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Correspondence and Reply

A limitation regarding the association between intranasal corticosteroid use and better COVID-19 outcomes: Nasal symptoms matter



To the Editor:

We read with great interest the article by Strauss et al.¹ Their study investigated the possible association between intranasal corticosteroid (INCS) therapy and risk for hospitalization, intensive care unit admission, or death owing to COVID-19. One strength of the study is that the authors analyzed a large-scale database about COVID-19 and adjusted for many clinically relevant confounding factors using a causal inference method (ie, propensity score matching). In addition, they confirmed the robustness of results by performing sensitivity analyses that accounted for the use of prescription inhaled corticosteroids, blood absolute eosinophil count, and allergic rhinitis. Although the results may support the potential effectiveness of INCS use in COVID-19 outcomes, we point to a possible limitation that might influence the interpretation of study results. We have an additional suggestion regarding this study.

The limitation is regarding preexisting nasal symptoms such as rhinorrhea and nasal congestion. Because this study is a retrospective observational design, most INCS users in this study experienced some kind of nasal symptom. Under such a condition, this study examined only the association between INCS use for preexisting nasal symptoms and COVID-19 outcomes, not the effectiveness of INCS on COVID-19 outcomes. Importantly, patients with mild COVID-19 present with nasal congestion or rhinorrhea as well as cough or hyposmia.² Thus, it might be that early nasal symptoms caused by COVID-19 rather than INCS potentially predict better COVID-19 outcomes. To clarify the effectiveness of INCS use in COVID-19 outcomes, a consideration is needed of the association between nasal symptoms and COVID-19 severity. To compensate for this limitation, we have a simple suggestion. If available, the authors should both describe and adjust for nasal symptoms (eg, rhinorrhea, nasal congestion), which are clearly distinguished from flu-like symptoms in clinical presentations. Because preexisting nasal symptoms are the common cause of both INCS use and COVID-19 outcomes,² these may be an important residual confounding factor that require adjustment.³ Hence, if the authors could identify and adjust for preexisting nasal symptoms among COVID-19 patients who used INCS, they could clarify the association between INCS users and COVID-19 outcomes, considering the presence of nasal symptoms.

We could not entirely interpret INCS use to be associated with good COVID-19 outcomes, although this study is well-designed. This limitation might be attributed to the observational study design. Therefore, randomized controlled trials are essential to prove the causal effects of INCS use on COVID-19 outcomes. However, we believe that considering the limitation and suggestion mentioned here will help

clinicians and future researchers interpret this study accurately.

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Reply to "A limitation regarding the association between intranasal corticosteroid use and better COVID-19 outcomes: Nasal symptoms matter"



To the Editor:

We thank the editors for the opportunity to respond to the comments by Maeda et al¹ regarding our article, and appreciate their positive comments. We acknowledge that our article was limited by its retrospective design and the information available in the Cleveland Clinic COVID-19 Research Registry (CCRR). Despite this, the significant associations between intranasal corticosteroid (INCS) and improved COVID-19 outcomes highlight the need for a randomized controlled trial (RCT) to determine whether INCS are effective in treating or preventing COVID-19.

Maeda et al¹ hypothesized that the association of early nasal symptoms with improved COVID-19 outcomes was confounded by INCS therapy and recommended repeat analysis adjusting for nasal symptoms. Although we appreciate their recommendation, the CCRR does not include data on nasal symptoms. Nonetheless, adding nasal symptoms as a covariate to our models, although helpful, does not preclude the need for a prospective cohort study or an RCT to corroborate our findings.

We note that observational studies of nasal symptoms in COVID-19 have been limited by small sample sizes and missing data. Kim et al² demonstrated that both nasal congestion (34.3%) and rhinorrhea (26.2%) were relatively common in a cohort of