

Prevalence of the metabolic syndrome among the Inuit in Greenland. A comparison between two proposed definitions

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Abstract

Aims To estimate the prevalence of the metabolic syndrome among Greenland Inuit according to the World Health Organization (WHO) definition and the definition suggested by the National Cholesterol Education Program (NCEP).

Methods From 1999 to 2001, 917 adult Inuit participated in a health survey in Greenland. The examination included a 75-g oral glucose tolerance test (OGTT). Body mass index (BMI), waist circumference, waist-to-hip ratio and blood pressure were measured. Plasma glucose, serum insulin, lipids and urine albumin/creatinine ratio were measured. The metabolic syndrome was diagnosed according to the WHO criteria 1999 and to the working definition suggested by the NCEP 2001.

Results Using the WHO and the NCEP criteria, 20.7% and 17.9% of the participants had the metabolic syndrome, respectively. There was a moderate agreement between the two definitions, $\kappa = 0.56$ (95% CI 0.51–0.61). Of those with the WHO metabolic syndrome, 37.9% did not have the NCEP syndrome, and 28.5% of those with the NCEP syndrome were not classified with the metabolic syndrome under the WHO criteria. Compared with the WHO syndrome, men with the NCEP syndrome had higher mean values of waist circumference, BMI and triglycerides, and lower mean values of high-density lipoprotein (HDL) cholesterol; among women, triglycerides were higher with the NCEP syndrome.

Conclusion The metabolic syndrome is common among Inuit using either the WHO definition or the proposed NCEP definition. The classification disagreement is considerable and a universally accepted definition is needed.

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Keywords definition, Greenland, Inuit, insulin resistance, metabolic syndrome

Abbreviations BMI, body mass index; CVD, cardiovascular disease; EGIR, European Group of the study of Insulin Resistance; HDL cholesterol, high-density lipoprotein cholesterol; IGT, impaired glucose tolerance; IHD, ischemic heart disease; HOMA, homeostasis model assessment; NCEP, National Cholesterol Education Program; OGTT, oral glucose tolerance test; WHO, World Health Organization; WHR, waist-hip ratio

Introduction

The Inuit populations in Greenland, Canada and Alaska show increasing prevalence of diabetes and impaired glucose tolerance; and obesity and physical inactivity are the reason for the increase in diabetes prevalence [1,2].

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Previously, the Inuit populations were considered relatively free of ischaemic heart disease (IHD). The traditional arctic diet with its high content of monounsaturated and polyunsaturated fatty acids of marine origin is suggested to protect against IHD. However, this hypothesis is not based on systematic studies and a new review shows that the combined cardiovascular disease (CVD) mortality is similar or probably higher among Inuit compared with whites [3].

The high diabetes prevalence among Inuit may indicate increasing insulin resistance. To what extent glucose intolerance is associated with cardiovascular risk among Inuit is not known. Insulin resistance is the possible link between glucose intolerance, central fat distribution, hypertension and dyslipidaemia. This cluster of metabolic disturbances is called the metabolic syndrome and is assumed to increase the risk of future diabetes and cardiovascular disease [4]. Because of the worldwide epidemic of obesity and sedentary lifestyle, knowledge about the prevalence of this syndrome and its impact on future CVD in various populations is important. However, no internationally agreed definition of the syndrome exists and estimates of the metabolic syndrome vary substantially across populations because many different criteria have been used [5]. The World Health Organization (WHO) proposed a definition of the metabolic syndrome in 1998 [6] and the National Cholesterol Education Program Expert Panel published a working definition (NCEP) in 2001 [7].

Thus, our study aimed to estimate the prevalence of the metabolic syndrome among the Inuit in Greenland according to the WHO definition and the definition suggested by the NCEP.

Methods

Participants

Data were collected from March 1999 to April 2001, in random samples of adult Greenlanders. The total population of Greenland is 56 000 of which 90% are ethnic Greenlanders (Inuit). Genetically, Greenlanders are Inuit (Eskimos) with a substantial admixture of European, mainly Danish, genes. They are closely related to the Inuit and Yupik in Canada, Alaska and Siberia.

Until the 1950s most Greenlanders made their living by small-scale hunting and fishing. Over the past decades substantial changes have occurred in Greenland with a rapid westernization, especially in the towns. However, today, hunting and fishing are still important leisure-time activities and traditional Greenlandic food makes up a significant proportion of the diet.

The study sample comprised Greenlanders aged 35 and above living in three areas of West Greenland, i.e. Nuuk (pop. 14 000), Qasigiannuit (pop. 1400) and four villages in the district of Uummanaq (pop. 240–275 in each village). In Nuuk, a random sample of the population was invited to participate, while in Qasigiannuit and Uummanaq everyone was invited. Only Inuit, defined as persons with at least one Inuit parent, were included in the study. The details of this study are described previously [8].

For all participants, informed consent was obtained in writing and orally. The Ethics Review Committee for Greenland approved the study.

Physical measurements

The participants underwent anthropometric measurements, blood samples and a 75-g standardized oral glucose tolerance test (OGTT). Weight and height were measured with the participants wearing undergarments and body mass index (BMI) was calculated. On the standing participant, waist circumference was measured midway between the iliac crest and the costal margin, and hip circumference at its maximum.

Three sitting blood pressures were measured using a standard mercury sphygmomanometer with an appropriate cuff size after at least 5 min rest. The mean of the two last blood pressures was calculated.

Participants with known diabetes did not have an OGTT, but fasting venous plasma glucose was measured. Plasma samples were immediately put on ice and spun at 4°C within 30 min of sampling. Plasma glucose was determined by the hexokinase/G6P-DH method (Boehringer Mannheim, Mannheim, Germany). Glucose tolerance was classified according to the WHO criteria 1999 [6]. The determination of serum insulin was made by enzyme-linked immunoassay, and the laboratory of the Steno Diabetes Centre, Denmark, performed the analyses of plasma glucose and serum insulin. Serum-cholesterol was determined using enzymatic calorimetric techniques (Code No K6219, Dako Diagnosis, Boehringer Mannheim, Germany). Analyses were performed at the Department of Clinical Chemistry, Bispebjerg Hospital, University of Copenhagen, Denmark.

Urine-albumin was determined turbidimetrically using reagents from Dako (Glostrup, Denmark) and urine-creatinine was determined by creatinine Jaffé method (kinetic colorimetric assay) (Boehringer Mannheim).

The metabolic syndrome

The WHO criteria defined the metabolic syndrome as insulin resistance and/or impaired glucose regulation in combination with two or more of the following components: serum triglycerides ≥ 1.7 mmol/l or serum HDL-cholesterol < 0.9 mmol/l in men and < 1.0 mmol/l in women, blood pressure $\geq 140/90$ mmHg, BMI > 30 kg/m² or waist-hip ratio > 0.90 for men and > 0.85 for women, or urinary albumin/creatinine ratio ≥ 30 mg/g. Impaired glucose regulation is defined by WHO as impaired glucose tolerance, impaired fasting glycaemia or diabetes. Insulin resistance required a euglycaemic, hyperinsulinaemic clamp. We adopted the modification suggested by the EGIR [9] and used fasting serum insulin above the upper quartile for the non-diabetic background population as a surrogate measure of insulin resistance.

The NCEP ATPIII panel defined the metabolic syndrome as the presence of three or more of the following: fasting plasma glucose ≥ 6.1 mmol/l, serum triglycerides ≥ 1.69 mmol/l, serum HDL-cholesterol ≤ 1.04 mmol/l in men and ≤ 1.29 mmol/l in women, blood pressure $\geq 130/85$ mmHg, or waist circumference ≥ 102 cm in men and ≥ 88 cm in women.

Statistics and data analysis

Analyses were performed using SAS version 8.2 (SAS Institute, Cary, NC, USA). Analyses were run separately for men and women. Means (SD) and proportions of baseline characteristics were compared by definition of the metabolic syndrome using *t*-tests and χ^2 tests, respectively. To test the agreement between the two definitions, we used the kappa test and interpreted the values according to Landis and Koch [10].

Results

A total of 1345 Inuit aged 35 years and above was invited to participate in the study. Of those, 917 attended the study (68.2%). The participation rate was 66, 72 and 64% in Nuuk, Qasigiannuit and Uummanaq, respectively (*P* = 0.025). The median age of the sample was 49 years (range 35–86) and 44% were males.

We classified 20.7% (95% CI: 18.1–23.3%) and 17.9% (95% CI: 15.4–20.4%) of the participants as having the metabolic syndrome using the WHO definition and the NCEP definition, respectively. There was a moderate agreement between the two definitions, κ = 0.56 (95% CI 0.51–0.61). Of those with the metabolic syndrome under the WHO definition, 37.9% did not have the metabolic syndrome under the NCEP definition, and 28.5% of those with the metabolic syndrome under the NCEP were not classified with the metabolic syndrome under the WHO criteria (Fig. 1).

The frequency of both syndromes increased with age (Fig. 2). Among men, the WHO syndrome was more frequent than the NCEP syndrome in all age groups; among women this was only the case in the oldest age group.

Table 1 shows the phenotypic characteristics of the two definitions. Men with the WHO syndrome had lower mean values of waist circumference, BMI and triglycerides, and higher mean values of HDL cholesterol, whereas there was no difference in age, plasma glucose, serum insulin, and blood pressure. Among women, there was no difference in levels of risk factors, except from HDL cholesterol which was higher among women with the WHO syndrome.

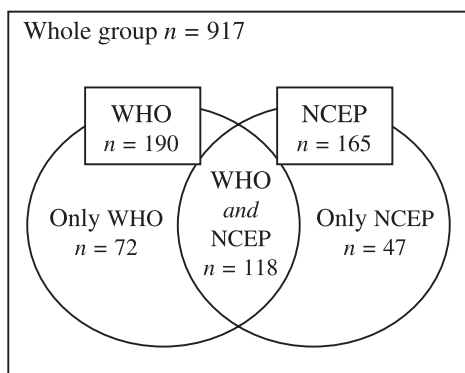


Figure 1 Overlap of the metabolic syndrome as defined by the NCEP or by the WHO.

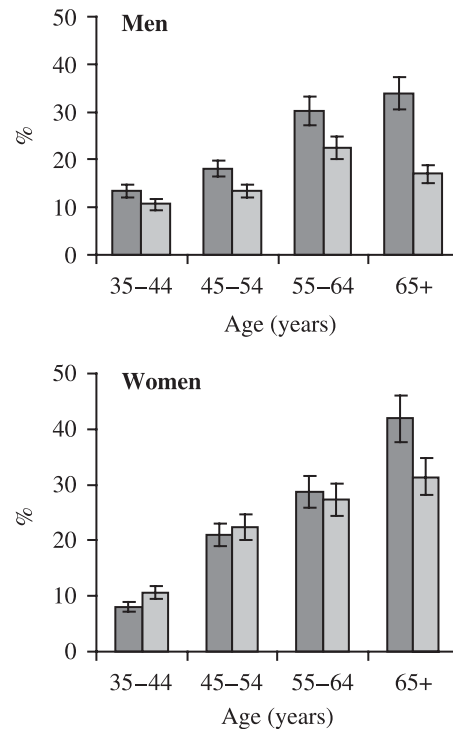


Figure 2 Age-specific prevalence with 95% CIs of the metabolic syndrome according to definition in males and females (■, WHO; □, NCEP).

For the whole population, the prevalence estimates of the individual criteria of the metabolic syndrome according to the two definitions are listed in Table 2.

Glucose abnormality was more frequent for women with the WHO syndrome than the NCEP syndrome as 72% of women with IGT and 43% of women with diabetes were not classified as glucose intolerant according to the NCEP definition (data not shown).

The frequency of obesity was much higher with the WHO syndrome than the NCEP syndrome, and this high prevalence was largely driven by the fact that 72% of men had a waist-to-hip ratio > 0.90 and 69% of women had a waist-to-hip ratio > 0.85.

The prevalence of hypertension and combined dyslipidaemia was higher with the NCEP definition because lower thresholds were used.

Discussion

The metabolic syndrome is common among Greenland Inuit, using either the proposed WHO definition or the NCEP definition. Among men, the WHO syndrome was more frequent than the NCEP syndrome; among women, the prevalence of the two syndromes was the same.

There are only few published data on the prevalence of the WHO metabolic syndrome in different populations. The NHANES study compared the two definitions and, although the two definitions yielded similar prevalence estimates for the

Table 1 Anthropometric and metabolic characteristics of individuals with the metabolic syndrome according to the two definitions

	Men		Women	
	WHO	NCEP	WHO	NCEP
Age (years)	56 (11)	54 (11)	57 (12)	54 (11)
Fasting Plasma glucose, mmol/l	6.5 (0.97)	6.7 (1.05)	6.9 (2.4)	6.9 (2.3)
2-h Plasma glucose, mmol/l	7.4 (2.96)	7.8 (3.31)	9.2 (4.8)	8.9 (4.9)
Fasting serum insulin pmol/l†	60 (14–1157)	73 (20–1157)	73 (18–374)	69 (17–374)
Waist circumference, cm	103 (12)	109 (11)*	101 (13)	103 (12)
BMI, kg/m ²	30 (6)	33 (5)*	32 (7)	32 (5)
Waist-hip ratio, %	100 (7)	102 (6)	96 (9)	96 (8)
Triglycerides, mmol/l†	1.37 (0.45–11.6)	1.67 (0.71–11.6)*	1.48 (0.49–8.0)	1.63 (0.27–8.0)
HDL cholesterol, mmol/l	1.42 (0.51)	1.21 (0.43)*	1.42 (0.47)	1.31 (0.38)*
Systolic blood pressure, mmHg	138 (20)	138 (20)	138 (22)	135 (23)
Diastolic blood pressure, mmHg	82 (13)	84 (12)	78 (12)	79 (12)

* $P < 0.05$ for a significant difference between the mean values for the two definitions.

†Geometric means with range in parentheses.

Means with SD.

BMI, body mass index; HDL cholesterol, high-density lipoprotein cholesterol.

Table 2 Frequency of the metabolic syndrome abnormalities according to the two definitions

	Men		Women	
	WHO	NCEP	WHO	NCEP
Metabolic syndrome	20%	13%	22%	22%
Glucose abnormality	39%	36%	35%	27%
Insulin resistance	26%	—	32%	—
Obesity	72%	19%	71%	51%
Hypertension	21%	36%	23%	35%
Microalbuminuria	9%	—	11%	—
Dyslipidaemia	15%	—	14%	—
Hypertriglyceridaemia	—	12%	—	13%
Low HDL cholesterol	—	12%	—	20%

HDL cholesterol, high-density lipoprotein cholesterol.

whole study sample, the classification disagreement was considerable in some of the ethnic groups [11]. Similar to our findings, the WHO estimates were higher than the NCEP estimates in African-American and in Mexican-American participants.

The WHO and NCEP definitions are similar in their focus on obesity, dyslipidaemia, hyperglycaemia and hypertension as constituent traits. Still substantial differences exist. The WHO criteria for overall and central obesity account for much of the higher prevalence of the WHO-defined syndrome. It is evident that abdominal fat distribution is a more important risk factor than overall obesity [12,13], and validation studies using magnetic resonance imaging and computed tomography have shown that waist circumference is the best anthropometric correlate of the amount of visceral adipose tissue [14]. However, the NCEP critical waist circumference values of 102 cm for men and 88 cm for women is developed in white men and women [12], and its impact on metabolic factors should not be uncritically extrapolated to other ethnic groups.

Among Inuit, given levels of BMI, WHR and waist circumference are associated with lower levels of blood pressure, triglycerides, post-challenge plasma glucose and serum insulin, and with higher levels of HDL cholesterol than in a northern European population [15]. It is therefore most likely that both definitions tend to overestimate the cardiovascular risk among Inuit.

The reliance on fasting plasma glucose alone in the NCEP definition to assess glycaemic status may overlook a large proportion of subjects with IGT and diabetes, solely diagnosed by 2-h plasma glucose values. A number of studies have demonstrated that 2-h glycaemia is associated with higher risk for both fatal and non-fatal CVD compared with fasting glycaemia [16,17]. An Australian study of five different ethnic groups found that 2-h plasma glucose was inversely associated with clamp-detected insulin sensitivity in all ethnic groups, whereas fasting serum insulin was not associated with either insulin sensitivity or homeostasis model assessment (HOMA) of insulin resistance [18].

Blood pressure threshold is higher in the WHO criteria compared with the NCEP, leaving a lower prevalence, but of more severe hypertension. However, mean blood pressure was not different in the two groups, indicating that individuals with relatively low blood pressure included in the NCEP definition do not meet the other inclusion criteria.

The NCEP criteria assign two 'points' for dyslipidaemia (HDL cholesterol and triglycerides). It is unlikely that each trait confers equivalent disease risk and weighting each trait equally may overweight the contribution of dyslipidaemia to the syndrome.

The inclusion of microalbuminuria has also been discussed widely. Microalbuminuria is associated with endothelial dysfunction and increases the risk for CVD, both in diabetic and non-diabetic individuals [19]. However, the association between insulin abnormalities and microalbuminuria is tenuous [9].

An important point when estimating the prevalence of the metabolic syndrome using the WHO definition, is how to define insulin resistance. The proposed definition requires a hyperinsulinaemic euglycaemic clamp which is considered the gold standard. However, this method is not feasible for clinical or epidemiological purposes. A number of surrogate measures have been used (fasting serum insulin concentration, HOMA modelling, etc.) in several ways. Clamp data on 1308 non-diabetic individuals from the European Group of the study of Insulin Resistance (EGIR) demonstrated that individuals with insulin resistance are characterized by central fat distribution and elevated lipolysis and endogenous glucose production, whereas individuals with hyperinsulinaemia have higher blood pressure and suppressed insulin clearance, endogenous glucose production and lipolysis [20]. Although the EGIR data were not population based, the observed pathophysiologic mechanisms may at least partly explain why prospective studies of the association between surrogate markers for insulin resistance and CVD have shown inconsistent results [21,22]. Among women and in the non-Caucasian population particularly, insulin resistance is not consistently associated with incident CVD [22,23]. Because the diagnosis of insulin resistance or hyperinsulinaemia is not a part of usual clinical practice, the NCEP syndrome does not include insulin resistance in the definition, which makes the NCEP definition easily implemented clinically. However, the constituent traits are rather common, and it may occur in many individuals without insulin resistance as the underlying unifying pathophysiology.

Few prospective surveys have studied the association between the proposed definitions of the metabolic syndrome and subsequent CVD, and the results are inconsistent. The Finnish Botnia study found an association between the metabolic syndrome as defined by the WHO and cardiovascular and overall mortality was higher in 35–70-year-old persons with a family history of Type 2 diabetes [24]. In the Finnish Kuopio Ischemic Heart Disease Risk Factor Study of 42–60-year-old men, both the WHO and the NCEP definitions were associated with increased IHD mortality, whereas only the WHO definition was associated with increased mortality from CVD and all-cause mortality [25]. Among North American Indians in the Strong Heart Study, the NCEP syndrome was not a predictor of fatal or non-fatal CVD in non-diabetic individuals after a follow-up period of 7.6 years [23]. However, comparisons between these studies are difficult because of important differences in methods, population characteristics, age ranges and diagnostic criteria.

In conclusion, the metabolic syndrome is common among the Inuit of Greenland using both proposed definitions; additionally, our data have demonstrated that the classification disagreement is considerable in this population. The way that both definitions weigh each component in the syndrome equally and independently may cause a substantial lack of sensitivity and specificity in detecting future disease; however, only prospective studies in different populations can determine the most appropriate definition of the syndrome for treatment

and intervention purposes and decide whether population specific thresholds for some of the abnormalities should be included.

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