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THE SAN DIEGO CONSENSUS FOR LARYNGOPHARYNGEAL SYMPTOMS AND LARYNGOPHARYNGEAL REFLUX DISEASE

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Abstract

Background: The term ‘laryngopharyngeal reflux’ (‘LPR’) is frequently applied to aerodigestive symptoms despite lack of objective reflux evidence. This initiative aimed to develop a modern care paradigm for LPR supported by otolaryngology and gastroenterology disciplines.

Methods: A 28-member international inter-disciplinary working group developed practical statements within the following domains: definition/terminology, initial diagnostic evaluation, reflux monitoring, therapeutic trials, behavioral factors and therapy, and risk stratification. Literature reviews guided statement development and were presented at virtual/in-person meetings. Each statement underwent 2 or more rounds of voting per the RAND Appropriateness Method; statements reaching appropriateness with $\geq 80\%$ agreement are included as recommendations.

Results: The term ‘laryngopharyngeal symptoms’ (LPS) applies to aerodigestive symptoms with potential to be induced by reflux and include cough, voice change, throat clearing, excess throat phlegm, and throat pain. ‘Laryngopharyngeal reflux disease’ (LPRD) refers to patients with LPS and objective evidence of reflux. Importantly, the presence of LPS does not equate to LPRD. Laryngoscopy has value in assessing for non-reflux laryngopharyngeal processes, but laryngoscopic findings alone cannot diagnose LPRD. LPS patients should be categorized as with or without concurrent esophageal reflux symptoms. While lifestyle modification and empiric trials of acid suppression $\pm$ alginates are appropriate when esophageal reflux symptoms coexist, upper endoscopy and ambulatory reflux monitoring are required for LPRD diagnosis when symptoms persist, when LPS is isolated, or when management needs to be escalated to include invasive anti-reflux management. The two recommended ambulatory reflux monitoring modalities, 24h pH-impedance and 96h wireless pH monitoring, are not mutually exclusive with distinct roles for the evaluation of LPS. Laryngeal hyperresponsiveness and hypervigilance commonly contribute to both LPS and LPRD presentations and are responsive to laryngeal recalibration therapy and neuromodulators.

Conclusions: The San Diego Consensus represents the formal modern-day inter-disciplinary care paradigm to evaluate and manage LPS and LPRD.

INTRODUCTION

The term “laryngopharyngeal reflux” (“LPR”) is used widely in clinical practice and research, both as a descriptor of proximal esophageal and aerodigestive symptoms as well as a diagnosis^{1, 2}. Despite the lack of finite diagnostic criteria, LPR accounts for as much as 10% of otolaryngology and gastroenterology visits³. Health care costs of LPR are reported to be 5.4 times higher than for gastroesophageal reflux disease (GERD), partly from prolonged acid suppression trials and diagnostic uncertainty⁴. There is a significant negative impact on quality of life, with higher rates of anxiety, depression and impaired social functioning regardless of whether LPR is diagnosed based on symptoms or objective testing^{5–8}. However, life-threatening long-term sequelae from “LPR”, such as cancer, are infrequent⁹.

While a variety of symptoms are attributed to the retrograde flow of gastric contents to the upper aerodigestive tract^{1, 2}, in actuality, few laryngopharyngeal symptoms (LPS) are

directly linked to this mechanism^{10, 11}. Evidence of GERD is not uniformly present, despite the categorization of “LPR” as part of extraesophageal GERD¹². As many as 60% of patients diagnosed with “LPR” have normal objective ambulatory reflux monitoring studies, which challenges the theory that reflux is the mechanism underlying most presentations¹³ and suggests that objective evidence of reflux (LPR disease [LPRD]) is low.

A modern care paradigm for LPS, supported by otolaryngology and gastroenterology disciplines, is critically needed. Thus, an international inter-disciplinary group aimed to develop evidence-based recommendations for the evaluation and management of LPS.

METHODS

The 28-member international inter-disciplinary working group included 12 esophageal expert gastroenterologists/physiologists (GIs), 9 laryngologists (ENTs), 6 speech-language pathologists (SLPs), and 1 clinical psychologist (Supplemental Table 1). The one-year initiative (October 2023 to October 2024) comprised seven working group meetings: five virtual and two hybrid with in-person meetings in Hong Kong (May 2024) and Austria (October 2024) as well as several rounds of independent voting and sub-group meetings.

First, 14-members were assigned to the following sub-groups: 1) Definition & Terminology; 2) Initial Diagnostic Evaluation; 3) Reflux Monitoring; 4) Therapeutic Trial; 5) Behavioral Factors & Therapy; 6) Risk Stratification. Each sub-group was led by two inter-disciplinary co-chairs tasked with performing a literature review, developing statements, and presenting evidence at working group meetings. Fourteen additional members were nominated and recruited for the voting panel.

The RAND Appropriateness Method (RAM), a formally validated methodology for determining the appropriateness of statements, was utilized. This method included independent electronic voting to determine the appropriateness of each statement per RAM using the University of California San Diego Research Electronic Database Capture (REDCap). Statements ranked as appropriate with $\geq 80\%$ agreement are included as final recommendations^{14, 15}. (Tables 1 & 2; Figure 1). Statements not meeting criteria as appropriate are including in Supplemental Tables 2 and 3.

DEFINITION & TERMINOLOGY

Key points:

- Laryngopharyngeal symptoms (LPS) refer to chronic and frequent throat and upper airway symptoms that have potential to be induced by retrograde flow of gastric content to the upper esophagus, pharynx and larynx.
- Laryngopharyngeal symptoms include cough, voice hoarseness/change, throat clearing, excess phlegm in the throat, throat pain/sore throat.
- Multiple mechanisms can lead to laryngopharyngeal symptoms, and the term LPS does not implicate reflux as the etiology of symptoms.

- A diagnosis of laryngopharyngeal reflux disease (LPRD) requires chronic troublesome LPS AND objective evidence supporting the relationship between symptoms and gastro-esophageal reflux.
- The presence of LPS does not equate to LPRD.

Characterization and definition of “LPR” have proven challenging over the past several decades, primarily because the term equates the presenting symptoms with a reflux-based etiology when, in fact, objective GERD is infrequently demonstrated. The panel sought to differentiate and define presenting symptoms with suspicion of reflux as LPS, from the diagnosis of the disease resulting from objective reflux, termed laryngopharyngeal reflux disease (LPRD).

Laryngopharyngeal Symptoms (LPS): To qualify as LPS, the panel agreed that symptoms must be frequent, occurring at least twice weekly, and present for more than 8 weeks^{16–18}. The group agreed that commonly cited “LPR” symptoms meeting criteria for LPS include (with the level of agreement in parentheses): cough (89%), regurgitation (89%), throat pain/sore throat (89%), throat clearing (86%), excess phlegm (82%), and hoarseness/voice change (80%)^{16–18}.

Although globus approached but did not reach agreement for inclusion as an LPS, the panel felt that globus is an important symptom warranting further evaluation and is often a negative predictor of reflux physiology^{19–21}. Several other symptoms that did not reach agreement to be considered LPS included tongue burning, nasal burning, post-nasal drip, halitosis, belching and dysphagia (Supplemental Table 2).

Importantly, all aforementioned symptoms are poorly specific for true LPRD. In other words, *the presence of LPS does not equate to LPRD*²².

Additionally, LPS can occur with esophageal reflux-like symptoms such as heartburn, regurgitation, or chest pain, or can occur independent of esophageal symptoms²³. Hence, early in the evaluation of LPS, the presence of esophageal symptoms should be assessed as the diagnostic and management algorithms differ for isolated LPS and LPS with concurrent esophageal reflux symptoms.

Laryngopharyngeal Reflux Disease (LPRD): While the prevalence of LPS is high, the proportion of individuals found to have objective LPRD on diagnostic evaluation is low, approximately 35%²⁴. *Thus, while many individuals experience LPS, true LPRD is much less common.*

Therefore, both LPS *and* objective evidence of gastro-esophageal reflux are needed for a diagnosis of LPRD. Such evidence could include reflux metrics on esophageal testing or, in the setting of concurrent esophageal reflux symptoms, a positive response to a pharmacologic trial. Irrespective of symptom presentation, there was strong agreement that diagnostic evidence supporting the relationship between LPS and gastroesophageal reflux is required for all patients prior to invasive anti-reflux management.

DIAGNOSTIC EVALUATION OF LPS

Role of Laryngoscopy

Key point

- Laryngoscopy is a necessary part of evaluation of LPS to assess for other non-reflux related otolaryngologic processes including malignancy; however, LPRD cannot be diagnosed based on laryngoscopy findings alone.

Laryngoscopy was agreed by the expert panel to be a necessary step in evaluating LPS, primarily to rule out alternate laryngeal pathologies including neoplasia. However, findings on laryngoscopy alone cannot diagnose LPRD^{22, 25}. Laryngoscopic findings on white light examination such as infraglottic edema, interarytenoid mucosal hypertrophy, erythematous changes and post-cricoid mucosal edema are non-specific for LPRD and may result from other causes of laryngeal inflammation or be found in healthy, asymptomatic individuals²⁵. LPRD is often erroneously assumed to cause LPS despite changes in other vibratory parameters such as symmetry, amplitude, mucosal wave, and glottic closure, visualized by stroboscopy. In addition, benign vocal fold lesions are common, as are lesions of epithelial origin, such as keratotic, pre-malignant dysplastic and malignant lesions²⁶. All of these can present with dysphonia, chronic throat clearing, globus sensation and other irritative complaints often ascribed to LPRD²⁷. When LPS includes hoarseness that is not explained by white light flexible laryngoscopy, videostroboscopic examination should be performed to evaluate for other etiologies. Additionally, the panel suggested that laryngoscopic finding instruments such as the Reflux Finding Score (RFS) and the Reflux Sign Assessment (RSA) should not be used to diagnose LPRD, given their suboptimal specificity^{28–30}.

Symptom Characterization & Role of Medical Trials

Key points

- The presence of concurrent esophageal reflux symptoms versus absence, referred to as isolated LPS, should be determined.
- In patients with LPS & esophageal reflux symptoms, a trial of medical anti-reflux management, along with dietary and lifestyle modification, is appropriate.
- In patients with isolated LPS, esophageal evaluation is recommended instead of empiric medical trials.
- Medical anti-reflux trial includes twice daily PPI for 3 months with or without alginate therapy.

The diagnostic and management algorithms differ for concurrent esophageal symptoms with LPS versus isolated LPS. When gastroesophageal reflux is implicated as the etiology of LPS, either based on typical esophageal reflux symptoms or positive diagnostic testing, initial therapeutic trials can include anti-secretory therapy, as well as barrier alginate therapy and lifestyle optimization. The latter are low-risk strategies that may complement and enhance the effectiveness of anti-secretory therapy in patients with LPRD^{31–33}. A 3-month trial of standard-dose potent acid suppression such as PPI (e.g. omeprazole 20 mg) taken twice a day is considered adequate for the assessment of LPS symptom response. LPS

have been shown to decrease with alginate therapy taken four times daily (after meals and before bedtime) compared to vocal hygiene and lifestyle management³⁴, and can augment acid suppression^{35, 36}. In patients with isolated LPS, acid-reducing medications are not recommended as first-line therapy without demonstration of diagnostic evidence of reflux^{37, 38}.

Esophageal Evaluation

Esophageal evaluation, including upper GI endoscopy and/or ambulatory reflux monitoring, is the next step in the investigation of LPS with typical esophageal symptoms when unresponsive to empiric treatment trials, and in isolated LPS.

Upper GI Endoscopy

Key Points:

- Conclusive evidence of GERD on upper GI endoscopy includes Los Angeles grades B, C, D esophagitis and/or biopsy proven Barrett's esophagus.

Using Lyon Consensus paradigms, upper GI endoscopy off acid suppressive therapy can establish GERD presence if Los Angeles grades B, C, D esophagitis and/or biopsy proven Barrett's esophagus are encountered³⁹, and can raise suspicion that reflux may be contributing when found in patients with LPS. The presence of disrupted esophagogastric junction on endoscopy, such as hiatal hernia, may serve as adjunctive evidence for LPRD. The potential value of upper endoscopy was demonstrated in a recent multicenter study of patients presenting with LPS, where up to 47% of patients demonstrated erosive findings and/or hiatal hernia⁴⁰. Notably, these findings may be present both in patients with esophageal symptoms and those with isolated LPS. The expert panel, therefore, agreed that upper GI endoscopic evaluation for signs of esophageal mucosal injury may be of value in patients with LPS. Office-based transnasal esophagoscopy (TNE) has been shown to be similarly diagnostic for Barrett's esophagus and certain other esophageal pathologies compared to standard upper endoscopy^{41–43}. While TNE may provide a convenient, point-of-care screening tool for esophageal signs of reflux or other pathologies, it should be performed by providers with specialized training in esophageal endoscopy to ensure proper identification of relevant findings.

A cervical inlet patch is an area of heterotopic gastric mucosa in the proximal esophagus found on upper endoscopy that may secrete acid, mucus, or pepsin. Inlet patches can be associated with LPS and globus⁴⁴, and ablation of inlet patch has been shown to reduce LPS in small case series⁴⁵. Despite these observations, the panel could not reach agreement on the value of identifying and treating inlet patch to reduce LPS, as current evidence remains limited. Further research, including controlled studies of the impact of ablation, is needed to more clearly establish the importance of identifying this endoscopic finding in patients with LPS.

Ambulatory Reflux Monitoring for Evaluation of LPS

Key Points:

- Ambulatory reflux monitoring is the reference standard for diagnosing LPRD.

- LPRD diagnosis is required prior to invasive anti-reflux management.
- In patients with isolated LPS, reflux testing can personalize management better than empiric treatment trials.
- Diagnostic evaluation for LPRD should be considered if long-term medical anti-reflux management is recommended.

The diagnostic evaluation of whether LPS are potentially related to reflux first requires determining whether pathologic gastro-esophageal reflux is present. Although objective evidence of GERD on reflux testing in patients with LPS does not necessarily implicate reflux as causative of a patient's LPS, the absence of GERD makes it unlikely that GERD is the mechanism underlying LPS or that anti-reflux therapies will improve LPS.¹⁶ Thus, ambulatory reflux monitoring has a role in multiple LPS settings to distinguish the presence of pathologic GERD, and determine the value of anti-reflux therapies.

Evidence of abnormal reflux burden is *essential* prior to endoscopic or surgical anti-reflux interventions as these are invasive, irreversible, and expensive. Since patients with isolated LPS have a lower pre-test likelihood of GERD, early ambulatory reflux monitoring can help to confirm or exclude GERD and thereby personalize management^{39, 46, 47}. In the absence of endoscopic evidence of GERD, ambulatory reflux monitoring is the reference standard for diagnosing LPRD. Ambulatory reflux monitoring is the next step in evaluating patients with LPS and concurrent esophageal symptoms who do not respond to empiric trials of anti-secretory and/or alginate therapy, in the absence of endoscopic evidence of GERD. Further, ambulatory reflux monitoring should be considered in patients requiring long-term medical anti-reflux management, primarily to confirm pathologic reflux burden prior to long term acid suppressive therapy, similar to recommendations in esophageal reflux symptoms⁴⁸.

Modality & Interpretation of Ambulatory Reflux Monitoring

Key Points:

- Ambulatory reflux monitoring for evaluation of LPRD in patients with unproven GERD should be performed off acid suppression therapy.
- pH-impedance and wireless pH monitoring measure different properties of LPRD and are not mutually exclusive.
- pH-impedance monitoring is a diagnostic option for LPRD, particularly in patients with isolated laryngopharyngeal symptoms.
- Prolonged wireless pH testing is a diagnostic option for LPRD, particularly in patients with concomitant esophageal reflux symptoms and prior to escalation of reflux management.
- Distal esophageal acid exposure time (AET) greater than 6.0% on ambulatory reflux monitoring meets criteria for proven GERD.
- AET less than 4.0% on all four days of 96-hour wireless pH monitoring predicts low likelihood of symptom response with anti-secretory therapy.

- Oropharyngeal pH monitoring alone has poor specificity for LPRD in patients with laryngopharyngeal symptoms.

The two primary modalities of reflux monitoring utilized to diagnose LPRD are 24-hour multichannel intraluminal impedance-pH monitoring and prolonged wireless pH monitoring, both performed off antisecretory therapy in unproven GERD²⁴ (Table 3). Each of these two modalities provides differing capabilities and value in the evaluation of LPS, and thus are not mutually exclusive. Both provide measurement of distal esophageal acid exposure time (AET). pH-impedance offers the added ability to detect proximal reflux events with greater detail depending on probe placement and catheter configuration, especially since hypopharyngeal events may be more likely to contribute to LPS. For both modalities, prospective and blinded trial data suggest a distal esophageal AET >6.0% is definitively abnormal and consistent with pathologic acid exposure, meeting criteria for proven GERD whereas distal esophageal AET <4.0% is considered physiologic, especially if present on all 4 days of a 96-hour prolonged wireless study^{49, 50 39}.

Early studies demonstrated that pH-impedance monitoring is superior to traditional esophageal pH monitoring in detecting proximal esophageal reflux events⁵¹. Hypopharyngeal reflux events were demonstrated using dual channel or hypopharyngeal-esophageal multichannel intraluminal impedance with dual pH (HEMII-pH) catheters, often occurring as weakly-acidic or non-acidic reflux episodes that have potential to predict treatment outcomes^{51–54}. These catheter configurations were able to identify pharyngeal reflux events in 81% of 42 patients with suspected reflux-mediated pathology in LPS, including 72% who tested negative for esophageal-only criteria, highlighting the diagnostic gap addressed by standard dual-channel pH-impedance monitoring. Identifying clinically relevant reflux episode thresholds requires further research, and the expert panel could not reach agreement for thresholds of >80 esophageal reflux events and >10 hypopharyngeal events to be considered abnormal.

Wireless pH monitoring utilizes a single pH sensor positioned in the distal esophagus during sedated endoscopy that wirelessly transmits data to a recorder for up to 96-hours^{55, 56}. Given significant day-to-day variability in esophageal acid exposure, a major advantage of wireless pH testing is the capacity to monitor for prolonged periods and capture variability rather than relying solely on a 24-hour snapshot⁵⁷. When the goal is to achieve the highest diagnostic accuracy in demonstrating pathologic GERD, 96-hour prolonged wireless pH monitoring outperforms 24- or 48-hour studies in predicting need for acid suppressive and anti-reflux therapies, primarily because day-to-day variation in acid burden can confound shorter studies^{48, 58–60}. In a double-blind, multi-center trial of 100 patients with troublesome esophageal reflux symptoms and inadequate PPI response, participants with 0 days of an elevated AET had 10 times increased odds of stopping PPI when compared to those with 4 days of an elevated AET. When AET was elevated on two or more days, the odds ratio for predicting need to continue PPI treatment was 5.3 (95% CI 2.19–13.44)⁵⁰. Given these findings, recent guidance positions 96-hour wireless pH testing off anti-secretory therapy as the preferred test for unproven GERD⁶¹. Prolonged pH monitoring also provides a higher diagnostic yield of pathologic GERD in patients with LPS. In a recent multicenter international study of 813 patients, the diagnostic yield of GERD in patients referred for

LPS was 50% on prolonged monitoring versus 27% on 24-h pH impedance monitoring, including HEMII-pH^{24, 62}.

Oropharyngeal pH testing (Restech Dx-pH probe, Respiratory Technology Corp, San Diego, CA) was introduced as a minimally invasive pharyngeal pH probe to detect pharyngeal acid, including aerosolized acid⁶³. However, this technique is not specific, cannot detect weakly-acidic or non-acidic reflux, has poor concordance with traditional pH-impedance monitoring, and does not correlate with clinical outcomes^{64–67}.

The expert panel agreed that both pH-impedance monitoring and wireless pH monitoring are diagnostic options for assessing LPS. pH-impedance monitoring provides information on mechanisms of LPS, especially isolated LPS, while prolonged wireless pH monitoring provides direction on the role of anti-reflux therapy in LPS. The panel reached near agreement in the value of HEMII-pH providing useful information when traditional esophageal reflux monitoring is inconclusive, and suspicion of a reflux-mediated mechanism remains high. The panel did not support oropharyngeal pH monitoring as a stand-alone tool in LPS evaluation.

LARYNGEAL HYPERRESPONSE AND HYPERVIGILANCE

Laryngeal Behavioral Factors

Key Points:

- Hyperresponsive laryngeal behaviors, with or without true LPRD, may contribute to or be the primary etiology of LPS.
- Laryngeal symptom-specific anxiety and hypervigilance may contribute to or be the primary etiology of LPS.
- The Laryngeal Cognitive Affective Tool can help identify individuals with symptom-specific anxiety and hypervigilance.

The larynx is a critical intersection of breathing, communication and swallowing. These processes can become measurably disrupted⁶⁸ with pathologic reflux, stress, vagal sensitivity and sequelae from medical comorbidities^{69–72}. The term “laryngoresponders” was first coined by Aronson in 1990 to describe a predisposition, by physical makeup or personality, to manifest emotional distress through sensory changes in the larynx or voice. In recent years, various studies have shown the relationship between emotion and the larynx^{73–76}. A survey investigation of 1,217 adults found that 16% to 46% of the general population self-identified as laryngoresponsive⁷⁷. Laryngeal hyperresponse can manifest as repetitive laryngeal behaviors such as throat clearing or coughing, breath-holding, or as biomechanical strain at the vocal folds altering one’s voice quality or causing globus sensation. Laryngeal hypervigilance, defined as increased threat-induced attention to the larynx, and symptom-specific anxiety, defined as fear/worry about LPS and perceived consequences, are psychological processes that can influence LPS. The Laryngeal Cognitive Affective Tool (LCAT) is a validated patient reported outcome (PRO) instrument to distinguish candidates with elevated levels of hypervigilance and anxiety related to their LPS, and who may improve with behavioral intervention^{78, 79}.

Laryngeal Behavioral Therapy

Key Points:

- Individuals with LPS can undergo initial laryngeal recalibration therapy (LRT) provided by a voice-specialized speech-language pathologist.
- LRT involves combined voice therapy techniques, autonomic regulation and cognitive reframing to address perceived and confirmed irritation manifesting as cough, throat-clearing, dyspnea and voice change.
- Behavioral therapies used to address psychological targets, such as cognitive behavioral therapy, can be used alone or in combination with other modalities (e.g. LRT, neuromodulators) in patients with LPS.

Behavioral therapy can effectively address hyperresponsive laryngeal behaviors and laryngeal hypervigilance. SLPs specializing in voice and upper airway disorders offer interventions aimed at modifying dysregulated patterns using mechanical reorganization and healthful cognitive perspectives associated with LPS. There is precedent for these interventions working in individuals with confirmed reflux⁸⁰, isolated cough⁸¹, inducible laryngeal obstruction/paradoxical vocal fold movement^{82, 83} and muscle tension dysphonia⁸⁴. Laryngeal Recalibration Therapy (LRT)⁸⁵ is a novel structured approach that infuses traditional SLP techniques with heart rate variability biofeedback as well as acceptance and commitment therapy⁸⁶.

If psychological processes continue to impact LPS and/or patients experience incomplete relief after LRT or pharmacologic neuromodulation, cognitive behavioral therapy can be used to target and modify the specific cognitive (e.g., my symptoms will never get better), emotional (e.g. fear, worry), physiological (increased autonomic arousal), and behavioral (e.g., avoidance of foods, laryngeal hypervigilance) processes exacerbating symptoms and interfering with quality of life. Psychological interventions in this context are not designed to address comorbid general mental health disorders. Instead, they are focused on targeting psychological processes specifically impacting LPS and are delivered by a mental health professional with specialized health psychology training.

Neuromodulation

Key Points:

- Neuromodulators may improve laryngeal hypersensitivity. These include tricyclic antidepressants, as well as gabapentin and pregabalin (particularly studied in cough).

Pharmacologic neuromodulation may attenuate laryngeal hypersensitivity and may be considered in LPRD patients with suboptimal response to anti-secretory therapy or SLP intervention and in isolated LPS with negative esophageal testing. Current clinical evidence for neuromodulators, notably gabapentin and pregabalin, focus primarily on the treatment of chronic cough through mediation of vagal hypersensitivity⁸⁷. Tricyclic antidepressants, commonly prescribed for the treatment of functional GI disorders, should be used with caution because of anticholinergic effects which may cause dry mouth and aggravate LPS⁸⁸. While there is a paucity of data for selective serotonin reuptake inhibitors and

serotonin norepinephrine reuptake inhibitors, they can be considered in individuals who have concomitant anxiety and depression.

PRO INSTRUMENTS & RISK STRATIFICATION TOOLS

Common PRO instruments for GERD (GERDQ, GERD-HRQL) are valuable in assessing the severity and treatment response of esophageal symptoms, but have suboptimal diagnostic yield for LPS and LPRD⁸⁹. The expert panel agreed that currently available LPRD-specific PRO instruments should not be used to diagnose LPRD due to insufficient specificity. In particular, the symptoms assessed by reflux symptom index (RSI) are non-specific for LPRD but can be used to follow many laryngological complaints over time⁹⁰. An RSI cutoff previously considered clinically significant (≥ 13) also could not distinguish patients with increased proximal/pharyngeal reflux or significant symptom correlation on HEMII-pH testing^{91, 92}. The more recent Reflux Symptom Score (RSS), developed in conjunction with HEMII-pH testing, demonstrates a higher specificity and sensitivity in predicting increased proximal reflux burden and treatment outcome^{93, 94}, but was not considered by the panel to be definitively diagnostic of LPRD based on current evidence. The value of other general voice and cough instruments, such as the Voice Handicap Index-10 (VHI)⁹⁵, Leicester Cough Questionnaire (LCQ)⁹⁶, and the Cough Severity Index (CSI)⁹⁷, should be only be used as prescribed – as PROs and not diagnostic instruments.

Some clinical risk stratification tools (HAS-BEER¹³, COuGH RefluX⁹⁸) were developed in recent years to help direct initial diagnostic and management strategies in patients with LPS. While they hold promise in aiding clinicians by classifying patients into risk categories for LPRD based on clinical and demographic factors, the panel agreed that more data are needed before they can be fully adopted in the consensus algorithm for LPS/LPRD. Further validation of these scores for treatment outcomes and in diverse populations represent important areas of future research.

DISCUSSION

The San Diego Consensus for LPS & LPRD (SD-LPRD) is a modern-day evidence-based paradigm for evaluation and management of LPS developed utilizing formal methodology amongst an international expert inter-disciplinary group of ENTs, GIs, SLPs, and psychologist.

The physiological mechanisms underlying “LPR” are often unclear. Simplistically, reflux of gastric contents to the upper aerodigestive tract implies incompetence of both the lower and upper esophageal sphincters. However, there are several potential mechanisms for LPR giving rise to symptoms, namely: neurogenic, inflammatory, behavioral or motility related. For example, it is hypothesized that injury to the larynx and pharynx occurs directly (via exposure to gastric acid, pepsin and bile salts) or indirectly (via repetitive mucosal trauma from vagally mediated or reactive cough and throat clearing)⁹⁹. Further, esophageal dysfunction may impact the tracheobronchial airway by a reflux pathway (micro-aspiration) or reflex pathway (vagally mediated airway stimulation). Additionally, heightened cognitive-behavioral responses may perpetuate laryngeal behaviors (Figure 2). Traditional anti-reflux

therapies do not address these varied mechanisms, likely explaining why fewer than 50% of LPS patients respond to anti-secretory therapy and why anti-reflux surgery frequently yields suboptimal outcomes. Therefore, a critical aim of SD-LPRD was to develop a clinically practical paradigm to guide the use of anti-reflux strategies and objective testing, while highlighting the critical roles of laryngeal hyperresponsiveness and hypervigilance in symptom persistence.

A major distinction made by the expert panel is between presenting symptoms pertaining to the upper aerodigestive tract, termed LPS, from confirmed reflux-mediated pathophysiology based on objective findings, termed LPRD. Although both LPS and LPRD contribute to health care burden, only LPRD stands to benefit from management of gastroesophageal reflux. Hence identification of LPRD is a key step in the diagnostic evaluation of LPS. Standardized definition for LPS versus LPRD is also critical for future research efforts in the field, as the prior ambiguity of the term “LPR” limited generalizability of prior literature.

An expert evaluation of the larynx using laryngoscopy ± stroboscopy is an important step in evaluating any patient with LPS, not only to document findings, but also to rule out non-reflux etiologies for LPS. However, laryngoscopic findings are poorly specific for LPRD and may result from other causes of laryngeal inflammation or be found in healthy, asymptomatic individuals²⁵. Although spontaneously forming vocal process granulomas (i.e. not from intubation trauma) have historically been considered pathognomonic for LPRD¹⁷, there remains uncertainty in this relationship. A recent survey of academic laryngologists suggested the most likely etiology of vocal process granulomas was phonotrauma (88%), followed by reflux (67%) and glottic insufficiency (48%). Other common non-reflux etiologies of LPS include allergy and glottic pathology^{100, 101}, and rarely neoplasia, all of which could be recognized on careful laryngoscopic examination.

The presence of typical esophageal symptoms should be assessed as evaluation and management algorithms differ for isolated LPS and concurrent LPS with esophageal reflux symptoms. Empiric acid suppressive therapy may be trialed when LPS coexists with esophageal symptoms of GERD. While the type, dose, frequency and duration of acid-reducing therapies vary widely in the literature, unit dose PPI (e.g. omeprazole 20 mg) up to twice daily for 3 months is recommended for LPS response^{46, 47, 102–108}. A novel class of potent acid suppression, potassium competitive acid blockers (PCABs), is approved for reflux driven conditions including non-erosive reflux disease and erosive esophagitis, and could be used in place of PPI therapy. Outcomes research focused on LPS will further clarify the role of PCABs.

Further, alginate therapies are inexpensive, generally well-tolerated, may reduce patient perception of globus¹⁰⁹, and may offer increased benefit compared to PPI monotherapy^{35, 36}. Lifestyle modifications for managing GERD include reduction of intra-gastric pressure (e.g., weight loss/management and avoiding tight fitting clothing around the abdomen), minimizing post-prandial reflux (e.g., maintaining upright posture/avoiding recumbency 2–3 hours following meals, practicing diaphragmatic breathing), modifying sleeping position in cases of nocturnal reflux (e.g. head of bed elevation, sleeping in the left lateral position), and avoiding foods that trigger symptoms^{31–33}.

Prior to initiating anti-reflux therapy in isolated LPS, or when empiric treatment trials fail in LPS associated with esophageal symptoms, further esophageal evaluation includes upper GI endoscopy and ambulatory reflux monitoring, to determine the presence or consequences of abnormal levels of gastroesophageal reflux. Although objective evidence of GERD (AET>6.0%) in patients with LPS does not necessarily implicate reflux as causative of LPS, the absence of objective GERD (AET<4.0%) makes it unlikely that GERD is the mechanism, or that anti-reflux therapies will improve LPS.¹⁶ In patients without previously proven GERD, ambulatory reflux monitoring is performed off acid suppression in order to measure baseline levels of esophageal acid exposure and the nature of reflux episodes.

In planning ambulatory reflux monitoring, the diagnostic evaluation of LPS potentially related to reflux may require the determination of whether symptoms arise from a reflux mediated mechanism (where acid or non-acid reflux events cause direct tissue irritation), or a reflex mechanism (where reflux triggers a vagally mediated response without direct tissue contact)⁹⁹. Demonstration of a reflux-mediated mechanism requires evaluation of both the proximal extent of reflux events and non-acidic or weakly acidic episodes that may contribute to symptoms. pH-impedance monitoring, particularly using a HEMII-pH or dual pH impedance catheter, can distinguish between these mechanisms and provide definitive evidence of reflux events, their characteristics, and their temporal relationship to symptoms. pH-impedance monitoring also provides baseline impedance values, which can offer information regarding esophageal mucosal integrity, especially in the distal esophagus, although this has not been extensively studied in LPS. Important limitations include the lack of day-to-day variability information⁶⁷, and suboptimal value in ruling out reflux disease^{65, 110}. Thus, pH-impedance monitoring has the highest value in providing information about whether LPS is related to a reflux-related inflammatory mechanism, especially with isolated LPS, but may not provide the best guidance regarding the role of anti-reflux management.

Since many patients with LPS require an upper GI endoscopy, ideally performed off antisecretory therapy in unproven GERD, the decision to place a wireless pH capsule can be made real-time during endoscopy if no evidence of reflux is observed endoscopically¹¹¹. This is a cost-effective strategy and is particularly relevant since prolonged wireless pH-monitoring provides precise information regarding the presence or absence of pathologic acid burden, which is a primary determinant of the need for antisecretory therapy, and especially irreversible invasive anti-reflux therapies. Prolonged wireless reflux monitoring is better tolerated by patients when compared to catheter-based testing, with the main adverse effect being chest discomfort that rarely necessitates removal^{112, 113}. Limitations of wireless pH-monitoring include absence of proximal esophageal and/or pharyngeal reflux monitoring, lack of baseline impedance, and inability to directly ascribe LPS to reflux.

Recommendations regarding reflux management are beyond the scope of the current initiative. Personalizing management to the individual patient requires consideration of available expertise and response to prior treatment trials. In the case of isolated LPS or when LPS fail to respond to anti-reflux therapies even in confirmed LPRD, overlap with laryngeal hyperresponsiveness and hypervigilance should be considered, and behavioral therapy and/or neuromodulation recommended. Laryngeal involvement does not implicate a mental health disorder; instead, a symbiotic relationship exists between various stressors and

laryngeal hyperresponsiveness independent of a diagnosed disorder of affect (Figure 3). A robust mechanistic comprehension of how “normal” stresses of daily life might manifest in the larynx will improve our understanding of symptom generation, and metrics to measure such triggers could clarify intervention paradigms. The LCAT holds potential to identify patients with LPS who could benefit from behavioral therapies and/or neuromodulation⁷⁸.

Laryngeal behavioral therapies offered through trained SLPs and other behavioral therapists can hold value in disorders with laryngeal hyperresponsiveness and hypervigilance independent of the underlying mechanism. LRT utilizes a combination of traditional SLP techniques with vagal biofeedback and cognitive interventions⁸⁵. Patients who experience incomplete relief after LRT may benefit from psychological interventions such as cognitive behavioral therapy, used alone or in combination with other treatments such as dietary adjustments and neuromodulation¹¹⁴. Although relatively new to LPS, the field of psychogastroenterology utilizes brain-gut behavioral therapies for a range of gastrointestinal disorders with LPS overlap including functional heartburn¹¹⁵ and globus sensation¹¹⁶. Disordered brain-larynx interaction may also improve with pharmacological neuromodulation, since laryngeal hypersensitivity is implicated as a major contributor to LPS¹¹⁷. Delta ligands such as gabapentin and pregabalin have demonstrated value in cough⁸⁷. Other neuromodulator classes include tricyclic antidepressants, SSRIs and SNRIs, where anticipated benefits need to be balanced taking concomitant affective disorders and potential for anticholinergic side effects.

The main limitations of this initiative are that the levels of agreement are based on existing literature, and may reflect the mostly observational evidence available, often with risk of indirectness when applied to the statement in question, and lack of outcomes data to confirm recommendations. The fact that we used a RAND methodology without GRADE methodology is also a reflection of the quality of available literature.

The San Diego Consensus for LPS & LPRD represents an initial step towards better characterization of the clinical conundrum represented by the term “LPR”. Distinction of the symptomatic state (LPS) from objective reflux-related aerodigestive symptoms (LPRD) will allow categorization of patients who need escalation of reflux therapy from those who need symptomatic and behavioral interventions, with the recognition of the potential of overlap between true LPRD and laryngeal hyperresponsiveness and hypervigilance. Further collaborative research utilizing the introduced paradigms and standardized terminologies will help to delineate the mechanisms underlying LPS and develop targeted therapies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

LPR	Laryngopharyngeal reflux
GERD	Gastroesophageal reflux disease
LPS	Laryngopharyngeal symptoms
LPRD	Laryngopharyngeal reflux disease
GIs	Gastroenterologists
ENTs	Laryngologists
SLPs	Speech-language pathologists
RAM	RAND Appropriateness Method
TNE	transnasal esophagoscopy
AET	acid exposure time
HEMII-pH	hypopharyngeal-esophageal multichannel intraluminal impedance with dual pH
LRT	laryngeal recalibration therapy
PRO	Patient reported outcome
RSI	reflux symptom index
RSS	Reflux Symptom Score
VHI	Voice Handicap Index-10
LCQ	Leicester Cough Questionnaire
CSI	Cough Severity Index
SD-LPRD	San Diego Consensus of LPS & LPRD

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SUMMARY BOX**WHAT IS KNOWN:**

- “Laryngopharyngeal reflux” (LPR) is a widely used non-specific term applied to aerodigestive symptoms, often without objective evidence of gastro-esophageal reflux
- Patients with laryngopharyngeal symptoms (LPS) undergo numerous tests and treatments, often without success, however with significant quality of life impairment and health care burden

WHAT IS NEW HERE:

- The term laryngopharyngeal symptoms (LPS) describes chronic and frequent throat & airway symptoms (cough, voice change, throat clearing, excess throat phlegm and throat pain) that have potential to be induced by gastro-esophageal reflux
- LPS does not equate to laryngopharyngeal reflux disease (LPRD), which requires both LPS and objective evidence supporting a relationship with gastro-esophageal reflux
- Laryngoscopy cannot diagnose LPRD but is important in the evaluation of LPS to assess for non-reflux related otolaryngologic processes
- Objective evidence supporting LPRD can be derived from upper GI endoscopy and/or ambulatory reflux monitoring (24h pH impedance or prolonged wireless pH monitoring), or when a patient with LPS & concurrent esophageal reflux symptoms responds to a 3-month trial of antisecretory therapy ± alginates & lifestyle modification
- Laryngeal hyperresponsiveness and laryngeal hypervigilance commonly contribute to LPS as well as LPRD, and can be targeted with laryngeal recalibration therapy or neuromodulation

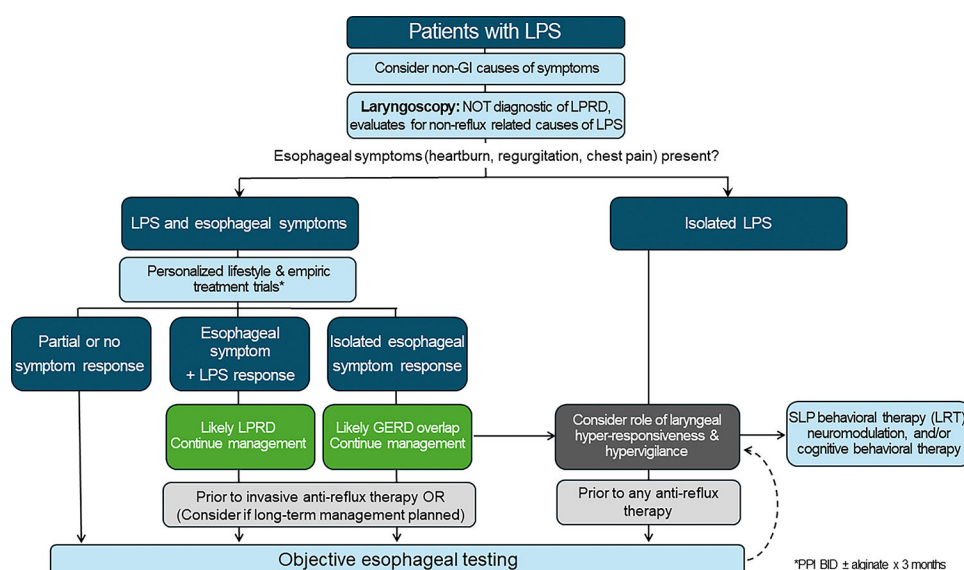


Figure 1. San Diego Consensus for Laryngopharyngeal Symptoms & Laryngopharyngeal Reflux Disease.

The initial evaluation for patients meeting definition for LPS include considering non-GI causes of symptoms, laryngoscopy to evaluate for non-reflux related causes of LPS, and discerning presence of concomitant esophageal reflux symptoms (heartburn, regurgitation). For LPS with concomitant esophageal reflux symptoms (left side of diagram) personalized lifestyle and empiric trials of acid suppression are appropriate followed by symptom assessment in 3 months. Those with esophageal symptom and LPS response likely have LPRD and can continue management. Those with isolated esophageal symptom response however ongoing LPS may have GERD overlap and can continue management; however, it is also important to consider a disordered laryngeal behavioral response. For patients with partial or no response of esophageal symptoms or LPS, the next step is objective esophageal testing and consideration of a disordered laryngeal behavioral response. For any patient with LPS and concomitant esophageal reflux symptoms, objective esophageal testing to assess for GERD/LPRD is indicated prior to invasive anti-reflux therapy such as endoscopic or surgical intervention and should be considered if long-term anti-reflux management is planned. On the other hand, for patients with isolated LPS (right side of diagram) it is critical to consider a disordered laryngeal behavioral response and it is suggested to proceed with objective esophageal testing prior to any anti-reflux management in order to personalize management. The dashed curved arrow highlights that disordered laryngeal behaviors can co-exist/overlap in the setting of objective GERD/LPRD and be a driver of symptoms. If disordered laryngeal behaviors are suspected, speech-language pathology guided behavioral therapy (e.g., laryngeal recalibration therapy), neuromodulation and/or cognitive behavioral therapy can be trialed.

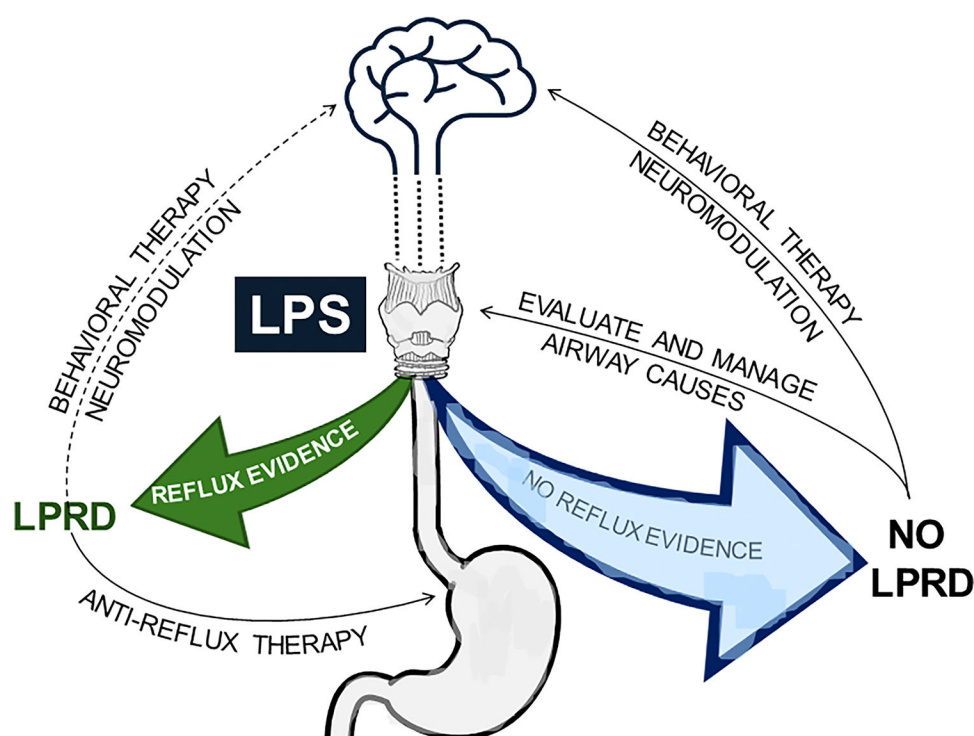


Figure 2. Paradigm of Laryngopharyngeal Symptoms & Laryngopharyngeal Reflux Disease.

The presence of LPS does not equate to LPRD. More commonly, patients with LPS have no objective evidence of reflux, in which case the evaluation should focus on non-gastrointestinal causes of symptoms including the brain-larynx interaction. For patients with objective evidence of LPRD therapeutic constructs include anti-reflux management and therapy focused on laryngeal behavioral responses.

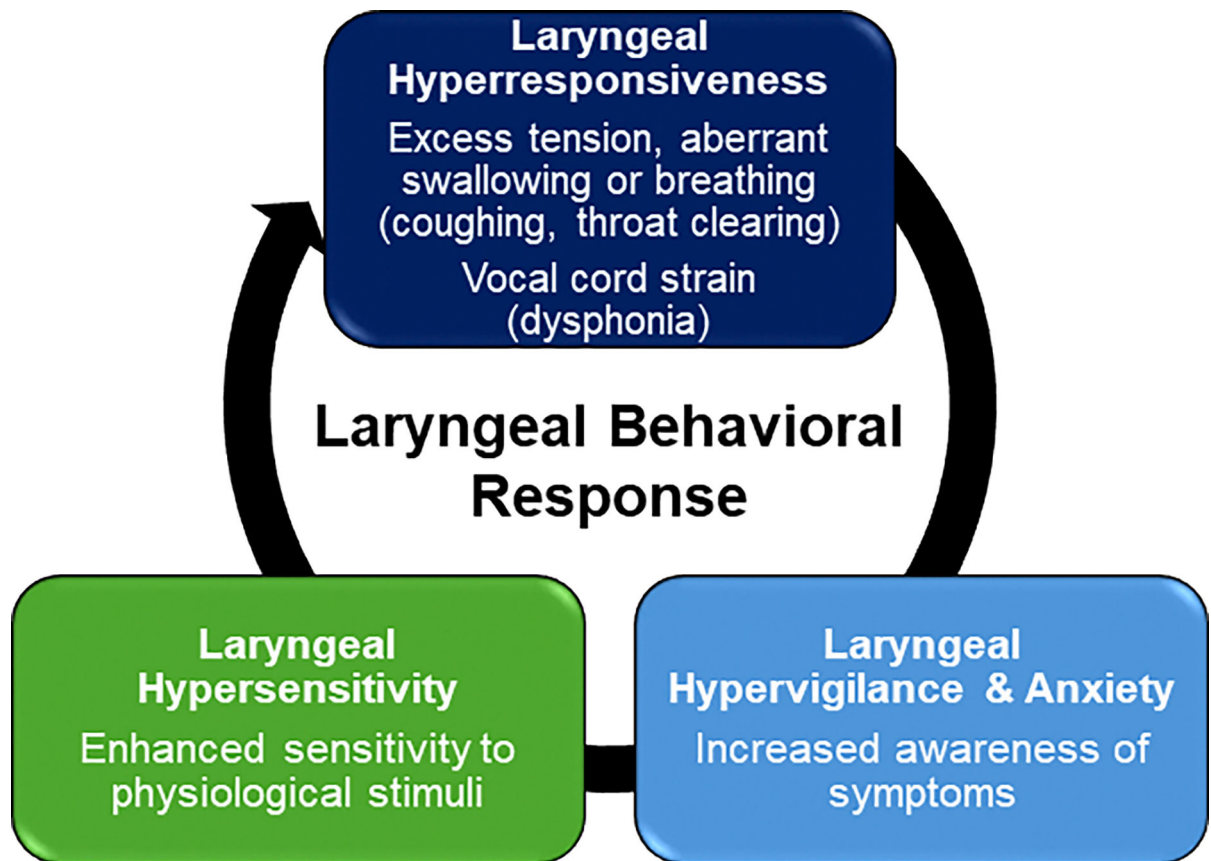


Figure 3. Laryngeal Behavioral Response.

The model of laryngeal behavioral responses involves a cyclical relationship between laryngeal hypersensitivity, laryngeal hyperresponse, and laryngeal hypervigilance, which can contribute to or drive laryngopharyngeal symptom (LPS) burden.

Table 1. Recommendation Statements for the San Diego Consensus for Laryngopharyngeal Symptoms and Laryngopharyngeal Reflux Disease.

Statements meeting criteria as appropriate are presented with the percent agreement as appropriate (ranked with a score of 7 or greater) as well as the median score.

Statement	% Agree	Median
Definition & Terminology		
Laryngopharyngeal symptoms (LPS) refer to chronic and frequent throat and upper airway symptoms that have potential to be induced by retrograde flow of gastric content to the upper esophagus, pharynx and larynx	96%	9
Frequent refers to symptoms occurring at least twice weekly	96%	8
Chronic refers to symptoms present for 8 weeks or more	93%	9
Laryngopharyngeal symptoms include cough, voice hoarseness/change, throat clearing, excess throat phlegm, throat pain/sore throat	See text for specific level of agreement	
Globus is a laryngopharyngeal symptom that warrants evaluation and management	88%	8
Multiple mechanisms can lead to laryngopharyngeal symptoms, and the term LPS does not implicate reflux as the etiology of symptoms	93%	9
A diagnosis of laryngopharyngeal reflux disease (LPRD) requires troublesome LPS AND objective evidence supporting the relationship between symptoms to gastro-esophageal reflux	82%	8
LPS can be isolated, or concurrent with typical esophageal reflux symptoms (heartburn, regurgitation, chest pain)	100%	9
The cost burden of LPS and LPRD is high, primarily related to prolonged therapeutic trials and diagnostic uncertainty	92%	8
LPS are highly prevalent and empirically managed more often than LPRD is proven on objective testing	92%	8
LPS and LPRD have a significant negative impact on quality of life	96%	9
Asthma and other pulmonary disorders have been reported in conjunction with LPS as well as LPRD	80%	7
Laryngoscopy		
Laryngoscopy should be performed to assess for non-reflux related causes of LPS prior to further diagnostic evaluation and/or LPRD treatment	93%	9
Laryngoscopy findings are neither specific nor pathognomonic for diagnosis of LPRD	93%	9
LPRD cannot be diagnosed based on laryngoscopy findings alone	89%	9
The primary role of laryngoscopy in the evaluation of LPS is to evaluate for other non-reflux related otolaryngologic processes including malignancy	93%	9
Laryngoscopic finding instruments based on laryngoscopic findings such as the Reflux Finding Score (RFS) and the Reflux Sign Assessment are not diagnostic of LPRD	86%	8
When white-light laryngoscopy is unrevealing in patients with hoarseness, videostroboscopy should be performed to evaluate for other causes of voice change prior to further diagnostic evaluation and/or LPRD treatment	89%	8
Symptom Characterization & Role of Medical Trial		
In patients with LPS, the presence of typical esophageal reflux symptoms (heartburn, esophageal chest pain, regurgitation) should be assessed	96%	9
In patients with LPS & typical esophageal reflux symptoms, a trial of medical anti-reflux management is appropriate	93%	8
If PPI is being trialed for LPS, twice daily therapy for 3 months is sufficient to determine if there is a symptomatic response	85%	8
A trial of alginates can be used in conjunction with PPI trial in patients with LPS and typical esophageal symptoms	90%	8
Anti-reflux medication interventions for LPS should be accompanied by dietary and lifestyle modifications	88%	8

Statement	% Agree	Median
In patients with isolated LPS, reflux testing can personalize management better than empiric treatment trials	81%	8
Upper GI Endoscopy		
Esophageal mucosal injury on upper endoscopy (>LA grade B erosive esophagitis or Barrett's esophagus) is conclusive evidence of gastroesophageal reflux and raises suspicion of LPRD in patients with LPS	89%	8
Endoscopic classification of the esophagogastric junction (hiatal hernia, Hill grade, AFS grade) provide supplementary evidence but are not conclusive for LPRD diagnosis	86%	9
When esophageal symptoms coexist with LPS, office-based transnasal esophagoscopy can screen for erosive esophagitis and Barrett's esophagus	82%	8
Role of Ambulatory Reflux Monitoring for Evaluation of LPRD		
Ambulatory reflux monitoring is the reference standard for diagnosis of LPRD	86%	8
Objective evaluation for LPRD should be considered if long-term medical anti-reflux management is recommended	86%	8
In patients with isolated LPS, evidence of abnormal reflux burden is required prior to escalation of anti-reflux management	86%	7
LPRD diagnosis is required prior to invasive anti-reflux management	93%	9
Modality & Interpretation of Ambulatory Reflux Monitoring		
Ambulatory reflux monitoring for evaluation of LPRD in patients with unproven GERD should be performed off acid suppression therapy	89%	8
pH-impedance and wireless pH monitoring measure different properties of LPRD and are not mutually exclusive	82%	9
pH-impedance monitoring is a diagnostic option for LPRD	93%	8
pH impedance monitoring is a diagnostic option for LPRD, particularly in patients with isolated laryngopharyngeal symptoms	82%	8
Prolonged wireless pH testing is a diagnostic option for LPRD, particularly in patients with concomitant typical esophageal reflux symptoms	82%	8
Prolonged wireless pH testing is a diagnostic option for LPRD, particularly prior to escalation of reflux management	82%	8
Distal esophageal acid exposure time greater than 6.0% on ambulatory reflux monitoring meets criteria for proven GERD	93%	8
Acid exposure time less than 4.0% on all four days of 96-hour wireless pH monitoring predicts low likelihood of symptom response with anti-secretory therapy	89%	8
Positive association between reflux event and laryngopharyngeal symptom on 96-hour wireless pH monitoring strengthens diagnostic confidence for LPRD	93%	8
Oropharyngeal pH monitoring alone has poor specificity for LPRD in patients with laryngopharyngeal symptoms	93%	8
Laryngeal Hyperresponsiveness & Hypervigilance		
People may be predisposed to manifest emotional distress through their larynx, which may contribute to or be the primary etiology of LPS	80%	8
Both general psychological processes (e.g., depression) and symptom-specific cognitive and behavioral processes (e.g. laryngeal hypervigilance, symptom-specific anxiety) can contribute to LPS symptom perception, with and without pathologic reflux	88%	8
The Laryngeal Cognitive Affective Tool can help identify individuals with symptom-specific anxiety and hypervigilance	80%	7.5
Patients with LPS and typical esophageal symptoms may report increased psychological symptoms, such as depression, hypervigilance, and/or symptom-specific anxiety	88%	8
Patients with LPS being evaluated for LPRD who have negative reflux monitoring studies and have had non-response to a trial of acid reducing therapy should be considered for a disorder of brain-larynx interaction, hypervigilance and/or a non-gastrointestinal process	83%	8

Statement	% Agree	Median
Laryngeal Behavioral Therapy		
Laryngeal recalibration involves combined voice therapy techniques, autonomic regulation and cognitive reframing to address perceived and confirmed irritation manifesting as cough, throat-clearing, dyspnea and voice change	85%	8
Individuals with LPS can undergo initial laryngeal recalibration training provided by a voice-specialized speech-language pathologist	83%	8
If LPS is accompanied by typical reflux symptoms, LRT can follow a trial of dietary/lifestyle modification and acid suppression	80%	8
Upon completion of laryngeal recalibration training, patients with ongoing hypervigilance, anxiety, depression and LPS symptoms may benefit from psychological intervention	80%	8
Behavioral therapies used to address psychological targets can be used alone or in combination with other modalities (e.g., laryngeal recalibration training, neuromodulators, dietary management) in patients with LPS	85%	8
Pharmacologic Neuromodulation		
If individuals with isolated LPS and negative reflux testing experience persistent symptoms after laryngeal recalibration training, pharmacologic neuromodulation may be helpful	83%	7
Neuromodulators and laryngeal recalibration training may be helpful in patients with LPRD and partial or poor response to acid suppression therapy	83%	8
Neuromodulators may improve laryngeal hypersensitivity	92%	8
Tricyclic antidepressants (TCAs) may help LPS symptoms but anticholinergic side effect such as xerostomia should be observed	92%	7.5
Gabapentin and pregabalin may be an effective adjunct to laryngeal recalibration training for LPS, especially cough	92%	8
While SSRIs and SNRIs have not been studied in LPS, individuals with LPS and clinical anxiety and/or depression may derive benefit	80%	7
If individuals with isolated LPS and negative reflux testing experience persistent symptoms after laryngeal recalibration training, pharmacologic neuromodulation may be helpful	83%	7
Patient Reported Outcome Instruments & Risk Stratification		
Common patient-reported outcome instruments for gastroesophageal reflux disease (GERDQ, GERD-HRQL) are useful for assessment of esophageal symptoms severity and evaluating treatment response	86%	8
Common patient-reported outcome instruments for gastroesophageal reflux disease (GERDQ, GERD-HRQL) are not specific for LPS and LPRD	96%	8
LPRD-specific patient-reported outcome instruments (LPR-HRQL, RSI, RSS) are not specific for diagnosing LPRD	86%	9
General voice and cough symptom instruments (VHI, CSI, LCQ) have unclear value in diagnosing LPRD	93%	8

Table 2.

Glossary of Terms for the San Diego Consensus for Laryngopharyngeal Symptoms and Laryngopharyngeal Reflux Disease.

Laryngopharyngeal symptoms (LPS):	Chronic and frequent throat and upper airway symptoms that have potential to be induced by retrograde flow of gastric content to the upper esophagus, pharynx and larynx. Laryngopharyngeal symptoms include cough, voice hoarseness/change, throat clearing, excess throat phlegm, throat pain/sore throat.
Laryngopharyngeal reflux disease (LPRD):	Requires chronic troublesome LPS AND objective evidence supporting the relationship between symptoms to gastro-esophageal reflux.
Objective Evidence Supporting LPRD:	LPS AND 1) concurrent esophageal reflux like symptoms with LPS that respond to trial of anti-reflux therapy, OR 2) diagnostic evidence of gastro-esophageal reflux on upper GI endoscopy or ambulatory reflux monitoring
Diagnostic evidence of gastroesophageal reflux:	Los Angeles B, C, or D esophagitis, and/or biopsy proven Barrett's esophagus on upper GI endoscopy, and/or distal esophageal acid exposure time >6.0% on ambulatory reflux monitoring off acid suppression
Empiric Anti-Reflux Trial:	PPI BID (Omeprazole 20mg BID equivalent) +/- alginate therapy x 3 months
Invasive Anti-Reflux Therapy:	Endoscopic or surgical anti-reflux interventions such as endoscopic fundoplication, surgical fundoplication, magnetic sphincter augmentation
Laryngeal Hyperresponse:	Repetitive laryngeal behaviors such as throat clearing or coughing, breath-holding, or as biomechanical strain at the vocal folds altering one's voice quality
Laryngeal Hypervigilance:	Increased threat-induced attention to the larynx, often co-existing with symptom-specific anxiety, fear/worry about LPS and perceived consequences
Laryngeal Recalibration Therapy:	Structured therapy integrating traditional SLP techniques with heart rate variability biofeedback and acceptance and commitment therapy to target laryngeal hyperresponsiveness and hypervigilance

Table 3. Role of Tools in the Diagnosis of Gastroesophageal Reflux Disease (GERD) and/or Laryngopharyngeal Reflux Disease (LPRD).
Hypopharyngeal Esophageal Multichannel Intraluminal Impedance-pH (HEMII-pH).

Diagnostic Tool	Confirmatory for GERD/LPRD	Supportive of GERD/LPRD	Exclusionary for GERD/LPRD	Considerations
Laryngoscopy	None		None	Not a diagnostic tool for LPRD
Upper GI Endoscopy	• Los Angeles B, C, D Esophagitis • Biopsy proven Barrett's Esophagus • Peptic Stricture	• Disrupted esophagogastric junction (e.g., hiatal hernia)	None	Inlet patch is not diagnostic of GERD/LPRD though may contribute to globus
pH-impedance monitoring	• Acid exposure time (AET) > 6.0%	• >80 distal esophageal reflux events • >10 proximal esophageal reflux events • Elevated hypopharyngeal reflux events on HEMII-pH • Positive symptom-reflux association • Low mean-nocturnal baseline impedance	• AET < 4.0%	24 hour monitoring limits ability to account for variability in reflux physiology Lower diagnostic yield for GERD
Prolonged wireless pH monitoring	• AET > 6.0% on 2 or more days of monitoring	• Positive symptom-reflux association • AET > 4.0% on 1 or more day of monitoring	• AET < 4.0% on all four days of monitoring	Unable to directly link laryngopharyngeal symptom (LPS) to proximal reflux physiology
Oropharyngeal pH monitoring (Restech)	None		None	Not a diagnostic tool for LPRD