Should FEV1/FEV6 replace FEV1/FVC ratio to detect airway obstruction? A meta-analysis

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CRD summary
The authors concluded that the FEV1/FEV6 ratio was a valid alternative for FEV1/FVC in diagnosis of airway obstruction. Although the generalisability of its application to different clinical populations was limited, this was a generally well-conducted review and the authors’ conclusion is likely to be reliable.

Authors' objectives
To evaluate the efficacy of the forced expiratory volume (FEV) test in six seconds (the FEV1/FEV6 ratio) as a surrogate for the FEV1/forced volume vital capacity (FVC) ratio in the detection of airway obstruction.

Searching
MEDLINE, EMBASE, The Cochrane Library and Web of Science were searched without language restriction from 1966 to 2008. Search terms were reported. Reference lists of primary studies and review articles were searched and conference proceedings were consulted for additional material.

Study selection
All studies that included at least 10 patients and assessed diagnostic accuracy of FEV1/FEV6 compared with FEV1/FVC (the gold standard) were eligible for inclusion in the review. Sensitivity and specificity data had to be available in order to construct a 2x2 contingency table for individual patients. Spirometry had to be performed according to guidelines set by American Thoracic Society or European Respiratory Society. Most studies used the fixed gold standard (FEV1/FVC<70%). Other studies diagnosed airway obstruction with a percentage below the lower limit of normal (LLN) or used a fixed cut-off. Mean age of patients ranged from 37 to 69 years. Males and females were represented equally. Study populations largely comprised adults; some were recruited from the community and others were described as workers or current smokers.

Two independent reviewers selected studies for inclusion. Any disagreements were resolved by consensus.

Assessment of study quality
Study quality assessment was carried out by two independent reviewers using an adapted Cochrane Collaboration checklist and the QUADAS tool for diagnostic accuracy studies. Maximum quality score was 14.

Data extraction
Sensitivity, specificity, positive and negative likelihood ratios (PLR and NLR), diagnostic odds ratio (DOR) and diagnostic scores, with 95% confidence intervals (CIs), were calculated for each study. Authors were contacted for additional study details where necessary.

Two independent reviewers extracted the data.

Methods of synthesis
Data were pooled in a random-effects meta-analysis (DerSimonian and Laird). A summary receiver operating characteristic (SROC) curve was presented to assess overall test performance. A Q* point was presented to indicate a joint maximum sensitivity and specificity. The threshold effect was tested with a regression model using the least-squares method weighted by the inverse of the variance. Statistical heterogeneity was assessed and explored using the Cochrane Q test and the I² statistic (>50% indicated substantial heterogeneity). Further exploration of heterogeneity was carried out with inverse variance-weighted univariate meta-regression analysis using prevalence and quality scores as variables to arrive at the relative diagnostic odds ratio. Publication bias was examined with funnel plots and by the Egger test. The trim and fill method was used in the presence of publication bias to impute missing data.
Results of the review
Eleven studies (n=31,333, sample size range 63 to 11,676) were included in the review: seven cross-sectional studies (n=19,243); and four retrospective studies (n=12,090). The quality scores ranged from 8 to 11. There was no evidence of publication bias.

Pooled results showed that the FEV$_1$/FEV$_6$ was an acceptable surrogate for FEV$_1$/FVC. Sensitivity was 0.89 (95% CI 0.83 to 0.93) and specificity was 0.98 (95% CI 0.95 to 0.99). Positive likelihood ratio was 45.46 (95% CI 18.26 to 113.21) and negative likelihood ratio was 0.11 (95% CI 0.08 to 0.17). Diagnostic odds ratio was 396.02 (95% CI 167.32 to 937.31) and the diagnostic score was 5.98 (95% CI 5.12 to 6.84). The SROC curve showed a high level of overall accuracy, with an area under the curve of 0.97 (95% CI 0.95 to 0.98; Q* point: 0.95). There was no evidence of a threshold effect, but there was statistically significant heterogeneity between the studies (p<0.001).

Multiple regression analysis showed that prevalence of airway obstruction had a statistically significant effect on diagnostic odds ratio (relative DOR 1.12, 95% CI 1.00 to 1.25, p=0.05). There was no statistically significant effect in terms of choice of cut-off point.

Authors' conclusions
FEV$_1$/FEV$_6$ was a valid alternative for FEV$_1$/FVC in diagnosis of airway obstruction.

CRD commentary
The review question was clear and supported by detailed inclusion criteria for all aspects other than patient characteristics. The search strategy included some relevant sources. Attempts were made to minimise publication and language biases. The review process was conducted with sufficient protection against potential errors and bias. An appropriate quality assessment tool was used for diagnostic accuracy studies. Study details were provided, but the absence of fuller information on included patient characteristics limited the interpretation of generalisability. Heterogeneity was assessed and its presence was fully explored. This was a generally well-conducted review and the authors' conclusion is likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that FEV$_1$/FEV$_6$ should be included in diagnostics guidelines and in clinical practice for airway obstruction.

Research: The authors did not state any implications for research.

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