

Original Article

Exercise improves lung function and habitual activity in children with cystic fibrosis

Shruti M. Paranjape^{a,*}, Laura A. Barnes^a, Kathryn A. Carson^b, Karen von Berg^c,
Holly Loosen^c, Peter J. Mogayzel Jr.^a

^a Eudowood Division of Pediatric Respiratory Sciences, Department of Pediatrics, Johns Hopkins University, 200 North Wolfe Street, Baltimore, MD, 21287

^b Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, 2024 East Monument Street, Suite 2–500, Baltimore, MD, 21287

^c Department of Physical Medicine and Rehabilitation, Johns Hopkins Medical Institutions, 600 North Wolfe Street, Baltimore, MD 21287

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Abstract

Background: Cystic fibrosis (CF) lung disease leads to progressive deterioration in exercise capacity. Because physical activity has been shown to improve lung function and quality of life (QoL), developing routine exercise programs can benefit this patient population.

Methods: Lung function, nutritional status, and exercise capacity and assessments of habitual activity and QoL were measured before and after a two-month, subject-designed exercise regimen based on self-reported activity assessment. Statistical analysis included Wilcoxon signed-rank, Wilcoxon rank sum, and Fisher's exact tests.

Results: Subjects completing the study demonstrated significant improvement in exercise capacity and body image perception, a CF-specific QoL measure ($p < 0.001$). In secondary analyses, subjects improving exercise capacity showed significant increases in lung function and self-reported habitual activity.

Conclusions: Increases in exercise capacity over a two-month period resulted in significantly improved lung function and self-reported habitual activity. Longer, controlled trials are needed to develop individualized exercise recommendations.

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Keywords: Exercise; Lung function; Quality of life; Habitual activity; Cystic fibrosis

1. Introduction

Cystic fibrosis (CF) lung disease leads to progressive deterioration in lung function and exercise capacity. Recent studies have demonstrated the benefits of exercise for CF patients [1,2] and include: slowing lung function decline [3] and enhancing airway clearance [4,5]. More importantly, higher exercise capacity has been associated with improved survival [6]. The additional benefits of exercise for CF patients do not differ from those for healthy individuals and include improved conditioning and endurance, bone density, muscle strength,

posture and quality of life [7]. Moreover, exercise as a therapeutic tool is underutilized [8]. There are many barriers to exercise and physical activity in CF patients, including low lung function, malnutrition, and cardiorespiratory deconditioning, as well as emotional barriers relating to the burden of care in chronic disease [9,10].

In light of these barriers and the demonstrated benefit of exercise for CF patients, efforts are being made to incorporate exercise into routine care. While both hospital-based conditioning programs and home-based programs have been shown to be beneficial [11], the latter may present more opportunities to

Abbreviations: BMI, body mass index; CF, cystic fibrosis; FEV₁, forced expiratory volume in 1 second; HAES, habitual activity estimation scale; MSWT, modified shuttle walk test; QoL, quality of life.

* Corresponding author at: Eudowood Division of Pediatric Respiratory Sciences, 200 North Wolfe Street, David M. Rubenstein Child Health Building, Johns Hopkins University, Baltimore, MD 21287. Tel.: +1 410 955 2795; fax: +1 410 955 1030.

E-mail address: sparanj1@jhmi.edu (S.M. Paranjape).

individualize the regimen and involve the patient, family, and other caregivers. Furthermore, to maximize the long-term benefits, any exercise program must be sustainable with a primary goal to modify behaviors toward achieving a more active lifestyle. Home-based programs have been shown to offer long-lasting benefits for physical fitness, activity and lung function in CF patients more than a year after the completion of the intervention [12]. The purpose of this study was to determine if specific, subject-driven exercise recommendations can improve selected outcomes in CF patients with the hypothesis that increasing activity in CF patients with a two-month exercise regimen leads to improved exercise capacity, lung function, nutritional status, and quality of life.

2. Patients and methods

2.1. Subjects

For this study approved by the Johns Hopkins University Institutional Review Board, pediatric subjects with CF were recruited at routine clinic visits after obtaining written informed assent and consent from the patients and their parents or guardians. Inclusion criteria were a confirmed diagnosis of CF, an age of 6–16y, no concurrent IV antibiotic treatment and the ability to perform exercise. Subjects were excluded if spirometry demonstrated more than 10% decline in lung function (measured by percent predicted FEV₁) compared to the previous clinic visit or required treatment with oral or intravenous antibiotics for a pulmonary exacerbation. Seventy-eight subjects consented to participate in the study; however, two did not perform the Modified Shuttle Walk Test (MSWT) [13,14] at the first study visit, six subjects withdrew voluntarily because they did not keep up with the recommended exercise regimen and five subjects did not complete the second study visit within the allotted follow-up window. Of the sixty-five subjects who completed both study visits, data from six of these subjects were not used because of illness or minor unrelated injury at the time of the second study visit.

2.2. Study design

Exercise capacity was assessed before and after a two-month, at-home exercise regimen. The study consisted of two clinical visits. At the first study visit, exercise capacity was assessed using a field test and two surveys were conducted to evaluate habitual activity and quality of life. Routine spirometric and anthropometric data were obtained. Based on an assessment of self-reported activity, the two-month exercise regimen consisted of activities chosen by the subject and was designed in conjunction with the clinic physical therapist. Participants were encouraged but not required to keep an exercise log. After one month, adherence to the exercise regimen and habitual activity was assessed by telephone. After two months, at the second study visit, subjects repeated the exercise capacity field test and the habitual activity and quality of life surveys with assessment of adherence.

2.3. Exercise capacity assessment

Exercise capacity was assessed using the MSWT [14]. The MSWT is a validated field test of exercise capacity in pediatric CF patients in which the participant walks 10 m lengths at progressively increasing paces [13]. The number of completed shuttles was recorded and used to express exercise capacity.

2.4. Habitual activity

Each subject's self-reported activity was assessed using the Habitual Activity Estimation Scale (HAES), which has been determined to be a valid and reliable instrument in the pediatric and adult CF patient populations [15,16]. For this study, habitual activity was expressed as the percentage of time when the study subject was awake and engaged in moderate-vigorous activity and recorded for a typical weekday and weekend.

2.5. Quality of life

The Revised CF Quality of Life Questionnaire (CFQ-R) was administered to assess the subject's quality of life. The CFQ-R is a validated instrument for CF patients that scores quality of life in twelve general and CF-specific domains [17–19]. This study focused on five exercise-related domains: physical functioning, emotional functioning, social functioning, body image perception, and respiratory wellness. Scores for each domain were expressed on a scale of 0–100.

2.6. Exercise intervention

At visit 1, the physical therapist recommended an individualized, two-month, at home exercise regimen consisting of regular, developmentally appropriate, and where applicable, family-oriented physical activities. The regimen consisted of 20–30 minutes of moderate to vigorous activity at least five times a week. The duration and intensity of the activity was based on the patient's self-reported activity on the HAES. For example, subjects who rated themselves overall as "inactive" were given 20 minutes of moderate activity, while those who reported themselves as "very active" were given 30 minutes of vigorous activity. The types of activity were chosen by the study subject in consultation with the physical therapist and included a wide variety of sports, play, and physical extracurricular activities. Emphasis was made to make the activities continuous for the recommended duration. Subjects left the study visit with a written copy of the exercise recommendation.

2.7. Statistical considerations

Demographic and clinical characteristics were summarized using medians and ranges or frequencies and percentages. Change from baseline at the two-month follow-up was calculated for the clinical characteristics and quality of life measures, and Wilcoxon signed-rank tests were used to test for significant improvement. Subgroup analyses comparing boys to girls and comparing those that improved by at least 10 shuttles

on the MSWT to those that did not were performed using Wilcoxon rank sum tests for continuous measures and Fisher's exact tests for categorical measures. Analysis was performed using SAS version 9.2 (SAS Institute, Inc., Cary, NC). All reported *P* values are two-sided, and significance was set at $p < 0.05$.

3. Results

3.1. Demographics

Baseline demographic and clinical characteristics of the 78 subjects are presented in Table 1. Overall, subjects showed normal lung function (median FEV₁ 99% predicted) and optimal nutritional status (median BMI percentile-for-age 56). The subject sample included patients with severe lung disease and growth failure. Self-reported activity was significantly higher on typical weekends than on weekdays (median 63.2% vs. 55.7%; $p = 0.004$). Median baseline scores for five exercise-related QoL measures ranged from 71.4–90.3.

3.2. Effects of a two-month exercise regimen

Baseline and two-month follow up data for the 59 subjects who completed the study are summarized in Table 2. Exercise capacity measured by the MSWT increased from 100 to 105 shuttles ($p < 0.001$). At the two-month follow up visit, changes in nutritional status, measured by BMI percentile, and lung function, measured by percent predicted FEV₁, were not statistically significant. Self reported activity, using the HAES, demonstrated that weekend habitual activity increased but was not statistically significant. Of the five exercise-related QoL measures assessed using the CFQ-R, physical functioning did not change over the two-month period, while body image perception, a CF-specific measure, showed a significant increase from baseline ($p < 0.001$). Emotional functioning, social functioning, and respiratory wellness showed increases that were not statistically significant over the two-month period.

Table 1
Baseline demographic and clinical characteristics of the 78 patients^a enrolled in the study.

| Characteristic | No. of Patients (%) | Median (range) |
|--------------------------------|---------------------|-------------------|
| Gender, female | 33 (42) | |
| Age, in years | | 10 (6 – 16) |
| BMI, % for age | | 56 (2 – 96) |
| FEV ₁ , % predicted | | 99 (32 – 132) |
| HAES | | |
| Weekday activity | | 55.7 (6.0 – 93.7) |
| Weekend activity | | 63.2 (0.0 – 95.8) |
| Number of shuttles | | 100 (20 – 150) |
| CFQ-R scores | | |
| Physical | | 90.3 (27.8 – 100) |
| Emotional | | 79.7 (20.8 – 100) |
| Social | | 71.4 (33.3 – 100) |
| Body image | | 88.9 (0 – 100) |
| Respiratory | | 83.3 (33.3 – 100) |

^a Two patients did not complete the baseline visit and only contribute gender and age data, and one patient was unable to perform pulmonary function tests.

Table 2

Medians (ranges) of clinical and quality of life measures at baseline and follow-up for the 59 subjects that completed the study.

| Characteristic | Baseline | 2-Month Follow-up | P value ^a |
|---|-------------------|--------------------|----------------------|
| BMI, % for age | 59 (2–96) | 56 (2 – 93) | 0.43 |
| FEV ₁ , % predicted ^b | 100 (52–132) | 104 (41 – 130) | 0.50 |
| HAES | | | |
| Weekday activity | 56.7 (6.0 – 93.7) | 50.1 (14.8 – 89.8) | 0.40 |
| Weekend activity ^c | 63.0 (4.4 – 92.3) | 67.3 (12.2 – 97.8) | 0.17 |
| Number of shuttles | 100 (21 – 150) | 105 (44 – 150) | <0.001 |
| CFQ-R scores | | | |
| Physical | 94.4 (27.8 – 100) | 94.4 (44.4 – 100) | 0.11 |
| Emotional | 75.0 (20.8 – 100) | 79.2 (33.3 – 100) | 0.06 |
| Social | 71.4 (33.3 – 100) | 72.2 (28.6 – 100) | 0.53 |
| Body image | 88.9 (11.1 – 100) | 100 (0 – 100) | <0.001 |
| Respiratory | 83.3 (33.3 – 100) | 91.7 (25 – 100) | 0.10 |

^a P value from Wilcoxon signed-rank test.

^b One subject did not have FEV₁ data.

^c Two subjects did not have HAES weekend activity data at follow-up.

Thirteen subjects did not complete the study; of these, 77% were girls compared to 35% of those who did complete the study ($p = 0.01$). At baseline, self-reported activity was higher and physical functioning and respiratory wellness scores by QoL assessment were lower in the non-completers compared to the completers, but these differences were not statistically significant. The non-completers had comparable nutritional status, lung function and exercise capacity to the completers.

3.3. Relationship of exercise capacity to lung function and habitual activity

To assess the utility of the MSWT as an instrument to measure exercise capacity in the clinical setting and define clinically relevant changes, the change from baseline in clinical and QoL measures was analyzed with respect to improvement in exercise capacity measured by the number of completed MSWT shuttles (Table 3). In this secondary analysis, patients were stratified by an improvement of at least 10 shuttles on the MSWT, which corresponds to a distance walked of 100 m. Because the MSWT has a defined maximum of 150 shuttles, three subjects who had completed at least 140 shuttles during the initial visit were excluded from this analysis. Of the 56 subjects included, 30 improved by at least 10 shuttles (median increase of 16 shuttles) and 26 did not improve by at least 10 shuttles (median change of –1 shuttle). Both FEV₁ and the number of shuttles performed at baseline were comparable for the group that improved by at least 10 shuttles and those that did not (median: FEV₁ at baseline: 99 vs. 102; $p = 0.16$, shuttles at baseline: 97 vs. 100; $p = 0.63$, respectively). Fifty percent of the subjects whose exercise capacity did not improve by at least 10 shuttles were girls, compared to twenty percent of subjects whose exercise capacity improved by at least 10 shuttles ($p = 0.02$). Subjects that improved exercise capacity showed significant increases compared to subjects that did not in median percent predicted FEV₁ (6% vs. –3%, $p = 0.03$) as well as in self-reported weekend activity (5.9% vs. –1.4%, $p = 0.03$). Between the two groups, there was no difference in change in BMI percentile for age and differences in changes from

Table 3

Demographic characteristics and change from baseline in clinical and quality of life measures by improvement in number of shuttles for completers that did < 140 shuttles at baseline. Medians (ranges) are presented unless otherwise stated.

| Characteristic | Change in Shuttles | | P value ^a |
|--------------------------------|----------------------------------|---------------------------------|----------------------|
| | < 10 | ≥ 10 | |
| No. of patients | 26 | 30 | |
| Female gender, N (%) | 13 (50) | 6 (20) | 0.02 |
| Age, years | 10 (6 – 15) | 10.5 (6 – 16) | 0.20 |
| BMI, % for age | 1.5 (–13 – 21) | 1.5 (–28 – 12) | 0.61 |
| FEV ₁ , % predicted | –3 (–18 – 10) ^b | 6 (–16 – 37) | 0.03 |
| HAES | | | |
| Weekday activity | –7.0 (–62.5 – 26.3) | 1.4 (–38.3 – 36.5) | 0.08 |
| Weekend activity | –1.4 (–56.6 – 30.1) ^c | 5.9 (–17.3 – 61.5) ^c | 0.03 |
| Number of shuttles | –1 (–21 – 8) | 16 (11 – 42) | |
| CFQ-R scores | | | |
| Physical | 0.0 (–38.9 – 55.6) | 0.0 (–38.9 – 27.8) | 0.91 |
| Emotional | 4.2 (–26.7 – 33.3) | 0.0 (–13.3 – 20.8) | 0.51 |
| Social | 0.0 (–33.3 – 28.6) | –4.8 (–16.7 – 28.6) | 0.30 |
| Body image | 0.0 (–55.6 – 55.6) | 11.1 (–44.5 – 66.7) | 0.56 |
| Respiratory | 0.0 (–16.7 – 41.7) | 0.0 (–50.0 – 50.0) | 0.75 |

^a P value from Wilcoxon rank sum test or Fisher's exact test (gender).

^b One patient in this group did not have FEV₁ data.

^c One patient in this group did not have HAES weekend activity data.

baseline in the five exercise-related QoL measures were not statistically significant.

3.4. Comparison by gender in changes from baseline of clinical and QoL measures

Of the 59 subjects who completed the study, 40 were boys and 19 were girls (Table 4). Boys showed a marginal improvement from baseline in exercise capacity compared to girls (11 vs. 5;

Table 4

Demographic characteristics and change from baseline in clinical and quality of life measures by gender for completers. Medians (ranges) are presented unless otherwise stated.

| Characteristic | Gender | | P value ^a |
|--------------------------------|---------------------------------|---------------------------------|----------------------|
| | Boys | Girls | |
| No. of patients | 40 | 19 | |
| Age, years | 10 (6 – 16) | 11 (6 – 15) | 0.51 |
| BMI, % for age | –1 (–28 – 16) | 2 (–14 – 21) | 0.61 |
| FEV ₁ , % predicted | 3 (–18 – 37) ^b | –2 (–11 – 21) | 0.16 |
| HAES | | | |
| Weekday activity | –1.0 (–62.5 – 36.5) | –1.3 (–39.6 – 29.5) | 0.94 |
| Weekend activity | 0.9 (–56.6 – 61.5) ^c | 3.2 (–46.1 – 41.8) ^c | 0.79 |
| Number of shuttles | 11 (–21 – 42) | 5 (–21 – 21) | 0.06 |
| CFQ-R scores | | | |
| Physical | 5.6 (–38.9 – 55.6) | –5.6 (–27.8 – 11.1) | <0.001 |
| Emotional | 0.0 (–13.3 – 20.8) | 0.0 (–26.7 – 33.3) | 0.51 |
| Social | –0.0 (–28.6 – 28.6) | 0.0 (–33.3 – 28.6) | 0.71 |
| Body image | 11.1 (–55.6 – 66.7) | 0.0 (–0.0 – 44.4) | 1.0 |
| Respiratory | 0.0 (–50.0 – 50.0) | 0.0 (–38.9 – 33.3) | 0.64 |

^a P value from Wilcoxon rank sum test.

^b One patient in this group did not have FEV₁ data.

^c One patient in this group did not have HAES weekend activity data.

$p=0.06$). Differences in the changes from baseline in nutritional status, lung function, and habitual activity were not statistically significant between boys and girls. With respect to exercise-related QoL measures, boys showed a positive change from baseline in physical functioning that was highly significant (+5.6 vs. –5.6; $p<0.001$). The median changes from baseline in the other QoL measures for girls were unchanged.

4. Discussion

The results of this study demonstrated that a patient-driven outpatient exercise program significantly improves exercise capacity in children with CF and indicate that exercise can and should be incorporated into a care regimen geared toward improving respiratory and general physical health. An exercise regimen can improve certain exercise-relevant quality of life measures as well as increase exercise capacity, which is beneficial, based on the results of this study, in the short term. Moreover, the use of three validated instruments, the HAES, CFQ-R, and MSWT, illustrates their applicability for both exercise assessment and prescription in a practical clinical setting.

Exercise testing and training have long been recognized as important aspects of CF care that are underutilized and warrant further study, preferably using randomized, controlled clinical trials [11], with respect to specific recommendations toward the development of practical and effective exercise training programs in the CF population [20]. Both formal and field tests of exercise are primarily limited by costs, equipment, space, and time [21]. Exercise training and habitual physical activity have been shown to be effective in children with CF and to slow the rate of decline of FEV₁, particularly in girls [10,16]. In a randomized controlled trial analyzing the long-term effects of a partially supervised conditioning program in children and adults with CF, the investigators concluded that a 6 month home based partially supervised and individualized program led to long-lasting beneficial effects on physical fitness, activity, and lung function over a 1–2 year period, indicating that such programs can result in changing behaviors toward physical activity [12].

Certain CF-specific risks [20,22] associated with exercise require careful consideration by patients, families, and care providers, specifically with respect to design of a therapeutic exercise program. These can include the potential risks of prolonged exercise, such as dehydration, excessive salt loss, bronchoconstriction, and hypoxemia. Other concerns include the possibility of hypoglycemia in a patient with CF-related diabetes or impaired glucose tolerance, or spontaneous fractures in patients who may have unrecognized or untreated bone disease or exhibit excessive cough during physical activity. Additional exercise-related risks include pneumothorax, cardiac arrhythmias, hemoptysis, and variceal bleeding [20]. Specific precautions to avoid contact sports should be taken in patients who have known portal hypertension and hepatosplenomegaly. It should be mentioned that while the risk of serious adverse reactions to exercise have not been systematically studied, the incidence of exercise-related serious adverse reactions appears

to be low with respect to exercise testing, inpatient exercise therapy, and independent exercise in the CF population [22].

Education of the CF care team regarding the advantages and potential risks of exercise is vital to the success of designing exercise programs for CF patients [10]. Consideration of potential physical and psychosocial barriers to exercise in conjunction with those related to the burden of chronic disease can facilitate the implementation of exercise into the therapeutic regimen toward improving compliance with habitual physical activity as well as other components of the care regimen. Moreover, using this information can enable CF care teams to utilize exercise testing in a practical setting to further assess lung function and overall physical health.

The major advantage of this study was the use of validated instruments to assess exercise capacity and habitual activity toward the design of an individualized exercise regimen and track progress, particularly in exercise capacity and lung function, over a two-month period. Given the strong correlation between distance walked and peak oxygen consumption [23], the MSWT is a valid measure of peak exercise performance that can be used in a clinical setting. In our study, girls reported lower habitual activity and had poorer lung function than boys, which supports the conclusion of previously published studies [16]. Another striking and concerning finding was 68% of girls completing the study did not improve exercise capacity over a 2-month period. It is unclear if this lack of improvement was related to disease severity or other factors, such as choice of activity or extent of participation in activities and adherence to the recommended exercise regimen. Based on these results, girls may benefit from implementing routine exercise programs as part of an overall regimen to maintain general health. The collaborative aspects of this study utilized the expertise in physical therapy and engaged the subject to design an exercise program based on self-reported habitual physical activity. In particular, choosing enjoyable activities and emphasizing family participation may have promoted the incorporation of activity into the daily life of the patient. The use of developmentally appropriate, family-friendly, and enjoyable activities chosen by the patient rather than concrete exercise plans prescribed by the CF care team promotes both patient adherence and the long-term incorporation of exercise into the lifestyle of the patient.

Study limitations include: small sample size, which limited the power to detect significant results; the lack of a control group to fully assess the effect of the intervention; selection bias with respect to enrollment of healthy patients with normal lung function and nutritional status; decreased capability to account for overreporting on the HAES by the subject's parent due to time constraints in the outpatient clinic; and adherence to the prescribed exercise regimen. Some subjects reported limitations of activity based on season, time of year, intercurrent illnesses or minor unrelated injuries at the second study visit. Other subjects did not complete the study because of the timing of the second study visit, which was to take place earlier than the routine clinic visit, and posed a scheduling conflict for families with other constraints such as insurance authorizations for routine clinic visits. The MSWT has been validated for pediatric CF patients [13,23–25]. Nevertheless, the study results may

have been influenced either by a training effect, in which subjects may have improved exercise capacity because they learned to perform the test [14], or a ceiling effect, in which subjects would not have shown an improvement in exercise capacity above the test-defined maximum of 150 completed shuttles. From the clinician's perspective, other limitations include the ability to encourage patients to maintain increased activity levels over time in order to demonstrate whether the exercise program had a sustained effect and determine how much of an increase in activity is needed to achieve a beneficial response.

Despite these limitations, this study has demonstrated the potential of the MSWT and HAES as objective clinical measures of exercise tolerance and habitual activity, as well as the advantage of an at-home exercise regimen to improve clinical outcomes. Additionally, we found that testing and development of an exercise plan could be carried out during routine clinic encounters. This study utilized three validated instruments, the CFQ-R, HAES, and MSWT, to clinically assess exercise capacity and use the data to design individualized exercise programs for children with CF and track their clinical progress. The results of this study showed that regular exercise over a two-month period improved exercise capacity and certain QoL measures, and that improvements in exercise capacity improved lung function and habitual activity.

5. Conclusion

We conclude that a two-month, at-home exercise regimen is beneficial for pediatric CF patients. The MSWT and the HAES questionnaire have practical applications in the outpatient setting for measuring exercise tolerance and habitual activity that are well tolerated by the patients and easily implemented. Future studies will include a longer follow-up period in order to assess the sustainability of the exercise regimen and long-term benefits and applications to help patients adopt a healthy lifestyle. In addition, a longer controlled trial is needed to determine if incorporating these tools into clinical practice to standardize exercise assessment and prescribing an individualized exercise regimen as an adjunct to conventional therapies can lead to improved lung function and quality of life.

Contributor's statement page

All authors attest to the following roles in the preparation of this manuscript:

- 1) Substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data – Paranjape, Barnes, Carson, von Berg, Loosen, Mogayzel
- 2) Drafting the article or revising it critically for important intellectual content – Paranjape, Barnes, Mogayzel, Carson, von Berg, Loosen
- 3) Final approval of the version to be published – Paranjape, Barnes, Carson, von Berg, Loosen, Mogayzel.

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References

- [1] Orenstein DM, Higgins LW. Update on the role of exercise in cystic fibrosis. *Curr Opin Pulm Med* Nov. 2005;11(6):519–23.
- [2] Smidt N, de Vet HC, Bouter LM, et al. Effectiveness of exercise therapy: a best-evidence summary of systematic reviews. *Aust J Physiother* 2005;51(2):71–85.
- [3] Schneiderman-Walker J, Pollock SL, Corey M, et al. A randomized controlled trial of a 3-year home exercise program in cystic fibrosis. *J Pediatr* March 2000;136(3):304–10.
- [4] Zach MS, Oberwaldner B. Chest physiotherapy—the mechanical approach to antiinfective therapy in cystic fibrosis. *Infection* 1987;15(5):381–4.
- [5] Zach MS, Purrer B, Oberwaldner B. Effect of swimming on forced expiration and sputum clearance in cystic fibrosis. *Lancet* Nov. 28 1981;2(8257):1201–3.
- [6] Nixon PA, Orenstein DM, Kelsey SF, Doershuk CF. The prognostic value of exercise testing in patients with cystic fibrosis. *N Engl J Med* Dec. 17 1992;327(25):1785–8.
- [7] Sawyer MG, Reynolds KE, Couper JJ, et al. Health-related quality of life of children and adolescents with chronic illness—a two year prospective study. *Qual Life Res* Sept. 2004;13(7):1309–19.
- [8] Barker M, Hebestreit A, Gruber W, Hebestreit H. Exercise testing and training in German CF centers. *Pediatr Pulmonol* April 2004;37(4):351–5.
- [9] Boucher GP, Lands LC, Hay JA, Hornby L. Activity levels and the relationship to lung function and nutritional status in children with cystic fibrosis. *Am J Phys Med Rehabil* Jul-Aug. 1997;76(4):311–5.
- [10] Wilkes DL, Schneiderman JE, Nguyen T, et al. Exercise and physical activity in children with cystic fibrosis. *Paediatr Respir Rev* Sept. 2009;10(3):105–9.
- [11] van Doorn N. Exercise programs for children with cystic fibrosis: A systematic review of randomized controlled trials. *Disabil Rehabil* June 2009;26:1–9.
- [12] Hebestreit H, Kieser S, Junge S, et al. Long-term effects of a partially supervised conditioning programme in cystic fibrosis. *Eur Respir J* March 2010;35(3):578–83.
- [13] Coelho CC, Aquino Eda S, de Almeida DC, et al. Comparative analysis and reproducibility of the modified shuttle walk test in normal children and in children with cystic fibrosis. *J Bras Pneumol* April 2007;33(2):168–74.
- [14] Singh SJ, Morgan MD, Scott S, Walters D, Hardman AE. Development of a shuttle walking test of disability in patients with chronic airways obstruction. *Thorax* Dec. 1992;47(12):1019–24.
- [15] Wells GD, Wilkes DL, Schneiderman-Walker J, et al. Reliability and validity of the habitual activity estimation scale (HAES) in patients with cystic fibrosis. *Pediatr Pulmonol* April 2008;43(4):345–53.
- [16] Schneiderman-Walker J, Wilkes DL, Strug L, et al. Sex differences in habitual physical activity and lung function decline in children with cystic fibrosis. *J Pediatr* Sept. 2005;147(3):321–6.
- [17] Quittner AL. Measurement of quality of life in cystic fibrosis. *Curr Opin Pulm Med* Nov. 1998;4(6):326–31.
- [18] Quittner AL, Buu A, Messer MA, Modi AC, Watrous M. Development and validation of The Cystic Fibrosis Questionnaire in the United States: a health-related quality-of-life measure for cystic fibrosis. *Chest* Oct. 2005;128(4):2347–54.
- [19] Quittner AL, Sweeny S, Watrous M, et al. Translation and linguistic validation of a disease-specific quality of life measure for cystic fibrosis. *J Pediatr Psychol* Sept. 2000;25(6):403–14.
- [20] Williams CA, Benden C, Stevens D, Radtke T. Exercise training in children and adolescents with cystic fibrosis: theory into practice. *Int J Pediatr* 2010;2010:1–7, doi:10.1155/2010/670640.
- [21] Radtke T, Stevens D, Benden C, Williams CA. Clinical exercise testing in children and adolescents with cystic fibrosis. *Pediatr Phys Ther* Fall 2009;21(3):275–81.
- [22] Ruf K, Winkler B, Hebestreit A, Gruber W, Hebestreit H. Risks associated with exercise testing and sports participation in cystic fibrosis. *J Cyst Fibros* Sept. 2010;9(5):339–45.
- [23] Bradley J, Howard J, Wallace E, Elborn S. Validity of a modified shuttle test in adult cystic fibrosis. *Thorax* May 1999;54(5):437–9.
- [24] Cox NS, Follett J, McKay KO. Modified shuttle test performance in hospitalized children and adolescents with cystic fibrosis. *J Cyst Fibros* Aug. 2006;5(3):165–70.
- [25] Brown CD, Wise RA. Field tests of exercise in COPD: the six-minute walk test and the shuttle walk test. *COPD* Sept. 2007;4(3):217–23.