Youth Overweight and Metabolic Disturbances in Predicting Carotid Intima-Media Thickness, Type 2 Diabetes, and Metabolic Syndrome in Adulthood: The Cardiovascular Risk in Young Finns Study

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OBJECTIVE

Our objective was to assess cardiovascular risk and metabolic complications in adulthood in subjects with or without overweight and metabolic disturbances (i.e., elevated blood pressure, glucose, triglycerides, low HDL cholesterol, and high LDL cholesterol) and their combinations as youth.

RESEARCH DESIGN AND METHODS

Using data from the population-based Cardiovascular Risk in Young Finns study, we examined the utility of four age- and sex-specific youth phenotypes (group I: normal weight, no metabolic disturbances; group II: normal weight, one or more metabolic disturbances; group III: overweight/obese, no metabolic disturbances; group IV: overweight/obese, one or more metabolic disturbances) in predicting adult high carotid intima-media thickness (IMT), type 2 diabetes mellitus (T2DM), and metabolic syndrome (MetS). The study included 1,617 participants 9–24 years of age at baseline who were followed up 21–25 years later.

RESULTS

IMT (mean ± SEM) was higher among participants in groups II (0.627 ± 0.005 mm, $P = 0.05$), III (0.647 ± 0.010 mm, $P = 0.005$), and IV (0.670 ± 0.010 mm, $P < 0.0001$) compared with group I (0.616 ± 0.003 mm). In addition, subjects in group IV had significantly higher IMT compared with those in group II ($P = 0.002$). Participants in groups II, III, and IV were at increased risk of the development of MetS in adulthood compared with those in the control group. For group II participants, the difference was attenuated after risk factor adjustments. Additionally, participants in group III and IV were at increased risk of the development of T2DM compared with those in groups I and II.

CONCLUSIONS

While metabolic risk factors associated with overweight increase future risk for MetS, T2DM, and increased IMT, overweight in isolation is also a risk factor. Therefore, overweight should be prevented and treated wherever possible.

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The prevalence of overweight has increased among youth worldwide (1–3). The age-standardized prevalence of obesity (defined as a BMI ≥95th percentile for age and sex) in youth (12–19 years of age) between 1976–1980 and 2009–2010 has increased from 5.3 to 17.1% in girls and from 4.8 to 19.6% among boys in the U.S. (1,2). Youth and early adulthood overweight have been found to predict the development of type 2 diabetes mellitus (T2DM) and cardiovascular disease later in life (4–7).

Among adults, there has been increased interest in the division of individuals based on the presence or absence of overweight and the presence or absence of metabolic abnormalities (8,9). Metabolically healthy overweight (10) is the term used to define overweight individuals with no associated metabolic complications, whereas those with metabolic abnormalities despite having a normal weight have been termed as normal weight metabolically abnormal individuals. Previous studies in middle-aged adults have shown metabolically healthy overweight individuals to have decreased heart failure risk compared with normal weight, insulin-resistant individuals (11–13). However, the evidence base for youth is not established. Given the increase in the prevalence and severity of overweight in youth, there is a need to identify individuals who will benefit most from potential weight loss and screening for metabolic disturbances. In addition, a recent consensus statement from the American Heart Association (14) called for more research, particularly in longitudinal studies from youth to adulthood, in a number of areas relating to overweight and metabolic disturbances in early life. Thus, our aim was to assess the relative ability of youth overweight and metabolic complications to predict future cardiometabolic risk.

In this study, we assessed the 21-year risk of the development of subclinical atherosclerosis, assessed by carotid intima-media thickness (IMT), and the 21- to 25-year risk of the development of T2DM and metabolic syndrome (MetS) among youth 9–24 years of age at baseline according to their BMI and metabolic status.

RESEARCH DESIGN AND METHODS

Subjects and Study Design

The Cardiovascular Risk in Young Finns study was launched in 1980 when 3,596 participants 3–18 years of age were examined. Subjects were randomly selected from the national register from different parts of Finland to produce a representative sample of Finnish children. Thereafter, follow-up studies have been conducted regularly. Total of 2,779 participants 9–24 years of age attended the 6-year follow-up in 1986. In the 21-year follow-up in 2001, noninvasive ultrasound studies were introduced to the study protocol to assess markers of subclinical atherosclerosis. The latest follow-up with ultrasound measurements was performed in 2007, when the study subjects had reached age 30–45 years. In 2007, a total of 2,204 subjects were examined. The most recent follow-up was performed in 2011, and included blood samples and questionnaires but not ultrasound data. The sample for the present analysis included those subjects who had participated in the 1986 survey (baseline) and had undergone ultrasound examinations during the 2007 follow-up (N = 1,617). For individuals who participated in multiple follow-up surveys (2007 and 2011), those measures (T2DM and MetS data) that provided the longest time period between baseline and follow-up were used. Subjects with MetS with either incomplete metabolic risk factor data from these study years (N = 94) or type 1 diabetes (N = 12), as well as females who were pregnant (N = 30) at either time point were excluded from the study. A study flow diagram is shown in Supplementary Fig. 1.

We have previously shown that participants who attended follow-up studies shared characteristics similar to those who attended at baseline (15,16). We used the 1986 data as the baseline sample for this study as that was the first follow-up that collected data on fasting glucose levels. Measures available in 1986 and 2007 included the following: height and weight, blood pressure, and lipid, glucose, and insulin levels. Each study was approved by the appropriate institutional review boards, and written informed consent was obtained from all of the study participants or their parents if they were <18 years of age.

Carotid Ultrasound Measurements

Ultrasound studies were performed for the 2007 follow-up by trained sonographers following a standardized protocol. A moving scan with a duration of 5 s was recorded including the beginning of the carotid bifurcation and the common carotid artery. Measurements were made afterward from stored digital images by one reader who was blinded to participants' clinical characteristics. Carotid IMT was measured a minimum of four times from the posterior wall of the left common carotid artery ~10 mm proximal to the carotid bifurcation. We used an ultrasound imaging device with a high-resolution system (ACUSON Sequoia C512; Siemens Healthcare, Erlangen, Germany) and a 13-MHz transducer. A total of 57 participants (2.5%) were randomly selected to be reexamined 3 months after the first visit to assess intraindividual reproducibility. The coefficient of variation between visits was 6.4%.

Biochemical Measurements

Venous blood samples were drawn after a 12-h fast. Serum triglycerides and HDL cholesterol were measured as described previously (17). LDL cholesterol was calculated using the Friedewald formula (18). Serum glucose level was determined enzymatically (Glucose Reagent; Olympus, Ireland), and high-sensitivity serum C-reactive protein level was determined turbidimetrically (CRP-UL; Wako) on an automated analyzer (AU400; Olympus, Japan). Serum insulin concentration was determined by a microparticle enzyme immunoassay (IMx Insulin Reagent; Abbott Diagnostics) on an IMx instrument (Abbott Diagnostics). The interassay coefficient of variation was 2.1%.

Blood Pressure and Anthropometric Measurements

Body height and weight were measured. BMI was calculated as weight (kg)/height (m^2). Blood pressure was measured using a random zero sphygmomanometer with the average of three measurements used in the analyses. Skin-fold thicknesses were measured by Harpenden calipers (John Bull British Indicators Ltd.) to 0.2 cm in 1986. The sum of three skin-fold thickness measurements (subscapular, triceps, and biceps) was used in the analysis. Waist circumference (measured in duplicate at the level of the 12th rib or the level of the navel in thin subjects) was measured only in 2007.

Classification of Metabolic Disturbances and Overweight at Youth

Because there are no universal cutoff points for pediatric metabolic disturbances, we took an approach based on prevalence data from the National Cholesterol Education Program, Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents (19), which was used in previous reports (20,21). First, we generated age- and sex-specific percentiles of systolic and diastolic blood pressures, and HDL cholesterol, triglyceride, and glucose levels. Participants were categorized as having a metabolic disturbance if he/she had any of the following components: systolic blood pressure ≥90th percentile and/or diastolic blood pressure ≥90th percentile; LDL cholesterol level ≥90th percentile; triglyceride level ≥90th percentile; and HDL cholesterol level ≤10th percentile or glucose level ≥90th percentile. For consistency, a similar approach to defining metabolic disturbances was used for participants 18–24 years of age. In addition, alternative results, when "metabolically abnormal" was characterized by a homeostasis model assessment (HOMA) index of ≥90th percentile (22), are provided separately in the RESULTS and are detailed in the Supplementary Data. As a check of the sensitivity of the findings to the cut points used to define metabolic disturbances, analyses were repeated using alternate cut points to define metabolic disturbances of systolic blood pressure ≥80th percentile and/or diastolic blood pressure ≥80th percentile, and levels of LDL cholesterol ≥80th percentile, triglycerides ≥80th percentile, HDL cholesterol ≤20th percentile, or glucose ≥80th percentile. In addition, analyses were further repeated using Centers for Disease Control and Prevention (CDC) growth charts of those persons with BMI values >85th percentile (age- and sex-specific) to define youth overweight/obesity. The results for these definitions were essentially similar to the results presented (data not shown) except for continuous IMT using the CDC definition to classify overweight/obesity (data shown in the Supplementary Data).

For the definitions of youth overweight, we used the age- and sex-specific international BMI percentiles of Cole et al. (23) for participants 9–15 years of age, which correspond to adult BMI values of 25 kg/m^2 (overweight). Among those participants 18–24 years of age, a BMI of ≥25 kg/m^2 was used to define overweight.

Participants were categorized into four groups on the basis of adiposity and metabolic status in youth. Group I included participants with normal BMI and no metabolic disturbances (normal weight, metabolically healthy); group II, those who were normal weight but had one or more metabolic disturbances (normal weight, metabolically abnormal); group III, those who were overweight but had no metabolic disturbances (overweight/obese, metabolically healthy); and group IV, those who were overweight and had one or more metabolic disturbances (overweight/obese, metabolically abnormal).

Classification of Study Outcomes in Adulthood

To classify adult MetS, we used the recent definition proposed in a joint statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; the National Heart, Lung, and Blood Institute; the American Heart Association; the World Heart Federation; the International Atherosclerosis Society; and the International Association for the Study of Obesity (24). Participants were classified as having T2DM if they (*1*) had a fasting plasma glucose ≥7.0 mmol/L (126 mg/dL), (*2*) had an A1C level of ≥6.5% (48 mmol/mol), (*3*) reported receiving oral hypoglycemic agents and/or insulin injections and did not have type 1 diabetes, or (*4*) reported a history of physician-diagnosed T2DM (25). Women who reported having physician-diagnosed diabetes only during the term of their pregnancy were considered to have had gestational diabetes mellitus and were classified as not currently having T2DM provided their plasma glucose levels were <7.0 mmol/L. We defined high-risk IMT in adulthood as an IMT ≥90th percentile for age- and sex-specific values (26). Insulin resistance was estimated according to the HOMA index as the product of fasting glucose and insulin levels divided by 22.5 (27).

Statistical Methods

The normality assumptions of the residuals were assessed by examining histograms of the residuals and normal probability plots. Values for plasma triglycerides, insulin, C-reactive protein, and glucose were $\log_e$-transformed to correct for skewness. The characteristics of study subjects in 1986 and 2007 were summarized for each youth phenotype using ANCOVA or χ^2 test, as appropriate. Comparisons of the baseline characteristics of the study subjects among the study groups were performed with the use of linear or logistic regression. ANCOVA followed by Tukey multiple-comparison post hoc test was used to compare the mean IMT at follow-up among the study groups. Relative risks and Poisson robust CIs were calculated using the GENMOD procedure to examine associations between study groups and dichotomous outcomes. Statistical analyses were performed with SAS version 9.1, and statistical significance was inferred as a *P* value of ≤0.05.

RESULTS

Participant Characteristics

Characteristics of the 1,617 participants at baseline (1986) and follow-up (2007) are shown in Table 1. BMI was higher at baseline and follow-up in the overweight groups. Participants with normal weight and one or more metabolic disturbance (group II) had higher diastolic blood pressure, higher levels of plasma glucose and triglycerides, and lower levels of HDL cholesterol in 1986 ($P < 0.05$) compared with those who were overweight but had no metabolic disturbances (group III). Those participants who were overweight and had metabolic disturbances (group IV) had a more adverse risk factor profile compared with those in the remaining groups. In 2007, there was no difference among groups for diastolic blood pressure, and levels of plasma glucose or triglycerides.

Youth Phenotypes and Future Outcomes

Figure 1 shows the mean values of IMT in 2007 across the four study groups. A significant increasing trend in IMT was observed from group I to group IV (*P* for trend <0.0001). Overweight/obese youth (groups III and IV) had higher IMT values compared with group I (*P* for difference 0.005 and <0.0001, respectively). No difference was observed between groups II and III ($P = 0.09$). After adjusting for baseline levels of glucose, triglycerides, HDL cholesterol, and LDL cholesterol, and systolic blood pressure, no statistically significant difference was

Table 1—Participant characteristics in 1986 and 2007

Characteristics	Normal weight		Overweight*		
	No metabolic disturbances‡ (*N* = 1,032)	One or more metabolic disturbances§ (*N* = 390)	No metabolic disturbances‡ (*N* = 90)	One or more metabolic disturbances§ (*N* = 94)	*P* value†
Male sex (%)	48	45	51	53	0.41
Characteristics in 1986					
Age (years)	16.0 (4.9)	16.2 (5.0)	16.2 (5.7)	16.5 (5.5)	0.78
BMI (kg/m^2)	19.4 (2.7)	19.7 (2.6)	24.9 (3.1)	25.5 (3.4)	<0.0001
Systolic blood pressure (mmHg)	112 (12)	116 (13)	117 (13)	123 (12)	<0.0001
Diastolic blood pressure (mmHg)	64 (9)	65 (11)	65 (10)	70 (11)	<0.0001
Glucose (mmol/L)	4.52 (0.36)	4.89 (0.61)	4.49 (0.35)	4.94 (0.49)	<0.0001
Triglycerides (mmol/L)	0.82 (0.22)	1.10 (0.49)	0.88 (0.40)	1.42 (0.70)	<0.0001
HDL cholesterol (mmol/L)	1.53 (0.27)	1.52 (0.30)	1.47 (0.23)	1.35 (0.24)	<0.0001
LDL cholesterol (mmol/L)	2.84 (0.71)	3.45 (1.06)	2.96 (0.75)	3.44 (0.96)	<0.0001
Insulin (units/L)	8.9 (4.3)	10.6 (7.3)	11.8 (6.2)	15.8 (10.3)	<0.0001
Characteristics in 2007					
BMI (kg/m^2)	25.0 (4.0)	25.6 (3.9)	31.3 (5.2)	31.6 (5.5)	<0.0001
Systolic blood pressure (mmHg)	119 (13)	122 (14)	123 (14)	127 (14)	<0.0001
Diastolic blood pressure (mmHg)	75 (11)	76 (11)	78 (12)	82 (12)	<0.0001
Glucose (mmol/L)	5.22 (0.48)	5.37 (0.61)	5.39 (1.08)	5.82 (2.01)	<0.0001
Triglycerides (mmol/L)	1.26 (0.73)	1.46 (1.01)	1.48 (0.69)	1.97 (1.23)	<0.0001
HDL cholesterol (mmol/L)	1.35 (0.32)	1.30 (0.30)	1.27 (0.28)	1.19 (0.34)	<0.0001
LDL cholesterol (mmol/L)	2.98 (0.74)	3.28 (0.86)	3.09 (0.72)	3.18 (0.81)	<0.0001
Insulin (units/L)	8.0 (6.3)	8.79 (6.2)	12.8 (10.2)	13.4 (8.8)	<0.0001

Data are mean (SD), unless otherwise indicated. *The age- and sex-specific international BMI percentiles of Cole et al. (23) for participants 9–18 years of age that correspond to adult BMIs of 25 kg/m^2 (overweight). Among those 18–24 years of age, a BMI of ≥25 kg/m^2 was used to define overweight. †*P* values are for comparisons across phenotypes using analysis of variances. ‡No metabolic disturbances (<90th percentile systolic blood pressure and/or diastolic pressure, <90th percentile glucose, <90th percentile triglycerides, <90th percentile LDL cholesterol). §One or more metabolic disturbances (≥90th percentile systolic blood pressure or diastolic pressure, ≥90th percentile glucose, ≥90th percentile triglycerides, ≤10th percentile HDL cholesterol, ≥90th percentile LDL cholesterol).

observed in IMT at follow-up between group I and group II (*P* for difference 0.35). Otherwise, the results remained similar. Further adjustment for smoking or family history of coronary artery disease did not influence the results. When the model was adjusted for adult BMI in 2007, differences among groups became nonsignificant. When metabolically abnormal was characterized as having a HOMA index ≥90th percentiles or overweight/obesity was defined according to CDC growth charts, IMT was higher in group III compared with group II ($P < 0.04$) (Supplementary Figs. 2 and 5). Supplementary Fig. 4 shows the results for IMT among different groups when overweight according to BMI was replaced by an index of adiposity (skin-fold thickness >90th percentile). The results were essentially similar when BMI was used to assess adiposity.

Table 2 displays the relative risks and 95% CIs of adulthood outcomes (in 2007) according to youth (in 1986) phenotypes. Overweight/obese youth (groups III and IV) were at increased risk of the development of T2DM in adulthood compared with those in group I. Differences between groups I and II were attenuated after adjusting for baseline systolic blood pressure, and levels of glucose, triglycerides, HDL cholesterol, and LDL cholesterol. When the models were adjusted for adult BMI (2007–2011), the associations were attenuated or eliminated (Table 2). When metabolically abnormal was characterized as having an insulin or HOMA index ≥90th percentile, participants in group III were at increased risk of the development of high-risk IMT (odds ratio 2.3 [95% CI 1.5–3.5]) compared with group I. Otherwise, similar results were observed, as shown in Table 2.

Does Youth Overweight Predict Future Outcomes Over Metabolic Disturbances?

Figure 2 shows that participants who were overweight but with no metabolic disturbances (group III) had a significantly higher risk of the development of T2DM (3.9-fold) 21–25 years later as adults compared with normal weight, metabolically abnormal individuals. The comparison between group III and group IV (overweight/obese and metabolically abnormal) is additionally shown in Fig. 2. Participants in group IV had a higher risk of the development of MetS (2.3-fold) compared with those in group III. When metabolically abnormal status was characterized as having a HOMA index ≥90th percentile, we observed that participants in group III had a higher risk of the development of MetS (1.8-fold) and high-risk IMT (1.8-fold) compared with those in group II. In addition, no differences were observed between groups III and IV. Results are shown in Supplementary Fig. 3.

CONCLUSIONS

This study addresses important areas regarding overweight subgroups in youth who were partially outlined in the recent scientific statement from the American Heart Association (14). First, individuals who were either overweight or metabolically abnormal in youth shared a similar increased risk of the development of elevated IMT compared with the control group in adulthood. Second, our data show that overweight youth are at increased risk of the development of T2DM in adulthood when compared with normal

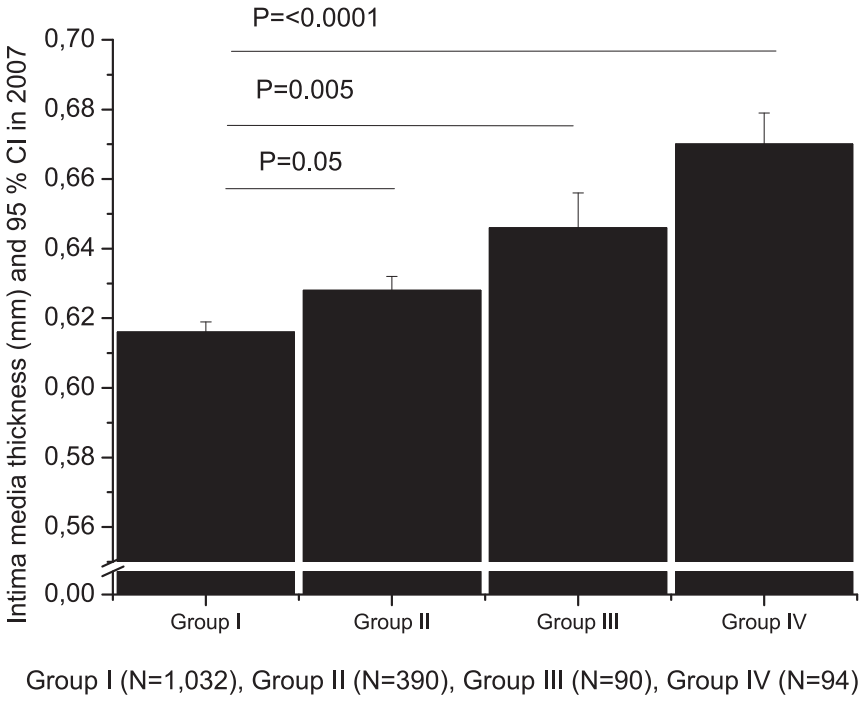

Figure 1—Carotid IMT in 2007 between youth phenotypes in 1986.

weight individuals. Third, the effect on future cardiometabolic risk was further increased in the presence of metabolic disturbances and overweight in combination.

To the best of our knowledge, this is the first study to investigate whether metabolically healthy but overweight youth share a similar risk as normal weight or overweight but metabolically unhealthy counterparts. The findings demonstrate an increased risk of future raised IMT in pediatric overweight individuals, even in those without metabolic derangement in youth—a finding that assists with clinical decision making in screening and pediatric overweight and obesity management. Previous studies (11–13) in middle-aged subjects have shown that metabolically healthy obese individuals have a decreased heart failure risk, when compared with normal-weight, insulin-resistant individuals. In the current study, participants were divided into four different subgroups to study whether individuals 9–24 years of age share similar risks for the development of cardiovascular problems. In contrast, Bo et al. (22) recently demonstrated in their 9-year follow-up study (baseline ages 45–64 years) that insulin-sensitive overweight individuals showed increased cardiometabolic risk similar to that of normal weight insulin-resistant subjects, thus questioning the clinical usefulness of stratifying obese individuals into subgroups. Our data confirm this notion but extend it to a much younger stage of the life course with some alternate outcomes and longer follow-up time. From a clinical perspective, the current

Table 2—Relative risk of adulthood outcomes (in 2007) according to youth (in 1986) phenotype

Outcome and phenotype	*n/N*	%	RR (95% CI)	*P* value	RR (95% CI) (adjusted*)	*P* value (adjusted*)	RR (95% CI) (adjusted†)	*P* value (adjusted†)
MetS 2007–2011								
Group I	126/1,039	12	Reference		Reference		Reference	
Group II	87/390	22	1.8 (1.4–2.4)	<0.0001	1.3 (0.9–1.8)	0.11	1.6 (1.2–2.1)	0.0005
Group III	25/90	28	2.3 (1.5–3.5)	<0.0001	2.0 (1.2–3.1)	0.004	0.9 (0.5–1.4)	0.49
Group IV	60/94	64	5.2 (3.8–7.1)	<0.0001	3.4 (2.2–5.2)	<0.0001	2.5 (1.7–3.8)	<0.0001
T2DM 2007–2011								
Group I	15/1,039	1.4	Reference		Reference		Reference	
Group II	10/390	2.6	1.8 (0.8–3.9)	0.16	1.3 (0.5–3.9)	0.56	2.3 (0.8–6.5)	0.11
Group III	9/90	10.0	6.9 (3.0–15.8)	<0.0001	6.1 (2.5–14.0)	0.004	2.2 (0.8–6.1)	0.14
Group IV	9/94	9.6	6.6 (2.9–15.1)	<0.0001	3.1 (1.0–9.9)	0.05	2.4 (0.8–6.7)	0.11

Group I, normal weight, no metabolic disturbances; Group II, normal weight, one or more metabolic disturbances; Group III, overweight/obese, no metabolic disturbances; Group IV, overweight/obese, one or more metabolic disturbances; Metabolic disturbances, ≥90th percentile systolic blood pressure and diastolic pressure, ≥90th percentile glucose, ≥90th percentile triglycerides, ≤10th percentile HDL cholesterol, ≥90th percentile LDL cholesterol; *n/N*, number of case patients/total number of subjects within the group. RR, relative risk. *Adjusted for baseline systolic blood pressure, glucose, triglycerides, HDL cholesterol, and LDL cholesterol. †Adjusted for adulthood BMI (2007–2011).

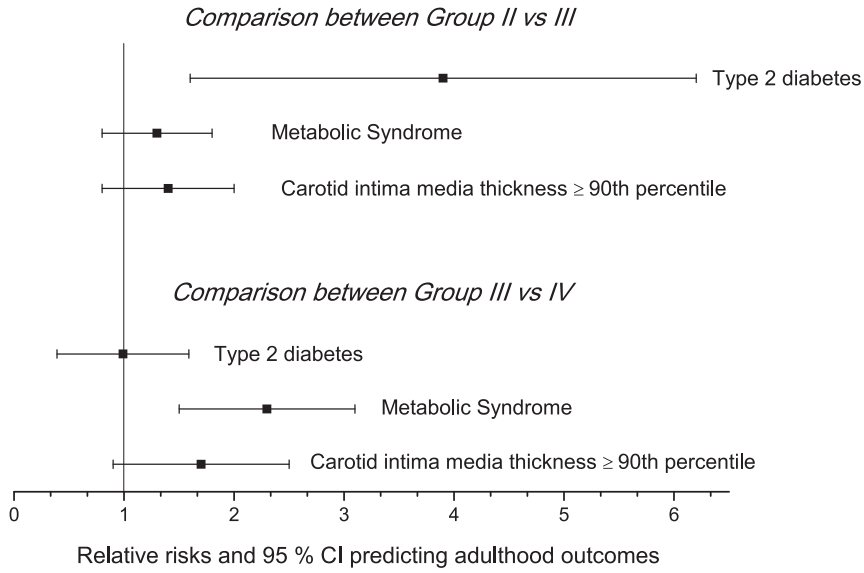

Figure 2—Relative risks and 95% CIs predicting adulthood outcomes between group II vs. group III (*top*) and between group III vs. group IV (*bottom*).

study showed no clear evidence for the healthy cardiovascular and metabolic overweight concept in youth assessed by IMT, T2DM, and MetS as future outcomes. The results and conclusions were not altered after adjustments with baseline risk factors, in sensitivity analysis or by using alternative ways of classifying overweight (using skin-fold thickness) and metabolic disturbance (using HOMA index >90th percentile).

Recently, Cunningham et al. (28) showed in their large cohort study that being overweight before entering kindergarten (mean age 5.6 years) was a strong predictor for incident obesity between the ages of 5–14 years, suggesting that preventive efforts may need to be focused on the first years of life. Furthermore, childhood BMI is a strong predictor of adult BMI, and established overweight/obesity is hard to treat (29). Previously, we (30) and others (31) have examined the associations of childhood BMI and adulthood cardiovascular risk factors, adjusting for adult BMI. The results show mainly eliminated associations for childhood BMI and adulthood risk, thus suggesting that the relationship was partly explained by significant tracking of BMI from youth to adulthood. In line with the current study, the differences among study groups predicting future T2DM, MetS, and IMT were attenuated or eliminated after adjusting for adulthood BMI. However, evidence for the potential benefits of reducing BMI in children and adolescents was recently observed in the International Childhood Cardiovascular Cohort Consortium (5). These data showed that the increased risk of the development of T2DM and preclinical atherosclerosis associated with youth overweight and obesity was attenuated among those who became nonobese by adulthood to a level similar to those who were never obese. The study suggested that those who were able to normalize their weight from youth to adulthood may overcome the increased risk for cardiometabolic outcomes associated with childhood overweight. Although the observational nature of our study precludes making clinical recommendations, these data indicate that all children and young adults, irrespective of their metabolic profile, should avoid overweight and obesity.

We (32) and others (33,34) have shown that pediatric MetS is associated with increased risk of the development of adult MetS, T2DM, and high-risk IMT. However, pediatric MetS predicted meaningful outcomes in adulthood at a level equivalent or inferior to predictions obtained from the status of high BMI in youth (32). Our results are in line with the result of these reports and were confirmed by performing an alternative analysis using only insulin resistance to define metabolically abnormal individuals. We showed that the risk of the development of cardiometabolic outcomes among overweight, metabolically healthy youth was similar or superior the risk in normal weight, metabolically abnormal youth. Further, BMI does not take into account potential differences in body composition among individuals with the same weight and thus may not be the best indicator of adiposity in childhood. However, we show that the indirect measurement of body adiposity, by substituting the sum of subscapular, biceps, and triceps skin-fold thickness, gives results similar to those observed for BMI. Although overweight and adiposity are not interchangeable per se, the results correspond well with each other. Nevertheless, considering the relatively poor tracking (32,35) of risk factor clustering compared with BMI, and the reproducibility of skin-fold measurements compared with BMI (32), this emphasizes the benefits of screening for overweight and obesity in the pediatric setting.

Study Strengths and Limitations

The strengths of our study were the long follow-up time from youth and the extensive baseline measurements of risk factors from a large community-based population sample. However, several limitations of our study should be considered. One explanation for why the predictive value of metabolic disturbances was lower than that of BMI may be that one measurement of BMI is more accurate than measures of each of the laboratory components and/or blood pressure. As such, BMI would be less susceptible to measurement error, as we have previously detailed (32). The results for adult outcomes were attenuated when models were adjusted for adult BMI, suggesting that the

associations with weight status may have been more profound because obesity tracks more than metabolic parameters. However, we have previously shown in this population that, in addition to BMI, childhood blood pressure and serum lipid levels correlate strongly with values measured in middle age (29). The low numbers with T2DM, and the use of fasting glucose levels and self-report data to indicate adult T2DM mean that associations with T2DM should be interpreted cautiously. However, the prevalence for T2DM was high in groups III and IV even though the absolute number of subjects was low. Second, any misclassification would rather attenuate the relative risk. Finally, because participants in the Young Finns Study are still of relative young age, it was not possible to study associations between risk factors and clinical outcome of cardiovascular events. Instead, vascular ultrasound measure was used as an indicator of an atherogenic process.

Conclusion

This study addresses important areas regarding overweight subgroups in youth. Together, our analysis of data from a longitudinal observational study supports the encouragement of young individuals to avoid being overweight/obese, irrespective of their metabolic profile.

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