ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Esophagogastric Junction Morphology is Associated with Ambulatory Reflux Monitoring Phenotypes in Patients Evaluated for Gastroesophageal Reflux Disease

Özofagogastrik Bileşke Morfolojisi, Gastroözofageal Reflü Hastalığı Şüphesiyle Değerlendirilen Hastalarda Objektif Reflü Yükü ile İlişkilidir

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ABSTRACT

Aim: *To evaluate whether high-resolution manometry-defined esophagogastric junction (EGJ) morphology is associated with objective reflux burden in adults evaluated for suspected gastroesophageal reflux disease.*

Materials and methods: *Consecutive adults evaluated between January 2021 and December 2025 were retrospectively screened. After exclusions, 243 patients who completed 36-channel high-resolution manometry and off-proton-pump-inhibitor pH-metry were included. Abnormal acid exposure time (AET) was defined as AET >6%. Associations were assessed using non-parametric tests and logistic regression adjusted for age, sex, hiatal hernia size, and lower esophageal sphincter pressure.*

Results: *Mean age was 42.0 years and 146 patients (60.1%) were male. Esophagogastric junction morphology was Type I in 111 patients, Type II in 81, and Type III in 51. Abnormal AET occurred in 38.7%, 22.2%, and 78.4% of Types I, II, and III, respectively (p<0.001). Median AET was 3.66%, 3.75%, and 10.79% (p<0.001). In the extended model, Type III remained associated with abnormal AET compared with Type I (OR 5.08, 95% CI 1.21–21.24; p=0.026).*

Conclusion: *Type III EGJ morphology was associated with higher objective reflux burden, whereas Type II showed a heterogeneous pattern. Esophagogastric junction morphology may complement, but should not replace, ambulatory reflux testing.*

Key words: *gastroesophageal reflux disease; esophagogastric junction; high-resolution manometry; acid exposure time; pH monitoring*

ÖZET

Amaç: *Bu çalışmanın amacı, yüksek çözünürlüklü manometri ile tanımlanan özofagogastrik bileşke (EGJ) morfolojisinin, gastroözofageal reflü hastalığı (GÖRH) şüphesi ile değerlendirilen erişkinlerde objektif reflü yükü ile ilişkili olup olmadığını değerlendirmektir.*

Gereç ve Yöntem: *Ocak 2021–Aralık 2025 tarihleri arasında değerlendirilen ardışık erişkin hastalar retrospektif olarak tarandı. Dışlama kriterleri uygulandıktan sonra, 36 kanallı yüksek çözünürlüklü manometri ve proton pompa inhibitörü (PPI) kullanılmayan dönemde pH-metri değerlendirmesi tamamlanan 243 hasta çalışmaya dâhil edildi. Anormal asit maruziyet süresi (AET), AET >%6 olarak tanımlandı. İlişkiler parametrik olmayan testler ve yaş, cinsiyet, hiatal herni boyutu ve alt özofagus sfinkter basıncı için düzeltilmiş lojistik regresyon analizleri ile değerlendirildi.*

Bulgular: *Hastaların ortalama yaşı 42,0 yıl olup 146'sı (%60,1) erkekti. Özofagogastrik bileşke morfolojisi 111 hastada Tip I, 81 hastada Tip II ve 51 hastada Tip III olarak sınıflandırıldı. Anormal AET sırasıyla Tip I, Tip II ve Tip III gruplarında %38,7, %22,2 ve %78,4 oranında saptandı (p<0,001). Medyan AET değerleri sırasıyla %3,66, %3,75 ve %10,79 idi (p<0,001). Genişletilmiş modelde, Tip III EGJ morfolojisi Tip I ile karşılaştırıldığında anormal AET ile bağımsız olarak ilişkili bulunmaya devam etti (OR 5,08; %95 GA 1,21–21,24; p=0,026).*

Sonuç: *Tip III EGJ morfolojisi daha yüksek objektif reflü yükü ile ilişkili bulunurken, Tip II heterojen bir patern göstermiştir. Özofagogastrik bileşke morfolojisi ambulatuvar reflü testlerini tamamlayıcı bir araç olabilir ancak bu testlerin yerine kullanılmamalıdır.*

Anahtar kelimeler: *gastroözofageal reflü hastalığı; özofagogastrik bileşke; yüksek çözünürlüklü manometri; asit maruziyet süresi; pH monitörizasyonu*

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Introduction

Gastroesophageal reflux disease (GERD) is heterogeneous, and symptoms, mucosal injury, and objective reflux burden do not always overlap (1). Therefore, current guidelines emphasize objective reflux testing, especially in patients with atypical, refractory, or preoperative presentations (2,3).

Ambulatory reflux monitoring quantifies acid exposure time (AET), reflux-event burden, and symptom association. According to the Lyon Consensus, AET <4% is physiological, AET >6% supports pathological reflux, and AET 4–6% requires supportive evidence (4,5).

High-resolution manometry (HRM) is not diagnostic for GERD, but it defines esophageal motor function and the esophagogastric junction (EGJ). Esophagogastric junction morphology reflects the relationship between the lower esophageal sphincter and crural diaphragm and is categorized as Type I, II, or III (6). Greater separation may impair antireflux-barrier function and increase reflux burden (7).

Although this mechanism is biologically plausible, clinical data linking EGJ morphology with pH-metry phenotypes remain limited (8). We therefore evaluated the association between EGJ morphology and reflux-monitoring outcomes in adults investigated for suspected GERD.

Material and Methods

Study Design and Population

We retrospectively analyzed consecutive adults evaluated for suspected GERD at a single tertiary referral center between January 2021 and December 2025. Reflux symptoms included heartburn, regurgitation, non-cardiac chest discomfort, or extra-esophageal symptoms prompting objective reflux evaluation. Of 267 screened patients, 8 were excluded for incomplete HRM, 11 for incomplete pH-metry, and 5 because pH-metry was performed on proton pump inhibitor (PPI) therapy; 243 patients were analyzed.

High-Resolution Manometry and EGJ Morphology

High-resolution manometry was performed using a 36-channel Medtronic system according to Chicago Classification v4.0 principles (6). Esophagogastric junction morphology was categorized as Type I, Type II, or Type III by an experienced gastrointestinal motility expert who was not blinded to clinical evaluation. Lower esophageal sphincter (LES) pressure, integrated relaxation pressure, distal latency, and distal contractile integral were recorded.

Ambulatory Reflux Monitoring

Ambulatory pH-metry was performed after a 10-day PPI washout. Acid exposure time was defined as the percentage of recording time with distal esophageal pH <4 and categorized using Lyon thresholds: normal <4%, inconclusive 4–6%, and abnormal >6% (4,5). The primary outcome was abnormal AET >6%. Secondary outcomes included continuous AET, DeMeester score, reflux-event counts, positional reflux metrics, and symptom association probability (SAP). Symptom association probability was treated as exploratory because positivity was uncommon.

Statistical Analysis

Continuous variables were summarized as mean with standard deviation or median with interquartile range, as appropriate. Categorical variables were summarized as counts and percentages. Between-group comparisons across EGJ morphology types used Kruskal-Wallis tests for continuous variables and chi-square tests for categorical variables. Ordinal trends across EGJ Types I to III were assessed with Spearman correlation. Pairwise non-parametric comparisons used Holm correction. Multivariable logistic regression estimated associations with abnormal AET. The primary model adjusted for age and sex; an extended model additionally adjusted for hiatal hernia size and LES pressure to evaluate whether Type III retained an independent association after accounting for key antireflux-barrier variables. A quadratic ordinal model was used as a sensitivity analysis to assess non-linear morphology effects, particularly the unexpected Type II pattern. Upright and supine reflux metrics were analyzed separately. Two-sided p values <0.05 were considered statistically significant. Statistical analyses were performed using IBM Statistical Package for Social Sciences (SPSS) program version 23.0 for Windows (IBM Corp., Armonk, NY, USA).

Results

Cohort Characteristics

A total of 267 consecutive patients underwent evaluation for suspected GERD during the study period. After exclusion of patients with incomplete HRM, incomplete ambulatory pH-metry, or pH monitoring

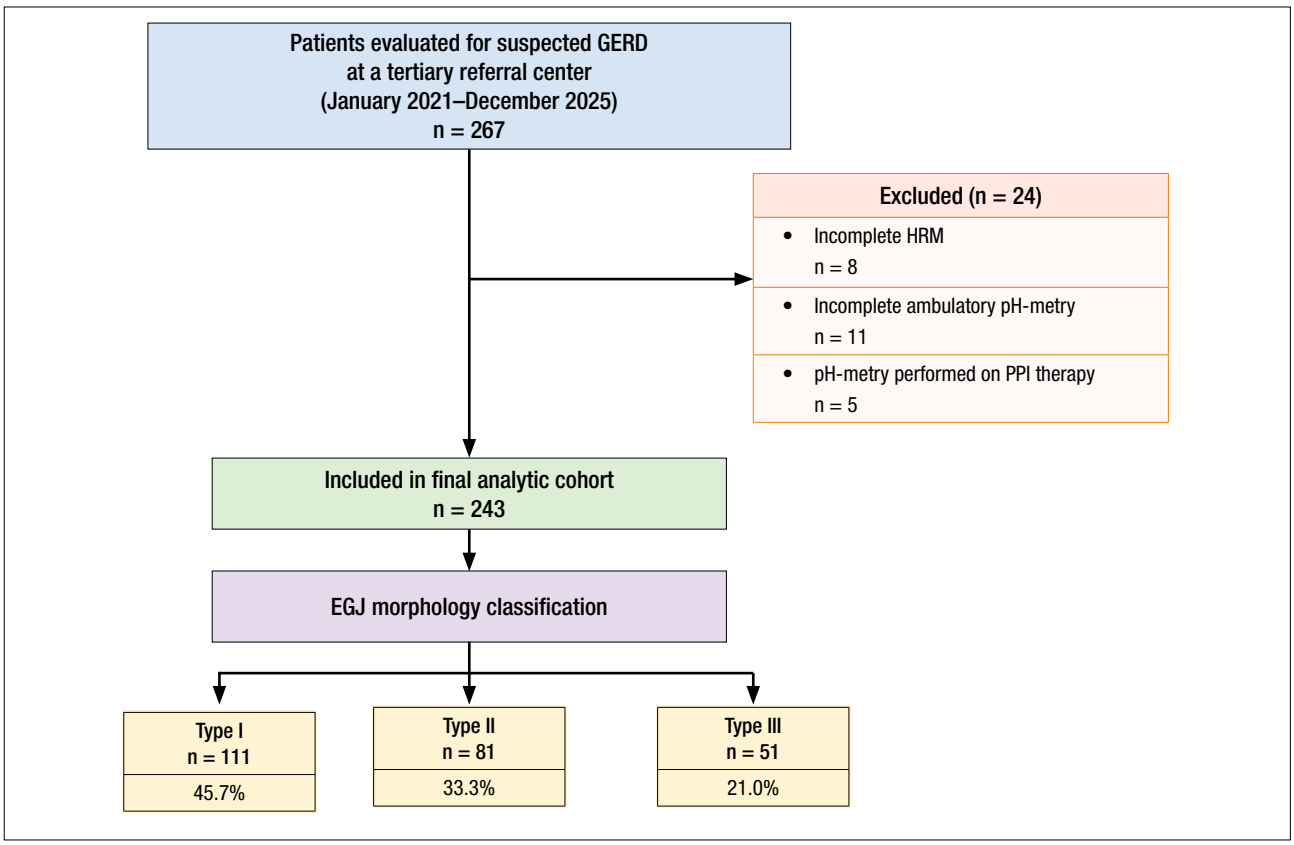


Figure 1. *Patient selection flowchart (GERD: gastroesophageal reflux disease; EGJ: esophagogastric junction; AET: acid exposure time).*

Table 1. *Baseline, manometric, reflux-monitoring characteristics, and Lyon AET category distribution by EGJ morphology*

Characteristic	Type I	Type II	Type III
n	111	81	51
Age, mean (SD)	42.2 (9.8)	41.8 (10.2)	41.8 (10.1)
Male, n (%)	69 (62.2)	46 (56.8)	31 (60.8)
AET, median (IQR)	3.66 (2.14–8.4)	3.75 (2.44–5.42)	10.79 (7.56–14.12)
DeMeester score, median (IQR)	14.6 (14.0–31.1)	14.6 (12.2–20.1)	37.5 (24.6–51.8)
Total reflux events, median (IQR)	44.0 (29.0–69.5)	41.0 (28.0–58.0)	96.0 (73.0–112.5)
LES pressure, mean (SD)	22.2 (5.1)	18.1 (4.1)	14.2 (3.7)
Hiatal hernia, median (IQR)	0.5 (0.4–0.7)	1.5 (1.1–1.9)	2.8 (2.25–4.0)
Positive SAP, n (%)	3 (2.7)	1 (1.2)	4 (7.8)
Normal (<4%)	58 (52.3)	44 (54.3)	8 (15.7)
Inconclusive (4–6%)	10 (9.0)	19 (23.5)	3 (5.9)
Abnormal (>6%)	43 (38.7)	18 (22.2)	40 (78.4)

Values are n (%), mean (SD), or median (IQR).
AET categories were defined as normal <4%, inconclusive 4–6%, and abnormal >6% according to Lyon Consensus thresholds.
AET: acid exposure time; EGJ: esophagogastric junction; LES: lower esophageal sphincter; SAP: symptom association probability.

performed during PPI therapy, 243 patients were included in the final analysis (Fig. 1). Esophagogastric junction morphology was classified as Type I in 111 patients (45.7%), Type II in 81 (33.3%), and Type III in 51 (21.0%).

Baseline demographic, physiological, and reflux characteristics according to EGJ morphology are summarized in Table 1. Age and sex distribution did not differ significantly across morphology groups.

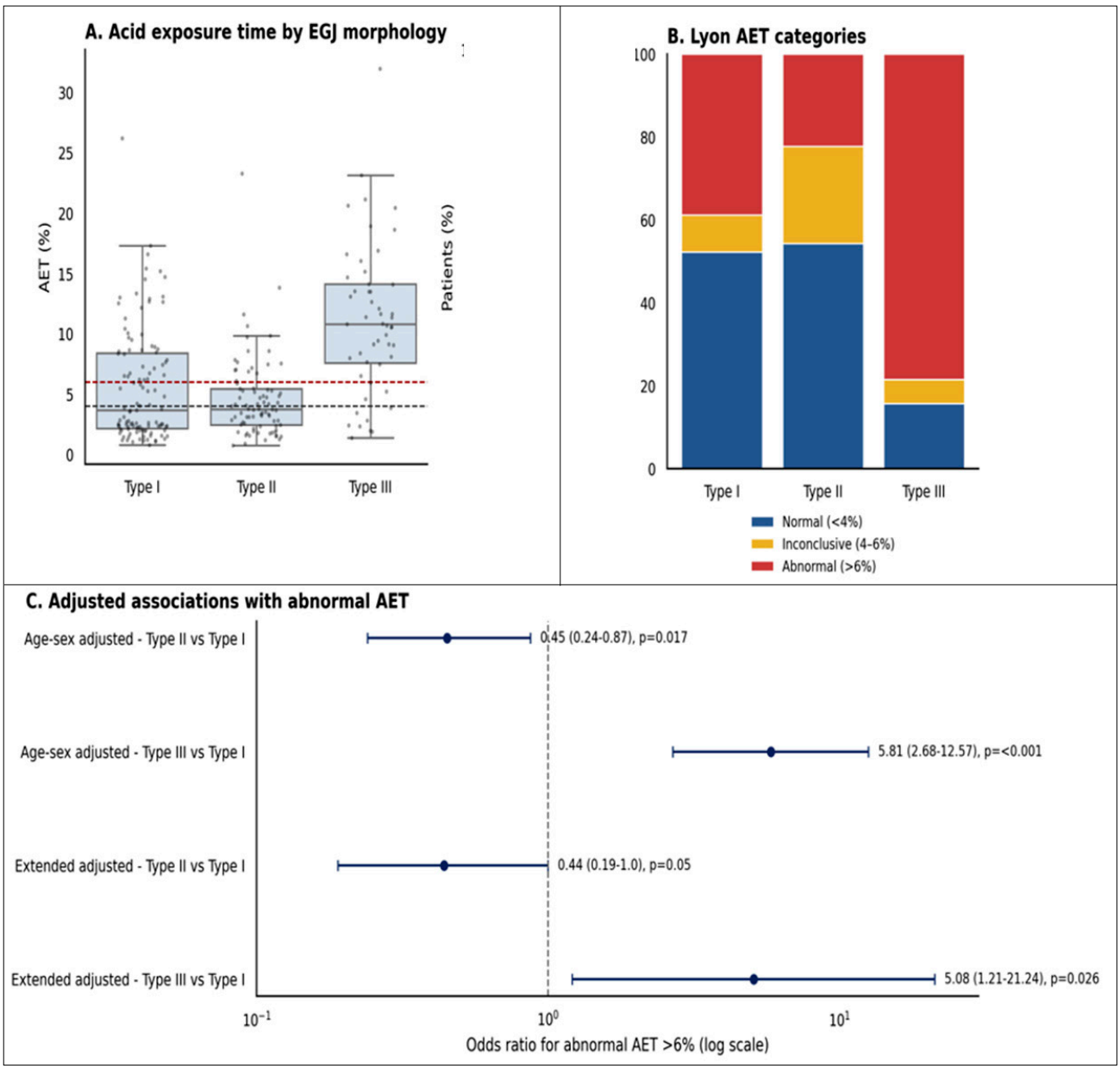


Figure 2. *Association of EGJ morphology with acid exposure burden, Lyon AET categories, and adjusted odds of abnormal reflux (AET: acid exposure time; EGJ: esophagogastric junction).*

Reflux Burden According to EGJ Morphology

Continuous reflux burden differed across EGJ morphology categories, with Type III demonstrating the highest acid exposure time (AET), DeMeester score, and reflux-event burden (Table 1; Fig. 2A).

Categorical reflux outcomes showed a similar distribution pattern. The proportion of patients meeting criteria for abnormal reflux differed across EGJ categories, whereas normal reflux profiles became less frequent in Type III morphology (Table 1; Fig. 2B).

Manometric and Anatomical Correlates

Manometric and anatomical characteristics varied across EGJ morphology groups. Lower LES pressure and greater hiatal hernia size were observed with increasing EGJ disruption severity (Table 1).

Adjusted Analyses

In age- and sex-adjusted regression analyses, Type III morphology was associated with higher odds of abnormal AET compared with Type I, whereas Type II showed lower odds than Type I (Table 2).

These associations remained directionally consistent in exploratory extended models incorporating hiatal hernia size and LES pressure, although effect estimates were attenuated after adjustment (Table 2).

Positional reflux analyses demonstrated that EGJ morphology was associated with both upright and supine reflux metrics across continuous and frequency-based measures (Table 3).

Pairwise post-hoc analyses demonstrated that Type III remained associated with higher odds of abnormal reflux compared with both Type I and Type II morphology, whereas Type II showed a lower probability of abnormal reflux relative to Type I (Table 4).

Sensitivity analyses supported a non-linear relationship across EGJ morphology categories and did not materially alter the overall interpretation of reflux burden findings (Tables 2 and 4).

Table 2. *Extended logistic regression models for abnormal AET >6%*

Model	Variable	OR (95% CI)	P value
Age-sex adjusted	Type II vs Type I	0.45 (0.24–0.87)	0.017
Age-sex adjusted	Type III vs Type I	5.81 (2.68–12.57)	<0.001
Extended adjusted	Type II vs Type I	0.44 (0.19–1.0)	0.05
Extended adjusted	Type III vs Type I	5.08 (1.21–21.24)	0.026
Extended adjusted	Hiatal hernia size, per cm	1.14 (0.74–1.76)	0.561
Extended adjusted	LES pressure, per mmHg	1.02 (0.96–1.09)	0.47

The extended model adjusted for age, sex, hiatal hernia size, and LES pressure.
AET: acid exposure time; CI: confidence interval; LES: lower esophageal sphincter; OR: odds ratio.
Extended adjusted estimates should be interpreted as exploratory rather than causal because selected covariates may represent intermediate physiological mechanisms.

Table 3. *Positional reflux metrics according to EGJ morphology*

Outcome	Type I, median (IQR)	Type II, median (IQR)	Type III, median (IQR)	Spearman rho	Trend P	Group P
Upright reflux, %	2.19 (1.12–5.21)	2.12 (1.37–3.33)	5.94 (3.58–8.0)	0.276	<0.001	<0.001
Supine reflux, %	1.31 (0.77–3.45)	1.67 (0.83–2.23)	4.39 (2.7–6.74)	0.288	<0.001	<0.001
Upright reflux frequency	26.0 (16.5–41.0)	24.0 (17.0–31.0)	55.0 (34.0–73.5)	0.28	<0.001	<0.001
Supine reflux frequency	17.0 (11.5–26.0)	16.0 (10.0–25.0)	35.0 (26.0–44.5)	0.255	<0.001	<0.001

Spearman rho and trend p values evaluate ordinal EGJ morphology from Type I to Type III.
Group p values are from Kruskal-Wallis tests.

Table 4. *Pairwise post-hoc comparisons of reflux outcomes according to EGJ morphology*

Comparison	Delta median AET, percentage points	Adjusted OR for abnormal AET	P value
Type II vs Type I	0.09	0.45 (0.24–0.87)	0.018
Type III vs Type I	7.13	5.74 (2.66–12.40)	<0.001
Type III vs Type II	7.04	13.90 (5.74–33.66)	<0.001

Delta median AET was calculated as the median AET of the first group minus the median AET of the comparator group.
Adjusted odds ratios were estimated using pairwise logistic regression models adjusted for age and sex.
AET: acid exposure time; EGJ: esophagogastric junction; OR: odds ratio.

Symptom Association

Symptom-association findings were less pronounced than reflux burden measures. Binary SAP positivity remained uncommon across all morphology groups and did not demonstrate a clear morphology-dependent pattern despite differences in continuous physiological measures (Table 1).

Discussion

In this 243-patient cohort, HRM-defined EGJ morphology was associated with objective reflux-monitoring phenotypes. The principal finding was that Type III morphology was associated with a high-reflux-burden phenotype, with abnormal AET in nearly four of five patients and substantially higher DeMeester score and total reflux-event burden than Types I and II. These findings support the current concept that GERD should be defined by objective evidence of pathological reflux rather than symptoms alone and suggest that abnormal EGJ morphology may provide supportive mechanistic information when interpreted alongside ambulatory reflux monitoring (4,5,9).

Our findings align with and extend previous studies linking LES-crural diaphragm separation with abnormal reflux monitoring. Tolone et al. demonstrated increasing AET and reflux episodes across EGJ morphology categories, with Type III patients showing the highest probability of positive impedance-pH

monitoring (8). More recent studies also support the relationship between EGJ disruption and reflux burden, suggesting that separation length may be more informative than morphology category alone (10,11). In our cohort, Type III morphology clustered with larger hiatal hernia size, lower LES pressure, and greater reflux burden.

This association is biologically plausible because the antireflux barrier depends on coordinated function of the intrinsic LES and crural diaphragm; separation reduces the composite high-pressure zone and may impair both reflux prevention and esophageal clearance (7,10). Consistent with this concept, Vespa et al. reported that disrupted EGJ integrity was associated particularly with increased recumbent reflux exposure (12). This supports evaluating upright and supine reflux separately in future studies and suggests that EGJ-disrupted patients may represent a mechanically driven GERD phenotype.

Type II findings require careful interpretation. Although Type II morphology showed larger hiatal hernia size and lower LES pressure than Type I, abnormal AET was not increased. This supports the view that Type II morphology is heterogeneous and may represent an intermediate rather than uniformly pathological phenotype (5,6,10,11). Additional metrics such as EGJ contractile integral, provocative HRM maneuvers, impedance-derived markers, and prolonged wireless pH monitoring may improve risk stratification in this subgroup (5,9,10).

The present findings also support the Lyon Consensus 2.0 framework, in which EGJ morphology should be interpreted as an adjunctive mechanistic marker rather than a replacement for reflux monitoring (5,9). Although Type III morphology increased the likelihood of pathological reflux, objective reflux testing remains necessary, particularly before invasive antireflux procedures (2,3,9).

Symptom-association findings were less robust than acid-burden findings. Symptom association probability positivity was uncommon and did not differ significantly across morphology groups, consistent with the known limitations of symptom-based analyses (13–15). Therefore, patients with Type III morphology may demonstrate substantial objective reflux burden despite negative SAP results.

Overall, our findings support a precision-phenotyping model of GERD in which EGJ morphology is integrated with reflux burden and physiological testing. Morphology alone does not diagnose GERD; however, Type III morphology identified a subgroup with internally consistent evidence of antireflux barrier impairment and objective reflux burden (4,5,7–12,16).

Strengths and Limitations

Strengths include a moderate esophageal physiology cohort, minimal missingness in core analyzed variables, use of Lyon AET thresholds, and evaluation of continuous, categorical, positional, and adjusted reflux outcomes.

Limitations include the retrospective cross-sectional design, lack of causal inference, and unavailable variables such as body mass index, smoking, symptom duration, endoscopic esophagitis grade, PPI response, mucosal impedance, EGJ contractile integral, and treatment outcomes. Symptom association probability morphology was assessed by an experienced motility expert but not blinded. Symptom association probability positivity was uncommon, reducing power for symptom-association analyses. Type II morphology appeared heterogeneous and requires more detailed physiological characterization.

The extended adjustment model should be interpreted as exploratory because hiatal hernia size and LES pressure may represent intermediate mechanisms rather than true confounders.

Prospective multicenter studies incorporating EGJ contractile integral and impedance-derived markers are warranted.

Conclusion

In this cohort, HRM-defined EGJ morphology was associated with objective reflux-monitoring phenotypes, with Type III morphology showing markedly higher acid exposure time, DeMeester score, and reflux-event burden.

These findings suggest that EGJ morphology may serve as a practical adjunct for GERD phenotyping and interpretation of ambulatory reflux testing, while objective reflux monitoring should remain the diagnostic reference standard.

Prospective multicenter studies incorporating EGJ contractile integral, impedance-derived markers, and standardized physiological assessment are warranted to validate and refine these observations.

Acknowledgments

The authors wish to express their sincere appreciation to Ayten Erdem for her long-standing dedication to the motility laboratory and for her invaluable technical support, which contributed significantly to the successful completion of this study.

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