



ABSTRACT

Reinke's edema is a benign inflammatory swelling of the superficial lamina propria of the vocal folds, termed Reinke's space. It is most often associated with cigarette smoking, but literature suggests laryngopharyngeal reflux and voice overuse contribute to the edema. It is suspected that coincident infection with *Helicobacter pylori*, a gram-negative, spiral bacterium, may worsen the severity of Reinke's edema. The purpose of this investigation is to assess the incidence of *H. pylori* infection in patients with Reinke's edema, and to assess the correlation of *H. pylori* infection with disease severity.

INTRODUCTION

Although Reinke's edema shares risk factors with malignancy, it is a benign disease of the vocal folds with a 0-3% chance of dysplasia.¹ Patients presenting with Reinke's edema commonly complain of dysphonia with females presenting more than males. The reasoning for this suggests women notice more subtle changes in the frequency of their voices. In addition to cigarette smoking, the primary risk factor, laryngopharyngeal reflux (LPR) is associated with an increased risk of Reinke's edema through gastric contents traveling up the esophagus and bathing the vocal folds.

H. pylori is a gram-negative, spiral bacterium that colonizes gastric mucosa and is protected from stomach acid contents by its motility and urease. The relationship between *H. pylori* and LPR has somewhat limited and controversial research. A literature review showed some studies finding no relationship between LPR and *H. pylori*.³ Another study, however, found that treatment of *H. pylori* positive patients experiencing LPR with triple therapy antibiotics had a 90% symptom improvement. The group of *H. pylori* positive patients treated just for LPR showed only a 40% symptom improvement.³ A 43.9% prevalence of *H. pylori* in LPR patients were found through a meta-analysis.² Another study found *H. pylori* in the laryngeal biopsy in more than one third of their patients but concluded further studies need to be done to confirm the relationship of laryngeal disorders and *H. pylori*.⁴ Based on existing literature, the relationship between *H. pylori* and LPR has yet to be confirmed or rejected.

MATERIALS & METHODS

Potential subjects were identified during their visits to the Otolaryngology clinic. Flexible laryngoscopic examination was used to diagnose patients with Reinke's edema. Once diagnosed with Reinke's edema, patients either received a *H. pylori* IgG blood test or a laryngeal biopsy was taken during surgery to identify *H. pylori* infection. Severity of Reinke's edema was determined by grade and type. Grades 1-4 were determined by how much of the glottic airway was obstructed and the severity of the polypoid lesion. Grade 1 is characterized as minimal polypoid degeneration involving 25% of the glottic airway, grade 2 as an expanding polypoid lesion involving 25-50% of the glottic airway, 3 as an expanded polypoid lesion involving 50-75% of the glottic airway, and 4 as obstructive lesion involving greater than 75% of the glottic airway. Types 1-4 were determined as type 1 involving one vocal fold, 2 involving both vocal folds, 3 involving one vocal fold with a polypoid lesion, and 4 involving both vocal folds with polypoid lesions. Severity was determined by a fellowship trained laryngologist. VHI-10 surveys, a 10-question survey, were given to patients at the time of the visit and was used to measure voice outcome.

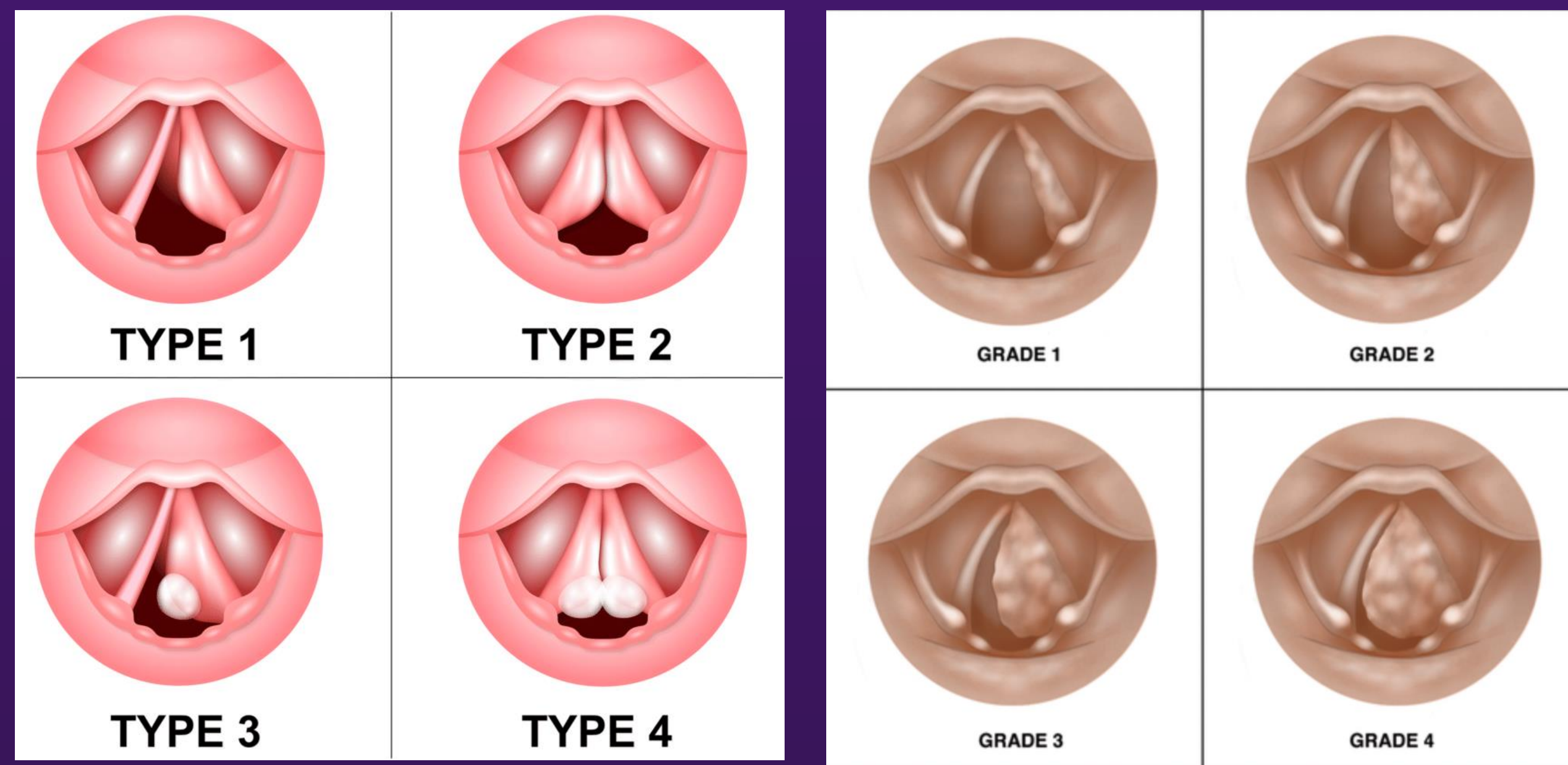


Figure 1. Reinke's edema typing scheme as proposed by De Vincentiis, Marco, et al. in "Reinke's Edema: A Proposal for a Classification Based on Morphological Characteristics".

Figure 2. Reinke's edema grading scheme as proposed by Tan, Melin, et al. in "Clinical Grading of Reinke's Edema".

OBJECTIVES

- Assesses the incidence of *H. pylori* in Reinke's edema patients
- Evaluate and compare the disease severity of patients who are *H. pylori* positive with those who are *H. pylori* negative

HYPOTHESIS

It is anticipated that patients with *H. pylori* infection will have a greater severity of Reinke's edema. Secondly, a higher VHI-10 score will be seen in the *H. pylori* patients.

RESULTS

	H. pylori (+)	H. pylori (-)	p value
VHI-10 Total	10	30.5	0.05
My voice makes it difficult for people to hear me.	4	3.5	0.04
People have difficulty understanding me in a noisy room.	1	3.5	0.04
My voice difficulties restrict personal and social life.	1	3	
I feel left out of conversations because of my voice.	2	2.67	0.02
My voice problem causes me to lose income.	1	1.17	
I feel as though I have to strain to produce voice.	1.25	3.33	
The clarity of my voice is unpredictable.	1	3.5	
My voice problem upsets me.	1.25	3.33	
My voice makes me feel handicapped.	1.25	3.17	
People ask, "What's wrong with your voice?"	1	3.33	0.05

Table 1. The average score of *H. pylori* positive and *H. pylori* negative patients in each domain of the VHI-10 as well as the total score.

The cohort included 16 patients, 13% of whom were male with an average age of 55.88 +/- 9.6 years. The average duration of smoke exposure was 28.32 +/- 20 years. 37.5% of the cohort had a positive *H. pylori* test. It was found that men had a significantly greater smoking exposure in pack years than the females (p=0.003). The total VHI-10 score was significantly greater in patients with a negative *H. pylori* (p=0.05). This was also true for three of the VHI domains "People have difficulty understanding me in a noisy room." (p=0.04), "I feel left out of conversations because of my voice." (p=0.02), and "People ask, "What's wrong with your voice?" (p=0.05). One domain, "My voice makes it difficult for people to hear me.", showed those with *H. pylori* scoring higher than those negative for *H. pylori* (p=0.04).

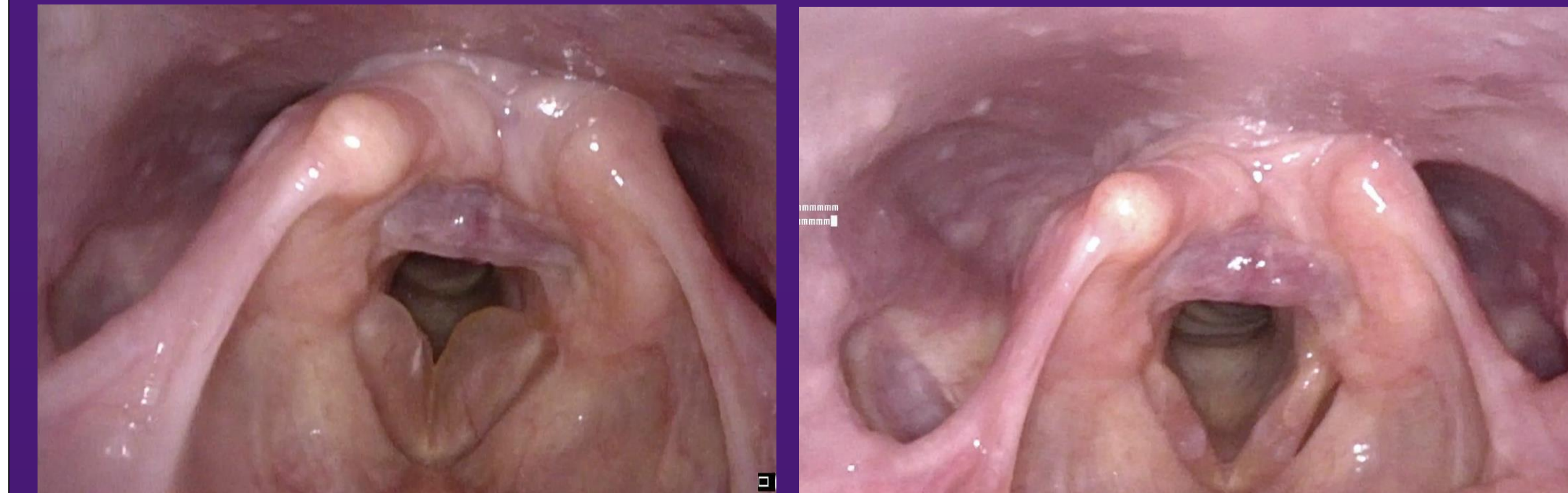


Figure 3. The left picture depicts a *H. pylori* positive female with Grade 3 Type 4 Reinke's edema preoperatively. The picture on the right depicts the same patient post-op Reinke's excision.

CONCLUSION

The data presented is not able to answer the question – does *H. pylori* status impact Reinke's severity. Hopefully with a larger sample size that question will be answered in the future. Although there was no significant relationship between *H. pylori* status and severity of Reinke's edema, there is a significant relationship between *H. pylori* status and dysphonia, a subjective Reinke's symptom. The interim analysis shows *H. pylori* positive patients scoring significantly lower than *H. pylori* negative patients. This perhaps suggests *H. pylori* infection provides a protective effect. The inflammatory response to the *H. pylori* may protect against prolonged heat or smoke exposure, limiting dysphonia.

The cohort being only 13% males agrees with research suggesting females present with Reinke's edema more than men. Women notice a change in their voice more often than men and will be diagnosed earlier. This correlated with men in the cohort presenting later, they have a longer history of smoking and a greater threshold to seek care because voice change is less obvious in men. The two methods of assessing disease burden are type and grade. While these methods are meant to be objective and create a common language in assessing Reinke's edema, neither are very effective in communicating the severity of the disease and depend on the experience of the individual performing the laryngoscopy and viewing it.

ONGOING STUDIES

Power calculations indicate that this study requires 25 subjects. After accounting for attrition, it was determined that at least 30 patients would need to be included. The data presented here represents a preliminary data analysis. Given the small cohort size, it is likely that statistical significance will be different at the time of final data analysis. It is anticipated that recruitment will be complete one year after initial enrollment. Given the current rate of recruitment, study personnel expect completion in June 2023.