



Correspondence

Fractional exhaled nitric oxide

Signaling lung function changes in obstructive lung diseases



We read with great interest the well-presented article entitled, “The Clinical Role of Fractional Exhaled Nitric Oxide in Asthma Control” by Sato et al.¹ which suggested an association between mean fractional exhaled nitric oxide (FeNO) levels and annual changes in forced expiratory volume in 1 second (FEV₁) as one of the characteristics of FeNO during asthma. The authors proposed FeNO as a risk factor involved in airway remodeling of asthma, thus making it a useful tool for detecting individuals with a coming decrease in pulmonary function.¹ Similarly, an association between higher FeNO levels and annual decrease in FEV₁ has been previously demonstrated.² In support of these observations, a recent study has identified that FeNO correlates with bronchial wall thickening visible on 3-dimensional computed tomography in patients with asthma.³

Along those lines, FeNO is expected to play a role in persistent chronic airway obstruction characterized as chronic obstructive pulmonary disease (COPD). Specifically, our team has recently highlighted a significant role of FeNO measured at a flow rate of 50 mL/s (FeNO₅₀) as a useful preoperative predictive marker regarding pulmonary complications in smoking patients with COPD who are undergoing abdominal surgery.⁴ In detail, we revealed that patients with elevated FeNO₅₀ were at highest risk for presenting with perioperative and postoperative bronchospasm that demands bronchodilator administration, as well as postoperative tachypnea and dyspnea.⁴ Furthermore, increased exhaled nitric oxide levels have been reported in hospitalized patients during an exacerbation of COPD.⁵ These findings are highly suggestive of an additional important signaling role of FeNO in cases of emerging airway stress in patients with COPD who may require local nitric oxide release for antimicrobial host defense or preservation of ventilation and perfusion matching within the lung.⁵

These findings could be further explained by the fact that endogenous nitric oxide represents an important airway protective mechanism indicative of an eosinophilic airway inflammation, released in cases of reversible or persistent airway obstruction.^{6,7} In these terms, asthma-COPD overlap, which is an umbrella term that encompasses patients with COPD and eosinophilic inflammation and smoking patients with asthma with non-fully reversible airflow obstruction, characterized by high FeNO levels.⁸

On the other hand, long-term smoking and more severe disease have been reported as the most important factors that influence exhaled nitric oxide levels in patients with severe COPD who had lower levels of FeNO than exsmokers and patients with mild to

moderate COPD.⁵ Moreover, severe α_1 -antitrypsin deficiency has been characterized by lower FeNO level compared with healthy non-smokers and patients with COPD.⁵ Hence, FeNO concentration in the airways seems to be reduced when there is a long-lasting oxidative stress, which is substantially correlated to the pulmonary function impairment.^{5,9}

In other words, FeNO should no longer be considered solely as an inflammation biomarker but rather as a biomarker that integrates with both airway inflammation and lung function changes.^{4,10} Overall, a classification based on the inflammatory profile, irrespective of the taxonomy, not only provides a more clear distinction of patients with obstructive airway diseases but also crucially reveals acute or progressive changes in lung architecture and function and could guide treatment in cases of obstructive lung diseases.

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Disclosures: Author has nothing to disclose.