Spirometric thresholds and biased interpretation of test results

In an effort to elucidate what constitutes irreversible airways obstruction (ie, COPD), Bhatt *et al*[1] used CT-defined emphysema and gas trapping to determine whether a fixed FEV_1:FVC ratio or the lower limit of normal (LLN) is a clinically more discriminating index of COPD. There are, however, several methodological limitations that need to be considered when interpreting these results.

1. The study assumes a paradigm that radiographic signs of emphysema and/or air trapping are specific of COPD. Alterations in pulmonary structure due to senescence and COPD are to some extent intertwined;[2] therefore, radiographic findings which do not consider the effects of normal ageing may well explain the higher prevalence rate of emphysema in the fixed ratio group.
2. Tables 2 and 3 in Bhatt *et al*[1], present 100 single-inference procedures for testing significant differences; for each comparison, type I error is fixed at 0.05, therefore each comparison runs a 5% chance of an erroneous conclusion. Multiple single-inference results lead to a greatly increased number of false-positive results. Correcting for the false discovery rate would alter the number of 'significant' findings.[3] The interpretation of significant differences is further complicated by the fact that several indices are correlated.
3. The study also grossly misrepresents the COPD population. Only including smokers implies that airflow limitation is solely attributable to smoking. The prevalence of COPD in non-smokers has been estimated at 25%–45%.[4] Second, 'One-quarter of the fixed-only group were initiated on home oxygen following the baseline visit'. It is astounding that so many people with no signs of airflow limitation, or at best mild COPD according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, receive home oxygen. The reason can hardly be COPD.
4. The paper would have benefitted from considering longitudinal studies that are at odds with the authors' conclusions,[5] and from evidence that 'exacerbations' were COPD related.

In light of these weaknesses, the findings of Bhatt *et al* need to be interpreted cautiously and certainly do not offer definitive proof that GOLD staging is advantageous over the LLN. Further studies which fairly compare the two criteria to a gold standard in a representative sample of patients with COPD are urgently needed to address this important issue.

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