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ORIGINAL CONTRIBUTION

Markers of metabolic syndrome in obese children before and after 1-year lifestyle intervention program

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Abstract
Purpose Excess weight may be related to the development of adverse cardiometabolic risk factors in children. The aim of this study was to evaluate the effect of a lifestyle intervention program (nutrition and exercise counseling) on anthropometric parameters and metabolic syndrome (MS) components in Portuguese overweight/obese children.
Methods A total of 83 overweight/obese children aged 7–9 years were assigned to a 1-year individual or group-based treatment (GT); 61 children (z-score BMI (zBMI): 1.93 ± 0.28; 27 boys and 34 girls) completed the program. Anthropometric and biochemical parameters were assessed at baseline, at 6 months and at 1 year.
Results The overweight/obese children, compared to normal-weight ones, presented significantly higher blood pressure, total-cholesterol, total-cholesterol/high density lipoprotein cholesterol (HDL) ratio, triglycerides, Apolipoprotein B and C-reactive protein levels, while HDL and Apolipoprotein A-I were significantly lower. At baseline, the prevalence of MS was 16.4% in overweight/obese and 0% in normal-weight children. The number of components of MS was significantly higher in children with higher zBMI. Lifestyle intervention led to a significant improvement in zBMI, waist circumference/height ratio, HDL, triglycerides, Apolipoprotein A-I, and Apolipoprotein B levels. The prevalence of MS decreased to 14.8%. The GT intervention seems to be more successful, with a significant decrease in zBMI and an increase in HDL and a lower drop-out rate.
Conclusions Overweight/obese children have multiple risk factors associated with the MS. Lifestyle intervention, both individual and group-based treatment, led to an improvement in the degree of overweight/obesity and in MS components.

Keywords Children · Metabolic syndrome · Obesity · Nutrition · Lifestyle intervention

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Introduction

In the past decades, the prevalence of childhood obesity has increased worldwide, reaching epidemic proportions and becoming a serious and growing public health problem [1]. An excessive increase in body mass index (BMI) during early childhood may be related to the development and acceleration of adverse cardiovascular and metabolic risk factors [2]. The constellation of symptoms such as hyperinsulinemia, glucose intolerance, hypertension, high plasma levels of triglycerides (TG), decreased levels of high-density lipoprotein (HDL) cholesterol and obesity is known as metabolic syndrome (MS) [3]. This condition increases the risk for cardiovascular diseases (CVD) and type 2 diabetes (DM2) [3, 4]. The definition of MS is not consensual in pediatric populations [5]. Many different MS criteria have been employed, and the cut-offs used to

diagnose this syndrome in young have varied considerably among studies [4–7]. Recently, a new consensus definition has been published [8]. While the concept of MS has strengths in terms of professional and public health education and awareness, critics argue that it has some limitations [4, 9].

MS is rapidly increasing in prevalence with rising childhood obesity and sedentary lifestyles worldwide. It has been reported to be relatively low in normal-weight children (1% or less) contrary to what occurs in obese (18–50%) [10]. In addition, parameters associated with MS have been shown to originate early in life [7], and tend to track into adulthood [7, 11]. Data from the Princeton LRC Follow-up Study showed that the risk was almost ninefold for CVD and almost fourfold for DM2 in children with MS compared with children without MS [11]. A proper approach to reduce the obesity-related health risks, both in children and adults, is losing weight. Lifestyle programs that tackle diet and physical activity as well provide psychosocial support, may help prevent or reduce obesity and its associated comorbidities, including the MS [12–16].

The MS has been widely studied in adults and adolescents; however, there is little research focusing on its prevalence during lifestyle intervention with younger children (<10 year old). The aims of our study were to evaluate the changes in the degree of overweight/obesity and in the prevalence of MS and its components in a sample of Portuguese overweight/obese schoolchildren enrolled in a 1-year outpatient lifestyle intervention program. We hypothesized that reduction of the degree of obesity will result in improvement of MS components, while increasing the degree of obesity will result in worsening of this syndrome.

Subjects and methods

Study population

We invited to participate in the study 127 children classified as obese (≥95th BMI percentile) according to the US Centers for Disease Control and Prevention (CDC) [17]. These children were identified in a previous population-based study [18]. Eighty-three accepted the invitation, and 61 (27 boys, 34 girls) concluded the 1-year study protocol. Between the assessment at school and the first visit at the Hospital Infante D. Pedro, 10 children initially classified as obese became overweight (85–95th BMI percentile). These children were also included in the study. The normal-weight (NW) children (≤85th BMI percentile; 7–9 years old; 13 boys, 9 girls) were recruited from the outpatient Pediatric Clinic, and they performed only the baseline assessment. None of the children had primary dyslipidemia, hypertension, diabetes or glucose intolerance, secondary obesity, and were not receiving pharmacological treatment. Each parent gave written informed consent, and children gave assent for participation. Assessments were done at the Department of Endocrinology, Diabetes and Nutrition. The study was approved by the Hospital Ethics Committee.

Study protocol

The children were randomly assigned to one of the two treatments: an individual conventional treatment (IT) or a group-based treatment (GT). Since GT implies more visits, and due to staff and space limitations, GT was assigned with probability 1/3 and IT with probability 2/3. The main objective of both interventions was to promote lifestyle changes in children and their families, and consequently to stop weight gain and promote weight loss. At baseline, anthropometric and biochemical measurements were carried out to all children. In IT, a healthy eating plan meeting nutrient needs according to the recommended daily allowance (≈1,800 kcal) was prescribed and explained to children and their parents. The diet recommended the reduced intake of refined carbohydrates and saturated fats, with an increased consumption of vegetables and fruits. Additionally, physical activity was encouraged and sedentary behaviors, such as TV watching and computer/video game playing, were discouraged. Follow-up visits were held at 3- and 6 months and 1 year after the first visit. In GT, children and their parents participated in a group-based nutrition education program (4 children per group), which consisted of 4 consecutive sessions each of 60 min duration, conducted by a nutritionist. These sessions covered several topics regarding childhood obesity and comorbidities, healthy eating habits, healthy cooking methods, portion size control, food labeling and physical activity promotion. The acquired knowledge was reinforced at each session and whenever necessary at follow-up visits that were held at 3- and 6 months and 1 year after the first visit. Forty-two children at the IT and 19 at the GT completed the 1-year follow-up visit.

Anthropometric measures

Weight, height, and waist circumference (WC) were measured according to standardized procedures [19]. Weight was measured to the nearest 0.1 kg using an electronic column scale (SECA-780); height was measured to the nearest 0.1 cm using a stadiometer (SECA-220); WC was measured to the nearest 0.1 cm at the mid-point between the iliac crest and the lower edge of the ribs at the end of a normal expiration. BMI was calculated with measured height and weight and was standardized (zBMI) by using

age- and gender-normative data from the CDC [17, 20]. The term overweight/obese (OW/OB) includes children with a BMI percentile ≥85th. Abdominal obesity was defined using the sex and age-specific 90th WC percentile by McCarthy et al. [21]. All measurements were repeated at each follow-up visit. Birth weight and length were obtained from the children's health booklet.

Clinical and biochemical measures

A physical examination was performed, and puberty status was assessed according to Tanner stages [22]. Blood pressure (BP) was measured on the right arm with the patient seated, after rest, using a digital sphygmomanometer (OMRON M6) and appropriate sized cuff. After three measurements, the lowest blood pressure value was recorded. Children were classified according to sex, height, and age-specific charts [23]. Baseline blood samples were collected in the morning (8:00 to 9:00) after an overnight fast (10 to 12 h) and after a local application of a topical anesthetic patch (EMLA). Plasma and serum were separated by centrifugation. The glucose oxidase method (Siemens Healthcare Diagnostics Inc., Newark, DE, USA) was used to determine blood glucose levels. Both serum lipids (total cholesterol (T-chol), HDL-cholesterol (HDL), LDL-cholesterol (LDL), triglycerides) and plasma liver enzymes (alanine aminotransferase (ALT), aspartate aminotransferase (AST), gama-glutamyltransferase (GGT)) levels were measured by enzymatic colorimetric methods (Siemens Healthcare Diagnostics Inc.). Apolipoprotein A-I and Apolipoprotein B were measured by an immuno-turbidimetric assay (Olympus America Inc., Center Valley, PA, USA). C-reactive protein (CRP) was determined using a turbidimetric immunoassay (Siemens Healthcare Diagnostics Inc.). Outcome measures were obtained at follow-up visits at 6 months and 1 year.

Physical activity

A questionnaire concerning children activities was applied at baseline and at 1-year follow-up visit. The children were asked, with the help of parents, about the time spent at school, watching TV, playing computer/video games and sleeping. The frequency and duration of physical activities performed at school and/or extracurricular were also quantified.

Family history

Parents were asked about the presence of overweight/obesity and associated co-morbidities such as diabetes, hypertension, dyslipidemia, CVD, and hyperuricemia, as well as its presence in children's grandparents. The parents were not measured for height and weight.

Definition of MS

MS was defined according to the National Cholesterol Education Program Adult Treatment Panel III criteria modified by Cook [6], with adjustment for fasting glucose according to the recent American Diabetes Association definition for impaired fasting glucose [24]. This definition was chosen since it is based on age- and gender-specific cut-offs and it has been used in other pediatric studies [5, 25]. MS was considered if three or more of the following criteria were present: (1) abdominal obesity (WC ≥90th percentile for age and sex) [21]; (2) fasting triglycerides ≥110 mg/dl; (3) HDL ≤40 mg/dl; (4) systolic/diastolic BP ≥90th percentile for age, sex and height [23]; (5) fasting glucose ≥100 mg/dl [24].

Statistical analysis

Descriptive statistics were executed. Pearson (R) and Spearman (ρ) correlation coefficients were used. Partial correlation was computed controlling for gender, age, and Tanner stage. Chi-square test was used in nominal categorical variables. Independent samples t test was performed in continuous variables with normal distribution and Mann–Whitney test in those without normal distribution. General Linear Model (GLM) for repeated measures was used to compare the evolution of each of the variables, and time (baseline, 6-month and 1-year follow-up), treatment assignment (IT and GT) and treatment × time interaction were included as fixed effects, controlling for gender and Tanner stage. The differences between 1-year follow-up and baseline values (Δ) were calculated. In order to reduce the number of variables, a principal components analysis on Δ of anthropometric, metabolic, and physical activity variables was performed and the components to extract were selected applying Cattell's method (scree plot). The principal components extracted were used in a multivariate GLM to study the effect of both treatments, controlling for gender, age, and Tanner stage. Normal distribution was assessed using the Kolmogorov–Smirnov test. We considered a significance level of 0.05. Analysis was performed using SPSS version 14.0, 2005.

For the purpose of sample size estimation, the primary outcome was a decrease in zBMI between baseline and 1-year follow-up. According to our previous experience, a standard deviation of zBMI near 0.35 and a dropout rate under 30% was estimated. From our baseline sample, the number of participants in the smaller treatment group (GT) was estimated to decrease from 25 to 18. From these

assumptions, a power analysis was conducted using a sample size for each group of 18, obtaining an estimated power of 0.81 for a paired samples *t* test.

Results

Of the 83 OW/OB children that were evaluated at first visit, 73.5% ($n = 61$) completed the program. No significant differences between dropouts ($n = 22$) and those who finished the study were observed at baseline. The attrition rate was similar in both treatment types: 27.6% in IT and 24.0% in GT. The main reason referred to dropout of the study was the lack of time due to school/work schedules. No statistical differences were found between the IT and GT subjects with respect to baseline parameters. The dropouts were excluded from the subsequent analysis.

Baseline characteristics

The anthropometric and clinical characteristics of the 61 OW/OB (51 obese, 10 overweight) and 22 NW children are shown in Table 1. No differences were found between both groups in age and gender. Gestational data (weight, length, and weeks of gestation) were also similar between groups. The OW/OB children presented significantly higher BP, T-chol, T-chol/HDL ratio, triglycerides (TG), Apolipoprotein B and C-reactive protein (CRP) levels; HDL and Apolipoprotein A-I were significantly lower. At baseline, the prevalence of MS was 16.4% in OW/OB children, without significant differences between gender ($p = 0.321$). None of the children fulfilled the five MS components. In NW children, MS was absent. Acanthosis nigricans was detected in 19.7% of the OW/OB children at baseline. Most children were prepubertal at baseline (Tanner stage: I—70.5%; II—29.5%). There were no statistical differences between gender, except for CRP (girls: 0.45 ± 0.91 mg/dl vs. boys: 0.31 ± 0.77 mg/dl; $p = 0.020$) and ALT (girls: 17.6 ± 4.9 U/L vs. boys: 21.3 ± 7.3 U/L; $p = 0.020$) in OW/OB children.

Table 1 Anthropometric and metabolic characteristics of overweight/obese and normal-weight children

	OW/OB ($n = 61$)	NW ($n = 22$)	*p*
Gender			
Male	4 (55.7%)	13 (59.1%)	0.233[a]
Female	27 (44.3%)	9 (40.9%)	
Metabolic syndrome	10 (16.4%)	0 (0.0%)	0.043[b]
Age (year)	8.6 ± 0.7	8.4 ± 0.7	0.133[b]
Weight (kg)	42.0 ± 6.6	26.7 ± 3.1	<0.001[b]
Height (cm)	134.9 ± 6.1	129.6 ± 5.8	0.001[b]
BMI (kg/m^2)	22.94 ± 2.29	15.86 ± 1.06	<0.001[b]
Z score BMI	1.93 ± 0.28	-0.12 ± 0.62	<0.001[b]
Waist circumference (cm)	72.8 ± 6.4	55.6 ± 3.7	<0.001[b]
Systolic BP (mmHg)	115.6 ± 8.2	103.2 ± 9.9	<0.001[b]
Diastolic BP (mmHg)	62.9 ± 9.6	53.8 ± 7.7	<0.001[b]
Glucose (mg/dl)	80.7 ± 5.7	80.3 ± 6.2	0.749[b]
T-chol (mg/dl)	169.6 ± 27.5	159.8 ± 15.3	0.046[b]
HDL (mg/dl)	49.7 ± 9.7	55.2 ± 10.6	0.030[b]
T-chol/HDL	3.51 ± 0.77	3.00 ± 0.67	0.008[b]
LDL (mg/dl)	107.8 ± 23.8	97.6 ± 17.8	0.073[b]
Triglycerides (mg/dl)	77.7 ± 52.1	52.3 ± 26.5	0.005[c]
Apolipoprotein A-I (mg/dl)	122.7 ± 15.6	141.8 ± 10.5	0.010[b]
Apolipoprotein B (mg/dl)	78.3 ± 15.1	69.4 ± 12.1	0.017[b]
Apolipoprotein A-I/B (mg/dl)	1.62 ± 0.38	1.93 ± 0.41	0.085[b]
C-reactive protein (mg/dl)	0.39 ± 0.84	0.11 ± 0.06	0.004[c]
AST (U/L)	25.1 ± 5.0	26.8 ± 4.9	0.089[c]
ALT (U/L)	19.3 ± 6.3	17.8 ± 4.4	0.552[c]
GGT (U/L)	15.6 ± 6.8	17.1 ± 3.3	0.016[c]
Birth weight (g)	3,412 ± 457	3,358 ± 455	0.638[b]

Data presented as *n* (%) for gender and MS, and as mean ± standard deviation (SD) for other variables

Statistic tests comparing OW/OB children with controls

OW/OB overweight/obese, *NW* normal weight, *BP* blood pressure, *T-chol* total cholesterol, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *GGT* gama-glutamyltransferase

[a] Chi-square test

[b] *t* student

[c] Mann–Whitney

Primary outcome

At follow-up, both groups showed a significant ($p < 0.001$) decrease in zBMI (−0.18 and −0.25 in IT and GT, respectively) and in WC/height ratio, although weight and height increased (Table 2). This decrease was more pronounced in the GT subjects ($p = 0.042$ for zBMI and WC/height ratio). An increase in zBMI was associated with an increase in WC ($R = 0.783$; $p < 0.001$), WC/height ratio ($R = 0.781$; $p < 0.001$) and GGT ($R = 0.261$; $p = 0.045$), and a decrease in HDL ($R = -0.357$; $p = 0.006$).

Secondary outcome

Along the study, we observed an improvement of HDL ($p = 0.019$), higher in the GT children ($p = 0.042$) (Table 3). TG levels evolved differently between genders ($p = 0.001$) and between Tanner stages ($p = 0.001$): it increased in time in girls (76.6 ± 41.8 mg/dl at baseline vs. 82.4 ± 42.8 mg/dl after 1 year) and in stage II children (67.8 ± 31.6 mg/dl at baseline vs. 83.3 ± 47.9 mg/dl after

Table 2 Baseline and follow-up anthropometric and clinical characteristics of the population study according to treatment assignment

($n = 61$)	Treat. type	Baseline	6-Month follow-up	1-Year follow-up	p^a		
					t	*t*T*	*T*
Weight (kg)	IT	42.6 ± 6.8	44.0 ± 7.3	46.5 ± 8.0	<0.001	0.431	0.270
	GT	40.7 ± 6.2	42.3 ± 6.9	43.9 ± 6.4			
BMI (kg/m^2)	IT	23.23 ± 2.52	23.08 ± 2.69	23.39 ± 2.77	0.842	0.579	0.107
	GT	22.30 ± 1.57	22.28 ± 1.75	22.14 ± 1.81			
zBMI	IT	1.96 ± 0.29	1.83 ± 0.34	1.78 ± 0.33	<0.001	0.582	0.042
	GT	1.86 ± 0.25	1.73 ± 0.35	1.61 ± 0.34			
WC (cm)	IT	73.6 ± 6.5	73.5 ± 6.9	74.9 ± 7.5	0.081	0.803	0.079
	GT	70.9 ± 6.0	71.1 ± 6.2	71.6 ± 5.6			
WC/height	IT	0.54 ± 0.04	0.53 ± 0.04	0.53 ± 0.04	<0.001	0.760	0.042
	GT	0.53 ± 0.03	0.52 ± 0.04	0.51 ± 0.03			
SBP (mmHg)	IT	115.2 ± 8.6	116.3 ± 8.8	114.3 ± 8.5	0.403	0.493	0.668
	GT	116.3 ± 7.5	111.9 ± 9.2	114.1 ± 9.9			
DBP (mmHg)	IT	62.3 ± 8.4	62.3 ± 8.4	60.5 ± 6.9	0.047	0.382	0.687
	GT	64.3 ± 12.0	58.4 ± 7.0	61.3 ± 6.5			

Data presented as mean ± standard deviation (SD) for continuous variables

Treat treatment, *IT* individual treatment ($n = 42$), *GT* group-based treatment ($n = 19$), *WC* waist circumference, *SBP* systolic blood pressure, *DBP* diastolic blood pressure

[a] GLM repeated measures, controlling for gender and Tanner stage: t = time effect; T = treatment effect; $t*T$ = time × treatment interaction

Table 3 Baseline and follow-up metabolic characteristics of the population study according to treatment assignment

($n = 61$)	Treat. type	Baseline	6-Month follow-up	1-Year follow-up	p^a		
					t	*t*T*	*T*
Glucose (mg/dl)	IT	80.7 ± 5.7	79.0 ± 6.2	77.4 ± 7.2	0.177	0.343	0.730
	GT	80.9 ± 6.2	78.7 ± 7.7	80.1 ± 10.8			
T-chol (mg/dl)	IT	166.0 ± 27.4	169.4 ± 27.2	168.6 ± 24.4	0.091	0.024	0.546
	GT	177.4 ± 26.8	170.6 ± 26.5	180.6 ± 30.4			
HDL (mg/dl)	IT	48.5 ± 9.9	49.8 ± 8.8	50.4 ± 10.6	0.019	0.235	0.042
	GT	52.4 ± 9.0	50.5 ± 9.7	55.9 ± 9.7			
T-chol/HDL ratio	IT	3.52 ± 0.79	3.48 ± 0.69	3.47 ± 0.76	0.377	0.413	0.145
	GT	3.47 ± 0.72	3.45 ± 0.67	3.30 ± 0.68			
LDL (mg/dl)	IT	105.4 ± 24.5	106.9 ± 21.9	105.4 ± 22.3	0.119	0.013	0.955
	GT	112.9 ± 21.9	107.4 ± 20.3	114.8 ± 26.4			
TG (mg/dl)	IT	79.2 ± 55.9	76.2 ± 27.8	77.2 ± 35.4	0.009	0.482	0.158
	GT	74.6 ± 43.8	65.1 ± 28.5	73.5 ± 42.1			
Apo A-I (mg/dl)	IT	121.5 ± 16.8	126.2 ± 16.8	122.9 ± 15.2	0.026	0.057	0.293
	GT	125.3 ± 12.6	122.2 ± 14.0	130.9 ± 14.2			
Apo B (mg/dl)	IT	77.2 ± 15.8	74.3 ± 13.8	75.1 ± 14.3	0.033	0.501	0.533
	GT	80.8 ± 13.4	75.9 ± 13.4	77.8 ± 14.5			

Data presented as mean ± standard deviation (SD)

Treat treatment, *IT* individual treatment ($n = 42$), *GT* group-based treatment ($n = 19$), *T-chol* total cholesterol, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *TG* triglycerides, *Apo A-I* apolipoprotein A-I, *Apo B* apolipoprotein B

[a] GLM repeated measures, controlling for gender and Tanner stage: t = time effect; T = treatment effect; $t*T$ = time × treatment interaction

1 year), while it decreased in boys (80.4 ± 65.1 mg/dl at baseline vs. 67.7 ± 28.3 mg/dl after 1 year) and in stage I (73.2 ± 48.6 mg/dl at baseline vs. 71.4 ± 31.5 mg/dl after 1 year). At 1 year, the MS prevalence decreased from 16.4 to 14.8% (Fig. 1), more significantly in boys ($p = 0.030$). BP levels ≥90th percentile decreased from 63.9 to 49.2%

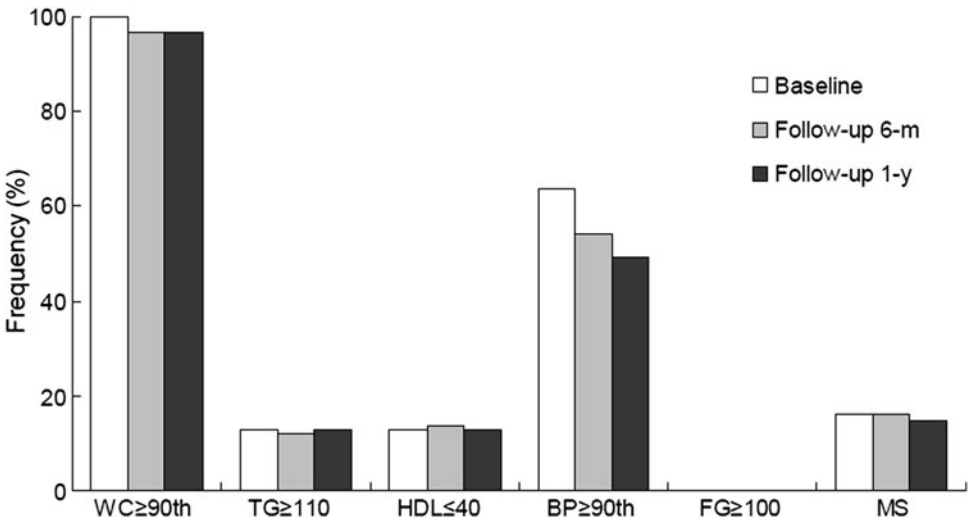

Fig. 1 Prevalence of Metabolic Syndrome and its criteria at baseline and at the follow-up visits at 6 months and at 1 year in overweight/obese children. *WC* waist circumference, *TG* triglycerides, *HDL* high density lipoprotein, *BP* blood pressure, *FG* fasting glucose, *MS* metabolic syndrome

Table 4 Sedentary and extra-curricular physical activities at baseline and at 1-year follow-up visit in overweight/obese and normal-weight children

	Overweight/Obese				Normal-weight				p^b
	Total ($n = 61$)	Boys ($n = 27$)	Girls ($n = 34$)	p^a	Total ($n = 22$)	Boys ($n = 13$)	Girls ($n = 9$)	p^a	
At baseline									
School (h/day)	7.3 ± 1.9	7.3 ± 2.2	7.4 ± 1.7	0.860[c]	8.3 ± 0.8	8.1 ± 0.8	8.6 ± 0.7	0.141[c]	0.001[c]
Sleeping (h/day)	9.5 ± 0.7	9.4 ± 0.5	9.6 ± 0.8	0.152[d]	10.2 ± 0.6	10.4 ± 0.7	9.9 ± 0.5	0.107[d]	0.000[d]
Watching TV (h/day)	1.7 ± 0.9	1.4 ± 0.6	2.0 ± 1.0	0.012[d]	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	0.637[d]	0.000[d]
Playing computer/videogames (h/day)	0.6 ± 0.5	0.8 ± 0.5	0.4 ± 0.4	0.001[d]	0.6 ± 0.4	0.6 ± 0.4	0.6 ± 0.4	0.621[d]	0.450[d]
Extra-curricular physical activities (min/day)	14.8 ± 15.3	21.7 ± 17.0	9.4 ± 11.4	0.005[d]	19.0 ± 24.3	21.9 ± 24.8	14.8 ± 24.3	0.510[d]	0.886[d]
At 1-year follow-up									
Extra-curricular physical activities (min/day)	15.6 ± 14.6	24.4 ± 15.7	8.7 ± 9.0	<0.001[c]	–	–	–	–	–

Data presented as mean ± standard deviation (SD)

[a] Significance level for the differences between boys and girls

[b] Significance level for the differences between overweight/obese and normal-weight children

[c] *t* student test

[d] Mann–Whitney test

($p = 0.063$). No child presented impaired fasting glucose levels, and acanthosis decreased to 11.5% 1 year later. Children with higher than average zBMI presented a higher than average number of MS criteria ($\rho = 0.418$, $p < 0.001$). OW/OB children with MS presented higher zBMI (2.15 ± 0.20 vs. 1.88 ± 0.23; $p = 0.006$), systolic BP (120.9 ± 8.6 vs. 114.5 ± 7.8 mmHg; $p = 0.023$), TG (159.6 ± 85.2 vs. 61.7 ± 18.6 mg/dl; $p < 0.001$), T-chol/HDL (4.54 ± 0.99 vs. 3.30 ± 0.53; $p = 0.003$) and Apolipoprotein B levels (87.6 ± 16.9 vs. 76.5 ± 14.2 mg/dl; $p = 0.033$) than those without MS, while HDL (39.5 ± 8.8 vs. 51.7 ± 8.6 mg/dl; $p < 0.001$), Apolipoprotein A-I (111.4 ± 14.6 vs. 124.9 ± 14.9 mg/dl; $p = 0.011$) and Apo A-I/B ratio (1.31 ± 0.25 vs. 1.69 ± 0.37; $p = 0.003$) were lower.

Physical activity and sedentary behavior

OW/OB children had statistically fewer hours of sleep and spent more hours watching TV than NW ones (Table 4). OW/OB girls spent more time watching TV ($p = 0.012$), while OW/OB boys spent more time playing computer ($p = 0.001$) and in extra-curricular activities ($p = 0.005$). Time devoted to extra-curricular exercise did not improve over time. No differences were found between the IT and GT subjects. MS children spent fewer hours in extra-curricular

exercise, both at baseline (3.0 ± 6.4 vs. 17.2 ± 15.5 min/day; $p = 0.004$) and after 1 year (5.9 ± 10.9 vs. 17.3 ± 14.6 min/day; $p = 0.030$).

Family history

Overweight/obesity was present in 42.6% of the mothers, 37.7% of the fathers and 14.8% of both parents of the OW/OB children (65.6% had at least one of their parents with excess weight). In grandparents, excess weight was present in 63.9%. Other comorbidities were also referred, such as dyslipidemia (21.3% mother, 21.3% father, 39.3% grandparents), hypertension (9.8% mother, 8.2% father, 47.5% grandparents) and diabetes (0% mother, 1.6% father, 57.4% grandparents). In NW children, overweight/obesity was present in 19.0% of the mothers, 9.5% of the fathers and 4.8% of both parents.

Principal components analysis

Seven principal components (PCs) were extracted with eigenvalues above 1. The first PC (PC1) was correlated mainly with anthropometric variables (Δweight, ΔBMI, ΔzBMI, ΔWC, ΔWC/height) and explained 24.0% of total variance (Table 5). The second PC (PC2) was correlated mainly with metabolic variables (ΔT-chol, ΔHDL, ΔLDL, ΔApoA-I, ΔApoB, ΔALT, ΔGGT) and explained 21.6% of total variance. The other PCs explained less than 8%. The physical activities variables had very weak correlations with both PCs. The only exception was the association between physical activity at school and PC1 ($R = -0.450$). According to the multivariate GLM, no significant association between PC1 and PC2 and the Δ of the number of MS components ($p = 0.639$) was found. Treatment type alone did not have a significant effect ($p = 0.412$), but its interaction with gender did ($p = 0.026$). For PC1, girls responded better to IT than to GT (−0.430 ± 1.220 vs. 0.438 ± 1.029), while boys responded better to GT (0.160 ± 1.337 vs. −0.773 ± 1.114). For PC2, girls did not show large discrepancies between IT and GT (0.160 ± 1.257 vs. 0.321 ± 1.060), while boys responded better to IT (−0.416 ± 1.377 vs. 0.321 ± 1.148). No significant differences between Tanner stages were found in both PCs; however, children that evolved from stage I to stage II over 1-year period had significantly lower values in both ($p = 0.023$).

Table 5 Correlation matrix between the principal components (PC) and the differences between baseline and 1-year follow-up variables (Δ)

Variables	PC1	PC2
ΔWeight	**0.860**	–0.299
ΔHeight	0.095	–0.350
ΔBMI	**0.906**	–0.200
ΔzBMI	**0.916**	–0.207
ΔWC	**0.865**	–0.328
ΔWC/height	**0.865**	–0.263
ΔSystolic BP	0.126	–0.097
ΔDiastolic BP	0.046	–0.318
ΔGlucose	–0.150	0.222
ΔTotal cholesterol	0.377	**0.840**
ΔHDL	–0.257	**0.686**
ΔLDL	0.394	**0.807**
ΔTriglycerides	0.401	0.372
ΔApolipoprotein A-I	0.036	**0.709**
ΔApolipoprotein B	0.458	**0.694**
ΔC-reactive protein	0.045	–0.080
ΔAST	–0.024	0.473
ΔALT	0.045	**0.567**
ΔGGT	0.359	**0.621**
ΔPhysical activities at school	–0.450	–0.092
ΔExtra-curricular physical activities	0.147	0.052

WC waist circumference, *BP* blood pressure, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *GGT* gama-glutamyltransferase

The bold correspond to the variables significantly correlated to each PC

Discussion

Our study presents the first report on the impact of an outpatient lifestyle intervention on MS and their components among OW/OB Portuguese children aged 7–9 years, recruited from the general population. We found a high prevalence of MS (16.4%) in OW/OB children, while it was absent in the NW. Similar results were found by Dubose et al. [26]. In other European countries, a similar prevalence of MS is found [5, 25, 27], however, with differences when considering the definition applied [5, 27].

OW/OB children in comparison with NW ones presented several cardiovascular and metabolic risk factors. BP levels have shown to be strongly predicted by BMI [28]; however, when compared to other studies [26, 27], we found a greater prevalence of elevated BP levels. This may be due to distinct dietary habits in our population, namely high sodium intake [29]. Our results are in agreement with data from Bogalusa Heart Study that showed significantly higher levels of T-chol, LDL and TG and lower HDL levels in overweight children [30]. CRP levels were also increased in our OW/OB subjects. This is in line with previous studies and seems to be related to an increased risk of CVD and diabetes [31]. Also, in our study, the number of children with 3 or more components of MS increased in parallel to the increasing severity of obesity. None of our children presented impaired fasting glucose

levels. Indeed, our sample is very young, and high fasting glycemia is not common in the pediatric age [32]. However, we found a high frequency (19.5%) of acanthosis nigricans, a known dermatologic feature of insulin resistance [33].

In this study, both approaches (IT and GT) were effective in zBMI change and, in general, clinical and metabolic parameters improved after 1 year. A significant reduction in WC/height ratio, an index associated with cardiovascular risk factors in children [30], was also observed at 1 year. Although weight, BMI, and waist circumference did not change significantly in this period, height increased significantly, which is associated with an anthropometrical improvement during growth. In this order, the use of percentiles or *z*-scores is preferred in the evaluation of children. Since our study was not hospital-based, the severity of obesity was moderate (zBMI: 1.93 ± 0.28), which may also account to less severe comorbidities. Both zBMI and WC/height ratio showed a more pronounced decrease in children enrolled in the GT.

In addition to a reduction in zBMI, an improvement of blood pressure and lipid profile was also shown over time. BP levels ≥90th percentile decreased by 23%, yet after 1 year we still found an alarming prevalence of elevated BP levels. In girls, we found an increase in TG levels at 1 year, which may be associated with the higher number of girls at Tanner stage II, since puberty is associated with an increase in TG levels [34]. The relative normal baseline lipid levels in these children may have limited our ability to show a more substantial change. These results are in line with previous pediatric studies showing that a reduction in obesity leads to an improvement in CVD risks factors [12, 35].

Mostly in GT-children, we observed a fluctuation in the mean values of some parameters between the follow-up visits at 6 months and 1 year, namely an initial improvement followed by a small setback. This may be associated with more visits held in the first semester, allowing greater compliance between children and staff. This suggests the need for the development of continuous care models, helping maintaining initial weight loss [36].

A slight decrease in the MS prevalence was observed. However, in girls and in Tanner stage II children a higher prevalence of MS was found at 1 year. This may be explained by pubertal development, since it is associated with an increase in insulin resistance [37] and with several changes in plasma lipids [34]. Among those children who never developed MS ($n = 47$) or no longer presented it after 1 year ($n = 5$), most of them improved their zBMI, while among those who developed MS ($n = 4$), all either worsen or maintained their degree of overweight/obesity. This is in accordance with a recent study which showed that the amount of overweight reduction is a predictive factor for the improvement of MS components [15]. The fact that MS phenotype tends to persist and worsen over time if no preventive actions are taken [7], highlights the value of diet and exercise intervention. Other authors obtained more significant results in response to lifestyle intervention [15, 35, 38]; however, those are accomplished with a stronger dietary restriction (1,000–1,200 kcal).

Besides small differences between the outcome measures in both interventions, the GT seems to be more successful, with a significant decrease in zBMI and an increase in HDL. A family-based group treatment has been described as more effective than individual treatment in the management of childhood obesity at long term [13, 39, 40]. The response to the treatment, IT or GT, was different according to gender, which may alert us to the need for different approaches at this age. In particular, girls in IT and boys in GT improved more in PC1 ("anthropometric"). In respect to PC2 ("metabolic"), girls did not show differences between IT and GT, while boys in IT presented better results. Further studies are needed to better understand these results in order to choose the optimal intervention.

OW/OB children were more prone to sedentary activities. Indeed, OW/OB and MS subjects spent usually around 2 h per day watching TV and playing computer or videogames, while only about 15 min in extra physical activities. Results from the Framingham Children's Study confirm that the number of hours spent watching television or playing videogames is an important risk factor for the development of excess body fat during childhood [41]. Boys are generally more active than girls [42], as we observed. The time devoted to extra-curricular exercise remained nearly constant over time. Some of the reasons pointed out were the short time available, lack of appropriate infrastructures and insecurity in the practice of outdoor activities. On the other hand, an increase in physical activity performed at school had a positive effect in PC1, which may argue for a key role of school in promoting healthy lifestyles. Since sedentary and physical activities were obtained by self-report, this may limit the validity of these measures. Many intervention studies with exercise in their programs have shown that the combination of these approaches improves metabolic outcomes [13–15].

Overweight/obesity was present in about 2/3 of the family members of the OW/OB children. However, these may be underestimated since data on parents were obtained by self report. Other comorbidities were also reported, such as CVD and DM2, mainly in grandparents. Indeed, a family environment that promotes obesity and comorbidities in one member may be more likely to promote it in others [43]. The advantage of family interventions is that they address children and their parents. This is especially important for younger children, as our sample, since the influence of the parents on food habits and physical activity is higher on earlier ages [44].

Our study presents some limitations. First, the final sample size, despite an acceptable drop-out rate. Second, most children presented normal values at baseline for most metabolic parameters, which may contribute to decrease the statistical power for detecting significant differences. Third, both groups were subjected to treatment, not allowing comparing the outcomes with children not enrolled in any.

In conclusion, our results showed a significant prevalence of MS and its components, namely abdominal obesity, higher blood pressure and dyslipidemia in Portuguese OW/OB children. Both treatment interventions led to a decrease in zBMI and a moderate improvement of those components, more effective in the GT. Even in the absence of weight loss, OW/OB children may improve their cardiovascular and metabolic risk profile by lifestyle changes—diet, exercise, and behavior therapies. This may lead to improved child health. The modest magnitude of the benefits observed argues for a longer term and perhaps more intensive intervention. Hence, longer-term studies and larger cohorts are necessary to evaluate whether the improvements are clinically relevant, how the changes are incorporated into the lives of children and families and are sustained over time.

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Conflict of interest The authors declare that they have no conflict of interest.

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