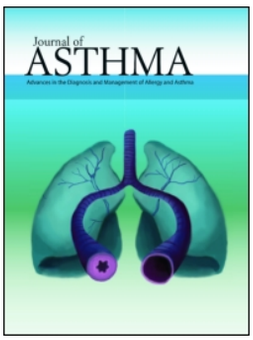

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Diagnostic value of FeNO and MMEF for predicting cough variant asthma in chronic cough patients: Methodological issues

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Dear Editor,

We were interested to read an article that recently published by Chen LC and colleagues in Dec 2019 issue of the Journal of Asthma (1). The purpose of the authors was to investigate the diagnostic value of fractional exhaled nitric oxide (FeNO) and maximum mid-expiratory flow (MMEF) for differentiating cough variant asthma (CVA) from chronic cough in patients with or without allergic rhinitis (1). 328 patients with chronic cough who underwent spirometry and FeNO tests were retrospectively reviewed. Diagnostic efficiency and prediction of CVA were assessed by Receiver Operating Characteristic (ROC), sensitivity, specificity, predictive values and optimal cutoff points of (FeNO and MMEF), respectively. The authors reported that the optimal cutoff values of FeNO and MMEF to discriminate CVA from chronic cough were 24.5 ppb (AUC, 0.76; sensitivity, 69.6%; specificity 72.9%; PPV, 61.2%; NPV, 79.5%) and 66.2% (AUC, 0.77; sensitivity, 67.2%; specificity 78.3%; PPV, 65.6%; NPV, 79.5%). Also, the optimal cutoff values of combining FeNO with MMEF to discriminate CVA from chronic cough were >22 ppb for FeNO and <62.6% for MMEF (AUC, 0.87) (1).

Despite these interesting results, there are some methodological issues that we will mention below: We must first distinguish between the concept and application of two words of prediction and diagnostic value. For clinical purposes, the accuracy and precision of a test must be considered together to determine the diagnostic value and presentation of each of them cannot explain the value of a diagnostic test. In summary, for calculating test accuracy and reliability, it is inevitable to provide values (sensitivity, specificity, predictive values, likelihood ratios, ROC) and (intraclass correlation coefficient (ICC) and Bland Altman Plot for quantitative and weighted kappa for qualitative variables). Another noteworthy point in this study is the prediction. Inorder to predict an outcome, we need to have atleast acohort dataset to develop and validate a prediction model (2-4). Our prediction model can easily be validated by applying methods such as split file, bootstrapping, or other well-known validation methods. Lastly, without assessing interaction between important predictors, most of the time our prediction will be a misleading message (2,5,6).

Authors concluded that FeNO and MMEF might have greater value as negative parameters for differentiating CVA from chronic cough and their combination gives a better prediction than either

alone and finally the diagnostic accuracy of FeNO for predicting CVA in chronic cough patients with allergic rhinitis was higher than in chronic cough patients without allergic rhinitis (1). In this letter, we discussed how to properly evaluate the diagnostic value of a test and how to predict an outcome. Any conclusions on these fields should be supported by the abovementioned methodology issues. Otherwise, misinterpretation cannot be avoided.

Keywords: Chronic cough; cough variant asthma; maximum mid-expiratory flow; fractional exhaled nitric oxide; allergic rhinitis; methodological issue

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