Available online at www.sciencedirect.com
ScienceDirect
Metabolism Clinical and Experimental 56 (2007) 614–622
Metabolism
Clinical and Experimental
www.elsevier.com/locate/metabol

Cardiovascular risk factor levels and their relationships with overweight and fat distribution in children: The Fleurbaix Laventie Ville Santé II study[☆]

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Received 3 April 2006; accepted 19 December 2006

Abstract

This study aimed to document for the first time in a general population of French children the prevalence and levels of cardiovascular risk factors and to assess separately in boys and girls whether these risk factors were associated with fat mass distribution independently of subcutaneous overall adiposity. A cross-sectional analysis of baseline data from 452 children (235 boys and 217 girls) aged 8 to 17 years included in a 1999 population-based epidemiologic study (the Fleurbaix Laventie Ville Santé II study) was made. Overweight was defined according to the International Obesity Task Force references and the 90th percentiles of the French body mass index curves. The thresholds of parameters defining cardiovascular and metabolic risks were the 95th percentile of the Task Force Report on High Blood Pressure in Children and Adolescents for blood pressure and those of the American Academy of Pediatrics for lipids. Anthropometric and biological parameters were described by sex and according to overweight status. Partial correlations between cardiovascular risk factors and anthropometric measures of adiposity (body mass index, sum of 4 skinfold thicknesses, waist circumference, waist-to-height ratio) were calculated. Then, these correlations were additionally adjusted for the sum of 4 skinfold thicknesses. High plasma triglycerides, high insulin concentration, and low plasma high-density lipoprotein cholesterol (HDL-C) concentration were associated with all measures of adiposity ($|r| \geq 0.20$, $P <$ .002). When obese children were excluded, overweight children already had high triglycerides and low HDL-C levels, respectively, 2 and 20 times more frequently than normal-weight children did. Among overweight children, 7.7% had at least 2 risk factors among high blood pressure, high plasma triglycerides or glucose, and low HDL-C concentration vs 0.25% among normal-weight children (P = .002). After adjusting for the sum of skinfolds, an independent association between the risk factors and waist circumference was found in girls. In conclusion, (*a*) modest excess weight is associated with increased levels of cardiovascular risk factors. (*b*) In girls, abdominal fat distribution is associated with cardiovascular risk factors, independently of overall adiposity. (*c*) International definition of abdominal obesity in children is required to standardize studies and to progress in the evaluation of childhood obesity and its consequences.

1. Introduction

The prevalence of adult obesity has been increasing in France in the last 2 decades [1] as well as in other industrialized countries [2,3]. Relationships between obesity and cardiovascular and metabolic risk factors [4,5] and between obesity and mortality [6,7] have been unequivocally established in adults. Both the total amount of fat and

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0026-0495/$ – see front matter © 2007 Elsevier Inc. All rights reserved.
doi:10.1016/j.metabol.2006.12.006

its distribution contribute to these relationships: increased abdominal fat is clearly associated with cardiovascular risk factors in adults [8-11].

Overweight and obesity prevalences are also increasing in children worldwide [12-14], and France is not spared [15,16]. Moreover, the recent increase in mean body mass index (BMI) in children has been reported to be accompanied by an even steeper increase in waist circumference (WC) [17], an acceptable surrogate marker for abdominal fat mass. In children, an increase in abdominal fat mass is also associated with increased levels of cardiovascular risk factors [18,19], and WC could be better than BMI in identifying children susceptible to develop cardiovascular diseases in adulthood [20,21]. Few studies have tested whether abdominal fat is associated with cardiovascular risk factors irrespective of the total amount of fat in children [22,23]. None of these studies analyzed sexes separately.

Our first aim was to report the prevalence of high levels of cardiovascular risk factors in association with overweight, as defined by the International Obesity Task Force (IOTF) [24], in a sample of French nonobese children aged 8 to 17 years from the general population. The prevalence of the cluster of cardiovascular risk factors included in the National Cholesterol Education Program definition of the metabolic syndrome in adults (ie, plasma blood glucose, triglycerides, high-density lipoprotein cholesterol [HDL-C] concentration, and blood pressure) was also evaluated. Our second aim was to assess, for the first time separately in boys and girls, whether cardiovascular risk factors are associated with children's abdominal fat mass independently of subcutaneous fat mass, as already shown in adults.

2. Population and methods

2.1. Population

The children were recruited in 1992 in Fleurbaix and Laventie, 2 neighboring towns in northern France with 2488 and 4426 inhabitants, respectively, when the Fleurbaix Laventie Ville Santé (FLVS) study started. The first part of the study, FLVS I, was a 5-year follow-up of children involved in a nutritional education program that recruited all families with at least one child in the classes from the last section of preschool to the last section of primary school [25].

The second part, FLVS II, was an epidemiologic study on the determinants of weight change in the population. This study was proposed in 1999 to every family who participated in the FLVS I study. We recruited and examined 294 families among the 393 families still living in the 2 towns who could be contacted (acceptance rate, 75%). All family members aged 8 years or older (1113 participants, including 251 girls and 256 boys aged 8 to 17 years) were examined in their homes in 1999. The FLVS II study was reviewed by an ethics committee (Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale [CCPPRB], Lille, France). Confidentiality of data complied with French regulations (Loi Informatique et Liberté). Before participants entered into the study, a written consent was obtained from them and from their parents for those younger than 18 years.

This article used cross-sectional data collected from the children when they were included in the FLVS II study in 1999. The 34 girls and 21 boys who had at least one missing parameter in anthropometric, blood pressure, or biological measurements were excluded from all analyses. They were younger (12.7 ± 2.8 vs 13.6 ± 2.5 years, $P = .01$), and after age adjustment, boys were shorter (152 ± 18 vs 161 ± 15 cm, $P = .007$) than those with complete data. None of the other parameters were significantly different between excluded and nonexcluded children. Most of the missing values (62%) concerned biological parameters. Missing blood samples were more often due to the refusal of the younger children, and this partly accounts for this age difference. Thus, the present article concerned 217 girls and 235 boys.

2.2. Measurements

Trained physicians collected anthropometric data. Weight was measured to the nearest 0.1 kg with participants wearing light clothes and without shoes, and height was measured to the nearest centimeter. Waist circumference was measured to the nearest 0.5 cm during expiration when breathing normally at the smallest diameter between the iliac crest and the lower rib. The thickness of 4 skinfolds was measured in duplicate to the nearest 0.1 mm using Harpenden calipers on the left side of the body: tricipital (posterior aspect of the arm at the midpoint between the acromion and the olecranon), bicipital (anterior aspect of the arm at the midpoint between the acromion and the olecranon), subscapular (1 cm below the inferior angle at the scapula), and suprailiac (1 cm over the iliac crest at the midaxillary line). The duplicate measures were averaged. The sum of skinfolds and BMI (weight in kilograms divided by the square of height in meters) were calculated. Because WC is positively correlated with height in children after taking age and Tanner stage into account ($r = 0.30$ in our population), a waist-to-height ratio was also calculated, as previously suggested [26]. Pubertal stage was determined according to Tanner classification [27].

A 20-mL blood sample was obtained after an overnight fast for the measurement of total cholesterol, HDL-C, triglyceride, glucose, and insulin concentrations (Bi-insulin IRMA kit, Sanofi Pasteur, Marne-la-Coquette, France). Low-density lipoprotein cholesterol (LDL-C) was calculated using Friedewald estimation [28]. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured using an automatic device (OMRON 705CT, OMRON Matsusaka Co Ltd, Japan), with an adapted cuff on the right arm after approximately 5 minutes of rest in a sitting position. Three measurements at 2-minute intervals were recorded and averaged.

Table 1
Characteristics by sex

	Boys (n = 235)	Girls (n = 217)	P[a]
General characteristics			
Age (y)	13.6 ± 2.4	13.6 ± 2.6	.87
Tanner stage			
1	19% (45)	18% (39)	.10
2	20% (47)	12% (26)	
3	19% (45)	21% (45)	
4	28% (65)	28% (62)	
5	14% (33)	21% (45)	
Weight (kg)	49 ± 15	47 ± 13	.0002
Height (cm)	161 ± 15	156 ± 12	<.0001
Adiposity parameters			
BMI (kg/m^2)	18.3 ×/÷ 1.17	18.8 ×/÷ 1.17	.24
Sum of the 4 mean skinfolds (mm)	33.2 ×/÷ 1.61	45.5 ×/÷ 1.53	<.0001
WC (cm)	67.7 ± 8.8	65.2 ± 7.6	<.0001
Waist-to-height ratio	0.42 ± 0.04	0.42 ± 0.04	.36
F-normal	91% (214)	92% (199)	.79
F-overweight[b]	9% (21)	8% (18)	
IOTF[c]-normal	90% (212)	89% (193)	.68
IOTF-overweight	8% (20)	9% (19)	
IOTF-obese	1% (3)	2% (5)	
Cardiovascular and metabolic risk factors			
Total cholesterol (mmol/L)	4.05 ×/÷ 1.19	4.30 ×/÷ 1.20	<.0001
LDL-C (mmol/L)	2.16 ×/÷ 1.31	2.36 ×/÷ 1.32	<.0001
HDL-C (mmol/L)	1.55 ± 0.34	1.55 ± 0.34	.55
Triglycerides (mmol/L)	0.662 ×/÷ 1.50	0.735 ×/÷ 1.45	.003
Glucose (mmol/L)	4.76 ×/÷ 1.08	4.65 ×/÷ 1.09	.001
Insulin (pmol/L)	33.1 ×/÷ 1.78	39.3 ×/÷ 1.78	.002
SBP (mm Hg)	110.1 ± 12.0	105.0 ± 11.1	<.0001
DBP (mm Hg)	61.8 ± 9.0	62.3 ± 8.6	.79
High blood pressure	5.5% (13)	3.2% (7)	.25

Data are expressed as mean ± SD, geometric mean ×/÷ geometric SD, or percentage (number).
[a] Student t test for sex comparisons of quantitative variables and χ^2 or exact Fisher test for sex comparisons of qualitative variables.
[b] Defined as the 97th percentile of the French BMI reference curves.
[c] Overweight and obesity defined by IOTF cutoff.

2.3. Definitions and cutoff points

We used recommended cutoff points whenever specific recommendations were made for higher values in children.

Overweight and obesity were defined according to the IOTF sex- and age-specific BMI cutoffs [24]. For comparison with other French data, we also used the 97th percentiles of the French BMI reference curves for age and sex to define F-overweight [29].

The 95th percentiles of age, sex, height, SBP, and DBP reference curves established by the US National High Blood Pressure Education Program defined high blood pressure [30]. High blood lipid concentrations were defined according to the American Academy of Pediatrics' recommendations for children: thresholds of 5.2 mmol/L (2.0 g/L) for total cholesterol, 3.4 mmol/L (1.3 g/L) for LDL-C, and 0.9 mmol/L (0.35 g/L) for HDL-C [31]. We chose the threshold of 1.5 mmol/L (1.3 g/L) for triglycerides. It corresponds to the 95th percentile during the second decade of life [32]. Fasting plasma glucose higher than 6.1 mmol/L (1.10 g/L) was considered as impaired fasting glucose according to the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus [33].

2.4. Data analysis

Results are given as arithmetic mean ± SD, geometric mean ×/÷ geometric SD for log-transformed variables, or percentage (number). Body mass index and sum of skinfolds were log-transformed as were total cholesterol, LDL-C, triglycerides, plasma glucose, and insulin. All comparisons between sexes or weight-status groups used Student, χ^2, or exact Fisher tests, as appropriate.

Quantitative analyses were performed separately in boys and girls because of different patterns between sexes and some interactions between anthropometric parameters and sex for the biological parameters.

Comparisons of mean values between normal and overweight groups were adjusted for age and Tanner stage by analysis of covariance using general linear models.

Prevalences of cardiovascular and metabolic risk factors were compared between normal and overweight children in separate logistic models, with each cardiovascular risk factor

Table 2
Anthropometric variables and cardiovascular risk factors according to the IOTF-overweight status

Variable	Boys		Girls	
	Not IOTF-OW (n = 212)	IOTF-OW (n = 20)	Not IOTF-OW (n = 193)	IOTF-OW (n = 19)
Age (y)	13.6 ± 2.5	13.6 ± 1.8	13.6 ± 2.6	12.8 ± 2.8
Weight (kg)	47.4 ± 13.3***	64.6 ± 13.7	45.8 ± 11.3**	54.5 ± 12.9
Height (cm)	161 ± 15	162 ± 13	156 ± 12	152 ± 12
BMI (kg/m^2)	17.7 ×/÷ 1.14***	24.2 ×/÷ 1.09	18.3 ×/÷ 1.14***	22.9 ×/÷ 1.12
WC (cm)	66.0 ± 6.9***	81.9 ± 7.3	63.9 ± 6.3***	73.8 ± 7.4
Waist-to-height ratio	0.41 ± 0.03***	0.51 ± 0.03	0.41 ± 0.03***	0.48 ± 0.04
Sum of skinfolds (mm)	30.0 ×/÷ 1.43***	80.3 ×/÷ 1.29	42.0 ×/÷ 1.44***	81.5 ×/÷ 1.31
Total cholesterol (mmol/L)	4.04 ×/÷ 1.18	4.14 ×/÷ 1.21	4.29 ×/÷ 1.20	4.32 ×/÷ 1.14
LDL-C (mmol/L)	2.14 ×/÷ 1.31	2.36 ×/÷ 1.38	2.34 ×/÷ 1.33	2.51 ×/÷ 1.20
HDL-C (mmol/L)	1.58 ± 0.34**	1.29 ± 0.34	1.58 ± 0.31**	1.40 ± 0.39
Triglycerides (mmol/L)	0.64 ×/÷ 1.49***	0.93 ×/÷ 1.48	0.72 ×/÷ 01.45	0.83 ×/÷ 1.47
Glucose (mmol/L)	4.75 ×/÷ 1.09	4.82 ×/÷ 1.06	4.63 ×/÷ 1.09	4.80 ×/÷ 1.08
Insulin (pmol/L)	31.3 ×/÷ 1.76***	54.8 ×/÷ 1.56	37.7 ×/÷ 1.75*	52.3 ×/÷ 1.93
SBP (mm Hg)	110 ± 12	113 ± 13	105 ± 11	106 ± 12
DBP (mm Hg)	61.6 ± 9.3	64.0 ± 6.9	61.5 ± 8.2*	65.9 ± 8.9

Data are expressed as mean ± SD or geometric mean ×/÷ geometric SD. The IOTF-obese were excluded from the comparison because they were too few to constitute a separate group. OW indicates overweight.

* $P < .05$ (Student t test for comparisons between the 2 groups of overweight status).

** $P < .01$ (Student t test for comparisons between the 2 groups of overweight status).

*** $P < .0001$ (Student t test for comparisons between the 2 groups of overweight status).

as dependent variable and overweight status as a dichotomous explicative variable, with adjustment for sex, age, and Tanner stage. As the number of overweight subjects in both sexes was small, boys and girls were pooled for this analysis. Obese children were excluded from these comparisons, as they were too few to constitute a separate group.

Partial Pearson correlations, adjusted for age and Tanner stage, were calculated between anthropometric variables and cardiovascular risk factors. Then, to test for an effect of abdominal fat variables (WC and waist-to-height ratio) on cardiovascular risk factors independently of subcutaneous fat mass, they were additionally adjusted for the sum of skinfolds.

Because of the presence of siblings in our study population, analysis had to take into account familial resemblance. In the analysis of quantitative variables, we introduced a nuclear family variable as a random effect in a linear mixed model. The partial correlation coefficient between 2 variables, $X1$ and $X2$, was obtained by the Pearson correlation between the residuals of the regressions of $X1$ and $X2$ on the adjustment factors that included a random effect for the nuclear family variable [34].

SAS software version 8.2 (SAS Institute, Cary, NC) was used for all analyses. All significance tests were 2-sided, and a probability value of less than .05 was considered significant.

3. Results

3.1. Descriptive characteristics

The children studied had a mean age of 13.6 years, with no difference between boys and girls (Table 1). More girls (21%) than boys (14%) had reached Tanner stage 5. The sum of skinfold thicknesses was higher in girls than in boys ($P < .0001$). Waist circumference was significantly larger in boys ($P < .0001$), but the waist-to-height ratios were similar ($P = .36$). Body mass index was not significantly different between sexes; approximately 10% of children were overweight or obese according to the

Table 3
Percentage of children with high level of cardiovascular risk factors according to IOTF-overweight status (girls and boys pooled)

	Cutoffs	Not IOTF-OW (n = 405)	IOTF-OW[a] (n = 39)	P[b]
Total cholesterol	≥5.2 mmol/L	10%	13%	.58
LDL-C	≥3.4 mmol/L	5.9%	5.1%	1.0
HDL-C	≤0.9 mmol/L	0.5%	13%	<.0001
Triglycerides	≥1.5 mmol/L	3.7%	10%	.08
Glucose	≥6.1 mmol/L	1.0%	0.0%	1.0
SBP	≥95th percentile	3.2%	13%	.01
DBP	≥95th percentile	0.7%	2.6%	.31
≥2 risk factors[c]	≥2	0.25%	7.7%	.002

[a] IOTF-obese were excluded.

[b] P values of a logistic regression, with cardiovascular risk factors as dependent variables; overweight status as explicative variable; and sex, age, and Tanner stage as adjustment variables.

[c] Among those pertaining to the adult definition of the metabolic syndrome (high plasma triglyceride and glucose, low plasma HDL-C, high blood pressure).

Table 4
Pearson correlation coefficients between cardiovascular and metabolic risk factors and anthropometric parameters, adjusted for age and Tanner stage in boys (n = 235) and girls (n = 217)

	Height	BMI[a]	Sum of skinfolds[a]	Waist-to-height ratio
Boys				
Total cholesterol[a]	−0.10	0.00	0.02	0.03
LDL-C[a]	−0.09	0.09	0.12	0.16*
HDL-C	−0.13*	−0.31***	−0.32***	−0.32***
Triglycerides[a]	0.08	0.22**	0.26***	0.20**
Glucose[a]	0.07	0.09	0.13*	0.05
Insulin[a]	0.14*	0.34***	0.37***	0.28***
SBP	0.08	0.19**	0.16*	0.16*
DBP	0.07	0.20**	0.12	0.14*
Girls				
Total cholesterol[a]	−0.18**	0.06	0.06	0.14*
LDL-C[a]	−0.16*	0.14*	0.17*	0.19**
HDL-C	−0.06	−0.24**	−0.33***	−0.23**
Triglycerides[a]	−0.09	0.26***	0.27***	0.36***
Glucose[a]	0.20**	0.16*	0.11	0.16*
Insulin[a]	0.11	0.34***	0.26**	0.27***
SBP	0.01	0.13	0.01	0.12
DBP	0.00	0.31***	0.22**	0.26**

[a] Log-transformed variables.
* $P < .05$.
** $P < .01$.
*** $P < .0001$.

IOTF definition, and 9% were overweight or obese according to the French definition.

Triglycerides were slightly, but significantly, higher in girls (0.66 ×/÷ 1.50 vs 0.74 ×/÷ 1.45 mmol/L, $P = .003$) as were LDL-C and total cholesterol ($P < .0001$ for both); however, HDL-C concentration was similar in boys and girls ($P = .55$). Plasma glucose concentration was slightly higher in boys than in girls (4.76 ×/÷ 1.08 vs 4.65 ×/÷ 1.09 mmol/L, $P = .001$), and plasma insulin was lower in boys ($P = .002$). Systolic but not diastolic blood pressure was significantly higher in boys. High blood pressure was not significantly different even if it was more prevalent in boys (5.5% vs 3.2%, $P = .25$).

3.2. Cardiovascular risk factors and overweight

Mean values of cardiovascular and metabolic risk factors and anthropometric parameters are presented by sex and according to IOTF BMI cutoffs (excluding obesity) in Table 2. Mean height was not significantly different between BMI groups, and, as expected, all other anthropometric parameters were higher in overweight children. In both sexes, HDL-C was significantly lower, and triglycerides and insulin were significantly higher in IOTF-overweight children. Glucose and total cholesterol or LDL-C were not significantly different according to the overweight status in either sex.

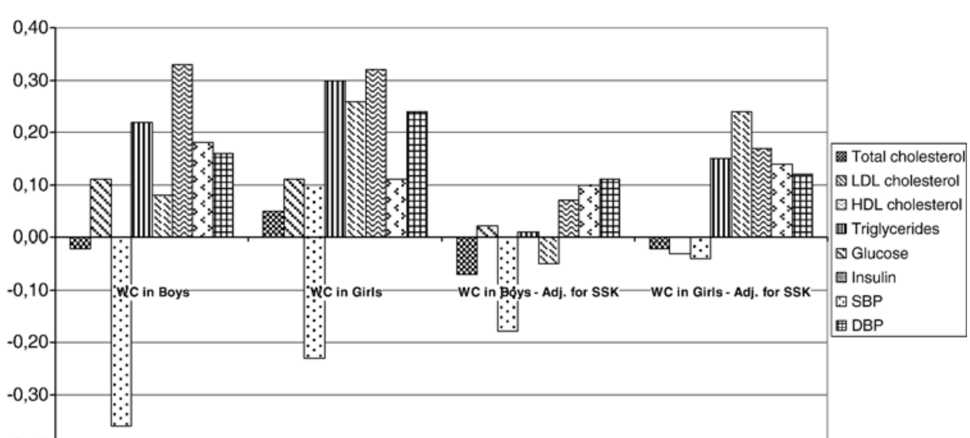

Fig. 1. Pearson correlation between cardiovascular risk factors and WC adjusted for age and Tanner stage, with and without an additional adjustment for the sum of skinfolds (Adj. for SSK) in 235 boys and 217 girls (statistical significance, $|r| > 0.13$).

The percentages of children with high levels of cardiovascular risk factors (as defined in the Population and methods section) are presented according to IOTF-overweight status in Table 3, with both sexes pooled. The most striking difference between normal- and overweight children was the low HDL-C, which reached 13% in IOTF-overweight children vs 0.5% in normal-weight children ($P < .0001$). High SBP was more prevalent in overweight children (13% in IOTF-overweight vs 3.2% in normal weight, $P = .01$). Prevalences of other risk factors tended to be higher in overweight children, but the differences did not reach significance. Only 4 children had at least 2 of the biological cardiovascular risk factors of the adult National Cholesterol Education Program definition of the metabolic syndrome exceeding the thresholds adapted to children: 1 with normal weight (0.25%) vs 3 overweight (7.7%, $P = .002$).

3.3. Correlations between anthropometric measurements and cardiovascular risk factors

Pearson correlation coefficients between anthropometric variables and cardiovascular risk factors adjusted for age and Tanner stage are presented in Table 4, and those between WC and cardiovascular risk factors are presented in Fig. 1.

Height was correlated with HDL-C ($r = -0.13$) and insulin ($r = 0.14$) in boys and with total cholesterol, LDL-C, and plasma glucose in girls ($r = -0.18$, $r = -0.16$, and $r = 0.20$, respectively). Among the cardiovascular risk factors, HDL-C, triglycerides, and insulin concentration ($|r| \geq 0.20$, $P < .002$) were strongly correlated with all other anthropometric parameters in boys and girls. Although correlations with LDL-C were lower, significant coefficients were observed with sum of skinfolds ($r = 0.17$) and BMI ($r = 0.14$) in girls and with waist-to-height ratio in both sexes ($r = 0.16$ in boys and $r = 0.19$ in girls). Total cholesterol was not significantly correlated with the anthropometric parameters except for waist-to-height ratio in girls ($r = 0.14$). Plasma glucose concentration was correlated with all anthropometric parameters in girls but not significantly so with sum of skinfolds. In boys, however, there was a weak relationship with sum of skinfolds only ($r = 0.13$, $P = .05$). Both SBP (range, 0.16-0.19) and DBP (range, 0.12-0.20) were correlated with almost all of the anthropometric variables in boys (correlations were not significant between DBP and sum of skinfolds), whereas only DBP was significantly associated with adiposity in girls (range, 0.22-0.31).

3.4. Additional adjustment for the sum of skinfolds

Fig. 1 presents the correlation coefficients between WC and the cardiovascular risk factors adjusted for age and Tanner stage, with and without an additional adjustment for the sum of skinfolds. Correlations between waist-to-height ratio and cardiovascular risk factors are only cited when different from those with WC.

Most of the cardiovascular risk factors were significantly correlated with WC in girls as in boys except for total cholesterol and LDL-C in both sexes, glucose in boys, and SBP in girls. The stronger correlations were observed between WC and HDL-C ($r = -0.36$) and insulin concentration ($r = 0.33$) in boys and between WC and triglycerides ($r = 0.30$) and insulin concentration in girls ($r = 0.32$).

In boys, once subcutaneous fat mass was accounted for, none of the relationships with cardiovascular risk factors remained significant except for HDL-C, which was still negatively associated with WC ($r = -0.18$, $P = .005$) but not with waist-to-height ratio ($r = -0.12$, $P = .07$).

In girls, correlations remained significant between WC and triglycerides ($r = 0.15$), glucose ($r = 0.24$), and insulin concentration ($r = 0.17$) and were increased with SBP ($r = 0.14$, $P = .04$). The strong correlation between waist-to-height ratio and triglycerides persisted ($r = 0.24$, $P = .0003$), but the waist-to-height ratio was no longer significantly associated with plasma glucose concentration ($r = 0.11$, $P = .10$).

Finally, the very strong correlation between insulin concentration and WC or waist-to-height ratio disappeared in boys ($r = 0.33$ to 0.07 and $r = 0.28$ to -0.02, respectively) and decreased in girls ($r = 0.32$ to 0.17 and $r = 0.27$ to 0.08, respectively) after adjusting for subcutaneous adiposity.

4. Discussion

In our population of healthy French children, the cardiovascular risk factors most strongly associated with overweight or adiposity parameters were fasting plasma triglycerides, insulin concentrations and blood pressure (positively), and plasma HDL-C concentration (negatively). After adjusting for subcutaneous fat, an association between these risk factors and abdominal fat distribution persisted for triglycerides and blood pressure in girls only, but this mostly disappeared for insulin concentration.

A limitation of our study is that adiposity was assessed with anthropometric measurements, which are less accurate than those of dual-energy x-ray absorptiometry (DXA). However, DXA is not applicable to large epidemiologic studies. Moreover, WC is considered as an appropriate marker of abdominal obesity in children [22], and the sum of skinfolds as a good indicator of overall adiposity [35-37]. Furthermore, our sample is not representative of the French children population. Indeed, the included children lived in 2 towns in northern France. They underwent a special nutritional education program at school for 5 years and accepted to participate in a longitudinal epidemiologic study [25]. The prevalence of overweight (including obesity) was approximately 10%, whereas it was closer to 15% in contemporary samples of French children [16,38]. This relatively low prevalence is probably due to the low participation rate of the overweight children in the longitudinal FLVS II study compared with the FLVS I (8.0% vs 13.5%) rather than to the effect of the nutritional education program. Indeed, we documented a rise in the mean BMI and in the prevalence of obesity in girls in cross-sectional studies of 5- to 12-year-old children performed before and 8 years after the beginning of the program in the schools [15]. To our knowledge, no other descriptive report on cardiovascular risk factors in overweight French children has been published so far. Because of these limitations, we believe that our reported prevalences and correlations represent a minimal estimate of the true situation.

We can therefore conclude from our study that overweight, as defined by IOTF, is associated with biological signs of insulin resistance and its associated dyslipidemia. The prevalence of clustered risk factors is low in the overweight nonobese children. Only 4 children (0.90%) in the overall overweight nonobese population presented with 2 or more of the metabolic syndrome risk factors; 3 (7.7%) among the overweight children did. A German study on overweight children also found noticeable prevalences of dyslipidemia, with figures even higher than those in our population: 16% for high triglyceride levels (defined as >1.7 mmol/L) and 17% for low HDL-C [39]. However, these children were selected in obesity centers and had probably a mean BMI (not reported) higher than that of our overweight children.

Waist circumference was the adiposity parameter most strongly associated with cardiovascular risk factors in our study as in most other studies [19,21]. It has been widely demonstrated that WC is a good predictor of cardiovascular risk factors in adults [40-42], and it is now used in the adult definitions of metabolic syndrome [43]. Several studies showed that in children, WC is also a good anthropometric parameter to evaluate cardiovascular and metabolic risks [20,21].

Another indicator of abdominal adiposity is waist-to-height ratio. Several studies reported that this was a better indicator of cardiovascular risk factors than BMI or WC itself [20,44-46], but others have not found any difference [21,47]. In our study, the correlations between the cardiovascular risk factors and WC or waist-to-height ratio were roughly similar. However, total cholesterol in girls and LDL-C in both sexes were significantly associated with waist-to-height ratio and not with WC, similar to a previous report [48].

When cardiovascular risk factors were associated with height, the correlation pattern between WC or waist-to-height ratio and cardiovascular risk factors was different. This could be a strength of using waist-to-height ratio as a parameter less influenced by height. After taking age and Tanner stage into account, WC was still closely related to height in our population (r = 0.30, P < .0001). Moreover, WC was dependent on age and sex, whereas waist-to-height ratio was not, as shown in another study [21]. Hence, as suggested before [40] and confirmed more recently [48], one particular advantage of the waist-to-height ratio may be that effects independent of age, sex, and height could be identified. It may be possible to define a unique cutoff for all children to define high WC whatever the age and sex. For example, Ho et al [49] suggested that in adults, a simple message that one's WC should not exceed half the stature could be recommended to the public. This threshold has already been used in a population of young adult students [50]. This parameter should be validated in large cohorts of children as a simple measurement allowing the screening of children at risk for cardiovascular diseases.

It is still not clear whether the effects of abdominal fat on cardiovascular risk factors are independent of the effects of total body fat [51]. We evaluated in our study whether WC was associated with cardiovascular risk factors independently of subcutaneous fat mass level in children. Other studies have looked at the differential relationship of fat localization measures and cardiovascular risk factors. One such study found that trunk skinfolds predicted cardiovascular disease risk factors to the same extent as did total fat mass by DXA, and in some cases independently of total fatness [23]. In another study, authors included both the percentage of body fat and fat distribution in a stepwise multiple linear regression analysis and found that fat distribution was a more important independent correlate of cardiovascular risk factors (high triglycerides, low HDL-C, high systolic blood pressure, high left ventricular mass) than percentage of fat mass [52].

These 2 studies did not perform analyses separately according to sex, whereas we consider that this was more appropriate. Indeed, boys and girls present quite different growth patterns in fat mass, lean mass, and fat distribution especially during puberty. Even in our relatively small population, some interactions were significant between anthropometric parameters and sex in relation with some biological parameters (eg, in the relation between waist-to-height ratio and triglycerides, P = .02).

The associations found only in girls between WC parameters and cardiovascular risk factors after taking the sum of skinfolds into account were primarily surprising. A central fat distribution is considered as a male-specific pattern and an explanation for the high prevalence of cardiovascular disease in men compared with women [53]. We hypothesized that the fat distribution is more homogeneously centrally distributed in boys and its effect on cardiovascular risk factors would not be distinguished from that of subcutaneous fat mass. Conversely, in girls, there is more variability in the fat distribution, from a gynoid to an android pattern, for a given level of total fat mass. However, we only found a slightly higher correlation between WC and the sum of 4 skinfolds in boys (r = 0.83) than in girls (r = 0.68).

One particular result from our study was that the very high positive correlations between anthropometric parameters and insulin concentration disappeared after the adjustment for subcutaneous fat mass, suggesting that subcutaneous fat mass has a role in the relation between abdominal fat distribution and hyperinsulinemia in these children. Furthermore, plasma glucose was more correlated with anthropometric parameters in girls than in boys. This may be in agreement with the higher prevalence of type 2 diabetes mellitus in adolescent girls than in adolescent boys [54].

5. Conclusion

In conclusion, modest excess weight using the IOTF definition of overweight, is associated with higher levels of metabolic markers of insulin resistance in boys and girls. In girls only, some metabolic factors were significantly related to the fat distribution independently of the overall amount of fat. An international definition of abdominal obesity in children is required to standardize studies, and to evaluate and prevent consequences of childhood obesity. Our study is important to consider in the context of the increase of obesity and particularly the associated increase in WC in women. How it could affect in the long-term the relative protection of women against cardiovascular diseases remains to be determined.

Acknowledgments

Marie-Aline Charles received grants from the Association de Langue Française pour l'étude des diabètes et du métabolisme and from the Mutuelle Generale de l'Education Nationale. We thank Laboratoires Knoll, CEDUS (Centre d'Etudes et de Documentation du Sucre), Groupe Fournier, Lesieur, Nestlé France, Produits Roche, and TEPRAL (Centre de recherche des brasseries Kronenbourg) for their support to the FLVS studies.

We thank the parents and their children who agreed to participate in the study.

References

[1] Charles MA, Basdevant A, Eschwege E. Prevalence of obesity in adults in France: the situation in 2000 established from the OBEPI Study. Ann Endocrinol (Paris) 2002;63(2 Pt 1):154-8.
[2] Flegal KM, Carroll MD, Ogden CL, et al. Prevalence and trends in obesity among US adults, 1999-2000. JAMA 2002;288:1723-7.
[3] Sundquist K, Qvist J, Johansson SE, et al. Increasing trends of obesity in Sweden between 1996/97 and 2000/01. Int J Obes Relat Metab Disord 2004;28:254-61.
[4] Huang KC, Lin WY, Lee LT, et al. Four anthropometric indices and cardiovascular risk factors in Taiwan. Int J Obes Relat Metab Disord 2002;26:1060-8.
[5] Must A, Spadano J, Coakley EH, et al. The disease burden associated with overweight and obesity. JAMA 1999;282:1523-9.
[6] Allison DB, Faith MS, Heo M, et al. Hypothesis concerning the U-shaped relation between body mass index and mortality. Am J Epidemiol 1997;146:339-49.
[7] Heitmann BL, Erikson H, Ellsinger BM, et al. Mortality associated with body fat, fat-free mass and body mass index among 60-year-old Swedish men—a 22-year follow-up. The study of men born in 1913. Int J Obes Relat Metab Disord 2000;24:33-7.
[8] Van Gaal L, Rillaerts E, Creten W, et al. Relationship of body fat distribution pattern to atherogenic risk factors in NIDDM. Preliminary results. Diabetes Care 1988;11:103-6.
[9] Von Eyben FE, Mouritsen E, Holm J, et al. Intra-abdominal obesity and metabolic risk factors: a study of young adults. Int J Obes Relat Metab Disord 2003;27:941-9.
[10] Walker SP, Rimm EB, Ascherio A, et al. Body size and fat distribution as predictors of stroke among US men. Am J Epidemiol 1996;144:1143-50.
[11] Bertrais S, Balkau B, Vol S, et al. Relationships between abdominal body fat distribution and cardiovascular risk factors: an explanation for women's healthier cardiovascular risk profile. The D.E.S.I.R Study. Int J Obes Relat Metab Disord 1999;23:1085-94.
[12] Frye C, Heinrich J. Trends and predictors of overweight and obesity in East German children. Int J Obes Relat Metab Disord 2003;27:963-9.
[13] Matsushita Y, Yoshiike N, Kaneda F, et al. Trends in childhood obesity in Japan over the last 25 years from the national nutrition survey. Obes Res 2004;12:205-14.
[14] Ogden CL, Flegal KM, Carroll MD, et al. Prevalence and trends in overweight among US children and adolescents, 1999-2000. JAMA 2002;288:1728-32.
[15] Heude B, Lafay L, Borys JM, et al. Time trend in height, weight, and obesity prevalence in school children from Northern France, 1992-2000. Diabetes Metab 2003;29:235-40.
[16] Rolland-Cachera MF, Castetbon K, Arnault N, et al. Body mass index in 7-9-y-old French children: frequency of obesity, overweight and thinness. Int J Obes Relat Metab Disord 2002;26:1610-6.
[17] McCarthy HD, Ellis SM, Cole TJ. Central overweight and obesity in British youth aged 11-16 years: cross sectional surveys of waist circumference. BMJ 2003;326:624.
[18] Goran MI, Gower BA. Relation between visceral fat and disease risk in children and adolescents. Am J Clin Nutr 1999;70(1 Part 2):149S-56S.
[19] Maffeis C, Corciulo N, Livieri C, et al. Waist circumference as a predictor of cardiovascular and metabolic risk factors in obese girls. Eur J Clin Nutr 2003;57:566-72.
[20] Lin WY, Lee LT, Chen CY, et al. Optimal cut-off values for obesity: using simple anthropometric indices to predict cardiovascular risk factors in Taiwan. Int J Obes Relat Metab Disord 2002;26:1232-8.
[21] Savva SC, Tornaritis M, Savva ME, et al. Waist circumference and waist-to-height ratio are better predictors of cardiovascular disease risk factors in children than body mass index. Int J Obes Relat Metab Disord 2000;24:1453-8.
[22] Daniels SR, Khoury PR, Morrison JA. Utility of different measures of body fat distribution in children and adolescents. Am J Epidemiol 2000;152:1179-84.
[23] Teixeira PJ, Sardinha LB, Going SB, et al. Total and regional fat and serum cardiovascular disease risk factors in lean and obese children and adolescents. Obes Res 2001;9:432-42.
[24] Cole TJ, Bellizzi MC, Flegal KM, et al. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ 2000;320:1240-3.
[25] Maillard G, Charles MA, Lafay L, et al. Macronutrient energy intake and adiposity in non obese prepubertal children aged 5-11 y (the Fleurbaix Laventie Ville Sante Study). Int J Obes Relat Metab Disord 2000;24:1608-17.
[26] Patel S, Unwin N, Bhopal R, et al. A comparison of proxy measures of abdominal obesity in Chinese, European and South Asian adults. Diabet Med 1999;16:853-60.
[27] Tanner JM. Growth at adolescence. Oxford (UK): Blackwell Scientific Publications; 1962.
[28] Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499-502.
[29] Rolland-Cachera MF, Cole TJ, Sempe M, et al. Body mass index variations: centiles from birth to 87 years. Eur J Clin Nutr 1991;45:13-21.
[30] National High Blood Pressure Education Program Working Group on Hypertension Control in Children and Adolescents. Update on

the 1987 Task Force Report on High Blood Pressure in Children and Adolescents: a working group report from the National High Blood Pressure Education Program. Pediatrics 1996;98(4 Pt 1): 649-58.
[31] American Academy of Pediatrics. Committee on Nutrition DL. Cholesterol in childhood. Pediatrics 1998;101(1 Pt 1):141-7.
[32] Freedman DS, Dietz WH, Srinivasan SR, et al. The relation of overweight to cardiovascular risk factors among children and adolescents: the Bogalusa Heart Study. Pediatrics 1999;103(6 Pt 1): 1175-82.
[33] Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 2003;26(Suppl 1): S5-S20.
[34] Brown H, Prescott R. Applied mixed models in medicine. Chichester (UK): John Wiley and Sons Ltd; 1999.
[35] Durnin JV, Womersley J. Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 years. Br J Nutr 1974;32:77-97.
[36] Gutin B, Litaker M, Islam S, et al. Body-composition measurement in 9-11-y-old children by dual-energy X-ray absorptiometry, skinfold-thickness measurements, and bioimpedance analysis. Am J Clin Nutr 1996;63:287-92.
[37] Lean ME, Han TS, Deurenberg P. Predicting body composition by densitometry from simple anthropometric measurements. Am J Clin Nutr 1996;63:4-14.
[38] De Peretti C, Castebon K. Surpoids et obésité chez les adolescents scolarisés en classe de troisième. Etudes et Résultats, no. 283, janvier 2004, DREES.
[39] Reinehr T, Andler W, Denzer C, et al. Cardiovascular risk factors in overweight German children and adolescents: relation to gender, age and degree of overweight. Nutr Metab Cardiovasc Dis 2005;15: 181-7.
[40] Rexrode KM, Carey VJ, Hennekens CH, et al. Abdominal adiposity and coronary heart disease in women. JAMA 1998;280:1843-8.
[41] Wang J. Waist circumference: a simple, inexpensive, and reliable tool that should be included as part of physical examinations in the doctor's office. Am J Clin Nutr 2003;78:902-3.
[42] Wang Z, Hoy WE. Waist circumference, body mass index, hip circumference and waist-to-hip ratio as predictors of cardiovascular disease in Aboriginal people. Eur J Clin Nutr 2004;58:888-93.
[43] Grundy SM, Brewer Jr HB, Cleeman JI, et al. Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation 2004;109:433-8.
[44] Ashwell M, Cole TJ, Dixon AK. Ratio of waist circumference to height is strong predictor of intra-abdominal fat. BMJ 1996;313: 559-60.
[45] Ashwell M, Lejeune S, McPherson K. Ratio of waist circumference to height may be better indicator of need for weight management. BMJ 1996;312:377.
[46] Hara M, Saitou E, Iwata F, et al. Waist-to-height ratio is the best predictor of cardiovascular disease risk factors in Japanese schoolchildren. J Atheroscler Thromb 2002;9:127-32.
[47] Hsieh SD, Yoshinaga H, Muto T. Waist-to-height ratio, a simple and practical index for assessing central fat distribution and metabolic risk in Japanese men and women. Int J Obes Relat Metab Disord 2003;27:610-6.
[48] Kahn HS, Imperatore G, Cheng YJ. A population-based comparison of BMI percentiles and waist-to-height ratio for identifying cardiovascular risk in youth. J Pediatr 2005;146:482-8.
[49] Ho SY, Lam TH, Janus ED. Waist to stature ratio is more strongly associated with cardiovascular risk factors than other simple anthropometric indices. Ann Epidemiol 2003;13:683-91.
[50] Bertsias G, Mammas I, Linardakis M, et al. Overweight and obesity in relation to cardiovascular disease risk factors among medical students in Crete, Greece. BMC Public Health 2003;3:3.
[51] Dietz WH. Childhood weight affects adult morbidity and mortality. J Nutr 1998;128(2 Suppl):411S-4S.
[52] Daniels SR, Morrison JA, Sprecher DL, et al. Association of body fat distribution and cardiovascular risk factors in children and adolescents. Circulation 1999;99:541-5.
[53] Price JF, Fowkes FG. Risk factors and the sex differential in coronary artery disease. Epidemiology 1997;8:584-91.
[54] Rosenbloom AL, Joe JR, Young RS, et al. Emerging epidemic of type 2 diabetes in youth. Diabetes Care 1999;22:345-54.