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Editorial

A Case for Using Indian Prediction Equations for Pulmonary Function Tests in Indians

Pulmonary function tests (PFTs) are an integral part of evaluation of patients with chest diseases. These find application in confirmation of diagnosis, evaluation of functional impairment, assessment of therapeutic response, monitoring for occupational and environmental lung damage, pre-operative risk stratification and for following the course of disease.[1] PFTs also find application in studies on public health as well as in settling legal claims for lung injuries. Being non-invasive, relatively less expensive and almost entirely without any hazards to the patient, these tests are also carried out periodically to aid in management decisions. The range of PFTs a laboratory can offer is wide and it is possible to obtain clinically useful information about lung mechanics including airway, parenchymal, chest wall and muscle function, gas exchange, exercise capacity, metabolic function as well as respiratory drive. Among these tests, spirometry is by far the most frequently performed investigation because it provides clinically useful objective information on a wide range of chest diseases, both obstructive and restrictive, that can be readily applied in the management of the patients. Low cost, ease of operation and maintenance, and portability have led to its wider availability even in resource-limited countries.

Few measurements in medicine have the kind of inherent variability and uncertainty in accuracy that characterises PFTs and few measurements are so dependent on factors related to equipment, operator and the patient. Proper maintenance of equipment, meticulous adherence to technique and strict quality control are mandatory to reduce errors and misleading information. The technical aspects of equipment and the procedure of the test have been well-standardised and revised from time-to-time.[2]

The final step in any investigation is to interpret the observations and provide the input to the clinician for the management decisions. The ultimate question is whether the observations indicate an abnormality. For most laboratory investigations, this is quite straightforward and involves a comparison with the range of values or the pattern or the picture known to be associated with a healthy state and any deviation is labelled as abnormal. However, pulmonary function parameters are unique as there is no constant or single "normal" value or range. These parameters vary among different populations globally by ethnic origins, by gender and other factors, and even in an individual with every year of age and changing anthropometric characteristics. Thus, every person will have a different "normal" value and that is not constant but ever-changing with time.[1] The normal value is calculated using "prediction" equations that take into account the known and the unknown predictors or determinants of the parameter of interest. These equations are developed by studying lung function of a large sample of carefully selected and well-defined "normal" subjects. Interpretation of measured parameters requires a comparison with "normal" or "predicted" values.

Prediction equations have been developed for different PFTs in several populations all over the world. Selection of prediction equations is a crucial step in the interpretative strategy. The PFT softwares usually offer a wide choice of prediction equations for different ethnicities and populations and the operator or the technician is required to exercise this choice even before the test is performed. Equipment software may not provide any equation for a patient's ethnicity and this has till recently been an unmet need in the Indian scenario. The software should preferably have an editing function that allows the users to add their own locally developed equations if these are not pre-loaded. In India, prediction equations have been developed from time to time in several populations, mainly for spirometry, though most of these are considered out-dated by current guidelines. Technicians as well as directors of pulmonary function laboratories are expected to select the right prediction equations and also be aware of the errors in interpretation that can occur if due care is not exercised in this step. However, audits of laboratory practices have shown that selection of prediction equations is often an ignored area and default choices are very often accepted.[3]

Lung function differs substantially among regions of the world. A recent study of 20,000 spirometry tests from 30 countries revealed that healthy African and Asian people have a mean forced vital capacity (FVC) that is 20% to 30% lower than for white people of the same height, age, and sex.[4] This explains why large differences exist among prediction equations. As results are expressed as "percent of predicted", there will be wide differences in results depending on the prediction equation selected. Clearly, interpretation would also vary widely rendering the test meaningless unless the "right" prediction equation is selected. Excessively high rates of falsely positive and falsely negative interpretations for airway obstruction and spirometric restriction will occur, especially with borderline or poor quality results. This may be misleading, resulting in management errors and has been documented in several studies.[5] Use of prediction equations from the European-American men consistently over-predicted FVC by 0.3 to 0.4L and forced expiratory volume in the first second (FEV_1) by 0.15L in Japanese in one study.[6] Aggarwal *et al*[7] showed that the use of previously used Caucasian equations resulted in mis-interpretation of spirometry data in a significant proportion of Indian patients. Nevertheless, it is common to see Caucasian prediction equations being used in PFT reports of Indian patients,

clearly a wrong practice borne out of ignorance. Chhabra and Madan[8] have recently shown that the US NHANES III (National Health and Nutrition Examination Survey III) and the recently developed Global Lung Function Initiative (GLI)-Caucasian equations, and to a lesser extent, the GLI-Mixed equations, predicted higher values and labelled more measurements as abnormal compared to the recently published prediction equations for north Indian population using the currently standardised protocols.[9] In up to one-thirds of the patients these differed from Indian equations in categorising ventilatory patterns with more patients classified as having restrictive and mixed disease.

A frequently used practice is to use adjustment factors with Caucasian equations. As Caucasians are known to have higher vital capacity than Indians by 15% to 20% or more, a typical correction factor would be 0.85 or 0.9, *i.e.* the predicted FVC by the Caucasians equations is multiplied by this factor to obtain the predicted FVC for Indians. Although this practice is popular, it is a flawed concept and an over-simplification, and can lead to substantial errors in interpretation. Hankinson *et al*[10] evaluating the performance of correction factors for applying NHANES III Caucasian equations to Asian-Americans have cautioned that a single correction factor may not be valid across all ages. Ip *et al*[11] have also demonstrated that the blanket application of correction factors for Asian populations may not be appropriate. The practice of using correction factors needs to be abandoned.

Therefore, selection of the right prediction equation cannot be over-emphasised and it is incumbent upon the technician and the laboratory directors to exercise due caution at this step to avoid misleading information and consequent management errors. It has been strongly recommended that due to the well-known differences in lung functions between subjects of different ethnic origins, equations developed in the population with the same ethnicity as the subject being tested must be selected.[1,2] The equations also need to be gender-specific. That means using Indian equations for Indian subjects. Collating published lung function data and using the LMS method, the Global Lung Function Initiative has developed equations for four defined ethnic groups globally, and for populations not included in these, the GLI-Mixed equation may be an option.[12] These are now the standard in Europe replacing the previously used European Community for Steel and Coal (ECSC) equations and are also being used increasingly in the US where the NHANES III equations agree very closely with GLI-Caucasians. This has for the first time made possible application of uniform equations for different ethnicities globally. However, data from Indian subcontinent has not been included in GLI, and therefore at present, there are no recommendations on the use of GLI equations for Indians. A recent study showed that the GLI equations are not appropriate for Indian population as these substantially over-diagnose abnormality and mis-classify ventilatory patterns on spirometry in Indian patients.[8] With the development of prediction equations for Indian population, both for adults[9] and children,[13] using the current standardisation protocols, an unmet need in the field of PFT has been resolved and it is now possible to select Indian equations for Indian population. These equations have now been made available by some manufacturers in their software and several other lung function softwares also have the provision for manual editing by the users. These equations also provide the standard errors of estimate, and therefore, it is possible to define the lower limits of normal more scientifically than using the erroneous method of a fixed percentage of predicted.

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