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Evolution of muscular oxygenation parameters during walking test in pre-term children : a pilot study.

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ABSTRACT

OBJECTIVE: Premature children tend to be less involved in physical activities than their full-term contemporaries. This behaviour could be partly explained by pulmonary impairment but also by a muscular impairment. NIRS technology could offer interesting way of investigation of muscular adaptation. The aim of the study was to explore parameters of peripheral muscular oxygenation, coupled to gait characteristics, between premature (PT) and full-term (FT) children during a 6-minute walking test (6MWT).

STUDY DESIGN: Prepubescent children performed a 6MWT. During the test, changes in muscular oxyhaemoglobin (ΔHbO_2), deoxyhaemoglobin (ΔHHb) and total haemoglobin (ΔtHb) were measured with NIRS technology, positioned on subjects' calves. Gait parameters were monitored with an OPTOGAIT system.

RESULTS: 45 children (33 FT children and 12 PT children) participated in this study (mean age \pm SD: 4.9 \pm 0.7 and 4.6 \pm 0.9 years, respectively). Statistical analysis highlighted a decreased walking performance for PT children, with significantly lower walking distance ($p<0.05$) than FT ones (405.1 \pm 91.8m vs. 461.0 \pm 73.3m respectively, -9%). A concomitant increase of oxygen extraction (over ΔHHb time course) was observed from the third minute of the test ($p<0.05$). No statistically significant difference was found for other NIRS parameters. Lastly, the analysis of gait parameters highlighted a group effect for walking speed ($p<0.05$) and stride length ($p<0.01$).

CONCLUSION: Premature children showed decreased walking performance and greater change in peripheral muscular oxygen extraction, associated with lower walking speed and stride length. This may point out a muscular maladjustment and reduced functional capacities for PT children. These phenomena could be responsible of a greater muscular fatigue.

List of abbreviations

6MWT: 6-Minute Walking Test

ΔHbO_2 : Variation of Oxyhemoglobin

ΔHbTot : Variation of Total Hemoglobin

ΔHHb : Variation of Desoxyhemoglobin

BPD: Bronchopulmonary Dysplasia

COPD: Chronic Obstructive Pulmonary Disease

FT: Full-term children

NIRS: Near Infra-Red Spectroscopy

PT: Pre-term children

Evolution of muscular oxygenation parameters during walking test in pre-term children.

Keywords: Preterm - Walking test - NIRS – Muscular oxidative capacity – functional capacity

INTRODUCTION

In the last decade, numerous factors, like obstetrical (uterine malformation), generic (increase of multiple pregnancies) or maternal (addiction, pregnancy disease or socio-economical factors) risk factors, can be responsible of the ratio (from 6 to 11%) of premature births worldwide, e.g. children born before 37 weeks of gestation (1,2). The degree of prematurity and birth weight are key factors in the risk for long-term impaired development (3,4): children born before 28 weeks of gestation are considered as extremely preterm, between 28 and 32 weeks great preterm and late preterm for those born after 34 to 36 weeks of gestation. Prematurity leads to multiple consequences and, in particular, causes an interruption of lung development, impacting the normal pulmonary vascular and alveolar development (5).

The major respiratory pathology developed in great prematurity is bronchopulmonary dysplasia (BPD), affecting up to 40 % of preterm (PT) children with birthweight inferior to 1000g (4). This pathology is defined as the need of oxygen supply during more than 28 days following birth with severity assessed at 36 weeks for infants born at gestational ages of less than 32 weeks (6). It is characterized by fewer and larger alveoli and a reduction in pulmonary vascularization. As a result of BPD, there is ~~a decrease in gas exchange efficiency,~~

higher dead space and gas trapping, along with lower pulmonary function and higher airway resistance (3).

During exercise, children with BPD show ventilatory limitations and a higher oxygen uptake for the same power output than full term (FT) children (7). Moreover, long term consequences seem to be important as adult survivors of preterm birth, with or without BPD, globally exhibit mechanical constraint to increase tidal volume during near-maximal exercise, associated with severe dyspnea and leg discomfort (8). Prematures show lower values of maximal oxygen uptake ($\dot{V}O_{2max}$) and forced expiratory volume in one second (FEV1) than FT controls (9,10). As a consequence, PT children are less involved in physical activities (1,11,12). Still, little information is available to explain how impaired lung function in PT children alters exercise capacity (3).

Chronic Obstructive Pulmonary Disease (COPD) model of deconditioning could be an interesting hypothesis for explaining the link between impaired lung function and exercise capacity alteration in PT children. In fact, several studies report muscular dysfunction secondary to respiratory impairment in COPD population (13,14). Strengthened by the fact that BPD children exhibit a high risk of COPD in later life (4–6,13), the impairment of lung function, as mentioned above, could have consequences on muscle function of PT children. In COPD patients, this muscular dysfunction is associated with alterations of morphological and structural skeletal muscle, atrophy, loss of type I fibers and mitochondrial dysfunction and represents a major element of COPD functional impairments (15). Nowadays, one way for muscle function investigation is related to non-invasive techniques like Near Infra-Red Spectroscopy (NIRS) (13). NIRS technology has been previously used in neonate and premature to measure tissue oxygenation and perfusion in regions of interest, e.g. the brain, kidneys or peripheral muscles, in early states of shock (16). It has also been used in children

with muscular pathologies and chronic heart disease, in whom different profiles of muscular oxygenation were evidenced, compared to healthy subjects (17,18). This method already reveals a decrease in oxidative capacities in lower leg muscle that contributed to exercise intolerance in these patients (19). Similarities between BPD and COPD suggest that PT children may present a high risk of exhibiting the same muscular disorders, also responsible for the reduced functional capacities reported in this population (20). However, muscular oxygenation in PT children during physical activity of daily living, like walking task, has not been studied yet.

The objective of this study was to compare parameters of peripheral muscular oxygenation using NIRS between PT and FT children during a 6-minute walking test (6MWT). We hypothesize that PT children present impaired muscular oxygenation parameters, compared to FT ones.

Methods

Population

This cross-sectional **pilot** study was conducted on two populations: i) **an experimental group with extreme and great** PT children; and ii) a control population of FT children. PT children were recruited at the ‘Hopital Mère Enfant’ (HME) in Limoges (France), followed by the ‘Centre d’Action Médico-Sociale Précoce’ (CAMSP) until their sixth birthday. The control population was composed of FT children recruited in several recreational centres in Limoges. Patients were eligible aged from 3 to 6 years old. Inclusion criteria for PT children included an age of birth before 32 weeks of gestation and a birth after 37 weeks of gestation for the full-term population. Exclusion criteria were **moderate PT children**, major neurological disabilities (cerebral palsy) or cardiac pathologies that would interfere with protocol realization **and any refusal of participation by the child or parents**. Parents were signed an informed consent and authorization before the participation of their children to this protocol. The study was carried out as per the standards set by the Declaration of Helsinki.

Protocol design

The study period took place over a 3-month period. At their arrival children were asked to sit and the NIRS probe was placed on the right medial gastrocnemius (Figure 1) (21). They were asked to walk as fast as possible once the start had been given and this for 6 minutes (6MWT). The starting line and the turning area were materialized by a line and a cone. The NIRS measurements began before the walking test once children were asked to stand up (allowing NIRS baseline determination). At the end of the test, children were asked to sit and the NIRS records were ended and collected ended.

*** Insert Figure 1 near here ***

Muscle oxygenation: NIRS setup and acquisition

Changes in muscle oxygenation and blood volume during the 6MWT was measured with a NIRS device (PortaMon, Artinis, Netherlands) (22). The NIRS probe was placed on the right medial gastrocnemius as illustrated in Figure 1.

NIRS acquisition was made through the Oxysoft software (version 3.0.97.1), with a 2 Hz sample frequency. Differential Pathlength Factor (DFP) was set on 4 (23). A 0.1 Hz low-pass filter was applied to the signal to remove physiological and instrumental noise. The relative concentrations in oxy- and deoxyhemoglobin (ΔHbO_2 and ΔHHb , respectively, $\mu\text{mol.L}^{-1}$) during the last 10 seconds of each minute of the 6MWT were then normalized by subtracting to them the mean value of the last 15 s of baseline, immediately before the beginning of the task, i.e., standing up. From these data was extracted the total haemoglobin ($\Delta\text{HbTot} = \Delta\text{HbO}_2 + \Delta\text{HHb}$).

Walking performance and gait parameters

A 6MWT was conducted in accordance with American Thoracic Society recommendations (24,25). Children were asked to walk back and forth along a 30-meter flat corridor as quickly as possible for 6 minutes. The covered distance (6MWT, in meters) was then recorded upon the completion of the test. During the 6MWT realization, gait parameters were measured using an OPTOGAIT system (Microgate, Bolzano, Italy) (26), placed at the beginning of the walking path 2 meters after the starting line in order to eliminate the acceleration and deceleration phase. Speed (m.s^{-1}), cadence (st.min^{-1}), stride step (cm) and stride time (s) were collected at each passage.

Statistical analysis

Unless otherwise stated, data are expressed as mean \pm SD.

Data analysis was performed, for all the tests described below, with the help of Prism software (software version 6.0c, GraphPad, San Diego, CA, USA).

For each statistical test performed, significant level was set for $p < 0.05$. The normality of data distribution was verified with the D'Agostino & Pearson normality test. Depending of the normality of data distribution, parametric and non-parametric were applied for further statistical analysis.

Mean walking performance was compared between both groups using an unpaired t-test.

All the muscular oxygenation parameters (ΔHbO_2 , ΔHHb and ΔHbTot) and gait parameters were analyzed by considering the entire 6-minute walking test. NIRS data were analyzed by repeated-measures two-way analysis of variance (ANOVA) protocol, with "Group" and "Time (minute)" factors. In case of significant interaction, a multiple comparison procedure was done by applying Bonferroni's multiple comparisons test.

Results

Population

Fifty-three children (38 FT and 15 PT) were recruited for this study and 33 FT children and 12 PT completed the entire protocol and were included for data analysis. The study flow chart is presented in Figure 2.

*** Insert Figure 2 near here ***

Population characteristics are presented in Table 1. **All the PT children had BPD diagnosis.** As expected, PT children had lower birthweight, weight and height at the same age than FT children ($p < 0.001$, $p < 0.05$ and $p < 0.05$, respectively). The gait acquisition was also earlier for FT children than for PT ones ($p < 0.001$), as well as independent walking ($p < 0.001$). The two populations were similar in terms of average age ($p > 0.05$).

*** Insert Table 1 near here ***

At the end of the 6MWT, FT children walked a greater distance than PT ones (461.0 ± 73.3 vs. 405.1 ± 91.8 m, $p < 0.05$).

The time-course variations of NIRS parameters (i.e. ΔHbO_2 , ΔHHb and ΔHbTot) are illustrated in Figure 3. ΔHbO_2 decreases during the 6MWT, indicating that peripheral muscle shows a greater deoxygenation (defined as a fall of HbO_2) at the onset of the 6MWT. This was followed by a plateau phase at the third minute, with no difference between the two populations ($p > 0.05$).

On the contrary, we observed an increase of ΔHHb , then reaching also a plateau at the third minute (cf. Figure 3). The peripheral oxygen extraction is enhanced at the beginning of exercise and will then stabilize after 3 minutes of moderate intensity activity. There is a significant difference between the two populations starting at the third minute of the 6MWT ($p<0.05$), with greater oxygen extraction (i.e. increase of ΔHHb) for PT group in comparison with FT group. This variation is maintained until the end of the test.

Lastly, there is no difference for ΔHbTot between the two populations during the 6MWT. ΔHbTot starts by slightly decreasing and then increases after 3 minutes of exercise.

*** Insert Figure 3 near here ***

Time-course evolution of gait parameters are resumed in Figure 4. The statistical analysis highlights similar results for walking speed and stride length, with a significant “Group” effect ($p<0.05$ and $p<0.01$, respectively), but with no significant effect of “Time” factor and without factors interaction. Stride cycle time presents no significant of both factors and no significant interaction.

*** Insert Figure 4 near here ***

Discussion

In this work, our main finding highlights a decreased walking performance in the PT population. Thus, prematures exhibit a reduced functional capacity, associated with a greater variation in peripheral muscular oxygen extraction (ΔHHb) and a specific gait adaptation, compared to FT, during a standardized walking evaluation. Other results show no difference in terms of oxygen supply (ΔHbO_2) or blood volume (perfusion ΔHbTot). All of these results are really interesting as it offers original and novel knowledge about exercise adaptation of muscle function in PT children. In fact, to the best of our knowledge, no study previously used skeletal muscular NIRS monitoring during exercise in PT children. It provides then new fundamental insight on peripheral muscular oxygenation in premature children aged from 3 to 6 years old and on the consequences of PT birth.

The major result of the current study is that great preterm children highlight a significantly lower walking performance, in comparison with full-term population, with a difference of 56 meters (-9%) between the mean walking distance of both groups ($p < 0.05$). The lower performance reported for PT population has been previously observed in PT children with very low birthweight (9,20). **Several hypotheses could be raised up for explaining this decreased performance in PT group. First of all, difference in anthropometric factors could explain this difference. FT children show significantly higher height, associated with higher stride length normalized to height. Therefore, with the same exercise time, higher body dimensions could help FT children to reach higher distance. Secondly, this lower functional capacity could be the expression of lung impairment and a global desadaptation to exercise in PT population. This could also be explained by a lesser muscle mass, as the significant difference for body weight between both populations ($p = 0.012$) could be an indicator of**

hypotrophy, one of major characteristics of prematurity. This hypotrophy could lead to a decreased muscle adaptability to exercise and therefore to an increased muscle fatigability. In order to investigate the potential impairment of muscle function in PT population, we decide to use a non-invasive monitoring method (NIRS), that uses near-infrared light for exploring muscular oxygenation and its adaptation to exercise. Peripheral muscular oxygenation measured with NIRS has been previously used in PT children to detect early states of shock and in different pathologies with muscular disorders (17) and could be an interesting method for muscular evaluation in PT population.

The variations of muscular oxygen parameters observed in the two populations from a general point of view are consistent with the NIRS data measured in adults and children (18,21–23). In both groups, walking task first led to a simultaneous reduction of ΔHbO_2 and increase of ΔHHb , reflecting a temporary inadequacy between O_2 consumption and delivery (27–29). After 3 minutes of walking, a plateau phase is then observed, as noted before: O_2 delivery is then sufficient to compensate for metabolic requirements (30). However, ΔHHb increases more in the PT population after 3 minutes of walking and until the end of the 6MWT. In previous studies, a greater O_2 consumption was observed in BPD children during exercise (3). Cardiac and muscular pathologies, such as Becker Muscular Dystrophy (BMD), also have a negative impact on O_2 extraction, due to an insufficient blood delivery. O_2 extraction is then optimized and ΔHHb enhanced in order to compensate disorders in O_2 delivery (18,31). The oxygen supply in children with BMD would be slower (cardiac insufficiency or capillarity default) and related to the degree of muscular and functional deficit (17). Alteration of muscular perfusion and impaired oxygen supply would contribute to exercise intolerance and premature fatigue observed in these children (18). However, this higher O_2 consumption could also be associated to mechanical ventilatory constraints (7), that could induce greater

work of breathing for PT population and may explain higher O₂ consumption during exercise in PT population.

The skeletal muscular oxygenation parameters show a higher oxygen extraction during exercise in PT children compared to FT, reflecting the metabolic state of the activated muscle. Prematurity has numerous consequences for child development. Cardiovascular disorders are rarely evoked in BPD children to explain impairments in muscular oxygenation (11,32,33). A previous study of Lewandowski et al. reports specific left cardiac adaptations due to prematurity (34). This could lead notably to reduced cardiac volume and reduced O₂ delivery, that could explain the greater O₂ extraction for PT population. However, in this study, the kinetics of oxyhaemoglobin (HbO₂) do not differ between PT and FT children. This could indicate that the lower performance (distance) observed for PT children for the walking test could be mainly associated to a muscle dysfunction, explaining the greater O₂ extraction. ~~and there is no difference in Δ HbTot between these two populations. Furthermore, the pulmonary function is altered, particularly in children affected by BPD, who exhibit air trapping, decreased alveolarization and pulmonary microvascular development in their lungs (7). Gas exchanges are impaired and~~ As a consequence, physical activity leads to various physiological responses (1,6,7).

In healthy subjects, muscular performance partially depends on the proportion of the different types of muscular fibers in the activated muscle. Prematurity has negative impacts on the respiratory function similar to COPD patients in which muscle morphologic adaptations such as fat infiltration, fibrosis, inflammation, increased subcutaneous adipose, loss of type I fibers and mitochondrial density may hamper NIRS measurement of muscle oxidative capacity (13,19). Muscular physiological characteristics of PT children with BPD could be close to COPD patients. Indeed, Wenrich et al. (2002) showed a reduction of the number of mitochondrial proteins and activity of the PDH and COX enzymes in very PT

neonates (35). The muscular oxygen metabolism is then impaired, and the subsequent ATP production is reduced. Skeletal muscle dysfunction and peripheral factors are major determinants of reduced exercise capacity and exercise intolerance, and could contribute to their reduced involvement in physical activities (18). Very PT children would be more prone to fatigue, as for a same moderate intensity physical activity, requiring a greater O₂ extraction in activated muscle in order to respond to the metabolic needs.

Another potential explanation for the lower performance observed for PT population, related to the muscle function, could be the difference for gait parameters observed in this study. Despite the absence of significant interaction for both factors (Time and Group), gait parameters seem to be influenced by group condition (PT vs. FT). In fact, walking speed and stride length are both lower for the PT group, in comparison with FT group, throughout the 6-minute walking test. Walking speed could be directly linked to muscle function and contractile capacity but also to the efficiency of the walk for each child, PT children having a higher age for independent walk. Lastly, the length of lower limbs could influence the length of the stride, as confirmed by a significant difference for normalized stride length to height between the two groups. But this hypothesis requires a more precise assessment of sitting height, for the determination of the length of lower limbs. Overall, gait parameters, linked with NIRS adaptation results, are interesting and tend to highlight a global muscle dysfunction of lower limbs in PT.

Limitations

They are a few limitations to report for this study. First, children aged from 3 to 6 years old may present various degree of psychomotor maturity within this age range (Cf. Table 1). Nevertheless, the mean age between the two populations was not significantly different, which allowed comparisons between the populations of PT and FT children. Furthermore, this

range of age for PT children is representative of real-life population monitored and cared for in paediatric units.

Then, the NIRS technique is a technology that is sensitive to methodological considerations and evaluates oxygenation parameters in a limited area of a targeted muscle group. Also, muscle microvascular oxygenation is heterogeneous within the studied muscle (36); in order to avoid this issue, the probe disposition was standardized (Cf. Figure 1). In order to have a global approach, it would have been interesting to couple the NIRS measures with V O₂ measurements and cardiorespiratory adaptations. Furthermore, NIRS only offers a peripheral point of view and NIRS measurement could be influenced by central factors linked to cardio-vascular characteristics (like blood flow and blood volume variation, haemoglobin or haematocrit levels). Therefore, this implies to couple NIRS assessment with other complementary measurement in order to provide a more global point of view.

In order to take account of these principal limits, it could be interesting to investigate muscle function of PT population with the help of complementary assessment tools (like oxygen uptake evaluation, muscle function evaluation (with bio-impedancemeter or force assessment) or multi-site NIRS assessment). This would help a better and more comprehensive vision of prematurity effect on body function (pulmonary, muscle functions). It could be also interesting to consider long-term follow-up studies in order to observe a cohort of PT subjects throughout the growing process. Physical activity level and lifestyle could also be interesting to monitor in order to determine the effects of these parameters on exercise performance in PT population. Lastly, studies investigating the effect of intervention specifically focused on muscle function could also be interesting to design in order to observe potential effects on physical activity participation and muscle function evolution.

Conclusion

This study is the first to provide new and original data on peripheral muscular oxygenation in PT children with BPD. This work allows to investigate some hypothesis in order to understand why PT children, and in particular great PT, are less involved in physical activities. In this study PT children with BPD showed reduced functional capacities during the 6MWT compared to FT children, due to specific adjustments. A better understanding of PT impact could be interesting in order to design and optimize specific intervention strategies.

Proposition :

This study is the first to provide new and original data on peripheral muscular oxygenation in PT children with BPD. PT children with BPD showed reduced functional capacities during the 6MWT compared to FT children. This study supports the hypothesis that prematurity has pulmonary impact on childhood. Further studies are needed to clarify the strategy for respiratory monitoring these children during childhood and adulthood.

Clinical messages

- Prematurity induces specific oxygenation adaptation during walking task
- Better knowledge of exercise adaptation for PT population is of great importance for the optimization of interventions. These ones should include specific focus on muscle function, as this function seems to be directly impacted in PT condition.

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Authors contributions

The different authors contributed at different levels to the different steps of the study conception, data acquisition, data analysis and manuscript writing and reviewing process.

Z.O-J: study conception, data acquisition, data analysis, manuscript writing and reviewing

A.P: study conception, manuscript writing and reviewing

E.H: data acquisition, data analysis and reviewing

L.F: study conception and reviewing

B.B: study conception, data analysis, manuscript writing and reviewing

References

1. Tikanmäki M, Tammelin T, Sipola-Leppänen M, Kaseva N, Matinolli H-M, Miettola S, et al. Physical Fitness in Young Adults Born Preterm. *Pediatrics*. janv 2016;137(1).
2. Torchin H, Ancel P-Y, Jarreau P-H, Goffinet F. [Epidemiology of preterm birth: Prevalence, recent trends, short- and long-term outcomes]. *J Gynecol Obstet Biol Reprod (Paris)*. oct 2015;44(8):723- 31.
3. MacLean JE, DeHaan K, Fuhr D, Hariharan S, Kamstra B, Henderson L, et al. Altered breathing mechanics and ventilatory response during exercise in children born extremely preterm. *Thorax*. nov 2016;71(11):1012- 9.
4. O'Donnell DE. Adult survivors of preterm birth. What spirometry conceals, exercise tests reveal. *Ann Am Thorac Soc*. déc 2014;11(10):1606- 7.
5. Narang I. Review series: What goes around, comes around: childhood influences on later lung health? Long-term follow-up of infants with lung disease of prematurity. *Chron Respir Dis*. 2010;7(4):259- 69.
6. Simpson SJ, Turkovic L, Wilson AC, Verheggen M, Logie KM, Pillow JJ, et al. Lung function trajectories throughout childhood in survivors of very preterm birth: a longitudinal cohort study. *Lancet Child Adolesc Health*. 2018;2(5):350- 9.
7. Kriemler S, Keller H, Saigal S, Bar-Or O. Aerobic and lung performance in premature children with and without chronic lung disease of prematurity. *Clin J Sport Med Off J Can Acad Sport Med*. sept 2005;15(5):349- 55.
8. Lovering AT, Elliott JE, Laurie SS, Beasley KM, Gust CE, Mangum TS, et al. Ventilatory and sensory responses in adult survivors of preterm birth and bronchopulmonary dysplasia with reduced exercise capacity. *Ann Am Thorac Soc*. déc 2014;11(10):1528- 37.
9. Edwards MO, Kotecha SJ, Lowe J, Watkins WJ, Henderson AJ, Kotecha S. Effect of preterm birth on exercise capacity: A systematic review and meta-analysis. *Pediatr Pulmonol*. mars 2015;50(3):293- 301.
10. Malleske DT, Chorna O, Maitre NL. Pulmonary sequelae and functional limitations in children and adults with bronchopulmonary dysplasia. *Paediatr Respir Rev*. mars 2018;26:55- 9.
11. Farrell ET, Bates ML, Pegelow DF, Palta M, Eickhoff JC, O'Brien MJ, et al. Pulmonary Gas Exchange and Exercise Capacity in Adults Born Preterm. *Ann Am Thorac Soc*. août 2015;12(8):1130- 7.
12. Lowe J, Cousins M, Kotecha SJ, Kotecha S. Physical activity outcomes following preterm birth. *Paediatr Respir Rev*. mars 2017;22:76- 82.
13. Maltais F, Decramer M, Casaburi R, Barreiro E, Burelle Y, Debigaré R, et al. An Official American Thoracic Society/European Respiratory Society Statement: Update on Limb Muscle Dysfunction in Chronic Obstructive Pulmonary Disease. *Am J Respir Crit Care Med*. mai 2014;189(9):e15- 62.
14. Ramon MA, Ter Riet G, Carsin A-E, Gimeno-Santos E, Agustí A, Antó JM, et al. The dyspnoea–inactivity vicious circle in COPD: development and external validation of a conceptual model. *Eur Respir J*. sept 2018;52(3):1800079.
15. Allaire J, Maltais F, Doyon J-F, Noël M, LeBlanc P, Carrier G, et al. Peripheral muscle endurance and the oxidative profile of the quadriceps in patients with COPD. *Thorax*. août

2004;59(8):673- 8.

16. Höller N, Urlesberger B, Mileder L, Baik N, Schwabegger B, Pichler G. Peripheral Muscle Near-Infrared Spectroscopy in Neonates: Ready for Clinical Use? A Systematic Qualitative Review of the Literature. *Neonatology*. 2015;108(4):233- 45.

17. Allart E, Olivier N, Hovart H, Thevenon A, Tiffreau V. Evaluation of muscle oxygenation by near-infrared spectroscopy in patients with Becker muscular dystrophy. *Neuromuscul Disord NMD*. août 2012;22(8):720- 7.

18. Moalla W, Elloumi M, Chamari K, Dupont G, Maingourd Y, Tabka Z, et al. Training effects on peripheral muscle oxygenation and performance in children with congenital heart diseases. *Appl Physiol Nutr Metab Physiol Appl Nutr Metab*. août 2012;37(4):621- 30.

19. Adami A, Cao R, Porszasz J, Casaburi R, Rossiter HB. Reproducibility of NIRS assessment of muscle oxidative capacity in smokers with and without COPD. *Respir Physiol Neurobiol*. 2017;235:18- 26.

20. Tsopanoglou SP, Davidson J, Goulart AL, Barros MC de M, dos Santos AMN. Functional capacity during exercise in very-low-birth-weight premature children. *Pediatr Pulmonol*. janv 2014;49(1):91- 8.

21. Kutsuzawa T, Kurita D, Ikeuchi M. Oxygenation state of the calf muscle during the 6-min walk test in patients with COPD. *Eur Respir J [Internet]*. 1 sept 2015 [cité 19 mai 2020];46(suppl 59). Disponible sur: https://erj.ersjournals.com/content/46/suppl_59/PA2294

22. Boushel R, Langberg H, Olesen J, Gonzales-Alonzo J, Bülow J, Kjaer M. Monitoring tissue oxygen availability with near infrared spectroscopy (NIRS) in health and disease. *Scand J Med Sci Sports*. août 2001;11(4):213- 22.

23. Leclair E, Borel B, Baquet G, Berthoin S, Mucci P, Thevenet D, et al. Reproducibility of measurement of muscle deoxygenation in children during exercise. *Pediatr Exerc Sci*. mai 2010;22(2):183- 94.

24. Singh SJ, Puhan MA, Andrianopoulos V, Hernandez NA, Mitchell KE, Hill CJ, et al. An official systematic review of the European Respiratory Society/American Thoracic Society: measurement properties of field walking tests in chronic respiratory disease. *Eur Respir J*. déc 2014;44(6):1447- 78.

25. Holland AE, Spruit MA, Troosters T, Puhan MA, Pepin V, Saey D, et al. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. *Eur Respir J*. déc 2014;44(6):1428- 46.

26. Lienhard K, Schneider D, Maffiuletti NA. Validity of the Optogait photoelectric system for the assessment of spatiotemporal gait parameters. *Med Eng Phys*. avr 2013;35(4):500- 4.

27. Moalla W, Merzouk A, Costes F, Tabka Z, Ahmaidi S. Muscle oxygenation and EMG activity during isometric exercise in children. *J Sports Sci*. nov 2006;24(11):1195- 201.

28. van Beekvelt MCP, van Engelen BGM, Wevers RA, Colier WNJM. In vivo quantitative near-infrared spectroscopy in skeletal muscle during incremental isometric handgrip exercise. *Clin Physiol Funct Imaging*. mai 2002;22(3):210- 7.

29. Murthy G, Kahan NJ, Hargens AR, Rempel DM. Forearm muscle oxygenation decreases with low levels of voluntary contraction. *J Orthop Res Off Publ Orthop Res Soc*. juill 1997;15(4):507- 11.

30. DeLorey DS, Kowalchuk JM, Paterson DH. Relationship between pulmonary O₂ uptake

kinetics and muscle deoxygenation during moderate-intensity exercise. *J Appl Physiol Bethesda Md* 1985. juill 2003;95(1):113- 20.

31. Barroco AC, Sperandio PA, Reis M, Almeida DR, Neder JA. A practical approach to assess leg muscle oxygenation during ramp-incremental cycle ergometry in heart failure. *Braz J Med Biol Res Rev Bras Pesqui Medicas E Biol.* 2 oct 2017;50(12):e6327.

32. Vardar-Yagli N, Inal-Ince D, Saglam M, Arikan H, Savci S, Calik-Kutukcu E, et al. Pulmonary and extrapulmonary features in bronchopulmonary dysplasia: a comparison with healthy children. *J Phys Ther Sci.* juin 2015;27(6):1761- 5.

33. Jacob SV, Lands LC, Coates AL, Davis GM, MacNeish CF, Hornby L, et al. Exercise ability in survivors of severe bronchopulmonary dysplasia. *Am J Respir Crit Care Med.* juin 1997;155(6):1925- 9.

34. Lewandowski AJ, Augustine D, Lamata P, Davis EF, Lazdam M, Francis J, et al. Preterm Heart in Adult Life: Cardiovascular Magnetic Resonance Reveals Distinct Differences in Left Ventricular Mass, Geometry, and Function. *Circulation.* 15 janv 2013;127(2):197- 206.

35. Wenchich L, Zeman J, Hansíková H, Plavka R, Sperl W, Houstek J. Mitochondrial energy metabolism in very premature neonates. *Biol Neonate.* 2002;81(4):229- 35.

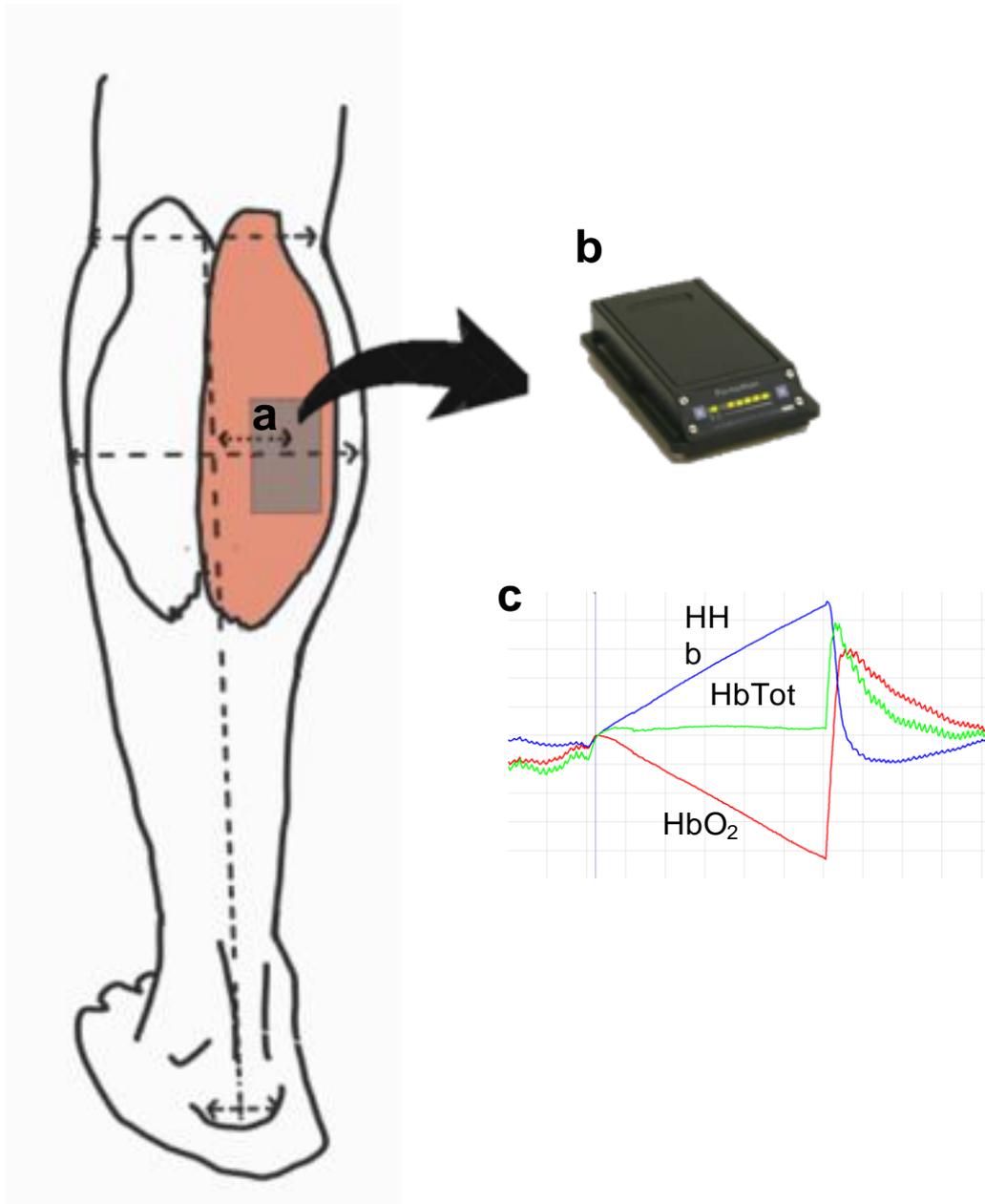
36. Miura H, McCully K, Chance B. Application of Multiple NIRS Imaging Device to the Exercising Muscle Metabolism. *Spectroscopy.* 2003;17(2- 3):549- 58.

Table 1 : Population characteristics

	<i>FT (N=33)</i>	<i>PT (N=12)</i>	<i>P-value</i>
<i>Parameters</i>			
<i>Age (years)</i>	4.9 ± 0.7	4.6 ± 0.9	0.216
<i>Weight (kg)</i>	18.6 ± 4.0	15.7 ± 2.8	0.012
<i>Height (m)</i>	1.1 ± 0.1	1.0 ± 0.1	0.011
<i>Body mass index (kg/m²)</i>	15.1 ± 2.4	14.5 ± 1.6	0.426
<i>Birthweight (kg)</i>	3.3 ± 0.6	0.9 ± 0.3	0.000
<i>Gestational age (weeks)</i>	39.9 ± 1.5	27.6 ± 1.1	0.000
<i>Perinatal variables</i>			
<i>Independent walking age (months)</i>	12.6 ± 2.0	17.8 ± 3.5	0.000
<i>Days with supplemental oxygen</i>	/	42.5 ± 29.9	/
<i>Gait parameters</i>			
<i>Speed (m/s)</i>	1.4 ± 0.3	1.3 ± 0.3	NS
<i>Cadence (step/m)</i>	152.8 ± 18.6	151.6 ± 45.9	NS
<i>Stride length (cm)</i>	105.3 ± 13.5	92.6 ± 13.0	NS
<i>Normalized Stride length</i>	94.7 ± 8.4	86.5 ± 9.3	0.009
<i>Stride time (s)</i>	0.8 ± 0.1	0.8 ± 0.1	NS

Values are expressed as mean ± SD. Stride length was normalized to height of children, in order to consider significant difference for height between the two groups.

Figure 1 : NIRS setup on the lower limb of children



A/ Position of the probe on the calf during walking test realization ; B/ Near Infra-Red Spectroscopy (NIRS) probe (Portamon, Artinis) ; C/ Schematic representation of the evolution of NIRS parameters (HbO₂ : oxyhemoglobin, HHb : Deoxyhemoglobin, HbTot : total hemoglobin) during exercise.

First, a straight line (ST) between the middle of the popliteal fossa and calcaneus was traced. Larger calf circumference (LCC) was then measured and traced. At the intersection between the LCC and ST the probe was moved medially from LCC/8 cm and finally secured around the lower leg.

Figure 2 : Flow chart

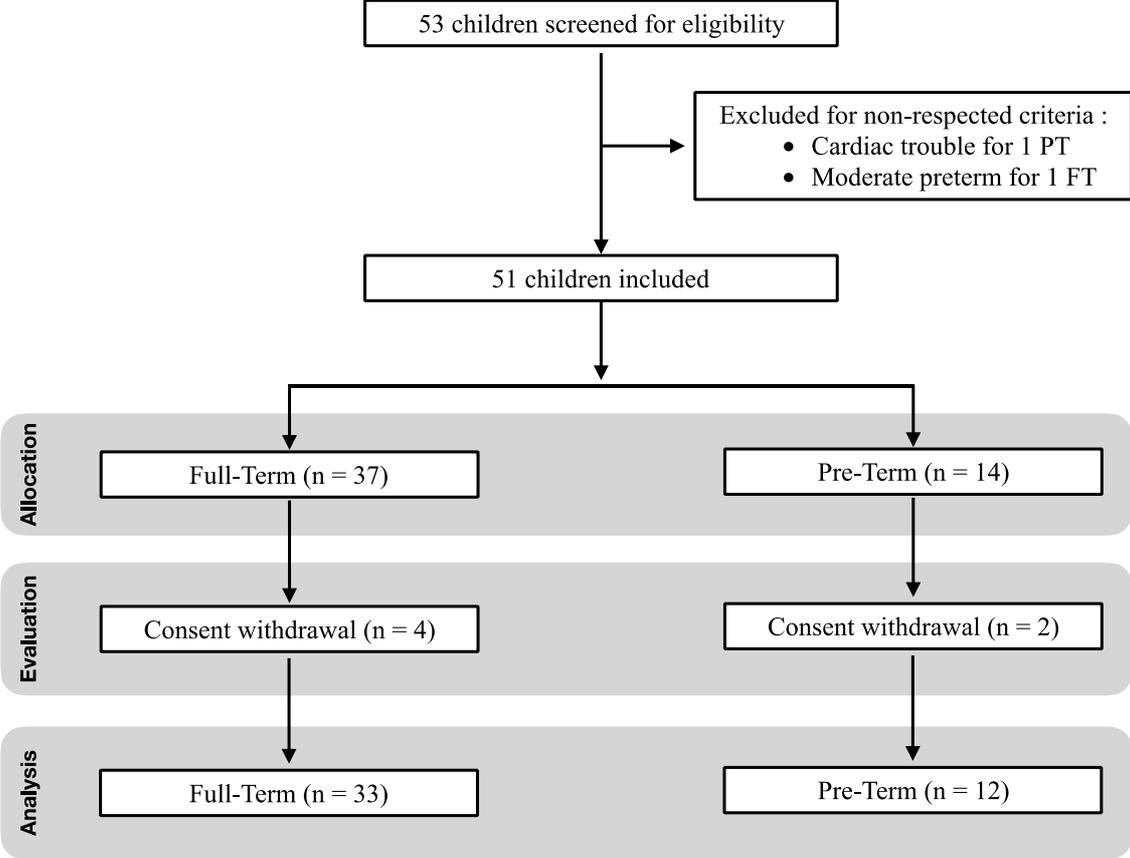
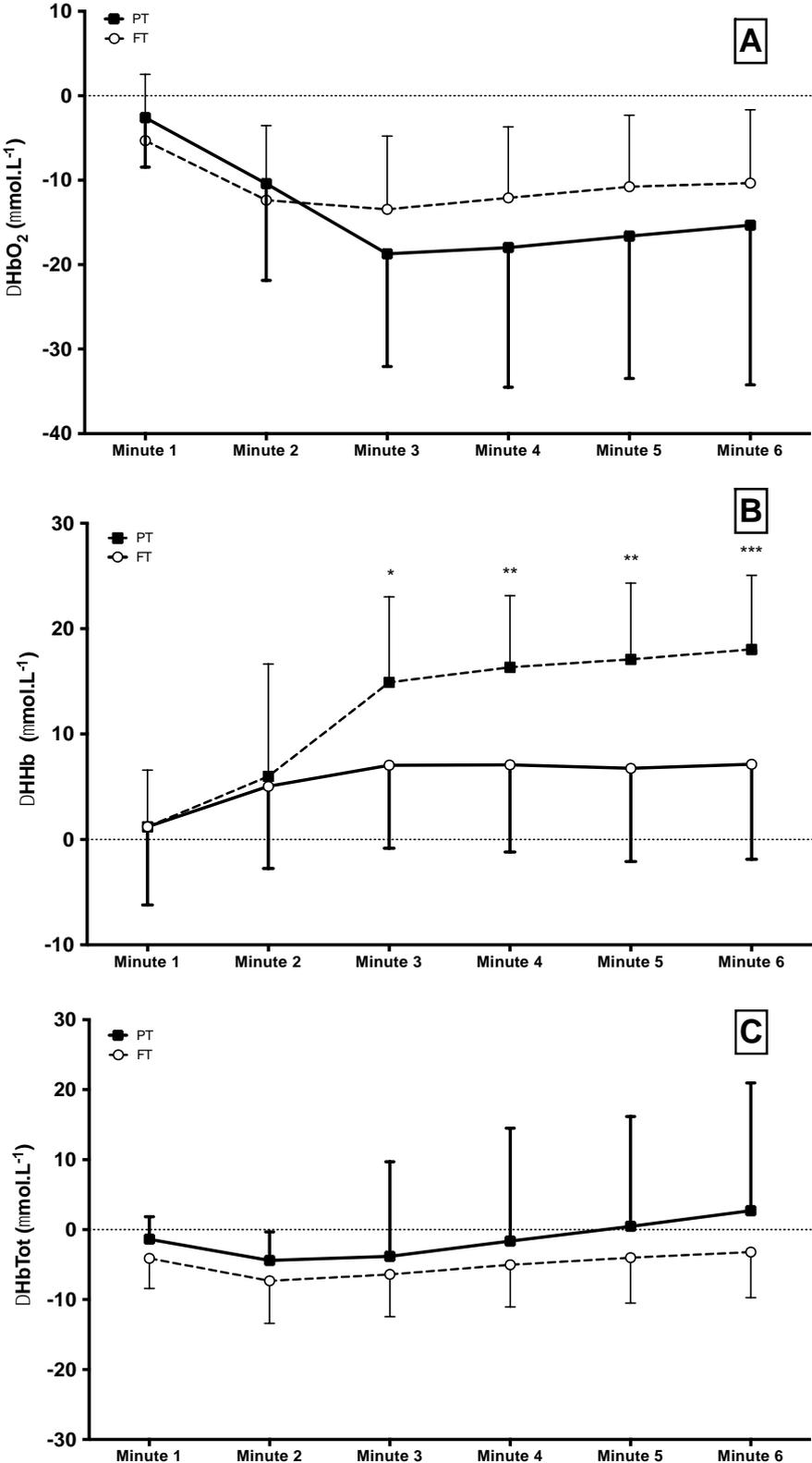


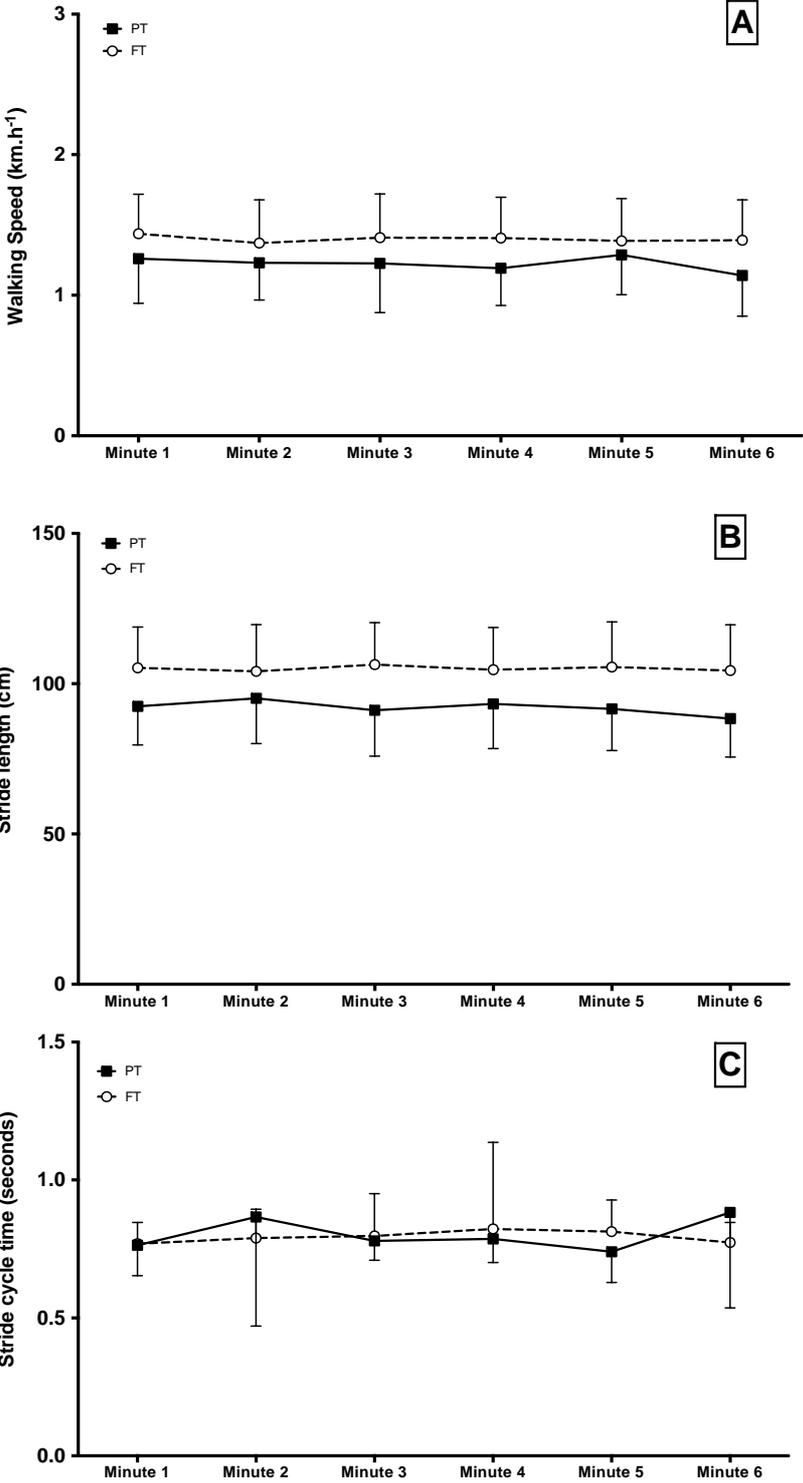
Figure 3 : Evolution of muscular oxygenation parameters during the 6MWT



Caption : PM : Pre-term children ; FT : Full-term children. Graph A (Top) : Oxyhemoglobin variation ; Graph B (Middle) : Deoxyhemoglobin variation ; Graph C (Bottom) : Total Hemoglobin variation.

* : p<0.05 ; ** : p<0.01 ; *** : p<0.001

Figure 4 : Evolution of gait parameters throughout the walking test



Caption : PM : Pre-term children ; FT : Full-term children. Graph A (Top) : walking speed (m.s-1) ; entre Graph B (Middle) : stride length (cm) ; Graph C (Bottom) : stride cycle time (seconds).