Sedentary Behaviour, Physical Activity, Physical Fitness and Subclinical Atherosclerosis in 11-12 Years-old Children

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Abstract: Aim: Examine the influence of sedentary behaviour (SED), physical activity (PA), muscular strength (MS) and cardiorespiratory fitness (CRF) on subclinical atherosclerosis in 11-12 years-old children. Methods: We assessed intima-media thickness (IMT) of the common carotid artery in 366 children aged 11-12 years-old (191 girls). Measures included IMT assessed with high-resolution ultrasonography, pulse pressure (PP), a maximal handgrip strength test, body mass index, waist circumference, body fat mass and lean mass (LEAN) from DXA and CRF determined using a maximal cycle ergometer test. SED and PA were assessed by accelerometry. MS was adjusted for LEAN yielding relative MS (RMS). Association between IMT and RMS adjusted for SED, PA and CRF were tested with multiple linear regression analysis. Differences in risk factors among RMS groups were tested with ANOVA/ANCOVA. Results: RMS was related to IMT independently of PA, CRF, age, gender, maturity and PP ($p<0.05$). As compared with the higher RMS group, subjects in the lower RMS group had increased body composition phenotypes, hemodynamics and IMT, and lower moderate-vigorous PA, MS and CRF ($p<0.05$). Full modelling exposed the detrimental and independent role of RMS in arterial structure in 11-12 years-old children. Greater RMS is associated with improved vascular health even in children.

1 INTRODUCTION

Children are not generally considered at risk for having clinical cardiovascular disease (CVD) events in the short term. However, the high prevalence of sedentary behaviour (SED), low cardiorespiratory fitness (CRF) as well as clustering of cardio-metabolic risk factors during youth sets the stage for heart disease in the middle and older ages (Carnethon et al., 2005); (Sattelmair et al., 2011) coupled with premature changes in carotid intima-media thickness (IMT), an intermediate phenotype for early atherosclerosis and a solid predictor of future vascular events (Lorenz et al., 2007).

Another important health related component of fitness is muscular strength (MS) and despite receiving far less attention than CRF, recent studies support the hypothesis that low muscular strength in childhood (Ortega et al., 2012); (Sato et al., 2009), and adulthood also predicts all-cause mortality, as well as mortality due to cardiovascular disease and cancer in healthy and diseased people (Gale et al., 2007); (Katzmarzyk and Craig, 2002); (Ruiz et al., 2008).

This study examined the influence of relative MS (RMS), SED, PA and CRF measures on IMT in 11-12 years-old children. In addition we examined whether differences among RMS tertiles translated to physiologically relevant differences increasing both metabolic and cardiovascular risk.

2 METHODS

Participants were 366 children (191 girls) aged 11-12 years-old from 6 schools of the Lisbon district.

Height and sitting height were measured to the nearest 0.1 cm and body mass was measured to the nearest 0.1 kg on a scale with an attached stadiometer (model 770, Seca; Hamburg,

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Deutschland). Waist circumference (WC) was measured to the nearest millimeter with an inelastic flexible metallic tape (Lufkin - W606PM, Vancouver, Canada) midway between the lower rib margin and the iliac crest.

Total-body scans were performed by dual-energy radiographic absorptiometry (DXA) and analysed using an extended analysis program for body composition (Hologic Explorer-W, fan-beam densitometer, software QDR for windows version 12.4, Waltham, Massachusetts, USA) to determine body fat mass (BFM), trunk fat mass (TFM) and lean body mass (LEAN).

Maturity offset was predicted with the equation of Mirwald et al., (2002).

Physical activity was assessed by accelerometry (ActiGraph GT1M model; Fort Walton Beach, FL) during four consecutive days, including two weekdays and two weekend days (Trost et al., 2005).

MS was measured on the dominant arm using a highly reliable portable electronic dynamometer (Jamar, EN-120604, Lafayette Instrument Company, USA) according to previously published instructions (De Smet and Vercammen, 2001); (Holm et al., 2008). The mean effort of 2 attempts (10 s of contraction with a rest period of at least 60 s) was used as peak absolute force (MS; kg) and relative handgrip strength (RMS; kg.kg $LEAN^{-1}$).

CRF was indirectly determined by a cycle test with progressively increasing workload using an electronically braked cycle ergometer (Monark 828 E Ergomedic; Monark, Vansbro, Sweden). Initial and incremental workloads were 20 W for children weighing less than 30 kg and 25 W for children weighing 30 kg or more. The workload was increased every 3 minutes until the maximal effort of the participants was reached (Klasson-Heggebø et al., 2006).

The heart rate at rest (HR_{rest}), brachial systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured after 10 min with the participants in the supine position using an automated oscillometric cuff (HEM-907-E, Omron, Tokyo, Japan). Two measurements were taken and if these values deviated by >5 mmHg, a third measurement was performed. The pressure difference between the SBP and DBP (PP) was calculated for adjustment purposes since SBP and DBP were positively correlated with the mean IMT of both the common and internal carotid arteries in a total of 128 Greek children and adolescents aged 10-19 yers-old (Stabouli et al., 2012).

The IMT of the common carotid artery (CCA) was defined as the distance between the leading edge of the lumen–intima interface to the leading edge of the media–adventitia interface of the far wall of the carotid artery. Carotid ultrasound was performed on the right carotid artery using an ultrasound scanner equipped with a linear 13 MHz probe (MyLab One, Esaote, Genova, Italy) and implemented with a previously validated radiofrequency-based tracking of arterial wall that allows a real-time determination of common carotid far-wall thickness (QIMT®) with high spatial and temporal resolution (Hoeks et al., 1997).

Multiple linear regression analysis was used to estimate the association between the exposure variable (IMT) and PA and physical fitness. Additionally we categorize subjects in tertils according to handgrip strength adjusted to LEAN of the individual (RMS). Hence, lower MS (LRMS): ≤0.65, middle MS (MRMS): >0.65 and <0.75, and higher MS (HRMS): ≥0.75 differences in strength and CRF measures were assessed with ANOVA. LSD test was used for post hoc comparison of means between each pair of groups. The statistical significance level was $p < 0.05$.

3 RESULTS

The characteristics of the study group are present in Table 1.

The determinants of IMT were examined in multivariate regression analyses in the entire cohort (Table 2). SED and MVPA were not associated with IMT (1^{st} model). CRF was the most important determinant of IMT (2^{nd} model) independent of age, gender and maturity.

Table 1: Means of the basic characteristics of the study group.

Variables	Unit	All
Age	(years)	11.35
BMI	($kg.m^{-2}$)	19.46
Maturity	(years)	-0.88
HR_{rest}	(bpm)	89.57
SBP	(mmHg)	110.99
DBP	(mmHg)	61.69
IMT	(mm)	0.50

Abbreviations: SBP: systolic blood pressure; DBP: diastolic blood pressure; IMT: intima-media thickness of the common carotid artery.

However, when RMS was added to this model, CRF was no longer a determinant of IMT over RMS even when controlled for pulse pressure.

As compared to HRMS group (Table 3), subjects in the LRMS group had higher mean values of body mass index (BMI), WC, BFM, SBP, DBP and IMT, and lower LEAN, maturity offset, MS, moderate-vigorous PA (MVPA) and CRF ($p<0.05$).

Table 2: Multiple regression analysis with IMT as dependent variable and SED, PA, CRF and RMS as determinants.

IMT	Variables	Beta	SEE	P
Model 1	SED	-0.01†		0.23
	PA	-0.02†		0.08
Model 2	CRF	-0.11	0.82	0.04
Model 3	RMS	-0.13	0.82	0.01
	CRF	-0.08†		0.16

The models are adjusted for age, gender, maturity and pulse pressure. † Excluded variable.

Abbreviations: RMS: Relative muscular strength; MVPA: moderate and vigorous physical activity per day; SED: Sedentary behaviour; CRF: Cardiorespiratory fitness; IMT: intima-media thickness of the common carotid artery

4 DISCUSSION

Results from this cohort study suggest that RMS is an independent predictor of intima-media thickness in 11-12 years-old children. Children with lower RMS have increased IMT, higher hemodynamic values, total and abdominal body fatness coupled with lower MVPA and CRF, apparently setting the stage for cardiovascular complications in adulthood.

The breakthrough finding from this study was that IMT, suggested to be predictor of CVD factors in adults (Lorenz et al., 2007), was associated with RMS independently of age, gender, maturity, PP, SED, MVPA and CRF.

These results strengthen up the data from cross-sectional studies (Artero et al., 2011); (Steene-Johannessen et al., 2009). The latter, using a cohort of 9- and 15-yr-old Noregian children (N = 2818), showed that MS was independently and inversely associated with clustered metabolic risk after adjustment for confounding factors.

To what public health policies are concerned, the evidence provided from our study along with the findings from the prospective population-based study of Grøntved et al., (2013) and Grøntved et al., (2013) suggesting that greater MS in youth is associated with lowers levels of CVD risk factors and a healthy insulin sensitivity and beta-cell function in young adulthood, independent of CRF and adiposity, is of particular importance supporting the inclusion of a specific recommendation for activities that increase MS as part of the guidelines for physical activity in youth for primordial prevention of CVD risk later in life.

Table 3: Means of the characteristics the muscular strength groups.

Variables	Unit	LRMS	MRMS	HRMS
n	(n)	122	123	121
Age	(years)	11.29	11.37	11.40
Boys/Girls	(n)	45/77	67/56	63/58
Weight	(Kg)	48.11	44.77	41.55*#†
Height	(cm)	153.19	150.88	149.50*#
BMI	(kg.m^{-2})	20.36	19.54	18.46*†
WC	(cm)	69.24	66.60	64.17*#†
BFM	(Kg)	14.66	12.23	11.13*#
LEAN	(Kg)	33.21	32.10	30.13*#
Maturity	(years)	-0.55	-1.01	-1.10*#
MS	(Kg)	19.47	22.42	24.36*#†
SED	(min)	542.18	536.19	525.84
MVPA	(min)	45.48	57.40	60.27*#
Wmax	(Watts.$^{kg-1}$)	2.43	2.75	2.80*#
HR_{rest}	(bpm)	91.20	88.28	89.23
HR_{max}	(bpm)	193.77	195.84	195.25
CRF	(ml.kg^{-1}.min^{-1})	38.99	43.09	44.54*#
SBP	(mmHg)	113.62	110.11	109.24*#
DBP	(mmHg)	62.92	61.68	60.45*
DIAM	(mm)	6.28	6.30	6.18
IMT	(mm)	0.51	0.50	0.48*

* Significantly differences between LRMS and HRMS ($p<0.05$; # Significantly differences between LRMS and MRMS ($p<0.05$); † Significantly differences between MRMS and HRMS ($p<0.05$).

Abbreviations: LRMS: lower relative muscular strength group; MRMS: middle relative muscular strength group; HRMS: higher relative muscular strength group; BMI: body mass index; WC: waist circumference; BFM: body fat mass by DXA; Maturity: maturity offset; MS: muscular strength; MVPA: moderate and vigorous physical activity per day; SED: Sedentary behaviour; Wmax: Maximal power output, HRrest: Heart rate at rest; HRmax: Heart rate at peak effort; CRF: Cardiorespiratory fitness; SBP: systolic blood pressure; DBP: diastolic blood pressure; DIAM: diameter of the common carotid carotid artery; IMT: intima-media thickness of the common carotid artery.

The differences among groups in fat accumulation, MVPA, CRF, BP and IMT translate to physiologically relevant differences increasing both metabolic and CVD risk. Exercise training reduces primary and secondary cardiovascular events, which is, at least partly mediated through the direct effects on vascular function and structure (Green et al., 2008).

Intervention studies have provided mixed results on the ability of exercise training to reverse vascular function and structure in children. Seeger et al., (2011) for example, showed that an 18-week exercise training program with predominantly running exercise in children with T1DM (10.9 ± 1.5 years) improved flow-mediated dilation (FMD) without altering IMT or WC. Woo et al. (2004)

showed that dietary and/or exercise intervention programs in 82 overweight children (BMI, 25±3), 9-12 years-old produced only small changes in IMT despite a 4.9% change in %BFM and Meyer et al. (2006) concluded that regular exercise over 6 months restores endothelial function and improves carotid IMT associated with an improved cardiovascular risk profile in obese 14.7±2.2 years-old children.

Yet, the relative risk of both myocardial infarction and stroke rises with increasing IMT (Lorenz et al., 2007). Hence, the larger IMT by 0.03 mm (30% of 0.1 mm) in LRMS group compared with HRMS group in this study may result in a higher risk of CVD later in life, highlighting the importance of increasing physical fitness.

Additionally, we can not disregard the fact that CRF and MS explained 15% of the variability in cardiovascular health outcomes in a study where Janz et al., (2002) assessed CRF, MS, vigorous and sedentary activity, maturation, blood pressure, lipids, and body composition in 125 healthy children for a period of five years (mean baseline age, 10.5 years). The results indicated that maintaining high levels of CRF and MS during late childhood were associated with low levels of overall and abdominal adiposity during adolescence.

Different possibilities exist as to why we did not observe an association of MVPA with IMT. First, given the young age of our sample, it is likely that it has not been exposed to the extent that would affect the structural measures that could be identified later in adolescence as in Meyer, et al. (2006) and Pahkala, et al. (2011). Second, structural adaptations may occur early in life but are not detectable with the ultrasound (Virmani et al., 2000).

5 CONCLUSIONS

Full modelling of SED, PA, CRF and RMS exposed the detrimental role of RMS in arterial structure in 11-12 years-old children. Greater MS for any given LEAN mass is associated with improved vascular health even in children.

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