

## Systematic Review Article

# LARYNGOPHARYNGEAL REFLUX RELATED DYSPHONIA: A SYSTEMATIC REVIEW

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## ABSTRACT

**Background:** Laryngopharyngeal reflux (LPR) is increasingly recognized as a significant contributor to voice disorders, particularly dysphonia. However, variability in diagnostic criteria and treatment outcomes has led to ongoing debate regarding its clinical relevance. This review is to evaluate the association between LPR and dysphonia, including diagnostic approaches, treatment outcomes, and improvements in voice quality.

**Materials and Methods:** PRISMA guidelines were followed in conducting the systematic review. Pubmed and Cochrane library were searched for the review. Recently conducted systematic reviews and/or meta-research were summarized, covering domains of voice outcome measurements, diagnostics and therapeutic interventions.

**Results:** Around 50-61% of patients with LPR report symptoms of dysphonia. Behavioural voice therapy overall resulted in improved voice outcomes and proton pump inhibitors (PPIs) yielded a variable effect. Reliable associations were not achieved through use of symptomatic but objective diagnostic techniques.

**Conclusion:** LPR is also highly associated with dysphonia and should also be analysed as a possible factor but no detailed conclusions can be drawn in view of various diagnoses. Treatment strategies must be individualized and multimodal assessment is recommended.

**Keywords:** Dysphonia, Laryngopharyngeal reflux, Voice quality, Proton Pump Inhibitors.

## INTRODUCTION

LPR describes a unique clinical state which is characterized by reflux of gastric contents into larynx and pharynx and may result in wide spectrum of symptoms affecting upper aerodigestive tract. [1] LPR resembles classically defined “gastroesophageal reflux disease (GERD)”, but it frequently occurs without symptoms of heartburn or regurgitation, and is a major diagnostic challenge in routine clinical practice. [2]

Esophageal mucosa has greater protective mechanisms than laryngeal epithelium and is thus less prone to injury from reflux. [3] Upon exposure, pepsin, gastric acid, bile salts, other enzymes may cause inflammation, edema, damage to epithelial surface, alter vocal fold vibration. [4] These pathophysiological changes result in laryngeal

symptoms such as dysphonia, one of most common and clinically significant symptoms. [5]

LPR-associated dysphonia may seriously affect quality of life in people who use their voice function extensively, like teachers, singers, health care professionals. [6] Symptoms involve hoarseness, fatigue of voice, clearing of throat, globus sensation, chronic cough. [7] The symptoms are not specific, however, and may coincide with other laryngeal and functional voice disorders, complicating diagnosis even further. [8]

Over past 2 decades, a variety of symptom-based indices, including Reflux Symptom Index (RSI) and endoscopic scoring systems, such as Reflux Finding Score (RFS), [9] have been developed as diagnostic tools which have been used in identification of LPR. These are extensively utilized tools because of their practicality; concerns remain about their specificity

and interobserver variability.<sup>[10]</sup> Objective diagnostic modalities, especially 24-hour multichannel intraluminal impedance-pH monitoring, are regarded as more reliable and are not routinely employed as they are costly, invasive, and not widely available.<sup>[11]</sup>

The association between LPR and dysphonia continues to be a topic of ongoing debate.<sup>[12]</sup> Many studies indicate there is high prevalence of voice disorder in LPR patients as well, but there have been some concerns about strength as well as causality of association. In addition, variable efficacy, including PPIs in improving voice-related symptoms has been found consistent with treatment response. Recent studies have revealed that factors, namely non-acid reflux, pepsin activity, hypersensitivity of larynx, may be involved in symptom generation and hence challenge conventional acid-centric paradigm of LPR.<sup>[13]</sup> The importance of rehabilitative and behavioural interventions in management of dysphonia associated with LPR has been recognized in recent years. Voice therapy techniques, namely semi-occluded vocal tract exercises and resonant voice therapy techniques, have demonstrated promising results, facilitating improvement in vocal function alleviating symptom burden. This demonstrates multifactorial nature of dysphonia in LPR and emphasises importance of comprehensive, multidisciplinary approach to management.<sup>[14]</sup>

Previous reviews focused either treatment outcomes or diagnostic approaches of LPR. This review is designed to assess present evidence on correlation between LPR and dysphonia with special emphasis on diagnostic procedures, results of treatment, voice quality assessment techniques. This study aims to synthesize findings of recent systematic reviews and meta-analyses to obtain improved understanding of this complex relationship and to suggest future research directions.<sup>[15,16]</sup>

## MATERIALS AND METHODS

**Study Design:** Systematic review performed according to PRISMA guidelines.

**Search Strategy:** An extensive literature search has been conducted through:

- PubMed
- Scopus
- BioMed Central
- Cochrane Library

**Keywords used:** “laryngopharyngeal reflux,” “dysphonia,” “voice therapy,” “proton pump inhibitors.”

### Inclusion Criteria

This systematic review includes studies evaluating the association between LPR and dysphonia, studies utilizing subjective including Voice Handicap Index (VHI) and/or objective voice outcome measures (acoustic, aerodynamic analysis), studies employing defined diagnostic criteria for LPR (symptom-based tools such as RSI/RFS and/or objective diagnostic

methods), Systematic reviews, “randomized controlled trials (RCTs)”, meta-analyses, observational studies, Articles published in the English language, Studies with clearly reported outcomes related to voice quality or dysphonia.

### Exclusion Criteria

This excludes investigations including presence of structural laryngeal pathologies, Studies lacking clear diagnostic criteria for LPR, Case reports, case series having limited number of subjects, Non-English publications.

**Study Selection:** Titles and abstracts have been screened, followed by full-text review for eligibility.

### Data Extraction

Extracted variables included:

- Study design
- Sample size
- Diagnostic method
- Voice outcomes
- Treatment modality

**Assessment of Risk of Bias:** Risk of bias has been assessed employing design-specific validated tools.

RCTs have been evaluated employing Cochrane Risk of Bias 2 tool, observational studies utilizing ROBINS-I, systematic reviews applying AMSTAR 2. In general, investigations showed predominantly moderate study risk of bias, primarily because of study variation in design and reliance on subjective outcome measures.

This systematic review has been evaluated for methodological quality according to AMSTAR 2 checklist. The review exhibited low to moderate confidence, mainly due to limitations of protocol registration and incomplete reporting of publication bias.

### PRISMA Overview

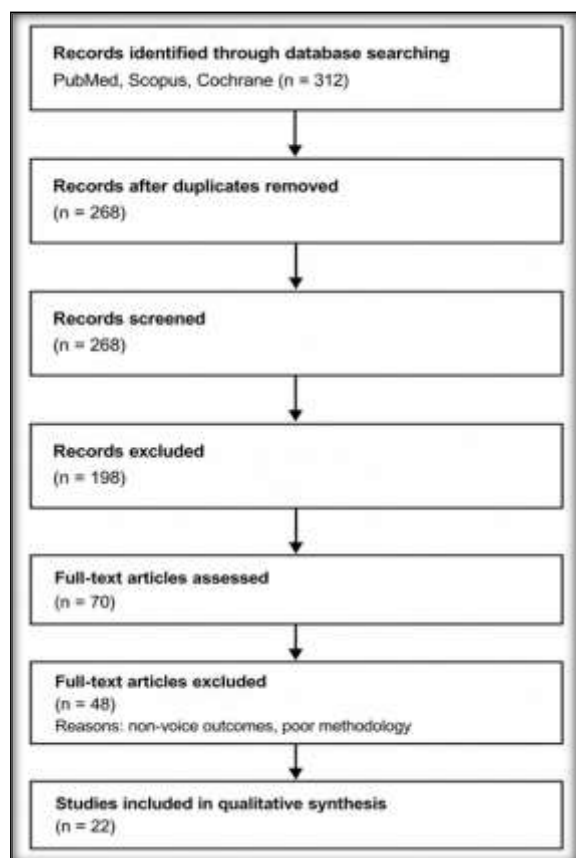
Most systematic reviews adhered to PRISMA guidelines based on:

- Comprehensive database search (PubMed, BioMed Central, Scopus, Cochrane).
- Established inclusion/exclusion criteria specific to voice outcomes related to LPR.
- Extraction of subjective (VHI) and objective (acoustic/aerodynamic) measures.
- Meta-analytical synthesis employing random-effects models in selected investigations

### PRISMA Flow Diagram

Records retrieved through searching in databases (PubMed, BMC, Scopus, Cochrane) (n = 245).

Other sources acknowledged through additional records (n = 15). Total number of records after duplicates were eliminated (n = 210). Records screened (title/abstract) (n = 210). Records excluded (n = 150). Evaluation of full-text articles for eligibility (n = 60). Exclusion of full-text articles (n = 38). Studies involved in qualitative synthesis (n = 22). Not related to dysphonia (n = 12). Inadequate diagnostic criteria (n = 10). Pediatric population (n = 6). Insufficient outcome data (n = 10). Investigations involved in quantitative synthesis (meta-analysis) (n = 10).



**Figure 1: PRISMA flowchart illustrating study selection process.**

## RESULTS

### Study Characteristics:

Rajput et al,<sup>[1]</sup> (n≈500) and Chen et al,<sup>[2]</sup> (n≈400), and Koufman,<sup>[4]</sup> provided focused clinical cohort (n=225). Also, Belafsky et al,<sup>[5,6]</sup> validation studies introduced widely employed diagnostic instruments, i.e., RSI and RFS. These results are compared with earlier systematic reviews that showed that high

burden of voice disorders in LPR populations is high. <sup>[7,15]</sup>

### Prevalence of Dysphonia in LPR:

In literature reviewed, between 50-61% of individuals diagnosed with LPR experience dysphonia. <sup>[1]</sup> Differences in prevalence were attributed to differences in diagnostic criteria, patient selection, assessment tools.<sup>[2,13]</sup>

### Diagnostic Approaches:

There was significant heterogeneity in diagnostic strategies used.<sup>[2]</sup> Objective diagnostic modalities, including impedance-pH monitoring and 24-hour pH monitoring (as in Koufman,et al), showed highly consistent and significant relationship between LPR and dysphonia.<sup>[4]</sup> In contrast, symptom-based tools such as RSI and RFS, although validated by Belafsky et al,<sup>[5,6]</sup> showed limited specificity and variable correlation with objective findings.<sup>[11]</sup> Systematic reviews relying primarily on symptom-based diagnosis reported more inconsistent outcomes.<sup>[12]</sup>

### Treatment Outcomes:

Behavioural voice therapy appeared as most consistently effective treatment. Rajput et al. showed improvement in voice outcomes with integrated PPI therapy and voice therapy, while studies that utilized mixed or pharmacological therapy alone had various outcomes. <sup>[1,2]</sup> The effectiveness of PPIs varied, with some trials demonstrating minimal or no improvement in voice-related parameters. Medical treatment also emerged to improve laryngeal outcomes, although not consistently for all voice parameters, and adjunctive treatment such as lifestyle modifications and combined treatment strategies appeared to be beneficial in selected populations of patients. <sup>[8]</sup> These results confirmed earlier controlled trials, which found that PPIs had variable therapeutic effects. <sup>[10]</sup>

**Table 1: Study Characteristics**

| Author(year)           | Study design                      | Sample size | Diagnostic criteria   | Intervention         | Key outcome                         |
|------------------------|-----------------------------------|-------------|-----------------------|----------------------|-------------------------------------|
| Rajput et al. (2025)   | Systematic Review & Meta-analysis | N ≈ 500     | RSI/RFS + pH study    | PPI vs Voice therapy | Moderate voice improvement          |
| Chen et al (2025)      | Systematic Review                 | N ≈ 400     | Symptom-based         | Mixed therapies      | Variable outcomes                   |
| Koufman (1991)         | Clinical Study                    | 225         | 24-hour pH monitoring | Medical therapy      | Correlation with laryngeal findings |
| Belafsky et al. (2002) | Validation Study                  | NA          | RSI                   | NA                   | Validated symptom index             |
| Belafsky et al. (2001) | Validation Study                  | NA          | RFS                   | NA                   | Validated laryngoscopic score       |

**Table 2: Risk of Bias Assessment**

| Study           | Study Design      | Domains                                        | Overall Risk  |
|-----------------|-------------------|------------------------------------------------|---------------|
| Noordzij et al. | RCT               | Randomization, deviations, outcome measurement | Some concerns |
| Koufman         | Observational     | Confounding, selection, outcome measurement    | Moderate      |
| Rajput et al.   | Systematic Review | Study selection, bias consideration            | Moderate      |
| Chen et al      | Systematic Review | Heterogeneity, reporting bias                  | Moderate      |
| Belafsky (RSI)  | Validation        | Tool validation                                | Low           |
| Belafsky (RFS)  | Validation        | Tool validation                                | Low           |

**Table 3: Summary of Major Findings**

| Domain           | Major Finding                  |
|------------------|--------------------------------|
| Prevalence       | Dysphonia in 50–61%            |
| Diagnosis        | pH monitoring more reliable    |
| RSI/RFS          | Useful but limited specificity |
| PPIs             | Variable efficacy              |
| Voice Therapy    | Consistent improvement         |
| Combined Therapy | Most favourable outcomes       |

## DISCUSSION

The current systematic review reveals that association between LPR and dysphonia is consistent and its prevalence has been reported to vary between 50-61%.<sup>[1]</sup> Nevertheless, this association is challenging to measure heterogeneity in diagnostic criteria, patient selection, outcome measures across studies is considerable.<sup>[2]</sup>

The main limitation that is established in literature is extensive dependence of symptom-based measures like RSI and RFS. <sup>[5,6]</sup> In spite of these tools being convenient and extensively employed in practice, limited specificity is a concern regarding overdiagnosis of LPR, especially in patients with coexisting functional voice disorder. <sup>[11,13]</sup> Such diagnostic ambiguity might result in heterogeneity in described prevalence and treatment response. <sup>[12,13]</sup>

More robust evidence of laryngopharynx reflux events can be obtained by objective diagnostic modalities, such as 24-hour multichannel intraluminal impedance and pH monitoring. <sup>[12]</sup> However, their application in routine practice in clinics is still limited because of their cost, limited accessibility, patient concerned factors. As a result, significant proportion of studies is based on subjective measures, consequently impacting overall quality and comparability of evidence. <sup>[11,13]</sup>

These outcomes of this review also emphasize inconsistencies in therapeutic outcomes. PPIs are widely utilized as first-line treatment, but their use has been found to be inconsistent in enhancing voice-related outcomes. <sup>[13]</sup> This observation indicates that acid reflux alone might not be entirely appropriate explanation of pathophysiology of LPR-related dysphonia. There is ever-growing indication of importance of non-acid reflux, pepsin-mediated mucosal injury, laryngeal hypersensitivity, which is considered not to be adequately addressed by use of acid suppression therapy alone. <sup>[8,13]</sup>

Conversely, voice therapy based on behavioural approaches appeared to be consistently effective intervention in all studies. Semi-occluded vocal tract exercises and resonant voice therapy procedures address maladaptive vocal behaviours, enhance vocal efficiency, minimize phonatory strain. These results highlight significance of addressing functional aspect of dysphonia and managing reflux. <sup>[14]</sup>

Moreover, there emerges a multifactorial and possibly bidirectional relationship between LPR and dysphonia. <sup>[14]</sup> Vocal misuse or overuse might

exacerbate laryngeal inflammation and reflux-induced mucosal alterations might influence vocal fold functioning, thus perpetuating a symptom persistence cycle. This explains necessity of a multidisciplinary management which comprises otolaryngologists, speech-language pathologists, gastroenterologists. <sup>[14]</sup>

Although clinical relevance of given topic is undeniable, there are numerous limitations persist in current evidence base. These involve heterogeneity in definition of diagnosis, variability in outcome measures, small sample sizes, limited long-term follow-ups. <sup>[1,2,7]</sup> The absence of standardized practices makes it difficult to compare findings across studies meaningfully and develop evidence-based clinical guidelines. <sup>[8,13]</sup>

Future studies must emphasize well-designed RCTs that encompass objective diagnostic measures and standardized voice outcome measures. <sup>[7,8]</sup> Longitudinal studies with long-term follow-ups are utilized to assess sustained treatment effects and recurrence patterns. <sup>[10]</sup>

Overall, although the relationship between LPR and dysphonia is significant, existing evidence is limited due to methodological limitations. <sup>[1,2,7]</sup> A comprehensive and individualized approach that integrates objective diagnostics, specific medical therapy, structured voice rehabilitation is suggested to achieve optimized patient results. <sup>[8,15]</sup>

### Limitations

Several important limitations were observed in studies included. A range of heterogeneous diagnostic criteria were used in various studies, so results might not be fully comparable, and interpretation of results may be limited. Furthermore, the limited use of gold-standard impedance-pH monitoring reduced diagnostic accuracy in some cases. Inconsistencies in results were also due to variability of voice outcome measures. The majority of primary studies had small sample size, and results were not generalizable. Follow-up durations have been short frequently, restricting ability to determine long-term findings. In addition, there was high dependence on subjective reporting, which could lead to potential reporting bias, and decreased overall robustness of evidence.

## CONCLUSION

LPR is typically related to dysphonia, but given inconsistencies in diagnostic criteria and treatment response, it is difficult to obtain definite conclusions. Behavioural voice therapy emerges as

having most consistent and effective interventions across studies. Moreover, emerging evidence specifies that combination approaches by which pharmacological therapy, dietary modification, lifestyle alteration are applied might result in enhanced mono-therapy, especially in specific patient groups. Early identification and early intervention will probably enhance resolution of symptoms and avoid chronic voice impairment. The need for objective diagnostic techniques, including impedance pH monitoring, as a means to increase accuracy in diagnoses provided and decrease over-reliance on symptom-based approach is also emphasized in current body of literature. Furthermore, outcome measures need to be standardized, and follow up periods extended to obtain more accurate assessment of long-term treatment efficacy and patterns of recurrence. Overall, an integrated, multi-disciplinary approach involving clear diagnostics and individualized treatment plans essential to ensure best treatment outcomes and further study.

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