Research Article

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Applicability of Narrow Band Image (NBI) to diagnose Laryngopharyngeal reflux disease (LPRD).

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ABSTRACT

Objectives: Laryngopharyngeal reflux disease (LPRD) can be challenging to diagnose due to its variable and non-specific symptoms, often leading to multiple doctor visits and delayed diagnosis. While conventional methods like flexible fiberscope examination are commonly used, they may lack the specificity needed to accurately identify LPRD.

Study design: Narrow band imaging (NBI), a technique that enhances visualization of submucosal capillaries, could offer a more reliable diagnostic tool. This study explores the potential of NBI for detecting LPRD by examining the correlation between nasopharyngeal capillary patterns and the Frequency Score of the Symptoms of GERD (FSSG) questionnaire. A total of 170 patients from the Nihon University Matsudo Dental Hospital between 2016 and 2023 were studied.

Methods: All patients underwent NBI to assess their nasopharyngeal capillary pattern, which was categorized as occupying more than 50%, less than 50%, or absent in the nasopharynx. Additionally, the patients completed the 14-question FSSG questionnaire to evaluate gastroesophageal reflux disease (GERD) and related symptoms. The correlation between the NBI findings and the FSSG results were statistically analyzed using correlation coefficients.

Results: The NBI results showed that 63.5% of patients had more than 50% nasopharyngeal capillary pattern, 30% had less than 50%, and 6.5% had no capillary pattern. There was a significant correlation between the NBI score and FSSG question 7, indicating that enhanced nasopharyngeal capillaries are associated with greater symptom severity. Most patients experienced symptom improvement within 1-3 months of treatment with rabeprazole sodium.

Conclusion: Taken together, the NBI shows promise as a diagnostic tool for LPRD. NBI can visualize distinctive patterns in the nasopharyngeal capillaries that correlate with specific symptoms identified through the FSSG questionnaire. The findings highlight NBI's potential to improve the accuracy of LPRD diagnosis, and suggest the FSSG questionnaire, particularly question 7, may be a useful supplementary screening tool for LPRD patients.

Keywords

LPRD, NBI, FSSG, MCP, PPI

INTRODUCTION

Laryngopharyngeal reflux disease (LPRD) can be challenging to diagnose due to its variable symptoms, often leading patients to see multiple doctors before receiving a proper diagnosis[1]. Common LPRD symptoms include throat discomfort, hoarseness, a burning sensation, and frequent throat clearing. Gastric acid is believed to be a cause and has also been linked to middle ear symptoms in some patients[2]. Flexible fiberscope examination is a common diagnostic tool for LPRD. However, the findings are often subtle, and interpretations can vary depending on the specialist[3]. LPRD shares many symptoms with upper aerodigestive tract inflammation, which leads to a lack of specificity and sensitivity in diagnostic tests. As a result, a diagnosis of LPRD typically relies on a combination of signs and symptoms[4]. Although several diagnostic methods, including pH monitoring, have been proposed, none have demonstrated consistent reliability due to practical constraints[5 6]. Narrow Band Imaging (NBI) has emerged as a powerful diagnostic tool, surpassing conventional fiberoptic examination in its ability to clearly visualize submucosal capillaries, making it invaluable for early cancer detection[7 8 9].

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Additionally, NBI has demonstrated utility in diagnosing benign conditions[10]. NBI has revealed distinct patterns of submucosal capillaries in the nasopharynx of patients with laryngopharyngeal reflux disease (LPRD) that are not as clearly visible with traditional fiberscope methods. Additionally, the Frequency Scale for the Symptoms of GERD (FSSG), developed by Kusano et al. in Japan, has become a widely used and reliable tool for assessing GERD symptoms in gastroenterology[11]. The 14-question FSSG questionnaire has proven effective not only in diagnosing GERD, but also in identifying symptoms in non-GERD patients[12]. Given that LPRD is considered a form of extra-esophageal GERD3 , FSSG has been suggested as a useful screening tool for patients with LPRD symptoms like throat discomfort[13 14]. This study evaluated the use of NBI to assess submucosal capillary patterns in the nasopharynx as a means of diagnosing LPRD. We also examined the correlation between these NBI findings and patient responses to the FSSG questionnaire.

PATIENTS AND METHODOLOGY

From 2016 to 2023, patients were observed at the Nihon University Matsudo Dental Hospital. We obtained Institutional Review Board (IRB) approval from our institution (EC-22-017). For both age and the improvement period (in months), we calculated the median and interquartile ranges. At the initial visit, patients completed the FSSG questionnaire. All patients underwent flexible fiberscope examination, which was performed using the NBI system (VISERA OTV-S7Pro CLV-S40Pro, OEV 191H, ENF Type VQ Olympus Optical Co, Ltd, Tokyo, Japan). The NBI examination employed blue light with a narrow 415 nm band filter, which has the shortest wavelength to effectively penetrate mucosal tissues[7]. This enhanced the visualization of submucosal tissues and capillaries, as the nasopharyngeal submucosal tissue and capillaries exhibit maximum hemoglobin absorption at this 415 nm wavelength. As a result, the blue light filter enabled a more precise definition of the vascular structures and patterns compared to conventional endoscopy. In patients with LPRD, the submucosal capillary pattern observed via NBI in the nasopharynx exhibited distinct, enhanced mucosal capillary shapes. All fiberscope examinations were conducted with the scope placed at the posterior edge of the nasal cavity, covering the area from the eustachian tube orifice to the posterior wall of the nasopharyngeal mucosa. These nasopharyngeal capillary patterns were categorized into three groups based on the extent of capillary enhancement: more than 50%, less than 50%, and no enhancement. Each category was scored as follows: 2 for more than 50% enhancement, 1 for less than 50%, and 0 for no enhancement. The FSSG consisted of 14 questions, with symptom frequency scored as: never (0), occasionally (1), sometimes (2), often (3), and always (4) (**Table 1**). All patients were prescribed 10 mg or 20 mg of rabeprazole sodium.

Table 1: The FSSG (Frequency Scale for the Symptoms of GERD questionnaire

Questions		Frequency				
		Never	Occasionally	Sometimes	Offen	Always
1	Do you get heartburn?	0	1	2	3	4
2	Do you sometimes subconsciously rub your chest with your hand?	0	1	2	3	4
3	Do you get heartburn after meals?	0	1	2	3	4
5	Do you get bitter liquid (acid) com ing up into your throat?	0	1	2	3	4
6	Do you get heartburn if you bend over?	0	1	2	3	4
7	Do you have an unusual (e.g burning) sensation in your throat?	0	1	2	3	4
8	Does your stom ach get bloated?	0	1	2	3	4
9	Does your store ach ever feel heavy after meals?	0	1	2	3	4
10	Do you ever feel sick after meals?	0	1	2	3	4
11	Do you feel full while eating = eals?	0	1	2	3	4
12	Do you burp a lot?	0	1	2	3	4
13	Do you get epigastric pain (burning) af ter meals?	0	1	2	3	4
14	Do you get epigastric pain (burning) before meals?	0	1	2	3	4

Statistical analysis

The correlation coefficients were calculated to analyze the relationship between responses to question 7 of the FSSG and NBI scores. The variables were defined as follows: X (0, 1, 2, 3, 4) represented the score for question 7, and Y (0, 1, 2) represented the corresponding NBI score. The formula for the correlation coefficient r is defined when $\bar{X}$ and $\bar{Y}_i$ represent the respective mean values of variables X and Y:

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$$r_i = \frac{S_{XY_i}}{\sqrt{S_X S_{Y_i}}}$$

The components of this formula are as follows:

$$S_X = \frac{1}{n}\sum_{k=1}^{n}(X_k - \bar{X})^2 \; S_{Y_i} = \frac{1}{n}\sum_{k=1}^{n}(Y_k - \bar{Y_i})^2 \; S_{XY_i} = = \frac{1}{n}\sum_{k=1}^{n}(X_k - \bar{X})^2 (Y_k - \bar{Y}_i)^2$$

This analysis used the following variables: n is the number of data, i is the value of NBI (i = 0, 1, 2), S_{XY_i} is the covariance, and S_X and S_{Y_i} represent the variance of X and Y_i, respectively. The mean frequency scores from the FSSG were analyzed using the Steel-Dwass test.

RESULTS

The study population consisted of 170 patients with a median age of 66 years (IQR: 55–74 years). The cohort included 119 males (70%) and 51 females (30%). Prior to referral to our department, 19 patients (11.2%) had visited one clinic, while 17 patients (10%) had visited two or more clinics. Of the 170 patients, 28 (16.5%) were treated with rabeprazole alone, while the remaining 142 patients (83.5%) received multiple medications. Patients were prescribed a combination of antibiotics, antihistamines, and mucolytic drugs only after their sinusitis symptoms and CT scan findings were confirmed. All patients experienced improvement in LPRD symptoms, with the post-treatment improvement period lasting a median of 2 months (interquartile range: 1-3 months), as shown in **Table2**. The capillary patterns in the nasopharynx were categorized into three groups: more than 50% capillary occupancy (**Figure 1**), less than 50% capillary occupancy (**Figure 2**), and no visible capillaries (**Figure 3**). Among the evaluable patients, the majority (63.5%, n=108) exhibited more than 50% capillary occupancy, while 30% (n=51) showed less than 50% occupancy, and 6.5% (n=11) had no visible capillaries. The FSSG questionnaire results revealed that question 7 had a notably higher proportion of patients with the maximum frequency score of 4 (always) compared to all other questions (**Figure 4**). Additionally, the frequency score for question 7 showed a statistically significant difference from the scores of all other questions ($p<0.01$) (**Figure 5**). Patients with a nasopharyngeal mucosal capillary pattern covering over 50% exhibited higher FSSG scores (**Table 3**). The FSSG score and NBI score had a strong positive correlation, ranging from r0 = 0.67 when NBI=0 to r1 = 0.95 when NBI=1 and r2 = 0.92 when NBI=2. Furthermore, the graph's slope became increasingly steep as the NBI score increased (**Figure 6**).

Table 2 : PPI+: Patients were prescribed a combination of antibiotics, antihistamines, and mucolytic drugs only after their sinusitis symptoms and CT scan findings were confirmed.

	n (%)
Age (years)	66 (55, 74)
Gender	
Female	119 (70.0)
Male	51(30.0)
NBI	
None	11(6.5)
< 50%	51(30%)
> 50%	108 (63.5)
PPI Type	
PPI	28 (16.5)
PPI+	142(83.5)
Improvement Period (months)	2 (1, 3)
Prior hospitals visited	
None	134 (78.8)
One	
Two or more	17 (10.0)

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Table 3: Patients numbers between score of NBI and frequency score of question.

Question 7		Score of Question				
		0	1	2	3	4
Score of NBI	0	1	2	2	1	5
	1	2	4	8	13	24
	2	3	4	21	23	57

Figure 1: Nasopharyngeal mucosal capillaries pattern occupying more than 50%.

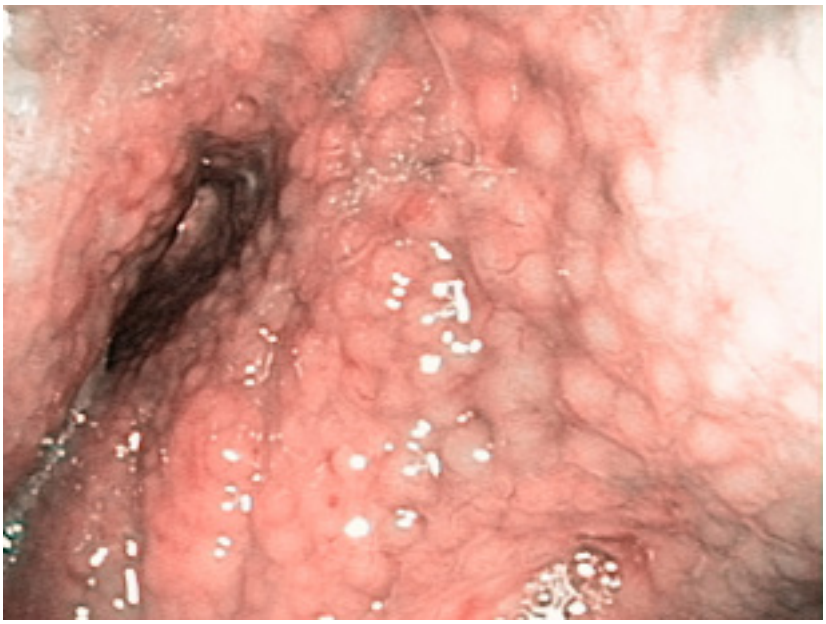

Figure 2: Nasopharyngeal mucosal capillaries patten occupying less than 50%.

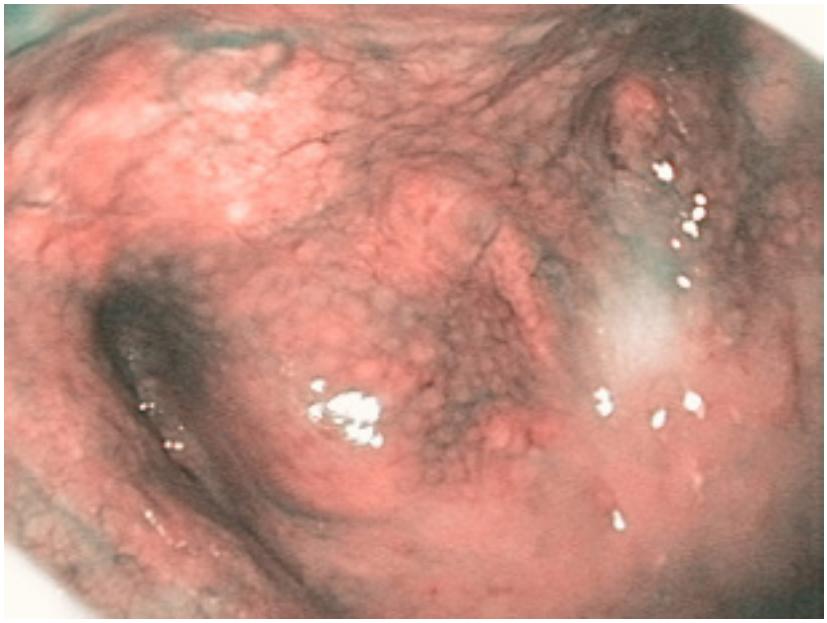

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Figure 3: No nasopharyngeal mucosal capillaries pattern.

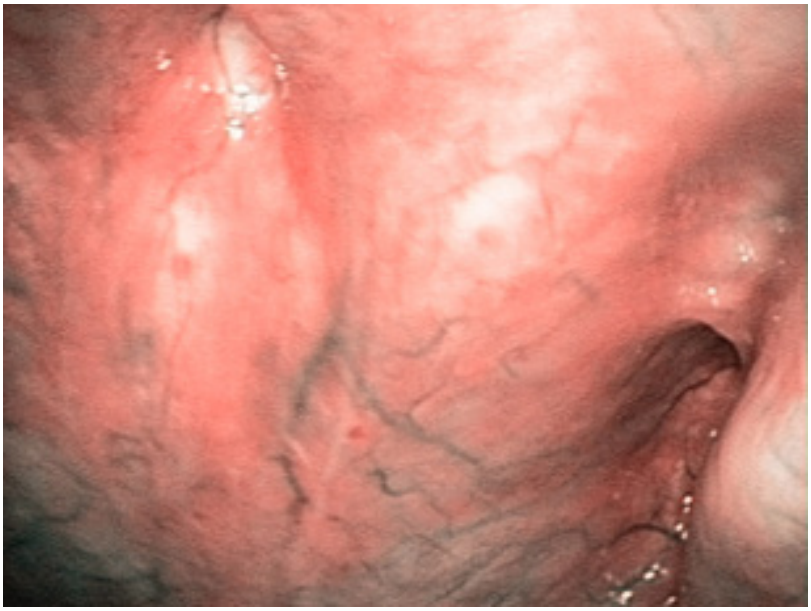

Figure 4: This graph shows frequency score 4 of question7 is the largest number of patients in all questions. Right square: never;0, 1, occasionally; 2, sometimes; 3, often; 4, always

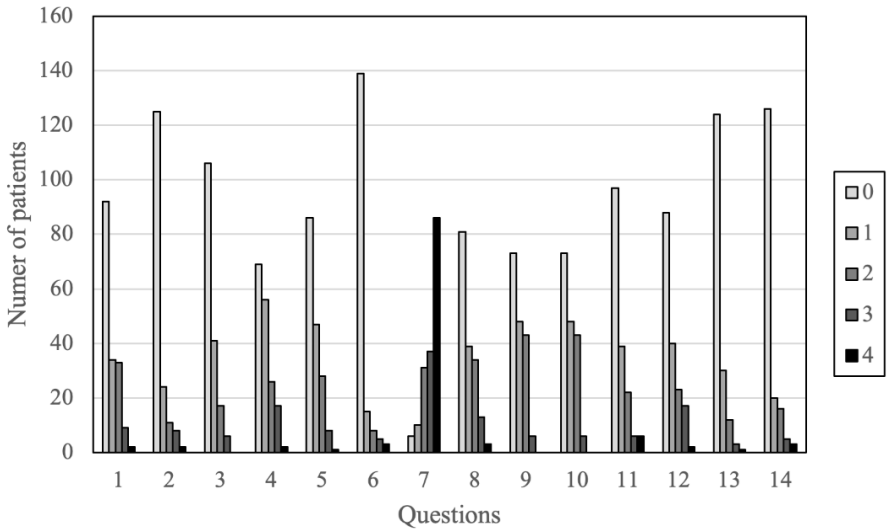

Figure 5: Mean frequency score in FSSG). The frequency score of question 7 showed significant differences between question 7 and all other questions ($p<0.01$) **.

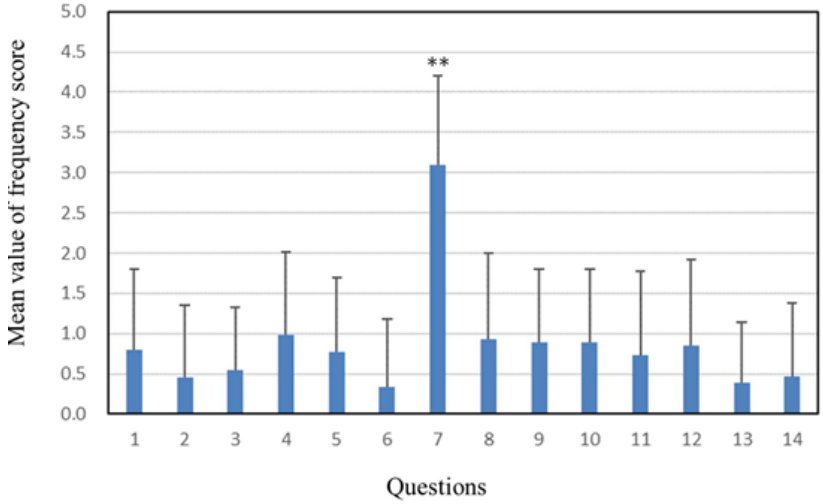

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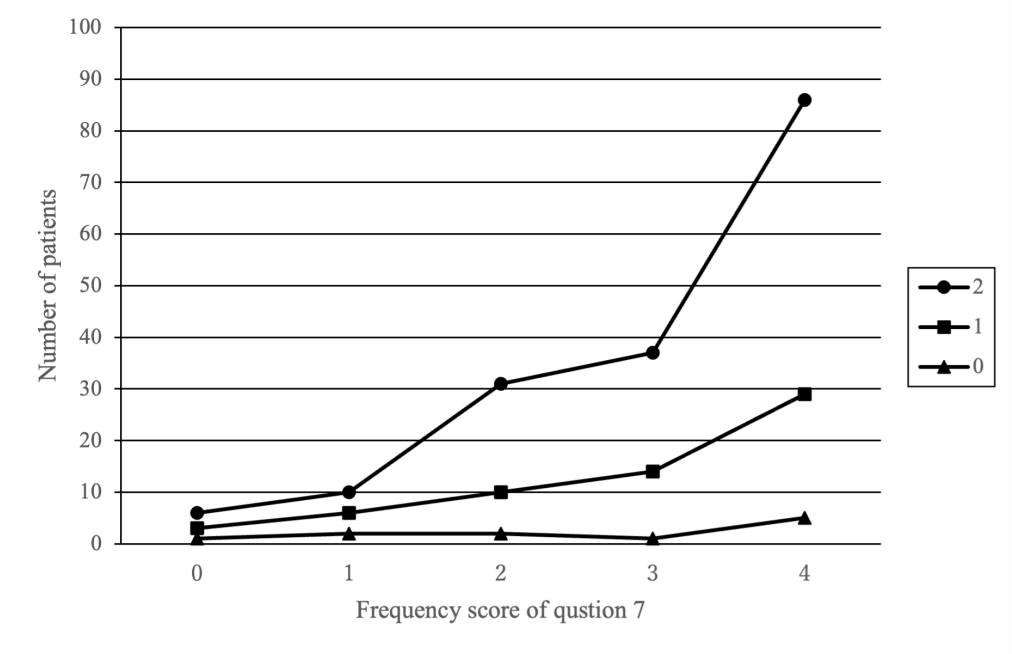
Figure 6: A correlation can be observed in the graph, indicating a sharper slope with an elevation in NBI score. When the NBI score was 0, the correlation coefficient r_0 was 0.67, when the NBI score was 1, the correlation coefficient r_1 was 0.95, and when the NBI score was 2, the correlation coefficient r_2 was 0.92.



DISCUSSION

Patients with LPRD commonly report throat discomfort as their primary complaint. However, despite undergoing examinations with fiberoptic laryngoscopy, CT scans, and MRI, many patients show no clear physical evidence of their reported symptoms. As a result, diagnosing LPRD can be challenging when relying solely on conventional laryngoscope assessments[5]. NBI technology enhances the visualization of microvasculature and mucosal patterns[15]. This is because the penetration depth of light in NBI varies by wavelength, allowing blue light's shorter wavelength to produce clearer imaging of mucosal tissue. As a result, NBI can more accurately detect vascular structure and patterns compared to conventional fiberscope[9]. In this study, NBI imaging of the nasopharynx in LPRD patients revealed distinctive features, including polygonal cells. The nasopharyngeal epithelium displayed a mixed, patchy arrangement of polyhedral cells with columnar and rounded shapes, as well as both squamous and ciliated cell types. NBI can detect capillary structures within the epithelial cells of the nasopharynx[16]. However, it remains unclear whether the nasopharyngeal submucosal capillary is distinctly accentuated in patients with LPRD. Clinicians typically assess the severity of GERD by examining macroscopic changes in the esophageal mucosa caused by the gastric acid regurgitation[17]. Likewise, prolonged exposure to gastric acid reflux can degrade the nasal and pharyngeal mucosal tissues. Prolonged irritation from gastric acid reflux may degrade the nasopharyngeal epithelial mucosa. Based on its resemblance to fish scales, we have provisionally dubbed the distinctive capillary pattern observed in LPRD patients the "Mackerel Cloud Pattern" (MCP) (Figure 1). The characteristic MCP pattern was readily identifiable, even in patients presenting with other primary concerns. When clinicians detected MCP and asked about pharyngeal discomfort, many of these patients confirmed experiencing such symptoms. This suggests MCP could serve as an indicator to alert clinicians to the possibility of LPRD. The FSSG, a diagnostic tool, has proven useful not only for identifying GERD, but also for evaluating patients without GERD[12]. Specifically, we found that question 7 of the FSSG is particularly effective for screening for LPRD (Figure 5). As shown in Table 3, among patients with MCP covering over 50% of the nasopharynx, the most numerous were those who scored 4 (always) on question 7. Furthermore, Figure 6 demonstrates a correlation between the score on question 7 and the percentage of nasopharynx occupied by MCP - the graph exhibits a steeper slope as the question 7 score increases alongside a larger MCP percentage. This study found a correlation between MCP and high scores on question 7 of the FSSG. Interestingly, even in cases without MCP, participants still exhibited elevated scores on question 7. Further analysis revealed that most of these cases involved laryngeal arytenoid hyperemia, suggesting that a comprehensive LPRD diagnosis should consider both

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laryngeal findings and FSSG score[2]. All patients experienced relief from pharyngeal discomfort within one to three months of treatment. Rabeprazole proved to be an effective medication, as many patients had previously been prescribed other proton pump inhibitors (PPIs) at other hospitals before visiting our department. High dose rabeprazole (20 mg/day) significantly improved LPRD symptoms compared to placebo[18]. However, symptoms often recurred after discontinuing treatment in this study, suggesting that long-term, high dose rabeprazole may be necessary for some patients. Recent reports have raised concerns about the serious side effects associated with long-term use of PPIs, such as hypomagnesemia, hypokalemia, hypocalcemia, enteric infections, and cardiovascular events[19]. Except for rabeprazole, most PPIs are primarily metabolized by the CYP2C19 enzyme. Genetic polymorphisms in CYP2C19 can lead to enzyme deficiency in certain populations, potentially resulting in reduced gastric acid suppression and increased side effects[19]. NBI, a novel diagnostic approach, can effectively identify LPRD by visualizing the instinctive nasopharyngeal capillary patterns that correlate with specific symptoms, as assessed by the FSSG questionnaire. This study demonstrates that NBI has the potential to enhance the accuracy of diagnosing LPRD. Additionally, the findings suggest the FSSG questionnaire, especially question 7, may serve as a valuable supplementary tool for screening patients with LPRD. Additional research is required to develop accurate diagnostic techniques for LPRD and to optimize long-term PPI therapy.

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