Quality Improvement Project to Implement a Systematic Assessment of Gross Motor Skills in School-Aged Children with Cystic Fibrosis

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Abstract

Introduction: Limited data exist on the gross motor abilities of children with cystic fibrosis (CF). The objective of this quality improvement project was to implement a systematic gross motor assessment in children with CF ages 4-12 years. Methods: Physical therapists aimed to evaluate at least 50% of eligible children at our CF Center over 1 year using the Bruininks-Oseretsky Test of motor Proficiency, second edition (BOT-2), a norm referenced assessment for gross motor skills, with delays defined by scores less than 18 th percentile. Demographic and clinical data including body mass index, hospitalizations, genotype, and comorbidities were collected. Basic descriptive statistics summarized patient information. Parametric and non-parametric methods compared groups of interest. Linear regression assessed associations between BOT-2 measures and clinical characteristics. Results: Of the 105 eligible children, 72 (69%) completed the BOT-2 over 1 year. Forty-five (62.5%) scored below average in at least one category. Impaired strength (22.2%) was most common, followed by impaired balance (16.7%), running speed and agility (15.3%), and bilateral coordination (8.3%). Eleven (15.5%) scored below average on their total motor composite score (TMC). Increased age, comorbidities and hospitalizations were associated with a lower TMC. Conclusions: The BOT-2 was successfully implemented as part of routine CF care to screen for gross motor delays. Results suggest that a high percentage of children with CF, especially older children with comorbid conditions or a history of hospitalization, have impaired gross motor function. These findings support the need for routine gross motor evaluations and physical therapy interventions within pediatric CF clinics.

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Conclusions: The BOT-2 was successfully implemented as part of routine CF care to screen for gross motor delays. Results suggest that a high percentage of children with CF, especially older children with comorbid conditions or a history of hospitalization, have impaired gross motor function. These findings support the need for routine gross motor evaluations and physical therapy interventions within pediatric CF clinics.

Introduction:

Little data exists on the gross motor abilities of school aged children with cystic fibrosis (CF)(1). Persons with CF (pwCF) are less likely to participate in vigorous physical activity (2-4). It is unclear if this is due to CF related delays in gross motor skills, fear-avoidance, time constraints, nutritional status, or peripheral skeletal muscle weakness(5). The exercise recommendations for pwCF are to participate in 60 minutes of exercise daily. Since physical activity positively affects lung function in pwCF(3, 6), evaluation for gross motor impairments and delays influencing ability to participate is indicated. Historically, physical therapy (PT) evaluations in CF clinics have not included standardized gross motor assessments, and instead have focused on exercise evaluations in older children(7). Gross motor skills are the foundational skills for a child to participate successfully in recreation, school, peer and family activities, and are a precursor for exercise participation and tolerance.

The Bruininks-Oseretsky Test of Motor Proficiency, second edition (BOT-2) is a pediatric assessment tool that assesses gross and fine motor skills including coordination, balance, strength, running speed and agility(8, 9). It is norm referenced and has excellent validity and test-retest reliability (8-10). For this quality improvement project, we aimed to implement a process to perform gross motor testing in >50% of our eligible CF population over 1 year using the BOT-2. Secondary objectives were to describe gross motor findings and examine demographic and clinical factors that may be associated with impaired gross motor function in children with CF.

Methods:

A variety of outcome measures were considered in the development of this quality improvement project. The tests that were considered included the Peabody (PDMS), Test of Gross Motor Development (TGMD), Movement Assessment Battery for kids (MABC) and BOT-2 (see **Table 3**)(11). Ultimately, the BOT-2 was selected for the following reasons: 1) The BOT-2 is norm referenced, valid and reliable (8), 2) the age range of the test met the goal to assess comprehensive motor skills in school aged children and 3) the information that the BOT-2 provides is specific and relevant to the skills that are necessary for participation in school, recreational and peer activities. The BOT-2 also includes specific strength and balance sections, which are skill areas that may be impacted in children with CF due to gene expression in skeletal muscle, or side effects of medications on the vestibular system.

Once BOT-2 was selected as the screening tool, children between 4 and 12 years of age with a diagnosis of CF based on a sweat chloride [?]60mEq/L and/or the presence of two known disease-causing variants in the CF gene were eligible to participate in this quality improvement project. An algorithm was developed to guide timing of the BOT-2 assessment in CF clinic and follow up recommendations (**Figure 1**). Eligible children were identified in pre-clinic rounds. In an effort to identify a clinic visit where the number of additional assessments (i.e., labs, imaging) were not needed, we targeted the half birthday visit for the BOT-2 evaluation. To increase the number of BOT-2 assessments over the year, the BOT-2 assessment was performed at the end of a hospitalization in a small subset, with historically infrequent outpatient clinic visits, when acute symptoms of a pulmonary exacerbation were improved. Parents were educated on the purpose of the assessment and observations of their child's performance and follow-up PT recommendations were made based on the results.

The BOT-2 requires a testing kit and scoring booklet, which costs $685(11). The equipment that is needed for the gross motor sections are a BOT-2 balance beam, a line on the floor, a tape measure, two cones, a scoring sheet, and a scoring booklet. An exercise mat can also be used for some of the strength tests but is not required. Testing was performed by two trained, board-certified PTs (only 1 PT required to do each test), and typically took 25-30 minutes to complete the 26 gross motor tasks to compile a full gross motor BOT-2 score. Children can perform the test in a clinic room or gym space, but testing does require a 50 foot shuttle run course. PTs found it helpful to partner with other CF care team members during clinic when BOT-2 testing was performed. With child and parent permission, PT would take a child to the gym to complete testing while other care team members (i.e., social worker, psychologist or dietitian) met with the child's parents. Separating children and parents was not a barrier to completing testing, as children generally expressed excitement about participating in BOT-2 testing during their clinic visit.

Data collected during the BOT-2 evaluation included scale scores, standard scores, percentile rankings, descriptive categories (well below average, below average, average, above average, well above average), and the total motor composite (TMC), an average of all subsections of the test. As defined by the BOT-2 tool, a percentile ranking of less than 18% was considered below average (3 to 17%) (10). A percentile ranking of less than 25% was also recorded since this qualifies a child in Colorado for school district and state services. Scale scores are assigned for the following components of the BOT-2: bilateral coordination, balance, running speed and agility and strength with normal scale score values defined as 11 to 19. Standard scores (normal values 41-59) and percentile score are given for body coordination (bilateral coordination plus balance) and strength and agility (running speed and agility plus strength). The descriptive categories of below average and well below average (<2%) indicate impairment. We utilized these scores and rankings to then customize individual exercise plans and follow up.

Our CF center clinical database was utilized to collect demographic data for all participants including age, sex, BMI, number of lifetime hospitalizations (defined as a hospital stay of 3 or more days), CF genotype, lung function including forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) and the presence of any of the following comorbidities: CF related diabetes, type I diabetes, asthma, Gastroesophageal Reflux Disease, history of intestinal surgery, anxiety, depression, Attention Deficit Hyperactivity Disorder, toe walking, gastrostomy tube, and other miscellaneous conditions (scoliosis, short gut, migraines, congenital heart disease). This quality improvement project was approved by Children's Hospital Colorado

Organization Research Risk & Quality Improvement Review Panel (ORRQIRP).

Statistical analyses:

Baseline clinical characteristics and BOT-2 measures were summarized as either median (Interquartile range [QR]; min – max), mean ± standard deviation (SD) or frequency (%). For group comparisons, participants were dichotomized into two groups based on their percentile score for TMC, Bilateral Coordination and Strength and Agility, corresponding to clinically meaningful cutoffs of below 18% and below 25%. Associations between continuous measures were assessed via Pearson correlation, continuous and categorical measures with one-way ANOVA and categorical via Chi-square tests for independence. Studentized jack-knife residuals were plotted to examine the assumption of linear regression. When categorizations had intrinsic ordering, tests for linear trends were conducted. When appropriate, non-parametric methods such as Wilcoxson Rank Test and Fisher's exact were used. Regression coefficients and correlation estimates are presented with 95% confidence intervals. No adjustments for multiple comparisons were made as this project was viewed as retrospective and hypothesis generating. All analyses were conducted in SAS version 9.3 (Cary, NC).

Results:

Between January 2019 and January 2020, 105 children with CF between 4-12 years were seen in clinic and eligible for a PT evaluation. PT collected BOT-2 Test scores on 72 children (69%) over the course of one year. Of the 72 completed evaluations, 7 (10%) were performed at the end of a hospital admission for pulmonary exacerbation and the remainder were tested during a routine outpatient clinic visit. Identified barriers to completing BOT-2 assessment during routine clinic visits included: 1) Poor clinic attendance, 2) Family opting out of participating due to high co-pay for PT assessments, 3) Inappropriate attire/footwear to complete testing, 4) Acute illness, 5) Family declining evaluation due to scheduling conflicts and 6) Lack of PT coverage in clinic due to illness or scheduled vacation.

Demographic data for the 72 evaluated children are included in**Table 1** . Children had a median age of 7 years, 90% had at least one F508 mutation. About half were diagnosed with a comorbidity (49%) and 55% had a clinical history of one or more lifetime hospitalizations with 25% having 3 or more lifetime hospitalizations. Spirometry data were available in a subset of children (n=55, 76%). Median [IQR] percent predicted (pp) FEV_1 and FVC were 100 [92, 107], and 104 [95.5, 111.5], respectively, at the time of the BOT-2 assessment.

A summary of BOT-2 scores is shown in **Table 2** . Eighteen (35%) scored below average (<18%) in either total motor composite (TMC), body coordination (BC) or strength and agility (SA) scores. Decreased SA (18.1%) was the most common delay at the 18% percentile cutoff, followed by TMC (15%) and BC (14%). Overall, these children had a median total motor composite (TMC) score of 50 [IQR: 45 to 56]. This corresponded to a TMC percentile (TMC%) median 50% [IQR: 30%-73%]. Eleven (15%) children scored below the 18^{th} percentile on their TMC and 17 (24%) scored below the 25^{th} percentile. Using the descriptive categories of well below average and below average to indicate impairment, impaired strength (22.2%) was the most common finding, followed by impaired balance (16.7%), impaired running speed and agility (15.3%), and impaired bilateral coordination (8.3%).

Clinical and demographic characteristics associated with Total Motor Composite Scores and Percentiles.

Age, a lifetime history of hospitalizations and the presence of any comorbidities were each associated with TMC and TMC% scores. Age was inversely associated with TMC. For every one-year increase in age, there was an estimated 1.2 point (95% CI: 0.3 to 2.1) decrease (p=0.0089) in TMC, and an estimated 3.5% (95% CI: 0.9% to 6.2%) decrease (p=0.0099) in TMC%. A history of hospitalization was also associated with significantly lower TMC scores (linear trend test, p= 0.0014) and TMC% (linear trend test, p=0.0005). Those diagnosed with any comorbidity had a significantly lower TMC score (8.9 points lower, CI 5.3- 12.5; p<0.0001) and lower TMC % (27.8% lower, CI 17.3% to 38.4%; p<0.0001). **Figure 2** illustrates TMC scores by age, hospitalizations, and presence of any comorbidities.

In univariable regression models, $ppFEV_1$ and ppFVC were positively correlated with both TMC and TMC%

(**Figure 3 A and B**). For every 1 percent increase in ppFEV1 there was an estimated 0.61 point (95%CI: 0.15 to 1.06) increase in TMC (p=0.0101). For every 1 percent increase in ppFVC there was an estimated 0.61 point (95%CI: 0.20 to 1.01) increase in TMC (p=0.0043). For every 1 percent increase in ppFEV1 there was an estimated 19.0% (95%CI: 4.4% to 33.6%) increase in TMC% (p=0.0118). For every 1 percent increase in ppFVC there was an estimated 19.2% (95%CI: 6.2% to 32.2%) increase in TMC% (p=0.0046).

Children with the F508del/Other genotype had the highest rate of total motor skill delays (27% with a TMC% below 18%). Comparatively, the F508del homozygous genotype group and the Other/Other group had a 6% and 10% rate of TMC% below 18%. Although this difference was not statistically significant (p=0.0706), it may be clinically meaningful. There were no observed associations between TMC and TMC% and body mass index (BMI). The only observed difference in the six BOT-2 subset components and scores between sexes was in running speed and agility with girls scoring higher than boys in this category (**Supplemental table 1**).

CFTR Modulator use and motor proficiency

Thirty-five individuals were receiving treatment with CFTR modulators at the time of the BOT-2 assessment. Nine (26%) individuals reported using ivacaftor, 25 (71%) lumacaftor-ivacaftor and 1 (3%) tezacaftor-ivacaftor. Of note, data were collected prior to the approval of elexacaftor-tezacaftor-ivacaftor. The median TMC for the group with modulator use was 51 [IQR: 47 to 57] compared to a median 49 [IQR: 41 to 55] in those not receiving modulator therapy. There were no observed differences in TMC or TMC% between those treated with modulators compared to those not treated with modulators (p=0.0777, p=0.0863 respectively).

Discussion:

In this quality improvement project, we successfully introduced a PT evaluation of gross motor skills in school-aged children with CF utilizing the BOT-2. Within a year we completed evaluations in over two-thirds of eligible children. This study is one of the few published gross motor assessments using a standardized tool in school-age children with CF. Prior studies have been very small, although the results were similar to our findings. In an observational study of 14 infants with CF, 27% had motor delays using The Bayley Scales of Infant and Toddler Development® - III Edition(1). In another cross-sectional study examining 12 school aged children with CF, 33% had motor delays using the Movement Assessment Battery for Children 2ndedition (MABC-2)(12).

The most common area of impaired gross motor function was strength. There is CFTR expression in the skeletal muscle of humans(5, 13). Decreased CFTR function in skeletal muscle affects sodium transport and calcium release, which is crucial for a robust muscle contraction(5, 13). In addition, impaired CFTR function impacts ATPase and mitochondria, which is essential for energy production(5). While this quality improvement project was not designed to determine the cause of gross motor delays in this CF cohort, there may be intrinsic CF-related factors leading to skeletal muscle weakness and peripheral muscle atrophy in pwCF(5). We did not identify a difference in gross motor assessments in those receiving CFTR modulators compared to those not eligible. However, relatively few of these children were receiving highly effective modulator therapy (HEMT). Further evaluation of the impact of CFTR modulators on gross motor assessment is indicated now that elexacaftor-tezacaftor-ivacaftor is approved for those down to 2 years of age. A better understanding of how CFTR modulators impact strength and gross motor skills in CF may also help to explain the potentially clinically significant differences seen between genotypes in this cohort given the higher rate of gross motor delays found in those with the F508del/Other mutations (27%) compared to those with F508 homozygous (6%) and Other/Other (9%) genotypes. This is clinically important as skeletal muscle strength impacts exercise capacity, which is a known predictor of survival in CF(14).

The relationship between lung function and gross motors skills is not fully understood. Our data suggests that lower FEV_1 and FVC measurements were associated with lower TMC and TMC% scores. It is unknown whether this association is independent or if other factors, such as hospitalizations or presence of comorbidities could be contributing. A study by Wilkes and coworkers highlighted the longitudinal relationship

between physical activity and lung health in CF, determining that a greater increase in habitual physical activity was associated with a slower rate of decline in FEV_1(2). This, along with the evidence by Nixon and colleagues that children with CF participate in less physical activity than their healthy non-CF peers(4), emphasizes the need for targeted evaluation and interventions in young children with CF to facilitate successful participation in exercise and recreation. If exercise improves lung function, it is possible that optimizing gross motor skills may be one way to improve pulmonary outcomes for children with CF. This would be important for those who are ineligible for or cannot tolerate CFTR modulator therapy.

In our cohort, hospitalizations were also associated with lower TMC scores. We elected to report hospitalizations that lasted 3 days or longer, expecting that brief hospitalizations would have less of an impact on gross motor skills. Gruet and coworkers found that hospitalizations in adults with CF intensified peripheral muscle dysfunction, specifically quadricep strength, which is likely due to disuse and systemic inflammation(15). Decrease in quadricep strength after hospitalization may contribute to decreased gross motor skills. However, a prospective assessment of gross motor delays would better clarify the relationship between physical function, FEV_1decline and hospitalizations.

Forty-seven percent of the children in this sample were found to have one or more comorbidities, and those with comorbidities had statistically lower TMC scores compared to those without comorbidities. In this evaluation we compared individuals with any comorbidities to those without. Therefore, it remains unclear the role each separate comorbidity has on gross motor evaluations, due to the infrequency of many of them within this cohort. Understanding the role of individual comorbidities could be helpful in determining the need for specific PT interventions in this population.

Surprisingly, in our sample, we did not observe an association between BMI and gross motor skills given the close association between FEV_1 and BMI and prior studies demonstrating this relationship (2, 16-18). Lack of an association may be attributed to fat free mass depletion that can be seen in pwCF with a normal BMI(19, 20). Despite advancements in the nutritional status of many pwCF, a recent study demonstrated high rates of fat-free mass depletion in a cohort of children with CF.

There was also no significant difference in BOT-2 scores between males and females in our sample. This may be related to the age range evaluated (4 to 12 years) as previous studies have demonstrated no gender differences in activity level in prepubescent children with CF but increased activity levels in post-pubescent males compared to females(21). Evaluation with the BOT-2 in the adolescent population may help to better define the relationship between gross motor skills and gender.

Implementation of a 6-week exercise program has been shown to significantly improve pulmonary function, walking distance on 6 minute walk test (6MWT), and scores on the modified Munich fitness test, which assesses flexibility, balance, strength and coordination(22). Similarly, significant improvements in 6MWT, quadricep strength and fat free mass has been demonstrated after an 8-week program(23). A longer-term exercise program has also been shown to be beneficial for children and adolescents with CF by improving motor performance fitness(24). This is very reassuring data to support the implementation of a home program in children with CF, when impairments are identified using a gross motor assessment and exercise testing. As a next step we will be longitudinally evaluating BOT-2 scores in school-aged children in our clinic to determine the impact of a home program on gross motor skill acquisition.

Limitations of these results include that it is a convenience sample and observational with the primary purpose being a quality improvement project to implement gross motor assessments in children with CF. In terms of the BOT-2 assessment tool, it is important to note the TMC is an average of all subsections. For a child that scored high in the body coordination section and low in the strength agility section, they may appear to have average gross motor abilities in evaluating TMC alone. Data from individual sections must therefore be considered when determining the plan of care, PT interventions, and how a child may be functioning in relation to same-age peers. Although associations between gross motor findings and clinical outcomes and demographic characteristics were noted, a causal relationship cannot be established. The strengths of this project include the number of children evaluated, which is the largest published assessment

of gross motor skills in children with CF. Additionally, we report novel information on the prevalence of gross motor delays in children with CF including outcomes using the BOT-2 and components of the TMC that were abnormal in this cohort.

The results of this intervention support the need for a PT in the care of children with CF to assess for gross motor delays. This assessment could ultimately lead to earlier detection of delays, improved quality of care, and allows PT to provide individualized recommendations to facilitate participation and success in physical activity from an early age. If, based on clinic workflow, PT is not embedded within CF clinic or cannot be involved in assessing all children with CF, priority should be given or an outpatient referral to PT should be considered, in those with a history of repeat hospitalizations and co-morbidities, due to the increased rate of gross motor delays in children with these risk factors. More data are needed to understand how motor delays impact health outcomes, and how PT interventions impact clinically meaningful outcomes in children. Longitudinal data are needed to trend changes in gross motor abilities in the CF population and determine risk factors for gross motor delays. Finally, as we enter the era of highly effective CFTR modulator therapies for younger children, it will be important to understand the impact of these therapies on gross motor abilities.

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Table 1: Summary of baseline clinical characteristics (N=72)

Demographics	Median [min - max] N (%)
Age in years	7 [4, 11]
Body mass index percentile	60.09 [9.25, 96.38]
Genotype	
F508 homozygous	32 (44.4)
F508/Other genotype	30 (41.7)
Other/Other genotype	10 (13.9)
Comorbidities	
Yes	35 (48.6)
No	37 (51.4)
Hospitalizations in lifetime (HIL)	
0 Hospitalizations in lifetime (%)	32 (44.4)
1-2 Hospitalizations (%)	22 (30.6)
[?]3 Hospitalizations (%)	18 (25.0)
FEV_1 percent predicted	100 [57, 132]
FVC percent predicted	104 [57, 132]

Table 2: Summary of Motor Proficiency (N=72)

		Median [min - max] N (%)
Total motor composite percentile		50 [6, 96]
Delay in TMC score (below the 18th percentile), N, (%)		11 (15.3)
TMC score below the 25th percentile, N (%)		17 (23.6)
Body coordination (Balance plus coordination) percentile		48 [6, 98]
Delay in body coordination (below 18th percentile), N (%)		10 (13.9)
Body coordination below 25th percentile, N (%)		19 (26.4)
Strength and agility percentile		46 [6, 99]
Delay in Strength and agility (below 18th percentile), N (%)		13 (18.1)
Strength and agility below 25th percentile, N (%)		18 (25.0)
Descriptive category body coordination	Above	17 (23.6)
	Average	49 (68.1)
	Below	6 (8.3)
Descriptive category balance	Above	10 (13.9)
	Average	50 (69.4)
	Below	12 (16.7)
Descriptive category running speed	Above	16 (22.2)
	Average	45 (62.5)
	Below	11 (15.3)
Descriptive category strength**	Above	8 (11.1)
	Average	48 (66.7)
	Below	16 (22.2)
Sum total delays below 18th percentile*	0	54 (75.0)
	1	8 (11.1)
	2	4 (5.6)
	3	6 (8.3)
Sum total delays below 25th percentile*	0	44 (61.1)
	1	12 (16.7)
	2	6 (8.3)
	3	10 (13.9)

*Delays could occur in TMC score, body coordination or strength and agility.

**Descriptive category for strength: Well above average (n=1) was grouped with the Above Category.

Table 3: Outcome Measures that were considered(11)

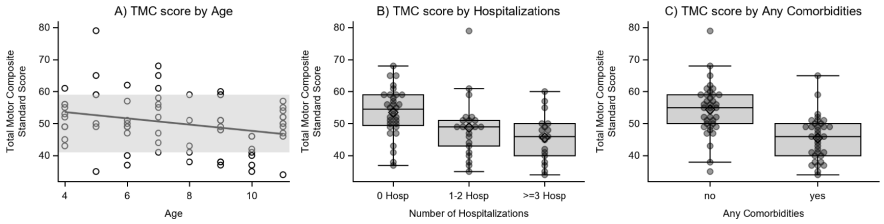
Test	Age range	Cost (for full kit)	Time	Considerations
PDMS-3	0-5	$781	20-30 minutes	Access to stairs, different step heights to jump off, tennis ball r
TGMD	3-10	$170	30-40 minutes	Bean bags, baseball T, tennis ball, soccer ball, paddle, cones ne
MABC	3-16	$1350	20-40 minutes	Bean bags, chairs, stopwatch needed for testing
BOT-2	4-21	$685	25-30 minutes	Space for 50 ft shuttle run, specific balance beam

Figure 1: Clinical Algorithm for BOT-2 Administration

Figure 2: Baseline Clinical Characteristics associated with Total Motor Composite Standard Score.

Figure shows the association between TMC Standard Score by age (A), hospitalizations (B) and presence of

any comorbidities (C). Note the reference band is the range of normal TMC standard scores of 41-59.



Figures 3: Association between TMC and Lung Function (FEV_1 and FVC).

Figures A and B show the association between TMC standardize scores observed lung function measures as FEV_1 (A) and FVC (B). Note the reference band is the range for TMC standard scores of 41-59.