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Correlation between "White Line" of Pharyngeal Posterior Wall and Laryngopharyngeal Reflux Disease

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Abstract: Objective: To explore the relationship between the "white line" of the posterior pharyngeal wall and laryngopharyngeal reflux disease (LPRD). **Methods:** The subjects were examined by fiberlaryngoscopy, and RSI and RFS scores were performed. The posterior pharyngeal wall was observed to determine the "white line", the mucosal boundary between the nasopharynx and oropharynx. **Results:** There was a significant difference in RFS values of the three types of white lines (P = 0.017), and the significant difference was between type I and III (P = 0.006). Age, gender, RSI, and RFS were included to construct the ordered multi-classification logistics regression equation. The effect of RFS on the white line was statistically significant (OR = 0.8, 95%CI −0.326∼−0.053, P = 0.008). **Conclusions:** The "white line"—the mucosal boundary between nasopharynx and oropharynx—has a correlation with laryngopharyngeal reflux.

Keywords: "White Line"; Throat Reflux Disease; RSI; RFS

1. Introduction

The 2006 Montreal consensus defines GERD as a disease caused by reflux of gastric contents causing discomfort symptoms and/or complications, and GERD is divided into esophageal symptom syndrome and extra-esophageal symptom syndrome [1]. In otolaryngology, extra-esophageal reflux is called laryngopharyngeal reflux disease (LPRD), which is defined as the reflux of gastric contents to the parts above the upper esophageal sphincter muscle (including the nasal cavity, oral cavity, pharynx, larynx, trachea, lung, etc.). Laryngopharyngeal reflux disease is a general term for a series of symptoms and signs caused by reflux of gastric contents to the site above the upper esophageal sphincter (UES) [2]. The clinical presentation of LPRD differs from gastroesophageal reflux disease. It manifests as globus pharyngeus, throat clearing, persistent cough, etc.

The gold standard for diagnosis is hypopharyngeal impedance pH monitoring. However, pH monitoring is expensive and invasive and can be poorly tolerated in patients. The reflux symptom index (RSI) and the reflux finding score (RFS) are recognized as important diagnostic tools for laryngopharyngeal reflux disease [3, 4].

The reflux is not only limited to the laryngopharynx, but also may involve the nasopharynx. It is considered that the reflux is involved in the pathogenesis of secretory otitis media and adenoid hypertrophy. We sometimes notice a clear boundary on the posterior pharyngeal wall—a white line during laryngoscopy in clinical practice. We speculate that this white line is related to reflux. This study aims to investigate the relationship between the pharyngeal "white line" and laryngopharyngeal reflux using the above two scales as an important reference.

2. Materials and Methods

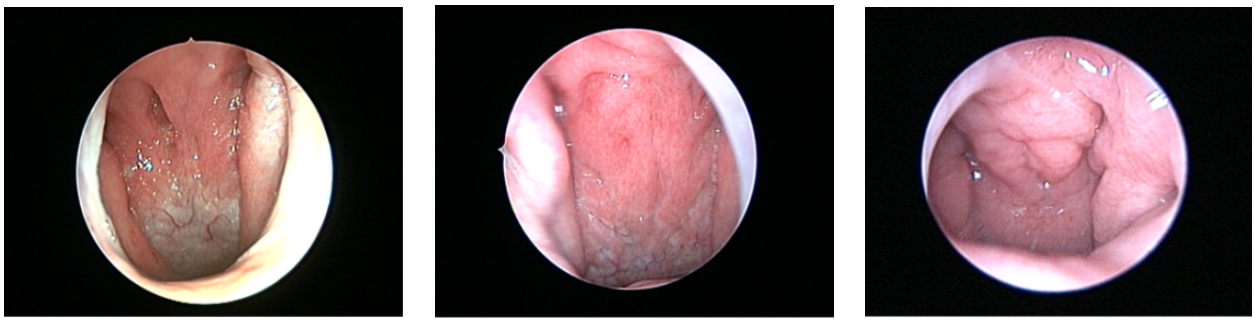
Ethics approval for this study was obtained from the Ethics Committee of Peking University International Hospital (2023-KY-0012). Seventy patients complained of throat discomfort, including foreign body sensation in the pharynx, cough, hoarseness, and other nonspecific symptoms. The medical history is more than one month. Exclusion criteria: acute and chronic inflammation, malignant tumors, allergic diseases, and severe neurological diseases, etc. The voluntary consent was obtained. All patients who met the criteria completed the Chinese version of the RSI, guided by the medical staff if necessary. This scale was accurately translated from the original RSI scale and contained assessment of nine subjective symptoms. According to the severity of the different symptoms, the score for a specific symptom ranged from 0 (no symptom) to 5 (very severe), and the total score could be between 0 and 45 points [5].

All patients underwent assessment by transnasal fiberoptic laryngoscopy (PENTEX). According to the RFS scale developed by Belafsky, for the 8 physical signs, the score can be between 0 and 26 points. Two physicians of different levels scored patients' RFS separately and took their average value. During the fiberlaryngoscopy, the boundary between the nasopharynx and oropharyngeal mucosa of the posterior pharyngeal wall was carefully observed and assessed by both physicians.

According to the morphology of the posterior pharyngeal wall we observed, it was artificially divided into three types:

"White line" classification (Figure 1) :
Type I: The color of the nasopharyngeal mucosa was significantly different from that of oropharyngeal mucosa. The color of the nasopharyngeal mucosa was light red, and the color of the oropharyngeal mucosa was light white, with a clear boundary of approximately horizontal between the two. White line is strong positive.
Type II: The color of the nasopharyngeal mucosa and oropharyngeal mucosa could still be distinguished, but the dividing line between the two was blurred or irregular. White line is positive.
Type III: There was no significant difference in color between the nasopharyngeal mucosa and oropharyngeal mucosa, and the boundary between them could not be distinguished. White line is negative.

SPSS 20.0 statistical software was used for statistical analysis of the data. Mean ± standard deviation was used to describe the data conforming to normal distribution, analysis of variance was used for the patients with three types of white lines, and the Chi-square test was used to compare the rates. Age, gender, RSI and RFS were included in the white line results to construct the ordered multi-classification logistics regression equation. Test value $\alpha \leq 0.05$.



(**a**) Type I (**b**) Type II (**c**) Type III

Figure 1. While Line classification, three types can be observed. (**a**) Type I: A clear boundary of approximately horizontal between nasopharyngeal and oropharyngeal mucosa. (**b**) Type II: The boundary is blurred or irregular, but still be distinguished. (**c**) Type III: The boundary could not be distinguished.

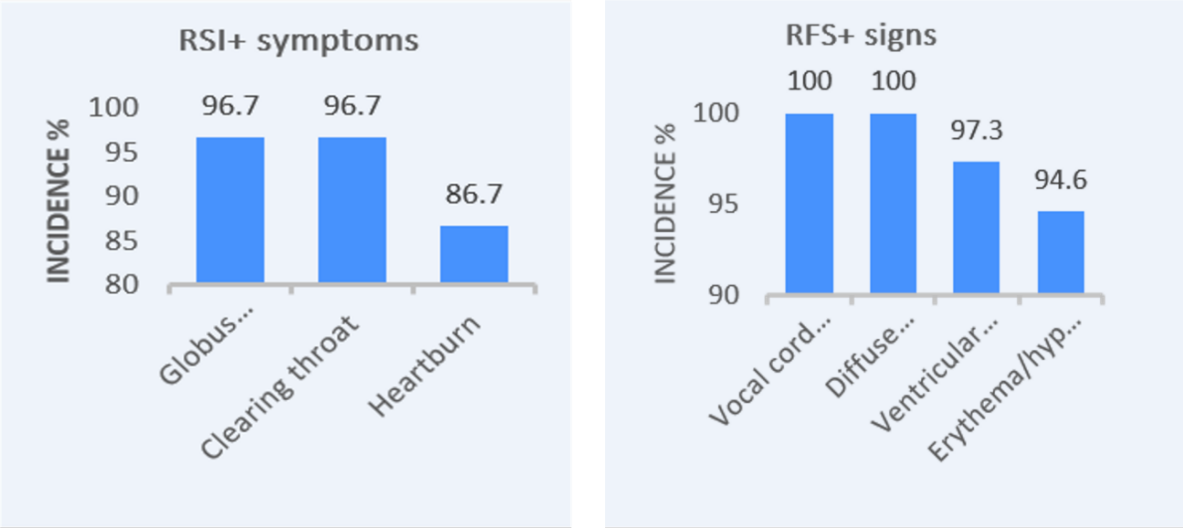
3. Results

RSI scores of patients ranged from 0 to 29 points, and the data were in line with normal distribution, with an average score of 12.64 ± 7.25. Among them, the positive rate (>13 points) was 42.9% (30 cases). The scores of RFS

ranged from 2 to 18 points, and the data were in line with normal distribution, with an average score of 7.66 ± 3.37. Among them, the positive rate (>7 points) was 52.9% (37 cases). The positive rate of both RSI and RFS was 25.7% (18 cases), the positive rate of RSI or RFS was 44.3% (31 cases), the positive rate of RSI and/or RFS was 70%, and the negative rate of both RSI and RFS was 2.9% (21 cases).

The most common symptoms of RSI positive patients were: foreign body sensation in pharynx 96.7% (29/30 cases), with an average score of 3.8; continuous throat clearing was 96.7% (29/30 cases), with an average score of 3.2. Heartburn, chest pain and stomach pain were 86.7% (26/30 cases), with an average score of 2.7 (Figure 2a).

The most common signs in patients with positive RFS were: vocal cord edema and diffuse laryngeal edema were 100% (37/37 cases), with an average score of 1.7 and 1.5, respectively; ventricular disappearance 97.3% (36/37 cases), with an average score of 2.3. Erythema/hyperemia and posterior commissure hypertrophy were 94.6% (35/37 cases), with average scores of 2.1 and 1.6, respectively. Only 7 cases of thick endolaryngeal mucus, and only 1 case of granuloma was found (Figure 2b).



(**a**) (**b**)

Figure 2. The most common symptoms of RSI positive patients and RFS positive patients. (**a**) Globus hysterics 96.7%; Clearing throat 96.7%; Heartburn 86.7%. (**b**) Vocal cord edema and Diffuse laryngeal edema 100%; Ventricular disappeared 97.3%; Erythema/hyperemia and Posterior commissure hypertrophy were 94.6%.

The RSI and RFS data after the white line classification were in line with normal distribution (Table 1). Among the 70 subjects, 22 cases were type I, 31 cases were type II, and 17 cases were type III. There was no statistical difference in the RSI value of three types of white line (P = 0.521). However, there was a significant difference in RFS values of the three types of white lines (P = 0.017), and the significant difference was between type I and III (P = 0.006). Age, gender, RSI and RFS were included to construct the ordered multi-classification logistics regression equation. The results showed that the influence of age, gender and RSI on the "white line" was not statistically significant. However, the effect of RFS on the white line was statistically significant (OR = 0.8, 95%CI −0.326~−0.053, P = 0.008).

Table 1. The RSI and RFS data of the white line.

White Line	N	RSI	RFS
Type I	22	13.82 ± 5.93	8.64 ± 3.70
Type II	31	12.65 ± 7.18	8.03 ± 3.07
Type III	17	11.12 ± 8.92	5.71 ± 2.80
P	-	0.521	0.017 (I and III 0.006)

Note: RSI: reflux symptom index; RFS: reflux finding score.

4. Discussion

The literature reports a worldwide incidence of laryngopharyngeal reflux disease of 7.1 to 30% in the general population [6]. A recent study of a large sample multicenter epidemiological survey (n = 90,440) [7] in China found that the incidence of LRPD (RSI positive) was about 10.15% among outpatients visiting otolaryngology head and neck surgery clinics. According to Koufman [8], LRPD (pH monitoring) accounts for 50% of throat diseases. This study found that the positive rate of RSI and/or RFS in outpatient throat diseases is 70%, and LPRD is one of the important causes of throat discomfort.

In recent years, studies have shown that pepsin can be detected and/or accompanied by a decrease in pH value in the nasopharynx, Eustachian tube, and even middle ear cavity in addition to throat diseases. It is suggested that reflux is not only limited to the laryngopharynx, but also may involve the nasopharynx and middle ear cavity. This pathological process may also be involved in the occurrence and development of diseases such as adenoid hypertrophy and secretory otitis media. Brunworth [9] compared 20 patients with Eustachian tube dysfunction and 21 normal subjects and found that the nasopharyngeal pH, reflux events and RFS in the Eustachian tube dysfunction group were different from those in the normal group. By comparing adenoid hypertrophy and normal children's dual pH probes, KELES [10] found that the rate of laryngopharyngeal reflux in children with adenoid hypertrophy was 46.7%, and that in the control group was 8.3%. We concluded that there was a relationship between adenoid hypertrophy and laryngopharyngeal reflux, which may be an important reason. In O'Reilly's study [11], pepsin was detected in 20% of 509 children with recurrent secretory otitis media compared with only 1.4% of 64 controls, thus suggesting that pepsin is an independent risk factor for secretory otitis media.

The pharynx is bounded by the soft palate and divided into the nasopharynx and oropharynx. The pharyngeal mucosa is composed of epithelium and lamina propria, the oropharynx surface is stratified flat epithelium, and the nasopharynx and laryngopharynx are pseudostratified ciliated columnar epithelium. Up to now, the surface boundary of nasopharyngeal and oropharyngeal mucosa has not been unified, and no relevant literature has reported the change of mucosal color. Neri et al. [12] observed 60 patients with nasopharyngeal foreign body sensation, whose 24h-pH and RSI all confirmed the presence of definite laryngopharyngeal reflux, and observed a clear boundary line of the posterior pharyngeal wall, which was called the "white line". The main pathological manifestation below the line is parakeratosis, which may be related to laryngopharyngeal reflux. This study also found that nasopharyngeal reflux may cause mucosal changes in the posterior pharyngeal wall, resulting in mucosal differentiation—white line.

The pathogenesis of laryngopharyngeal reflux disease is still not well understood. Current studies suggest that the anatomical basis of laryngopharyngeal reflux disease is relaxation of the upper esophageal sphincter. Szczesniak [13] found that all laryngopharyngeal reflux occurred in the upright position, and 91% were related to active relaxation of the upper esophageal sphincter. The study of Postma [14] showed that the time of esophageal acid clearance in LPRD patients was significantly longer than that in healthy controls, and the abnormal esophageal peristalsis weakened the mucosal acid resistance. Furthermore, the acid resistance of the pharyngeal mucosa is weaker than that of the esophageal mucosa.

Under the action of gastric acid and pepsin, the pharyngeal epithelial mucosa undergoes inflammatory infiltration, edema and hyperplasia [15], which promote cell proliferation, differentiation and apoptosis [16]. During swallowing, the saliva undergoes acidic neutralization after the reflux comes into contact with the pH sensor [17]. However, the nasopharynx, which is generally not exposed to swallowed saliva and lacks acid neutralization, may be more markedly affected by reflux.

5. Conclusions

Laryngeal reflux disease is one of the most important causes of laryngeal discomfort in the outpatient department. The incidence of laryngeal reflux disease (RSI and/or RFS positive rate) in patients with throat discomfort was 70%. The mucosal boundary between nasopharynx and oropharynx—the "white line", has correlation with pharyngeal reflux.

Author Contributions

Data curation, L.Z.; writing, J.X.; supervision, H.G. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Peking University International Hospital (2023-KY-0012).

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.
Written informed consent has been obtained from the patient(s) to publish this paper.

Data Availability Statement

The research data is all included in the article.

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Conflicts of Interests

All the authors declare that there is no conflict of interest regarding the publication of this paper.

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