Title page

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

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Abstract

Compared to 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 nutritional status. This Quality Improvement (QI) project explored the feasibility of measuring GS in medically stable youth with CF, ages 6-21 years old. Three hundred sixty-one (361) GS measurements were performed using a digital hand dynamometer in youth from a single CF center. Using reference tables which were created for this project by merging data from the 2011-2012 and 2013-2014 National Health and Nutrition Examination Surveys (NHANES), youth with CF were found to be weaker than age and gender matched peers, even when controlled for differences in size. A positive association ($p < 0.001$) was found between GS percentile and lung function as measured by Forced Expiratory Volume in one second percent predicted (FEV1pp). Statistical analysis revealed that both BMI percentile and absolute GS percentile were positively associated with FEV1pp and with each other, primarily at the lower levels of BMI percentile (< 50%) and absolute GS percentile (<50%). GS may provide a reliable, less expensive and clinically feasible alternative to body composition measurements in monitoring nutritional status in youth with CF, especially in youth whose BMI is < 50th percentile.

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

Introduction

Nutritional 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 or above since 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) nor does it allow the identification of non-obese 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 displacement plethysmography (ADP) 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 (TSF) and mid-arm circumference (MAC) to calculate arm muscle area (AMA) has a wide margin of error and measurements are often unreliable due to low interrater reliability.[8] Bioelectrical impedance analysis (BIA), even when using the more expensive multi-frequency BIA machines ($5000-19,000 USD), also have reliability issues. A recent validation study of 110 recreationally active 18-25 year old adults found that BIA measured a 4-9% difference in percent body fat compared to DEXA, with BIA tending to underestimate percent body fat compared to 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 to 12 hours and avoid exercise 6 to 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 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 (e.g. $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 intra- and inter-tester reliability and validity as studied in multiple disciplines and populations.[8, 13]

While GS measures have been used in children without CF,[13, 14, 15] there is only one small, pilot study which measured GS in 23 children with CF (ages 6–18 years).[8] In this pilot study, GS measurements were taken 5 months before, days 5-7 during a hospital admission for pulmonary exacerbation and then again about 6 weeks post-hospitalization. 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 has been reported in a larger sample of medically stable, non-hospitalized children with CF. . Moreover, associations between 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 with CF who are medically stable and compare it to their peers without CF, using robust, normative GS reference tables which were created for this project by merging population-level reference data from the 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 between GS, lung function and BMI in children with CF who are medically stable.

Methods

Study Population

Two hundred and one (201) children with CF, ages 6–21 years old, were included in this QI project which measured GS, BMI and pulmonary function (as measured by FEV1pp). The CF diagnosis was confirmed via 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 children also had a follow up GS measurement. This QI project was approved by the Institutional Review Board.

Study Design and Measurement

Anthropometric data was 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 using a wall-mounted stadiometer (Holtain Limited, fitted with a Veeder-Root counter, Crymych, Dyfed, Britain). Weights, with the individuals wearing street clothes, but no shoes or outer garments, were measured within 100 grams using a digital scale (Scale-tronix, serial #6702 5913, White

Plains, NY,). Both the stadiometer and the scale are inspected and maintained by the Biomedical Technical Service. BMI is calculated using weight in kilograms (kg) divided by height in meters squared (m^2).

One of two registered dietitians measured each individual's GS with a Jamar Plus+ digital hand dynamometer (Patterson Medical, Warrenville, IL) which is recalibrated yearly by the manufacturer. Per standard protocols, individuals must be at least 6 years old in order to be physically and developmentally ready to accurately follow the instructions for measuring GS. The American Society of Hand therapists' measurement protocol as described by Mathiowetz is associated with a high intra-test and inter-test reliability and was used for this project.[16,17] Individuals were in a seated position with their shoulders adducted, elbow flexed at 90 degrees, 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 10-15 sec 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, age 6-19 years old.[19] This data set represents 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 Hispanic persons and non-Hispanic black and Asian persons as well as persons who identified as non-Hispanic white or "other" and were at or below 130 percent of poverty level or 80 years and older (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 grip strength protocol, the highest measurement from either hand was used to determine the age and gender specific percentile for absolute grip strength (ABS). Normalized grip strength (NGS) was calculated by dividing ABS by body weight in kg 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 is presented in four (4) reference tables: ABS for boys, ABS for girls, NGS for boys and NGS for girls. (See Supplementary Material: Tables S1-S4)

Statistical Analysis

Reference percentiles were calculated using SAS version 9.4, and all other analyses were done using R version 3.6.1. Grip strength percentiles were calculated using the combined 2011-2012 and 2013-2014 NHANES datasets of muscle strength, body measures and demographics. The highest grip strength measurement in kg from either hand (ABS) was used for percentile estimates for males and females in each 1-year age increment from 6 to 19 years. Sample weights were used to account for complex survey design (including survey oversampling), survey non-response, and post-stratification. The sample weights from the two survey cycles were combined according to the procedures outlined at 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 standard errors for most percentile estimates in each age-sex grouping. The estimated percentiles were used to transform the raw grip strength measurements from this project into percentiles. Pearson correlations and two sample t-tests were used to assess the associations of ABS, NGS, and BMI percentiles with FEV1pp. One sample t-tests were used to examine the change scores from the first to second study assessments. Plotting and LOESS curve fitting were used to visualize the association of FEV1pp, BMI and group strength and their percentiles. To examine the independent association of grip strength and BMI with FEV1, the sample was stratified at the median and at the quartile of BMI and ABS percentiles, and correlations were calculated within each stratum. For all tests, p value of < 0.05 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 6-21 years old at the time of the project. Three hundred and sixty-one 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 and adolescents 6-19 years old, were available for 186 individuals. Fifteen individuals were 20 years old or older at the time of the initial measurement so were not included in analyses which used BMI percentile.

One hundred and sixty out 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 (i.e. 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 due to time constraints, 3 were not measured due to 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).

Overall, the youth with CF that were tested were found to be weak for their age and gender compared to their peers without CF. Forty percent of the 6-19 year old group (75 out of 186 individuals) were very weak (ABS $\leq 10^{th}$ percentile). When these 75 very weak individuals were divided into two groups by BMI (BMI $< 50^{th}$ percentile: n = 31; BMI $\geq 50^{th}$ percentile: n = 44), the difference between the groups was not statistically significant. [Table 3]

When normalizing grip strength by dividing ABS by weight, individuals with a BMI < 50% percentile were significantly stronger for their size at any given age than individuals with a BMI $\geq 50^{th}$ percentile. Moreover, 40.7% of individuals with a BMI $\geq 50^{th}$ percentile were weak for their size (NGS percentile of $< 25^{th}$) compared with only 20.6% of individuals with a BMI $< 50^{th}$ percentile. [Table 3]

The ABS percentile was positively associated with FEV1pp across all BMI percentiles ($p < 0.001$), even when the BMI percentiles were divided into two groups: BMI <

50%ile ($p < 0.002$) and BMI ≥ 50%ile ($p <0.05$.) [Table 4] When the group was divided into four BMI subcategories, this correlation continued to be statistically significant for those with a BMI < 25th percentile ($p < 0.022$). This suggests that individuals who have a low BMI (< 25%ile) but a high ABS may be at an advantage in term of respiratory status as determined by FEV1pp.

NGS percentile was also positively associated with FEV1pp across all BMI percentiles ($p<0.001$), but this significance did not hold when divided into BMI percentile subcategories. [Table 4].

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

Discussion

Our QI project presents the largest data set to date of GS measurements in medically stable youth 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 and adolescents were receptive, and even excited, to show how strong they were by performing GS measurements using a hand dynamometer. The American Society of Hand Therapists protocol 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 less than 5 minutes in the clinic setting. Only 8 individuals (5%) out 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 was merged to form robust, normative GS reference tables which reflect contemporary ethnic, educational and economic diversity.[19] This is in contrast to the Mathiowetz data which was taken from a 7 county area near Milwaukee, Wisconsin in 1984. Table 1 compares the GS reference data that is currently available. Wang et. al. found that NHANES grip strength 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 breakdown the age categories into 1 year rather than 2 year increments and the percentiles into 5% increments rather than larger ones, resulting in 14 centiles as opposed to 7 centiles as in Peterson's table.[20] A more granular data reference set and a larger sample size (n = 186) likely allowed for statistical significance between FEV1pp and GS percentile where Gibson's pilot study (n = 23) did not.[8] Clinically, these new GS reference tables can be effectively used to determine cut offs 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 ≥ 50^{th} percentile but they have an ABS ≤ 10^{th} 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 lean body mass.

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 Gibson's sample (n = 23).[8] Whereas Gibson's sample 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 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 Gibson's sample who had a mean BMI *z score* of only -0.17 +/- 0.63 five months prior to hospitalization and +0.06 +/- 0.54 six weeks after hospitalization.

Our findings are congruent with Gibson's study that showed children with CF are weak compared to their peers of the same gender and age. Using the Mathiowetz reference data from 1985, Gibson 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 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).

ABS is defined as the largest value from either hand after taking a total of 3 altering measurements on each hand. ABS percentile describes how strong someone is for their age, compared to their peers of the same age and gender. Forty percent of individuals age 6 –19 years old had an ABS of ≤ the 10th percentile (75 out of 186). [Table 3] In a normal study population, one would expect only 10% of the population to have a ABS ≤ 10th percentile. According to a small study in medically stable pediatric patients who were s/p bone marrow transplant (BMT), a ABS < 10th percentile was correlated with weakness and poor nutritional status ($P < 0.05$).[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 a FEV1pp.[7] Comparatively, our GS project shows ABS, a surrogate for LBM, is positively associated with FEV1pp. A patient who is strong for their age (high ABS) is more likely to have a higher FEV1pp than someone who is weak for their age (low ABS). Moreover, this is especially true for children and adolescents with a lower BMI (< 50%ile). [Figure 1B] This finding is strikingly similar to the results reported by Sheikh et. al. which also revealed that LBM index is more strongly associated with pulmonary function compared to BMI, especially in individuals with lower BMIs (< 50%ile).[7] The clinical implications of this finding is that if a child or adolescent has a BMI < 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 ABS percentile is also positively associated FEV1pp. [Figure 1B]. Both ABS percentile and BMI percentile were positively associated with FEV1pp and with each other, but primarily at the lower levels (<50%ile). The clinical implications of this finding is to continue to try to achieve a goal of BMI ≥ 50%ile (especially if ABS is < 50%ile), but also work to achieve ABS ≥ 50%ile (especially if BMI is < 50%ile).

NGS percentile describes the strength of someone in relation to their size, compared to peers of the same age and gender. Thirty-three percent of the 6-19 year olds had a NGS < 25th percentile (62 out of 186). [Table 3] According to the study which looked at medically stable pediatric patients who were s/p bone marrow transplant, a NGS < 25%ile percentile for age and gender distinguished an "over-nutrition" group from the "normal nutrition" group (P < 0.05). Over-nutrition, as defined by the pediatric BMT study, meant a BMI z score ≥ 1, i.e. BMI ≥ 85th percentile, sedentary 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.[24] Our findings suggest that as BMI increases in youth with CF, grip strength 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 in order 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 increasing body fat. Clinicians can encourage youth to “eat like an athlete,” i.e. 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 grip strength. This information can be used in future interventions studies as evidence that the intervention, and not the testing itself, was likely responsible for changes in GS. In order 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 nutritional status in youth with CF, especially in youth whose BMI is < 50th percentile. Merging two 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.

Supplementary Material

Reference Charts for Grip Strength in Children and Young Adults Ages 6-19 years, Tables S1 – S4 are available online at http://ncp.sagepub.com

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):583-91.

[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, Tran PH, Tangpricha V, Hunt W, Stecenko A, Ziegler T, Alvarez J. Visceral adipose tissue is associated with poor dietary quality and higher fasting glucose in adults with cystic fibrosis. *J Cyst Fibrosis* 2019; 18:430-435.

[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:e035261. doi:10.1136/ bmjopen-2019-035261

[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 Multi-frequency Bioelectrical Impedance Analyzer versus DXA for Body Fat Percentage Analysis. *Journal of Exercise Physiology* 2016;19(5):71-78.

[10] Charatsi AM, Dusser P, Freund R, Maruani G et. al. Bioelectrical impedance in young patients with cystic fibrosis: Validation of a specific equation and clinical relevance. *Journal of Cystic Fibrosis* 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;169:281-287.

[13] Bouma S, Peterson M, Gatza E, Choi SW. Nutritional status and weakness following pediatric hematopoietic cell transplantation. *Pediatric Transplantation* 2016;20(8):1125-1131. doi:10.1111/petr.12821

[14] Mathiowetz V, Wiemer DM, Federman SM. Grip and pinch strength: norms for 6-to 19-year-olds. *American Journal of Occupational Therapy* 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;29:380-385.

[16] Fess E, Moran C. American Society of Hand Therapists Clinical Assessment Recommendations. 1981. American Society of Hand Therapists manual.

[17] Mathiowetz V, Weber K, Volland G, Kashman N. Reliability and validity of grip and pinch strength evaluations. *The Journal of hand surgery* 1984; 9(2): 222-226.

[18] Roberts HC, Denison HJ, Martin HJ, Patel HP, Syddall H, Cooper C *et al.* A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. *Age and 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. *Journal of Hand Therapy* 2019;32(4):489-496.

[20] Peterson MD, Krishnan C. Growth Charts for Muscular Strength Capacity With Quantile Regression. *American Journal of Preventive Medicine* 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. *Digestive Diseases and Sciences* 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. *Clinical nutrition* 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] Peterson MD, Saltarelli WA, Visich PS, Gordon PM, Strength capacity and cardiometabolic risk clustering in adolescents. *Pediatrics* 2014;133:e896-e903.

[25] 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; 66:69-74.

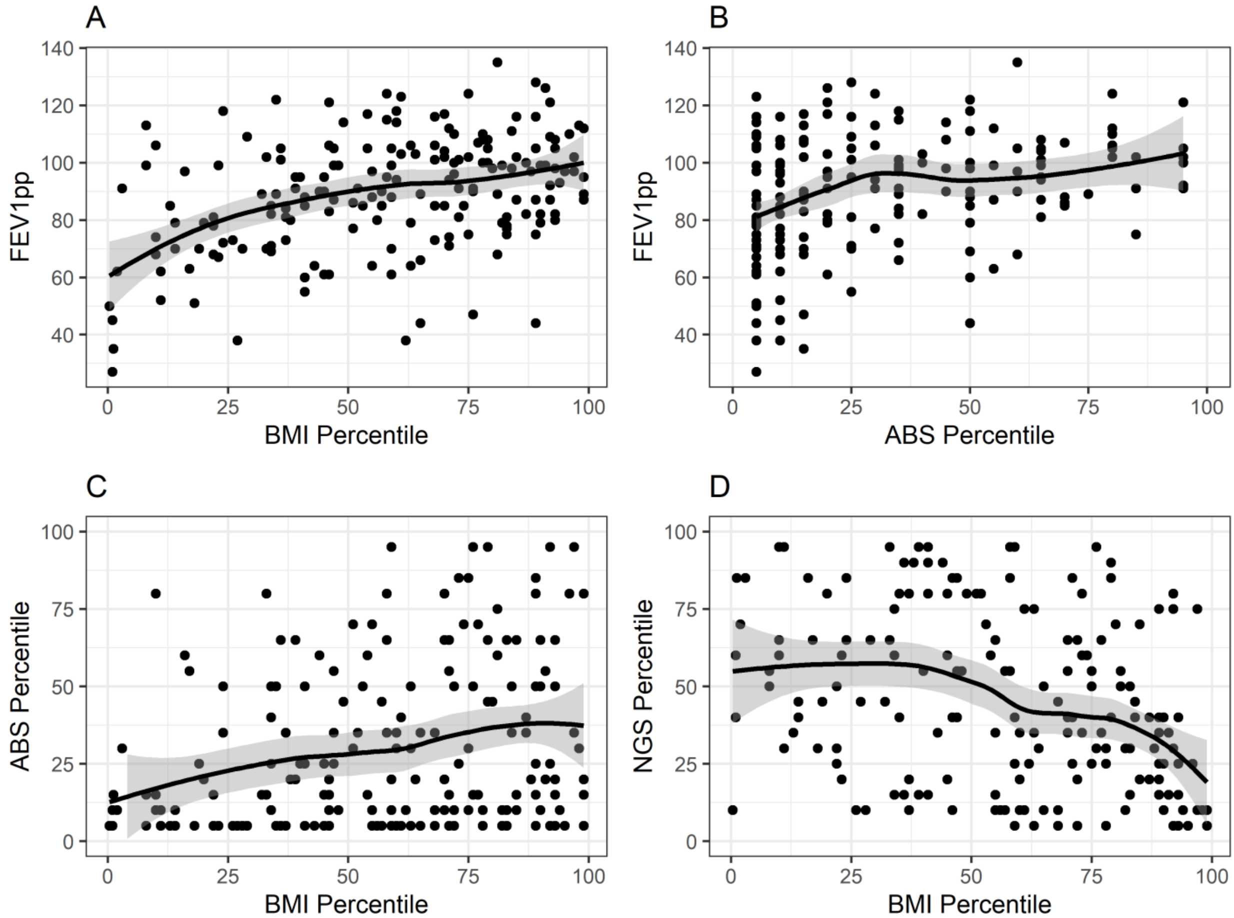

Fig. 1. Associations between Forced Expiratory Volume in One Second Percent Predicted (FEV1pp), Absolute Grip Strength (ABS) Percentile, Normalized Grip Strength (NGS) Percentile and Body Mass Index (BMI) Percentile. (A) FEV1pp and BMI percentile, (B) FEV1pp and ABS Percentile, (C) ABS Percentile and BMI Percentile, (D) NGS Percentile and BMI Percentile

Reference Data Set	Population used	Age range	Years data was collected	Number of individuals (6-19 years old) included	Measurement used	Method of evaluating
Reference data that comes with the Jaymar Digital dynamometer (Mathiowetz 1985/1986)[14, 25]	Healthy School Children & Adults from a 7 county Milwaukee, WI area	6 – 75+ years old	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 old	2011-2012	2431 (Total sample including adults = 7119)	Highest measurement out 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 old	2011-2012 & 2013-2014	4672 (Total sample including adults = 13,676)	Highest measurement out of 6 measurements (3 from each hand)	14 Quantile ranges (5% increments from 5% to 95%; i.e. 5%, 10%, 15%, 20%, etc.)

Table 1: Comparison of Three U.S. Reference Data Sets for Grip Strength

Table 2. Descriptive Statistics of Project Participants

N =	201
Age (mean (SD))	13.25 (4.57)
Gender = female (%)	99 (49.3)
Height (m) (mean (SD))	1.48 (0.20)
Weight (kg) (mean (SD))	45.29 (17.07)
BMI (kg/m2) (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 (kg) (mean (SD))	18.49 (10.28)
Average GS – right hand (kg) (mean (SD))	20.43 (11.06)
ABS (kg) (mean (SD))	22.21 (11.86)
ABS 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 (%)	
heterozygous	73 (36.3)
homozygous	103 (51.2)
other	25 (12.4)
Sweat (mmol/L) (mean (SD))	95.44 (21.18)

GS, Grip Strength; BMI, Body Mass Index; FEV1pp, Forced Expiratory Volume in one second percent predicted; ABS, Absolute Grip Strength; NGS, Normalized Grip Strength, i.e. ABS/Weight (kg)

Table 3. Comparison of FEV1 and Grip Strength parameters for two 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)	<0.001*
Right average GS (kg) (mean (SD))	19.43 (10.47)	19.25 (10.49)	0.914
Left average GS (kg) (mean (SD))	18.08 (9.93)	17.11 (9.45)	0.512
ABS (kg) (mean (SD))	21.31 (11.45)	20.78 (10.92)	0.757
NGS (mean (SD))	0.51 (0.13)	0.44 (0.11)	<0.001*
ABS <=10%ile = yes (%)	31 (45.6)	44 (37.3)	0.339
NGS <25%ile = yes (%)	14 (20.6)	48 (40.7)	0.008*
Right GS *z score* [a]	-1.81 (0.97)	-1.4 (1.21)	0.017*
Left GS *z score* [a]	-1.5 (0.98)	-1.26 (1.22)	0.173

GS, Grip Strength; BMI, Body Mass Index; FEV1pp, Forced Expiratory Volume in one second percent predicted; ABS, Absolute Grip Strength; NGS, Normalized Grip Strength, i.e. ABS/Weight (kg); *p< 0.05

[a]Using the Mathiowetz reference data for comparison purposes[14]

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
ABS percentile (Strength for age)	All	186	0.294	0.157	0.420	<0.001*
	[0-49)	68	0.377	0.152	0.565	0.002*
	[50-100)	118	0.181	0.000	0.350	0.050*
	[0-24)	28	0.431	0.069	0.693	0.022*
	[25-49)	40	0.290	-0.024	0.552	0.070
	[50-74)	54	0.238	-0.031	0.476	0.083
	[75-100)	64	0.111	-0.139	0.347	0.384
NGS percentile (Strength for age & size)	All	186	0.294	0.157	0.420	<0.001*
	[0-49)	68	0.199	-0.041	0.418	0.103
	[50-100)	118	0.117	-0.065	0.292	0.206
	[0-24)	28	0.177	-0.210	0.516	0.368
	[25-49)	40	0.232	-0.086	0.507	0.150
	[50-74)	54	0.182	-0.090	0.429	0.189
	[75-100)	64	0.095	-0.155	0.333	0.457

GS, Grip Strength; BMI, Body Mass Index; FEV1pp, Forced Expiratory Volume in one second percent predicted; ABS, Absolute Grip Strength; NGS, Normalized Grip Strength, i.e. ABS/Weight (kg); *p≤ 0.05