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Preliminary report: homeostasis model assessment of insulin resistance, an indicator of insulin resistance, is strongly related to serum insulin: practical data presentation and the mathematical basis

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Abstract

The homeostasis model assessment for insulin resistance (HOMA-R) is frequently used as an indicator of insulin resistance. The purpose of this study was to clarify the advantage of HOMA-R as an indicator of insulin resistance. A population of 3008 Japanese male workers (34 to 64 years old), who have no history of diabetes mellitus, hypertension, dyslipidemia, hyperuricemia, coronary and/or cerebrovascular disease and their fasting plasma glucose were under 140 mg/dL. The Spearman's rank correlation coefficient between HOMA-R and the serum insulin was 0.982. Although HOMA-R is also regulated by the plasma glucose, insulin and plasma glucose are not independent. The lower and upper 2.5%ile data of plasma glucose were prepared, which were used for mathematical basis of strong correlation between HOMA-R and serum insulin. Subjects with higher insulin had higher plasma glucose, which was resulted in higher HOMA-R. In the same manner, HOMA-R would become lower in the area of lower insulin levels. As two lines of the lower and upper 2.5%ile data of plasma glucose exists near, the correlation between HOMA-R and serum insulin became very strong. Although HOMA-R is a popular indicator of insulin resistance, we recommend that HOMA-R could be substituted simply by serum insulin. This may be valid in the general population with no remakable medical condition.

1. Introduction

The homeostasis model assessment for insulin resistance (HOMA-R) has frequently been used as an indicator of insulin resistance. Insulin resistance is associated with glucose intolerance, hypertension, and dyslipidemia, which are the main risk factors for coronary artery disease [1]. Insulin resistance is also a risk factor for the development of diabetes mellitus [2]. Although the kinetics of serum insulin is complicated and modified by many factors [3], insulin resistance plays a crucial role in the development of systemic vascular disease [4]. Validation studies of measurement of insulin resistance, including HOMA-R, have been reported. Vaccaro et al [5] concluded that there were no significant differences among the serum insulin, HOMA-R, quantitative insulin sensitivity check index, and revised quantitative insulin sensitivity check index using receiver operator characteristic curve analysis with minimal model-derived estimates of insulin sensitivity as the criterion standard for the detection of insulin resistance.

However, HOMA-R appears to be equivalent in clinical significance to serum insulin itself. The purpose of this study was to clarify the strong correlation between HOMA-R and serum insulin, with demonstration of the epidemiologic data with the mathematical (theoretical) basis.

2. Methods

The author studied a population of 3584 Japanese male workers ranging in age from 34 to 64 years who were working at a company in Gunma Prefecture, Japan. Subjects with a current history of treatment of diabetes, hypertension, dyslipidemia, hyperuricemia, coronary, and/or cerebrovascular disease were excluded. Participants with

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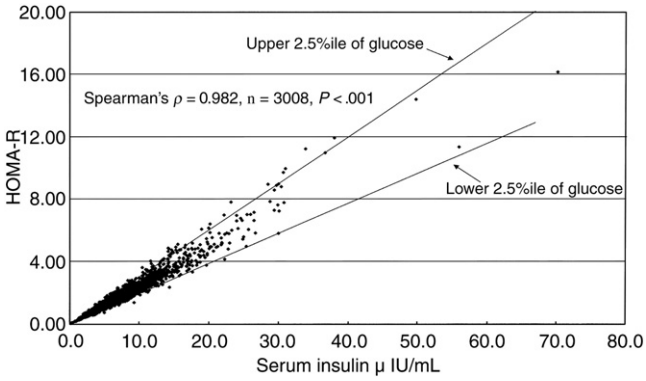

Fig. 1. Relationship between serum insulin and HOMA-R.

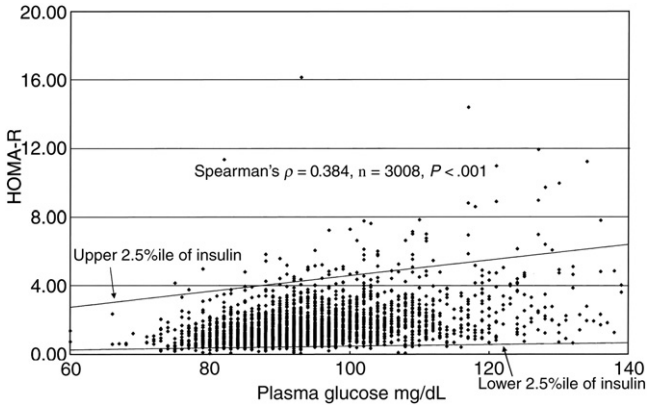

Fig. 2. Relationship between plasma glucose and HOMA-R.

fasting plasma glucose levels of 140 mg/dL or higher were also excluded. Finally, data from 3008 participants were included in the analysis. Informed consent was obtained from all the study participants, and the study protocol was approved by the ethics committee of the company where the participants were employed.

Venous blood samples were drawn from each subject after they had fasted for 9 hours, and the samples were stored at −80°C until the following assays were performed. The plasma glucose level was determined using the hexokinase method, and the serum insulin level was measured by chemiluminescent enzyme immunoassay (Fujirebio, Tokyo, Japan) with a detection sensitivity of 0.3 μIU/mL [6]. The intraassay coefficient of variation for repeated measurements was 2.1% (First IRP National Institute for Biological Standards and Control code: 66/304). As an insulin resistance indicator, the HOMA-R [7] was calculated as follows: fasting plasma glucose (in milligrams per deciliter) × fasting serum insulin (in micro–international units per milliliter)/405.

All the statistical analyses were conducted using SPSS 16.0 for Windows (SPSS Japan, Tokyo, Japan).

3. Results and discussion

Plasma glucose was normally distributed, whereas the distribution of serum insulin and HOMA-R was skewed to the left. The Spearman rank correlation coefficient between HOMA-R and the serum insulin was 0.982. The scatter diagram revealed a strong linear correlation between 2 indicators (Fig. 1). Although HOMA-R is also regulated by the plasma glucose, insulin and plasma glucose are not independent; and a dynamic physiologic correlation exists. As a matter of fact, the Spearman rank correlation coefficients between plasma glucose and serum insulin or HOMA-R were determined to be 0.224 and 0.384, respectively (Fig. 2). As additional information, the Spearman rank correlation coefficients between HOMA-R and serum lipids such as triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and total cholesterol were determined to be 0.420, −0.403, 0.288, and 0.215, respectively.

In the next step, the author presents the mathematical basis for the strong correlation between HOMA-R and insulin using the lower (upper) 2.5 percentile data of serum insulin and plasma glucose, which were 1.9 (18.5) μIU/mL and 78 (121) mg/dL, respectively. These values were calculated using the epidemiologic data mentioned above. If it were assumed that subjects with higher insulin may have a tendency to show higher plasma glucose based on the Spearman rank correlation coefficient, HOMA-R would become higher in the area of higher insulin levels in the upper part of Fig. 1. In the same manner, HOMA-R would become lower in the area of lower insulin levels in the lower part of Fig. 1. As a consequence, the correlation between HOMA-R and serum insulin is very strong.

Homeostasis model assessment for insulin resistance would also become higher in the area of higher glucose in the higher part of Fig. 2. In the same manner, HOMA-R would become lower in the area of lower glucose in the lower part of Fig. 2. As there is a distance between the 2 lines in Fig. 2, the correlation between HOMA-R and plasma glucose is relatively weak.

A very strong correlation exists between HOMA-R and serum insulin, and the author concludes that insulin and HOMA-R are of almost equivalent efficacy in determining the presence of insulin resistance in nondiabetic subjects at the workplace. This may also be valid in the general population with no remarkable medical condition. Homeostasis model assessment for insulin resistance, a popular indicator of insulin resistance, provides information not different from the serum insulin itself. Thus, HOMA-R may be useful to check the longitudinal data in subjects who might go on to develop abnormal glucose tolerance [8], whereas it may be more difficult to calculate in subjects with increased fasting plasma glucose. Homeostasis model assessment for insulin resistance could be substituted simply by serum insulin, with no need for data on plasma glucose.

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