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Letter

Clinical Scoring Systems in Cystic Fibrosis – What Are the Options for Developing Countries?

Brenda May Morrow [1, *]

[1] Department of Pediatric Medicine, University of Cape Town, Cape Town, South Africa

*Corresponding author: Brenda May Morrow, Department of Pediatric Medicine, University of Cape Town, Cape Town, South Africa. Tel: +27216585074, Fax: +27216891287, E-mail: brenda.morrow@uct.ac.za.

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Dear Editor,

Cystic fibrosis (CF) is recognized as a serious, life-limiting autosomal recessive inherited condition, affecting multiple organs. Improvements in both diagnosis and management of CF has led to the recognition of a range of phenotypes, from mild to severe, with varying rates of disease progression. Pulmonary disease is still the main predictor of morbidity and mortality associated with CF (1). There are currently nearly 2000 recognized cystic fibrosis trans-membrane regulator (CFTR) mutations (2).

Over the past few decades, there has been a surge of developments in the management of people with cystic fibrosis, spurred on by many clinical trials. Along with improved management and longer life-span, comes the need to objectively monitor the disease progression and response to therapeutic interventions. Previously-valid outcome measures such as FEV1 (forced expiratory volume in one second) and mortality, are no longer considered useful in isolation, as the median age of death has increased well into adulthood; and FEV1 has improved in response to new therapies with a low rate of annual decline of between 1% and 5% in different settings (3-5).

Today, in technologically advanced countries, standard of care in monitoring disease progression and determining disease status has shifted away from clinical scores and basic spirometry to highly objective, repeatable and reliable measures of lung disease such as high resolution computed tomography (HRCT) scanning (6) and advanced pulmonary function measurement [with multiple-breath inert gas washout being more sensitive than spirometry, plain radiography or even plethysmography (7, 8)].

But what is reasonable in poorly-resourced countries? HRCT scan is the most sensitive technique to monitor structural changes in the lung (9). However, high costs and significant radiation exposure (especially for children) prevent CT from being useful in the routine monitoring of CF lung disease in most centers, especially in poorly resourced areas (10, 11). The majority of centers have access to basic pulmonary function measurement by spirometry, but this is only useful from the age of five or six when children can cooperate with the forced expiratory manoeuvre. In these cases, it might be appropriate to use a clinical scoring system which has been validated for use in children, and also ideally validated for use in the under-test population.

The first clinical scoring system described for CF was the Shwachman and Kulczycki (S-K) score (12), which combined clinical and radiographic findings for the first time (13). Since then, numerous scoring systems have been introduced or suggested, ranging from purely radiological, quality of life, pulmonary function, nutritional, and clinical (12, 13).

The use of any of these scoring systems should be determined on the basis of the question being asked. The system chosen will likely differ if one monitors individual disease progression; audits quality of care of a CF clinical service; compares severity of CF disease between sites; determines the need for or response to therapeutic interventions; for prediction of mortality or as an outcome measure of a clinical trial. Furthermore, costs (in terms of potential harm for the patient and financial costs to the hospital, patient, and state) and potential benefits need to be weighed up to determine the most cost-effective option for the context. The chosen clinical scoring system needs to reflect daily clinical practice and it needs to obtain objective clinical information in a standardized,

Implication for health policy/practice/research/medical education:
This manuscript is submitted by invitation as an editorial commentary for Khalilzadeh et al.; Shwachman Score in Clinical Evaluation of Cystic Fibrosis.

repeatable manner (13). In this journal, Khalilzadeh et al. (14) published a clinical evaluation of 23 CF patients admitted to a Pediatric Ward in an Iranian Hospital, using the S-K scoring system; including six patients who died.

It is unclear why the S-K scoring system was chosen, as this is generally considered to be obsolete, having been replaced in most centers by more reliable scoring systems (13). The reliability of the S-K test has not been determined and the validity is only partially determined. In addition, Kulczycki himself acknowledged the subjectivity of the S-K score; which has additional limitations in terms of overlapping of categories and no inclusion of pulmonary function parameters. It has also been found to be insensitive in mild disease (13). The modified S-K score presented by Doershuk et al. (15), and the NIH-score (16) are currently preferred options which have undergone limited validity and reliability studies in children, although Taussig et al. found both to be inadequate for regular clinical use and for use as endpoints of clinical trials (17). The Cystic Fibrosis Clinical Score (CFCS) may be useful for assessing current clinical status and need for hospitalization and may be helpful as a surrogate measure of assessing lung function in very young children (18).

We need to critically assess clinical scores in terms of what they were designed to measure. Until the 1970s, only about half of the children diagnosed with CF survived to eight years of age, even in well-resourced countries like the United Kingdom (13). Clearly, management and outcome, in terms of both longevity and quality of life, have changed substantially and new scores need to be developed to reflect these changes and different clinical settings.

The study by Khalilzadeh et al. (14) was further limited by the small sample size, the fact that the score seemed to be retrospectively applied, and the "snapshot" nature of the study (as opposed to longitudinal analysis of changes in the score over time). The fact that none of the children had "excellent" scores is not surprising given that the samples were selected from children who were admitted to hospital, and therefore likely had a more severe phenotype of CF. It would be interesting to determine S-K scores for all children being managed for CF in this community, and not only those requiring hospital admission. For future studies of this nature, it would also be helpful to have a clearer description of the included patients, such as genotype, pancreatic sufficiency, nutritional status, pulmonary function, bacterial lung colonization, and management (e.g. how many were receiving inhaled antibiotics, azithromycin, bronchodilators or steroids etc.). Without this information it is difficult to make meaningful comparisons between population groups and study sites.

Khalilzadeh et al.'s (14) concern about the effects of late diagnosis due to lack of neonatal screening is valid (19), and is a concern shared with other poorly resourced countries, and/or those of which screening may be considered impractical or inappropriate. We have previously reported the problem of late diagnosis and the potential impact of that on the outcome in a CF cohort from South Africa (5).

Perhaps we need to use all the information at hand to more accurately and holistically determine the disease state and progression. This would incorporate measures of structural lung pathology (radiography; HRCT where available), function (pulmonary function, using available measures, two minute walk test etc.), quality of life (choosing a validated instrument for the specific population), nutritional status (using standardized anthropometric measures), laboratory data [e.g. bacterial and viral culture, inflammatory markers (20)], and number of exacerbations and response to therapies over time. We could create a new score that covers all these areas of standard clinical assessment and is relevant to the local CF population, including those in poorly resourced countries. A richer assessment would allow more accurate detection of problems where they exist, and would enable targeted treatment and monitoring of the response thereto.

In developing and undeveloped nations, we may not have access to high-powered technologically advanced devices and laboratory techniques. We therefore need to pragmatically use all the tools at our disposal in order to effectively monitor and describe our progress in caring for all children with cystic fibrosis.

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