

The association between laryngopharyngeal reflux and COVID-19 is still not demonstrated

Dear Editor,

We read with interest the paper entitled "The impact of laryngopharyngeal reflux disease on 95 hospitalized patients with coronavirus disease 2019 (COVID-19) in Wuhan, China: A retrospective study."¹ The authors retrospectively reported that hospitalized patients with laryngopharyngeal reflux (LPR) had poorer clinical outcomes compared with those without LPR according to reflux symptom index (RSI). The LPR diagnosis was based on RSI > 13, which is the threshold used by Belafsky et al. to suspect LPR.² Many points have to be addressed regarding the methodology and the conclusion of the study.

First, the use of RSI > 13 as diagnosis approach is particularly problematic. RSI includes many nonspecific symptoms (eg, hoarseness, cough, throat clearing, sticky mucus, etc) that are usually encountered in many common inflammatory diseases of the upper aerodigestive tract, including allergy,³ rhinitis or chronic rhinosinusitis,⁴ and pharyngolaryngitis.⁵ The RSI is not designed to make the

LPR diagnosis but to suspect the LPR diagnosis when use in combination with laryngeal finding score, such as reflux finding score (sensitive approach).^{5,6} The use of objective approach, such as hypopharyngeal-esophageal multichannel intraluminal impedance-pH monitoring (HEMII-pH) is required to confirm the LPR diagnosis.⁵ It is unconceivable to state that patients have LPR if they did not have objective testing. In case of inability to use HEMII-pH, authors would consider fiberoptic findings (eg, posterior commissure hypertrophy, laryngeal erythema or arytenoid granulation tissue) or noninvasive objective approach such as pepsin saliva measurement to increase the accuracy of the diagnosis approach.⁵

The use of objective diagnosis approach of LPR would make sense regarding the non-specificity of the RSI symptoms, which are commonly found in both diseases. Thus, the ear, nose, and throat symptoms are frequently observed in patients with COVID-19.⁶ Regarding a recent European study, a significant number of patients

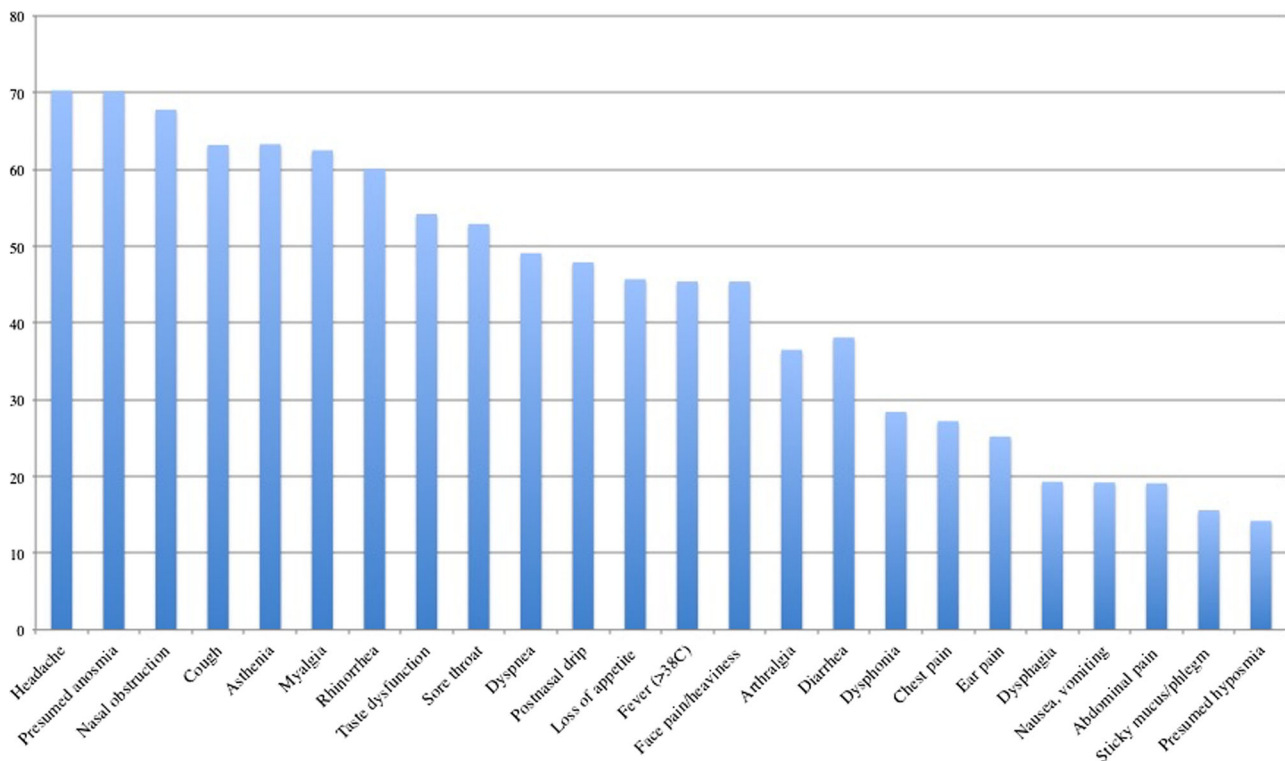


FIGURE 1 Main symptoms associated with COVID-19 infection. According to this study that included 1420 patients,⁷ the otolaryngological symptoms were prevalent. Cough, rhinorrhea, postnasal drip are all symptoms that may be associated with overall inflammation of the upper aerodigestive tract mucosa, leading to similar LPR-associated symptoms. COVID-19, coronavirus disease 2019; LPR, laryngopharyngeal reflux

with COVID-19 have rhinorrhea, postnasal drip, dysphonia or cough (Figure 1), which may be associated with laryngopharyngeal irritation.⁷ For this reason, it is probable that the RSI results found in the study of Jiang et al. would reflect the nonspecific inflammatory reaction of the laryngopharyngeal mucosa related to the infection.

Second, Jiang et al. stated that the LPR prevalence was higher in their patients, suggesting a potential impact of the virus on the upper esophageal sphincter.¹ In fact, the prevalence of LPR is still unknown.⁵ The studies that were cited by authors are epidemiological studies that assessed the LPR-symptoms in populations but the LPR diagnosis was not confirmed in these studies. About the potential impact of virus on the upper esophageal sphincter, this hypothesis has to be confirmed. We know that the main etiological factors of LPR are patient diet and stress; both acting on the upper esophageal sphincter tonus.^{8,9} If the patients of Jiang et al. would have a confirmed LPR diagnosis, the first etiological factor to investigate would be the stress related to the disease. Stress is associated with autonomic nerve dysfunction, especially with an alteration of the sympathetic-vagal balance through an increase of sympathetic "activity."^{9,10} The increase of the sympathetic activity related to stress leads to esophageal sphincter transient relaxations, which may be associated with an increase of distal, proximal, and hypopharyngeal reflux episodes.

In sum, we believe that the use of RSI is insufficient to state that patients had reflux. The otolaryngological symptoms found in the RSI would be related to COVID-19, which may entry into the pharyngeal cells through angiotensin converting enzyme-2 receptor.¹⁰ Future studies are needed to explore the relationship between LPR and COVID-19 infection. Regarding the sanitary situation, these studies have to involve adequate noninvasive objective approach such as pepsin saliva detection.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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REFERENCES

- Jiang G, Cai Y, Yi X, et al. The impact of laryngopharyngeal reflux disease on 95 hospitalized patients with COVID-19 in Wuhan, China: A retrospective study. *J Med Virol*. 2020;jmv.25998. <https://doi.org/10.1002/jmv.25998>
- Belafsky PC, Postma GN, Koufman JA. Validity and reliability of the reflux symptom index (RSI). *J Voice*. 2002;16(2):274-277.
- Eren E, Arslanoğlu S, Aktaş A, et al. Factors confusing the diagnosis of laryngopharyngeal reflux: the role of allergic rhinitis and inter-rater variability of laryngeal findings. *Eur Arch Otorhinolaryngol*. 2014;271(4):743-747. <https://doi.org/10.1007/s00405-013-2682-y>
- Brown HJ, Kuhar HN, Plitt MA, Husain I, Batra PS, Tajudeen BA. The impact of laryngopharyngeal reflux on patient-reported measures of chronic rhinosinusitis. *Ann Otol Rhinol Laryngol*. 2020;3489420921424. <https://doi.org/10.1177/0003489420921424>
- Lechien JR, Akst LM, Hamdan AL, et al. Evaluation and management of laryngopharyngeal reflux disease: state of the art review. *Otolaryngol Head Neck Surg*. 2018.
- Belafsky PC, Postma GN, Koufman JA. Laryngopharyngeal reflux symptoms improve before changes in physical findings. *Laryngoscope*. 2001;111(6):979-981.
- Lechien JR, Chiesa-Estomba CM, Place S, et al. Clinical and epidemiological characteristics of 1420 European patients with mild-to-moderate coronavirus disease 2019. *J Intern Med*. 2020;joim.13089. <https://doi.org/10.1111/joim.13089>
- Lechien JR, Bobin F, Muls V, et al. Patients with acid, high-fat and low-protein diet have higher laryngopharyngeal reflux episodes at the impedance-pH monitoring. *Eur Arch Otorhinolaryngol*. 2019;277:511-520.
- Wang AM, Wang G, Huang N, et al. Association between laryngopharyngeal reflux disease and autonomic nerve dysfunction. *Eur Arch Otorhinolaryngol*. 2019;276:2283-2287. <https://doi.org/10.1007/s00405-019-05482-w>
- Xu R, Cui B, Duan X, Zhang P, Zhou X, Yuan Q. Saliva: potential diagnostic value and transmission of 2019-nCoV. *Int J Oral Sci*. 2020;12(1):11. <https://doi.org/10.1038/s41368-020-0080-z>