Atherosclerosis xxx (2009) xxx–xxx

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Persistence of the metabolic syndrome and its influence on carotid artery intima media thickness in overweight Latino children

Claudia M. Toledo-Corral [a], Emily E. Ventura [a], Howard N. Hodis [a,c], Marc J. Weigensberg [b], Christianne J. Lane [a], Yanjie Li [c], Michael I. Goran [a,d,*]

[a] Department of Preventive Medicine, Keck School of Medicine, University of Southern California, United States
[b] Atherosclerosis Research Unit, Keck School of Medicine, University of Southern California, United States
[c] Department of Pediatrics, Keck School of Medicine, University of Southern California, United States
[d] Department of Physiology and Biophysics, Keck School of Medicine, University of Southern California, United States

ARTICLE INFO

Article history:
Received 27 December 2008
Received in revised form 14 March 2009
Accepted 16 March 2009
Available online xxx

Keywords:
CIMT
Obesity
Children
MetS

ABSTRACT

Objective: The objective of this study was to examine the influence of persistence of the metabolic syndrome (Mets) and its individual components over a 3-year period on carotid intima media thickness (CIMT) in overweight Latino children.
Methods: Ninety-seven healthy male and female overweight Latino children (mean age at baseline: 11.0 ± 1.8 years) were assessed for MetS on four annual evaluations and classified according to the persistence of MetS: NEVER (0 annual visits with the MetS, $n = 53$), INTERMITTENT (1 or 2 visits with the MetS, $n = 28$), and PERSISTENT (3 or 4 visits with the MetS, $n = 16$). CIMT was measured with high-resolution B-mode ultrasound (7.9 ± 0.7 months after the most recent MetS assessment; mean age: 14.6 ± 1.8 years).
Results: PERSISTENT MetS was associated with significantly higher CIMT (0.647 ± 0.018 mm compared to 0.600 ± 0.007 mm in those who NEVER had MetS, $p < 0.01$). This difference remained significant after controlling for gender, baseline age, total fat mass, total lean tissue mass and insulin sensitivity. PERSISTENT high waist circumference and PERSISTENT high blood pressure were also significantly associated with higher mean CIMT, but these differences were no longer significant after controlling for total fat and lean tissue mass. Baseline systolic blood pressure and 2-h glucose were significantly related to CIMT independent of all other MetS components ($p < 0.05$).
Conclusions: Persistence of the MetS over a 3-year period was uniquely associated with increased CIMT during childhood. Children with hypertension, persistent abdominal adiposity or impaired glucose tolerance may also be at higher risk for elevated CIMT.

Published by Elsevier Ireland Ltd.

1. Introduction

In adults, a clustering of risk factors collectively known as the metabolic syndrome (MetS) has been linked to cardiovascular disease (CVD) and atherosclerosis [1,2]. Some longitudinal studies have shown that MetS during childhood predicts the development of CVD by adulthood [3,4]. The escalating obesity rates in the pediatric population [5] and the association between obesity and MetS in childhood [6] substantiates the need to investigate the relationship of MetS and its components with atherosclerosis, especially in obese children. Children at highest risk are those who are overweight and have a family history of diabetes due the concomitant nature of metabolic and vascular dysfunction.

Common carotid artery intima media thickness (CIMT) has been used predominately in adults as a non-invasive measure of atherosclerosis. CIMT is a significant correlate to traditional vascular disease risk factors, such as cholesterol and blood pressure [7,8] and has been shown to be predictive of CVD in adults [9–11]. In pediatric populations, recent cross-sectional studies have shown that obesity [12–14] and the MetS [15] are associated with increased CIMT. Our cross-sectional study in overweight Latino children showed there was no association between the MetS and CIMT [16]. No studies to date have investigated the tracking of cardiometabolic risk factors and its effects on CIMT during childhood and adolescence. Our current objectives are therefore: (1) to investigate the effects of persistent MetS over a 3-year period on a subsequent single measure of CIMT and (2) to examine the individual effects of the persistence of each MetS component on a subsequent single measure of CIMT. We hypothesize

* Corresponding author at: Departments of Preventive Medicine and Physiology & Biophysics, University of Southern California, 2250 Alcazar Street, Los Angeles, CA 90089-9073, United States. Tel.: +1 323 442 3027; fax: +1 323 442 4103.
E-mail address: Goran@usc.edu (M.I. Goran).

0021-9150/$ – see front matter. Published by Elsevier Ireland Ltd.
doi:10.1016/j.atherosclerosis.2009.03.013

that persistent MetS will have a significant adverse effect on CIMT.

2. Methods

2.1. Subjects

Participants were enrolled in the Study of Latino Adolescents at Risk for Diabetes (SOLAR), a longitudinal study exploring metabolic risk factors for type 2 diabetes. Study participants satisfied the following criteria for inclusion at the initial baseline visit: 8–13 years of age, Latino ethnicity (i.e., parents and grandparents of Latino descent), age- and gender-specific BMI $\geq$ 85th percentile, positive family history for type 2 diabetes, and absence of diabetes as assessed by an oral glucose tolerance test (OGTT). Participants were excluded if they were using a medication or diagnosed with a condition known to influence body composition or insulin/glucose metabolism. Prior to testing procedures, written informed consent from parents and assent from the children were obtained. This investigation was approved by the Institutional Review Board of the University of Southern California. To be included in these analyses participants must have 3 or 4 annual MetS assessments prior to CIMT measurement.

2.2. Study protocol

As part of the full study protocol previously described [17], participants attended their annual visit to at the USC General Clinical Research Center (GCRC) for a comprehensive medical history and physical examination by a licensed health care provider, an oral glucose tolerance test (OGTT) and body composition measure by dual-energy X-ray absorptiometry (DEXA). Approximately 7–14 days following the outpatient visit, participants were admitted to the USC GCRC for their inpatient hospital visit and examined once more by a licensed health care provider and an MRI was completed. A single-slice axial TR 400/16 view of the abdomen at the level of the umbilicus was analyzed for cross-sectional area of visceral and subcutaneous adipose tissue. Following an overnight fast, a frequently sampled intravenous glucose tolerance test (FSIVGTT) was performed the following morning.

Fasting lipids were assessed using Vitros Chemistry DT Slides (Johnson and Johnson Clinical Diagnostics, Inc., Rochester, New York). Glucose was assayed using a Yellow Springs Instruments analyzer (YSI INC., Yellow Springs, OH) that uses a membrane bound glucose oxidase technique. Insulin was assayed using a specific human insulin enzyme-linked immunosorbent assay kit from Linco (St. Charles, MO; intra-assay coefficient of variation 4.7–7.0%, interassay coefficient of variation 9.1–11.4%; cross-reaction with human proinsulin 0%).

CIMT was determined at the USC Atherosclerosis Research Unit Core Imaging and Reading Center as previously described [11,18–22]. High-resolution B-mode ultrasound images were obtained using a Seimens Acuson CV70 (13 MHz linear array) imager. C-IMT was measured from computer processed images of the right distal common carotid artery approximately 1–2 cm from the bifurcation into external and internal carotids.

We defined the MetS using ATP-like criteria adapted for children, as previously described by our laboratory [17]. The MetS was determined at each annual visit, and the subjects were then classified into 1 of 3 categories according to the persistence of the MetS over the repeated annual visits: NEVER group (0 annual visits with the MetS), INTERMITTENT group (1 or 2 annual visits with the MetS), or PERSISTENT group (3 or 4 annual visits with the MetS). The persistence of each MetS component was examined in the same fashion, according to the criteria used in our definition of the MetS [23–26] (Table 2).

2.2.1. Statistical analyses

The Shapiro–Wilk's *W*-test was used to test the Gaussian distribution of the dependent variable, CIMT, which did not deviate from normality ($p > 0.05$). χ^2 tests and analysis of variance (ANOVA) with Bonferroni corrections were used to compare baseline characteristics of the three MetS groups. The analysis of covariance (ANCOVA) test was used to test for differences in CIMT by MetS group while adjusting for gender and the following covariates at baseline: age, total fat mass, total lean tissue mass, LDL-cholesterol, and insulin sensitivity. To test for differences in CIMT by persistence of the individual MetS components, ANOVA and ANCOVA analyses were performed to determine which component contributed the most to our initial result. To determine which of the MetS components contributed most to the results, linear regression models were employed with dependent variable, CIMT. Both models were adjusted for gender, age, total fat mass and total lean tissue mass (either at baseline or at time of CIMT measurement). Data were analyzed using SPSS for Windows version 13.0 (SPSS Inc., Chicago, IL), with an *apiori* significance level set at $p < 0.05$. Data are reported as mean $\pm$ S.D.

3. Results

The total sample was composed of 57.7% male participants with a mean overall age of 11.0 $\pm$ 1.8 years at baseline). In Table 1, baseline physical and metabolic characteristics are shown by the three MetS categories (NEVER, INTERMITTENT and PERSISTENT). There were significantly more males in the INTERMITTENT and PERSISTENT groups. The adiposity measures of BMI, total body fat mass and abdominal adipose tissue were not statistically different in any group. Insulin sensitivity was lowest in the PERSISTENT MetS group, but this difference did not reach statistical significance. MetS components at baseline are shown by mean differences by MetS group, followed by percent of subjects meeting the respective MetS component criterion. The PERSISTENT MetS group had a significantly higher percentage of participants with the MetS at baseline and the highest mean number of MetS components. Mean waist circumference, systolic blood pressure and triglycerides were significantly higher in the PERSISTENT MetS group whereas mean HDL-cholesterol was significantly lower than in the other MetS groups ($p < 0.05$).

Fig. 1 shows the significantly higher CIMT with increasing persistence of the MetS ($p = 0.01$), and this significance remained after adjusting for covariates (gender, baseline age, total fat mass, total lean tissue mass and insulin sensitivity, $p < 0.05$). Post hoc analyses

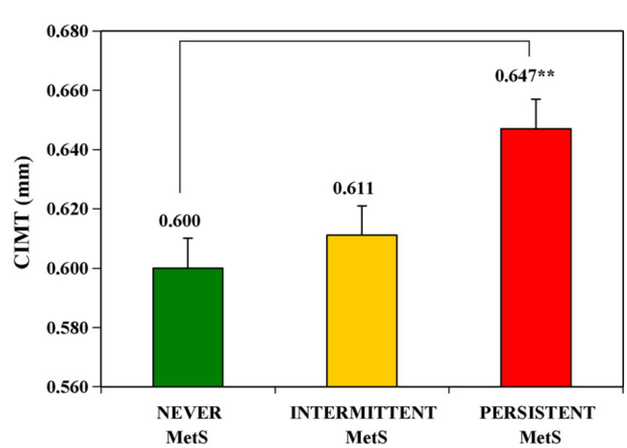

Fig. 1. CIMT by MetS group. Persistence of MetS defined as: NEVER (0 annual visits with the MetS, $n = 53$), INTERMITTENT (1 or 2 visits with the MetS, $n = 28$), and PERSISTENT (3 or 4 visits with the MetS, $n = 16$).

Please cite this article in press as: Toledo-Corral CM, et al. Persistence of the metabolic syndrome and its influence on carotid artery intima media thickness in overweight Latino children. Atherosclerosis (2009), doi:10.1016/j.atherosclerosis.2009.03.013

Table 1
Baseline physical and metabolic characteristics by MetS group.

	NEVER MetS ($n = 53$)	INTERMITTENT MetS ($n = 28$)	PERSISTENT MetS ($n = 16$)	Overall p-value (χ^2) or significant comparisons (ANOVA)
Male gender (%)	47.2%	64.3%	81.3%	0.03
Age (years)	10.9 ± 1.9	11.3 ± 1.6	10.6 ± 1.8	NS
Maturation stage by Tanner	2.2 ± 1.3	2.0 ± 1.1	1.7 ± 1.4	NS
Height (cm)	146.3 ± 11.6	150.3 ± 11.4	149.5 ± 14.8	NS
Weight (kg)	59.3 ± 20.2	66.8 ± 20.4	67.6 ± 21.2	NS
BMI (kg/m^2)	26.9 ± 5.4	28.9 ± 5.9	29.4 ± 4.5	NS
Total lean tissue mass (kg)	34.4 ± 9.9	37.7 ± 9.9	38.7 ± 12.0	NS
Total fat mass (kg)	22.7 ± 10.3	26.6 ± 11.1	26.4 ± 9.6	NS
Subcutaneous adipose tissue (cm^2)	306.7 ± 158.8	344.6 ± 134.9	348.1 ± 120.7	NS
Visceral adipose tissue (cm^2)	43.6 ± 20.7	50.5 ± 16.1	45.7 ± 17.9	NS
LDL-cholesterol (mg/dL)	91.9 ± 21.6	96.4 ± 25.8	96.2 ± 24.7	NS
Total cholesterol (mg/dL)	150.4 ± 26.0	151.5 ± 28.6	155.6 ± 25.9	NS
Adiponectin (μg/mL)	10.9 ± 3.1	10.2 ± 3.3	9.1 ± 2.3	NS
Fasting glucose (mg/dl)	90.5 ± 6.3	90.3 ± 5.5	91.1 ± 5.8	NS
Fasting insulin (μU/mL)	13.5 ± 8.2	18.0 ± 10.7	18.3 ± 12.6	NS

χ^2 test used to test for gender differences. ANOVA was used to compare means with Bonferroni corrections for multiple comparisons and data are means ± standard deviations.

Table 2
Baseline descriptive statistics of the individual MetS components by MetS group.

	NEVER MetS ($n = 53$)	INTERMITTENT MetS ($n = 28$)	PERSISTENT MetS ($n = 16$)	Overall p-value (χ^2) or significant comparisons (ANOVA)
Subjects with MetS (%)	0%	32.1%	87.5%	$p = 0.000$
Mean number of MetS components	1.4 ± 0.7	2.2 ± 0.9	2.9 ± 0.4	N vs. I**, N vs. P*
Waist circumference (WC) (cm)	85.5 ± 14.4	90.2 ± 10.9	93.1 ± 13.4	N vs. P†
Subjects with high WC (23)	58.5%	82.1%	100%	$p = 0.002$
HDL-cholesterol (HDL-C) (mg/dL)	41.0 ± 10.1	34.4 ± 6.4	33.7 ± 6.9	N vs. I**, N vs. P*
Subjects with low HDL-C (24)	43.4%	75.0%	81.3%	$p = 0.003$
Systolic blood pressure (SBP) (mmHg)	106.0 ± 8.4	110.3 ± 10.8	114.2 ± 8.8	N vs. P**
Subjects with high SBP [25]	11.3%	25.0%	31.3%	NS
Diastolic blood pressure (DBP) (mmHg)	62.5 ± 6.3	63.8 ± 6.7	65.8 ± 4.6	NS
Subjects with high DBP [25]	0%	0%	0%	NS
Triglycerides (TG) (mg/dL)	87.6 ± 43.2	103.5 ± 35.5	128.6 ± 44.8	N vs. P**
Subjects with high TG [24]	9.4%	21.4%	50%	$p = 0.002$
2-h glucose (mg/dL)	124.8 ± 16.6	123.4 ± 17.0	128.6 ± 13.4	NS
Subjects impaired glucose tolerance (IGT) [26]	20.8%	14.3%	31.3%	NS

χ^2 test used for data that were reported as percentages. ANOVA test was used to compare means with Bonferroni corrections for multiple comparisons and data are means ± standard deviations. $p < 0.001$.
† $p = 0.06$.
* $p < 0.05$.
** $p < 0.01$.

further revealed a significantly higher mean CIMT in the PERSISTENT than in the NEVER group (ANOVA means: 0.647 ± 0.018 mm vs. 0.600 ± 0.007 mm, $p < 0.01$) and a marginally significantly higher mean CIMT in PERSISTENT than in the INTERMITTENT group (0.647 ± 0.018 mm vs. 0.611 ± 0.008 mm, $p = 0.09$). Statistical significance remained in ANCOVA analyses.

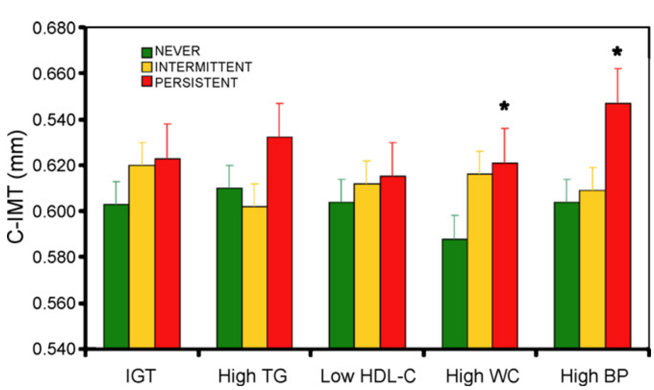

Fig. 2. CIMT by persistence of individual MetS component.

Examination of the persistence of each MetS component and their individual influences on CIMT are reported in Fig. 2. Participants with either PERSISTENT high waist circumference (HWC) or PERSISTENT high blood pressure (HBP) had significantly higher mean CIMT than those in the NEVER HWC or HBP groups ($p < 0.05$). Both models were no longer significant after adjustment for total body fat and lean tissue mass. All other PERSISTENT component groups had higher CIMT than the INTERMITTENT or NEVER group, but these differences did not reach statistical significance ($p > 0.05$).

In Table 3, it is shown that CIMT was significantly related with baseline systolic blood pressure ($p = 0.018$) and 2-hour glucose ($p = 0.02$), independent of gender, baseline age, body composition and all other MetS components. At time of CIMT measurement, CIMT was significantly related with age ($p = 0.008$) and total lean tissue mass ($p < 0.001$), but it was not associated with any of the MetS components.

4. Discussion

The overall objective of this study was to investigate, the effects of the persistence of the MetS over several years on CIMT (measured 7.9 ± 0.7 months following the most recent MetS evaluation). The

Please cite this article in press as: Toledo-Corral CM, et al. Persistence of the metabolic syndrome and its influence on carotid artery intima media thickness in overweight Latino children. Atherosclerosis (2009), doi:10.1016/j.atherosclerosis.2009.03.013

Table 3
Associations between CIMT and the individual components of the Mets at baseline and at time of CIMT measurement.

	At baseline			At time of CIMT measurement		
	Unstandardized beta	S.E.	*p*-Value	Unstandardized beta	S.E.	*p*-Value
Gender	−0.010056	0.012073	0.407	0.023653	0.014120	0.098
Age	−0.007905	0.004942	0.113	−0.010823	0.003952	0.008
Total lean tissue mass	0.000000	0.000001	0.930	0.000003	0.000001	0.000
Total fat mass	0.000002	0.000001	0.075	0.000000	0.000001	0.509
Systolic blood pressure	0.001625	0.000676	0.018	0.000941	0.000827	0.259
2-h glucose	0.000820	0.000347	0.020	0.000146	0.000275	0.598
Waist	0.001642	0.001078	0.113	0.000428	0.001641	0.795
Triglycerides	−0.000034	0.000134	0.803	−0.000052	0.000136	0.700
HDL-cholesterol	−0.000008	0.000645	0.990	0.000144	0.000858	0.867

analysis showed that children with persistent MetS over a 3-year period was associated with a 7% higher CIMT compared to those who never had MetS. This finding remained significant after adjusting for a variety of potential covariates including gender, baseline age, total body fat mass, total lean tissue mass and insulin sensitivity. Of the individual MetS components, persistent high waist circumference and high blood pressure were related to increased CIMT, although these effects may be explained by baseline total body fat and lean tissue mass. However, baseline measures of systolic blood pressure and 2-h glucose were independently related to increased CIMT.

To date, there are only two longitudinal studies focusing on the relationship between CVD risk factors in childhood and their long-term effects on CIMT in adulthood. The Bogalusa Heart Study found that clustering of increasing number of MetS components at the lower quartiles of risk predicted about a 0.1 mm decrease in CIMT at 26-year follow-up [3]. Secondly, the Young Finns Study found that adverse CVD clustering of risk factors (LDL-cholesterol, systolic blood pressure, BMI, smoking) in childhood predicted up to 0.1 mm higher CIMT at 21-year follow-up [4]. The present study is novel in that it shows that 0.047 mm greater CIMT can be observed in childhood following only 3 years of persistent MetS.

There are few studies examining the relationships between clustered cardiometabolic risk factors and subclinical atherosclerosis during childhood. A cross-sectional study of various pediatric MetS definitions and CIMT found that the definitions with higher BMI cut-offs and that utilized impaired glucose tolerance (Weiss et al. and Viner et al.) [6,27] were the ones with significant relationships with CIMT [28]. The present study showed that persistent MetS was related to elevated CIMT, using our pediatric definition of the MetS. This suggests that our pediatric definition, along with Viner et al. [27] and Weiss et al. [6], may be suitable matches for the concept of MetS in children. Our study also showed that all participants in the PERSISTENT MetS group were also part of the PERSISTENT high waist circumference group, which implies that abdominal adiposity may be driving the relationship between persistent MetS and CIMT. In contrast, only 37.5% of those in the PERSISTENT MetS group were also in the PERSISTENT high blood pressure group, suggesting this feature may be more of a stand-alone risk. Similar to Reinehr et al. [28], we found that baseline systolic blood pressure and 2-h glucose were the best predictors of CIMT, independent of the other MetS components. These data suggest that hypertension in conjunction with early insulin resistance and high waist circumference may be a plausible explanation for elevated CIMT in overweight Latino youth.

The PERSISTENT group's average CIMT was 0.047 mm higher than the NEVER group. The normal rate of progression reported in our control groups ranges from 0.003 mm to 0.005 mm increase/year [20,22]. Therefore, this 0.047 mm difference would represent about 10 years of increased atherosclerosis progression. Although we can only speculate, such an elevated CIMT may indicate an early state of diseased vessels in these adolescents, signifying a more rapid progression of atherosclerosis as compared to youth with no history of the MetS. Supportive evidence includes an adult longitudinal study that showed that every 0.030 mm increase in CIMT per year translates into a relative risk for any coronary event of 3.1 [11]. Although a direct comparison cannot be made to our current study, a 0.047 mm CIMT difference may signify a potential coronary risk in this high-risk youth group.

Our findings have other important clinical implications. The relatively short-term effects of MetS on CIMT during childhood and adolescence suggest that frequent measurement of MetS and more aggressive treatment for children with the MetS may be appropriate, particularly in overweight children. Waist circumference and blood pressure are easily accessible clinic measures that would allow for cost-effective and repeatable clinical evaluation. This could be an important predictive measure of atherosclerosis and premature CVD events, perhaps as early as young adulthood.

The strengths of this study stem from the methodological aspects, which included the longitudinal measures the MetS and a subclinical atherosclerosis measure completed by the same sonographer and reader for the ultrasound images. In addition, we used accurate measures of adiposity such as total and regional body composition (DEXA and MRI scans) and direct measures of insulin sensitivity (FSIVGTT with minimal modeling). The homogeneous sample of overweight, understudied minority youth also contributed to the strength of this study. Despite these strengths, there were several design limitations. The CIMT measure was only taken at a single time point and consequently, we could only speculate that persistent MetS caused increased thickening of the carotid artery in overweight Latino youth. Repeated measures of CIMT are currently being conducted within this cohort, but have yet to be reported. Another limitation of the study is the unequal gender distribution, resulting in more male participants within the PERSISTENT MetS group. Increased CIMT has been shown to be more prevalent in male adults [29] and male children [30], hence we cannot disregard male gender as a potential predictor as any gender differences may be masked. Finally, the results could only be generalized to overweight Latino adolescents with a family history of type 2 diabetes.

In summary, our main conclusion is that persistence of the MetS over a 3-year period was associated with increased CIMT during childhood. Persistent abdominal adiposity and/or hypertension may also have an effect on arterial structure even before adulthood. A comprehensive evaluation for presence of the MetS is warranted to intervene and prevent vascular disease in this especially high-risk group of overweight adolescents.

Disclosures

The authors have no disclosures.

Acknowledgements

We would like to thank the staff of the University of Southern California/Los Angeles County GCRC and the dedicated SOLAR coordinators, Quintilla Avila and Christina Ayala and the rest of the SOLAR staff over the past 6 years. Our gratitude is especially extended to the loyal participants and their families for their continued participation. This work is supported by NIDDK grants R01-DK59211 (M.I. Goran) and General Clinical Research Center for Health Resources grant (M01 RR 00043). Claudia Toledo-Corral is supported by a NIDDK fellowship (F31-DK081276) under the sponsorship of M.I. Goran.

References

[1] Dekker JM, Girman C, Rhodes T, et al. MetS and 10-year cardiovascular disease risk in the Hoorn Study. Circulation 2005;112:666–73.
[2] Hunt KJ, Resendez RG, Williams K, Haffner SM, Stern MP. National Cholesterol Education Program versus World Health Organization MetS in relation to all-cause and cardiovascular mortality in the San Antonio Heart Study. Circulation 2004;110:1251–7.
[3] Chen W, Srinivasan SR, Li S, Xu J, Berenson GS. MetS variables at low levels in childhood are beneficially associated with adulthood cardiovascular risk: the Bogalusa Heart Study. Diab Care 2005;28:126–31.
[4] Raitakari OT, Juonala M, Kahonen M, et al. Cardiovascular risk factors in childhood and carotid artery intima–media thickness in adulthood: the cardiovascular risk in Young Finns Study. JAMA 2003;290:2277–83.
[5] Flegal KM, Ogden CL, Carroll MD. Prevalence and trends in overweight in Mexican-American adults and children. Nutr Rev 2004;62:S144–148.
[6] Weiss R, Dziura J, Burgert TS, et al. Obesity and the MetS in children and adolescents. N Engl J Med 2004;350:2362–74.
[7] Poli A, Tremoli E, Colombo A, Sirtori M, Pignoli P, Paoletti R. Ultrasonographic measurement of the common carotid artery wall thickness in hypercholesterolemic patients. A new model for the quantitation and follow-up of preclinical atherosclerosis in living human subjects. Atherosclerosis 1988;70:253–61.
[8] Heiss G, Sharrett AR, Barnes R, Chambless LE, Szklo M, Alzola C. Carotid atherosclerosis measured by B-mode ultrasound in populations: associations with cardiovascular risk factors in the ARIC study. Am J Epidemiol 1991;134:250–6.
[9] Chambless LE, Folsom AR, Clegg LX, et al. Carotid wall thickness is predictive of incident clinical stroke: the Atherosclerosis Risk in Communities (ARIC) study. Am J Epidemiol 2000;151:478–87.
[10] O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson Jr SK. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. N Engl J Med 1999;340:14–22.
[11] Hodis HN, Mack WJ, LaBree L, et al. The role of carotid arterial intima–media thickness in predicting clinical coronary events. Ann Intern Med 1998;128:262–9.
[12] Reinehr T, Kiess W, de Sousa G, Stoffel-Wagner B, Wunsch R. Intima media thickness in childhood obesity: relations to inflammatory marker, glucose metabolism, and blood pressure. Metabolism 2006;55:113–8.
[13] Zhu W, Huang X, He J, Li M, Neubauer H. Arterial intima–media thickening and endothelial dysfunction in obese Chinese children. Eur J Pediatr 2005;164:337–44.
[14] Woo KS, Chook P, Yu CW, et al. Overweight in children is associated with arterial endothelial dysfunction and intima–media thickening. Int J Obes Relat Metab Disord 2004;28:852–7.
[15] Iannuzzi A, Licenziati MR, Acampora C, et al. Increased carotid intima–media thickness and stiffness in obese children. Diab Care 2004;27:2506–8.
[16] Toledo-Corral CM, Weigensberg MJ, Hodis HN, Goran MI. Influence of adiposity, insulin sensitivity, cardiovascular risk factors, and fasting glucose on Carotid Intima Media Thickness (C-IMT) in overweight Latino adolescents (abstract). Obesity 2007;15:A125.
[17] Cruz ML, Weigensberg MJ, Huang TT, Ball G, Shaibi GQ, Goran MI. The MetS in overweight Hispanic youth and the role of insulin sensitivity. J Clin Endocrine Metab 2004;89:108–13.
[18] Selzer RH, Hodis HN, Kwong-Fu H, et al. Evaluation of computerized edge tracking for quantifying intima–media thickness of the common carotid artery from B-mode ultrasound images. Atherosclerosis 1994;111:1–11.
[19] Selzer RH, Mack WJ, Lee PL, Kwong-Fu H, Hodis HN. Improved common carotid elasticity and intima–media thickness measurements from computer analysis of sequential ultrasound frames. Atherosclerosis 2001;154:185–93.
[20] Hodis HN, Mack WJ, Lobo RA, et al. Estrogen in the prevention of atherosclerosis: a randomized, double-blind, placebo-controlled trial. Ann Intern Med 2001;135:939–53.
[21] Xiang AH, Azen SP, Buchanan TA, et al. Heritability of subclinical atherosclerosis in Latino families ascertained through a hypertensive parent. Arterioscler Thromb Vasc Biol 2002;22:843–8.
[22] Hodis HN, Mack WJ, LaBree L, et al. Alpha-tocopherol supplementation in healthy individuals reduces low-density lipoprotein oxidation but not atherosclerosis: the Vitamin E Atherosclerosis Prevention Study (VEAPS). Circulation 2002;106:1453–9.
[23] Fernandez JR, Redden DT, Pietrobelli A, Allison DB. Waist circumference percentiles in nationally representative samples of African-American, European-American, and Mexican-American children and adolescents. J Pediatr 2004;145:439–44.
[24] Hickman TB, Briefel RR, Carroll MD, et al. Distributions and trends of serum lipid levels among United States children and adolescents ages 4–19 years: data from the Third National Health and Nutrition Examination Survey. Prev Med 1998;27:879–90.
[25] 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. National High Blood Pressure Education Program Working Group on Hypertension Control in Children and Adolescents. Pediatrics 1996;98:649–58.
[26] Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus 1997;20:1183.
[27] Viner RM, Segal TY, Lichtarowicz-Krynska E, Hindmarsh P. Prevalence of the insulin resistance syndrome in obesity. Arch Dis Child 2005;90:10–4.
[28] Reinehr T, Wunsch R, de Sousa G, Toschke AM. Relationship between MetS definitions for children and adolescents and intima–media thickness. Atherosclerosis 2008;199:193–200.
[29] Ebrahim S, Papacosta O, Whincup P, et al. Carotid plaque, intima media thickness, cardiovascular risk factors, and prevalent cardiovascular disease in men and women: the British Regional Heart Study. Stroke 1999;30:841–50.
[30] Osika W, Dangardt F, Montgomery SM, Volkmann R, Gan LM, Friberg P. Sex differences in peripheral artery intima, media and intima media thickness in children and adolescents. Atherosclerosis 2009;203:172–7.

Please cite this article in press as: Toledo-Corral CM, et al. Persistence of the metabolic syndrome and its influence on carotid artery intima media thickness in overweight Latino children. Atherosclerosis (2009), doi:10.1016/j.atherosclerosis.2009.03.013