










Original Research

Reduced handgrip and inspiratory muscle strength are associated with lower lung function and physical capacity in children and adolescents born preterm with very low birth weight



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ABSTRACT

Background: Individuals born preterm exhibit reduced physical capacity and muscle strength, along with cardiometabolic alterations, increasing the risk of early-onset chronic diseases. Data on muscle function and physical capacity in young individuals born preterm, especially those born in low- and middle-income countries, remain limited.

Objective: To compare handgrip and inspiratory muscle strength, lung function, and physical capacity in children and adolescents born preterm with very low birth weight (VLBW) to their term-born peers.

Methods: This cross-sectional study recruited 69 individuals born preterm with VLBW (<1500 g) and 59 peers born at term aged between 8 and 13 years. Assessments included bioelectrical impedance analysis for fat-free mass (FFM), inspiratory muscle strength (IP_{max}), handgrip strength, spirometry and six-minute walk test.

Results: Preterm group showed significantly lower IP_{max} of 12.8 cmHO [95% confidence interval(CI): 4.0, 21.5] compared with the term-born group (-78.7 vs. -91.5 cmH₂O), even after adjusting for sex or FFM, and significantly lower handgrip strength of 1.6 kg [95%CI: 0.04, 3.2] (15.5 vs. 17.2 Kg), even after adjusting for sex (not for FFM). Preterm group showed reduced lung function. Walk test was similar between groups. For the preterm group, a higher handgrip and inspiratory muscle strength were associated with higher lung function and longer walk distance.

Conclusion: Children and adolescents born preterm with VLBW had reduced strength, which was associated with lower lung function and physical capacity. These findings suggest that interventions targeting muscle function may be a potential strategy to improve respiratory health and overall physical capacity in this high-risk population.

Introduction

The prevalence of preterm birth in Brazil is 11.1%, positioning the country among the 10 nations with the highest prevalence of preterm births worldwide.¹ Individuals born preterm (<37 weeks' gestational

age), and especially those with very low birth weight (VLBW), experience long-term physical and neurodevelopmental impairments,²⁻⁴ increasing their risk for chronic health conditions⁴⁻⁷ and all-cause mortality as they reach adulthood.⁸

Recent studies indicate that individuals born preterm have reduced

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exercise capacity compared to term-born controls,^{9,10} which may be associated to altered motor abilities,¹¹ lower lean mass,¹² and adverse skeletal muscle adaptation.¹³ The latter may result from: early-life exposure to oxidative stress and inflammation due to preterm birth,^{14,15} lower insulin sensitivity and insulin-like growth factor-1 levels resulting in lower muscle protein synthesis;^{13,16} as well as increased muscle stiffness.¹⁷ Also, experimental models of preterm birth show muscle atrophy, fiber type switching (from type I to type IIb, which favors inflammation), and reduced mitochondrial oxidative capacity as signs of skeletal muscle adaptation.^{18,19} Clinical studies have shown that skeletal muscle mass and strength are affected by preterm birth, which in turn impacts exercise capacity.^{17,20,21} However, data on the impact of preterm birth on physical health, muscle strength, and cardiopulmonary function in young individuals remain scarce—particularly for those born preterm in low- and middle-income countries.^{22–27}

We hypothesize that children and adolescents born preterm with VLBW have reduced muscle strength, physical capacity, and lung function compared to term-born peers. The primary aim of the study was to compare handgrip and inspiratory muscle strength, along with lung function and physical capacity, between children and adolescents born preterm with VLBW and in term-born controls. We further aimed to identify whether neonatal characteristics (such as gestational age, birth weight, bronchopulmonary dysplasia diagnosis, number of days in mechanical ventilation) or current ones (fat-free mass, body mass index) were associated with muscle strength, lung function, and physical capacity.

Methods

Study design and population

We performed a cross-sectional observational study including

children and adolescents between 8 and 13 years of age born preterm with VLBW (< 1500 g) (preterm group) at our institution, a tertiary public university hospital in Southern Brazil. The hospital is a reference center for neonatal care and outpatient multiprofessional follow-up of high-risk preterm infants born before 32 weeks of gestation or with VLBW. These patients are monitored until five years of age. The preterm group was compared with children born at term (GA \geq 37 weeks and birth weight >2500 g), also delivered at our institution, to ensure access to complete perinatal records. All participants were born between 2008 and 2012. From 2008 to 2012, the neonatal care team recorded an average of 53 live births <1500 g annually. From 2020 to 2024, the neonatal team has recorded 76 live births <1500 g annually, along with 1040 yearly outpatient visits to the preterm follow-up clinic.

Matching preterm to term infants was based on the year of birth. We began recruitment with children born in 2008, based on available contact information in the outpatient database. The detailed recruitment process is presented in the [Supplementary Material](#), and participant flow is shown in [Fig. 1](#). Exclusion criteria for both groups were: major neurocognitive or physical impairments, and genetic syndrome or congenital malformations preventing assessments. Preterm children without VLBW were not eligible. Children older than 14 years at evaluation were also excluded due to age- and sex-associated changes in strength.²⁸

The study was approved by the Institution's Research Ethics Committee (number: 2019-0571; CAAE:20371119.6.0000.5327). All parents or guardians gave written consent for their children to participate. At the end of the recruitment conversation, parents were strongly encouraged to read the Informed Consent Form together with their children. Children gave verbal assent to participate in the study. They were assessed at the Clinical Research Center of our institution from March 2020 to September 2023.

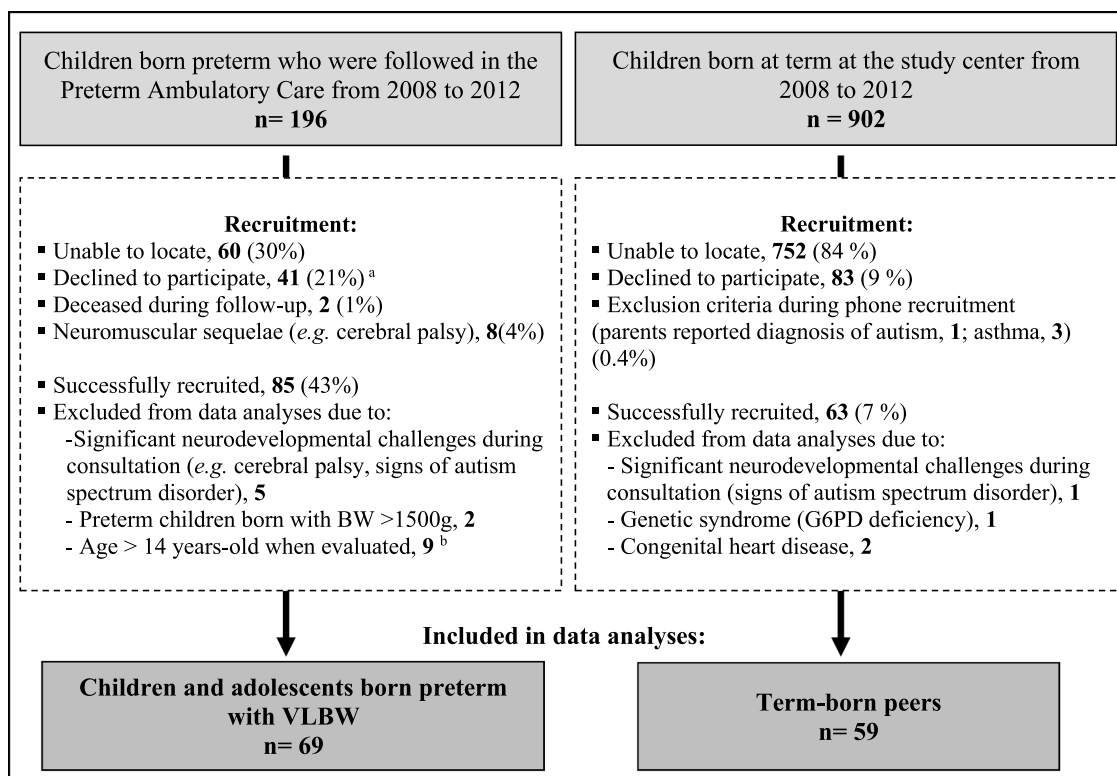


Fig. 1. Flowchart of the recruitment process for children and adolescents born preterm with very low birth weight (VLBW) and term-born peers from a public hospital in Southern Brazil.

^a The main reason reported from parents to not participate was their fear due to Sars-Cov-2 transmission (COVID-19). ^b Adolescents aged 14 years and older were not included due to age- and sex-associated differences in muscle²⁸ strength.

Anthropometric data

Body weight (scale Balmak-ELP-25BB) and height (Holtain stadiometer with veeder-root counter) were measured, and body mass index (BMI-for-age) was calculated using the application *WHO AnthroPlus* software. The bioelectrical impedance analysis device (InBody-770® - Biospace, South Korea) was used to assess fat-free mass (FFM), FFM Index (kg/m^2), and skeletal muscle mass, with the child wearing light clothes.

Lung function

Forced vital capacity (FVC), forced expiratory volume at the first second (FEV_1), FEV_1/FVC ratio, and forced expiratory flow 25–75% (FEF_{25-75}) were measured following ATS/ERS recommendations²⁹ with a portable spirometer Datospir Micro-C (Sibelmed, Spain; using a bacterial viral filter). Z-score was calculated following the Global Lung Function Initiative (GLI). Reduced lung function was defined as a z-score below -1.645 (the 5th percentile of a standard Gaussian distribution, which defines the lower limit of normal). The bronchodilator responsiveness test was performed with 400mcg of salbutamol using a volumetric spacer, and positive BD response was defined as FEV_1 and/or FVC changed $>10\%$ of the predicted value.²⁹ Flow-volume curves were evaluated by an independent pediatric pulmonary expert.

Physical capacity

Six-minute walk test (6MWT) was performed in a 30-m long corridor, following the ATS guidelines.³⁰ Vital signals were assessed at rest and immediately after the test. The predicted total distance was calculated using a multinational equation for all participants,³¹ and a Brazilian equation for children aged 6–12 years.³² As part of the physical activity evaluation, parents were asked how many hours per week their child engages in activities that are strenuous enough to cause sweating and fatigue, which was considered as moderate to intense physical activity.

Inspiratory muscle strength

Maximal inspiratory pressure (IP_{max}) was measured using an analogic manovacuometer (Murenas/Brazil, $+300/-300$ cmH_2O).^{33,34} The instrument was connected to a silicone tube, coupled to an isolating filter (pressure transducer TP41; GVS-Brazil) and to an inspiratory force adaptor (Rescal, internal diameter 15 mm and one extra-orifice of 1 mm to prevent the increase of intraoral pressure), which was connected to the mouthpiece. The measurements were performed in a sitting position, with both feet on the ground and the trunk at 90° , using a nose clip during the maneuvers. IP_{max} measurement was performed from the beginning of the residual volume, and the average of the three highest values with a variation of <10 cmH_2O was considered. Three to six maneuvers were performed, with 50–60 s between repetitions or until the child fully recovered. Predicted values were calculated from a multicenter study of healthy children aged 6 to 18 years.³⁵

Peripheral muscle strength

Handgrip was measured with an electronic dynamometer (Camry-EH-101, China). The test was performed with the participants sitting upright in an armless chair, with feet resting fully on the ground (knee at 90°). The tested arm was resting at the sides of the body, with shoulder abducted at a $5-10^\circ$ angle, not touching the rib cage, and elbows flexed at a 90° angle, forearms in a neutral position.³⁶ The opposite hand rested on the contralateral thigh. Three to six repetitions were performed to achieve three maximal contractions, with 50–60 s rest between sets and verbal encouragement. Results are presented as the mean of the three highest handgrip scores from the dominant, non-dominant arms and total handgrip (sum of both arms), based on supporting studies.³⁷⁻³⁹

Moreover, the results from the dominant hand were compared with reference values from healthy Brazilian children and adolescents ([Supplementary material](#)).³⁶

Neonatal and perinatal data

Neonatal characteristics of preterm children were collected from the medical charts: birth weight, gestational age (GA) (evaluated by the last menstrual period and confirmed by early obstetrical ultrasound until the end of the first trimester), small for GA (SGA, <10 th percentile; peditools.org/fenton2013/), necrotizing enterocolitis, *peri*/intraventricular hemorrhage (PIVH), leukomalacia, late-onset neonatal sepsis (positive blood or cerebrospinal fluid cultures), patent ductus arteriosus (PDA), and the number of days in mechanical ventilation. Bronchopulmonary dysplasia (BPD) was defined by the need of ventilatory support in the 36th post-menstrual week.⁴⁰ The same neonatal data of the term-born children was also collected.

Statistical analysis

The sample size to compare the means of IP_{max} and handgrip between preterm and term groups was calculated at 130 children, obtaining a power of 80% and significance level of 5%, based on a standard deviation of IP_{max} and handgrip of 26.1 cmH_2O ³⁴ and 7.96 kg,³⁶ respectively, with a mean difference of 10 cmH_2O and 3.5 kg. The power calculation was done using a PSS calculator.⁴¹ Comparison between preterm versus term-born groups was performed with Student's *t*-test (normally distributed variables), Mann-Whitney test (skewed distribution variables), and Chi-squared or Fisher's exact test for categorical data. Analyses were adjusted for sex and/or FFM, reporting as mean difference (MD) and 95% Confidence Interval (CI). Due to multicollinearity between height and FFM, only FFM was included as an independent variable. Linear regression models examined associations of the neonatal (birth weight and GA) and anthropometric (BMI and FFM) variables with functional outcomes (muscle strength, physical capacity, and lung function), within each group. Additional models explored relationship between inspiratory muscle strength with lung function and physical capacity, as well as handgrip strength with lung function and physical capacity, all adjusted for FFM. Regression assumptions were verified. Correlation analysis between functional, neonatal, and current characteristics are presented in [Supplementary Table S2](#). Children with overweight (BMI-for-age) are presented separately from eutrophic participants in [Supplementary Table S3](#). Analyses were performed using SPSS 18.0 (IBM® SPSS® Statistical, USA). The significance level was set as 0.05.

Results

Characteristics of the studied population

A total of 128 children and adolescents were included, 69 born preterm with VLBW, and 59 term-born peers ([Fig. 1](#)). The main clinical characteristics of the participants are shown in [Table 1](#). The mean age of the preterm and term-born participants evaluated was 11 years. The preterm group had significantly lower weight, height z-score, BMI-for-age, FFM, and skeletal muscle mass when compared to the term-born group ([Table 1](#)).

Lung function

The preterm group showed significantly lower z-score of FEV_1 , FVC, and FEF_{25-75} compared to term-born group ([Table 2](#)). Preterm individuals with BPD exhibited even lower lung function z-score values compared to the term-born group ([Supplementary Table S1](#)). Lung function below the lower limit of normal was more frequent among participants in the preterm group compared to the term-born group

Table 1

Characteristics of children and adolescents born preterm with very low birth weight and term-born peers in Southern Brazil.

Current characteristics, n	Preterm group 69	Term-born group 59	P value
Current age	11.1 (1.4)	11.0 (1.2)	0.619
Sex (male/female)	31/38	33/26	0.215
Body weight, kg	38.3 (33.0, 44.7)	46.5 (33.9, 55.8)	0.008
Height, cm	145.9 (9.3)	147.9 (10.0)	0.245
Height z-score	0.10 (0.92)	0.50 (1.12)	0.030
Body mass index (BMI), kg/m ²	17.5 (16.0, 20.6)	20.3 (16.7, 25.2)	0.007
BMI z-score	0.22 (1.46)	1.08 (1.63)	0.002
Fat-free mass (FFM), kg	30.1 (5.6)	32.8 (7.1)	0.018
FFM index (FFMI), kg/m ²	14.0 (1.2)	14.8 (1.8)	0.005
Skeletal muscle mass, kg	15.8 (3.3)	17.3 (4.2)	0.019
Sociodemographic characteristics			
Ethnicity			0.167
Caucasian, n (%)	44 (63.8%)	40 (67.8%)	-
African American, n (%)	13 (18.8%)	15 (25.4%)	-
Pardo (Other/Mixed-race), n (%)	12 (17.4%)	4 (6.8%)	-
Maternal educational level, years	11 (6.5, 11)	11 (11, 11)	0.005
Family income (Brazilian real) (x1000)	2.5 (1.8, 3.9)	3.6 (2.4, 4.9)	0.006
Maternal current smoking, n (%)	13 (18.8%)	16 (27.6%)	0.242
Children - secondhand smoke, n (%)	21 (30.4%)	28 (48.3%)	0.040
Neonatal characteristics			
Gestational age (GA), weeks	29.9 (2.2)	38.9 (1.0)	0.001
Birth weight (BW), g	1155 (236)	3277 (479)	0.001
Small Gestational Age (SGA), n (%)	15 (24.6%)	8 (14.0%)	0.249
Maternal age, years	27 (7)	27 (6)	0.633
Use of Surfactant, n (%)	41 (59.4%)	-	-
Mechanical ventilation, days	1 (0, 15)	-	-
Bronchopulmonary Dysplasia (BPD), n (%)	18 (26.1%)	-	-
Periventricular hemorrhage (PIVH), n (%)	17 (24.6%)	-	-
Periventricular leukomalacia (PVL), n (%)	4 (5.8%)	-	-
Patent ductus arteriosus, n (%)	18 (26.1%)	-	-
Necrotizing enterocolitis, n (%)	7 (10.1%)	-	-
Confirmed late onset sepsis, n (%)	22 (31.9%)	-	-
Newborn jaundice, n (%)	-	32 (54.2%)	-
Neonatal infection (antibiotic therapy), n (%)	-	5 (8.5%)	-
Transient tachypnea of the newborn, n (%)	-	6 (10.2%)	-
Length of hospital stay, days	59 (44, 83)	3 (2, 5)	0.001

Data presented as mean (SD), median (25th, 75th percentiles), absolute number (n), and proportion (%).

(15.3% vs. 4.8%, $P = 0.042$).

Physical capacity

No differences were found between preterm and term-born groups after the 6MWT (MD 7.9 m [95%CI: -15, 31]) (Table 2). After the 6MWT, systolic and diastolic blood pressure were significantly higher in the preterm group compared to the term-born group (systolic: 119 ± 21 versus 112 ± 12 mmHg, $P = 0.032$; diastolic: 73 ± 12 versus 68 ± 10 mmHg, $P = 0.043$, respectively), while heart rate, dyspnea, and leg fatigue were similar. Both groups walked <80% of the predicted distance based on multinational reference values, but exceeded 90% when the predicted distance was calculated using regional reference values (Table 2). According to parental reports on a subjective question, children and adolescents in the preterm group engaged in significantly more hours per week of moderate to intense physical activities (Table 2).

Inspiratory and handgrip muscle strength

IP_{max} was significantly lower in the preterm group compared to the term-born group (MD: 12.8 cmH₂O [95%CI: 4.0, 21.5], $P = 0.004$), this also held true when adjusted for sex ($P = 0.008$) or FFM ($P = 0.038$) (Table 3). Based on the predicted IP_{max} values from healthy young individuals, the preterm group achieved 82% of the predicted value, compared to 95% for term-born group (Table 3). Children diagnosed

Table 2

Lung function and physical capacity of children and adolescents born preterm with very low birth weight and term-born peers in Southern Brazil.

Lung function, n	Preterm group 59	Term-born group 53	P value
FVC z-score	0.04 (1.16)	0.55 (1.12)	0.022
FEV ₁ z-score	0.00 (1.24)	0.72 (1.01)	0.001
FEV ₁ /FVC z-score	-0.09 (0.99)	0.28 (0.96)	0.047
FEF ₂₅₋₇₅ z-score	-0.24 (1.07)	0.28 (0.79)	0.005
Lung function under LLN, n (%)	9 (15.3%)	2 (3.8%)	0.042
BD response (>10%) [†]	4/38 (10.5%)	1/34 (2.9%)	0.206
Physical capacity, n			
6MWT distance, m	555 (62)	547 (70)	0.491
Percent of predict, multinational eq., % ^{††}	78 (7)	80 (10)	0.479
Percent of predict, regional eq., % ^{†††}	91 (7)	92 (11)	0.432
Physical activity reported by parents, h/week	7 (3, 10)	3.5 (1.5, 7)	0.003

Data presented as mean (SD), median (25th, 75th percentiles), absolute number (n), and proportion (%).

FVC: forced vital capacity; FEV₁: forced expiratory volume at the first second; LLN: Lower Limit of Normal (z-score < -1.645 - the 5th percentile of a standard Gaussian distribution); z-score from Global Lung Initiative (GLI) equation.

[†] Bronchodilator (BD) response determined if >10% relative to the predicted value, based in the ATS/ERS technical standard on interpretation of lung function.

^{††} Percentage of predicted based on a multinational equation.³¹

^{†††} Percentage of predicted values based on an equation from a study conducted with healthy children (aged 8 to 12 years)³² from the same region as the present study. In this age range, the 60 preterm and 54 term-born participants were included.

Table 3

Inspiratory and handgrip muscle strength of children and adolescents born preterm with very low birth weight and term-born peers in Southern Brazil.

	Preterm group	Term-born group	Non-adjusted P value	Adjusted MD (95% CI) ^{a, OR^b}	Adjusted MD (95% CI) ^{a, AND^b}
Inspiratory muscle strength, n	68	58			
IP _{max} , cmH ₂ O	-78.7 (24.6)	-91.5 (24.7)	0.004	10.9 (2.8, 19.1) ^{a**}	7.5 (-0.4, 15.5)
IP _{max} percent of predict, %	82.2 (23.0)	95.4 (22.9)	0.002	11.5 (3.2, 19.7) ^{b**}	-
Peripheral muscle strength, n	68	59			
Handgrip dominant arm, kg	15.5 (4.4)	17.2 (4.6)	0.044	1.5 (-0.0, 3.1) ^a	0.1 (-0.9, 1.2)
Handgrip non-dominant arm, kg	13.7 (4.4)	15.4 (4.3)	0.030	1.7 (0.1, 3.2) ^{a*}	0.4 (-0.6, 1.5)
Total handgrip strength, kg	29.4 (8.7)	32.7 (8.9)	0.037	3.2 (0.1, 6.2) ^{a*}	0.6 (-1.5, 2.7)

Data presented as mean (SD), absolute number (n), and mean difference (MD) (95% Confidence Interval). IP_{max}: maximal inspiratory pressure; Total handgrip strength: sum of the dominant and non-dominant arms.

^a Adjusted for sex or.

^b adjusted for fat-free mass (FFM); ^{a+b} adjusted for sex and FFM; * $P < 0.05$. ** $P < 0.01$.

Note: The supplementary material presents a comparison of handgrip strength with reference values from healthy Brazilian children and adolescents.

with BPD had lower IP_{max} values (-75 ± 25 cmH₂O; preterm without BPD: -80 ± 24 cmH₂O). Moreover, preterm group presented a significantly lower handgrip strength compared to the term-born group (dominant arm: MD 1.6 kg [95%CI: 0.04, 3.2], $P = 0.044$; non-dominant arm: MD 1.7 kg [95%CI: 0.17, 3.3], $P = 0.030$; and total handgrip: MD 3.3 kg [95%CI: 0.19, 6.4], $P = 0.037$) (Table 3). When adjusted for sex and FFM, handgrip was not different between groups. When compared to reference values of healthy Brazilian children and adolescents, set as

100%, the preterm group showed a handgrip strength of 74.5%, whereas the term-born group exhibited a strength of 89% (Supplementary material). Preterm participants with BPD presented significantly lower IP_{max} compared to participants in the term-born group (Supplementary Table S1).

Association between functional variables, neonatal and current anthropometric characteristics

In addition to the neonatal complication of BPD being associated with a lower lung function and a lower IP_{max}, individuals born preterm with more extreme low birth weight were found to have weaker handgrip strength (Supplementary Table S2). GA and days on ventilatory support were not associated with muscle strength, lung function, or physical capacity in the preterm group (Supplementary Table S2).

Fat-free mass was the only independent variable positively associated with IP_{max} and handgrip strength in the preterm group; for every 5 kg increase in FFM, a gain of inspiratory pressure of 6.3 cmH₂O (95%CI: 0.44, 12.1) and handgrip strength of 3.1 kg (95%CI: 2.4, 3.9) was observed. In regard to the term-born group, FFM was positively associated with handgrip strength (a 5 kg increase in FFM was associated with a 3.1 kg [95%CI: 2.4, 3.8] increase in handgrip strength). On the other hand, BMI-for-age presented a negative association (a 5 units increase in BMI was associated with a decrease of 1.28 kg [95%CI: 2.1, 0.3] in handgrip strength).

Table 4 shows that higher inspiratory muscle strength and higher handgrip strength were significantly associated with higher FEV₁, FVC and walked distance in the preterm group.

Discussion

Our findings show that children and adolescents born preterm with VLBW have lower handgrip strength, inspiratory muscle strength and lung function when compared to their term-born peers. Physical capacity, assessed by a submaximal exercise test, was similar among groups. Furthermore, the preterm group showed a significant, positive association between both inspiratory and peripheral muscle strength and lung function, as well as with physical capacity, suggesting that a gain of strength and muscle mass may improve overall physical health in this population.

Table 4

Association analysis of inspiratory or handgrip muscle strength with lung function and physical capacity of children and adolescents born preterm with very low birth weight and term-born peers.

		Preterm group	Term-born group
Outcome	Predictor (5 units)	B coefficient (95% CI)	B coefficient (95% CI)
FVC, liters	IP _{max} , cmH ₂ O	-0.02 (-0.04, 0.00) *	0.00 (-0.02, 0.02)
FVC, liters	Handgrip strength, kg	0.23 (0.06, 0.39) **	0.09 (-0.09, 0.26)
FEV ₁ , liters	IP _{max} , cmH ₂ O	-0.02 (-0.04, 0.00) *	0.00 (-0.02, 0.02)
FEV ₁ , liters	Handgrip strength, kg	0.19 (0.04, 0.35) *	0.06 (-0.10, 0.26)
Distance walked, m	IP _{max} , cmH ₂ O	-3.17 (-6.36, 0.00) *	-2.28 (-6.54, 1.97)
Distance walked, m	Handgrip strength, kg	31.11 (6.09, 56.14) *	-0.40 (-31.53, 30.72)
IP _{max} , cmH ₂ O	Handgrip strength, kg	-10.05 (-20.07, -0.04) *	6.70 (-3.02, 16.42)

Data presented as B unstandardized coefficient and 95% Confidence Interval (lower and upper bound). Linear regression model adjusted for fat-free mass (FFM). *P < 0.05; **P < 0.01; ***P < 0.001.

IP_{max}: maximal inspiratory pressure, FVC: forced vital capacity, FEV₁: forced expiratory volume at the first second, Distance walked: distance after the six-minute walk test.

Muscle strength and lung function are key determinants for exercise capacity.⁴² In the present study, reduced lung function was observed in children and adolescents born preterm, which is in agreement with the current literature.⁷ An early decline in lung function is observed in children born preterm, aged 4 to 12 years, in the post-surfactant era, with an important decrease in spirometry z-scores over time compared to term controls.^{43,44} Moreover, individuals born preterm with BPD have been shown to experience a more pronounced decline in spirometry z-scores (at least 0.1 z-score decline per year).^{43,44} Further contributing to reduced respiratory function, inspiratory muscle strength was found to be reduced in the preterm group. To the best of our knowledge, only one study investigated inspiratory strength in school-age children.²⁶ Batista-Novais et al. reported a significant inspiratory muscle weakness in preterm subjects. Our study corroborates these findings, with a larger sample size, strengthening the knowledge surrounding the outcomes assessed. A reduction of 12.8 cmH₂O (95%CI: 4.0, 21.5) in the inspiratory strength in the preterm group might be clinically relevant as, for instance, the minimal important difference observed in COPD patients after inspiratory muscle training is 13.5 cmH₂O.⁴⁵ One can postulate that increasing muscle strength through respiratory muscle training protocols may improve lung volumes and function in individuals born preterm.⁴⁶⁻⁴⁸

Reduced handgrip strength is observed in preschoolers,^{20,21,49} adolescents,⁵⁰ and in adults born preterm,³⁹ and is a prognostic marker of all-cause mortality in adults.^{39,51} In the present study, handgrip strength was significantly reduced in the individuals born preterm when compared to term-born peers. Compared to reference values from healthy Brazilian young individuals (6–19 years), the preterm children showed a 25% reduction in handgrip strength (see Supplementary material). In contrast, a study with 21 healthy and physically fit adolescents born very or extremely preterm presented similar handgrip strength compared to term-born adolescents, despite their lower exercise capacity.³⁸ A meta-analysis that included studies with infant, children, and adolescent population (25 studies in total, with only 5 involving adults) concluded that individuals born preterm display alterations in muscle mass (thickness) and function (jump power).²¹ These data suggest that, along with morphological changes, muscle function of individuals born preterm might present an adapted and particular physiology that differs from individuals born at term.^{13,52} Delfrate & Girard-Bock et al. concluded that preterm young-adults present reduced muscle function due to altered muscle perfusion and metabolism based in the reduction of V̇O₂ to work rate relationship (ΔV̇O₂/ΔWR), commonly seen in various cardiopulmonary disorders.⁵³ Besides the morphophysiological factors, poor motor ability might be another factor contributing to lower muscle strength.¹¹ However, studies of children born preterm aged 8 to 11 show that most have normal motor development.^{54,55} We should also consider that a combination of altered motor coordination and skeletal muscle function could occur in the preterm population, especially in those born with extremely low birth weight, which warrants further investigation as they age.¹¹ These sets of results reinforce the importance of investigating muscle strength in early childhood, possibly allowing the implementation of early intervention programs in this at-risk population, especially in low- and middle income countries.⁵⁶

In our study, preterm children and adolescents showed the same performance in the submaximal 6MWT compared to their term-born peers. Our results are in agreement with studies that measured subjects activity levels using an accelerometer, showing no differences between children born preterm and term.^{57,58} Also, children born extremely preterm showed comparable aerobic capacity and exercise performance to those of peers born at term, measured through a maximal treadmill exercise.⁵⁹ Conversely, children born extremely preterm self-reported less exercise and lower endurance,⁶⁰ perceived inferior exercise capacity and difficult breathing compared to term-born peers.⁵⁸ Additionally, a population-based cohort study with healthy young men concluded that preterm birth predicts low physical capacity.² Despite the latter, our results show that the children and

adolescents of the preterm group appeared to be more physically active than their term-born peers. Indeed, the preterm group spent more hours per week on physical activities that left them tired and sweaty as reported by their parents. Furthermore, the lower BMI in the preterm group (z-score BMI near to the average of the population) compared to the term-born group, and a routine with a greater amount of physical activity may be linked to the positive outcomes from the close follow-up offered in our outpatient clinic.⁶¹ Additionally, more attentive care from families toward the health of their preterm children could contribute to improved health outcomes.^{62,63}

Our association analyses show that the higher the handgrip and inspiratory muscle strength, the greater the lung function and physical capacity in the preterm group. Gaining muscle strength through a well-designed training program may help delay the development and progression of pulmonary diseases.⁶⁴ It may also improve physical capacity later in life for in individuals born prematurely.^{65–67}

Finally, studies show that BPD, the most common complication of prematurity, leads to impaired lung function with higher risk of lung diseases later in life, and impairment of physical health.^{7,44} In our study, the sub-analysis of individuals born preterm with BPD revealed a more significant decline in lung function and inspiratory muscle strength compared to the term-born group, suggesting that preterm children with BPD may require additional attention from healthcare practitioners.

Study limitations must be acknowledged. First, 27.3% of participants in the preterm group showed an insufficient performance on the spirometry test, especially those born at earlier gestational ages. This could be associated with a higher prevalence of neurodevelopmental delays in those born extremely preterm.⁶⁸ Second, the lack of predicted values of handgrip strength for young people in the literature prevented us from performing comparisons of this outcome. To overcome this issue, we have compared our results with data from healthy Brazilian children and adolescents (Supplementary material). Third, the fact that the global health of our term-born group presented higher BMI-for-age and lower physical activity levels, as per the normative values of the worldwide population⁶⁹; this might have impacted functional comparisons. In order to mitigate this confounding factor in our statistical comparisons, we performed a sensitivity analysis considering eutrophic and overweight status (preterm vs. term-born) which further supports the impact of preterm birth over skeletal muscle function. Although the recruitment strategy for the term-born group may have introduced some bias, no physical limitations were observed in the children and adolescents during assessments. Moreover, we recruited a control group from the same socio-economic and environmental background as the preterm group. Finally, we evaluated children born preterm between 2008 and 2012 because this five-year period enhanced our recruitment success, as an average of 40 children per year were referred to the outpatient clinic during that time.

In conclusion, children and adolescents born preterm with VLBW present reduced handgrip strength, inspiratory muscle strength and lung function, contributing to their increased risk for early-onset chronic diseases. These findings highlight the importance of initiating an early interventional training program in childhood, to establish physical activity behaviors that track into adulthood, and to improve the overall physical health of preterm individuals. Our data, originating from a developing country with lower income families, contributes to the current literature focused mainly on high-income countries, by providing valuable insights into the long-term effects of preterm birth on physical health.

Authors' contribution

ROF conceptualized and designed the study, performed data analyses, and wrote the manuscript; ROF, SLR, MACR, LSM, VSB, ASE participated in recruitment and data collection; VCBGC performed data analyses, technical support, reviewed critically the manuscript; PMER conceptualized and designed study, reviewed critically the manuscript;

RSP, RCS conceptualized and designed study, funding acquisition, wrote and reviewed critically the manuscript. All authors revised and finalized the manuscript.

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Declaration of competing interest

The authors declare no competing interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.bjpt.2026.101582.

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