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Optimal threshold of homeostasis model assessment for insulin resistance in an Iranian population: The implication of metabolic syndrome to detect insulin resistance

Alireza Esteghamati[a,*], *Haleh Ashraf*[a], *Abdoul-Reza Esteghamati*[b], *Alipasha Meysamie*[c], *Omid Khalilzadeh*[a], *Manouchehr Nakhjavani*[a], *Mehrshad Abbasi*[a]

[a] *Endocrinology and Metabolism Research Center, Vali-asr Hospital, Tehran University of Medical Sciences, Keshvarz Blvd, Tehran 14197-33147, Iran*

[b] *Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran*

[c] *Department of Community and Preventive Medicine, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran*

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ABSTRACT

We assessed the threshold of homeostasis model assessment (HOMA) values to determine insulin resistance (IR) in a sample of Iranians and examined the associations of IR with metabolic syndrome (MetS). Study comprised 1327 non-diabetic and non-hypertensive subjects (438 men, 838 women; aged 20–77 years) incurred in four different locations (Tehran, Iran), 2005–2008. Lower limit of the top quintile of HOMA values in subjects without any metabolic abnormality was considered as the threshold of IR. This threshold was 1.8 (1.7 men; 1.8 women). Overall, 41.1% (36.3% men; 41.5% women) of subjects had IR. HOMA cut-off to determine MetS was 1.95 for ATPIII definition, and 1.85 for IDF. IR associated MetS (ATPIII: odds ratio (OR) = 2.9, 95% CI = 2.2–3.9, $p < 0.05$; IDF: OR = 2.94, 95% CI: 2.3–3.8, $p < 0.05$). Sensitivity of MetS to detect IR was 22.4% for IDF and 36.2% for ATPIII criteria. In multivariate models, HOMA was predicted by waist circumference, and inversely by age and serum HDL-cholesterol. In this study, the cut point of HOMA to detect IR was lower than other populations. IR is an unyielding correlate of MetS; but definitions of MetS are insensitive measures of IR in our population.

1. Introduction

The cluster of risk factors including obesity, impaired fasting glucose, hypertension and dyslipidemia has been referred to "metabolic syndrome" [1]. Metabolic syndrome (MetS) is considered to be a multidimensional risk condition for both atherosclerotic cardiovascular diseases (CVDs) and type2 diabetes [2].

The national prevalence rates of two major components of metabolic syndrome, hypertension and diabetes, are determined to be 26% and 7.7% in Iran in 2004 [3,4]. Prevalence of MetS in normotensive adults of Isfahan, a central province of Iran, was reported to be less than 13% in a sub-national survey, the Isfahan Healthy Heart Program [5]. Reportedly in one of the 20 districts of Tehran, the prevalence of MetS in normal-weight men and women were 9.9% and 11.0%, respectively [6]. Insulin resistance (IR) is thought to be the major abnormality in MetS, previously called the insulin resistance syndrome [7]; however, controversial findings are also reporting the discordance between IR and MetS [8]. The association of IR and MetS in our population is not yet studied.

* *Corresponding author*. Tel.: +98 2188417918/9121154577; fax: +98 2188428951.
E-mail addresses: esteghamati@tums.ac.ir (A. Esteghamati), mehrshad_abbasi@yahoo.com (M. Abbasi).
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The homeostasis model assessment of insulin resistance (HOMA-IR) provides a useful model to assess IR in epidemiological studies [9]. Nevertheless, the HOMA-IR cut points to diagnose IR cannot be readily applied to all populations and might be varied from race to race [10]. In this regard, we performed an analysis in a sample of healthy Iranian subjects to determine optimal cut-off value for HOMA-IR to identify a threshold for IR. We also examined performance of the National Cholesterol Education Program (NCEP) Third Adult Treatment Panel (ATPIII) and the International Diabetes Federation (IDF) criteria defining MetS to diagnose subjects with IR in our population. To the best of our knowledge, no evidences of this kind exist for Iranian population.

2. Materials and methods

2.1. Subjects

This uncontrolled-registry cross-sectional study was conducted in four different sites in Tehran (Iran) from September 2005 to January 2008. Participants were enrolled from individuals taking health examinations, or those who accompanied patients at three centers located in west, downtown, and south of Tehran as follows: (1) Valiasr Hospital, a university hospital (Tehran, Iran), (2) Bank Melli General Hospital (Tehran, Iran), (3) a referral private endocrine clinic (Tehran, Iran) and staffs of a private company located in eastern side of Tehran undergoing routine health examination. Individuals with a history of recent acute illness or known cardiovascular, kidney, liver, endocrine diseases (other than metabolic syndrome) were excluded. Pregnant or lactating women, hypertensive patients and smokers were not included. Also individuals aged <20 years were excluded from the analyses of this study. The study population consist of 1276 individuals (438 male and 838 female) aged 20–77 years.

Oral informed consent was obtained from all patients before study commencement. The present study was conducted in conformity with the Helsinki declaration.

2.2. Procedures

Detailed medical histories were obtained for all subjects and physical examinations were performed by one of the authors (i.e. AE).

Weight (kg) was measured while the patient dressed in light clothing and without shoes using digital scales and recorded to the nearest 0.5 kg. Height (to the nearest 0.5 cm) was measured in a standing position, without shoes, using stadiometer, while the shoulders were in a normal position. Blood pressure was measured by standard mercury sphygmomanometer with an appropriate sized cuff for arm diameter. Before measurement, the participant was questioned about drinking tea or coffee, physical activity, smoking and full bladder. The participants were required to rest for at least 5 min before having their blood pressure checked twice at an interval of at least 5 min. The mean value of these two measurements was used for the analyses.

Venous blood samples were obtained after at least 10 h overnight fasting in the morning between 07:00 and 09:00. Blood samples were taken in a sitting position according to the standard protocol and centrifuged immediately. Fasting blood sugar was measured by enzymatic colorimetric method using glucose oxidize test. Serum total cholesterol, triglyceride, and HDL-cholesterol were determined by enzymatic methods (Parsazmun, Karaj, Iran). LDL cholesterol was calculated using the formula of Friedewald et al. [11]. In case that serum triglyceride concentration was greater than 400 mg/dL, LDL cholesterol was determined directly with enzymatic method using commercial kits (Parsazmun, Karaj, Iran). Insulin was measured by radioimmunoassay (Immunotech, Prague, Czech Republic). Sensitivity was 0.5 μU/mL, and the upper limits of intra- and interassay coefficients of variation were 4.3 and 3.4, respectively.

Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in meters) squared. HOMA-IR was calculated as fasting insulin (U/l) × fasting glucose (mg/dL)/405, as described by Matthews et al. [9]. We defined metabolic syndrome according to updated 2005 NCEP-ATPIII [12] and IDF [13]. Under the NCEP-ATPIII criteria, MetS was defined as the presence of three or more of the following risk factors: abdominal obesity (waist circumference >102 cm [men] or >88 cm [women]), triglyceride ≥150 mg/dL, HDL-cholesterol <40 mg/dL (men) or <50 mg/dL (women), blood pressure ≥130/85 mmHg, and fasting glucose ≥100 mg/dL [12]. According to IDF definition, a person defined as having MetS must have central or abdominal obesity (waist circumference >94 cm in men and >80 cm in women) plus any two of the following four factors: (1) triglyceride ≥150 mg/dL; (2) HDL-cholesterol <40 mg/dL for men, <50 mg/dL for women; (3) systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg; (4) fasting blood sugar ≥100 mg/dL [13]. For both NCEP and IDF definitions, subjects who were taking antihypertensive medication were considered hypertensive individuals.

Those with triglyceride <150 mg/dL, HDL-cholesterol ≥40 mg/dL for men, ≥50 mg/dL for women, fasting blood sugar <100 mg/dL, systolic blood pressure <130 mmHg, diastolic blood pressure <85 mmHg, serum total cholesterol ≤200 mg/dL, and BMI ≤25.0 kg/m^2 are defined as subjects without any metabolic abnormality to determine reference values of HOMA-IR and cut-offs to detect IR. To compare our results with that of Bonora's study [14] we also applied the following criteria to define the normal subjects: BMI <25.0 kg/m^2, fasting blood sugar <140 mg/dL, serum total cholesterol <240 mg/dL, HDL-cholesterol >40 mg/dL, serum triglycerides <250 mg/dL, systolic blood pressure <160 mmHg and diastolic blood pressure <95.

2.3. Statistics

Statistical analyses were conducted using SPSS software (SPSS, Chicago, IL, USA; Version 15 for Windows Evaluation). For the descriptive analysis, after having checked for normality of variables using the Kolmogorov–Smirnov test, measures of normal dispersion were used: average ± standard deviation for quantitative variables and/or standard error (S.E.). To assess the correlations of the variables, independent sample Student's *t*-test was employed when the variables were parametric and Mann–Whitney *U*-test when the vari-