CLINICAL STUDY

The Frequency of Metabolic Syndrome in Women with Polycystic Ovaries at Reproductive Age and Comparison of Different Diagnostic Criteria for Metabolic Syndrome

Eray **ÇALIŞKAN**[1], Teoman **KILIÇ**[2], Harika **BODUR**[1], Şahin **ZETEROĞLU**[3]

[1]*Department of Obstetrics and Gynecology, Faculty of Medicine, Kocaeli University, Kocaeli, Turkey*
[2]*Department of Cardiology, Faculty of Medicine, Kocaeli University, Kocaeli, Turkey*
[3]*Department of Obstetrics and Gynecology, Faculty of Medicine, Mustafa Kemal University, Hatay, Turkey*

Received 12 December 2007; received in revised form 06 May 2007; accepted 06 May 2007; published online 15 May 2007

Abstract

Objective: To investigate the frequency of the metabolic syndrome (MetS) by using different criteria in women with polycystic ovary syndrome (PCOS).

Materials and Methods: The study group consisted of 182 patients diagnosed with PCOS according to the Rotterdam criteria and 182 age matched controls. MetS frequency was separately investigated in the two groups according to the National Cholesterol Education Program Expert Panel (NCEP), World Health Organization (WHO), American Heart Association/National Heart Lung Blood Institute (AHA/NCLBI), International Diabetes Federation (IDF) and the Rotterdam MetS criteria.

Results: Except for the AHA/NCLBI criterion, all criteria showed significantly higher MetS prevalence in patients with PCOS as compared to the control group. This difference was more prominent especially at younger age. The highest frequency of MetS (26%) was observed according to the International Diabetes Federation (IDF) definition. The lower cut-off values of waist circumference and fasting glucose level in the IDF criteria has made it the most discriminative MetS definition for identifying risky individuals for MetS in patients with PCOS.

Discussion: Development of MetS may begin at younger ages in PCOS patients by using IDF, NCEP and Rotterdam criteria. As the most important approach for treatment and management of MetS against future cardiovascular events is the preventive strategy, categorizing more women with MetS according to the most discriminative criteria can also be a useful method for identifying the individuals under greater risk to prevent the developmental effects of MetS in patients with PCOS.

Keywords: metabolic syndrome, polycystic ovary syndrome

Özet

Üreme Çağındaki Polikistik Over Sendromlu Hastalarda Metabolik Sendrom Sıklığı ve Farklı Metabolik Sendrom Tanı Ölçütlerinin Karşılaştırılması

Amaç: Farklı tanı ölçütleri kullanarak polikistik over sendromlu (PKOS) hastalarda metabolik sendrom sıklığını (MetS) araştırmak.

Materyal ve Metot: Rotterdam ölçütlerine göre PKOS tanısı konulmuş 182 kadın çalışma grubunu oluştururken, yaşa göre eşleştirilmiş 182 kadın da kontrol grubunu oluşturdu. Her iki grupta da MetS sıklığı Ulusal Kolesterol Eğitim programı (NCEP: National Cholesterol Education Program Expert Panel), Dünya Sağlık Örgütü (WHO: World Health Organization), Amerikan Kalp Derneği/Ulusal Kalp Akciğer Kan Enstitüsü (AHA/NCLBI: American Heart Association/National Heart Lung Blood Institute), Uluslararası Diyabet Federasyonu (IDF: International Diabetes Federation) ve Rotterdam MetS kriterleri kullanılarak araştırıldı.

Sonuçlar: PKOS grubunda AHA/NCLBI dışındaki diğer tüm ölçütlerle MetS tanısı konulmuş hasta sıklığı kontrol grubundan fazlaydı. Bu fark, özellikle daha genç yaşlarda daha belirgindi. En yüksek MetS sıklığı tanısı %26 ile IDF ölçütlerine göre

Corresponding Author: Dr. Eray Çalışkan
Kocaeli Üniversitesi Tıp Fakültesi, Kadın Hastalıkları ve Doğum AD,
Umuttepe Kampüsü, 41000 Kocaeli, Türkiye
Phone : +90 262 233 12 42
: +90 262 303 70 39
GSM : +90 532 434 61 86
E-mail : caliskan@artemisonline.net

konuldu. Bel çevresi ve açlık kan glukozunda kullanılan düşük kesme değerleri IDF ölçütlerini MetS tanısında en ayırt edici ölçütler yapmaktadır. Bu ölçütler PKOS hastalarında riskli kadınların ayırt edilmesinde ve MetS'e bağlı ileride oluşacak etkilerin önlenmesinde kullanılabilir.
Tartışma: IDF, NCEP ve Rotterdam ölçütleri göstermektedir ki, PKOS'lu kadınlarda MetS oluşumu daha genç yaşlarda başlayabilir. MetS'in gelecekteki kardiyovasküler etkilerinin tedavisi ve yönetimindeki en önemli strateji önleme olduğu için en ayırt edici ölçütler kullanılarak daha fazla kadını MetS olarak tanımlamak riskli kadınların MetS'in gelecekteki etkilerinden korunmalarını sağlayabilir.
Anahtar sözcükler: metabolik sendrom, polikistik over sendromu

Introduction

Polycystic ovary syndrome (PCOS) is a special clinical diagnosis, which is characterized by chronic oligo-anovulation, clinical or biochemical signs of hyperandrogenism and polycystic ovaries diagnosed by ultrasound (1). After the attention in PCOS has turned to insulin resistance, PCOS and the Metabolic Syndrome (MetS) were evaluated together as "intertwined insulin resistance syndromes" (2). The National Cholesterol Education Program Expert Panel (NCEP), World Health Organization (WHO), American Heart Association /National Heart Lung Blood Institute (AHA/NHLBI), International Diabetes Federation (IDF) and especially Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop established different criteria's for the clinical diagnosis of the MetS (3-6). Despite these excessive amounts of criteria, the frequency of MetS by using different definitions especially in special age groups of PCOS patients has not been evaluated. The aim of this study is to investigate the frequency of the metabolic syndrome by using five separate diagnostic criteria in patients with polycystic ovary syndrome (PCOS).

Materials and Methods

Study population

The study was designed as a case control study and carried out during a period of 2 years between the years 2004-2006 in Kocaeli University, Mustafa Kemal University and Van 100. Yıl University Clinics of Obstetrics and Gynecology. One hundred eighty two women with PCOS and 182 age-matched controls were enrolled in the study. Ethics committee approval was obtained and patients signed an informed consent before participating in the study.

Definition of PCOS and MetS

PCOS was diagnosed according the presence of minimally two criteria of the Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop. All the cases with PCOS were newly diagnosed subjects who had not used any medication known to affect sex steroid metabolism such as oral contraceptives, anti-androgenic drugs, or agents effective on carbohydrate and lipid metabolism for the last 3 months. Females with regular menses with either normal transvaginal ultrasound findings or no evidence of clinical or biochemical hyperandrogenism in the presence of polycystic ovaries (PCO) on ultrasound formed the control group. The volunteers in the control group were students of the nursing school and medical school, doctors, nurses and the healthy visitors of hospitalized patients.

Metabolic syndrome was separately defined according to the presence of ≥3 risk factors with the criteria of the National Cholesterol Education Program Expert Panel (NCEP), World Health Organization (WHO), American Heart Association/National Heart Lung Blood Institute (AHA/NHLBI), International Diabetes Federation (IDF) and especially Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop. None of the subjects received medications including oral contraceptives, anti-androgenic drugs, or agents effective on carbohydrate metabolism for the last 3 months.

Laboratory analysis

Blood samples were collected in the follicular phase, early in the morning following a 12-hour overnight fasting. The screening consisted of venopuncture followed by measurement of height, weight, waist and hip circumferences. Ferriman-Gallwey scores and the presence of acne were recorded. Right arm systolic and diastolic blood pressures were measured after 15 minutes in the sitting position. A random spot urine sample was collected for the measurement of urinary albumin concentration (Ualb). Plasma total cholesterol, high-density lipoprotein (HDL), and triglyceride (TG) levels were measured by using commercially available kits (Aeroset automated analyzer; Abbott Laboratories, Abbott, IL, USA). Low-density lipoprotein cholesterol (LDL-C) was calculated using Friedewald's Formula (Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of LDL-C in plasma, without the use of the preparative ultracentrifuge, Clin Chem 1972;18:499-502). Plasma glucose concentration was measured by glucokinase method while insulin levels were detected by chemiluminescent enzyme immunoassay (Immulite 2000, Diagnostic Products Corp. Los Angeles, CA, USA) with intra- and inter-assay coefficients of variation of 6.4%. All subjects underwent a 75 g oral glucose tolerance test (OGTT). Fasting plasma glucose (FG) and the 2-hour plasma glucose (PG) and insulin were measured during the OGTT. OGTT results were evaluated according to the criteria of Expert Committee on the Diagnosis and Classification of Diabetes Mellitus (Lepor, 2004); impaired FG was associated with levels of 100-125 mg/dl, and impaired glucose tolerance was associated with 120 minute plasma glucose levels of 140-199 mg/dl. A ratio of FG to fasting insulin (FI) of 4.5 was diagnosed as insulin resistance (Legro et al. 1998). Homeostatic model assessment (HOMA) is applied by using the formula "HOMA Insulin resistance (IR)=Fasting blood glucose (mg/dl)/18 x Fasting insulin (IU/L)/22.5" (Matthews et al. 1985).

Statistical analysis

SPSS V.11.5 software (SPSS Inc, Chicago, Illinois, USA) was used for statistical analysis of the study. Results are presented as mean (±SD) or as percentages and numbers for categorical data. Normality tests were used for all variables. Continuous variables that were normally distributed were analyzed with the two-tailed *t* test and unequally distributed variables were analyzed with the Mann-Whitney U test. Categorical data and proportions were analyzed with the χ^2, Fisher's exact test or likelihood ratio where appropriate. A *p* value of <0.05 was considered statistically significant.

Results

One hundred twenty five (68.7%) of PCOS patients had oligo/anovulation, 169 (92.9%) hyperandrogenism, and 95 (52.2%) women had PCO in ultrasound (Table 1). The mean ages in PCOS group and the control group were 23.21±4.5 and 24.6±4.6, respectively and no significant difference was determined (p=0.537).

Table 2 demonstrates that bodymass index (BMI), FG, FI, triglycerides (TGs), total and LDL cholesterol level were higher among PCOS patients, whereas HDL levels were lower than the age matched controls (p<0.001, p<0.001, p<0.001, p=0.002, p<0.001, p<0.001, respectively). FG scores were 16.4±8.8 in PCOS and 3.8±2.3 in control cases (p<0.001). There was no difference in waist-hip ratio between PCOS patients and controls (p=0.476).

Table 3 shows the frequency of the metabolic syndrome in the study population by using different criteria. Except the AHA/NHLBI criterion, all criteria showed significantly

Table 1. The distribution of clinical and biochemical findings of PCOS subjects compared to control cases according to Rotterdam criteria

	PCOS (n=182)	Control (n=182)	*p*
Oligo or anovulation (%)	125 (68.7)	0 (0)	<0.001*
Clinical/biochemical hyperandrogenism (%)	169 (92.9)	62 (34.1)	<0.001*
PCO in ultrasound (%)	95 (52.2)	5 (2.7)	<0.001*

The results are expressed as numbers and percentages.
*Statistically significant (p<0.05) $\chi 2$ test.

Table 2. Demographic, anthropometrical and biochemical parameters of PCOS and control groups are demonstrated

	PCOS (n=182) Mean ±SD	Control (n=182) Mean ±SD	*p*
Age (year)	23.21±4.5	23.6±4.6	0.41
BMI (kg/m^2)	25.04±5.1	23.52±2.9	<0.001*
Ferriman-Gallwey score	16.4±8.8	3.8±2.3	<0.001*
Waist/Hip ratio	0.77±0.06	0.75±0.06	0.001*
Fasting glucose (mg/dl)	88.15±14.3	87.98±8.8	0.89
Fasting insulin (µUI/ml)	27.64±39.4	6.06±2.42	<0.001*
Triglyceride (mg/dl)	91.5±34.4	79.7±28.6	<0.001*
Total cholesterol (mg/dl)	170.2±34.7	151.6±19.3	<0.001*
HDL cholesterol (mg/dl)	46.3±12	51.1±7.7	<0.001*
LDL cholesterol (mg/dl)	99.8±35.6	88.6±21.6	<0.001*

Data are expressed as mean ±SD.
*Statistically significant (p<0.05) independent samples *t*-test.

Table 3. Prevalence of metabolic syndrome in PCOS and control groups

	PCOS (n=182)	Control (n=182)	*p*
NCEP (%)	15 (8.2)	5 (2.7)	0.02*
IDF (%)	26 (14.3)	5 (2.7)	<0.001*
WHO (%)	15 (8.2)	5 (2.7)	0.02*
AHA/NHLBI (%)	19 (10.4)	12 (6.6)	0.18
Rotterdam (%)	18 (9.9)	5 (2.7)	0.005*

The results are expressed as numbers and percentages.
*Statistically significant (p<0.05) $\chi 2$ test.

Table 4. The distribution of cases according to selected metabolic syndrome criteria in the two groups

	PCOS (n=182) n (%)	Control (n=182) n (%)	*p*
Waist circumference >88 cm	35 (19.2)	6 (3.3)	<0.001*
Waist circumference >80 cm	70 (38.5)	45 (24.7)	0.005*
Waist/hip >0.85	26 (14.3)	17 (9.3)	0.14
TG >150	10 (5.5)	4 (2.2)	0.1
HDL <50	111 (61)	104 (57.1)	0.45
HDL <39	30 (16.5)	10 (5.5)	0.001*
Fasting glucose >100	32 (17.6)	16 (8.8)	0.01*
Fasting glucose >110	10 (5.5)	1 (0.5)	0.006*
HOMA-IR >2.5	44 (24.2)	11 (6)	<0.001*
BMI >30 kg/m^2	31 (17)	3 (1.6)	<0.001*
Hypertension defined as systolic BP ≥130 mmHg and Diastolic BP ≥85 mmHg	28 (15.4)	12 (6.6)	0.007*

The results are expressed as numbers and percentages.
*Statistically significant (p<0.05) $\chi 2$ test.

higher MetS prevalence in patients with PCOS. The highest frequency of MetS was observed according to the IDF criterion.

The frequency of cases with different cut-off values used as diagnostic criteria for MetS in NCEP, WHO, AHA/NHLBI, IDF and Rotterdam are presented in Table 4. Hypertension was more frequent in the PCOS group compared to the control group. Decreasing the waist cut-off value from 88 cm to 80 cm categorized 35 cases as risky in PCOS group and 39 cases as risky in the control group. Increasing HDL cut-off value from 39 to 50 mg/dl categorized 81 cases and 94 cases as risky in

Table 5. The distribution of metabolic syndrome positive cases with different criteria among PCOS and control group with respect to age groups

Age groups	<20 (n=65)	20-30 (n=243)	>31 (n=56)	*p*
NCEP				
PCOS (n=182)	2 (4.8%)	10 (8.4%)	3 (13.6%)	0.6
Normal (n=182)	0	2 (1.6%)	3 (8.8%)	0.03
p value	0.53	0.01*	0.67	
IDF				
PCOS (n=182)	6 (14.3%)	16 (13.5%)	4 (18.2%)	0.5
Normal (n=182)	0	2 (1.6%)	3 (8.8%)	0.03
p value	0.08	<0.001*	0.41	
WHO				
PCOS (n=182)	5 (11.9%)	8 (6.7%)	2 (9.1%)	0.7
Normal (n=182)	0	4 (3.2%)	1 (2.9%)	0.04
p value	0.15	0.2	0.55	
AHA				
PCOS (n=182)	4 (9.5%)	12 (10.1%)	3 (13.6%)	0.9
Normal (n=182)	0	7 (5.6%)	5 (14.7%)	0.02
p value	0.28	0.1	1	
Rotterdam				
PCOS (n=182)	4 (9.5%)	11 (9.3%)	3 (13.6%)	0.9
Normal (n=182)	0	2 (1.6%)	3 (8.8%)	0.03
p value	0.28	0.008*	0.67	

The results are expressed as numbers and percentages.
*Statistically significant (p<0.05) Fischer's exact test.

the PCOS and the control group, respectively. Decreasing fasting glucose level from 110 mg/dl to 100 mg/dl categorized 22 and 15 cases as risky in the PCOS and control groups.

Although, MetS frequency tends to increase with age within the control group according to different criteria, the frequency was similar within PCOS group of different age groups (Table 5). When PCOS cases were compared to the control group, MetS frequency was higher in the younger age groups especially between 20-30 years of age according to IDF, NCEP and Rotterdam criteria (Table 5).

Discussion

Women with PCOS run multiple risk factors for diabetes including obesity, a family history of type 2 diabetes, and abnormalities of insulin actions (7). Women affected by PCOS are at uncertain risk of developing cardiovascular disease (8,9). Limited epidemiological data have shown no increase in cardiovascular events. But, the young age of the study populations limits reality of this result.

Atherogenic dyslipidemia consist of raised TGs, small LDL particles, and low HDL cholesterol. Raised TGs commonly reflect the presence of remnant lipoproteins, which are widely believed to be atherogenic (5). In the Pathological Determinants of Atherosclerosis in Youth (PDAY) study, McGill et al. found that in young women, BMI was not associated with coronary atherosclerosis, but in those with a thick panniculus adipose, there was a trend toward greater coronary lesions. Postmortem blood analysis results in this study reflect that with increasing adiposity, non-HDL (LDL+VLDL) cholesterol, glycohemoglobin level and medial thickness of renal arteries as a marker of hypertension were higher, whereas HDL cholesterol levels were lower (6).

PCOS and the metabolic syndrome share insulin resistance as an important component in their pathophysiology. Legro et al. reported significantly higher percentile of impaired glucose tolerance among PCOS when compared with age and weight matched premenopausal controls (10). In our study, insulin resistance was evaluated. The percentile of contributors with HOMA-IR greater than 2.5 values was found to be statistically significant. This might be important on the development of cardiovascular effects with the long term exposure to high levels of insulin.

This study is a first report about the comparisons of different MetS criteria. Our findings point out that PCOS patients experience MetS earlier in life than the age matched controls. As the age increases the MetS prevalence among the control group also increases to a frequency similar to that of the PCOS patients. This might point out two conclusions. Either PCOS causes an earlier onset of MetS due to its hormonal milieu or a subgroup of MetS cases might also lead to PCOS syndrome. Whatever the mechanism, our data shows that PCOS patients have a considerable prevalence of MetS during their young adulthood.

The criteria of the IDF are based on expert opinion and are similar to the NCEP-ATP III definition. The principal differences are the requirement of 'abdominal obesity' and the threshold differences based on ethnicity. For the European population the cut-off value of waist circumference is accepted to be 94 cm for men and 80 cm for women. In subjects whose BMI is ≥30, the IDF proposes to not measure waist circumference (4). On the other hand, the World Health Organization (WHO) defines the MetS as glucose intolerance. Risk factors of metabolic syndrome of ATP III criteria, were well known predisposing factors for cardiovascular disease. Although insulin resistance is presumed to be the basic defect leading to the metabolic syndrome, neither assessment of insulin resistance nor hyperinsulinemia were among the proposed ATP III criteria (1). Study researching the capability of ATP III criteria to identify insulin resistant individuals, argued that ATP III guidelines are not very sensitive (14). However, they proposed to use larger number of criteria (four or five versus three) as indicative of insulin resistance.

In the US Third National Health and Nutrition Examination Survey (NHANES III), the prevalence of the syndrome was linearly related to age over the range of 20 to 70 years, and was approximately equal to age 20, given as a percentage (13). In our study, the mean age of healthy control was 24.6±4.6, and the prevalence of metabolic syndrome was 2.7% using the NCEP-ATP III, IDF, WHO and Rotterdam definitions which was similar with the previous results in literature (13). Surprisingly, there was no statistically significant difference between PCOS and the control when the AHA criterion was used for the diagnosis of MetS, because the 'impaired concentration' for FG was lowered to 100 mg/dl and the number of women with the MetS increased among the "healthy" controls (prevalence rose from 2.7% to 6.6%). In PCOS, the IDF criterion diagnosed more patients than did those of the AHA, Rotterdam, NCEP-ATP III, and the WHO. In a previous study, IDF was found more powerful to predict carotid atherosclerosis than NCEP and AHA in females (15) while the results were different in males. The abdominal obesity component of the IDF definition was independently associated with increased median carotid intimal thickness in females (15). Our results might be varying as a function of the ethnic difference of the group. Also, different data about the MetS prevalence and the presence of insulin resistance raises the question of the clinical utility of making the diagnosis of MetS on the basis of any specific number of criteria.

Among newly diagnosed PCOS patients, using the NCEP-ATP III criteria for the diagnosis of the MetS, Glueck et al. found that the incidence of MetS was 46% in this study population (11). Apridonidze et al. found, twofold greater prevalence of MetS in PCOS patients (43% of PCOS versus 24% of the controls) at all ranges of BMI. This result may suggest that PCOS itself causes an increased risk for the development of the MetS (12). In a previous study conducted

by Ford et al., when stratified by age, the prevalence of MetS was 45% in women with PCOS between the ages of 20 and 29 years and 53% in women 30 or older. These rates were substantially higher than the rates of 6% for women aged 20-29 years and 15% for women aged 30-39 years as reported in the general population (13).

PCOS should be considered a general health disorder with serious public health implications. Accordingly appropriate attention should be given to screen MetS in young PCOS patients to shorten the duration of MetS and postpone its possible detrimental effects on long-term cardiovascular complications. Preventive measures could be applied such as education on dietetic orientations and early lifestyle changes which would improve the quality of life in PCOS in the near future.

References

1. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adults Treatment Panel III): Final Report. Bethesda, MD. National Heart, Lung and Blood Institute; 2002.
2. Report of a WHO consultation. In: Alwan A, King H, eds. Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications. Part 1: Diagnosis and Classification of Diabetes Mellitus. Geneva: Word Health Organization, Department of Noncommunicable Disease Surveillance; 1999:1-59.
3. Grundy SM, Cleeman JI, Daniels SR et al. Diagnosis and management of the metabolic syndrome: an American heart association/national heart, lung, and blood institute scientific statement. Circulation 2005; 112:2735-52.
4. Alberti KG, Zimmet P, Shaw J. IDF Epidemiology Task Force Consensus Group. The metabolic syndrome; a new worldwide definition. Lancet 2005;366:1059-62.
5. Grundy SM. Obesity, metabolic syndrome, and coronary atherosclerosis. Circulation 2002;105:2696-8.
6. McGill HC Jr, McMahan CA, Herderick EE et al. Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group. Obesity accelerates the progression of coronary atherosclerosis in young men. Circulation 2002;105:2712-8.
7. The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril 2004;81:19-25.
8. Wild RA. Long-term health consequences of PCOS. Hum Reprod Update 2002;8:231-41.
9. Legro RS. Polycystic ovary syndrome and cardiovascular disease: a premature association? Endocrine Rev 2003;24:302-12.
10. Legro RS, Kunselman AR, Dodson WC, Dunaif A. Prevalence and predictors of risk for type 2 diabetes mellitus and impaired glucose tolerance in polycystic ovary syndrome: a prospective, controlled study in 254 affected women. J Clin Endocrinol Metab 1999;84(1):165-9.
11. Glueck CJ, Papanna R, Wang P et al. Incidence and treatment of metabolic syndrome in newly referred women with confirmed polycystic ovary syndrome. Metabolism 2003;52(7):908-15.
12. Apridonidze T, Essah PA, Iuorno MJ, Nestler JE. Prevalence and characteristics of the metabolic syndrome in women with polycystic ovary syndrome. J Clin Endocrinol Metab 2005;90:1929-35.
13. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA 2002;287:356-9.
14. Cheal KL, Abbasi F, Lamendola C et al. Relationship to insulin resistance of the Adult Treatment Panel III diagnostic criteria for identification of the metabolic syndrome. Diabetes 2004;53:1195-200.
15. Skilton MR, Moulin P, Sérusclat A et al. A comparison of the NCEP-ATPIII, IDF and AHA/NHLBI metabolic syndrome definitions with relation to early carotid atherosclerosis in subjects with hypercholesterolemia or at risk of CVD: Evidence for sex-specific differences. doi:10.1016/j.atherosclerosis.2006.02.019.