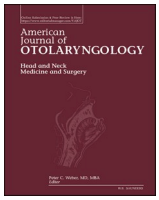
American Journal of Otolaryngology–Head and Neck Medicine and Surgery 45 (2024) 104223

Contents lists available at ScienceDirect

American Journal of Otolaryngology–Head and Neck Medicine and Surgery

journal homepage: www.elsevier.com/locate/amjoto



Acute or persistent mechanisms of dysphonia in COVID-19 patients

ARTICLE INFO

Keywords
Laryngeal
Laryngology
Head neck
Surgery
Otolaryngology
Reflux
COVID-19
SARS-CoV2
Voice
Dysphonia

Dear Editor,

We read the paper of Lin et al. entitled "COVID-related dysphonia and persistent long-COVID voice sequelae: A systematic review and meta-analysis [1]". In this systematic review, the authors reported that the prevalence of dysphonia during the coronavirus disease 2019 (COVID-19) infection was 25.1 % and decreased to 17.1 % after recovery [1]. The data of the meta-analysis indicated higher prevalence of dysphonia in females compared to males. We congratulate the authors for their valuable systematic review and meta-analysis investigating an important issue in clinical practice. In this letter, we would like to draw attention to the physiological mechanisms underlying the high prevalence of dysphonia during and post-COVID-19 infection.

Dysphonia is a multifactorial complaint, which may occur in inflammatory, neurological, or functional conditions involving the larynx. The observation of higher prevalence of dysphonia in females compared to males during the COVID-19 infection may reflect the overall highest prevalence of dysphonia in female gender, regardless of the etiological condition [2,3]. It is important to note that several genes located on the X chromosome encode proteins involved in inflammation, and escape to X chromosome inhibition [4], leading to a stronger inflammatory response in females. The gender-related immune differences were suggested by authors without providing the etiology of the laryngeal inflammatory process [1]. Several studies showed that COVID-19 infection is often associated with dysregulation of autonomic nerve function [5,6], which commonly involves an imbalance between the sympathetic and para-sympathetic nervous systems. A potential explanation for the gender differences in dysphonia prevalence could be the greater susceptibility of females to develop dysphonia in case of laryngopharyngeal reflux (LPR) compared to males [7,8]; LPR being itself associated with an autonomic nerve dysfunction [9,10]. This higher susceptibility in females might be due to vocal fold gender-related anatomical differences, since it has been supported that LPR has a stronger impact on the vocal folds of females, which are characterized by shorter and thinner mucosa, and smaller vibrating surface than males [11]. The potential autonomic nerve dysfunction induced by COVID-19 (and reflux), coupled with a high prevalence of LPR during COVID-19 [12] may explain the higher prevalence of laryngeal inflammation and associated dysphonia, which seems to develop more rapidly in females compared to males.

Another interesting issue is the persistence of dysphonia beyond the acute stage of COVID-19. Indeed, autonomic nerve dysfunction is currently one of the primary etiological hypotheses underlying long COVID-19 disease [6]. According to studies that supported the presence of vagus nerve inflammation in long COVID-19 [5], the infection sequelae may contribute to long-term esophageal dysmotility and potential chronic LPR. The evolution of dysphonia after the pandemic was studied by Al-Ani et al. who observed that in most of the cases persisted for more than a month [13]. The paper of Lin et al. supported that the follow-up of patients who developed dysphonia during the COVID-19 pandemic is an important yet overlooked field of research, which needs to consider the autonomic nerve dysfunction and its impact on vocal fold and esophageal (LPR) functions.

Acknowledgments

None.

References

[1] Lin CW, Wang YH, Li YE, Chiang TY, Chiu LW, Lin HC. Chang CT.COVID-related dysphonia and persistent long-COVID voice sequelae: a systematic review and meta-analysis. Am J Otolaryngol 2023;44(5):103950. https://doi.org/10.1016/j.amjoto.2023.103950.

DOI of original article: https://doi.org/10.1016/j.amjoto.2024.104286.

https://doi.org/10.1016/j.amjoto.2024.104223
Received 22 July 2023
Available online 16 January 2024

[2] Marchese MR, Longobardi Y, Di Cesare T, Mari G, Terruso V, Galli J, et al. Gender-related differences in the prevalence of voice disorders and awareness of dysphonia. Acta Otorhinolaryngol Ital 2022;42(5):458–64. https://doi.org/10.14639/0392-100X-N2018.
[3] Lai YT, Wang YH, Yen YC, Yu TY, Chao PZ, Lee FP, et al. The epidemiology of benign voice disorders in Taiwan: a nationwide population-based study. Ann Otol Rhinol Laryngol 2019;128(5):406–12. https://doi.org/10.1177/0003489419826136.
[4] Lefèvre N, Corazza F, Valsamis J, Delbaere A, De Maertelaer V, Duchateau J, et al. The number of X chromosomes influences inflammatory cytokine production following toll-like receptor stimulation. Front Immunol 2019 May;9(10):1052. https://doi.org/10.3389/fimmu.2019.01052.
[5] Woo MS, Shafiq M, Fitzek A, Dottermusch M, Altmeppen H, Mohammadi B, et al. Vagus nerve inflammation contributes to dysautonomia in COVID-19. Acta Neuropathol 2023. https://doi.org/10.1007/s00401-023-02612-x.
[6] Astin R, Banerjee A, Baker MR, Dani M, Ford E, Hull JH, et al. Long COVID: mechanisms, risk factors and recovery. Exp Physiol 2023;108(1):12–27. https://doi.org/10.1113/EP090802.
[7] Lechien JR, Huet K, Finck C, Khalife M, Fourneau AF, Harmegnies B, et al. Clinical and acoustical voice quality evolutions throughout empirical treatment for laryngopharyngeal reflux disease according to gender: a preliminary study. Folia Phoniatr Logop 2020;72(4):257–66. https://doi.org/10.1159/000500085.
[8] Lechien JR, Huet K, Khalife M, Fourneau AF, Finck C, Delvaux V, et al. Gender differences in the presentation of dysphonia related to laryngopharyngeal reflux disease: a case-control study. Eur Arch Otorhinolaryngol 2018;275(6):1513–24. https://doi.org/10.1007/s00405-018-4951-2.
[9] Lechien JR, Saussez S, Mayo-Yanez M, Iannella G, Vaira LA. Reflux symptoms may develop in cases of throat mucosa injury, stress and related-autonomic nerve dysfunction. Am J Otolaryngol 2023;44(1):103687. https://doi.org/10.1016/j.amjoto.2022.103687.
[10] Wang AM, Wang G, Huang N, Zheng YY, Yang F, Qiu X, et al. Association between laryngopharyngeal reflux disease and autonomic nervedysfunction. Eur Arch Otorhinolaryngol 2019;276(8):2283–7. https://doi.org/10.1007/s00405-019-05482-w.
[11] Zhukhovitskaya A, Battaglia D, Khosla SM, Murry T, Sulica L. Gender and age in benign vocal fold lesions. Laryngoscope 2015;125(1):191–6.
[12] Jiang G, Cai Y, Yi X, Li Y, Lin Y, Li Q, 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;92(10):2124–9. https://doi.org/10.1002/jmv.25998.
[13] Al-Ani RM, Rashid RA. Prevalence of dysphonia due to COVID-19 at Salahaddin general hospital, Tikrit City, Iraq. Am J Otolaryngol 2021;42(5):103157. https://doi.org/10.1016/j.amjoto.2021.103157.

Jerome R. Lechien[a,b,c,*], Antonino Maniaci[a,d], Isabelle M. Gengler[a,e], Maria Rosaria Barillari[a,f], Luigi A. Vaira[a,g,h], Miguel Mayo-Yanez[a,i]

[a] *Research Committee of Young Otolaryngologists of International Federation of Otorhinolaryngological Societies (World Ear, Nose, and Throat Federation), Paris, France*

[b] *Department of Laryngology and Bronchoesophagology, EpiCURA Hospital, Faculty of Medicine, UMONS Research Institute for Health Sciences and Technology, University of Mons (UMons), Mons, Belgium*

[c] *Department of Otolaryngology-Head & Neck Surgery, Foch Hospital, School of Medicine, UFR Simone Veil, Université Versailles Saint-Quentin-en-Yvelines (Paris Saclay University), Paris, France*

[d] *Department of Medical, Surgical Sciences and Advanced Technologies G.F. Ingrassia, ENT Section, University of Catania, Catania 95123, Italy*

[e] *Department of Otolaryngology-Head and Neck Surgery, University of Cincinnati Medical Center, Cincinnati, OH, USA*

[f] *Department of Mental and Physical Health and Preventive Medicine, "L. Vanvitelli" University, Naples, Naples, Italy*

[g] *Maxillofacial Surgery Operative Unit, Department of Medicine, Surgery and Pharmacy, University of Sassari, Italy*

[h] *Biomedical Science PhD School, Biomedical Science Department, University of Sassari, Italy*

[i] *Otorhinolaryngology-Head and Neck Surgery Department, Complexo Hospitalario Universitario A Coruña (CHUAC), A Coruña, Galicia, Spain*

[*] Corresponding author at: Department of Laryngology and Bronchoesophagology, EpiCURA Hospital, Faculty of Medicine, UMONS Research Institute for Health Sciences and Technology, University of Mons (UMons), Mons, Belgium.
E-mail address: Jerome.Lechien@umons.ac.be (J.R. Lechien).