



Correspondence

Fractional exhaled nitric oxide, methacholine, or forced expiratory flow between 25% and 75%



What's better in the daily clinical practice?

Nickels and Lim¹ retrospectively evaluated 774 adults who underwent methacholine challenge and fractional exhaled nitric oxide (FeNO) measurement. They reported that approximately 16% of tested individuals had positive methacholine challenge results (ie, bronchial hyperreactivity [BHR]) and that FeNO values were higher in those with BHR. A receiver operating characteristic curve revealed an area under the curve of 0.57, suggesting a poor association between FeNO and methacholine outcomes. Therefore, the authors concluded that in corticosteroid-naïve pulmonary patients with normal forced expiratory volume in 1 second values, FeNO poorly predicts the outcome of a methacholine challenge. However, the authors speculated about the economic context of the findings, suggesting that FeNO provides a potential treatment-guiding data point, is more sensitive to inhaled corticosteroids, and is quicker and cheaper than methacholine testing. Thus, they propose FeNO as an attractive first-line test in a patient with respiratory symptoms and normal baseline spirometry results. The current study is up-to-date, and the suggestions are surely intriguing. However, I believe that it deserves some consideration.

FeNO is a typical biomarker of type 2 bronchial inflammation, indicated only in patients with eosinophilic bronchial inflammation.² In this regard, the mean age of the cohort is 54.4 years: if the respiratory symptom occurrence was recent, it is likely that most patients had a nonallergic endophenotype. Strong inverse correlation between FeNO and BHR to methacholine was found in allergic children with asthma and rhinitis, and a cutoff of 32 ppb of FeNO was predictive of BHR.³ Another study, conducted in 211 patients with persistent allergic rhinitis, found a strong and inverse correlation between FeNO levels and BHR severity.⁴ FeNO was a predictive factor for BHR, and 37 ppb was found to be the best cutoff (area under the curve, 0.90) to define BHR. Finally, in 298 allergic patients, FeNO was considered a good predictor for BHR (area under the curve, 0.90 with 27.0 ppb as the cutoff).⁵

Currently, the practical use of FeNO in asthma management is still controversial, as recently pointed out.^{6,7} However, FeNO assessment may give useful information about endotyping and phenotyping patients with asthma only in those who are well screened patients.⁸

Because Nickels and Lim also considered the pharmaco-economic aspects of FeNO measuring, I would like to propose another potential biomarker in those with normal forced expiratory volume in 1 second values. Unfortunately, these authors did not

provide spirometry parameters, but forced expiratory flow between 25% and 75% (FEF_{25%–75%}) may provide fruitful insights, as acknowledged by the authors. It has been evidenced that impaired FEF_{25%–75%} values, such as less than 65% of predicted, may predict the following: BHR, reversibility to bronchodilation testing, high FeNO values, poor asthma control, and early bronchial involvement in allergic patients with rhinitis.^{9,10} Therefore, a simple spirometry may give important suggestions useful in the daily clinical practice.

In conclusion, I maintain that FeNO assessment may have a role in a definite situation, but FEF_{25%–75%} may give pragmatic information in a wider population of patients with respiratory symptoms.

Giorgio Ciprandi, MD
Department of Medicine

IRCCS - Azienda Ospedaliera Universitaria San Martino - IST
Genoa, Italy
gio.cip@libero.it

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