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Title: Simultaneous analysis of clinical markers for predicting increased lung function fluctability in stable asthma

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Body: Background: Airway hyperresponsiveness (AHR) has been shown to be associated with the loss of asthma control. Predicting the increased fluctuation of lung function might be useful to regulate the future risk of poor asthma control because peak expiratory flow (PEF) variability well correlates with AHR. Objective: We simultaneously analyzed the clinical markers for predicting increased PEF variability in stable asthma. Methods: We studied non-smoking asthmatic patients who were receiving conventional therapy and clinically stable for 8 weeks. Patient medical records were obtained and asthma control questionnaire (ACQ), spirometry, and exhaled nitric oxide fraction (FENO) were measured. Associations between these variables and PEF variability over a week (Min%Max) were prospectively assessed. Results: 52 of 297 asthmatics (17.5%) showed the increased PEF variability (Min%Max < 80%). These subjects were receiving more intensive therapy, but had more severe asthma symptoms, more airflow obstruction, and more evidence of airway inflammation. Especially, ACQ, forced expiratory volume in one second % of predicted (%FEV1), and FENO were identified to be independent predictors of Min%Max < 80%. When we combine baseline %FEV1 ≤ 85% and/or FENO ≥ 40 ppb, this index was associated with the highest combination of sensitivity (94.2%) and specificity (80.4%) for increased PEF variability. Conclusions: These results suggested that ACQ, %FEV1 and FENO can stratify risk for increased fluctuation of lung function among the clinically stable asthmatics.