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Association between Reflux Symptom Index scores and modified Mallampati class in adults undergoing upper gastrointestinal endoscopy: a prospective cross-sectional study

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Research Article

Keywords: Reflux Symptom Index, extraesophageal symptoms, Mallampati class, upper endoscopy, airway assessment

Posted Date: November 5th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10905065/v1

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Additional Declarations: No competing interests reported.

Abstract

Background

The modified Mallampati classification is a routine component of preoperative airway assessment. We examined whether throat-predominant symptom burden, measured with the Reflux Symptom Index (RSI), and typical esophageal symptom burden, measured with the Gastroesophageal Reflux Disease Questionnaire (GerdQ), are associated with modified Mallampati class in adults undergoing elective upper gastrointestinal endoscopy.

Methods

In this prospective cross-sectional exploratory study, 90 adults with reflux-type symptoms of more than one year's duration were enrolled. Participants using proton pump inhibitors were instructed to stop treatment for at least 14 days beforehand. Modified Mallampati class was graded from standardized photographs by a blinded assessor. The primary outcome was Mallampati class III–IV and the primary exposure was continuous RSI score. The main adjusted model included RSI, body mass index (BMI), neck circumference and current smoking, with Firth penalized logistic regression as a robustness analysis. Secondary analyses examined the four Mallampati categories.

Results

Thirty-five participants (38.9%) had Mallampati class III–IV. RSI scores were higher in the III–IV group than in the I–II group (13.97 ± 7.14 vs 8.27 ± 6.67; $p < 0.001$). In the main adjusted model each 1-point increase in RSI was associated with Mallampati III–IV (OR 1.13, 95% CI 1.04–1.22; $p = 0.002$; OR 1.84, 95% CI 1.24–2.73 per 5 points). Firth penalization and restriction to participants who were not current smokers (OR 1.26, 95% CI 1.04–1.52) gave a concordant direction of association. RSI did not rise monotonically across the four categories and the proportional-odds assumption was violated ($p = 0.0015$). GerdQ scores did not differ between groups ($p = 0.65$).

Conclusions

Higher RSI-defined throat symptom burden was associated with modified Mallampati class III–IV, and the association persisted after adjustment and in sensitivity analyses. No evidence of an association between GerdQ score and Mallampati class was observed. Because the relationship was not graded across all four categories and no objective reflux testing was performed, these exploratory findings describe a relationship between upper-airway symptom burden and oropharyngeal phenotype rather than evidence of reflux disease.

Background

Gastroesophageal reflux disease (GERD) is defined by troublesome symptoms or complications related to reflux of gastric contents, while current diagnostic frameworks distinguish symptom-based suspicion from disease confirmed by objective testing (1, 2). Throat-predominant complaints such as throat clearing, hoarseness, globus sensation, and chronic cough are often described within the spectrum of laryngopharyngeal reflux (LPR), but these symptoms are nonspecific and should not be considered diagnostic of reflux in isolation (2, 3). Symptom questionnaires therefore measure symptom burden rather than establishing a physiological diagnosis.

The Reflux Symptom Index (RSI) primarily captures throat-predominant symptoms. The Gastroesophageal Reflux Disease Questionnaire (GerdQ) instead focuses on typical esophageal symptoms such as heartburn and regurgitation (4, 5), so the two instruments assess related but distinct constructs. Experimental studies support the susceptibility of laryngeal mucosa to acid- and pepsin-mediated injury (3, 6), but whether symptom burden corresponds to clinically observable upper-airway features remains uncertain.

The modified Mallampati classification is a standard component of airway assessment and is generally interpreted together with other predictors of airway difficulty (7–9). Classes III and IV are commonly grouped as high grade because they reflect reduced visibility of the oropharyngeal structures (7–9). Mallampati class has also been associated with tolerance of unsedated peroral upper gastrointestinal endoscopy (10). Whether throat-predominant reflux symptom burden is associated with the routinely recorded Mallampati class has not been established.

We therefore evaluated the associations of RSI and GerdQ scores with modified Mallampati class in adults with chronic reflux-type symptoms undergoing elective upper endoscopy. The question addressed was whether throat-predominant symptom burden is associated with reduced oropharyngeal visibility as graded by the modified Mallampati classification, not whether reflux causes a high Mallampati class. We hypothesized that RSI, but not necessarily GerdQ, would be associated with Mallampati class III–IV. The study was exploratory and was not designed to diagnose reflux disease or to assess airway outcomes.

Methods

Study design and participants

This prospective cross-sectional exploratory study was conducted at the Endoscopy Unit of Medical Park Göztepe Hospital, İstanbul, Türkiye. Participants were enrolled between July 2019 and January 2020. Adults aged 18 years or older who were referred for elective upper gastrointestinal endoscopy and encountered by the study team were assessed against the eligibility criterion of reflux-type symptoms lasting more than one year that required an endoscopy; those who met that criterion and no exclusion criterion were invited to participate. The study team did not screen every patient attending the endoscopy unit during the study period, so the sample should not be regarded as a consecutive series of

all endoscopy attendees. Participants using proton pump inhibitors (PPIs) were instructed to discontinue treatment for at least 14 days before endoscopy and questionnaire assessment. Patients were excluded for known cardiac disease, previous surgery for obstructive sleep apnea, craniofacial or maxillomandibular abnormalities that could independently affect Mallampati class, previous upper gastrointestinal surgery, inability to complete the questionnaire, or an emergency procedure. Recruitment was completed before the introduction of COVID-19-related restrictions on elective endoscopy.

Ninety-seven eligible participants were enrolled; 7 were subsequently excluded from the complete-case analysis because primary Mallampati or RSI data were incomplete, leaving 90 participants (Fig. 1). All participants provided written informed consent. The Bahçeşehir University Clinical Research Ethics Committee approved the study on April 17, 2019 (decision/protocol No. 2019-08/01). The study was conducted in accordance with the Declaration of Helsinki and is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations for cross-sectional studies (11).

Data collection

Demographic and clinical data were collected prospectively. Recorded variables included age, sex, height, weight, modified Mallampati class, RSI score, GerdQ score, neck circumference, smoking status, and a history of sleep apnea and/or recurrent snoring with witnessed apneic episodes during sleep, based on repeated reports by a relative. Neck circumference was measured at the level of the cricothyroid membrane with the patient seated. Smoking was categorized as current smoking versus non-smoking, with former smokers classified as non-smokers after at least one year of abstinence. Data were entered into a structured database.

Measurements

Modified Mallampati classification

A board-certified anesthesiologist, blinded to the reflux questionnaire scores at the time of grading, performed all assessments. Standardized photographs were obtained immediately before endoscopy with the participant seated, the mouth fully open, the tongue maximally protruded, and without phonation, under consistent lighting. The anesthesiologist subsequently reviewed the photographs and assigned class I, II, III, or IV according to standard criteria (7–9). A second board-certified anesthesiologist, also blinded to the reflux questionnaire scores, reviewed the photographs and confirmed the assigned Mallampati classifications. Because separate paired ratings from the confirmatory assessment were not retained, formal interrater reliability could not be calculated. The photographs were not regraded to estimate intra-rater agreement. For the primary analysis, classes were grouped as I–II and III–IV; the four individual categories were retained for the secondary analysis.

Reflux symptom assessment

Symptom burden was assessed using two previously published questionnaires; neither instrument was developed specifically for the present study. The Reflux Symptom Index (RSI), originally developed and validated by Belafsky et al. (4), is a 9-item self-administered questionnaire in which each item is scored from 0 to 5, yielding a total score from 0 to 45. Eight items address upper-airway or throat complaints, while one item addresses heartburn, chest pain, indigestion and acid regurgitation. The RSI served as the primary exposure measure and asks about symptoms experienced within the preceding month.

The Gastroesophageal Reflux Disease Questionnaire (GerdQ), originally developed by Jones et al. (5), is a 6-item frequency-based questionnaire with a maximum score of 18 that emphasizes heartburn and regurgitation while also incorporating symptom-related sleep disturbance, additional medication use, epigastric pain and nausea; it refers to a 7-day recall period. GerdQ was evaluated as an exploratory secondary exposure.

Both questionnaires were administered in Turkish. Turkish translations of the published instruments were prepared for study administration, while the original item content, response structure, recall periods, and scoring systems were retained without modification. No additional study-specific questionnaire or structured interview was developed. Both questionnaires were completed after the protocol-defined PPI washout. Because the 14-day washout is shorter than the RSI recall window, part of the period covered by the RSI fell during PPI treatment in participants who had been receiving these drugs.

Objective reflux testing

Ambulatory pH-impedance monitoring was not performed, and routine endoscopic findings were not collected using a prespecified reflux-phenotyping protocol. Accordingly, the study evaluates questionnaire-defined symptom burden rather than objectively confirmed GERD or LPR (2, 3).

Statistical analysis

Descriptive statistics, group comparisons and the unadjusted and BMI-adjusted logistic regression models were performed with SPSS version 25.0 (IBM Corp., Armonk, NY, USA). The Firth penalized logistic regression, ordinal logistic regression, proportional-odds likelihood-ratio test, restricted cubic spline analysis and Jonckheere–Terpstra test were computed in Python 3 using the statsmodels and SciPy libraries, with Firth estimation implemented using profile penalized-likelihood confidence intervals. Distributional assumptions were evaluated with the Shapiro–Wilk test. Continuous variables are reported as mean ± standard deviation and, for non-normally distributed variables, median and interquartile range. Categorical variables are reported as number and percentage. Age was compared with an independent-samples t test; body mass index (BMI), RSI, GerdQ, and neck circumference were compared with the Mann–Whitney U test. Categorical variables were compared using the chi-square test, with continuity correction for 2 × 2 comparisons.

The primary analysis used binary logistic regression with Mallampati class III–IV as the dependent variable and continuous RSI score as the primary exposure. A single main adjusted model was specified on biological grounds and contained RSI, BMI, neck circumference and current smoking; covariates were not selected on the basis of univariable p values. Because only 35 participants had the outcome, the covariate set was deliberately restricted to limit model instability and overfitting(12), and Firth penalized logistic regression with profile penalized-likelihood confidence intervals was fitted as a robustness analysis (13, 14). Unadjusted and BMI-adjusted models, and a model adjusted for BMI, age and sex, are also reported for comparability with the original analysis plan. Age and sex were not added to the main model because neck circumference and sex were strongly collinear in this cohort ($r = -0.71$) and the resulting six-covariate model produced unstable estimates. Multicollinearity was assessed using variance inflation factors. RSI associations are reported per 1-point increase and, for clinical interpretation, per 5-point increase.

The linearity of the relationship between RSI and the logit of the outcome was examined by adding a quadratic term and by fitting a three-knot restricted cubic spline (knots at the 10th, 50th and 90th percentiles) and testing the nonlinear term by likelihood ratio. As a secondary analysis, the distribution of RSI across the four Mallampati categories was examined with the Kruskal–Wallis test and the Jonckheere–Terpstra test for ordered alternatives, and ordinal logistic regression was fitted with Mallampati class I–IV as the outcome; the proportional-odds assumption was assessed by a likelihood-ratio test comparing the proportional-odds model with a multinomial logistic model, supported by inspection of cutpoint-specific binary logistic estimates. Two post-hoc sensitivity analyses addressed smoking, which was imbalanced between Mallampati groups: the primary analysis was repeated among participants who were not current smokers, and an RSI × smoking interaction term was tested. These analyses were exploratory and underpowered, and are reported as effect estimates with confidence intervals. GerdQ was analyzed as an exploratory secondary exposure, and its correlation with RSI was assessed with the Spearman rank coefficient.

Associations are reported as odds ratios (ORs) with 95% confidence intervals (CIs). Statistical significance was defined as a two-sided p value below 0.05. No missing-data imputation was performed; analyses were restricted to participants with complete data for the variables included in each model.

Sample size

The enrollment target was pragmatic. A sample of approximately 90 participants was expected to estimate a Mallampati III–IV prevalence of about 40% with a 95% CI width of approximately ± 10%. This calculation addressed prevalence precision and did not constitute a formal power calculation for the multivariable association analyses; regression estimates should therefore be interpreted as exploratory. No post-hoc power calculation was performed.

Use of large language models

A large language model (Claude, Anthropic) was used during preparation of this manuscript for language editing and manuscript organization. It was not used for data collection. All statistical results were verified against the source dataset, and all manuscript content was critically reviewed and revised by the authors, who take full responsibility for the work.

Results

Participant characteristics

Of 97 enrolled participants, 7 were excluded from the complete-case analysis because primary study data were incomplete, leaving 90 participants (Fig. 1). No data were imputed. Modified Mallampati class was I in 18 participants (20.0%), II in 37 (41.1%), III in 30 (33.3%) and IV in 5 (5.6%); accordingly, 55 participants (61.1%) were classified as Mallampati I–II and 35 (38.9%) as Mallampati III–IV. The median age was 44 years (range 18–88). Age did not differ between groups (43.1 ± 14.2 vs 45.2 ± 13.1 years; $p = 0.49$). Female sex was more frequent in the III–IV group, although the difference was not statistically significant (58.2% vs 68.6%; $p = 0.44$). BMI was comparable (25.49 ± 4.69 vs 26.83 ± 6.24 kg/m²; $p = 0.25$). Neck circumference was numerically greater in the III–IV group (36.65 ± 3.50 vs 38.23 ± 3.68 cm; $p = 0.063$), and current smoking was more frequent (49.1% vs 77.1%; $p = 0.015$). Current smokers also had higher RSI scores than those who were not current smokers (12.78 ± 7.36 vs 7.06 ± 5.97; $p < 0.001$). Baseline characteristics are presented in Table 1.

Table 1
Baseline characteristics by modified Mallampati group.

Variable	Mallampati I–II (n = 55)	Mallampati III–IV (n = 35)	p value
Modified Mallampati class, n (%)	I: 18 (32.7%); II: 37 (67.3%)	III: 30 (85.7%); IV: 5 (14.3%)	—
Age (years), mean ± SD	43.1 ± 14.2	45.2 ± 13.1	0.49a
Sex, female, n (%)	32 (58.2%)	24 (68.6%)	0.44b
BMI (kg/m²), mean ± SD; median [IQR]	25.49 ± 4.69; 25.04 [22.10–27.43]	26.83 ± 6.24; 26.78 [23.27–30.92]	0.25c
Neck circumference (cm), mean ± SD; median [IQR]	36.65 ± 3.50; 36.6 [33.5–39.5]	38.23 ± 3.68; 37.9 [35.7–40.5]	0.063c
Current smoking, n (%)	27 (49.1%)	27 (77.1%)	0.015b
Recurrent snoring and witnessed apnea by a relative, n (%)	8 (14.5%)	6 (17.1%)	0.97b
RSI score, mean ± SD; median [IQR]	8.27 ± 6.67; 7.0 [3.5–12.0]	13.97 ± 7.14; 16.0 [8.5–19.0]	< 0.001c
GerdQ score, mean ± SD; median [IQR]	6.85 ± 2.84; 6.0 [5.5–8.0]	6.77 ± 2.38; 7.0 [6.0–8.0]	0.65c

a Independent-samples t test; b chi-square test with continuity correction; c Mann–Whitney U test. Percentages for the four-category Mallampati distribution are within the dichotomized group. BMI, body mass index; GerdQ, Gastroesophageal Reflux Disease Questionnaire; IQR, interquartile range; RSI, Reflux Symptom Index; SD, standard deviation.

Primary analysis

RSI scores were higher in participants with Mallampati III–IV than in those with Mallampati I–II (mean 13.97 ± 7.14; median 16.0 [interquartile range 8.5–19.0] vs mean 8.27 ± 6.67; median 7.0 [interquartile range 3.5–12.0]; $p < 0.001$). In univariable logistic regression, each 1-point higher RSI score was associated with 12% higher odds of Mallampati III–IV (OR 1.12, 95% CI 1.05–1.20; $p < 0.001$), corresponding to OR 1.79 (95% CI 1.28–2.51) per 5-point increase. In the main adjusted model containing RSI, BMI, neck circumference and current smoking, the RSI estimate was essentially unchanged (OR 1.13, 95% CI 1.04–1.22; $p = 0.002$; OR 1.84, 95% CI 1.24–2.73 per 5-point increase). Neck circumference was associated with the outcome after adjustment (OR 1.20, 95% CI 1.02–1.41; $p = 0.03$), whereas BMI (OR 1.01, 95% CI 0.92–1.12; $p = 0.78$) and current smoking (OR 2.01, 95% CI 0.65–6.19; $p = 0.23$) were not. Variance inflation factors in this model were below 1.4. Firth penalized estimates were

close to the maximum-likelihood estimates (RSI OR 1.12, 95% CI 1.04–1.21). The regression results are shown in Table 2.

Table 2
Associations of RSI and clinical covariates with modified Mallampati class III–IV.

Variable	OR	95% CI	p value
Univariable analysis			
RSI score (per 1-point increase)	1.12	1.05–1.20	< 0.001
RSI score (per 5-point increase)	1.79	1.28–2.51	< 0.001
Main adjusted model: RSI + BMI + neck circumference + current smoking			
RSI score (per 1-point increase)	1.13	1.04–1.22	0.002
RSI score (per 5-point increase)	1.84	1.24–2.73	0.002
BMI (per 1-unit increase)	1.01	0.92–1.12	0.78
Neck circumference (per 1-cm increase)	1.20	1.02–1.41	0.03
Current smoking (yes vs no)	2.01	0.65–6.19	0.23
Firth penalized logistic regression (same covariates)			
RSI score (per 1-point increase)	1.12	1.04–1.21	—
RSI score (per 5-point increase)	1.75	1.23–2.63	—
BMI (per 1-unit increase)	1.01	0.92–1.12	—
Neck circumference (per 1-cm increase)	1.18	1.02–1.39	—
Current smoking (yes vs no)	1.95	0.66–5.84	—
Additional models, for comparability with the original analysis plan			
RSI, adjusted for BMI	1.13	1.05–1.21	< 0.001
RSI, adjusted for BMI, age and sex	1.12	1.05–1.20	0.001
Post-hoc sensitivity analyses for smoking			
RSI, not current smokers (n = 36, 8 events)	1.26	1.04–1.52	0.017
RSI, not current smokers, Firth penalized	1.24	1.06–1.59	—
RSI, current smokers (n = 54, 27 events)	1.06	0.98–1.15	0.12
RSI × smoking interaction	—	—	0.16

Dependent variable: modified Mallampati class III–IV versus I–II, except for the ordinal model, in which the outcome is Mallampati class I–IV. The main adjusted model was specified on biological grounds; covariates were not chosen by univariable screening. Firth confidence intervals are profile penalized-likelihood intervals, for which no p value is reported. Variance inflation factors in the main adjusted model were below 1.4. Age and sex were not added to the main model because neck circumference and sex were collinear (r = − 0.71). BMI, body mass index; CI, confidence interval; GerdQ, Gastroesophageal Reflux Disease Questionnaire; OR, odds ratio; RSI, Reflux Symptom Index.

Variable	OR	95% CI	p value
Univariable analysis			
Secondary analyses			
RSI, ordinal model (Mallampati class I–IV)	1.07	1.01–1.14	0.02
GerdQ score (univariable, per 1-point increase)	0.99	0.84–1.16	0.88

Dependent variable: modified Mallampati class III–IV versus I–II, except for the ordinal model, in which the outcome is Mallampati class I–IV. The main adjusted model was specified on biological grounds; covariates were not chosen by univariable screening. Firth confidence intervals are profile penalized-likelihood intervals, for which no p value is reported. Variance inflation factors in the main adjusted model were below 1.4. Age and sex were not added to the main model because neck circumference and sex were collinear (r = − 0.71). BMI, body mass index; CI, confidence interval; GerdQ, Gastroesophageal Reflux Disease Questionnaire; OR, odds ratio; RSI, Reflux Symptom Index.

The RSI estimate was stable across the other models examined: OR 1.13 (95% CI 1.05–1.21; p < 0.001) after adjustment for BMI alone, and OR 1.12 (95% CI 1.05–1.20; p = 0.001) after adjustment for BMI, age and sex. There was no evidence of departure from linearity: adding a quadratic RSI term did not improve model fit (p = 0.21), and the nonlinear term of a three-knot restricted cubic spline was not significant (p = 0.83). The proportion of participants with Mallampati III–IV rose across RSI quartiles, from 20.8% in the lowest quartile (RSI 0–4) to 21.7% (RSI 5–9), 44.0% (RSI 10–16) and 77.8% (RSI 17–31) in successive quartiles (Fig. 2B).

Analysis across the four Mallampati categories

RSI scores did not increase monotonically across the four Mallampati categories (class I, mean 10.67 ± 7.02, median 10.5; class II, 7.11 ± 6.25, median 5.0; class III, 14.63 ± 5.85, median 16.0; class IV, 10.00 ± 12.75, median 2.0; Kruskal–Wallis p < 0.001; Fig. 2A). The overall test for an ordered trend was nominally significant (Jonckheere–Terpstra p = 0.018; Spearman ρ = 0.25, p = 0.016), but this reflected the high scores of class III rather than a graded increase across successive categories. In ordinal logistic regression with Mallampati class I–IV as the outcome, the RSI estimate was substantially smaller than in the dichotomized analysis (OR 1.07, 95% CI 1.01–1.14, p = 0.02 unadjusted; OR 1.07, 95% CI 1.00–1.14, p = 0.05 adjusted). The proportional-odds assumption was violated (likelihood-ratio test against a multinomial model, χ^2 = 12.97, 2 df, p = 0.0015). Cutpoint-specific estimates showed where this arose: the RSI odds ratio was 1.00 (95% CI 0.93–1.07) for class II or above, 1.12 (95% CI 1.05–1.20) for class III or above, and 0.99 (95% CI 0.87–1.12) for class IV. The association was therefore concentrated at the boundary between classes II and III, and the ordinal model is reported as an assumption check rather than as a supportive analysis. Only 5 participants were in class IV, so estimates involving that category are very imprecise.

Post-hoc sensitivity analyses for smoking

Current smoking was more common in the Mallampati III–IV group and was associated with higher RSI scores, so two post-hoc analyses examined whether it accounted for the primary finding. Among the 36 participants who were not current smokers, of whom 8 had Mallampati III–IV, the association was at least as strong as in the whole cohort (unadjusted OR 1.26, 95% CI 1.04–1.52; adjusted for BMI, OR 1.31, 95% CI 1.05–1.64; Firth penalized, OR 1.24, 95% CI 1.06–1.59). Among the 54 current smokers the estimate was smaller and its confidence interval included the null (OR 1.06, 95% CI 0.98–1.15). The RSI × smoking interaction was not significant (Wald p = 0.16; likelihood-ratio p = 0.11). These subgroup analyses are underpowered and are reported as effect estimates with confidence intervals rather than interpreted through significance testing, but they argue against current smoking as the sole explanation rather than excluding residual confounding by smoking history.

Secondary analysis: GerdQ

GerdQ scores were similar in the Mallampati I–II and III–IV groups (6.85 ± 2.84 vs 6.77 ± 2.38; p = 0.65). Across the whole cohort the median GerdQ score was 6.0 (interquartile range 6.0–8.0; range 0–15), and 31 participants (34.4%) scored 8 or above, with an almost identical proportion in the two Mallampati groups (34.5% vs 34.3%; p = 1.00). GerdQ was not associated with Mallampati III–IV in univariable analysis (OR 0.99, 95% CI 0.84–1.16; p = 0.88) or in adjusted analyses. In the exploratory model containing RSI, GerdQ, BMI, age and sex, RSI remained associated with the outcome (OR 1.13, 95% CI 1.05–1.22; p = 0.001), whereas GerdQ did not (OR 0.92, 95% CI 0.75–1.12; p = 0.38). RSI and GerdQ were only weakly correlated (Spearman ρ = 0.25, p = 0.019).

Discussion

In this cross-sectional cohort of adults with chronic reflux-type symptoms undergoing elective upper endoscopy, higher RSI scores were associated with Mallampati class III–IV, and the estimate changed little across adjustment models, under Firth penalization, and among participants who were not current smokers. GerdQ scores were similar in the two groups and showed no association with the outcome. The relationship was not, however, graded across all four Mallampati categories, and the proportional-odds assumption was violated, indicating that the observed association was concentrated at the boundary between classes II and III rather than as a dose–response gradient across the whole scale. These results describe an association between one symptom domain and the dichotomized Mallampati grouping; they do not show that Mallampati class identifies GERD or LPR.

The divergent results for RSI and GerdQ are plausible because the two questionnaires emphasize different symptom domains. Most RSI items address upper-airway or throat complaints such as hoarseness, throat clearing, cough and globus, although the instrument also contains one item addressing heartburn and acid regurgitation. GerdQ emphasizes heartburn and regurgitation while additionally incorporating symptom-related sleep disturbance, medication use, epigastric pain and nausea (4, 5). The GerdQ findings did not provide evidence that typical reflux symptom burden accounted for the RSI association in this cohort, although the restricted GerdQ distribution and the differing recall periods limit direct comparison of the instruments. The weak correlation between the two

scores therefore suggests partially distinct symptom patterns rather than wholly separate laryngeal and esophageal constructs. RSI symptoms are nonspecific, however, and can arise from smoking, upper-airway or respiratory disease, heavy voice use, and other causes (2, 3). The head-to-head model suggests that the two questionnaires captured different symptom patterns in our cohort, but it does not show that reflux caused the association.

At least three explanations should be considered for this association, and the present data cannot distinguish between them. First, reflux-related throat symptoms and upper-airway tissue changes could be related, since experimental work supports the susceptibility of laryngeal mucosa to acid- and pepsin-mediated injury (3, 6). We did not measure mucosal inflammation, edema, or anatomical change, so this remains a hypothesis for future work. Second, the association could reflect unmeasured upper-airway anatomy rather than reflux-mediated tissue change. Modified Mallampati class is influenced by the relationship between tongue size and the visible oropharyngeal space, by body habitus, and by examination technique (7–9). Detailed upper-airway anatomical variables such as tonsillar grade were not measured here, so a shared anatomical contribution to both the symptom score and the airway grade cannot be excluded; this would be consistent with the association we observed for neck circumference. Third, smoking and other airway irritants are potential confounders rather than established mechanisms here: current smokers in this cohort had substantially higher RSI scores than those who were not current smokers, and smoking was also more frequent in the Mallampati III–IV group. Our sensitivity analyses argue against smoking as the sole explanation, because the association persisted and was if anything stronger among those who were not current smokers, but they cannot exclude residual confounding by other irritant exposures. The small number of Mallampati III–IV events limited how many covariates could be entered simultaneously, so the adjusted models do not amount to full confounder control.

In a 2025 prospective study of 107 patients undergoing modified electroconvulsive therapy, in which laryngopharyngeal reflux was defined by salivary pepsin rather than by symptoms, Mallampati classification did not differ significantly according to reflux status ($p = 0.208$) (15). That cohort differed from ours in age, indication and reflux definition, and Mallampati class was one of many baseline variables screened rather than the focus of the analysis, so the two studies are not directly comparable. Taken together, however, the contrast suggests that what we observed may be a relationship between upper-airway symptom burden and oropharyngeal phenotype rather than between physiological reflux and the airway, which would also be consistent with the divergent results we found for RSI and GerdQ.

The clinical implications of these findings are limited. GERD is considered during preoperative assessment of regurgitation and aspiration risk, although the observational evidence linking esophageal reflux itself to perioperative aspiration is inconsistent (16, 17), but we did not measure regurgitation, gastric contents, aspiration, laryngoscopic view, or intubation difficulty. These results therefore cannot be used to diagnose reflux or to estimate aspiration risk at the bedside. They support only further study of whether routine airway findings and throat-symptom measures carry complementary information in broader preoperative populations.

Several limitations deserve emphasis. The cross-sectional design precludes causal and temporal inference. The cohort was restricted to symptomatic patients referred for upper endoscopy; without an asymptomatic comparison group, the results may not generalize to an unselected preoperative population. Reflux was assessed by questionnaire rather than by ambulatory pH-impedance monitoring or a standardized endoscopic or laryngoscopic phenotype. The Turkish translations used for questionnaire administration were not independently validated within the present study, which may have introduced measurement variability despite preservation of the original item content and scoring structure.

Mallampati class was graded from standardized photographs by a blinded board-certified anesthesiologist and subsequently confirmed by a second blinded board-certified anesthesiologist. Because separate paired ratings from the confirmatory assessment were not retained, formal interrater reliability could not be quantified. Intrarater reliability was also not assessed, and photographic grading may not fully reproduce routine bedside assessment; tonsillar grade was not recorded. RSI item-level responses were not retained in the study database, so we could not examine whether the association persisted after excluding the RSI item that captures heartburn and acid regurgitation. The association was not monotonic across the four Mallampati categories and the proportional-odds assumption was violated, so the finding should be understood as specific to the conventional I–II versus III–IV dichotomy; with only 5 participants in class IV, the behavior of the highest category is poorly estimated. Sleep-related breathing symptoms were based on repeated reports of snoring and witnessed apneic episodes by a relative rather than a validated obstructive sleep apnea questionnaire or polysomnography. Baseline PPI use was not recorded. Strong correlation between neck circumference and sex limited stable simultaneous adjustment for both in this small dataset. Smoking exposure was recorded only as current versus non-current smoking, so former smokers are included in the non-current group and cumulative exposure such as pack-years was unavailable; residual confounding by smoking history cannot be excluded. Finally, this was a small single-center cohort, and the multivariable estimates require external validation.

A confirmatory study should recruit an unselected perioperative population, retain the four Mallampati categories where sample size permits, include independent repeated airway assessments, collect detailed anthropometric and upper-airway variables, and use objective reflux testing. Such a study could show whether the association is reproducible and whether it adds useful information to established airway and reflux assessments.

Conclusions

Among adults with chronic reflux-type symptoms undergoing elective upper endoscopy, higher RSI scores were associated with modified Mallampati class III–IV after adjustment for BMI, neck circumference and smoking, and the association persisted among participants who were not current smokers and under penalized estimation. No evidence of an association between GerdQ score and Mallampati class was observed, although the restricted distribution of GerdQ scores and the sample size

limit inference. Because the relationship was not graded across the four Mallampati categories and no objective reflux testing was performed, these exploratory findings are best interpreted as a relationship between throat-predominant symptom burden and oropharyngeal phenotype. They do not confirm reflux disease and do not address airway or aspiration outcomes. Larger studies using objective reflux testing and independent repeated airway assessment are needed before the association can inform clinical practice.

Abbreviations

BMI
body mass index
CI
confidence interval
GERD
gastroesophageal reflux disease
GerdQ
Gastroesophageal Reflux Disease Questionnaire
IQR
interquartile range
LPR
laryngopharyngeal reflux
OR
odds ratio
PPI
proton pump inhibitor
RSI
Reflux Symptom Index
SD
standard deviation
STROBE
Strengthening the Reporting of Observational Studies in Epidemiology
VIF
variance inflation factor.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Bahçeşehir University Clinical Research Ethics Committee on 17 April 2019 (decision/protocol No. 2019-08/01). Written informed consent was obtained from all participants prior to enrollment.

Consent for publication

Not applicable.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Author Contribution

Authors' contributionsTK: Conceptualization, data collection, formal analysis, writing—original draft, writing—review and editing.MB: Data curation, writing—review and editing.SKB: Investigation, data curation, formal analysis.YB: Investigation, writing— original draft.CB: Supervision, writing—review and editing.All authors read and approved the final manuscript and agreed to be accountable for the work.

Acknowledgements

Not applicable.

Data Availability

The datasets generated and analyzed during the current study are not publicly available because they contain information that could compromise participant privacy, but are available from the corresponding author on reasonable request.

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Figures

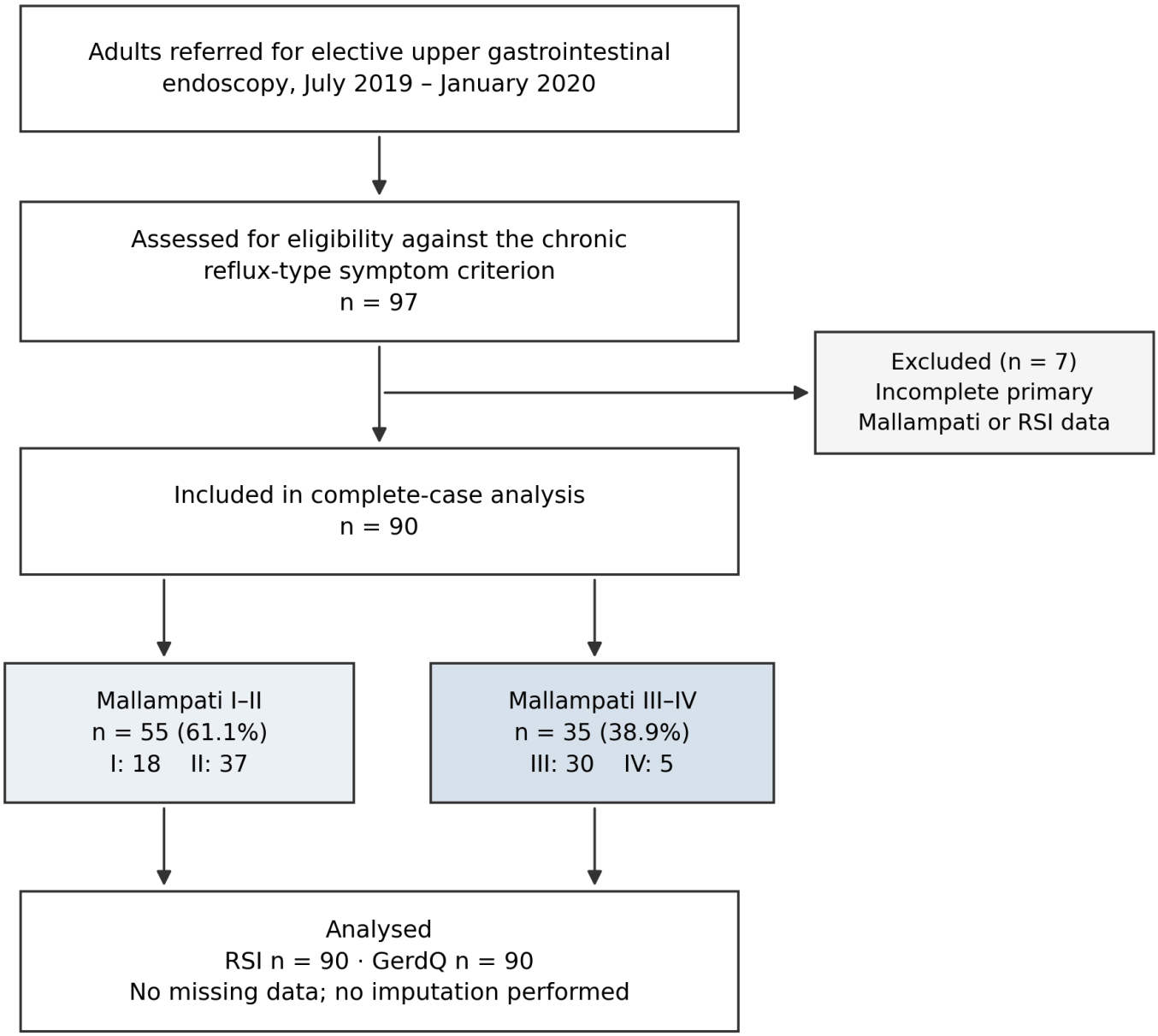


Figure 1

Participant flow through the study. Reported according to the STROBE recommendations for cross-sectional studies.

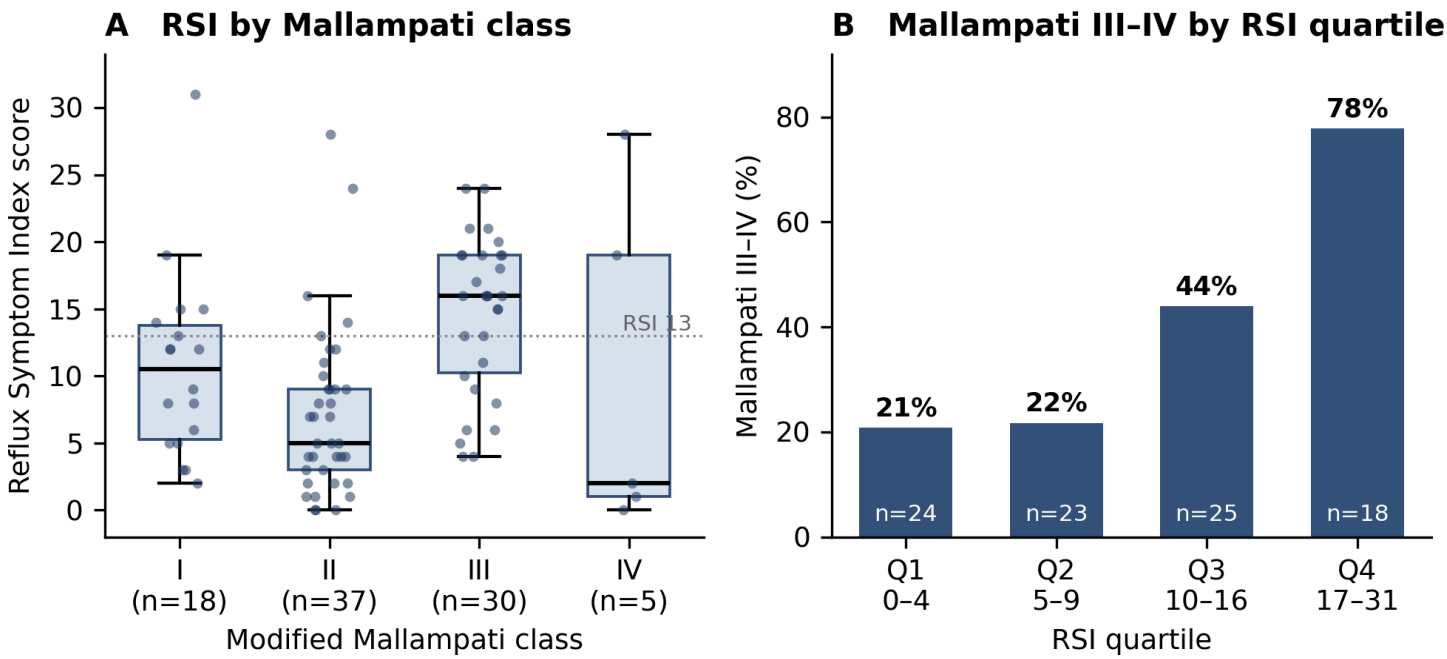


Figure 2

Reflux Symptom Index (RSI) scores and modified Mallampati class. (A) Distribution of RSI scores across the four Mallampati categories; boxes show the median and interquartile range, whiskers extend to 1.5 × IQR, and individual observations are overlaid. RSI does not increase monotonically across categories, and class IV contains only 5 participants. (B) Proportion of participants with Mallampati class III–IV by RSI quartile.