Nutrition in Clinical Practice
Volume 35 Number 6
December 2020 1110–1118

DOI: 10.1002/ncp.10583
wileyonlinelibrary.com
WILEY

The Association of Grip Strength, Body Mass Index, and Lung Function in Youth with Cystic Fibrosis

Sandra F. Bouma, MS, RDN, CSP[1]; Courtney Iwanicki, MS, RDN, CSP[1]; Harlan McCaffery, MA, MS[2]; and Samya Z. Nasr, MD, CPI[3]

Abstract

Compared with body mass index (BMI), lean body mass and fat-free mass are strongly associated with lung function in children and adolescents with cystic fibrosis (CF). Methods of measuring body composition in youth with CF are often unreliable, expensive, or not clinically feasible. Grip strength (GS), a measure of muscle function, is used as a surrogate for muscle mass and is an indicator of nutrition status. This quality improvement project explored the feasibility of measuring GS in medically stable youth with CF, aged 6–21 years. A total 361 GS measurements were performed by using a digital hand dynamometer in youth from a single CF center. Using reference tables that were created for this project by merging data from the 2011–2012 and 2013–2014 National Health and Nutrition Examination Surveys, youth with CF were found to be weaker than age- and gender-matched peers, even when controlled for differences in size. A positive association ($P < .001$) was found between GS percentile and lung function, as measured by forced expiratory volume in 1 second percent predicted (FEV1pp). Statistical analysis revealed that both BMI percentile and absolute GS (AGS) percentile were positively associated with FEV1pp and with each other, primarily at the lower levels of BMI percentile (<50%) and AGS percentile (<50%). GS may provide a reliable, less expensive, and clinically feasible alternative to body composition measurements in monitoring nutrition status in youth with CF, especially in youth whose BMI is in the <50th percentile. (*Nutr Clin Pract.* 2020;35:1110–1118)

Keywords

body mass index; cystic fibrosis; grip strength; lung function; nutrition assessment

Introduction

Nutrition status is positively associated with respiratory health and survival in individuals with cystic fibrosis (CF).[1,2] The CF Foundation (CFF) recommends that children and adolescents with CF maintain or achieve a body mass index (BMI) at the ≥50th percentile because individuals with a lower BMI are at greater risk of poor outcomes. Although BMI is a valid metric for stratifying the CF population into different risk categories, it is not without limitations. The goal of increasing BMI in individuals with CF arguably led to a focus on caloric quantity at the cost of dietary quality.[3] Moreover, the ability to maintain and build lean body mass (LBM) by improving physical activity, particularly strength conditioning, while eating a high-calorie, high-protein diet, is often lacking.[4] Another limitation of the BMI measurement is that it does not discriminate between adipose tissue and fat-free mass (FFM) and does not allow the identification of nonobese individuals with excess body fat.[5] LBM and FFM have been found to correlate more strongly than BMI with lung function in adults and children with CF.[6,7] Findings such as these have led to a growing interest in measuring body composition in individuals with CF; however, the various measurement methods are often unreliable, too costly, or not feasible in the CF population.[8] Dual energy x-ray absorptiometry (DEXA), hydrostatic weighing, and air

From the [1]Division of Pediatric Pulmonology, Nutrition Services, Michigan Medicine, Ann Arbor, Michigan, USA; [2]Center for Human Growth and Development, University of Michigan, Ann Arbor, Michigan, USA; and the [3]Department of Pediatrics, Division of Pediatric Pulmonology, Michigan Medicine, Ann Arbor, Michigan, USA.

Financial disclosure: None declared.

Conflicts of interest: Sandra F. Bouma served as a speaker for Abbott Nutrition and Health Institute. The other authors declare they have no conflicts of interest to disclose.

Received for publication May 19, 2020; accepted for publication September 13, 2020.

This article originally appeared online on October 7, 2020.

Corresponding Author
Sandra F. Bouma, MS, RDN, CSP, Nutrition Supervisor, Michigan Medicine, 1500 East Medical Center Drive, Ann Arbor, MI 48109-5212, USA.
Email: sbouma@umich.edu

displacement plethysmography are reliable gold standards for measuring body composition, but they are costly and, particularly in the case of hydrostatic weighing, not clinically feasible. Using triceps skin fold and mid-arm circumference measurements to calculate arm muscle area has a wide margin of error, and measurements are often unreliable because of low interrater reliability.[8] Bioelectrical impedance analysis (BIA), even when using the more expensive multifrequency BIA machines ($5000–$19,000 USD), also have reliability issues. A recent validation study of 110 recreationally active adults aged 18–25 years found that BIA measured a 4%–9% difference in percent body fat compared with DEXA, with BIA tending to underestimate percent body fat compared with DEXA.[9] One study group from France attempted to validate a CF-specific equation for estimating FFM using BIA in a small sample of young people with CF (n = 54).[10] But even if CF clinics could justify the expense, BIA has strict, inconvenient requirements, such as needing to fast from food for 4–12 hours and avoid exercise 6–12 hours prior to BIA testing, neither of which were addressed in the French study.[9,10]

Grip strength (GS), which measures hand muscle function by using a hand dynamometer, has been used as an indicator of overall muscle strength in healthy children and adults.[11,12] Muscle function, as determined by GS, reflects a dynamic surrogate for muscle mass. Measuring GS is affordable (eg, $300–$400 USD for a digital hand dynamometer) and has been shown to be feasible in a non-CF pediatric clinical setting.[13] When standard protocols are followed, clinicians can efficiently take GS measurements and be confident in the fidelity of repeated measurements by virtue of a well-established history of intratester and intertester reliability and validity, as studied in multiple disciplines and populations.[8,13]

Although GS measurements have been used in children and adolescents without CF,[13–15] there is only 1 small pilot study that measured GS in 23 children and adolescents ((aged 6–18 years) with CF.[8] In this pilot study, GS measurements were taken 5 months before hospitalization, days 5–7 during a hospital admission for pulmonary exacerbation, and then again ~6 weeks' posthospitalization. The study found that GS *z*-scores significantly increased after hospitalization, but there was no association between GS *z*-scores and BMI *z*-scores or GS *z*-scores and forced expiratory volume in 1 second percent predicted (FEV1pp). Limitations of this study were its small sample size (n = 23) and its use of a small, limited data reference set, which uses GS measurements from a sample of 471 children who lived in the greater Milwaukee area in 1985.[14] To our knowledge, no data on GS have been reported in a larger sample of medically stable, nonhospitalized children and adolescents with CF. Moreover, associations among GS, lung function, and BMI have not been explored in a larger CF population.

The primary aim of this quality improvement (QI) project was to determine the feasibility of collecting GS data on a large number of children and adolescents with CF who are medically stable and compare it with their peers without CF by using robust, normative GS reference tables that were created for this project by merging population-level reference data from the National Health and Nutrition Examination Surveys (NHANES) 2011–2012 and 2013–2014 survey cycles (Supplementary Material: Tables S1–S4). The secondary aims were to characterize changes in GS in individuals with CF over time and to look for associations among GS, lung function, and BMI in children with CF who are medically stable.

Methods

Study Population

A total 201 individuals aged 6–21 years with CF were included in this QI project, which measured GS, BMI, and pulmonary function (as measured by FEV1pp). The CF diagnosis was confirmed via a sweat chloride test and/or 2 disease-causing mutations. During a 52-month study period (April 7, 2017, through July 10, 2019), GS measurements were taken on children and adolescents when they came to their regularly scheduled clinic visits. GS measurements were taken at least once per year, and 160 of these individuals also had a follow-up GS measurement. This QI project was approved by the institutional review board.

Study Design and Measurement

Anthropometric data were collected and recorded in the individual's medical record, as per standard practice, by trained medical assistants at the pediatric pulmonology outpatient clinic. Standing heights, without shoes, were measured within 0.1 cm by using a wall-mounted Stadiometer fitted with a Veeder-Root counter (Holtain Ltd, Crymych, Dyfed, UK). Weights, with the individuals wearing street clothes but no shoes or outer garments, were measured within 100 grams by using a digital scale (Scale-tronix, White Plains, NY, USA). Both the Stadiometer and the scale are inspected and maintained by the biomedical technical service. BMI is calculated as weight in kilograms divided by height in meters squared.

One of 2 registered dietitians measured each individual's GS with a Jamar Plus+ digital hand dynamometer (Patterson Medical, Warrenville, IL, USA), which is recalibrated yearly by the manufacturer. Per standard protocols, individuals must be aged ≥6 years to be physically and developmentally ready to accurately follow the instructions for measuring GS. The measurement protocol of the American Society of Hand Therapists, as described by Mathiowetz, is associated with a high intratest and intertest reliability and was used for this project.[16,17] Individuals were in a

seated position with their shoulders adducted, elbow flexed at 90°, and forearms in a neutral position. The handle was positioned such that the individuals were able to wrap their thumb around one side of the handle and their fingers around the other side, with their intermediate phalanges covering the face of the handle and the tips of their fingers not coming into contact with the palm of their hand. Three measurements were taken on each hand, alternating between hands with a 10- and 15-second break between each measurement. Individuals were encouraged to squeeze harder until the number on the digital read-out stopped rising.[18]

Normative Reference Data

For this project, robust normative GS reference tables were created by merging data from the NHANES 2011–2012 and 2013–2014 survey cycles, resulting in GS measurements from 4672 individuals, aged 6–19 years.[19] These data sets represent an ethnically, educationally, and economically diverse national sample that is nearly 10 times larger than the data set used for the reference table included with the dynamometer.[14] The NHANES target population is noninstitutionalized civilian residents. In the 2011–2014 survey cycles, the survey sampled larger numbers of certain subgroups of particular public health interest, such as Hispanic persons and non-Hispanic Black and Asian persons, as well as persons who identified as non-Hispanic White or "other," who were at or below 130% of the poverty level or aged ≥80 years (https://wwwn.cdc.gov/nchs/nhanes/ContinuousNhanes/Overview.aspx?BeginYear=2013). A comparison of available GS reference tables is found in Table 1. As per the NHANES GS protocol, the highest measurement from either hand was used to determine the age- and gender-specific percentile for absolute GS (AGS). Normalized GS (NGS) was calculated by dividing AGS by body weight in kilograms for each individual.[20,21] Because age and gender are the largest determinants of muscle strength, age- and gender-specific percentiles were calculated from NHANES reference data to allow comparisons across age groups.[22,23] The data can be used in the clinical setting and are presented in 4 reference tables: AGS for boys, AGS for girls, NGS for boys, and NGS for girls. (See Supplementary Material: Tables S1–S4)

Statistical Analysis

Reference percentiles were calculated by using SAS version 9.4 (Cary, NC, USA), and all other analyses were done using R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria). GS percentiles were calculated using the combined 2011–2012 and 2013–2014 NHANES data sets of muscle strength, body measurements, and demographics. The highest GS measurement in kilograms from either hand (AGS) was used for

Table 1. Comparison of 3 US Reference Data Sets for Grip Strength.

Reference data set	Population used	Age range	Years data was collected	Number of individuals (aged 6–19 years) included	Measurement used	Method of evaluating
Reference data that comes with the Jaymar Digital dynamometer (Mathiowetz 1985/1986)[14,24]	Healthy school children and adults from a 7-county Milwaukee, WI, area	≥6–75 years	1985–1986	471 (total sample, including adults = 1109)	Average of 3 measurements on each hand	Mean ± SD
Reference data from Peterson & Krishnan 2015[20]	Healthy children and adults from an ethnically, educationally, and economically diverse national sampling	6–80 years	2011–2012	2431 (total sample, including adults = 7119)	Highest measurement of 6 measurements (3 from each hand)	7 quantile ranges (5%, 10%, 25%, 50%, 75%, 90%, 95%)
Reference data created by Bouma, McCaffery, Iwanicki & Nasr, 2020 (see supplement); expanded from Wang, 2019[19]	Healthy children and adults from an ethnically, educationally, and economically diverse national sampling	6–80 years	2011–2012 and 2013–2014	4672 (total sample, including adults = 13,676)	Highest measuremen of 6 measurements (3 from each hand)	14 quantile ranges (5% increments from 5% to 95%; ie, 5%, 10%, 15%, 20%, etc)

percentile estimates for males and females in each 1-year age increment from 6–19 years. Sample weights were used to account for complex survey design (including survey oversampling), survey nonresponse, and poststratification. The sample weights from the 2 survey cycles were combined according to the procedures outlined on the Center for Disease Control website (https://www.cdc.gov/nchs/tutorials/nhanes/SurveyDesign/Weighting). The estimated percentiles by age and sex were tabulated in 5% increments, which was the highest level of granularity that would enable calculating SEs for most percentile estimates in each age-sex grouping. The estimated percentiles were used to transform the raw GS measurements from this project into percentiles. Pearson correlations and 2 sample *t*-tests were used to assess the associations of AGS, NGS, and BMI percentiles with FEV1pp. One sample *t*-tests were used to examine the change in scores from the first to the second study assessments. Plotting and locally estimated scatterplot smoothing (LOESS) curve fitting were used to visualize the association of FEV1pp, BMI, and GS and their percentiles. To examine the independent association of GS and BMI with FEV1, the sample was stratified at the median and at the quartile of BMI and AGS percentiles, and correlations were calculated within each stratum. For all tests, a *P*-value of $<.05$ was considered statistically significant. *P*-values were not adjusted for multiple comparisons.

Results

The pediatric CF center has a total of 275 pediatric patients, of which 201 were aged 6–21 years old at the time of the project. A total 361 GS measurements were completed during the project's 52-month time span. Table 2 gives a description of the project's population. Initial GS measurements were completed on 201 individuals. BMI percentiles, which are used for children, adolescents, and young adults aged 6–19 years, were available for 186 individuals. Fifteen individuals were aged $\geq$20 years at the time of the initial measurement, so they were not included in analyses, which used BMI percentile.

A total 160 of 201 individuals had a second follow-up GS measurement. The average length of time between the initial GS measurement and the follow-up one was 10.2 months (range, 3–24.9 months), with all but 5 individuals having their second follow-up GS measurement done between 5 and 15.7 months apart.

Of the 41 individuals who did not have a follow-up GS measurement, 11 transitioned to the adult CF clinic, 11 were lost to follow-up (ie, no show, missed appointment), 6 were not due for their yearly GS measurement at the time the project ended, 4 moved out of the area, 4 were not measured because of time constraints, 3 were not measured because of lack of an available person trained in using the dynamometer, 1 refused to be measured again, and 1 was deceased. We found no statistically significant differences in descriptive characteristics between the 160 individuals who received a follow-up measurement and the 41 who did not (data not shown). There was also no statistically significant difference between the initial GS percentile and the follow-up GS percentile (data not shown), so other analyses were restricted to the first study assessment (n = 201, of which 186 were young enough to have a BMI percentile).

Table 2. Descriptive Statistics of Project Participants.

Characteristic	Value (N = 201)
Age, mean (SD), y	13.25 (4.57)
Female gender, n (%)	99 (49.3)
Height, mean (SD), m	1.48 (0.20)
Weight, mean (SD), kg	45.29 (17.07)
BMI, mean (SD)	19.89 (3.72)
BMI percentile, mean (SD)	58.51 (26.93)
Height-for-age *z*-score, mean (SD)	−0.42 (1.12)
Average GS (left hand), mean (SD), kg	18.49 (10.28)
Average GS (right hand), mean (SD), kg	20.43 (11.06)
AGS, mean (SD), kg	22.21 (11.86)
AGS percentile, mean (SD)	30.43 (26.49)
NGS, mean (SD)	0.48 (0.13)
NGS percentile, mean (SD)	44.76 (27.65)
FEV1pp (% predicted), mean (SD)	88.69 (20.57)
Genetics, mean (SD), %	
Heterozygous	73 (36.3)
Homozygous	103 (51.2)
Other	25 (12.4)
Sweat, mean (SD), mmol/L	95.44 (21.18)

NGS is calculated as AGS divided by weight in kilograms.
AGS, absolute grip strength; BMI, body mass index; FEV1pp, forced expiratory volume in 1 second percent predicted; GS, grip strength; NGS, normalized grip strength.

Overall, our project found that the children, adolescents, and young adults with CF aged 6–19 years who were tested were found to be weak for their age and gender compared with their peers without CF. Forty percent of the group (75 out of 186 individuals) were very weak (AGS $\leq$ 10th percentile). When these 75 very weak individuals were divided into 2 groups by BMI (BMI $<$ 50th percentile, n = 31; BMI $\geq$ 50th percentile, n = 44), the difference between the groups was not statistically significant. (Table 3)

When normalizing GS by dividing AGS by weight, individuals with a BMI $<$ 50th percentile were significantly stronger for their size at any given age than individuals with a BMI $\geq$ 50th percentile. Moreover, 40.7% of individuals with a BMI $\geq$ 50th percentile were weak for their size (NGS of the $<$25th percentile) compared with only 20.6% of individuals with a BMI $<$ 50th percentile. (Table 3)

The AGS percentile was positively associated with FEV1pp across all BMI percentiles ($P < .001$), even when the BMI percentiles were divided into 2 groups: BMI $<$ 50th percentile ($P < .002$) and BMI $\geq$ 50th percentile ($P < .05$.) (Table 4) When the group was divided into

Table 3. Comparison of FEV1 and Grip Strength Parameters for 2 BMI Percentile Categories.

BMI percentile	(0–49)	(50–100)	*P*-value
n	68	118	
FEV1pp, mean (SD)	80.85 (20.89)	94.50 (18.06)	<.001*
Right average GS, mean (SD), kg	19.43 (10.47)	19.25 (10.49)	.914
Left average GS, mean (SD), kg	18.08 (9.93)	17.11 (9.45)	.512
AGS, mean (SD), kg	21.31 (11.45)	20.78 (10.92)	.757
NGS, mean (SD)	0.51 (0.13)	0.44 (0.11)	<.001*
AGS ≤ 10th percentile = yes (%), n	31 (45.6)	44 (37.3)	.339
NGS < 25th percentile = yes (%), n	14 (20.6)	48 (40.7)	.008*
Right GS *z*-score[a]	−1.81 (0.97)	−1.4 (1.21)	.017*
Left GS *z*-score[a]	−1.5 (0.98)	−1.26 (1.22)	.173

NGS is calculated as AGS divided by weight in kilograms.
AGS, absolute grip strength; BMI, body mass index; FEV1pp, forced expiratory volume in 1 second percent predicted; GS, grip strength; NGS, normalized grip strength.
[a] Using the Mathiowetz reference data for comparison purposes.
* $P < .05$.

Table 4. Correlation of Absolute and Normalized Grip Strength with FEV1 by BMI Percentile Category.

GS variable	BMI percentile	N	ρ	Lower bound	Upper bound	*P* -value
AGS percentile (strength for age)	All	186	0.294	0.157	0.420	<.001*
	(0–49)	68	0.377	0.152	0.565	.002*
	(50–100)	118	0.181	0.000	0.350	.050*
	(0–24)	28	0.431	0.069	0.693	.022*
	(25–49)	40	0.290	−0.024	0.552	.070
	(50–74)	54	0.238	−0.031	0.476	.083
	(75–100)	64	0.111	−0.139	0.347	.384
NGS percentile (strength for age and size)	All	186	0.294	0.157	0.420	<.001*
	(0–49)	68	0.199	−0.041	0.418	.103
	(50–100)	118	0.117	−0.065	0.292	.206
	(0–24)	28	0.177	−0.210	0.516	.368
	(25–49)	40	0.232	−0.086	0.507	.150
	(50–74)	54	0.182	−0.090	0.429	.189
	(75–100)	64	0.095	−0.155	0.333	.457

NGS is calculated as AGS divided by weight in kilograms.
AGS, absolute grip strength; BMI, body mass index; FEV1pp, forced expiratory volume in 1 second percent predicted; GS, grip strength; NGS, normalized grip strength.
* $P \leq .05$.

4 BMI subcategories, this correlation continued to be statistically significant for those with a BMI < 25th percentile ($P < .022$). This suggests that individuals who have a low BMI (<25th percentile) but a high AGS may be at an advantage in terms of respiratory status, as determined by FEV1pp.

NGS percentile was also positively associated with FEV1pp across all BMI percentiles ($P < .001$), but this significance did not hold when divided into BMI percentile subcategories. (Table 4).

BMI percentile and AGS percentile were positively associated with FEV1pp and with each other, primarily at the lower levels of BMI percentile (<50%) and AGS percentile (<50%). Plotting and LOESS curve fitting revealed a nonlinear association of FEV1pp with both BMI and AGS percentiles, with the slope leveling off in higher percentiles (Figure 1A and B). AGS percentile and BMI percentile were positively correlated (Figure 1C), whereas NGS percentile dropped as BMI percentile increased (Figure 1D).

Discussion

Our QI project presents the largest data set to date of GS measurements in medically stable children, adolescents and young adults with CF. Our project obtained 201 initial-visit GS measurements and 160 follow up–visit measurements, which were, on average, 10 months later. Measuring GS in youth with CF in the clinic setting was feasible. Children

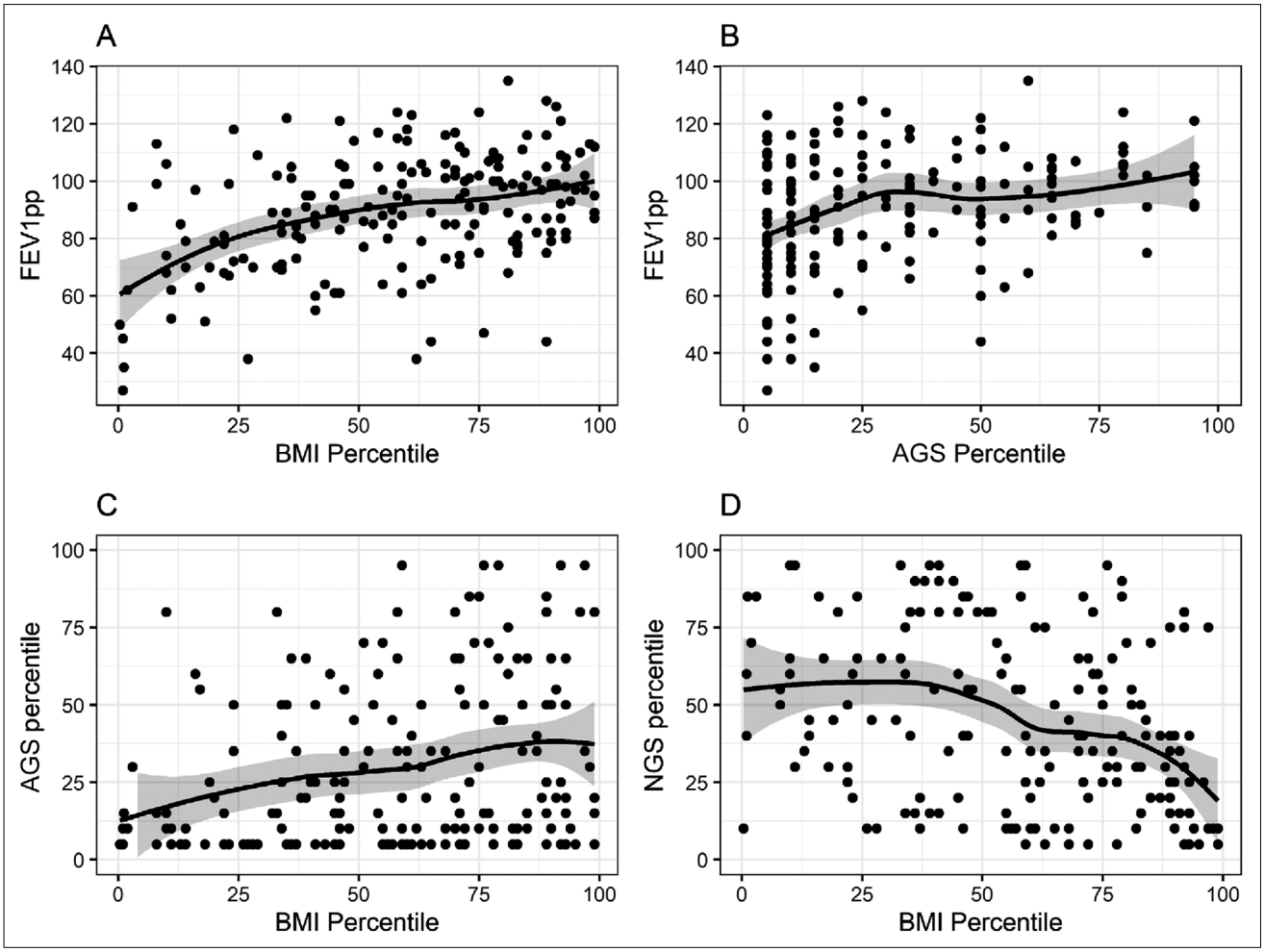

Figure 1. Associations between forced expiratory volume in 1 second percent predicted (FEV1pp), absolute grip strength (AGS) percentile, normalized grip strength (NGS) percentile, and body mass index (BMI) percentile. (A) FEV1pp and BMI percentile, (B) FEV1pp and AGS percentile, (C) AGS percentile and BMI percentile, (D) NGS percentile and BMI percentile.

and adolescents were receptive, and even excited, to show how strong they were by performing GS measurements using a hand dynamometer. The protocol of the American Society of Hand Therapists is simple to follow and requires a similar level of training as would be required to measure an individual's weight or height. After practicing on volunteers enough times to feel comfortable with the process, clinicians could perform GS measurements in <5 minutes in the clinic setting. Only 8 individuals (5%) of the 160 who came back for a follow-up appointment failed to get a follow-up GS measurement. GS was a well-received, efficient method to provide insight into an individual's muscle strength.

As part of this project, national GS data from the NHANES 2011–2012 and 2013–2014 survey cycles were merged to form robust, normative GS reference tables that reflect contemporary ethnic, educational, and economic diversity.[19] This is in contrast to the Mathiowetz data, which were taken from a 7-county area near Milwaukee, Wisconsin, in 1984. Table 1 compares the GS reference data that are currently available. Wang et al found that NHANES GS values showed stability across data-release cycles, which provided the rationale for the merger of survey cycles 2011–2012 and 2013–2014.[19] This merger also allowed for enough data to break down the age categories into 1-year rather than 2-year increments and the percentiles into 5% increments rather than larger ones, resulting in 14 percentiles as opposed to 7 percentiles, as in the table by Peterson and Krishnan.[20] A more granular data reference set and a larger sample size (n = 186) likely allowed for statistical significance between FEV1pp and GS percentile, whereas the pilot study by Gibson et al (n = 23) did not.[8] Clinically, these new GS reference tables can be effectively used to determine cutoffs and help develop nutrition care plans for children, adolescents, and young adults. For example, if youth with CF meet the CFF's recommended goal of having a BMI $\geq$ 50th percentile, but they have an AGS $\leq$ 10th

percentile for their age, the GS measurements provide individuals with objective, and potentially motivating, evidence from which the CF medical team can recommend increasing physical activity to try to build muscle and increase LBM.

Despite the difference in population size, our project's demographics were similar to the pilot study by Gibson et al in that the mean age of our group was 13.25 ± 4.47 years at the first visit (n = 201) compared to a mean age of 12.4 ± 4 years at the time of hospitalization in the Gibson et al sample (n = 23).[8] Whereas the sample in the study by Gibson et al was 66% female, our CF population was more balanced between males (50.7%) and females (49.3%) at the first visit. The average BMI percentile in our study population was the 59th ± 27th percentile, which in a normal distribution is the equivalent to a BMI *z*-score of +0.23 ± 0.6. This was higher than the sample by Gibson et al, which had a mean BMI *z*-score of only −0.17 ± 0.63 5 months prior to hospitalization and +0.06 ± 0.54 6 weeks after hospitalization.

Our findings are congruent with the study by Gibson et al, which showed children with CF are weak compared with their peers of the same gender and age. Using the Mathiowetz reference data from 1985, Gibson et al reported a dominant-hand mean GS *z*-score at 6 weeks after hospitalization of –1.59 ± 1.06.[8] Using the same reference data for comparison, we found that the right-hand value from our CF population had a highly comparable mean GS *z*-score of −1.53 ± 1.12 at their first visit and −1.46 ± 1.10 at their follow-up visit (data not shown).

AGS is defined as the largest value from either hand after taking a total of 3 altering measurements on each hand. AGS percentile describes how strong someone is for their age compared with their peers of the same age and gender. Forty percent of individuals aged 6–19 years had an AGS of in the ≤10th percentile (75 out of 186). (Table 3) In a normal study population, one would expect only 10% of the population to have an AGS in the ≤10th percentile. According to a small study in medically stable pediatric patients who were status post (s/p) bone marrow transplant (BMT), an AGS in the <10th percentile was correlated with weakness and poor nutrition status ($P < .05$).[13]

In children and adolescents with CF, Sheikh et al found that LBM index (LBM divided by height^2) correlated more strongly than BMI with an FEV1pp.[7] Comparatively, our GS project shows AGS, a surrogate for LBM, is positively associated with FEV1pp. An individual who is strong for their age (high AGS) is more likely to have a higher FEV1pp than someone who is weak for their age (low AGS). Moreover, this is especially true for children, adolescents, and young adults with a lower BMI (<50th percentile) (Figure 1B). This finding is strikingly similar to the results reported by Sheikh et al, which also revealed that the association between LBM index and pulmonary function was especially true in individuals with lower BMIs (<50th percentile).[7] The clinical implication of this finding is that if a child or adolescent has a BMI in the <50th percentile and is otherwise healthy, but has not been able to improve BMI through diet alone, they may be able to maintain or improve their lung function by improving their muscle strength (as measured by GS), regardless of their BMI. The cause and effect of this relationship is unknown, but it is reasonable to assume that strong muscle function is essential for optimal lung function.

It is well known that BMI percentile is positively associated with FEV1pp.[3] The data from our project confirmed this (Figure 1A). To our knowledge, this is the first project to show that AGS percentile is also positively associated FEV1pp. (Figure 1B). Both AGS percentile and BMI percentile were positively associated with FEV1pp and with each other but primarily at the lower levels (<50th percentile). The clinical implication of this finding is to continue to try to achieve a goal of BMI in the ≥50th percentile (especially if AGS is in the <50th percentile) but also to work to achieve AGS ≥ 50th percentile (especially if BMI is in the <50th percentile).

NGS percentile describes the strength of someone in relation to their size compared with peers of the same age and gender. Thirty-three percent of the patients aged 6–19 years had an NGS < 25th percentile (62 of 186). (Table 3) According to the study, which looked at medically stable pediatric patients who were s/p BMT, an NGS < 25th percentile for age and gender distinguished an "overnutrition" group from a "normal nutrition" group ($P < .05$). Overnutrition, as defined by the pediatric BMT study, meant a BMI *z*-score ≥ 1 (ie, BMI ≥ 85th percentile), a sedentary lifestyle by self-report, and signs of increased subcutaneous fat on physical exam.[13] A low NGS has been associated with poor cardiometabolic outcomes in adolescents.[25] Our findings suggest that as BMI increases in youth with CF, GS in relation to their size decreases (Figure 1D). Moreover, an individual with CF who is weak for their size may have less LBM, regardless of their BMI, which could negatively impact their lung function. Alavarez et al reported that excess adiposity, particularly in the form of normal-weight obesity, was inversely associated with lung function in adults with CF.[5] Since some CF centers have noticed a rapid weight gain in individuals taking modulators, it could be important to encourage physical activity during modulator therapy to promote gain in muscle, rather than adipose tissue, for optimal lung function. Indeed, with an overall increasing life span for individuals with CF, adjusting patient care goals to promote long-term health, such as focusing on improved muscle strength, is warranted. Given that muscle weighs 4–5 times more than an equal volume of fat, building muscle through strength training could increase both LBM and BMI. Consideration should be given to muscle building during a state of healthy homeostasis, since infection, inflammation, and steroid use can negatively affect muscle

mass and strength. Monitoring NGS in medically stable individuals with CF gives youth an objective finding, which could help motivate them to engage in physical activity that increases BMI by building muscle rather than defaulting to sedentary activity that, along with a high calorie diet, is more likely to increase body fat. Clinicians can encourage youth to "eat like an athlete," ie, a high-calorie, high-protein, nutrient-dense diet, with an emphasis on whole grains and healthy fats, while youth engage in muscle-building activity and then monitor NGS to evaluate results.

No statistically significant change in GS between the initial visit and the follow-up visit was noted. This suggests that merely measuring someone's GS does not result in a change in GS. This information can be used in future intervention studies as evidence that the intervention, and not the testing itself, was likely responsible for changes in GS. To increase GS, a planned, specific intervention would be recommended to lead to improvement.

Conclusion

GS provides a reliable, less expensive, and clinically feasible alternative to body composition measurements in monitoring nutrition status in children, adolescents, and young adults with CF, especially in those whose BMI is in the <50th percentile. Merging 2 recent cycles of NHANES data gives clinicians robust, normative reference data for GS that can be uniformly used to determine patient care goals. Additional QI projects, including a high-intensity training program, are needed to help determine if increased exercise, particularly muscle-building/strength-conditioning exercises, will improve GS and improve FEV1pp.

Statement of Authorship

S. Bouma, C. Iwanicki, and S. Nasr contributed to the conception and design of the research; S. Bouma and C. Iwanicki contributed to the acquisition of the data; S. Bouma, C. Iwanicki, H. McCaffery, and S. Nasr contributed to the analysis and interpretation of the data; and S. Bouma drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

References

1. Corey M, McLaughlin FJ, Williams M, Levison H. A comparison of survival, growth, and pulmonary function in patients with cystic fibrosis in Boston and Toronto. *J Clin Epidemiol*. 1988;41(6):583-591.
2. Stallings VA, Stark LJ, Robinson KA, Feranchak AP, Quinton H. Evidenced-based practice recommendations for nutrition-related management of children and adults with cystic fibrosis and pancreatic insufficiency: results of a systematic review. *J Am Diet Assoc*. 2008;108(5):832-839.
3. Bellissimo MP, Zhang I, Ivie E, et al. Visceral adipose tissue is associated with poor dietary quality and higher fasting glucose in adults with cystic fibrosis. *J Cyst Fibrosis*. 2019;18(3):430-435.
4. Denford S, van Beurden S, O'Halloran P, et al. Barriers and facilitators to physical activity among children, adolescents, and young adults with cystic fibrosis: a systematic review and thematic synthesis of qualitative research. *BMJ Open*. 2020;10(2):e035261.
5. Alvarez JA, Ziegler TR, Millson EC, Stecenko AA. Body composition and lung function in cystic fibrosis and their association with adiposity and normal-weight obesity. *Nutrition*. 2016;32(4):447-452.
6. Pedreira CC, Robert RG, Dalton V, Oliver MR, Carlin JB. Association with body composition and lung function in children with cystic fibrosis. *Pediatr Pulmonal*. 2005;39(3):276-280.
7. Sheikh S, Zemel BS, Stallings VA, Rubenstein RC, Kelly A, Body composition and pulmonary function in cystic fibrosis. *Front Pediatr*. 2014;2(33):1-6.
8. Gibson HT, McDonald CM, Derrick JW, Eggett DL, Bellini SG. Evaluating changes in hand grip strength in children with cystic fibrosis: a pilot study. *Nutr Clin Prac*. 2018;33(2):261-267.
9. Miller RM, Chambers TL, Burns SP. Validating InBody® 570 multifrequency bioelectrical impedance analyzer versus DXA for body fat percentage analysis. *J Exercise Physiol*. 2016;19(5):71-78.
10. Charatsi AM, Dusser P, Freund R, et al. Bioelectrical impedance in young patients with cystic fibrosis: validation of a specific equation and clinical relevance. *J Cyst Fibros*. 2016;15(6):825-833.
11. Bohannon RW. Is it legitimate to characterize muscle strength using a limited number of measure? *J Strength Cond Res*. 2008;22(1):166-173.
12. Wind AE, Takken T, Helders PJ, Engelbert RN. Is grip strength a predictor for total muscle strength in healthy children, adolescents, and young adults? *Eur J Pediatr*. 2010;169(3):281-287.
13. Bouma S, Peterson M, Gatza E, Choi SW. Nutritional status and weakness following pediatric hematopoietic cell transplantation. *Pediatr Transplant*. 2016;20(8):1125-1131.
14. Mathiowetz V, Wiemer DM, Federman SM. Grip and pinch strength: norms for 6-to 19-year-olds. *Am J Occup Ther*. 1986;40(10):705-711.
15. Silva C, Amaral TF, Silva D, Oliverira BM, Guerra A. Handgrip strength and nutrition status in hospitalized pediatric patients. *Nutr Clin Pract*. 2014;29(3):380-385.
16. American Society of Hand Therapists. *American Society of Hand Therapists Clinical Assessment Recommendations*. Accessed August 26, 2020. 1st ed. American Society of Hand Therapists manual; 1981.
17. Mathiowetz V, Weber K, Volland G, Kashman N. Reliability and validity of grip and pinch strength evaluations. *J Hand Surg [Am]*. 1984;9(2):222-226.
18. Roberts HC, Denison HJ, Martin HJ, et al. A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. *Age Ageing*. 2011;40(4):423-429
19. Wang YC, Bohannon R, Li X, Yen SC, Sindhu B, Kapellusch J. Summary of grip strength measurements obtained in the 2011–2012 and 2013–2014 National Health and Nutrition Examination Surveys. *J Hand Ther*. 2019;32(4):489-496.

20. Peterson MD, Krishnan C. Growth charts for muscular strength capacity with quantile regression. *Am J Prev Med*. 2015;49(6):935-938.
21. Bin CM, Flores C, Álvares-da-Silva MR, Francesconi CFM. Comparison between handgrip strength, subjective global assessment, anthropometry, and biochemical markers in assessing nutritional status of patients with Crohn's disease in clinical remission. *Dig Dis Sci*. 2010;55(1):137-144.
22. Norman K, Stobäus N, Gonzalez MC, Schulzke J-D, Pirlich M. Hand grip strength: outcome predictor and marker of nutritional status. *Clin Nutr*. 2011;30(2):135-142.
23. Guerra RS, Fonseca I, Pichel F, Restivo MT, Amaral TF. Handgrip strength and associated factors in hospitalized patients. *JPEN*. 2015;39(3):322-330.
24. Mathiowetz V, Kashman N, Volland G, Weber K, Dowe M, Rogers S. Grip and pinch strength: normative data for adults. *Arch Phys Med Rehabil*. 1985;66(2):69-74.
25. Peterson MD, Saltarelli WA, Visich PS, Gordon PM, Strength capacity and cardiometabolic risk clustering in adolescents. *Pediatrics*. 2014;133(4):e896-e903.