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Title: Meta-analysis of the accuracy of screening adult asthma using exhaled nitric oxide

Dr. Hideo 23327 Ichihashi ichihap0401@softbank.ne.jp MD ¹, Dr. Hiroyuki 23410 Sano hsano@ko-arena.med.kindai.ac.jp MD ², Dr. Katsuyuki 23411 Tomiya tomita-katsuyuki@nho-yonago MD ³, Dr. Akiko 23412 Sano asano@ko-arena.med.kindai.ac.jp MD ², Dr. Osamu 23413 Nishiyama nishiyama@ko-arena.med.kindai.ac.jp MD ², Dr. Takashi 23420 Iwanaga iwanaga@med.kindai.ac.jp MD ², Dr. Yuji 23421 Higashimoto higashimoto@ko-arena.med.kindai.ac.jp MD ², Dr. Hiroaki 23427 Kume hkume@ko-arena.med.kindai.ac.jp MD ² and Prof. Yuji 23502 Tohda tohda@med.kindai.ac.jp MD ². ¹ General Medicine, Yamatotakada Municipal Hospital, Yamatotakada, Nara, Japan ; ² Department of Respiratory Medicine and Allergology, Kinki University Faculty of Medicine, Osakasayama, Osaka, Japan and ³ Division Respiratory of Medicine, Yonago Medical Centre, Yonago, Tottori, Japan .

Body: Background: Exhaled nitric oxide (FENO) has been highlighted as a non-invasive inflammatory biomarker. However, the relationship between FENO and screening of asthma in the adult population is not clear. The aim of this study is to estimate the accuracy of FENO for screening adult asthma using a meta-analysis. Methods: We searched PubMed, EMBASE, and ISI Web of Science from December 1996 through December 2011 to obtain relevant studies for the meta-analysis. Prospective English-language studies that diagnosed adult asthma using FENO and included sufficient data for completion of 2 × 2 tables or the equivalent data calculated from sensitivity and specificity. We used a meta-analytic method to construct summary receiver operating characteristic (ROC) curves. Results: Of 230 potential studies, 22 articles were retrieved for detailed evaluation, and 19 studies with a total of 3,293 patients met the inclusion criteria. Study methodological quality was generally high, with average Quality Assessment for Diagnostic Accuracy Studies (QUADAS) scores of 9.3 of a total of 14 points (range, 8 to 11 points). The pooled sensitivity was 0.71 (95% confidence interval [CI], 0.67 to 0.76) and the specificity was 0.79 (95% CI, 0.75 to 0.82) with high heterogeneity (I² = 0.83). In a sub-analysis, high positive likelihood ratio (6.30) and lower heterogeneity (I² = 0.18) were obtained using the cutoff level of 45 ppb. Conclusions: We conclude that measurement of FENO is not sufficiently accurate to diagnose asthma without the assistance of other diagnostic tools; however, it is useful as a screening tool, when the cutoff level of ≥45 ppb was used.