Small lung syndrome: the need to reclassify chronic lung disease

In 1958, an international symposium defined a category of "non-specific lung disease", which excluded all neoplasms, infections, and diseases caused by other known (mostly occupational) exposures.[1] This grouping included bronchitis (defined by symptoms), emphysema (defined by histology), and airflow obstruction, both reversible (asthma) and irreversible (later called chronic obstructive pulmonary disease [COPD]). The term non-specific lung disease is no longer in general use, but since the eighth edition of the International Classification of Diseases (ICD-8, published in 1965), this cluster has appeared together, currently under the title "certain lower respiratory tract diseases". Despite this broad title, the ICD has also followed the symposium in excluding all restrictive lung disease from the group.

The omission of restrictive disorders from non-specific lung disease carries the mistaken implication that a low forced vital capacity (FVC) is found only among the specific lung diseases mentioned later in the classification (ICD-11 CA60-CA8Z, CB00-CB0Z). However, low FVC in the absence of any specific diagnosis, or mistakenly diagnosed as COPD, is widespread and associated with increased mortality.[2,3] This condition is particularly common in low-income countries in south and east Asia and sub-Saharan Africa, including countries with a very low prevalence of smoking.[4] Although these regional differences in vital capacity have often been discounted as normal variation, there is increasing evidence from the USA that the low FVC found, for instance, among African American people is associated with poor health outcomes, including increased mortality.[5]

Where there is substantial consumption of tobacco, smoking is by far the most common cause of airflow obstruction,[6] and there is a strong association between the prevalence of smoking and the prevalence of a low ratio of FEV_1 to FVC (FEV_1/FVC),[4] a measure of airflow obstruction. However, the association between smoking and COPD mortality is less clear. Barker and Osmond[7] noted that mortality from bronchitis and emphysema in England and Wales was associated with infant deaths from pneumonia and bronchitis 50 years earlier, but only weakly associated with lung cancer rates. This lack of association is also reflected in the global distribution of COPD mortality, with high rates in low-income countries in Asia and sub-Saharan Africa coinciding with areas of poverty and low FVC, but not with smoking or airflow obstruction.[4] This discrepancy suggests that many people dying with a low FVC are being misclassified as dying from COPD. The misclassification is understandable. Most people with a low FVC have symptoms, including breathlessness, that are commonly found in airflow obstruction.[8] Most will not have had any spirometry testing, but those who do will have a low FEV_1, which is commonly (and often wrongly) assumed to define airflow obstruction. As there is no alternative heading in the ICD under which to classify these people, it is not surprising if they are certified as dying of COPD.

Although low FVC can be associated with increased residual volume in selected patients with severe airflow obstruction, this is an unusual finding in general populations, in which there is no correlation between FVC and FEV_1/FVC,[9] and low FVC is more likely to reflect low total lung capacity. A low total lung capacity is important because this is associated with both increased arterial stiffness[10] and increased mortality.[11] Low FVC, which is a marker of low total lung capacity, has also been linked to increased mortality[2,3] and cardiovascular and metabolic abnormalities.[12] Although it has frequently been asserted that these comorbidities are associated with COPD, they are not associated with obstruction.[13] The confusion has come about from studies that defined obstruction from FEV_1 alone, without reference to FVC, and studies in clinical settings,[14] which are notably prone to admission rate bias.

If this condition is to be properly recognised, it requires a new diagnostic label. The term small lung syndrome would recognise both the basic abnormality (a low total lung capacity) and the associated comorbidities. In most surveys, the syndrome would be defined as a low FVC (ie, less than the fifth percentile of the normal, asymptomatic non-smoking population), regardless of the FEV_1, whereas in clinical environments it might be more accurately identified from a slow vital capacity or, in doubtful cases, from a low total lung capacity. Ignoring the condition would be to the detriment of populations in low-income and middle-income countries, and ethnic

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minority groups in high-income countries. Small lung syndrome is common. The proportion of the population over the age of 40 years with an FVC below the lower limit of normal (for Americans of European heritage) is between 10% and 20% in Europe and north Africa, but much higher, at 20–80%, in low-income and middle-income countries in Asia and sub-Saharan Africa.[4] Naming the condition should encourage physicians to identify it and could improve the quality of care and the collection of routine statistics. Not recognising this problem will perpetuate the error of believing that people with small lung syndrome have COPD, leading to inappropriate treatment and management.

Small lung syndrome is likely to be a disorder of lung development, but we know little else about its origins. Some genetic variants have been associated with the condition, although they explain very little of its variation.[15] There is no specific treatment, and the efficacy of different care packages is untested. However, care packages should emphasise the need to identify the condition and, at the very least, to monitor and control cardiovascular risks, including hypertension and diabetes. The heavier burden in poorer countries suggests that the main place for research should be low-income and middle-income settings.

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Peter Burney, Ben Knox-Brown, André F S Amaral
p.burney@imperial.ac.uk

National Heart Lung Institute, Imperial College London, London SW3 6LR, UK (PB, BK-B, AFSA); National Institute for Health Research Imperial Biomedical Research Centre, London, UK (AFSA)

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