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Salivary Pepsin Concentrations are Higher for Patients with Reflux Associated Laryngeal Symptoms: A Prospective Pilot Study

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Abstract:

Background: Confirming an association between laryngeal reflux symptoms and physiologic reflux is challenging. Pepsin, a proteolytic enzyme produced in the stomach, has been implicated in the pathogenesis of laryngopharyngeal reflux (LPR), and analysis of salivary pepsin may be of diagnostic utility. The aim of this study was to assess for differences in salivary pepsin for patients with LPR and gastroesophageal reflux disease (GERD) symptoms compared to controls.

Methods: We conducted an observational prospective cohort pilot study at a single tertiary care teaching institution. Volunteers were recruited and separated into 3 cohorts based on symptoms measured with validated symptom questionnaires (GerdQ and Reflux Symptom Index (RSI)): 1) Control (RSI ≤13, GerdQ <8); 2) LPR (RSI >13, GerdQ <8); 3) LPR+GERD (RSI >13, GerdQ ≥8). When applicable, proton pump inhibitors were held for ≥ 5 days prior to study. Saliva was collected on 2 consecutive days. Pepsin analysis was performed using a lateral flow device with 2 unique monoclonal antibodies to pepsin (Peptest™, RDBiomed Ltd). Pepsin concentration was estimated semi-quantitatively based on visual comparison to control line and reference to a standard curve, and considered positive if ≥ 1 sample tested positive with a lower limit of pepsin detection of 16 ng/mL. Findings were interpreted by the researchers and manufacturer.

Results: 17 control, 5 LPR, and 8 LPR+GERD subjects were recruited. Inter-rater reliability was 100% for identifying Peptest positivity and 85% for estimating pepsin concentration. LPR+GERD subjects had a significantly higher mean pepsin concentration when compared to controls (117.9 ng/mL *vs* 32.4 ng/mL; p=.01) or to the LPR cohort (7.5 ng/mL, p=.04). Mean pepsin concentration was not significantly different between the control and LPR cohort (32.4 ng/mL *vs* 7.5 ng/mL, p=.11) (Table). There was no statistically significant difference in the proportion of positive Peptest results amongst cohorts. 53% of control subjects compared to 75% of LPR+GERD subjects had a positive test, resulting in 75% sensitivity and 47% specificity for Peptest (Figure).

Conclusions: Peptest revealed higher concentrations of salivary pepsin for subjects with LPR+GERD compared to LPR and control subjects, suggesting that Peptest may be useful in identifying abnormal concentrations of salivary pepsin in patients with reflux associated laryngeal symptoms. However, the proportion of abnormal Peptests were not significantly different between cohorts, with >50% false positives for controls, suggesting that the upper limit of normal pepsin concentration may need to be redefined as >16ng/mL.

Table. Baseline & clinical characteristics for all cohorts

	Control	LPR	LPR + GERD	P-value
Gender (female)	8 (47%)	5 (100%)	6 (75%)	0.08
Ethnicity (Non-Hispanic)	15 (88%)	5 (100%)	5 (71%)	0.46
Body Mass Index (kg/m^2)	22.7 ± 3.3	23.8 ± 3.5	24.4 ± 5.8	0.69
Age (years)	27.1 ± 4.7	55.0 ± 14.3	37.0 ± 9.9	0.001
GerdQ Score	5.7 ± 1.6	5.2 ± 1.3	10.7 ± 3.1	0.0003
RSI Score	3.5 ± 4.5	24.6 ± 6.5	19.6 ± 7.3	0.0001
Abnormal Peptest Results	9 (53%)	2 (40%)	6 (75%)	0.48
Pepsin concentration, Mean (ng/mL)	32.4 ± 41.9	7.5 ± 11.2	117.9 ± 147.4	0.06

Statistical significance ($p<0.05$) determined via Kruskal-Wallis and Chi-square analysis.

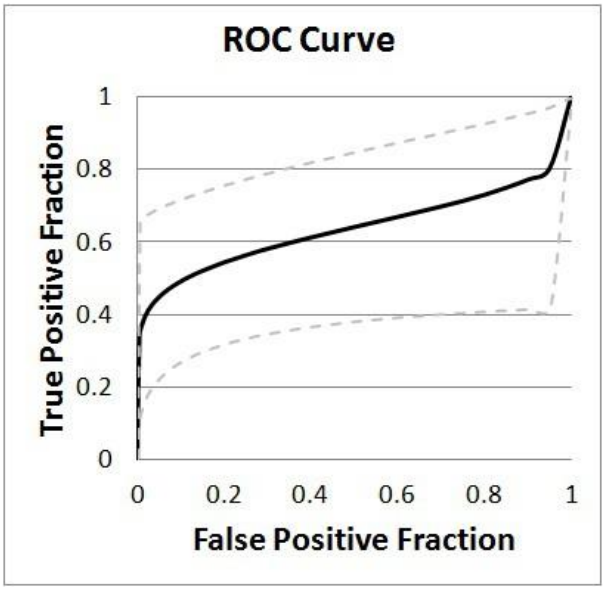

Figure. Receiver operating characteristics (ROC) curve for the detection of LPR+GERD *vs* control subjects with dashed grey lines indicating the 95% confidence interval.