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ORIGINAL REPORT

DIFFERENCES IN CARDIOVASCULAR HEALTH IN AMBULATORY PERSONS WITH CEREBRAL PALSY

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***Objective*: To compare cardiovascular health variables and physical activity levels of adolescents and adults with cerebral palsy who are Gross Motor Function Classification System (GMFCS) levels I and II.**
***Methods*: Eleven adolescents (mean age 13.1 (standard deviation (SD) 2.1) years) and 14 adults (mean age 31.7 (SD 10.4) years)) with cerebral palsy were included, grouped by their GMFCS level (level I (n=12); level II (n=13)). Assessments of cardiovascular health, body composition and physical activity levels were performed. Cardiovascular variables included resting blood pressure and carotid artery intima media thickness. Body composition included height, weight, body mass index, and waist circumference. Physical activity was measured using accelerometry.**
***Results*: Adjusting for age between GMFCS levels (GMFCS I mean 17.3 (SD 5.2); GMFCS II mean 29.3 (SD 14.1) years, p=0.011), significant differences were evident for moderate-to-vigorous physical activity per day (GMFCS I median 45.8 (interquartile range (IQR) 32.4–75.1); GMFCS II median 16.4 (IQR 13.0, 25.0) min/day, p=0.011), height (GMFCS I mean 1.63 (SD 0.14); GMFCS II mean 1.56 (SD 0.12) m, p=0.010), mean arterial pressure (GMFCS I mean 84.6 (SD 7.8); GMFCS II mean 89.4 (SD 8.5) mmHg, p=0.030), and carotid artery intima media thickness (GMFCS I mean 0.431 (SD 0.06); GMFCS II mean 0.489 (SD 0.04), p=0.026).**
***Conclusion:* Individuals with cerebral palsy who were GMFCS level I had lower mean arterial pressure, thinner carotid artery intima media thickness, and engaged in a greater amount of moderate-to-vigorous physical activity per day than those who were GMFCS level II. Clinicians should acknowledge that ambulatory individuals with cerebral palsy could have differing cardiovascular health profiles and should monitor these cardiovascular variables and discuss physical activity during healthcare visits, regardless of age.**

Key words: cerebral palsy; adolescent; adult; physical activity; cardiovascular health; body composition.

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LAY ABSTRACT

Physical activity has many health benefits, one of which is the health of the heart and blood vessels. People with cerebral palsy are at risk of developing unhealthy heart and blood vessels due to limitations in mobility reducing the amount of physical activity they can perform. We studied the differences in blood vessel health between people with cerebral palsy who walk without limitations compared with those who walk with limitations. The group who walk without limitations had better measures of vessel health, such as lower blood pressure, and engaged in more physical activity than those who walk with limitations. We recommend that healthcare providers measure blood pressure and discuss physical activity with people with cerebral palsy in order to help them maintain heart and blood vessel health.

Cerebral palsy (CP) is a well-recognized neurodevelopmental condition commencing in early childhood and continuing throughout life (1). CP is caused by non-progressive disturbances to the developing foetal or infant brain. The resulting motor disorders can be accompanied by secondary disturbances affecting cognition, communication, and behaviour, among others (2). As CP presents early in life, much research has focused on children with CP. However, researchers have recently started to examine the impact of CP and its secondary disturbances later in life, which is of interest given the increasing lifespan of persons with CP (3).

A prominent concern among clinicians and researchers regarding persons with CP, regardless of their age, is a lack of physical activity (PA) (4). Low levels of PA in persons with CP can partly be explained by the condition, as well as accompanying perceptions of physical pain and fatigue that worsen with age (5, 6). Studies in both children and adults with CP have shown that persons with CP engage in significantly less PA than the general population (4). While this finding is most evident in non-ambulatory individuals with CP (4), it also has been reported in the most functional, ambulatory individuals (i.e. individuals classified as Gross Motor Functional Classification System (GMFCS) (7) level I or II) (8). Compared with adolescents and adults in GMFCS level I, adolescents and adults in level II have limitations walking long distances and

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balancing, may use wheeled mobility when travelling long distances outdoors and in the community, require the use of a handrail to walk up and down stairs, and are not as capable of running and jumping (7).

Reduced PA in persons with CP is related to increased risks of cardiometabolic and cardiovascular disease (CVD) (9, 10) and co-morbidity (11), with these relationships becoming more prevalent later in life in this population (12). Descriptive data from our previous work showed that non-ambulatory adults with CP (GMFCS levels III–V) may be at greater risk of CVD compared with those who are ambulatory (GMFCS levels I, II) (13). A Medical Expenditure Panel Survey of over 200,000 adults (of whom 1,015 had CP) reported that adults with CP were at greater risk of cardiovascular-related diseases, such as diabetes (unadjusted odds ratios (OR); 2.63), hypertension (unadjusted OR; 3.13) and stroke (unadjusted OR; 4.08), compared with the general population (11). Importantly, age, physical disability status (i.e. moderate or severe) and self-reported PA were associated with cardiovascular-related disease in these adults with CP (11). Similarly, in a population-based cohort in Taiwan, patients with CP had a 2.17-fold greater risk of stroke than the general population (14).

While it is apparent that non-ambulatory (GMFCS level III–V) individuals with CP have increased susceptibility to physical inactivity and cardiovascular risk (12), there has been little research into the companion risk relationship for ambulatory individuals with CP. A secondary objective in a study by Ryan and colleagues was to examine the relationship between PA, measured by accelerometry, and cardiometabolic risk in adults with CP who were GMFCS levels I–III (9). They found that moderate activity was negatively associated with waist circumference, systolic blood pressure (SBP) and diastolic blood pressure (DBP). Indeed, previous research within our group revealed that adolescents with CP who were GMFCS levels I and II did not differ from their age- and sex-matched counterparts in measures of arterial health (15). However, a limitation of this study was that GMFCS I and II were combined and limited to adolescents only. Further risk stratification within an ambulatory population (GMFCS level I vs GMFCS level II) would permit identification of those individuals who would benefit from intensified monitoring and preventative management. Therefore, the primary objective of this exploratory study was to compare cardiovascular health variables and objectively measured PA levels of adolescents and adults with CP who are GMFCS level I vs those who are GMFCS level II. A secondary objective was to assess the relationships between objectively measured PA and cardiovascular health variables in this sample of persons with CP who are ambulatory. It is hypothesized that those who are GMFCS level I will have increased PA levels and healthier cardiovascular indices compared with those who are GMFCS level II. Secondly, it is hypothesized that PA levels will be inversely associated with cardiovascular health variables in this study sample.

METHODS

Data from the Stay-FIT Program of Research (https://www.canchild.ca/en/stay-fit), a multi-step research programme whose objectives are to understand physical health and encourage a healthy active lifestyle in children, adolescents and adults with CP, were reviewed for study eligibility. Specifically, adolescents and adults with CP who were GMFCS levels I or II were included in the present study. This resulted in a sample consisting of 11 adolescents (mean 13.1 (SD 2.1) years) and 14 adults (31.7 (SD 10.4) years) with CP. Data were previously collected in the Vascular Dynamics Laboratory at McMaster University, Hamilton, Ontario, Canada, with recruitment occurring in the years 2010–2012 (15) and 2012–2014 (12), respectively. The Hamilton Integrated Research Ethics Board granted study approval.

Methods for body composition data collection and non-invasive arterial structure and function measures are described elsewhere (12, 15). Physical activity was measured using an ActiGraph GT1M or GT3X accelerometer (ActiGraph, Pensacola, FL, USA) worn on the hip of each participant during all waking hours, with the exception of any water activities, over 7 consecutive days. All data were collected in 3-s sampling intervals, or epochs. The mean minutes of moderate-to-vigorous physical activity (MVPA) per day (min/day) were determined using age-appropriate cut-points, as previously described (16, 17). Accelerometer data were only included in the analysis if the participant wore the device for a minimum of 5 h on at least 4 days (18).

Participants included in the study had data pertaining to the following variables: age, height (cm), weight (kg), body mass index (BMI) (kg/m^2), waist circumference (cm), heart rate (beats per min), SBP (mmHg), DBP (mmHg), mean arterial pressure (MAP) (mmHg), carotid artery distensibility (mmHg^{-1}), carotid artery intima-media thickness (cIMT) (mm), absolute brachial artery flow mediated dilation (FMD) (mm), relative FMD (%), and MVPA per day. GMFCS level was recorded for each participant using a self-report version of the GMFCS-E&R (7). Participants were separated into 2 groups based on their GMFCS level (i.e. GMFCS level I or GMFCS level II).

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS 20. IBM, Armonk, NY, USA). Descriptive summary statistics were calculated as means and standard deviations for continuous variables and as percentages for nominal data (i.e. sex). Assumptions pertaining to the t-test for independent means were tested. Continuous variables were assessed for normality using the Shapiro-Wilk descriptive test in each GMFCS level. *t*-tests for independent means were performed for each continuous variable. An analysis of covariance (ANCOVA) was performed, where age, a continuous variable, was included as a covariate when examining between-group differences for body composition, cardiovascular variables, and MVPA per day. Age was chosen as a covariate due to the fact that it has been identified as a salient predictor of CVD in the general population (19), and was recently shown to be a significant predictor of cIMT and other non-traditional markers of CVD risk in adults with CP (12). Separate Pearson correlations were performed between MVPA per day (independent variable) and BMI, waist circumference, heart rate, SBP, DBP, MAP, carotid artery distensibility, FMD (both absolute and relative), and cIMT (dependent variables). A minimum criterion alpha level of $p \leq 0.05$ was used to determine statistical significance.

RESULTS

Data collection

One adolescent who was GMFCS level I did not have an FMD assessment performed and therefore was not included in the between-group analysis for absolute or relative FMD. Another adolescent who was GMFCS level II was not included in the between-group analysis for cIMT due to data acquisition error. Finally, 4 adolescents and 1 adult (4 GMFCS level I, 1 GMFCS level II) did not have MVPA values as a result of missing data files. Participants wore the accelerometer for a mean of 6.5 days (SD 0.9), equalling a total mean wear time of 77.4 (SD 15.5) waking hours.

Comparison between GMFCS level I and II

Participant characteristics and descriptive summary statistics are presented in Table I. Carotid artery distensibility ($p<0.001$) and MVPA per day ($p=0.001$) were not normally distributed, therefore natural log transformations of the data were performed prior to hypothesis testing. These transformations resulted in normal distributions of the data. Independent samples *t*-test revealed significant differences for age ($p=0.011$, 95% CI –20.9 to –3.0) and MVPA per day ($p=0.037$, 95% CI 2.2 to 57.9) between GMFCS levels I and II (Table I), with the GMFCS level II group being older in age and engaging in less MVPA per day than the GMFCS level I group.

With age included as a covariate, ANCOVA revealed statistically significant differences in height, MAP, cIMT and MVPA per day between individuals who were GMFCS level I compared with those who were GMFCS level II. More specifically, the GMFCS level I group was taller than the GMFCS level II group ($F_{1, 23} = 5.68$, $p=0.010$). The GMFCS level I group had lower MAP ($F_{1, 23}=4.11$, $p=0.030$) and smaller cIMT ($F_{1, 22}=4.34$, $p=0.026$) than the GMFCS level II group. Finally, the GMFCS level I group engaged in more MVPA per day than the GMFCS level II group ($F_{1, 18}=6.027$, $p=0.011$) (Table I).

Relationships between MVPA per day and cardiovascular health variables

Log-transformed values of MVPA per day and carotid artery distensibility were used in the Pearson correlations. Moderate-to-vigorous PA per day was inversely associated with waist circumference ($r=-0.608$, $p=0.004$), BMI ($r=-0.593$, $p=0.006$), and cIMT ($r=-0.563$, $p=0.010$) in this sample of persons with CP (Fig. 1). There were no significant relationships between MVPA per day and heart rate, SBP, DBP, MAP, carotid artery distensibility and FMD.

DISCUSSION

As research continues to investigate the relationship between physical (in)activity and CVD risk in the general population (20), the evidence has shown that persons with CP, who have an inherent physical disa-

Table I. Participant characteristics

	GMFCS I *n*=12	GMFCS II *n*=13	Unadjusted CIs	Age adjusted CIs
Sex (males), %	66.7	61.5		
Age, years, mean (SD)	17.3 (5.2)	29.3 (14.1)*	–20.8 to –3.0	
Height, m, mean (SD)	1.63 (0.14)	1.56 (0.12)	–0.04 to 0.17	0.04 to 0.25*
Weight, kg, mean (SD)	55.7 (25.5)	58.6 (18.3)	–21.3 to 15.5	–10.8 to 27.8
BMI, kg/m^2, mean (SD)	20.2 (6.2)	23.5 (5.1)	–8.0 to 1.4	–6.0 to 4.2
Waist circumference, cm, mean (SD)	72.1 (15.9)	80.6 (15.7)	–21.6 to 4.5	–16.4 to 12.3
Heart rate, bpm, mean (SD)	72.0 (11.8)	73.4 (10.3)	–10.5 to 7.8	–14.7 to 6.3
SBP, mmHg, mean (SD)	112 (13.8)	119 (12.9)	–17.6 to 4.5	–14.3 to 10.6
DBP, mmHg, mean (SD)	65.2 (7.3)	70.8 (10.5)	–13.2 to 1.9	–8.1 to 7.2
MAP, mmHg, mean (SD)	84.6 (7.8)	89.4 (8.5)	–11.6 to 1.94	–7.9 to –1.2*
Carotid distensibility, mmHg^{-1}[a], median (IQR)	0.004 (0.003–0.007)	0.006 (0.004–0.008)	–0.003 to 0.003	–0.005 to 0.002
Carotid IMT, mm, mean (SD)	0.431 (0.06)	0.489 (0.04)	–0.13 to 0.01	–0.09 to –0.01*
Absolute FMD, mm, mean (SD)	0.316 (0.150)	0.309 (0.179)	–0.13 to 0.15	–0.18 to 0.15
Relative FMD, %, mean (SD)	9.88 (5.83)	9.46 (6.41)	–4.8 to 5.6	–6.8 to 5.3
MVPA, min/day[a], median (IQR)	45.8 (32.4–75.1)	16.4 (13.0–25.0)*	2.2 to 57.9*	5.4 to 49.1*

*$p<0.05$.
[a]Variable not normally distributed.
Body mass index (BMI) percentiles for adolescents for each Gross Motor Function Classification System (GMFCS) level were calculated according to CDC criteria for age and reported as follows: GMFCS level I (4 males; 3 females) = 20.4±16.3; GMFCS level II (4 males) = 70.5±24.2.
SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; IMT: intima-media thickness; FMD: flow mediated dilation; MVPA: moderate-to-vigorous physical activity; CI: confidence interval; IQR: interquartile range; BMI: body mass index; SD: standard deviation.

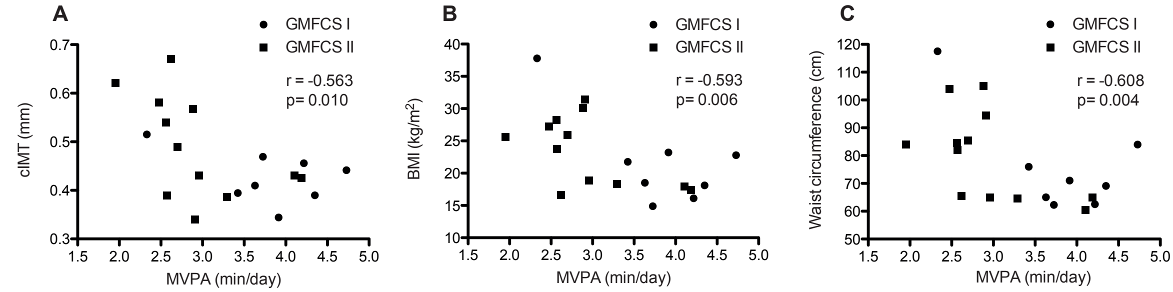

Fig. 1. Pearson correlations between moderate-to-vigorous physical activity per day and carotid artery intima media thickness (cIMT), body mass index (BMI), and waist circumference. (A) Moderate-to-vigorous physical activity (MVPA) (min/day) vs carotid artery intima media thickness (mm); (B) MVPA (min/day) vs BMI (kg/m^2); (C) MVPA (min/day) vs waist circumference (cm). Note: MVPA min/day is presented as log-transformed values. GMFCS: Gross Motor Function Classification System.

bility, may be at increased risk of CVD by virtue of engaging in less PA than the general population. Our previous work recently identified age as an important predictor of cardiovascular-related disease risk in adults with CP (12). Given this, as well as the fact that age was significantly different between GMFCS levels I and II in the present study, we adjusted for age differences by including age as a covariate in subsequent between-group analyses of body composition, PA and cardiovascular-related variables. We found that, after adjusting for age, the GMFCS level I group had lower MAP, smaller cIMT and engaged in greater amounts of MVPA per day than the GMFCS level II group.

In agreement with our primary hypothesis, our exploratory findings revealed that individuals who were GMFCS level I engaged in more MVPA than those who were GMFCS level II. These findings are in line with 2 previous studies, one in adolescents and another in adults, which reported higher levels of MVPA in GMFCS level I compared with GMFCS level II (9, 21). Our research is unique, in that we have analysed a sample that combined adolescents and adults with CP, whereas the aforementioned studies included participants who represented only one or the other group. Our study is also the first to report a negative relationship between MVPA per day and cIMT in persons with CP.

After adjusting for age, we found significant differences in cardiovascular health between groups, such that individuals who were GMFCS level I had lower MAP and reduced cIMT compared with those who were GMFCS level II. These differences in MAP and cIMT are in agreement with our hypothesis, that those who were GMFCS level I would present healthier cardiovascular variables compared with those who were GMFCS level II. Research has shown that increased cIMT in adults is a significant predictor for developing CVD (22). Specifically, the risk of having a myocardial infarction or stroke increased with intima-media thickness in individuals without a history of CVD, even after adjusting for traditional risk factors of CVD (23). This may be particularly important for persons with CP, as recent studies showed that persons with CP were at increased risk of stroke compared with the general population (11, 14) particularly at ages equal to or less than 50 years (14). Given that the mean age in both groups was less than 50 years and that cIMT was elevated in the GMFCS level II group, our findings highlight the importance of early screening for cardiovascular health, including cIMT assessment, particularly in individuals who are GMFCS level II. In the general population, a cIMT $\geq$1 mm is considered to be at high risk of atherosclerosis (24). Of the individuals with CP in the present study, no-one presented with a cIMT at or above this risk value. However, an important implication from our findings is that it should no longer be assumed that it is acceptable to combine GMFCS levels I and II when investigating cardiovascular and/or cardiometabolic disease risk in persons with CP.

The difference in MAP between GMCFS levels is also interesting. Previous research has shown that increases in MAP are related to increased CVD risk (25). Furthermore, increases in blood pressure are also related to cIMT (26). This combination of elevated MAP and cIMT seen in those who were GMFCS level II could identify a group that is at increased risk of the development of CVD in comparison to those who are GMFCS level I, which again alludes to the importance of separating individuals with CP who are GMFCS levels I and II in these investigations. Regarding body composition, research has shown that individuals with CP are significantly shorter in stature than age-matched controls due to a reduced growth development experienced during childhood in those with CP (27). Research in the general population revealed an inverse relationship between height and cardiovascular health, such that individuals who were shorter had poorer cardiovascular health (28). The results from our exploratory study may suggest a similar relationship even within persons with CP, particularly as individuals in GMFCS level II were statistically significantly shorter, had increased MAP, and increased cIMT compared with the GMFCS level I group.

Consistent with findings from Ryan and colleagues (9), we found an inverse relationship between MVPA per day and waist circumference in our sample of persons with CP. We also reported inverse associations between MVPA per day and BMI, as well as MVPA per day and cIMT. The latter is particularly interesting, as this is the first study to reveal a significant relationship between PA and cIMT in individuals with CP, thereby indicating a strategic target of PA interventions for CVD risk reduction in this population. In the general population, increased PA has been shown to be related to a decreased progression of intima-media thickness in adolescents (29). Future studies investigating the effect of PA/exercise interventions in people with CP should consider measuring changes in cIMT and body composition (i.e. waist circumference and BMI) as outcome variables of interest while adjusting for age and sex.

Study limitations

There are both technical and logistical limitations that should be considered. Different assessors collected data for non-invasive measures of arterial structure and function. However, assessors employed similar techniques that are comparable to studies that reported test-retest reliability for the FMD assessment (30) and cIMT (31) measures of 0.90 and 0.97, respectively. In addition, PA measurement via accelerometry may have been underestimated for some participants due to the device's sensitivity to water. Swimming is a preferred activity for individuals with CP and any time spent swimming would not have been recorded by the device. Furthermore, accelerometer cut points are commonly population- and age-specific (32). A limitation of the present study was the adoption of 2 sets of cut-points, 1 validated for children and adolescents with CP, and another developed for the general adult population (17). While there are no data to suggest whether these cut-points are comparable, the fact that they were used consistently between the 2 GMFCS levels in the present study allows for a more meaningful comparison between groups. Also, other noteworthy limitations include our small sample size, lack of statistical power analysis, and lack of a comparator group from the general population. However, the findings from this study should be considered knowledge building and should be explored in a larger sample of ambulatory individuals with CP, including those who are GMFCS level III.

Conclusion

In support of recent research identifying an increased risk of stroke in persons with CP compared with the general population, our findings show important differences in both MVPA levels and CVD health variables between GMFCS levels I and II. In particular, a combination of elevated blood pressure (MAP), increased cIMT, and lower levels of MVPA in individuals who were GMFCS level II could put this group at risk of CVD in comparison with individuals who were GMFCS level I. Therefore, we recommend clinicians to acknowledge that ambulatory individuals with CP could have differing cardiovascular health profiles and should monitor cardiovascular variables, including resting blood pressure, during regular clinical visits for persons with CP, regardless of age.

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