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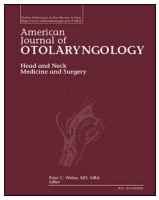

Translational research for elucidating the relationship between chronic cough and laryngopharyngeal reflux disease

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Dear Editor,

We read the paper of Watson et al. entitled "Manometric Abnormalities in Patients With and Without Chronic Cough [1]." In this study, the authors observed that chronic cough patients had upper esophageal sphincter (UES) relaxation duration (734 ms) significantly longer than the non-cough patients (582 ms), while the intrabolus pressure and the UES motility mean peak pressure did not differ between groups. They concluded that there are subtle differences in high-resolution manometry (HRM) between patients with and without chronic cough, and they proposed that the baseline alterations of UES function could manifest through potentially vagal hypersensitivity. We congratulate the authors for this interesting investigation of an important topic. Based on their observations, we would like to draw attention to some points.

First, the observations of a longer UES relaxation in chronic cough patients could indirectly support a potential relationship between chronic cough and laryngopharyngeal reflux disease (LPRD) [2], but the lack of 24-hour hypopharyngeal-esophageal multichannel intraluminal impedance-pH monitoring (HEMII-pH) limits the establishment of a causal association. From a pathophysiological standpoint, LPRD is defined as the occurrence of more than one pharyngeal reflux event at the 24-hour HEMII-pH, which involves lower and upper esophageal sphincter transient relaxations [3]. UES relaxation abnormalities are commonly observed in LPRD patients [2], who report gaseous, upright/daytime, and weakly acid pharyngeal reflux events [4]. In this way, the longer UES relaxation duration could be associated with a higher probability of having gaseous reflux events refluxing from the proximal esophagus to the hypopharynx, leading to the deposit of gastroduodenal enzymes into the upper aerodigestive tract mucosa. It has been suggested that chronic cough can develop in LPRD patients through gastroduodenal enzyme-induced mucosa irritation rather than a vagal sensitivity mechanism as the origin of the cough [5,6]. This possibility is strengthened by the current examples of the occurrence of cough as a reflex induced by the irritation of ear, nose, and throat mucosa/skin, by various stimuli, e.g. tobacco components, ear duct wax impaction, or allergens [7,8]. The origin of chronic cough in LPRD patients could be investigated through the protocol of Watson et al. [1], which can be improved considering the use of 24-hour HEMII-pH and the measurement of gastroduodenal enzymes in laryngopharyngeal sputum. For this last point, the consideration of bile acids, trypsin, elastase, and pepsin makes sense regarding the high rates of weakly acid or alkaline pharyngeal events in the LPRD [4,9]. Thus, the non-acid features of most LPRD can explain the lack of effectiveness of proton pump inhibitors (PPIs) or H2-blockers, which were prescribed in the study of Watson et al. in 62.5 % of patients with chronic cough [1]. Finally, the lack of significant abnormalities of the esophageal body contraction at the Chicago classification can be explained by the existence of several LPRD patient profiles, with 43.3 % of patients having esophageal body dysmotility, while others having impaired proximal esophageal contractility [10].

To conclude, the findings of Watson et al. are important in the understanding of the pathophysiological mechanisms of chronic cough associated with LPRD, and their results can indirectly suggest a potential direct link between LPRD and chronic cough. The HRE findings can encourage the conduction of future investigations combining objective additional examinations in the same cohort in a translational approach (HEMII-pH-HRM-enzyme measurements).

CRediT authorship contribution statement

Mejdeddine Al Barajraji: Conceptualization. **Jennifer Aoun:** Data curation, Formal analysis, Validation. **Manon Louvrier:** Writing – original draft. **Noémie Nemry:** Writing – original draft. **Jerome R. Lechien:** Writing – original draft, Writing – review & editing.

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