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Cardiorespiratory Fitness and Body Mass Index as Predictors of Metabolic Syndrome in Schoolchildren (PACH Study)

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Purpose: Metabolic syndrome (MetS) has become a condition not rarely diagnosed in children and adolescents, leading to changes in physical and mental health. Simple and cost-effective screening methods applied in schools are needed to take preventive measures and reduce the risk of the development of MetS in children.

Methods: This prospective longitudinal study aims to investigate the prevalence of MetS and its risk factors in 8–10-year-old schoolchildren (46 boys and 60 girls) over 3 consecutive years. General Linear Mixed Model (GLMM) was used to assess the effect of recommended daily levels of moderate to vigorous physical activity (MVPA), body mass index (BMI), waist circumference (WC), cardiorespiratory fitness (CRF), and obesity level on a new set of orthogonal variables formed from various parameters of MetS (eg blood pressure (BP), lipid panel and glucose homeostasis) determined by Principal Component Analysis (PCA).

Results: The prevalence of MetS was 2% in the years 2017, 2018 and 2019, while in 2020 prevalence reached 7.7%. The most prevalent combination of criteria defining MetS syndrome in children was increased WC, BP, and blood triglycerides (TG). PCA identified non-high-density lipoprotein (non-HDL), low-density lipoprotein (LDL), and total cholesterol (TCHOL) as important predictors of metabolic syndrome (MetS). Additionally, cardiorespiratory fitness (CRF) and body mass index (BMI) were found to significantly influence the variance in MetS criteria. However, moderate to vigorous physical activity (MVPA) did not have a notable effect on the variance of these criteria.

Conclusion: The prevalence of MetS in children is increasing with age. Non-HDL turned out to be the most influential parameter across all principal components. The CRF, being accessible, simple to use, non-invasive and cost-effective, proved to be a superior predictor of variance of glucose homeostasis compared to BMI.

Keywords: cardiorespiratory fitness level, cardiometabolic health, BMI, MVPA, pupils

Introduction

Establishing criteria for monitoring the prevalence of Metabolic Syndrome (MetS) in children has been regarded as less relevant since cardiometabolic diseases (CMD) primarily affect middle-aged and older individuals. However, a notable increase in MetS and CMD among the younger population over the last two decades necessitates a reevaluation of monitoring protocols for MetS in children.[1] The incidence of childhood obesity has doubled over the last 40 years and the prevalence of MetS in obese children varies from 6 to 39%, depending on the applied definition.[2] The most common definition of MetS criteria is provided by the International Diabetes Federation and the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III), although there is an increasing tendency to use a more specific definition proposed by Cook et al, to enhance the accuracy of MetS diagnosis in children.[3] Despite some nuances in

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definitions, MetS criteria in children involve increased WC, systolic, diastolic BP, TGs, fasting blood glucose (FBG) and decreased blood high-density lipoprotein (HDL).

Several predictors of MetS in children have been described previously, eg BMI, waist-to-height ratio (WHtr), BP, a sum of skinfolds, fat mass (kg) and fat-free mass (kg).[4–6] WHtr and BP proved sensitive in the early detection of MetS in children.[4] However, there is contrary evidence that BMI, WHtr, WC and sum of skin folds were found to be weak predictors of MetS in 7–15-year old children.[5]

Previously published data have reported a positive association between obese children and reduced fruit, and vegetable consumption, as well as breakfast skipping.[7] Additionally, increased BMI has been linked to eating in front of the screen and consumption of unhealthy snacks.[7]

Lifestyle habits such as diet, time spent in sedentary and physical activities (PA) can be modified on individual and social levels. Structured high-intensity PA is associated with healthier body composition and higher CRF levels.[8] Furthermore, childhood WC and CRF are both strongly associated with cardiometabolic health in later life.[9] Over the past 60 years, CRF in youth has decreased worldwide, probably due to an increase in inactivity and obesity, as well as a decrease in MVPA.[10]

Previously described methods have been found accessible, simple to use, non-invasive and cost-effective, however, there is still a debate on their precision. Furthermore, despite the rise of MetS in children, there are no internationally approved guidelines on MetS criteria and cut-off points to facilitate the identification of the diagnosis in children.[3,11] Thus, the rationale for conducting the present prospective, longitudinal study is to use PCA to refine the predictive value of existing criteria (total PA, MVPA, CRF, BMI, and WC) on a comprehensive set of blood biomarkers and functional parameters of the cardiovascular system to find out simple and cost-effective methods for prediction of MetS.

Material and Methods

Study Design and Participants

This paper presents prospective, longitudinal data of pupils enrolled in the Physical Activity and Children Overall Health (PACH) study. In total, 106 8–10-year-old pupils (53.5% (n = 46) boys and 46.5% (n = 60) girls) from 13 different schools were recruited in the study through convenience sampling. After introducing schools to the aim of the study and implementation process, class teachers were able to sign up their classes for this study. More than half of the study participants (56,5% of pupils) were participants of the Latvian Olympic Committee project "Sport for All Classes" (SFAC). Project SFAC is an initiative of the Latvian Olympic Committee and promotes structured physical activities in schools in Latvia ensuring 5 school-based physical education (PE) lessons per week in comparison to the regular curriculum (43,5% of participants had 2 PE lessons per week, respectively). To participate in SFAC, school authorities (principals, form teachers, and physical education teachers) had to submit an official application with the list of pupils and corresponding signatures of their parents.

The present PACH study is a collaboration project between the University of Latvia and the Latvian Olympic Committee (ZD2019/20861) and is conducted in line with the Declaration of Helsinki and approved by the Ethical Committee of the Institute of Cardiology and Regenerative Medicine, University of Latvia (Nr.179/2019; valid from 14.10.2019). Parents were asked to sign a detailed written consent explaining all procedures and possible risks, and data collection and management procedures for participation in the PACH study. Verbal consent from the pupils was obtained and they had the right to refuse further participation in the study without explanation at any point.

Measures

Anthropometric Measurements

Bodyweight, height, and WC were measured. BMI (kg/m^2) and the percentile[12] for each child were calculated, and then the obesity level was determined.

Physical Activity

It has been reported that regular participation in structured PA during childhood and early preadolescence leads to greater cardiovascular fitness and healthier body mass compared to non-exercising counterparts,[8] thus this study focused on

structured PA as PE classes at school and extra-curricular structured activities as training sessions in different types of sports. PA questionnaire included questions about the number of PE lessons in school and participation in sports training (team and individual sports). Responses provided by pupils were used to calculate time spent in light (<3 youth metabolic equivalents (METy), moderate (3–6 METy) and vigorous (>6 METy) PA,[13] as well as to estimate the prevalence of pupils meeting the World Health Organisation (WHO) recommendations of MVPA per week. Total PA included structured light, moderate and vigorous PA.

Cardiorespiratory Fitness Level

To determine CRF level, a physical exercise test for school-age children was carried out as previously described.[14] The study participants performed a 3-minute Kasch Pulse Recovery Test (KPR Test). The KPR Test consisted of stepping on a standard wooden exercise bench (30cm high, 25cm wide) for 3 minutes at a pace of 24 steps up and down per minute. The climbing pace was maintained by a metronome with a set of 96 beats per minute. Data on heart rate before, during and 1 minute in the recovery of the KPR Test was monitored with a Polar H7 heart rate (HR) detection sensor belt and Polar teams' software. During the recovery period, participants were in a seated position and were instructed to remain still, breathe normally, and avoid conversations. In the case HR during the test exceeded 180 beats per minute, the test was discontinued, and the study participant's CRF level was evaluated as very poor. CRF level on a scale of 1 (excellent)–6 (very poor) was determined by HR values of the post-exercise recovery period (arithmetic mean value).[14] For statistical analysis, inverse values were used.

Plasma Parameters

Glucose and lipid homeostasis plays an important role in monitoring health status throughout the life cycle. In this study, we investigated plasma parameters which serve as good predictors of early diagnosis of MetS,[15] and CMD.[16] Accordingly, determined plasma parameters were grouped in markers of a) lipid metabolism: total cholesterol (TCHOL, high-density lipoprotein (HDL), low-density lipoprotein (LDL), remnant cholesterol (RCHOL, calculated as [TCHOL] - [HDL] - [LDL]), non- high-density lipoprotein (non-HDL, calculated as [TCHOL] - [HDL]) and triglycerides (TG); b) glucose metabolism: fasting blood glucose (FBG), insulin, homeostatic model assessment for insulin resistance (HOMA-IR); c) inflammation: high-sensitivity C-reactive protein (hsCRP).

Blood Pressure and Heart Rate

Systolic, diastolic BP and resting HR were measured with an electronic blood pressure device (Microlife, BP B1 Classic, Microlife China) to investigate the effect of independent variables (eg BMI, WC, CRF, MVPA) on these parameters. To ensure resting BP and HR measurement, pupils were asked to maintain calmness before and during the procedure.

Metabolic Syndrome

MetS was defined in accordance with pediatric and adolescent MetS criteria adapted from the NCEP-ATP III. The NCEP-ATP III considered the following criteria for MetS in children: central obesity with WC≥ 90th percentile in both sexes, TGs ≥1.24 mmol/L, HDL ≤1.03 mmol/L; BP (systolic or diastolic) ≥90th percentile and FBG ≥5.6 mmol/L. Individuals need to have at least three abnormalities in the MetS criteria to be classified as having MetS.[3] To estimate the 90th percentile for WC – age and sex-specific reference data was used.[17] For the determination of the 90th percentile for BP – age, sex and height-specific reference data was used.[18]

Procedure

Study data were collected 4 times during 3 consecutive years in the following periods: September – November 2017; April – May 2018; April – May 2019; January – February 2020.

Blood samples were collected after the overnight fast. Handling, transport, and analysis of blood samples were subcontracted to and performed by an accredited clinical laboratory "E. Gulbis Laboratory". Study participants and their parents were informed not to have any food or beverages, besides water, before the blood tests. If the participant accidentally had food or drink in the morning, then the results of blood tests were excluded from the data set.

Anthropometric measurements were carried out according to a standardized protocol (COSI).[19] Body height was measured using a portable stadiometer (ADE MZ10042, ADE Germany), standing as straight as possible and with arms hanging freely along the sides. Height was measured in centimeters and the reading was taken until the last complete mm (0.1 cm). The body weight of the children was measured in kilograms and recorded to the nearest 100 g (0.1 kg) unit (medical scales, ADE M320000, ADE Germany). Pupils were weighed without shoes in light sportswear. Waist was measured to the nearest 0.5 cm with an anthropometric nonelastic measuring tape (ADE MZ10021, ADE Germany) after normal expiration, at the level of the umbilicus. After the collection of anthropometric data, the KPR Test was performed.

Questionnaires estimating PA levels were in paper format in the years 2017 and 2018. Researchers assisted individually every pupil in filling out the questionnaire by explaining the meaning of the questions or helping with reading. Starting from the year 2019 questionnaires were transformed into digital format and pupils filled them out on school computers with the assistance of their teacher and/or researcher.

Statistical Analysis

The data distribution of quantitative variables was evaluated by the Shapiro–Wilk test and exploring normal Q–Q plots. The presentation of variables involved expressing them as either mean with standard deviation (SD) when normally distributed or as median with interquartile range (Q1-Q3) when not normally distributed. The one-way repeated measures ANOVA or Friedman test was employed to assess the variation in multiple parameters (such as HDL, LDL, insulin, glucose, etc.; Tables 1 and 2) across the years from 2017 to 2020.

Principal Component Analysis is a widely used technique for dimensionality reduction and feature extraction. In this study, we applied Principal Component Analysis to reduce the dimensionality of the data. The dataset comprises 16 dependent variables repeatedly measured across the years from 2017 to 2020. Before Principal Component Analysis, the data was standardized to ensure that variables with different scales contributed equally to the analysis. The Kaiser–Meyer–Olkin (KMO) measure of sampling adequacy and Bartlett's test of sphericity were calculated to ensure that the data fit the model. The eigenvectors and eigenvalues were computed to determine the principal components.

As this observation study is replicated across years introducing random variables, the GLMM was performed to identify factors influencing components (obtained using Principal Component Analysis). A full model was initially specified, including all main effects of the predictors (BMI, WC, CRF, total PA, MVPA, and obesity level) and their possible two-way interactions. This comprehensive model served as the starting point for our analysis. Using the Akaike Information Criterion (AIC) as a guide, we systematically evaluated the significance of each interaction term. Interactions that did not contribute significantly to the model (ie, those with high p-values and minimal impact on AIC) were removed in a stepwise manner. This process ensured that the final model retained only the most relevant interactions, thereby

Table 1 Independent Variables

Parameter	Mean (SD) or Median (Q1–Q3)				p-value
	2017	2018	2019	2020	
MVPA, min	118 (54.7) [a]	127 (59.6) [a]	136 (69.4) [b]	139 (64.4) [b]	<0.001
Total PA, min	157 (71.8) [a]	168 (77.4) [a]	179 (89.5) [b]	183 (83.0) [b]	<0.001
Weight, kg	35 (9.1) [a]	37 (10.0) [b]	42 (12.0) [c]	46 (13.2) [d]	<0.001
Height, cm	140 (6.2) [a]	143 (6.5) [b]	148 (6.8) [c]	154 (7.1) [d]	<0.001
BMI, kg/m2	17.7 (3.4) [a]	18.1 (3.5) [b]	18.7 (3.9) [c]	19.3 (4.0) [d]	<0.001
WC, cm	60.7 (8.0) [a]	62.8 (9.0) [b]	68.7 (11.7) [c]	70.9 (10.1) [d]	<0.001
Obesity level	5 (4–7)	5 (4–7)	5 (4–7)	5 (4–6.5)	0.156
CRF level	2.5 (2–4)	2 (2–4)	2 (2–3)	3 (2–4)	0.676

Notes: Values with different superscript letters (a-d) on the same row are significantly different across the years ($p < 0.05$). [a] represents a significant difference to [b, c, d; b] represents a significant difference to [c, d; c] represents a significant difference to [d]. Q1-Q3 – interquartile range (the first and third quartile).
Abbreviations: SD, standard deviation; MVPA, moderate to vigorous physical activity; total PA, total physical activity; BMI, body mass index; WC, waist circumference; CRF level, cardiorespiratory fitness level.

Table 2 Dependent Variables

Parameter	Median (Q1–Q3)				p-value
	2017	2018	2019	2020	
HOMA_IR	1.4 (1.0–2.1) [a]	1.2 (0.8–1.9) [a]	1.8 (1.2–3.0) [b]	2.6 (1.8–3.6) [c]	<0.001
TG, mmol/l	0.7 (0.5–0.9) [a]	0.6 (0.5–0.8) [a]	0.7 (0.5–0.9) [a]	0.8 (0.6–1.1) [b]	<0.001
RCHOL, mmol/l	0.3 (0.2–0.4) [a]	0.4 (0.3–0.5) [b]	0.3 (0.1–0.4) [a]	0.2 (0.1–0.3) [c]	<0.001
LDL, mmol/l	2.4 (2.1–2.7) [b]	2.3 (1.9–2.6) [a]	2.3 (1.9–2.7) [b]	2.4 (1.8–2.6) [ab]	<0.001
Insulin, μU/mL	6.4 (4.5–9.5) [a]	5.6 (3.8–8.7) [a]	8.3 (5.6–13.4) [b]	11.5 (8.2–16.3) [c]	<0.001
Non-HDL, mmol/l	2.7 (2.3–3.1) [a]	2.6 (2.3–3.1) [a]	2.6 (2.2–2.8) [a]	2.5 (2.1–2.8) [b]	<0.001
TCHOL, mmol/l	4.2 (3.9–4.6) [a]	4.2 (3.8–4.5) [a]	4.0 (3.7–4.4) [b]	3.9 (3.5–4.2) [c]	<0.001
HDL, mmol/l	1.5 (1.3–1.7)	1.5 (1.4–1.7)	1.5 (1.3–1.7)	1.5 (1.3–1.7)	0.065
FBG, mmol/l	4.9 (4.7–5.1) [a]	4.7 (4.5–5.0) [b]	4.9 (4.7–5.2) [a]	5.0 (4.7–5.2) [c]	<0.001
hsCRP, mg/L	0.4 (0.2–1.1)	0.4 (0.2–0.8)	0.2 (0.2–1.0)	0.3 (0.2–0.8)	0.239
Systolic BP*	102 (94–106) [a]	101 (94–106) [a]	102 (94–109) [a]	107 (98–114) [b]	0.004
Diastolic BP*	67 (62–70)	66 (61–72)	65 (62–70)	67 (61–74)	0.738
HR, beats per min	85 (77–92)	85 (79–89)	84 (78–89)	81 (74–89)	0.665
KPRT (3min)	162 (151–168)	159 (150–168)	158 (150–169)	164 (154–172)	0.067
KPRT (4min)	110 (100–121)	110 (102–119)	109 (101–118)	113 (97–121)	0.995
PAQ - C, total score	1.8 (1.4–2.2)	1.9 (1.5–2.3)	2.0 (1.5–2.4)	1.8 (1.4–2.2)	0.187

Notes: Values with different superscript letters (a-d) on the same row are significantly different across the years ($p < 0.05$). [a] represents a significant difference to [b, c, d; b] represents a significant difference to [c, d; c] represents a significant difference to [d]. Q1-Q3 – interquartile range (the first and third quartile). *Blood pressure/mm Hg.

Abbreviations: HOMA-IR, homeostatic model assessment for insulin resistance; TG, triglycerides; RCHOL, remnant cholesterol; LDL, low-density lipoprotein; non-HDL, non-high-density lipoprotein; TCHOL, total cholesterol; HDL, high-density lipoprotein; FBG, fasting blood glucose; BP, blood pressure; hsCPR, high-sensitivity C-reactive protein; HR, heart rate; KPRT HR, Kasch Pulse Recovery Test; PAQ-C, physical activity questionnaire for older children.

improving model parsimony and interpretability. Throughout the model selection process, the assumptions of normality, homoscedasticity, and multicollinearity were tested by examining residual plots and variance inflation factors (VIF) to ensure that the inclusion of interaction terms did not violate these assumptions. The final GLMM included significant main effects and interactions that provided the best fit to the data, as indicated by the lowest AIC value. This model was then used to interpret the influence of BMI, WC, CRF, and their interactions on the principal components derived from the PCA. The statistical data analysis was performed using the Jamovi software (v 2.3), and the result was considered statistically significant if the p-value was less than 0.05.

Study Power

The sample size of this study, comprising 106 schoolchildren, was determined based on a power analysis conducted prior to the study. The power analysis was performed to ensure that the study would have sufficient power to detect significant differences and associations among the variables of interest. Using an alpha level of 0.05 and a desired power of 0.95, the sample size was calculated to detect medium effect sizes for the primary outcomes related to MetS criteria. The results of sample size calculation showed that the minimum sample size for this analysis is n=36.

Moreover, the longitudinal design of the study, with repeated measures over four consecutive years, enhances the robustness of the findings. The use of GLMM further strengthens the analysis by accounting for within-subject correlations and random effects, thereby improving the precision of the estimates.

Additionally, the application of PCA to reduce the dimensionality of the data and identify key predictors of MetS criteria contributes to the statistical power of the study. By focusing on the most influential parameters, it was possible to derive meaningful insights despite the sample size limitations.

Results

Time Spent in Structured Physical Activity and Cardiorespiratory Fitness Level

The majority (91,5%) of the pupils were not involved in extra-curricular physical activities in 2017 and 2018 (84%). Involvement in extra-curricular activities increased from year to year resulting in 28% of pupils taking part in additional extra-curricular physical activities in year 2020. Accordingly, there was no significant difference in time spent in MVPA in 2017 and 2018, but MVPA significantly increased in 2019 and 2020. Thus, also the total PA increased between 2019 and 2020 in comparison to 2017 and 2018 (Table 1). Even though on average pupils spent 21 more minutes in MVPA weekly in 2020 compared to 2017, most of them did not reach the recommended minimum of 300 minutes in MVPA on weekdays across all four years. Similarly, the increase in time spent in MVPA did not result in significant differences between CRF levels throughout these years.

According to the score reached in the self-reported PA questionnaire, pupils had similar PA levels during school PE lessons, school breaks, after school and leisure time in 2017, 2018, 2019 and 2020 (Table 1).

Anthropometric Measurements and Obesity Level

There was a significant increase in weight, height, WC and BMI parameters from year 2017 to 2020 in growing pupils, but no increase in obesity levels (Table 1).

Blood Pressure and Heart Rate

Systolic BP significantly increased from years 2017–2019 to 2020 and there were no significant changes in diastolic BP over the years (Table 2). HR at rest, during and post-exercise, remained unchanged throughout the years.

Blood Plasma Parameters

HOMA-IR and blood plasma insulin levels increased significantly from 2017 and 2018 till 2019, and even more in 2020. FBG concentrations differed from year to year, but the median values remained in reference ranges. A significant increase in TG levels while a decrease in TCHOL, RCHOL and non-HDL was observed in the year 2020. Plasma HDL and hsCRP levels remained unchanged throughout the study.

Metabolic Syndrome

The criteria of MetS (WC, BP, TG, HDL and FBG) across the years 2017–2020 were evaluated from data presented in Table 2. According to NCEP-ATP III criteria, the prevalence of MetS was similar from 2017 to 2019, but an increase in 2020 by 5.7% was observed (Table 3).

Table 3 Prevalence of MetS and Its Criteria

MetS Criteria	Central Obesity	High BP	High TG	Low HDL	High FBG	Prevalence of MetS
Year	WC ≥90th percentile	Systolic or diastolic BP ≥90% for age, sex, height	110mg/dL (≥1.24 mmol/L)	40mg/dL (≤1.03 mmol/L)	100mg/dL (≥5.6 mmol/L)	Pupils with 3 or more risk factors
2017	24 (n=104)	16 (n=104)	11 (n=100)	1 (n=100)	3 (n=98)	2 (2%)*
2018	25 (n=101)	16 (n=100)	6 (n=98)	2 (n=98)	2 (n=96)	2 (2.1%)*
2019	33 (n=93)	15 (n=92)	10 (n=90)	2 (n=90)	3 (n=90)	2 (2.2%)*
2020	33 (n=84)	14 (n=78)	16 (n=81)	5 (n=81)	4 (n=81)	6 (7.7%)*

Notes: Data presents the prevalence of MetS and its criteria in study participants across the years 2017–2020. Values are indicated as n (total n) representing the number of individuals with corresponding criteria and MetS. * The % was calculated from the number of participants with all criteria of MetS being measured.
Abbreviations: MetS, metabolic syndrome; WC, waist circumference; BP, blood pressure; TG, triglycerides; HDL, high-density lipoprotein; FBG, fasting blood glucose.

Reduction of the Dimensionality by Principal Component Analysis

Table 4 presents the component statistics for the first 5 principal components (PC) and represents % of variance for each component. Furthermore, even though each principal component contains all 15 measured parameters, loadings are displayed solely for the three most influential parameters within each specific PC. Variables with loadings greater than 0.5 or −0.5 are considered influential. The rest of the PCs are represented in supplement Table S1. Dependent variables such as grip strength of leading and other hand, and saliva cortisol level were excluded by PCA.

The first principal component (PC1) is characterized by high loadings of non-HDL, LDL and TCHOL which are predictors for cardiometabolic, cardiovascular and cerebrovascular health outcomes and explains ~20% of the data variance. The rest of the four principal components explain relatively similar data variance ranging from 11.4% to 15.3%. The second principal component (PC2) is dominated by HOMA-IR, insulin and FBG, indicating that this component reflects glucose homeostasis. The variables dominating the third principal component (PC3) are systolic, diastolic BP, and hsCRP – the determinants of cardiovascular health. The fourth principal component (PC4) is dominated by heart rate during rest and KPR Test. Such variables as TG, HDL and RHDL dominate in the fifth principal component (PC5). In total, the first five principal components explain more than 2/3 of data variance.

Furthermore, Table 4 presents the uniqueness of each measured parameter across all five different PC. In other words, that is a % of data that is not included in the formation of PCs. Thus, non-HDL was the most significant parameter in our data set, as more than 98% of data were included in the formation of PCs. Non-HDL is followed by LDL and TCHOL,

Table 4 Statistics of Principal Components

Eigenvalues **Variance %** **Cumulative %**	**Component**					**Uniqueness**
	1 **3.33** **18.7** **18.7**	**2** **2.71** **15.3** **34.0**	**3** **1.63** **12.2** **46.1**	**4** **1.40** **11.7** **57.8**	**5** **1.29** **11.4** **69.2**	
Non-HDL, mmol/l	0.959					0.0222
LDL, mmol/l	0.947					0.0768
TCHOL, mmol/l	0.946					0.0625
HOMA-IR		0.865				0.1042
Insulin, μU/mL		0.829				0.1427
FBG, mmol/l		0.687				0.5032
Diastolic BP*			0.840			0.2798
Systolic BP*			0.815			0.2787
hsCRP, mg/L			0.520			0.5975
KPRT, 4min				0.810		0.3171
KPRT, 3min				0.720		0.4741
HR, beats per min				0.572		0.6418
TG, mmol/l					0.798	0.2835
HDL, mmol/l					−0.676	0.4925
RCHOL, mmol/l					0.653	0.3411

Notes: The table represents five principal components. Each principal component includes all 15 measured parameters, however only the 3 most influential parameters determined by loadings are shown for convenience; loadings greater than 0.5 or −0.5 are considered influential. Uniqueness represents the variance of data across all principal components that are not included in the analysis (the greater the coefficient of uniqueness the lesser the variance of parameter). *Blood pressure/mm Hg.

Abbreviations: Non-HDL, non-high-density lipoprotein; LDL, low-density lipoprotein; TCHOL, total cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; FBG, fasting blood glucose; BP, blood pressure; hsCPR, high-sensitivity C-reactive protein; KPRT HR, Kasch Pulse Recovery Test; HR, heart rate; TG, triglycerides; HDL, high-density lipoprotein; RCHOL, remnant cholesterol.

respectively involving 92% and 94% of data in PCs. Surprisingly, parameters representing risk factors of MetS such as FBG, HDL, TG and BP included less data in the formation of PCs: 50%, 51%, 72%, and 72%, respectively.

General Linear Mixed Models

Table 5 represents the final general linear mixed models for each PC, indicating that the primary factors influencing PCs are CRF levels and BMI. Interestingly, only PC3 is influenced by the total amount of PA; however, the estimated impact (see *Estimate* value, Table 5) in comparison to BMI is very low. Other independent variables (eg MVPA, WC and obesity levels) did not influence any of the first 5 PCs. GLMM analysis shows that improved CRF levels decrease PC1, PC2 and PC4, thus also the parameters representing glucose and lipid metabolism, such as non-HDL, LDL, TCHOL, HOMA-IR, insulin, FBG, as well as parameters reflecting heart function, such as HR at rest and exercise. In turn, increasing BMI is associated with higher levels of HOMA-IR, insulin, FBG, systolic and diastolic BP, hsCRP, HR at rest and exercise, as well as increased TGs, RCHOL levels, while decreased HDL represented by PC2, PC3, PC4 and PC5.

Discussion

The prevalence of the MetS in the general population is 0–19,2%, but in obese children, it varies from 10% to 66%.[20] One important reason for such a variation in children is disagreement with the definition of MetS criteria for children.[2,20,21] In 2009, the European Youth Heart Study found that 0.2% of 10-year-old children and 1.4% of 15-year-olds were diagnosed with with MetS.[22] Similarly, in 2017 the prevalence of MetS in our study participants was 2%, with a following increase in 2020 when prevalence reached 7.7%, which is in line with published data at a time of increasing numbers of MetS in children.[2,21]

Undoubtedly PA is beneficial for physical and mental health, and PA is recommended for all people in different age groups, such as smaller children, adolescents, adults and seniors. Regular PA reduces the risk of cancer, cardiovascular diseases (CVD), diabetes, depression, and anxiety as well as improves overall well-being and quality of life.[23–26] Despite all the benefits, physical inactivity and a sedentary lifestyle is an increasing feature globally.[27,28] Most of the people in

Table 5 Regression Models of First Five Principal Components

Model, AIC	Variable	Estimate	95% CI	t	p
Principal component 1, 1387					
	intercept	−0.05	−0.64–0.54	−0.17	0.879
	CRF level	−0.43	−0.72 – −0.15	−2.99	0.003
Principal component 2, 1089					
	intercept	0.17	−1.05–1.39	0.27	0.802
	CRF level	−0.39	−0.56 – −0.21	−4.42	<0.001
	BMI	0.36	0.30–0.42	12.08	<0.001
Principal component 3, 1063					
	intercept	−0.003	−0.25–0.25	−0.03	0.978
	BMI	0.35	0.29–0.40	12.41	<0.001
	Total PA	0.003	0.001–0.005	2.95	0.003
Principal component 4, 977					
	intercept	0.009	−0.15–0.17	0.12	0.906
	BMI	0.11	0.06–0.16	4.48	<0.001
	CRF level	−1.04	−1.18 – −0.89	−14.25	<0.001
Principal component 5, 1091					
	intercept	0.12	−0.25–0.23	−0.07	0.945
	BMI	0.03	0.11–0.22	5.59	<0.001

Notes: Akaike information criteria (AIC) was used for determination the best general linear mixed model for particular data. Principal component analysis was performed on all 16 independent variables listed in Table 4 to form 5 PCs. Each PC in Table 4 represents only the three most influential parameters. Table 5 represents the main influential factors of PCs – CRF and BMI, p<0,05 indicates statistical significance. The estimate represents the effect of influential factors (CRF and BMI) on dependent variables in PCs.

Abbreviations: BMI, body mass index; CRF, cardiorespiratory fitness; PA, physical activity; PC, principal component.

the different age groups are not meeting PA recommendations, and there has been no progress since year 2001.[26] It has been found that at the age of 11, there is a higher risk for a decrease in PA in comparison to younger kids.[29] For instance, more than 80% of children aged 11–17 do not reach recommended levels of PA.[26] Physical inactivity has become a burden for health in a variety of aspects in sedentary individuals, as well as a burden for health systems and resources.[30] Our study showed that in the year 2017, none of the pupils reached the recommended MVPA on weekdays, while in the following years, only 1–2% of the pupils reached recommended MVPA levels.

PCA Analysis

The application of PCA in this study served as a pivotal statistical method to streamline the complex array of parameters influencing MetS in schoolchildren. By transforming a large set of interrelated variables into a smaller set of uncorrelated PCs, PCA enables a more straightforward and interpretable analysis of the data. This reduction in dimensionality not only simplifies the predictive modelling of MetS criteria but also enhances the robustness and reliability of the findings.

The WHO guidelines on PA recommend 60 minutes of MVPA per day, accordingly 300 minutes per weekdays and 420 minutes per week in total.[26] It has been suggested to add also vigorous type of aerobic PA.[26] However, lately, some studies reported that MVPA is not sufficient enough to induce cardiometabolic benefits in children, and vigorous PA has to be performed.[31,32] Further, a systematic review and meta-analysis showed an inconsistent relation between MVPA and individual risk factors of cardiometabolic health.[33] Also, the results of the present study suggest that there is no association between MVPA and parameters reflecting MetS score and cardiometabolic health. In the present study, we were not able to compare the effects of MVPA vs vigorous PA on blood biomarkers and functional parameters of the cardiovascular system, as the majority of pupils did not meet WHO recommendations for MVPA.

Previously it has been shown that the criteria of MetS vary considerably among adults in European countries. For instance, the cluster of risk factors of MetS in the UK and Germany consisted of WC, TG, and BP, but in Italy, Spain, Portugal and Belgium of WC, BP and FBG. Interestingly, in Lithuania, more adults with MetS had changes in all five risk factors of MetS in comparison to other countries.[34] Similar differences between studies estimating the most common risk factors of MetS in children and adolescents have been reported. Thus, a previously published scoping review reported that the most prevalent risk factors in children with MetS were high WC followed by increased TG levels, decreased HDL, elevated BP, and high FBG as the least prevalent risk factor.[3] Furthermore, meta-analysis showed that in low- and middle-income countries in overweight/obese children and adolescents who were diagnosed with MetS, the most common risk factor was abdominal obesity, but the least common high FBG level, while in children with normal weight it low HDL and high FBG levels, correspondingly.[35] Additionally, the European Youth Heart Study found high WC, elevated FBG and low HDL as the most common combination of risk factors determining MetS.[22] In the present study, the most common combination of MetS risk factors found in pupils with MetS was high WC, BP and TG. However, the least common risk factors were elevated FBG and decreased HDL. More than half of the pupils fulfilling the scores for MetS had elevated levels of LDL, a marker that is not included in the list of the risk factors for MetS but is closely related to cardiovascular health.[2] Variations in dietary patterns, cultural practices, and socio-economic factors, including income and the accessibility of high-quality food, may contribute to differences observed among countries.

As previously described five PCs found in our study accounted for 69% of the total variability of measured blood biomarkers and functional parameters of the cardiovascular system. Elevated values of non-HDL, LDL and TCHOL in PC1 are increasing the risk of metabolic syndrome,[2] non-alcoholic liver disease,[36] myocardial infarction and stroke.[37–39] Parameters HOMA-IR, insulin and FBG in PC2 represent glucose homeostasis, thus PC2 is also descriptive of cardiometabolic health.[40,41] Elevated BP in children is a significant health marker as hypertension stresses blood vessels and induces damage to the endothelium.[42] Furthermore, it is a constituent of MetS and increases cardiovascular mortality and morbidity in adulthood.[15,41,43] Both elevated BP, as well as hsCRP being an inflammatory marker, indicate higher risks of atherosclerosis.[42,44] Thus, the evidence suggests that variables (BP and hsCRP) in PC3 are associated with cardiovascular health and represent an increased risk of myocardial infarction and stroke. PC5 in our study was dominated by TG, HDL and RCHOL. Elevation in TG and a decrease in HDL are positively associated with MetS.[15] RCHOL reflects levels of very low and intermediate-density lipoproteins, which carry high amounts of triglycerides. Very LDL is associated with hypertension and atherosclerosis risks in MetS.[45,46] The variability of all previously

mentioned parameters included in PCs is largely dependent on CRF and BMI. Surprisingly, according to uniqueness, the most significant parameters in PCs were non-HDL, LDL and TCHOL, parameters which are not listed as criteria for MetS in current definitions.[3] LDL levels were increased in the majority of pupils with MetS. Contrary, parameters that are listed as criteria for MetS and were dominant in PC2, PC3 and PC5 (FBG, BP, TG and HDL, correspondingly) were less significant in comparison to the non-HDL, LDL and TCHOL according to uniqueness score. Our study data suggest that criteria for MetS in children might differ from adults and there is a need for further exploration of parameters describing this pathophysiological condition.

Over the years controversial reports have been published about CRF and the relation of this health marker with cardiometabolic health. A systematic review of longitudinal studies showed an inverse association with several factors like body fatness, BMI and MetS incidence, but there was no association with glucose homeostasis, lipid metabolism or blood pressure in children.[47] On the contrary, other studies reported a strong association between CRF level, MetS score and cardiovascular health in children.[9,48] Our findings suggest that CRF level has a positive effect on non-HDL, LDL, TCHOL, HOMA-IR, insulin, FBG, and HR at rest and exercise and that it is a superior predictor compared to BMI for these parameters. Estimation of CRF levels in children can be used to monitor risk for MetS relatively easily.[47]

Childhood obesity is another public health concern and plays an important role in various health outcomes and has a negative effect on the immune, skeletal, cardiovascular, endocrine, and nervous systems.[49] Lately, studies have found BMI a non-invasive and easy method for the prediction of MetS in children.[4,6] This is in line with the present study as an effect of BMI on MetS criteria (FBG, systolic and diastolic BP, increased TG) as well as other measured parameters such as HOMA-IR, insulin, hsCRP, resting and exercising heart rate, RCHOL levels, but an inverse effect on HDL levels was found over a period of three consecutive years. Thus, these data support previous findings on the impact of BMI on blood pressure regulation,[50,51] dyslipidemia[52] and glucose metabolism,[53,54] in children and adolescents.[44,55]

Limitations

One potential limitation of this study is the reliance on self-reported questionnaires to assess PA. The use of objective tools, such as accelerometers, could improve the accuracy of data collection in future research.

Conclusion

By employing PCA, we were able to simplify the complex interplay of various metabolic and cardiovascular parameters into a more manageable and interpretable form. The use of PCA allowed to identify non-HDL, LDL and TCHOL as the most significant parameters across all principal components, suggesting its potential as a key indicator for MetS in children. Furthermore, increased plasma LDL was found in most of the pupils with MetS, suggesting that this criterion could be another risk factor of MetS and the addition of it to existing criteria could facilitate the diagnosis of MetS in children. Moreover, the analysis revealed that CRF and BMI were the primary factors influencing the PCs. Even though both CRF and BMI can be used as feasible methods for predicting criteria of MetS in schoolchildren, CRF proved to be a superior predictor of variance of parameters of glucose homeostasis in comparison to BMI.

It can be argued that LDL should be included as a criterion for MetS. Additionally, CRF plays an important role in the prevention of MetS, and more emphasis should be placed on CRF as a relatively easy-to-modify risk factor.

Ethics and Consent Statements

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethical Committee of the Institute of Cardiology and Regenerative Medicine, University of Latvia approved the PACH study (Nr.179/2019; effective from 14.10.2019). Written informed consent for each participant was obtained from the parent/legal guardian.

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