Laryngopharyngeal Reflux (LPR) and Gastroesophageal Reflux (GERD)

Laryngopharyngeal reflux (LPR) is an inflammatory condition defined as the backflow of gastric contents into the laryngopharynx, where it comes in contact with the tissues of the upper aerodigestive tract. LPR is characterized by chronic inflammation of the laryngopharynx and, more broadly, the tissues of the upper aerodigestive tract. The mechanism of LPR requires bypassing both the upper and lower esophageal sphincters to achieve extraesophageal reflux of gastric contents. This is in contrast to gastroesophageal reflux disease (GERD), which involves backflow of gastric contents into the esophagus bypassing only the lower esophageal sphincter.

J.A. Koufman, J.E. Aviv, R.R. Casiano, et al. Laryngopharyngeal reflux: position statement of the committee on speech, voice, and swallowing disorders of the American Academy of Otolaryngology-Head and Neck Surgery Otolaryngol Head Neck Surg, 127 (2002), pp. 32-35.
J.R. Lechien, C. Finck, P. Costa de Araujo, et al. Voice outcomes of laryngopharyngeal reflux treatment: a systematic review of 1483 patients. Eur Arch Otorhinolaryngol, 274 (2016), pp. 1-23.

Anatomy and Physiology

Over time, liquid or aerosolized gastric contents, including acid, bile, and pepsin inflame the tissue of the laryngopharynx, leading to symptoms including cough, throat clearing, mucus sensation, globus sensation, and hoarseness as well as laryngeal findings such as postcricoid edema, arytenoid mucosal erythema, pachydermia, and pseudosulcus.

*Ford CN. Evaluation and management of laryngopharyngeal reflux. JAMA 2005;**294**:1534–1540.*
*Noordzij P, Khidr A, Evans B, et al. Omeprazole in treatment of reflux laryngitis. Laryngoscope 2001;**111**:2147–2151.*

Although gastroesophageal reflux GERD similarly involves the reflux of gastric contents, LPR, also referred to as extraesophageal or atypical reflux is a distinct diagnosis, is often present without the esophagitis, frank regurgitation or heartburn associated with GERD, and only 20% of LPR patients have frank GERD symptoms.

Koufman JA. The otolaryngologic manifestations of gastroesophageal reflux disease (GERD): a clinical investigation of 225 patients using ambulatory 24-hour pH monitoring and an experimental investigation of the role of acid and pepsin in the development of laryngeal injury. Laryngoscope *1991;**101**(4 pt 2 suppl 53):1–78*.
El-Serag HB, Lee P, Buchner A, et al. *Lansoprazole treatment of patients with chronic idiopathic laryngitis: a placebo-controlled trial*. Am J Gastroenterol *2001;**96**:979–983*.
Williams RBH, Szczesniak M, Maclean JC. Predictors of outcome in an open label, therapeutic trial of high-dose omeprazole in laryngitis. Am J Gastroenterol *2004;**99**:777–785*.

Assessment

As there is no gold standard, LPR diagnosis is probably the most controversial aspect of the disease. In 2018, the two most commonly used techniques to make the diagnosis consist of the use of Multi-channel impedance-pHmetry and, when it is unavailable or refused by the patient, the positive response to a well conducted empirical therapeutic trial.

Ford CN. Evaluation and management of laryngopharyngeal reflux. JAMA 2005; 294:1534-1540.
Gupta N, Green RW, Megwalu UC. Evaluation of a laryngopharyngeal reflux management protocol. Am J Otolaryngol 2016; 37:245-250.

Pathophysiology

Previous studies have shown that irritation of the laryngeal mucosa in LPR is due to two mechanisms. The main mechanism concerns the direct effect of the refluxed gastric content (acid, pepsin, trypsin, bile salts, and some gastroduodenal proteins) on the laryngeal mucosa.

Jiang A., Liang M., Su Z., et al. Immunohistochemical detection of pepsin in laryngeal mucosa for diagnosing laryngopharyngeal reflux. Laryngoscope, 121 (2011), pp. 1426-1430.
M. Sereg-Bahar, R. Jansa, I. Hocevar-BoltezarVoice disorders and gastroesophageal reflux. Logoped Phoniatr Vocol, 30 (2005), pp. 120-124.
N. Johnston, Yan J.C., C.R. Hoekzema, et al.Pepsin promotes proliferation of laryngeal and pharyngeal epithelial cells. Laryngoscope, 122 (2012), pp. 1317-1325.
J. Galli, L. Calò, S. Agostino, et al.Bile reflux as possible risk factor in laryngopharyngeal inflammatory and neoplastic lesions. Acta Otorhinolaryngol Ital, 23 (2003), pp. 377-382.

Stomach acid exposure does seem to play a role in many cases of LPR, although it is notoriously difficult to predict which patients will be refractory to medical, acid-suppression treatment, or be misdiagnosed from the onset. Non-acidic gastric reflux can also be symptomatic, causing liquid regurgitation, esophageal motility problems, and chronic inflammatory laryngitis. Furthermore, pepsin which requires an acidic environment to become active and produce tissue damage, can be reactivated within the larynx and pharynx by a later change in pH in this environment.

El-Serag HB, Lee P, Buchner A, *et al.* Lansoprazole treatment of patients with chronic idiopathic laryngitis: a placebo-controlled trial. *Am J Gastroenterol* 2001;**96**:979–983.
Williams RBH, Szczesniak M, Maclean JC. Predictors of outcome in an open label, therapeutic trial of high-dose omeprazole in laryngitis. *Am J Gastroenterol* 2004;**99**:777–785

Treatment

Patients who have relief of symptoms from empiric PPI trials are often recommended to stay on the reflux medication for 6 months before tapering to allow complete healing of laryngopharyngeal mucosa. This recommendation is based on an early position statement from the Academy of Otolaryngology–Head and Neck Surgery that continues to influence practice patterns as seen in a recent survey of the American Bronchoesophagological Association members that revealed an increase in empiric BID PPI use as first-line treatment for suspected LPR. More recent studies have shown that high dose AM PPI and QHS H2-blocker have

excellent patient compliance and near-equivalent effectiveness. With the multitude of suspected adverse effects of high-dose BID PPI, the step-wise approach may be considered for reluctant patients.

Gooi Z, Ishman SL, Bock JM, *et al.* Changing patterns in reflux care: 10-year comparison of ABEA members. *Ann Otol Rhinol Laryngol* 2015;**124**:940–946.
Koufman JA, Aviv JE, Casiano RR, *et al.* Laryngopharyngeal reflux: position statement of the Committee on Speech, Voice, and Swallowing Disorders of the American Academy of Otolaryngology–Head and Neck Surgery. *Otolaryngol Head Neck Surg* 2002;**127**:32–35.
Carroll TL, Werner A, Nahikah K, Dezube A, Roth DF. Rethinking the laryngopharyngeal reflux treatment algorithm: Evaluating an alternate empiric dosing regimen and considering up-front, pH-impedance, and manometry testing tom minimize cost in treating suspect laryngopharyngeal reflux disease. Laryngoscope. 2017;127 Suppl 6:S1-S13.