



Gastroesophageal reflux disease, laryngopharyngeal reflux, and nasopharyngeal reflux in chronic rhinosinusitis patients

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Dear Editor,

We read the paper of Chen et al. dedicated to the relationship between chronic rhinosinusitis (CRS) and gastroesophageal reflux disease (GERD) [1]. The authors extracted genome-wide association study data sets for GERD and CRS, and used Mendelian randomization to assess the causality between both conditions. They concluded that GERD increases the risk of developing CRS by 36% through genetic association [1]. We congratulate the authors for the investigation of a difficult and controversial topic. In this letter, we would like to draw attention to the difference between GERD, laryngopharyngeal reflux (LPR) and potential nasopharyngeal reflux (NPR), and the potential biases related to the lack of consideration of LPR/NPR in the author analyses.

According to the Lyon consensus, the GERD diagnosis is only confirmed when the patient has grade C or D

esophagitis, acid exposure time > 6% in the distal esophagus (pH monitoring), or esophageal stricture [2]. These criteria were not considered in the study of Chen et al., who based the diagnosis on the 10th edition of the International Classification of Diseases, which is not updated regarding the last consensus papers. For example, in the database used by Chen et al., some patients with GERD symptoms have been considered GERD patients. At the same time, it is demonstrated that the presence of GERD symptoms is not enough to confirm the diagnosis [2].

From a pathophysiological standpoint, the study of the association between reflux and CRS needs to consider more laryngopharyngeal reflux (LPR) or nasopharyngeal reflux (NPR) rather than GERD. Indeed, the esophageal reflux events of most GERD patients do not reach the pharynx [3, 4], while the proportion of hypopharyngeal events reaching the nasopharynx and the nasal cavities remains unclear. This point is particularly important. Indeed, the association between CRS and reflux needs to involve the deposit

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of gastroduodenal contents (e.g. pepsin, bile salts) into the nasopharyngeal and nasal mucosa, which leads to the development of inflammation, and the related CRS [5, 6]. Because GERD and CRS are both prevalent conditions affecting up to 30% of Western country populations [7, 8], there is a risk of finding potential biased or indirect associations that may be due to the high prevalence of both conditions, or the higher prevalence of LPR in GERD population compared to healthy populations. In that way, it should be possible that the significant association between GERD and CRS results more from an association between the patients with CRS and both GERD and LPR, rather than those with CRS and GERD.

In practice, future studies investigating the relationship between reflux and CRS should consider (1) the LPR diagnosis with hypopharyngeal–esophageal intraluminal multi-channel impedance–pH monitoring or, even better, the use of nasopharyngeal pH monitoring [3, 9], (2) the detection of gastroduodenal enzymes into the sinonasal secretions, and (3) the last criteria for the diagnosis of CRS, GERD, and LPR [2, 4, 10]. These criteria are important to differentiate the indirect association and causality relationship between reflux and CRS.

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Declarations

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