Original Article

Pulmonary function outcomes for assessing cystic fibrosis care

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Abstract

Background: Assessing cystic fibrosis (CF) patient quality of care requires the choice of an appropriate outcome measure. We looked systematically and in detail at pulmonary function outcomes that potentially reflect clinical practice patterns.
Methods: Epidemiologic Study of Cystic Fibrosis data were used to evaluate six potential outcome variables (2002 best FVC, FEV_1, and FEF_{25-75} and rate of decline for each from 2000 to 2002). We ranked CF care sites by outcome measure and then assessed any association with practice patterns and follow-up pulmonary function.
Results: Sites ranked in the top quartile had more frequent monitoring, treatment of exacerbations, and use of chronic therapies and oral corticosteroids. The follow-up rate of pulmonary function decline was not predicted by site ranking.
Conclusions: Different pulmonary function outcomes associate slightly differently with practice patterns, although annual FEV_1 is at least as good as any other measure. Current site ranking only moderately predicts future ranking.
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1. Introduction

Much has been written in recent years about improving quality of care for patients with cystic fibrosis (CF) [1–8]. Evidence points to improved patient outcomes associated with the development of quality improvement processes in CF care sites [9,10], and benchmarking efforts in both the United States and Germany have identified structural factors and care processes within care sites that are associated with improved patient outcomes [4,6]. Ideally one would like to know which therapies or practices result in better patient outcomes. Given the increasing

number of therapies for treating CF, comparative effectiveness studies looking at real world use of multiple different therapies are needed to counter the tendency to place every patient on every therapy proven beneficial by randomized controlled trials. However, benchmarking and comparative effectiveness studies are influenced by the choice of outcome. Different care sites may be identified as top performing, depending on whether one chooses survival as the outcome or chooses to focus on pulmonary, nutritional, or quality-of-life outcomes.

Since pulmonary function is most closely related to patient survival, we designed this study to look systematically at several baseline spirometric measures of pulmonary function that might be clinically useful and meaningful as indicators of respiratory outcomes in CF, and to see how closely these measures are associated with clinical practice patterns. Johnson

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et al. [11] reported on a study dividing care sites into quartiles based on the average forced expiratory volume in 1 s (FEV_1) percent predicted (%pred) and then compared care practices in upper and lower quartile sites. Although FEV_1 at a single time has been used historically as a surrogate for long-term pulmonary outcome and to assess mortality risk [12,13], other pulmonary function measures, such as forced vital capacity (FVC) and forced expiratory flow at mid-lung volume (FEF_{25-75}), might be more predictive depending on the severity of a patient's lung disease. Furthermore, rate of decline may be a more appropriate measure than a single value at one point in time [14,15].

We analyzed several approaches for determining site rankings. First we looked cross-sectionally at three pulmonary function measures: FVC, FEV_1, and FEF_{25-75}. Then we examined patient-specific rate of decline in lung function for each of these measures. Finally, to determine whether site ranking based on any of these pulmonary function measures is predictive of future pulmonary or nutritional outcomes, we compared patient-specific lung function rate of decline and weight for age or body mass index (BMI) rate of decline at upper and lower quartile sites for the 2 years following the initial site ranking. We also evaluated if there was any association between the site ranking and care patterns over this follow-up period.

2. Methods

We used data from the Epidemiologic Study of Cystic Fibrosis (ESCF), a multicenter, encounter-based observational study designed to characterize the natural history of patients with CF in North America [16], to develop site quartiles based on different measures of pulmonary function and to determine whether the use of specific CF therapies was associated with better site outcomes using an approach similar to that of Johnson et al. [11]. Informed consent was obtained according to the policies governing research at each participating institution.

We included data from 2000 to 2004 and divided patients into three groups based on their ages at the end of 2002 (6–12, 13–17, and 18+ years). To be included in the data for site rankings, each patient needed ≥ 1 spirometry in 2000, ≥ 1 in 2001, and ≥ 1 in 2002. Site quartiles were developed for each of six variables: best recorded value during 2002 for FVC, FEV_1, and FEF_{25-75}; and change from the best percent predicted value in 2000 to the best in 2002 (rate of decline) for FVC, FEV_1, and FEF_{25-75}. Annualized rates of decline took account of the dates of the best values and divided the difference in values by the time in years. Percent predicted values were calculated using reference equations from Wang et al. [17] through age 15 for girls and age 17 for boys and Hankinson et al. [18] for older patients.

Each site had to have participated in ESCF from 2000 to 2004 and had to have at least 10 eligible patients within an age group to receive a quartile assignment for that age group. Median values of each of the 6 measures for each of the 3 age groups were calculated for all eligible sites (up to 18 possible values per site). Sites were classified for each age group based on the median value for each measure.

After creating the site quartile variables (based on data from 2000 to 2002), we assessed the association between these quartile assignments and patient care patterns during 2002. Additionally we looked for any associations between these quartile assignments and follow-up care patterns and outcomes from 2002 to 2004. Patients were included in this analysis if they belonged to a site with at least one quartile assignment and had at least one visit and at least one spirometry in each year 2002, 2003, and 2004. Patient care patterns and outcome variables were analyzed within the three age groups.

Practice patterns evaluated for association with quartile ranking were healthcare use (4), use of chronic therapies (9), hospitalization and treatment of exacerbations (7), and nutritional status (2) (Tables 1, 2). We evaluated both 1-year values (2002) and 3-year values (2002 to 2004) for these practice patterns to assess associations with site pulmonary function quartiles. We also assessed the association between site ranking quartiles in 2002 and future pulmonary function outcomes from 2002 to 2004.

Patients from sites in the highest quartile were compared to patients from sites in the lowest quartile on these practice patterns and pulmonary function outcome measures. Comparisons were stratified by each patient's highest FEV_1 %pred in 2002 (<40, 40–69, 70–99, ≥ 100) so that patients with a similar stage of lung disease were compared regardless of their site's quartile. Patients, stratified by disease stage, at the highest and lowest quartile sites were compared using stratified Wilcoxon rank sum tests (for continuous outcome variables) and Mantel-Haenszel tests (for categorical outcome variables). No adjustment was made for multiple comparisons. Site rankings were compared using Spearman's rank correlation. All analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC).

3. Results

Data from 7729 patients were ranked by pulmonary function test outcomes in 2002, including 2033 age 6–12 years (85 sites), 2129 age 13–17 years (85 sites), and 3567 age 18 years or older (109 sites).

Associations between outcomes and practice patterns recorded in 2002 are shown in Table 1. The left column lists the processes considered, and the right columns represent the association with site quartiles ranked by average 2002 pulmonary function or by change in pulmonary function from 2002 to 2004. The right columns are divided by the spirometry value analyzed (FVC %pred, FEV_1 %pred, FEF_{25-75} %pred) and subdivided into age groups. Practice patterns associated with a positive site ranking (i.e. more likely to occur in upper quartile sites) are shown as either a single + ($p < 0.05$) or a double ++ ($p < 0.001$); those negatively associated with site ranking (less likely to occur in upper quartile sites) are shown as either a single − ($p < 0.05$) or a double − − ($p < 0.001$).

As an example, there are strong associations ($p < 0.001$) between site quartile as determined by the average FEF_{25-75} %pred in 2002 for the group age 6–12 years and the numbers of clinic visits, spirometries, and respiratory tract cultures and the likelihood of obtaining at least one respiratory tract culture during the year. If instead we use the change in FEF_{25-75} %pred from 2000 to 2002 as