Lifestyle Variables, Non-traditional Cardiovascular Risk Factors, and the Metabolic Syndrome in an Aboriginal Canadian Population

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Abstract

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Objective: To examine lifestyle factors associated with metabolic syndrome (MetS) and to explore the relationships between MetS and non-traditional cardiovascular disease risk factors [adiponectin, leptin, C-reactive protein (CRP), interleukin-6 (IL-6), and serum amyloid A (SAA)] in an isolated Aboriginal Canadian community.

Research Methods and Procedures: Data were obtained from 360 non-diabetic adults participating in a population-based study of Aboriginal Canadians. Fasting samples were drawn for glucose, insulin, lipids, adiponectin, leptin, CRP, IL-6, and SAA. Percentage body fat was measured using bioelectrical impedance analysis. Past year physical activity and fitness level were assessed. MetS was diagnosed according to the criteria of the National Cholesterol Education Program, the World Health Organization, and the International Diabetes Federation.

Results: The results showed that older age, higher percentage body fat, and lower fitness levels were associated with increased odds of MetS regardless of MetS definition and subject gender. Past year physical activity was independently related with the World Health Organization-MetS in male subjects. Subjects with MetS had significantly higher leptin, CRP, IL-6, and SAA levels and lower adiponectin levels; however, only adiponectin remained significantly low after adjustment for age and percentage body fat.

Discussion: The study showed that higher percentage body fat and lower physical activity and fitness were associated with a higher prevalence of MetS in this Aboriginal community and that hypoadiponectinemia was independently associated with MetS.

Key words: metabolic syndrome, lifestyle factors, inflammation, Aboriginal Canadians, adiponectin

Introduction

It is increasingly recognized that metabolic syndrome (MetS),[1] a constellation of risk factors including abnormal glucose tolerance, hypertension, dyslipidemia, and increased adiposity, is associated with an elevated risk of cardiovascular disease (CVD) (1–4) and type 2 diabetes (4–6). Although the pathophysiology of this syndrome re-

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[1] Nonstandard abbreviations: MetS, metabolic syndrome; CVD, cardiovascular disease; CRP, C-reactive protein; IL-6, interleukin-6; SAA, serum amyloid A; WHO, World Health Organization; NCEP, National Cholesterol Education Program; IDF, International Diabetes Federation; ADA, American Diabetes Association; EASD, European Association for the Study of Diabetes; WC, waist circumference; WHR, waist-to-hip ratio; Vo_{2max}, maximum oxygen uptake; MET, metabolic equivalent; INS, fasting insulin; TG, triglyceride; HDL-C, high-density lipoprotein-cholesterol; $HOMA_{IR}$, homeostasis model assessment index of insulin resistance; CI, confidence interval.

mains a subject of continuing controversy, insulin resistance and/or visceral adiposity have been considered major causes of developing this syndrome (7–11). Some lifestyle behaviors (high carbohydrate intake or high dietary glycemic index, inadequate physical activity, and cigarette smoking) may also contribute to the development of MetS (9,12–17). Moreover, a number of emerging risk factors for CVD, including adipokines such as adiponectin (18–20) and leptin (21,22), and inflammatory markers such as C-reactive protein (CRP), interleukin-6 (IL-6), and serum amyloid A (SAA) (23–26), have been found to be associated with obesity, diabetes, and MetS.

Although the appropriate way to define MetS is still being hotly debated, the World Health Organization (WHO) (27), the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (11), and, recently, the International Diabetes Federation (IDF) (28) have proposed criteria to define this syndrome for research purposes or early clinical identification, and the prevalence rates of MetS under these definitions have been assessed in various populations around the world (29). Over the past several decades, Aboriginal Canadian communities have experienced rapid lifestyle change, with dramatic reductions in physical activity and increases in the consumption of processed foods, resulting in an epidemic of obesity and diabetes in some Aboriginal communities (30,31). A limited number of recent papers have reported an extremely high prevalence of MetS in Aboriginal Canadian communities (32). However, very little is known about lifestyle risk factors for MetS in this population and whether emerging CVD risk factors such as adiponectin, leptin, and CRP are associated with the syndrome. Very recently, in a joint statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) (33), the value of including diabetes in the definition was questioned. Thus, the objectives of this study were to examine lifestyle factors associated with MetS and to explore the associations between MetS and emerging CVD non-traditional risk factors including adiponectin, leptin, CRP, IL-6, and SAA among non-diabetic individuals in an Aboriginal Canadian population.

Research Methods and Procedures

Study Population

Data were obtained from the Sandy Lake Health and Diabetes Project, a population-based cross-sectional survey that aimed to determine the prevalence of type 2 diabetes and its associated risk factors in an isolated Aboriginal community in northwestern Ontario, Canada. The methodology of the survey has been described in detail in previous publications (30,34–38). From July 1993 to December 1995, 728 of 1018 (72%) eligible residents of Sandy Lake, 10 to 79 years old, volunteered to participate in the survey. The analyses in the present paper are based on the 360 non-diabetic Oji-Cree adults who were ≥18 years of age at the time of the survey and had all of the relevant data available.

Anthropometry and Measurement of Blood Pressure

Anthropometric measurements included weight, height, waist circumference (WC), and hip circumference. Each measurement was performed twice, and the average was used in the analysis. BMI was calculated as weight (kilograms) divided by height squared (meters squared). Waist-to-hip ratio (WHR) was calculated as the ratio of the two circumferences. Percentage body fat was estimated by bioelectrical impedance analysis using the Tanita TBF-201 Body Fat Analyzer (Tanita Corp., Tokyo, Japan). Blood pressure was measured in the right arm with the participant seated. Two measurements were performed, and the average was used in the analysis. Information regarding smoking behaviors and physical activity was recorded on standardized interviewer-administered questionnaires.

Physical Activity and Fitness Level

We used the modifiable activity questionnaire to assess physical activity levels. This instrument has been shown to be valid and reliable in adults (39). The instrument was modified for use in the study community by including a list of items that were specific and comprehensive to the Sandy Lake community (30). The individual's physical activity level was determined by leisure and occupational activities over the past year and expressed as hours per week. Activities were also weighted by estimates of their relative intensity and expressed as metabolic equivalent (MET)-hours per week.

Maximum oxygen uptake ($V\mathrm{O}_{2\mathrm{max}}$), a standard measure of cardiorespiratory fitness level, was estimated using a validated submaximal step test developed by Siconolfi et al. (40). Exclusion criteria included a medical history of cardiovascular, respiratory, or severe muscular-skeletal disease or an unwillingness to perform the test; 77% of men and 66% of women in this study sample completed the step test protocol. In the analysis, $V\mathrm{O}_{2\mathrm{max}}$ was adjusted for lean body mass (estimated from bioelectrical impedance analysis).

Laboratory Tests

Participants provided fasting blood samples for glucose, insulin, lipids, and other variables after an 8- to 12-hour overnight fast. A 75-gram oral glucose tolerance test was administered, and a second sample for glucose was drawn after 120 minutes. Subjects were excluded from the oral glucose tolerance test if they had physician-diagnosed diabetes and were currently receiving treatment with insulin or oral hypoglycemic agents or if they had physician-diagnosed diabetes and a fasting blood glucose > 11.1 mM. Concentrations of fasting and 2-hour post-challenge glu-

cose, fasting insulin (INS), triglyceride (TG), high-density lipoprotein-cholesterol (HDL-C), adiponectin, leptin, CRP, IL-6, and SAA were measured using methods described in previous publications (36–38).

Definition of MetS

According to the NCEP criteria (11), subjects were considered to have MetS if they had any three or more of the following five disorders: abdominal obesity, WC > 102 cm in men or >88 cm in women; hypertriglyceridemia, ≥1.7 mM (≥150 mg/dL); low HDL-C, <1.0 mM (<40 mg/dL) in men or <1.3 mM (<50 mg/dL) in women; high blood pressure, ≥130/85 mm Hg or previously diagnosed hypertension with treatment (~3.5% of women and 7.4% of men had previously diagnosed hypertension); and high fasting glucose, ≥6.1 mM (≥110 mg/dL).

According to the WHO criteria (27), a participant had MetS if he or she had impaired glucose tolerance, impaired fasting glucose, or insulin resistance, plus two or more of the following abnormalities: high blood pressure, ≥140/90 mm Hg or previous diagnosed hypertension with treatment; dyslipidemia, TG concentration ≥ 1.7 mM (≥150 mg/dL) and/or HDL-C < 0.9 mM (<35 mg/dL) in men and <1.0 mM (<39 mg/dL) in women; and central obesity, WHR > 0.90 in men or >0.85 in women and/or BMI >30 kg/m^2. Diabetes, impaired glucose tolerance, and impaired fasting glucose were diagnosed according to the 1998 WHO criteria (26). Insulin resistance was defined as the highest quartile (>4.18 units) of the distribution of the homeostasis model assessment index of insulin resistance ($HOMA_{IR}$) among subjects with normal glucose tolerance, calculated from the following equation: $HOMA_{IR}$ = INS (microunits per milliliter) × fasting plasma glucose (millimolar)/22.5 (41). Microalbuminuria was excluded as a component of the WHO-defined MetS because information on albumin status was not available for Sandy Lake Health and Diabetes Project participants.

More recently, the IDF has published a new worldwide definition of MetS on its website (28). Because there is no specific cut-off point of WC for North American Native Americans in the new definition, the NCEP cut-off points were used. Therefore, subjects were considered to have MetS if they had central obesity defined as WC > 102 cm for men or >88 cm for women and any two of the following four factors: raised TG level, ≥1.7 mM (≥150 mg/dL); reduced HDL-C, <1.0 mM (<40 mg/dL) in men or <1.3 mM (<50 mg/dL) in women; raised blood pressure, ≥130/85 mm Hg or treatment of previously diagnosed hypertension; and high fasting glucose, ≥5.6 mM (≥100 mg/dL).

Statistical Analysis

All analyses were conducted using SAS version 8.2 (SAS, Cary, NC). Logistic regression analysis was performed to investigate the relationship between MetS and potential risk factors (age, percentage body fat, current smoking status, physical activity, or fitness). The mean differences in adipokines (adiponectin and leptin) and inflammatory markers (CRP, IL-6, and SAA) between groups were assessed using covariance analysis. The natural log transformations of skewed variables were used in the models, and least squares means were back transformed for data presentation. The effect modification of gender was also assessed by including interaction terms in regression models.

Results

Prevalence of MetS

The overall crude and age-standardized prevalence rates (using 1991 Canadian population) of MetS in the study sample were 21.4% [95% confidence interval (CI), 17.2% to 26%] and 27.5% (95% CI, 20.2% to 34.9%) based on the NCEP definition; 22.5% (95% CI, 18.3% to 27.2%) and 30.9% (95% CI, 22.8% to 38.9%) according to the WHO criteria; and 28.1% (95% CI, 23.4% to 33.0%) and 37.2% (95% CI, 28.4% to 45.9%) for the IDF criteria, respectively. The crude rates were higher for women than for men by the NCEP (26.3% vs. 15.4%, $p = 0.01$) and IDF (34.9% vs. 19.8%, $p = 0.001$) criteria but not by the WHO criteria (23.2% vs. 21.6%, $p = 0.71$). As expected, a strong agreement was found between IDF and NCEP definitions, with κ value of 0.75 (95% CI, 0.67 to 0.83), and there was moderate agreement between NCEP and WHO criteria (κ = 0.51; 95% CI, 0.41 to 0.62) and between IDF and WHO criteria (κ = 0.50; 95% CI, 0.40 to 0.60).

Associated Risk Factors of MetS

Because sex interactions were observed for the association of MetS with percentage body fat and age, gender-stratified analyses were performed for investigating the relationship between MetS and its risk factors. As shown in Table 1, subjects with MetS were substantially older and had significantly lower fitness levels and higher percentage body fat than those without MetS. A significantly lower physical activity level (in both frequency and intensity) was observed in male subjects with WHO-defined MetS.

In men, multiple logistic regression analysis (Table 2) showed that higher percentage body fat and smoking were associated with increased odds of the NCEP-defined MetS, and older age, percentage body fat, and lower total physical activity (either using hours per week or MET-hours per week) were associated with increased odds of WHO-defined MetS. In a model in which total physical activity was replaced by physical fitness, physical fitness and percentage body fat remained independently associated with MetS regardless of the definition used. In women, age, percentage body fat, and physical fitness,

Table 1. Characteristics of non-diabetic Oji-Cree men and women with or without MetS according to NCEP and WHO criteria

Variable	NCEP-MetS		WHO-MetS	
	Without	With	Without	With
Men				
*n**	137	25	127	35
Current smoking (%)	77.4	92.0	81.9	71.4
Age (years)‡	32.1 ± 13.3	36.2 ± 11.6	30.0 ± 10.8	42.5 ± 15.9¶
Body fat (%)‡	26.1 ± 7.6	33.3 ± 3.4¶	25.5 ± 7.4	33.6 ± 4.2¶
Total activity (h/wk)‡	30.7 ± 19.0	26.0 ± 16.2	32.1 ± 18.5	22.3 ± 17.5¶
Total activity (MET-h/wk)‡	159.3 ± 106.6	134.2 ± 83.1	166.3 ± 102.9	115.8 ± 97.2¶
Fitness (Vo_{2max}) (ml/min/kg)‡	61.5 ± 10.4	54.3 ± 7.68¶	62.2 ± 9.4	51.6 ± 11.0¶
Adiponectin (μg/mL)§	12.6 (9.4 to 16.8)	7.7 (5.4 to 11.1)¶	12.5 (9.1 to 16.9)	9.3 (5.9 to 14.6)¶
Leptin (ng/mL)§	4.7 (2.9 to 7.9)	8.8 (7.3 to 10.5)¶	4.5 (2.8 to 7.0)	9.1 (7.8 to 11.9)¶
CRP (mg/L)§	1.5 (0.6 to 3.2)	3.5 (2.1 to 5.0)¶	1.4 (0.6 to 3.2)	3.4 (1.7 to 5.6)¶
IL-6 (ng/L)§	0.6 (0.3 to 1.1)	0.9 (0.4 to 1.8)	0.5 (0.3 to 1.1)	0.9 (0.6 to 1.4)¶
SAA (mg/L)§	6.7 (4.7 to 9.9)	8.1 (6.0 to 13.1)	6.5 (4.4 to 9.9)	8.7 (6.1 to 12.7)
Women				
*n**	146	52	152	46
Current smoking (%)	74.7	55.8¶	76.8	63.0
Age (years)‡	30.0 ± 11.2	39.5 ± 14.6¶	31.0 ± 12.5	37.4 ± 12.9¶
Body fat (%)‡	42.8 ± 9.4	49.6 ± 5.4¶	43.3 ± 9.5	49.0 ± 5.7¶
Total activity (h/wk)‡	21.2 ± 16.8	19.7 ± 16.6	20.3 ± 16.5	22.4 ± 17.6
Total activity (MET-h/wk)‡	97.0 ± 79.7	87.8 ± 74.8	92.7 ± 77.7	100.9 ± 81.3
Fitness (Vo_{2max}) (ml/min/kg)‡	53.7 ± 5.7	50.5 ± 7.1¶	53.7 ± 6.0	50.5 ± 6.0¶
Adiponectin (μg/mL)§	13.7 (10.4 to 18.5)	11.7 (9.0 to 15.4)¶	14.1 (10.9 to 18.3)	11.7 (8.2 to 13.4)¶
Leptin (ng/mL)§	17.7 (11.4 to 26.5)	24.0 (17.7 to 32.7)¶	18.2 (11.7 to 26.6)	24.0 (16.9 to 32.5)¶
CRP (mg/L)§	2.5 (1.1 to 6.1)	5.5 (3.0 to 9.5)¶	2.5 (1.1 to 5.8)	6.1 (4.0 to 10.0)¶
IL-6 (ng/L)§	0.8 (0.4 to 1.4)	1.1 (0.7 to 2.1)¶	0.8 (0.4 to 1.4)	1.3 (0.7 to 2.1)¶
SAA (mg/L)§	7.7 (5.5 to 13.1)	11.6 (8.1 to 19.3)¶	7.7 (5.4 to 13.1)	11.6 (8.1 to 19.4)¶

MetS, metabolic syndrome; NCEP, National Cholesterol Education Program; WHO, World Health Organization; CRP, C-reactive protein; IL-6, interleukin-6; SAA, serum amyloid A.

* Various sample sizes for fitness.

‡ Means ± standard deviation.

§ Medians (interquartile range) and Student's *t* tests performed on log transformation.

¶ $p < 0.05$.

but not total physical activity, were independently associated with MetS. The findings were similar when the IDF definition was used (data not shown).

The unadjusted analysis showed that, except in male subjects under the NCEP definition, men and women who smoked had lower prevalence of MetS. However, this inverse association was due to the confounding effects of age and total body adiposity. In these study subjects, smokers were, on average, 7 years younger and more physically active, and had lower total body adiposity (percentage body fat and BMI) (data not shown).

Relation of Adipokines and Inflammatory Markers with MetS

Spearman's correlation coefficients between selected emerging CVD risk factors and variables of MetS were calculated. Adiponectin was significantly inversely correlated with BMI, WC, WHR, TG, fasting glucose, INS level,

Table 2. Multiple logistic regression for determinants of MetS among non-diabetic Oji-Cree adults from Sandy Lake (1993 to 1995), according to definition (NCEP and WHO)*

Variables	NCEP-MetS	WHO-MetS
Men		
n (total = 162)	25	35
Age (per 10-year increase)	1.25 (0.85 to 1.86)	2.27 (1.49 to 3.47)†
Body fat (per 5% increase)	3.78 (1.97 to 7.23)†	5.83 (2.74 to 12.41)†
Current smoking	10.8 (1.75 to 66.51)†	1.42 (0.42 to 4.75)
Past year activity (per 5 MET-h/wk increase)	0.98 (0.95 to 1.01)	0.96 (0.93 to 0.99)†
n (total = 128)	17	20
Age	0.81 (0.34 to 1.89)	0.94 (0.39 to 2.26)
Body fat	3.92 (1.70 to 9.03)†	6.25 (2.29 to 17.07)†
Current smoking	7.11 (0.78 to 64.69)	0.54 (0.13 to 2.30)
$V\text{O}_{2\text{max}}$ (per 10 mL/min per kilogram increase)	0.29 (0.10 to 0.87)†	0.16 (0.04 to 0.56)†
Women		
n (total = 198)	52	46
Age (per 10-year increase)	1.85 (1.39 to 2.48)†	1.47 (1.23 to 1.91)†
Body fat (per 5% increase)	1.95 (1.44 to 2.65)†	1.60 (1.23 to 2.09)†
Current smoking	0.68 (0.32 to 1.46)	1.04 (0.48 to 2.23)
Past year activity (per 5 MET-h/wk increase)	0.98 (0.96 to 1.01)	1.00 (0.98 to 1.03)
n (total = 139)	27	27
Age	1.46 (0.80 to 2.68)	1.94 (1.07 to 3.51)†
Body fat	2.65 (1.66 to 4.24)†	2.35 (1.51 to 3.65)†
Current smoking	1.06 (0.37 to 3.09)	1.15 (0.40 to 3.34)
$V\text{O}_{2\text{max}}$ (per 10 mL/min per kilogram increase)	0.30 (0.13 to 0.71)†	0.34 (0.15 to 0.79)†

Data are odds ratios (95% CI). MetS, metabolic syndrome; NCEP, National Cholesterol Education Program; WHO, World Health Organization.

* Logistic model with MetS as dependent variable, age, percentage body fat, current smoking status, and physical activity or fitness level as independent variables.

† $p < 0.05$

and HOMA_{IR}, as well as percentage body fat (correlation coefficient range −0.16 to −0.40, all $p < 0.05$), and positively correlated with HDL-C (female subjects, $r = 0.38$, $p < 0.0001$; male subjects, $r = 0.46$, $p < 0.0001$). Leptin was strongly correlated with all four measures of adiposity for both sexes (0.64 to 0.79; all $p < 0.0001$, except WHR in women, $r = 0.26$, $p = 0.0003$), INS, and HOMA_{IR} (0.60 to 0.67; all $p < 0.0001$). CRP was positively correlated with all adipose variables, blood pressure, TG, fasting glucose, INS, and HOMA_{IR} and negatively correlated with HDL-C for both sexes. IL-6 and SAA also showed positive correlations with adipose variables, fasting glucose, INS, and HOMA_{IR}, but associations were weaker than those observed for CRP. After adjustment for age and percentage body fat, correlation coefficients were attenuated, but associations of adiponectin with HDL, insulin, and HOMA_{IR}, as well as associations of leptin with insulin and other measures of adiposity, remained notable and significant (Table 3).

As shown in Table 1, both male and female subjects who had MetS had significantly lower concentrations of adiponectin and higher levels of leptin, CRP, and IL-6 than the subjects without MetS regardless of definitions. SAA concentrations were higher in female subjects with MetS. After adjustment for age and percentage body fat, adiponectin was significantly lower among subjects with MetS for both sexes regardless of the definitions, and leptin was moderately higher among male subjects who had WHO-defined MetS (Table 4). The differences in CRP and IL-6 concen-

Table 3. Spearman correlation coefficients between selected emerging CVD risk factors and variables of MetS after adjustment for age and percentage body fat

	WC	BMI	WHR	SBP	DBP	TG	HDL-C	FPG	INS	$HOMA_{IR}$
Men ($n = 162$)										
Adiponectin	−0.15	−0.10	−0.18*	0.08	0.07	−0.22*	0.37*	−0.09	−0.18*	−0.19*
Leptin	0.27*	0.15	0.15	0.19*	0.20*	0.04	−0.11	0.06	0.32*	0.32*
CRP	0.09	0.08	0.08	−0.07	0.05	0.03	−0.16*	0.05	0.14	0.14
IL-6	0.11	0.12	0.12	0.11	0.19*	0.00	−0.02	−0.01	0.05	0.04
SAA	−0.13	−0.09	0.04	0.01	−0.01	−0.10	0.08	0.07	0.07	0.08
Women ($n = 198$)										
Adiponectin	−0.11	−0.07	−0.24*	0.13	−0.04	−0.21*	0.30*	−0.10	−0.27*	−0.26*
Leptin	0.19*	0.25*	−0.02	0.07	−0.05	0.16*	0.05	0.04	0.26*	0.24*
CRP	0.10	0.08	0.10	0.04	−0.02	0.11	0.01	0.06	0.21*	0.20*
IL-6	0.04	0.04	0.08	0.11	0.00	0.12	−0.08	−0.03	0.13	0.12
SAA	0.01	−0.04	0.04	0.06	0.02	0.03	0.12	0.09	0.19*	0.19*

CVD, cardiovascular disease; MetS, metabolic syndrome; WC, waist circumference; WHR, waist-to-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglyceride; HDL, high-density lipoprotein cholesterol; FPG, fasting plasma glucose; INS, fasting insulin; $HOMA_{IR}$, homeostasis model assessment index of insulin resistance; CRP, C-reactive protein; IL-6, interleukin-6; SAA, serum amyloid A.
* $p < 0.05$.

trations between male subjects with and without MetS were not significant after adjustment for age and percentage body fat. CRP, IL-6, and SAA in female subjects with WHO-defined MetS remained high after covariate adjustment.

Discussion

In this population-based study of an Aboriginal Canadian population undergoing rapid epidemiological transition, we demonstrated that the prevalence rate of MetS was high among non-diabetic subjects in this community, with variation in prevalence depending on the definition used (21.4% for NCEP, 22.5% for WHO, and 28.1% for IDF), and that older age, higher percentage body fat, and lower fitness levels were associated with increased odds of MetS regardless of definition and gender. Past year physical activity was independently related to WHO-defined MetS in male subjects. Adiponectin, leptin, CRP, IL-6, and SAA were strongly correlated with most components of MetS, but the associations were attenuated after adjustment for age and percentage body fat. In both sexes, adiponectin was independently inversely associated with the syndrome no matter which definition was used. Female subjects with WHO-defined MetS had significantly higher levels of CRP, IL-6, and SAA after controlling for age and percentage body fat; however, no independent associations between the syndrome and these proinflammatory markers were found in male subjects.

The unique contributions of this study include the assessment of MetS prevalence and associated risk factors and CVD variables in a novel population that is undergoing rapid and dramatic changes in the burden of chronic diseases (including obesity, diabetes, and heart disease), as well as the use of three commonly used or recently proposed MetS definitions. Recently, the ADA and EASD called for a critical appraisal of MetS, including the current use of multiple definitions and varying components. Our finding that risk factors associated with MetS were generally similar across the definitions (and especially for NCEP and IDF) is informative in this context.

Physical activity has an impact on individual components of MetS. Physical exercise has been shown to decrease weight and visceral fat accumulation, decrease TG and increase HDL-C concentrations, decrease blood pressure, and prevent the development of type 2 diabetes (17,42–44). Traditionally, most activities of daily living for Aboriginal people involved vigorous physical exertion. However, over the past several decades, Aboriginal people have adopted a sedentary lifestyle with dramatic reductions in physical activity. Our results in this Aboriginal community extend findings from previous studies (15,17,43) indicating that MetS is inversely associated with physical activity and fitness. A prospective study from Finland (15) has shown that low levels of leisure-time physical activity and cardiorespiratory fitness predict development of MetS using both

Table 4. Non-traditional cardiovascular risk factors among individuals with and without MetS according to NCEP and WHO definitions by gender with adjustment for age and percentage body fat

	NCEP-MetS		WHO-MetS	
Variable	**Without**	**With**	**Without**	**With**
Men				
Adiponectin	12.1 (11.1 to 13.2)	9.0 (7.3 to 11.1)*	12.1 (11.1 to 13.3)	9.8 (7.9 to 11.7)*
Leptin	5.2 (4.9 to 5.7)	5.8 (4.8 to 7.0)	5.1 (4.7 to 5.5)	6.2 (5.2 to 7.4)†
CRP	1.8 (1.5 to 2.2)	2.7 (1.8 to 4.0)	1.9 (1.5 to 2.2)	2.3 (1.6 to 3.4)
IL-6	0.6 (0.5 to 0.7)	0.8 (0.5 to 1.2)	0.6 (0.5 to 0.7)	0.8 (0.6 to 1.2)
SAA	7.5 (6.6 to 8.7)	8.7 (6.2 to 12.3)	7.7 (6.6 to 8.9)	7.8 (5.7 to 10.7)
Women				
Adiponectin	13.6 (12.7 to 14.5)	11.9 (10.6 to 13.4)†	14.0 (13.1 to 14.9)	10.7 (9.5 to 12.0)*
Leptin	19.1 (17.9 to 20.4)	18.9 (16.9 to 21.2)	19.0 (17.9 to 20.2)	19.1 (17.0 to 21.4)
CRP	3.1 (2.6 to 3.6)	3.7 (2.8 to 4.8)	2.9 (2.5 to 3.3)	4.8 (3.7 to 6.2)*
IL-6	0.8 (0.7 to 0.9)	1.0 (0.8 to 1.3)	0.8 (0.7 to 0.9)	1.0 (0.8 to 1.3)†
SAA	9.2 (8.0 to 10.6)	10.5 (8.2 to 13.5)	9.0 (7.8 to 10.3)	11.7 (9.1 to 15.1)†

Data are least squares mean (95% confidence interval), natural log transformation used in the models, and back transformed for presentation. MetS, metabolic syndrome; NCEP, National Cholesterol Education Program; WHO, World Health Organization; CRP, C-reactive protein; IL-6, interleukin-6; SAA, serum amyloid A.

* $p < 0.05$.

† $0.05 < p \leq 0.07$.

WHO and NCEP definitions. Moreover, a recent study (43) demonstrated that nearly one-third of participants with the NCEP-defined MetS at baseline were no longer classified as having MetS after 20 weeks of a supervised aerobic exercise program.

Inflammation predisposes to atherothrombosis and is associated with features of MetS (23–25,45). However, many previous studies did not strictly define MetS using either the NCEP or WHO criteria. A recent report showed that subjects with the NCEP-defined MetS were more likely than individuals without the syndrome to have elevated levels of CRP (26). A prospective study also showed that CRP predicted the development of MetS (defined by both WHO and NCEP) and diabetes in men (46). The results from the current study, in which individuals with diabetes were excluded, illustrated that the association of inflammatory markers (CRP, IL-6, and SAA) with features of MetS and with NCEP-defined MetS itself no long remained after adjustment for age and percentage body fat. These findings suggest that the association is highly dependant on obesity, which might be expected because adipose tissue is a major source of proinflammatory cytokines (45). Several interventional studies have also demonstrated that weight loss can decrease proinflammatory marker (such as CRP and IL-6) levels (47,48). Including diabetes in the definition of MetS has been questioned by the joint statement of ADA and EASD (33) because the relation of diabetes with obesity, insulin resistance, and inflammation is well documented, and diabetes appears to account for most of the CVD predictive value. When we re-ran our analyses including diabetic subjects, the positive association between CRP and MetS remained significant after controlling for age and percentage body fat (data not shown).

Adiponectin, a collagen-like plasma protein, is produced and secreted exclusively by adipocytes. Although the physiological role of adiponectin has not yet been fully established, adiponectin appears to enhance insulin sensitivity (49) and to inhibit many steps in the inflammatory process (50). Several studies have shown that adiponectin was lower in obese subjects and in patients with type 2 diabetes (18,20,38) or dyslipidemia (19). Reversal of hypoadiponectinemia has been observed by lifestyle intervention in obese adolescents (51) and by gastric surgery in morbidly obese women (52). Our results showed that adiponectin was inversely related to percentage body fat, BMI, fasting glucose, INS, and TG and positively related to HDL-C. Subjects with MetS, regardless of the definition used, had significantly lower adiponectin levels than those without the syndrome, even after adjustment for age and percentage body fat. Thus, our results confirm that hypoadiponectinemia is associated with MetS.

In conclusion, our study showed that MetS was prevalent in this Aboriginal community, and MetS is positively associated with age and percentage body fat and inversely with

physical activity and fitness. Adiponectin is inversely associated with MetS, independently of obesity. Although the cross-sectional nature of the present study does not allow causality to be inferred, these findings suggest that lifestyle intervention (such as increasing physical activity and weight loss) may contribute to the reduction of the prevalence of MetS in Aboriginal Canadians.

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