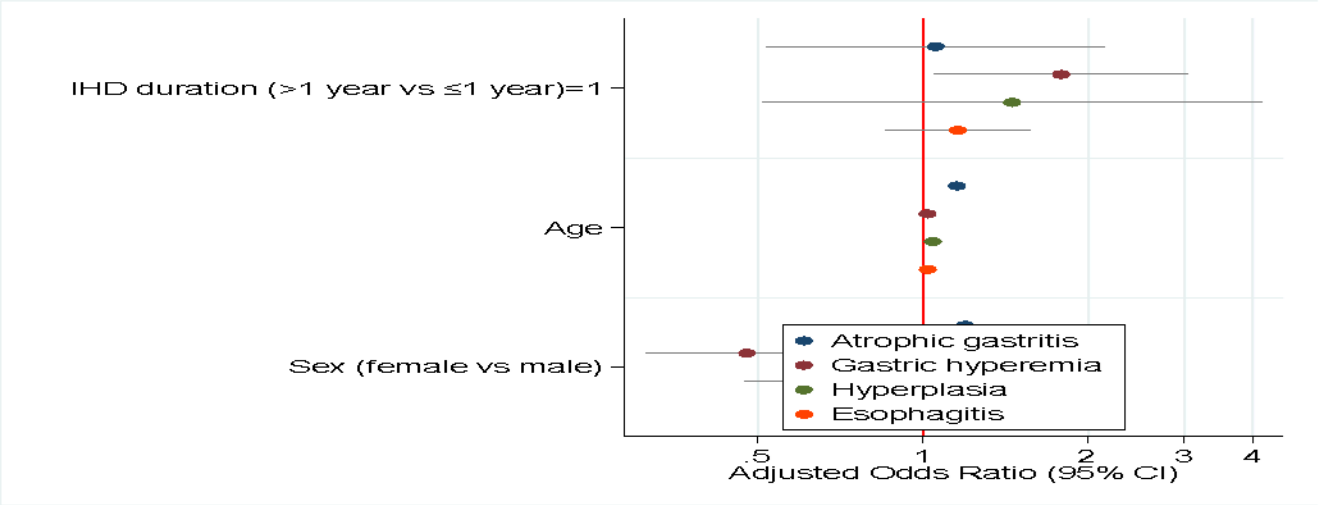


Figure 1

Multivariable logistic regression analysis of age-, sex-, and ischemic heart disease duration-related endoscopic gastric changes