

Safety and feasibility of symptom-limited cardiopulmonary exercise test using the modified Naughton protocol in children with cerebral palsy

An observational study

Ah-Ran Kim, MD^a, Min-Hwa Suk, PhD^b, Jeong-Yi Kwon, MD, PhD^{a,*} 

Abstract

Variables derived from the cardiopulmonary exercise test (CPX) provide objective information regarding the exercise capacity of children with cerebral palsy (CP), which can be used as the basis for exercise recommendations. Performing maximal CPX might not be appropriate, safe, or practical for children with CP. In the present study, the safety and feasibility of symptom-limited CPX using the modified Naughton protocol, a submaximal protocol, were investigated in children with CP, Gross Motor Function Classification System (GMFCS) level I or II. The present study included 40 children aged 6 to 12 years with CP who underwent symptom-limited CPX. CPX was performed to measure cardiopulmonary fitness using a treadmill with a modified Naughton protocol. Motor capacity was assessed using the Gross Motor Function Measure (GMFM), Pediatric Balance Scale (PBS), Timed Up and Go (TUG) test, and 6-minute walk test. Thirty-seven children with CP successfully completed testing without any adverse events during or immediately after CPX (dropout rate 7.5%). The reason for test termination was dyspnea (51.4%) or leg fatigue (48.6%). Based on the respiratory exchange ratio (RER), 21 of 37 (56.8%) children chose premature termination. The relationship between the reason for test termination and RER was not statistically significant (Spearman rho=0.082, $P=.631$). CPX exercise time was strongly correlated with GMFM (Spearman rho=0.714) and moderate correlation with PBS (Spearman rho=0.690) and TUG (Spearman rho=0.537). Peak oxygen uptake during CPX showed a weak correlation with GMFM and a moderate correlation with PBS. This study revealed that symptom-limited CPX using the modified Naughton protocol was safe and feasible for children with CP and GMFCS level I or II.

Abbreviations: 6MWT = 6-minute walk test, AT = anaerobic threshold, CP = cerebral palsy, CPX = cardiopulmonary exercise test, GMFCS = Gross Motor Function Classification System, GMFM = Gross Motor Function Measure, PBS = Pediatric Balance Scale, RER = respiratory exchange ratio, TUG = Timed Up and Go, VE = ventilation per minute, VO_2 = oxygen uptake, VO_{2peak} = peak oxygen uptake.

Keywords: cardiopulmonary exercise test, cerebral palsy, children

1. Introduction

Cerebral palsy (CP) is caused by damage to the immature brain.^[1] A study based on the Western Australian Cerebral Palsy Register found that 22% of individuals with mild CP had a survival rate up to 58 years of age, which is similar to that in the general

population.^[2] As expected, the standardized mortality ratio increased with serious impairment.^[2] Adults with CP reportedly have a higher prevalence of cardiometabolic diseases such as diabetes, asthma, high blood pressure, heart disease, and stroke than adults without CP.^[3] The increased risk of chronic diseases

Editor: Manal Kamel Youssef.

Posted history: Some of the contents of the abstract were previously posted to: doi: https://www.karm.or.kr/workshop/?abyear=201902&search=Y&class=4&mode=poster_view&sid=2868&search=Y&class=4.

This research was supported by a National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) (2017R1A2B4004615).

The authors have no conflicts of interest to disclose.

Supplemental Digital Content is available for this article.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

^a Department of Physical and Rehabilitation Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, ^b Department of Physical Education, Seoul National University of Education, Seoul, Republic of Korea.

* Correspondence: Jeong-Yi Kwon, Department of Physical and Rehabilitation Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 06351, Republic of Korea (e-mail: jeongyi.kwon@samsung.com).

Copyright © 2021 the Author(s). Published by Wolters Kluwer Health, Inc.

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Kim AR, Suk MH, Kwon JY. Safety and feasibility of symptom-limited cardiopulmonary exercise test using the modified Naughton protocol in children with cerebral palsy: an observational study. *Medicine* 2021;100:29(e26269).

Received: 21 January 2021 / Received in final form: 16 May 2021 / Accepted: 21 May 2021

<http://dx.doi.org/10.1097/MD.00000000000026269>

in people with CP is associated with deficits in physical fitness, such as cardiorespiratory fitness, muscle strength, muscle endurance, musculoskeletal flexibility, and body composition.^[4]

Maximal oxygen consumption (VO_2max) or peak oxygen consumption (VO_2peak) derived from the cardiopulmonary exercise test (CPX) is the gold standard for assessing exercise capacity in both adults and children^[5] and is frequently used for exercise recommendations. CPX combines conventional exercise testing procedures with ventilator-expired gas analysis, which allows for the concomitant assessment of 3 functional parameters: oxygen consumption (VO_2), carbon dioxide production (VCO_2), and minute ventilation (VE). Although CPX involves higher levels of training and proficiency, as well as equipment and cost, for many patients, the independent and additive information obtained justifies its use.^[5]

CPX studies on CP have rarely been reported because of difficulties in performing the test on subjects with mental and physical impairments. Children with CP generally have lower aerobic exercise capacity and higher oxygen costs for activities of daily living than children with typical development.^[6] The oxygen cost increases with increasing disability.^[7,8] Although maximal exercise tests such as the Bruce protocol are recommended for the pediatric population, performing maximal CPX might not be appropriate, safe, or practical for children with CP. Exercise testing in children presents unique challenges, largely due to their small body size in relation to testing equipment and less compliant nature to the exhaustive and monotonous exercise protocol.^[9] The modified Naughton protocol was used to reduce the time required to administer the test, and the protocol is often modified by reducing the duration of stages from 3 to 2 minutes. This reduction in stage duration can alter the relationship between exercise time and aerobic capacity.

Children with CP can develop various exercise-induced physiological signs or complaints that warrant termination of the test before obtaining the maximum value.^[10] In this special population, submaximal exercise testing to predict VO_2max is recommended.^[11] To date, in CPX studies on subjects with CP, researchers have used modified exercise protocols to adapt to the physical limitations of subjects.^[10,12–15] Therefore, comparing the results between subjects with and without CP is difficult. In the present study, a modified Naughton protocol, a submaximal test,^[16] was applied to children with CP to investigate the applicability of CPX for prevention, treatment, and rehabilitation of cardiopulmonary disease in patients with CP.

We hypothesized that symptom-limited CPX using the modified Naughton protocol would be feasible in ambulatory children with CP. Further, we hypothesized that children with Gross Motor Function Classification System (GMFCS) level I would have better cardiorespiratory fitness than children with GMFCS level II. Therefore, the objective of this study was to clarify the safety and feasibility of symptom-limited CPX using the modified Naughton protocol in children with CP and GMFCS level I or II.

2. Methods

2.1. Study design

This study was conducted in a tertiary university hospital in the Seoul metropolitan area, and the Institutional Review Board of Samsung Medical Center (Seoul, Republic of Korea) approved

Table 1

Participant characteristics.

Characteristic	Value (n = 40)
Age (yr)	7.40 ± 1.60
Height (cm)	123.84 ± 10.24
Weight (kg)	24.53 ± 5.29
Sex (male/female)	21/19
Distribution (unilateral/bilateral)	18/22
GMFCS distribution (level I/level II)	21/19

Values are expressed as mean ± standard deviation.

GMFCS = Gross Motor Function Classification System.

the study protocol (2017-06-045). This research was part of the “Effects of hippotherapy on physical activities, cardiopulmonary fitness and attention in children with CP” study (Clinicaltrials.gov, NCT03870893). The enrollment of participants began on August 1, 2017, and data collection was stopped on January 21, 2019. Children suitable for this study were identified using the Samsung Medical Center database. If the parents wanted their child to participate in the study, the primary investigator conducted a screening *via* telephone. Informed consent was obtained from the participants and their parents or guardians before screening.

2.2. Participants

The present study included 40 children with CP (Table 1). The inclusion criteria were as follows: (a) diagnosis of CP, (b) classified as GMFCS level I or II, (c) 6 to 12 years of age, and (d) body weight <35 kg. Exclusion criteria were as follows: (a) injection with botulinum toxin within 3 months, (b) selective dorsal rhizotomy or orthopedic surgery within 1 year, (c) poor visual acuity, (d) hearing impairment, (e) severe intellectual disability, (f) uncontrolled seizures, (g) hip dislocation, (h) scoliosis Cobb angle >30°, and (i) unhealed fracture.

2.3. Measurements

To determine aerobic capacity, a symptom-limited CPX test using the modified Naughton protocol was performed. The variables measured were VO_2peak (mL/kg/min), ventilation per minute (VE, mL/kg/min), anaerobic threshold (AT, %), respiratory exchange ratio (RER), heart rate, and blood pressure. To evaluate motor capacity, 2 experienced pediatric physical therapists administered the Gross Motor Function Measure (GMFM-66, GMFM-88, %), the Pediatric Balance Scale (PBS, score), and the Timed Up and Go (TUG, seconds) test. Two experienced exercise researchers measured the 6-minute walk test (6MWT, m). All the testers were blinded to the other results.

2.4. Field tests

2.4.1. 6MWT. Children were instructed to walk as fast as possible for 6 minutes in a straight, flat, hard-surfaced corridor. Additional standardized verbal comments or encouragement were allowed every minute, such as “you are doing well” and “you have only 1 minute to go.” Before starting the test, the children were told that the objective of the test was to walk as far as possible in 6 minutes. The tester stood during the test in a manner that did not influence the child’s walking speed, and no practice walk or warm-up was permitted. The total distance

walked was recorded as the 6MWT distance (m), which has shown test-retest reliability for school-aged children with CP (intra-class correlation coefficient, ICC=0.98).^[17]

2.4.2. GMFM. The GMFM-88 is a validated tool for assessing gross motor function in children with CP.^[18] The assessment consists of 88 items in 5 dimensions: (A) lying and rolling (17 items); (B) sitting (20 items); (C) crawling and kneeling (14 items); (D) standing (13 items); and (E) walking, running, and jumping (24 items). Each item is scored on a 4-point scale. The raw score for each dimension was converted into a percentage score, and the dimensions were equally weighted. GMFM-66 scores were calculated from the GMFM-88 using the Gross Motor Ability Estimator.

2.4.3. PBS. PBS is a criterion-referenced measure for evaluating functional balance in everyday tasks.^[19]

PBS aggregate scores (hereafter PBS scores) for the 14 tasks evaluated ranged from 0 to 56, with higher scores indicating better postural control. The evaluated tasks on PBS were as follows: (1) sitting to standing, (2) standing to sitting, (3) transfers, (4) standing unsupported, (5) sitting unsupported, (6) standing with eyes closed, (7) standing with feet together, (8) standing with one foot in front, (9) standing on one foot, (10) turning 360 degrees, (11) turning to look behind, (12) retrieving object from floor, (13) placing alternate foot on stool, and (14) reaching forward with outstretched arm. The scale consists of 14 items scored from 0 (lowest function) to 4 points (highest function), with a maximum score of 56 points.^[19] The scale has been validated as a good test for children with CP^[20]; PBS has excellent test-retest reliability (ICC > 0.9) and inter-rater reliability (ICC > 0.9) and validity.^[21]

2.4.4. TUG test. The TUG test was used to evaluate walking speed, posture control, functional mobility, and balance.^[22]

The test represents the time that a person takes to rise from a chair, walk 3 m, turn around, walk back to the chair, and sit down. A score of 10 seconds or less indicates normal mobility, 11 to 20 seconds are within normal limits for disabled patients, and greater than 20 seconds means the person needs assistance outside and indicates further examination and intervention. The TUG test showed test-retest reliability in children with CP (ICC = 0.99).^[23]

2.5. Cardiorespiratory exercise test

All subjects performed a symptom-limited treadmill exercise test using the modified Naughton protocol (Supplementary Table 1, <http://links.lww.com/MD/G270>). The modified Naughton protocol has 2-minute stages and starts at a lower metabolic equivalent of task (MET) workload and increases by 1 MET per stage.^[7] The grade increases by 3.5% every 2 minutes until maximal effort is achieved. The children were allowed to grip the support bars of the treadmill for safety and to wear their ankle foot orthoses (AFOs) if needed. Electrocardiograms were recorded during the test to observe abnormal heart rhythms. The electrocardiogram was checked using an exercise test device (Q-stress, Mortara Instrument Inc., Milwaukee, WI, USA), and cardiopulmonary fitness was estimated using a True One 2400 (Palvo Medics, Salt Lake City, UT, USA). All children were verbally encouraged to continue the test until exhaustion. The reasons for test termination included impaired breathing, lower limb fatigue, exhaustion, high heart rate, abnormal blood

pressure responses, heart arrhythmias, increasing chest pain during exercise, marked ST depressions during the test, and refusal to continue. At the end of the test, the child was asked why he or she had stopped. VO₂peak, VE, AT, and RER were obtained and analyzed. To reduce the child's psychological burden, one or more brief mock tests, a full explanation of the test procedure and meaning, and continued encouragement (before and during the test) was applied.

2.6. Statistical analysis

After certification of normality based on the Shapiro–Wilk test, the independent *t*-test or Mann–Whitney *U* test was performed to examine differences between groups. Pearson's chi-square test was used for the analysis of GMFCS level and RER. The relationship between aerobic capacity and motor capacity was analyzed using Spearman's correlation coefficient. A correlation coefficient of 0.70 to 0.89 represents a "strong" correlation. A correlation coefficient of 0.40 to 0.69 represents a "moderate" association, whereas 0.10 to 0.39 is a "weak" association. Data were analyzed using SPSS for Windows (version 21.0; SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Adverse events

Among the 40 participants, 3 dropped out of the CPX. Two (GMFCS level II) of the 3 children quit the test prematurely at stage 3 (<6 minutes) because of locomotor insufficiency and unwillingness to provide maximal exertion. One child (GMFCS level II) failed the treadmill test because of psychological difficulties (fear). A total of 37 children successfully completed the test without any adverse events during or after CPX.

3.2. Aerobic and motor capacities of children with CP

Values obtained through CPX were analyzed to evaluate the differences in aerobic capacities between children with GMFCS levels I and II. The exercise time of children with GMFCS level II (9.69 ± 2.31 minutes) was significantly shorter than of children with GMFCS level I (13.48 ± 2.77 minutes; *P* < .001). The other parameters did not show any statistical differences between the 2 groups (Table 2). In all field tests, including GMMF-66, GMFM-88, 6MWT, PBS, and TUG, children with GMFCS level I showed significantly higher motor capacity than children with GMFCS level II (*P* < .05; Table 2).

Based on the RER, 21 of 37 (56.8%) children chose premature termination. RER is the ratio between the amount of carbon dioxide (CO₂) produced during metabolism and the oxygen (O₂) used. An RER level ≥ 1 is indicative of carbohydrate as the predominant fuel source. A chi-square test of independence was performed to examine the relationship between GMFCS level and RER during CPX; the relationship between these variables was not significant (*P* > .05; Table 3). Among the 37 children who underwent CPX successfully, 19 (51.4%) stopped exercising due to dyspnea and the other 18 (48.6%) due to leg fatigue. The relationship between the reason for test termination and RER was not significant (Spearman's rho = 0.082, *P* = .631).

CPX exercise time showed a strong correlation with GMFM (Spearman rho = 0.714 with GMFM-66, Spearman rho = 0.717 with GMFM-88) and moderate correlation with PBS and TUG

Table 2
Aerobic and motor capacities of children with cerebral palsy.

Variable		All (n=37)	Level I (n=21)	Level II (n=16)	P value
Aerobic capacities	Exercise time (min)	11.84 ± 3.18	13.48 ± 2.77	9.69 ± 2.31	.000
	VO ₂ peak (mL/kg/min)	25.44 ± 3.73	26.20 ± 4.13	24.42 ± 2.94	.153
	VE (mL/min)	20.36 ± 6.05	21.04 ± 5.88	19.45 ± 6.32	.435
	AT (%)	46.49 ± 3.06	46.52 ± 3.44	46.44 ± 2.58	.934
	RER	0.98 ± 0.05	0.97 ± 0.05	0.99 ± 0.04	.303
	HR rest (beats/min)	90.97 ± 13.31	89.62 ± 13.21	92.75 ± 13.65	.751
	HR max (beats/min)	167.08 ± 12.75	165.38 ± 15.07	169.31 ± 8.83	.360
	SBP rest (mmHg)	103.03 ± 9.47	103.05 ± 9.27	103.00 ± 10.04	.988
	DBP rest (mmHg)	68.65 ± 8.33	67.57 ± 7.96	70.06 ± 8.84	.375
	SBP max (mmHg)	122.35 ± 11.72	122.52 ± 12.28	122.13 ± 11.33	.920
Motor capacities	DBP max (mmHg)	67.62 ± 5.85	66.76 ± 5.56	68.75 ± 6.19	.312
	GMFM-88 (%a)	97.17 ± 2.62	98.87 ± 1.10	94.95 ± 2.36	.000
	GMFM-66a	85.03 ± 10.04	91.56 ± 8.22	76.45 ± 3.69	.000
	PBS (score)a	53.32 ± 2.14	54.57 ± 1.43	51.69 ± 1.77	.000
	TUG test (sec)	7.97 ± 1.95	7.21 ± 1.15	8.96 ± 2.33	.004
	6MWT (m)	393.24 ± 63.30	426.71 ± 46.58	349.31 ± 55.65	.000

Values are expressed as mean ± standard deviation (SD).

6MWT = 6-minute walk test, AT = anaerobic threshold, DBP max = maximal diastolic blood pressure, DBP rest = diastolic blood pressure at rest, GMFM = Gross Motor Function Measure, HR max = maximal heart rate, HR rest = heart rate at rest, PBS = Pediatric Balance Scale, RER = respiratory exchange ratio, SBP max = maximal systolic blood pressure, SBP rest = systolic blood pressure at rest, TUG = Timed Up and Go, VE = ventilation per minute, VO₂peak = peak oxygen uptake.

(Spearman rho = 0.690 with PBS, Spearman rho = -0.537 with TUG). VO₂peak during CPX showed a weak correlation with GMFM (Spearman rho = 0.353 with GMFM-66, Spearman rho = 0.369 with GMFM-88) and moderate correlation with PBS (Spearman rho = 0.460; Table 4).

4. Discussion

In the present study, symptom-limited CPX using the modified Naughton protocol was safe and feasible for children with CP and GMFCS levels I or II. The dropout rate was only 7.5% in 3 children. The recommended total exercise duration is 6 to 12 minutes for children to avoid premature muscle fatigue and lack of attention and motivation.^[24] The average exercise time in the present study was within this range (11.84 ± 3.18 minutes).

The variables obtained from the CPX provide objective information regarding the exercise capacity of children with CP, which can be used as the basis for exercise recommendations. Because the modified protocol can be used for school-age children with CP, hypothetically, CPX using this protocol can be applied to adolescents and adults with CP. Management of cardiopulmonary disease in patients with CP has become an important medical issue as the coexistence of cardiopulmonary disease in patients with CP increases.^[3] The parameters measured using

CPX can potentially be used as biomarkers for the diagnosis, treatment, and rehabilitation of cardiopulmonary disease in patients with CP.

VO₂max is defined as the highest rate of oxygen uptake and utilization by the body during maximal exercise when further increases in the work rate cease to bring about additional increases in VO₂. VO₂peak, directly reflective of VO₂max, has the highest VO₂ value attained during an incremental or other high-intensity exercise test designed to bring the subject to their tolerance limit. The VO₂peak values in people with CP using the treadmill test have been reported to range from 28.7–42.0.^[12–14,25] The VO₂peak values obtained during the cycle ergometer test in children with CP (GMFCS level I, II, and III; 9.6–10.5 years) are reportedly similar to the treadmill test, ranging from 31.4 to 39.3 mL/kg/min.^[10,15,20] These values are higher than those measured using the modified Naughton protocol in the present study. A possible explanation is that maximal exercise was not performed in many children in this study, and the age and BMI were much lower than in previous reports. Furthermore, significant differences were not observed in VO₂peak between CP children with GMFCS levels I and II in this study, which is inconsistent with previous reports.^[13,15,20] The VO₂peak was weakly correlated with motor capacities (GMFM, PBS, and 6MWT) in children with CP and GMFCS level I or II in the present study.

Table 3
Respiratory exchange ratio (RER) and stages reached by participants during the cardiopulmonary exercise test.

GMFCS	RER	Stages								N	P value
		Stage 4	Stage 5	Stage 6	Stage 7	Stage 8	Stage 9	Stage 10			
Level I	<1.0	0	1	3	6	3	0	1	14	NS	
	≥1.0	0	0	1	4	0	2	0	7		
Level II	<1.0	2	1	2	2	0	0	0	7		
	≥1.0	2	1	5	1	0	0	0	9		
Total		4	3	11	13	3	2	1	37		

Values are number. Tests were performed with a modified Naughton protocol. GMFCS = Gross Motor Function Classification System.

Table 4
Correlations between aerobic and motor capacities.

	GMFM-66	GMFM-88	PBS	TUG test	6MWT
Exercise time	0.714 ^{***}	0.717 ^{***}	0.690 ^{***}	-0.537 ^{**}	0.702 ^{***}
VO ₂ peak	0.353 [*]	0.369 [*]	0.460 ^{**}	-0.152	0.409 [*]
VE	-0.008	-0.016	0.070	0.123	0.282
AT (%)	-0.047	-0.048	0.050	0.246	-0.051
RER	-0.143	-0.156	-0.091	-0.031	0.070

Values expressed Spearman rho.

6MWT = 6-minute walk test, AT = anaerobic threshold, GMFM = Gross Motor Function Measure, PBS = Pediatric Balance Scale, RER = respiratory exchange ratio, TUG = Timed Up and Go, VE = ventilation per minute, VO₂peak = peak oxygen uptake.

^{*} P < .05.

^{**} P < .01.

^{***} P < .001.

Several treadmill tests are available for maximal exercise tests, such as the modified Balke protocol and the modified Bruce protocol.^[26] However, these tests require a high treadmill inclination, which can be a drawback, especially for children with spasticity in their legs. To avoid this disadvantage, Maltais et al proposed a protocol in which the inclination did not increase.^[14] This type of protocol designed by individual researchers is disadvantageous because comparing results between subjects with and without CP is difficult. Submaximal tests can overcome the limitations of maximal stress tests, such as insufficient exercise time due to muscle fatigue rather than exertion and possible risks in people with CP. The modified Naughton protocol is a submaximal exercise test protocol originally designed for patients with congestive heart failure. In the present study, VO₂peak and exercise time measured using the modified Naughton protocol correlated with the 6MWT, a simple submaximal field test for children with CP.

The main disadvantage of VO₂peak is that VO₂max is underestimated because it is often not accompanied by maximum exertion.^[27] For participants to reach VO₂max, understanding why patients end CPX prematurely is important. Factors that cause premature termination of CPX include anxiety, lack of motivation to provide maximal exertion, locomotor insufficiency, or subjective reasons such as dyspnea and muscular fatigue.^[28–34] reasons for early discontinuation have not been adequately reported in children with CP. In the present study, 51.4% (n = 19) of the children completed the test due to dyspnea and 48.6% (n = 18) due to leg fatigue. Because this reason is not associated with RER, complaints for stopping CPX are regarded as subjective and less relevant in terms of exertion in children with CP. According to Santa Mina's study,^[27] the reasons for test termination in adults with cancer were as follows: equipment discomfort (49%), volitional peak meaning that participants did not want to attempt further exertion (36%), and physical discomfort including leg fatigue (14.9%). For subjects who met the VO₂max criteria, volitional peak was the most common reason for test termination (45.5%), followed by physical discomfort (36.4%), and equipment discomfort (18.2%). Among the 35 CPXs that were discontinued due to equipment discomfort, only 2 met the VO₂ max verification criteria. Although a small mask that fits a child was used in the present study, wearing a mask can cause discomfort and/or fear to the child. We attempted to reduce the child's psychological burden through one or more mock tests, a full explanation of the test procedure and meaning, and continued encouragement before and during the test.

5. Limitation

This study suggests the possibility of applying the modified Naughton protocol to patients with CP. Further studies are necessary to determine the reliability and validity of the symptom-limited CPX using the modified Naughton protocol in a large cohort of patients with CP and various GMFCS levels in all age groups. Future studies on CPX using the modified Naughton protocol are necessary to identify the cutoff points used to identify low, moderate, and high cardiorespiratory fitness across age and sex in patients with CP. Because this study suggested the possibility of applying the modified Naughton protocol in CP patients, future studies will use a large cohort to limit symptoms and CPX reliability and efficacy.

Author contributions

Conceptualization: Jeong-Yi Kwon.

Data curation: Jeong-Yi Kwon.

Formal analysis: Ah-Ran Kim, Min-Hwa Suk, Jeong-Yi Kwon.

Funding acquisition: Jeong-Yi Kwon.

Investigation: Ah-Ran Kim, Min-Hwa Suk, Jeong-Yi Kwon.

Methodology: Min-Hwa Suk, Jeong-Yi Kwon.

Project administration: Min-Hwa Suk, Jeong-Yi Kwon.

Resources: Jeong-Yi Kwon.

Software: Min-Hwa Suk, Jeong-Yi Kwon.

Supervision: Jeong-Yi Kwon.

Validation: Jeong-Yi Kwon.

Visualization: Jeong-Yi Kwon.

Writing – original draft: Ah-Ran Kim, Jeong-Yi Kwon.

Writing – review & editing: Ah-Ran Kim, Jeong-Yi Kwon.

References

- [1] Bax M, Goldstein M, Rosenbaum P, et al. Proposed definition and classification of cerebral palsy, April 2005. *Dev Med Child Neurol* 2005;47:571–6.
- [2] Blair E, Langdon K, McIntyre S, Lawrence D, Watson L. Survival and mortality in cerebral palsy: observations to the sixth decade from a data linkage study of a total population register and National Death Index. *BMC Neurol* 2019;19:1–11.
- [3] Peterson MD, Ryan JM, Hurvitz EA, Mahmoudi E. Chronic conditions in adults with cerebral palsy. *JAMA* 2015;314:2303–5.
- [4] Hombegen SP, Huisstede BM, Streur MF, et al. Impact of cerebral palsy on health-related physical fitness in adults: systematic review. *Arch Phys Med Rehabil* 2012;93:871–81.
- [5] Ross R, Blair SN, Arena R, et al. Importance of assessing cardiorespiratory fitness in clinical practice: a case for fitness as a clinical vital sign: a scientific statement from the American Heart Association. *Circulation* 2016;134:e653–99.

- [6] Unnithan VB, Dowling JJ, Frost G, Bar-Or O. Role of cocontraction in the O₂ cost of walking in children with cerebral palsy. *Med Sci Sports Exerc* 1996;28:1498–504.
- [7] Johnston TE, Moore SE, Quinn LT, Smith BT. Energy cost of walking in children with cerebral palsy: relation to the Gross Motor Function Classification System. *Dev Med Child Neurol* 2004;46:34–8.
- [8] Kamp FA, Lennon N, Holmes L, Dallmeijer AJ, Henley J, Miller F. Energy cost of walking in children with spastic cerebral palsy: relationship with age, body composition and mobility capacity. *Gait Posture* 2014;40:209–14.
- [9] Duff DK, De Souza AM, Human DG, Potts JE, Harris KC. A novel treadmill protocol for exercise testing in children: the British Columbia Children's Hospital protocol. *BMJ Open Sport Exerc Med* 2017;3:e000197.
- [10] Brehm MA, Balemans AC, Becher JG, Dallmeijer AJ. Reliability of a progressive maximal cycle ergometer test to assess peak oxygen uptake in children with mild to moderate cerebral palsy. *Phys Ther* 2014;94:121–8.
- [11] Satonaka A, Suzuki N, Kawamura M. Validity of submaximal exercise testing in adults with athetospastic cerebral palsy. *Arch Phys Med Rehabil* 2012;93:485–9.
- [12] Garcia CC, Alcocer-Gamboa A, Ruiz MP, et al. Metabolic, cardiorespiratory, and neuromuscular fitness performance in children with cerebral palsy: a comparison with healthy youth. *J Exerc Rehabil* 2016;12:124–31.
- [13] Verschuren O, Takken T. Aerobic capacity in children and adolescents with cerebral palsy. *Res Dev Disabil* 2010;31:1352–7.
- [14] Maltais DB, Pierrynowski MR, Galea VA, Bar-Or O. Physical activity level is associated with the O₂ cost of walking in cerebral palsy. *Med Sci Sports Exerc* 2005;37:347–53.
- [15] Balemans AC, van Wely L, Becher JG, et al. Longitudinal relationship among physical fitness, walking-related physical activity, and fatigue in children with cerebral palsy. *Phys Ther* 2015;95:996–1005.
- [16] American College of Sports Medicine ACSM's Guidelines for Exercise Testing and Prescription. Philadelphia: Wolters Kluwer; 2018. 111–142.
- [17] Thompson P, Beath T, Bell J, et al. Test-retest reliability of the 10-metre fast walk test and 6-minute walk test in ambulatory school-aged children with cerebral palsy. *Dev Med Child Neurol* 2008;50:370–6.
- [18] Rosenbaum PL, Walter SD, Hanna SE, et al. Prognosis for gross motor function in cerebral palsy: creation of motor development curves. *JAMA* 2002;288:1357–63.
- [19] Franjoine MR, Gunther JS, Taylor MJ. Pediatric balance scale: a modified version of the berg balance scale for the school-age child with mild to moderate motor impairment. *Pediatr Phys Ther* 2003;15:114–28.
- [20] Balemans AC, Van Wely L, De Heer SJ, et al. Maximal aerobic and anaerobic exercise responses in children with cerebral palsy. *Med Sci Sports Exerc* 2013;45:561–8.
- [21] Yi SH, Hwang JH, Kim SJ, Kwon JY. Validity of pediatric balance scales in children with spastic cerebral palsy. *Neuropediatrics* 2012;43:307–13.
- [22] Williams EN, Carroll SG, Reddihough DS, Phillips BA, Galea MP. Investigation of the timed 'up & go' test in children. *Dev Med Child Neurol* 2005;47:518–24.
- [23] Gan SM, Tung LC, Tang YH, Wang CH. Psychometric properties of functional balance assessment in children with cerebral palsy. *Neuro-rehabil Neural Repair* 2008;22:745–53.
- [24] Massin MM. The role of exercise testing in pediatric cardiology. *Arch Cardiovasc Dis* 2014;107:319–27.
- [25] Hoofwijk M, Unnithan V, Bar-Or O. Maximal treadmill performance of children with cerebral palsy. *Pediatr Exerc Sci* 1995;7:305–13.
- [26] Verschuren O, Ketelaar M, Keefer D, et al. Identification of a core set of exercise tests for children and adolescents with cerebral palsy: a Delphi survey of researchers and clinicians. *Dev Med Child Neurol* 2011;53:449–56.
- [27] Santa Mina D, Au D, Papadopoulos E, et al. Aerobic capacity attainment and reasons for cardiopulmonary exercise test termination in people with cancer: a descriptive, retrospective analysis from a single laboratory. *Support Care Cancer* 2020;28:4285–94.
- [28] Edvardsen E, Hem E, Anderssen SA. End criteria for reaching maximal oxygen uptake must be strict and adjusted to sex and age: a cross-sectional study. *PLoS One* 2014;9:e85276.
- [29] Jones LW, Eves ND, Haykowsky M, Joy AA, Douglas PS. Cardiorespiratory exercise testing in clinical oncology research: systematic review and practice recommendations. *Lancet Oncol* 2008;9:757–65.
- [30] Wagner DR, Clark NW. Similar results for face mask versus mouthpiece during incremental exercise to exhaustion. *J Sports Sci* 2016;34:852–5.
- [31] Jones LW, Eves ND, Mackey JR, et al. Safety and feasibility of cardiopulmonary exercise testing in patients with advanced cancer. *Lung Cancer* 2007;55:225–32.
- [32] Forman DE, Myers J, Lavie CJ, Guazzi M, Celli B, Arena R. Cardiopulmonary exercise testing: relevant but underused. *Postgrad Med* 2010;122:68–86.
- [33] Milani RV, Lavie CJ, Mehra MR, Ventura HO. Understanding the basics of cardiopulmonary exercise testing. *Mayo Clin Proc* 2006;81:1603–11.
- [34] Bart BA, Wolfel EE. Method of expired gas collection during cardiopulmonary exercise testing does not affect respiratory gas exchange measurements in patients with heart failure. *J Card Fail* 1994;1:91–6.