Relation of insulin resistance in metabolic syndrome components to levels of HOMA-IR and HOMA-AD

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Summary: HOMA-IR is a mathematical model that predicts insulin sensitivity by measuring the blood glucose and fasting insulin. Adiponectin is an adipocytokine with anti-inflammatory function, anti-atherogenic, insulin sensitizing and anti-platelet and can be a HOMA sensitive predictor. This study compared these indices and verified the effectiveness of HOMA-IR and HOMA-AD. Methods: One hundred and fifty-six healthy volunteers aged 48.7 ± 6.0 years were studied in relation to liver function, anthropometric parameters and HOMA-IR and HOMA-AD.

Keywords: HOMA-IR, HOMA-AD, insulin resistance, metabolic syndrome.

Introduction

HOMA-IR (Homeostatic Assessment Index) is a mathematical model that predicts insulin sensitivity, measured by fasting blood glucose and basal insulin. It is strongly correlated to the hyper insulimic-euglycemic clamp, the gold standard for assessing insulin resistance (IR) [1] and validated for the Brazilian population [2]. It is correlated positively to components of metabolic syndrome such as central obesity, lipid abnormalities, hypertension and atherosclerosis. Matsushita [2] used a new index, adapting HOMA (fasting glucose x fasting insulin). HOMA-IR was calculated from the product of serum insulin and plasma glucose levels divided by serum adiponectin levels (HOMA-AD). Adiponectin is an adipocytokine with anti-inflammatory function, anti-atherogenic, anti-platelet and insulin sensitizing. It is also the most abundant protein in serum insulin signaling pathways in muscle and liver and can be a sensitive predictor of HOMA. Individuals in the aging process physiologically accumulate larger amounts of truncal fat promoting the development of metabolic syndrome and thus increasing cardiovascular risk [3,4]. In this population, prevailing lower levels of adiponectin favored an increase in glucose and lipid levels and consequently insulin resistance.

When comparing the two indices to the other components of metabolic syndrome, in middle age it can be possible to define the more appropriate for each variable. Age is associated with negative nitrogen balance due to sarcopenia. In this population, physical activity can be a benefit increasing protein synthesis and improving fat mass control. The objective of this study was to compare the two indices, HOMA-IR and HOMA-AD, correlating them with lipid variables, anthropometric parameters and liver enzymes in individuals as they age.

Material and Methods

Were studied 156 healthy volunteers with mean age 48.7 ± 6.0; other parameters may be seen in Table 1. Patients were selected...
according to the rules of the Ethics Committee in Research - Faculty of Medical Sciences, State University of Campinas (CEP 695/2004), and signed a free consent form according to the guidelines of Resolution 196/96 of the Ministry of Health - Brazil. For the components of metabolic syndrome, the index according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII) was used. The index considers the presence of three or more components in a single individual: abdominal obesity, reduced glucose tolerance, elevated serum triglycerides, decreased levels of HDL cholesterol and high blood pressure. It also characterizes the presence of insulin resistance, a potential therapeutic target for prevention of type 2 diabetes and cardiovascular disease.

### Table I. Parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Value</th>
<th>Mean (S.D.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antropometric Values</td>
<td>Weight (kg)</td>
<td>83.97(14.21)</td>
</tr>
<tr>
<td></td>
<td>BMI (kg/m²)</td>
<td>28.20(4.29)</td>
</tr>
<tr>
<td></td>
<td>Waist (cm.)</td>
<td>100.27(11.46)</td>
</tr>
<tr>
<td></td>
<td>Hip (cm.)</td>
<td>100.99(8.01)</td>
</tr>
<tr>
<td>Enzimas Hepáticas</td>
<td>AST (mg/dL)</td>
<td>26.09(8.49)</td>
</tr>
<tr>
<td></td>
<td>ALT (mg/dL)</td>
<td>31.03(17.52)</td>
</tr>
<tr>
<td></td>
<td>GGT (mg/dL)</td>
<td>45.32(40.23)</td>
</tr>
<tr>
<td></td>
<td>AF (mg/dL)</td>
<td>71.01(20.59)</td>
</tr>
<tr>
<td>Lipídios</td>
<td>Total cholesterol (mg/dL)</td>
<td>214.94(44.36)</td>
</tr>
<tr>
<td></td>
<td>HDL-cholesterol (mg/dL)</td>
<td>47.49(10.10)</td>
</tr>
<tr>
<td></td>
<td>Triglycerides (mg/dL)</td>
<td>167.55(116.79)</td>
</tr>
<tr>
<td></td>
<td>Glycosilada Hemoglobin glicosilada (%)</td>
<td>5.36(0.58)</td>
</tr>
</tbody>
</table>

Analyses were performed using SPSS Statistics 12.0 (London, UK) and variance analysis by ANOVA method. For comparisons Student’s t test for paired data and Kruskal-Wallis for multiple comparisons were used. To compare the interest variables Pearson’s test was applied using a significance level of 5%.

### Results

Metabolic syndrome was found in 22.7% of the subjects. In this study 79.2% of the volunteers had high systolic blood pressure and 53% diastolic blood pressure changes. Regarding HDL, 25.6% of the volunteers had results below 40mg/dL and 69.1% had trigonel obesity. Triglycerides were increased in 41.7%. Only 10.4% of the subjects presented glucose blood levels above 102mg/dL and 49% presented HOMA-IR above 2.47. The mean of HOMA-IR was 2.29 ± 1.64 and HOMA-AD 125.17 ± 123.11. Regarding liver enzymes HOMA-AD was positively correlated to ALT (P < 0.001; r=0.311), HOMA-IR correlated to ALT (P < 0.001; r=0.362) and GGT (P = 0.012; r=0.202). In demographics HOMA-AD was positively correlated to weight (P < 0.001; r=0.31), BMI (P < 0.001; r=0.383), waist (P < 0.00; r=0.318), hip (P < 0.003; r=0.289), waist/hip ratio (P = 0.004; r=0.289), weight, fat mass by bioelectrical impedance (P < 0.001; r=0.397), percentage of fat mass (P < 0.001; r=0.358) and lean mass (P = 0.002; r=0.275). Concerning HOMA-IR, correlation was positive with weight (P < 0.001; r=0.477), BMI (P < 0.001; r=0.523), waist (P < 0.001; r=0.467), hip (P < 0.001; r=0.474), waist/hip ratio (P = 0.015; r=0.243), fat mass weight by bioelectrical impedance (P < 0.001; r=0.596), percentage of fat mass (P < 0.001; r=0.522) and lean mass (P < 0.001; r=0.419). In the biochemical lipids profile there was positive correlation to HOMA-AD with the parameters: total cholesterol (P = 0.024; r=0.190), with HDL-cholesterol (P = 0.003; r=0.222) and glycated hemoglobin (P = 0.003; r=0.252). Only a trend was shown with LDL (P = 0.051; r=0.166). In HOMA-IR correlation was positive with total cholesterol (P = 0.012; r=0.203), with triglycerides (P = 0.006; r=0.223), with HDL-cholesterol (P = 0.011; r=0.205) and the glycated hemoglobin (P < 0.001; r=0.275). There was a trend with the parameter LDL cholesterol (HOMA-AD com P = 0.13; r= 0.209 and HOMA-IR with P = 0.08; r= 0.14). The basal glucose and insulin had better correlation to log HOMA-IR.
Discussion

This study aimed to verify the performance of two indices of insulin resistance: the widely used HOMA-IR and HOMA-AD. HOMA-AD uses adiponectin as inflammatory marker which may be a predictor of insulin resistance when associated with HOMA in a specific population of men in the process of aging. Insulin resistance in the association of cardiovascular risk factors and components of metabolic syndrome can be found in several authors [6,7], Wallace [7] defined HOMA index as a real correlation with simple reproducibility, determined by the correlation between baseline levels of glucose and insulin, reflecting the balance between hepatic glucose and insulin secretion - maintenance feedback liver / β cell. Matsuhisa [3] refers to the HOMA-IR as a more simplified calculation of insulin resistance, but with some limitations, especially in subjects of fasting hyperglycemia, because it is induced by inadequate insulin secretion. Besides that, the level of glucose and insulin homeostasis between the baseline HOMA-AD has been proposed as a new index to address these limitations. Adiponectin as serous inflammation marker could be insulin resistance predictor in individuals who present moderately altered fasting glucose and show no changes in blood glucose. In this work we compared individuals with and without metabolic syndrome according to NCEP-ATPIII. Adiponectin group with metabolic syndrome did not correlate with any parameters, but the individuals in the group without metabolic syndrome were correlated to parameters of glucose (p<0.15 r<0.365) and glycated hemoglobin (p<0.05 r=-0.303), in agreement with other studies [5,8,9,11,12].

EBINÇ [13] presented a significant correlation between adiponectin and total cholesterol, LDL, insulin and HOMA-IR. In this study, adiponectin correlated only with GGT, considered a marker of hepatic insulin resistance and showed no correlation with HOMA-IR. It was also verified that HOMA-IR correlated better with lipids than HOMA-AD, being compatible with results reported on The Stopp DM2-prevention study group and Nowak [14, 15].

In this study it was observed that 22.7% of individuals presented metabolic syndrome, corroborating with Resnick [16] and Tipene-Leach [17], who related that metabolic syndrome and insulin resistance were prevalent in women. In this study 79.2% of the volunteers had high systolic blood pressure and 53%, diastolic blood pressure changes. Regarding HDL, 25.6% of the volunteers had results below 40mg/dL, and 69.1% had truncal obesity. In this study triglycerides were high in 41.7% of the volunteers, demonstrating that the factors that comprise metabolic syndrome as expected in aging outcome of insulin resistance. These results were consistent with Park [18] in black population, as well as Natali [19], who incorporated in the diagnosis of the metabolic syndrome cutoff more sensitive values to elevated blood pressure. The results from this study were similar to Taniguchi [20], Jaber [21] and Jeffs [22], who found a weaker association with HDL-c.

In addition, the frequency of metabolic syndrome cases in which only one of three components specifically related to insulin resistance was present, such as glucose. Although HOMA-AD is less effective than HOMA-IR, its use is justified by its best results of metabolic syndrome components were the feature of adipose truncal tissue (centripetal adiposity) and blood pressure changes. As adiponectin is a marker of inflammation, its association with HOMA (HOMA-AD) is an excellent choice to establish an index of insulin resistance. It also predicts cardiovascular risk and is inversely related to BMI and visceral fat.

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