

Spectrum of insulin sensitivity in the Korean population

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Abstract

The aims of the present study were to (1) examine the range of values for insulin sensitivity measures such as fasting serum insulin, homeostasis model assessment (HOMA), and quantitative insulin sensitivity check index (QUICKI) and (2) to identify cutoffs for indirect indexes of insulin sensitivity such as insulin, HOMA, and QUICKI that confer increased risk of metabolic syndrome in a large sample of Korean adults. The total number of study subjects involved was 83 186. All of them presented for a routine health status checkup at the Kangbuk Samsung Hospital between January 2003 and December 2004, and none of them was currently taking medication for hypertension, diabetes, or dyslipidemia. We used 3 measures of insulin sensitivity: the fasting serum insulin, the HOMA, and the QUICKI. The age- and sex-adjusted prevalence of metabolic syndrome was examined by tenths of the distribution of each index of insulin. The fasting serum insulin, HOMA, and QUICKI were compared by using receiver operating characteristic curves. The fasting serum insulin ranged from 1.71 to 70.40 $\mu\text{U/mL}$, with the 25th percentile = 5.97, the median = 7.69, and the 75th percentile = 9.82. The HOMA ranged from 0.34 to 17.72, with the 25th percentile = 1.33, the median = 1.74, and the 75th percentile = 2.27. The QUICKI ranged from 0.112 to 0.202, with the 25th percentile = 0.146, the median = 0.152, and the 75th percentile = 0.158. The insulin, HOMA, and QUICKI values at the point on the receiver operating characteristic curve closest to the ideal of 100% sensitivity and 100% specificity for detecting the presence of metabolic syndrome were 9.7 $\mu\text{U/mL}$, 2.43, and 0.145, respectively. In conclusion, these findings describe the spectrum of insulin sensitivity in Korean adults. This study is the first attempt to determine cutoff values for indirect indexes of insulin sensitivity such as insulin, HOMA, and QUICKI that confer an increased risk of metabolic syndrome. These findings may be useful for evaluating insulin resistance, particularly in epidemiological studies.

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1. Introduction

Insulin resistance is an independent risk factor for cardiovascular and cerebrovascular disease [1–9]. The gold standard for measuring insulin resistance is the hyperinsulinemic-euglycemic clamp [10]. The minimal model analysis of a frequently sampled intravenous glucose tolerance test is an alternative to the clamp technique [11]. However, these are invasive, cost-intensive, and labor-intensive procedures that are not applicable to routine clinical practice or to large-scale epidemiological studies. Therefore, indirect indexes of insulin sensitivity have been proposed.

To date, it has been shown that the homeostasis model assessment (HOMA) [12–14] or the quantitative insulin sensitivity check index (QUICKI) [15], which are calculated from fasting plasma glucose (FPG) and insulin, are useful surrogate indexes of insulin resistance in healthy subjects and diabetic subjects because of their high correlation with the indexes assessed by the hyperinsulinemic-euglycemic clamp method.

Although researchers have used the fasting serum insulin, HOMA, and QUICKI methods in clinical studies, little research has been done to evaluate the cutoff values for the HOMA and QUICKI tests. Moreover, the range of values for these measures has not been assessed in a large Korean population sample.

The aims of the present study were (1) to examine the range of values for insulin sensitivity measures such as

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fasting serum insulin, HOMA, and QUICKI and (2) to identify the cutoff values for the indirect indexes of insulin sensitivity such as fasting serum insulin, HOMA, and QUICKI that confer increased risk of metabolic syndrome in a large sample of Korean adults.

2. Methods

2.1. Subjects

The total number of subjects involved in our study was 128 737, all of whom presented for a routine health status checkup at the Kangbuk Samsung Hospital, College of Medicine at Sungkyunkwan University, between January 2003 and December 2004, and the subjects were without any specific medical complaint. The subjects were asked questions concerning the risk factors for general cardiovascular disease (ie, medical history and lifestyle factors such as smoking, alcohol consumption, and regular exercise). We limited our analysis to the participants aged 20 years or older (128 705, 99.9% of all subjects). Of these potential participants, 45 519 (35.4%) were excluded: 5825 (4.5%) were currently taking medication for hypertension, diabetes, or dyslipidemia; 10 527 (8.2%) did not have information about their medical history; 10 539 (8.2%) did not have the fasting laboratory measurements needed to obtain the fasting serum insulin, HOMA, or QUICKI; 18 501 (14.4%) did not have the blood pressure (BP) measurement; and 127 (0.1%) were pregnant. Finally, 83 186 subjects (52 141 men, 31 045 women) were included in this study.

2.2. Measurements

The blood samples were collected after more than 12 hours of fasting, and the total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) values were measured enzymatically using an automatic analyzer (Advia 1650 Autoanalyzer, Bayer Diagnostics, Leverkusen Germany). The BP was determined using a mercury manometer between 8:00 and 10:00 AM after the subject had been sitting upright for at least 10 minutes. When the systolic or diastolic BP exceeded 140 or 90 mm Hg, respectively, the BP was remeasured twice after the subject rested, and the values were then averaged. The waist circumference was measured at the midlevel between the lowest rib and the iliac crest or the narrowest part without adding pressure according to the recommendation of the World Health Organization [16]. The body mass index was calculated as the weight in kilograms divided by the square of height in meters to the nearest 0.1 from the measured body weight and height with the subject in a light gown using an automatic scale.

We used 3 measures of insulin sensitivity: fasting serum insulin expressed in microunits per milliliter, the HOMA, and the QUICKI. The serum insulin was measured by an immunoradiometric assay (Biosource, Nivelles, Belgium).

The maximum inter- and intra-assay coefficients of variation for the range of concentrations that were evaluated were 12.2% and 4.5%, respectively, for the fasting serum insulin. The HOMA was calculated from the equation $HOMA = [\text{fasting serum glucose (mmol/L)} \times \text{fasting serum insulin } (\mu\text{U/mL})]/22.5$ [12]. For both the fasting serum insulin and HOMA, increasing values corresponded to decreasing insulin sensitivity. The QUICKI was calculated from the equation $QUICKI = 1/\{\log [\text{fasting serum insulin } (\mu\text{U/mL})] + \log [\text{fasting serum glucose (mg/dL)}]\}$.

Metabolic syndrome was defined according to ATP III criteria. A participant has metabolic syndrome if he or she has 3 or more of the following: increased waist circumference (>102 cm in men and >88 cm in women), high triglycerides (≥ 150 mg/dL), low HDL-C (<40 mg/dL in men and <50 mg/dL in women), and high BP ($\geq 130/85$ mm Hg) and fasting glucose (≥ 110 mg/dL).

We defined 3 mutually exclusive categories of glucose metabolism (normoglycemia, impaired fasting glucose, and diabetes) based on the American Diabetes Association criteria [17]. Normoglycemia was defined as a normal fasting glucose level (an FPG concentration ≤ 99 mg/dL). Impaired fasting glucose was defined by an FPG level of 100 to 125 mg/dL. Diabetes was defined by an FPG level of 126 mg/dL or higher.

2.3. Statistical analyses

The Kolmogorov-Smirnov test was used to determine if continuous variables were normally distributed. To describe the spectrum of insulin sensitivity in this study, we used measures for both the spread of the data (range, 10th, 25th, 75th, and 90th percentiles, and SD) and of the central tendency of the data (median and mean). We did not transform either the fasting serum insulin or the HOMA to describe the spectrum of the fasting serum insulin and HOMA.

2.3.1. Frequency distributions

The prevalence of metabolic syndrome was determined in 83 186 subjects (52 141 men and 31 045 women). The age- and sex-adjusted prevalence of metabolic syndrome was examined according to the tenths of the distribution for each index of insulin sensitivity such as insulin, HOMA, and QUICKI. This approach was used because it provided the highest precision for examining the possible threshold effects while maintaining adequate numbers within each percentile band. The age and sex standardization was estimated using the direct method to the age and sex structure of the subjects.

2.3.2. Receiver operating characteristic analysis

In this study, the fasting serum insulin, HOMA, and QUICKI were compared by using the characteristic receiver operating characteristic (ROC) curves [18]. This method compares the diagnostic properties of a test by expressing sensitivity as a function of $1 - \text{specificity}$. The areas under the curve represent the probability that a subject chosen at

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