PROFESSIONAL ARTICLES

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SIGNIFICANCE AND ROLE OF HOMEOSTATIC MODEL ASSESSMENT IN THE EVALUATION OF GLUCOSE REGULATION MECHANISMS

ZNAČAJ I UPOTREBA PARAMETARA MODELTA HOMEOSTAZE U PROCENI GLIKOREGULATORNIH MEHANIZAMA

Stanislava NIKOLIĆ, Nikola ĆURIĆ, Romana MIJOVIĆ, Branislava ILINČIĆ and Damir BENC

Summary

Introduction. Mathematical formulas, such as homeostatic model assessment indexes, proved to be useful for the estimation of insulin resistance. Nevertheless, numerous published results point to a considerable variability of their reference values. The aim of this study was to use homeostatic model assessment indexes and evaluate levels of insulin resistance in non-diabetic patients.

Methods. The study included 486 individuals (mean age 36.84 ± 12.86; 17% of males and 83% of females). Blood sampling was performed in order to determine glucose and insulin plasma levels, at the 0th and 120th minute of the oral glucose tolerance test. The indexes were calculated by the use of homeostatic model assessment 2 calculator, homeostatic model assessment of insulin resistance, homeostatic model assessment of insulin sensitivity, and homeostatic model assessment of β-cells function. The results were statistically analyzed using a Data Analysis programme.

Results. In the examined population, the average glycemic values of the oral glucose tolerance test were within the euglycemic scope (Gluc 0 = 4.76 ± 0.45 mmol/L; Gluc 120 = 5.24 ± 1.17 mmol/L), while the average values of calculated homeostatic model assessment indexes were: insulin resistance - 1.41 ± 0.82; β-cells function - 131.54 ± 49.41%, and insulin sensitivity - 91.94 ± 47.32%. According to study cut-off values, homeostatic model assessment of insulin resistance was less than 2. We found 84 (17.28%) individuals with increased insulin resistance. Also, we set the lowest reference value for homeostatic model assessment of insulin sensitivity at less than 50%. With the probability of 66.67% (± 1SD), basal insulin level under 11.9 mIU/L can be considered to correspond to the physiological level of insulin resistance.

Conclusion. The follow-up of increased insulin resistance and altered secretion of pancreatic β-cells, at early stages of glucose regulation disturbances, may be useful in assessing dynamics and level of glucose regulation disturbances and their appropriate treatment.

Key words: Insulin Resistance; Prediabetic State; Insulin; Blood Glucose; Glucose Tolerance Test; Early Diagnosis; Models, Theoretical; Risk Factors; Diabetes Mellitus, Type 2; Insulin-Secreting Cells

Sažetak

Uvod. Za relativno brzu procenu insulinske rezistencije primenjuju se matematički izrazi, poput programa za procenu homeostaze. Međutim, podaci iz literature ukazuju na veliku varijabilnost njihovih graničnih vrednosti, namećući potrebu za njihovim određivanjem u našoj populaciji. Cilj rada bio je da se ispitu nivos insulinske rezistencije pomoću indeksa homeostaze u grupi pacijenata bez dijabetesa.

Materijal i metode. U studiju je uključeno 486 ispitanika, od kojih su 17% osobe muškog pola. Prosek godina života ispitanika je 36.84. Svim ispitanicima laboratorijski je određivana koncentracija glukoze i insulina, iz uzorka plazme, u toku nultog i 120. minuta oralnog testa tolerancije glukoze, a zatim primenom kalkulatora 2 homeostaze, izračunati sledeći indeksi: indeks insulinske rezistencije, indeks insulinske senzitivnosti i sekretorni indeks oslobađanja insulina. Rezultati su statistički obradivani programom Data Analysis i potom prikazani grafički i tabelarno.

Rezultati. Na ispitivanoj populaciji, srednje vrednosti glikemije u nultom i 120. minuto oralnog testa tolerancije glukoze su unutar euglikemijskog opsega (4.76 ± 0.45 mmol/L i 5.24 ± 1.17 mmol/L), dok su srednje vrednosti izračunatih indeksa homeostaze: indeks insulinske rezistencije (1,41 ± 0,82); sekretorni indeks oslobađanja insulina (131,54 ± 49,41%); i indeksa insulinske senzitivnosti (91,94 ± 47,32%). Prema preporucama iz literature i rezultatima studije, definisana je gornja granična vrednost indeksa insulinske rezistencije < 2. U ispitivanoj populaciji je bilo 84 ispitanika (17,28%) sa povišenom insulinskom rezistencijom. Takođe, postavili smo dojmu graničnu vrednost za indeks insulinske senzitivnosti na < 50%. Smerujućim faktorima su: glikemia i insulin hemolizacija, koja može da dovede do vrednosti bezazalnih insulinina ispod 11,9 mIU/L odgovaraju fiziološkom nivou insulinike sekrecije. Zaključak. Pracenu promene insulinske rezistencije i sekrecije beta-ćelija pankreasa, u početnim fazama pomećaja glikoregulatornog sistema, mogao bi biti od koristi u pravilnoj i eventualnoj preduzimanju pravovremenih, odgovarajućih terapijskih mera.

Ključne reči: insulinska rezistencija; prediabetes; insulinarne deficite; peću kod crvi; oralni glukogoja tolerant test; rana dijagnostika; teoretski modeli; faktori rizika; dijabetes melitus, tip 2; insulin-sekretnađećelije

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**Abbreviations**

T2DM – type 2 diabetes mellitus  
HOMA – homeostatic model assessment  
HOMA-IR – homeostatic model assessment of insulin resistance  
HOMA-S – homeostatic model assessment of insulin sensitivity  
HOMA-B – homeostatic model assessment of secretory \(\beta\)-cell capacity  
QUICKI – quantitative insulin sensitivity check index  
OGTT – oral glucose tolerance test  
CLIA – direct chemiluminescence immunoassay

**Acknowledgments and appreciation**

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**Introduction**

The incidence of type 2 diabetes mellitus (T2DM), associated with obesity, physical inactivity and unhealthy diet, is increasing worldwide, especially in developing countries [1]. It is characterized by abnormalities in insulin secretion and elevated insulin resistance leading to increased glucose levels [2]. Years before the T2DM is diagnosed, patients usually have a few or even no signs or symptoms typical for the disease itself. Therefore, it is of great importance to have a suitable diagnostic tool which may point to the initial pathophysiological processes in apparently healthy population.

The gold standard for the assessment of insulin sensitivity and/or resistance is the glucose clamp technique. However, these tests are expensive and difficult to perform, and as such they are not suitable for routine use [3].

According to the results primarily obtained by clamp techniques (euglycemic, hyperinsulinemic and hyperglycemic clamp), certain mathematical models were developed. These equations are based on simple, single determination of glucose, insulin or C-peptide levels, and as such, relatively accurately estimate the level of insulin resistance, as well as the secretory capacity of \(\beta\)-cells.

These mathematical equations, described in 1985, called homeostatic model assessment (HOMA) indexes, comprise two different formulas: homeostatic model assessment of insulin resistance (HOMA-IR), and homeostatic model assessment of \(\beta\)-cell capacity (HOMA-B) [4]. Since that time, other mathematical expressions have been developed, such as quantitative insulin sensitivity check index (QUICKI), and McAuley index which assesses the degree of insulin sensitivity [5]. At the same time, the existing formulas have been upgraded by glucose and insulin levels obtained from oral glucose tolerance test (OGTT), as well as the demographic and anthropometric data (body mass index, age, and gender). These equations are known as Stumvoll indexes [6].

The fact that these relatively simple mathematical models highly correlate with the clamp technique, has enabled their use in a large number of clinical and epidemiological studies. However, in clinical practice, the most widely used are HOMA indexes: HOMA-IR and HOMA-B, using both glucose and insulin under basal conditions.

Insulin resistance is associated with an increased cardio-metabolic risk in obese people as well as in individuals with altered glucose control. Considering that insulin resistance is the pathophysiological basis of T2DM, there is a need for its measurement, as well as for setting the reference (cut off) intervals, especially in people at increased risk of developing T2DM [7]. In most of the published papers, HOMA-IR value taken for the upper limit is less than 2.5 [8].

The aim of this study was to analyze the level of insulin resistance using HOMA indexes in subjects with clear euglycemic values in basal conditions, as well as at the 120th minute of the OGT-test.

**Table 1. Mean values and standard deviations of all of examined parameters (n = 486)**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>(\bar{x})</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>36.84</td>
<td>12.86</td>
</tr>
<tr>
<td>Gluc 0 (mmol/L)/Gluc 120 (mmol/l)</td>
<td>4.76</td>
<td>0.45</td>
</tr>
<tr>
<td>Gluc 120 (mmol/L)/Gluc 120 (mmol/l)</td>
<td>5.24</td>
<td>1.17</td>
</tr>
<tr>
<td>Ins 0 (mIU/l)/Ins 0 (mIU/l)</td>
<td>11.14</td>
<td>6.59</td>
</tr>
<tr>
<td>Ins 120 (mIU/l)/Ins 120 (mIU/l)</td>
<td>52.40</td>
<td>46.46</td>
</tr>
<tr>
<td>HOMA-IR/HOMA-IR</td>
<td>1.41</td>
<td>0.82</td>
</tr>
<tr>
<td>HOMA-B (%) / HOMA-B (%)</td>
<td>131.54</td>
<td>49.41</td>
</tr>
<tr>
<td>HOMA-S (%) / HOMA-S (%)</td>
<td>91.94</td>
<td>47.32</td>
</tr>
</tbody>
</table>

**Legend:** Gluc 0 and Gluc 120 – plasma glucose level during the 0th and 120th OGT test; Ins 0 and Ins 120 – plasma insulin level during the 0th and 120th OGT test; HOMA-IR - calculated index of insulin resistance (homeostasis model assessment, calculator HOMA 2); HOMA-B - calculated index of insulin secretion (homeostasis model assessment, calculator HOMA 2); HOMA-S - calculated index of insulin sensitivity (homeostasis model assessment, calculator HOMA 2)

**Legend:** Gluc 0 i Gluc 120 – koncentracija glukoze u toku oralnog testa tolerancije glukoze; Ins 0 i Ins 120 – koncentracija insulina u toku oralnog testa tolerancije glukoze; HOMA-IR – izračunati indeks insulinске rezistencije; HOMA-B% - izračunati indeks insulinске sekrecije; HOMA-S% - izračunati indeks insulinске senzitivnosti
Table 2. The significance of differences of examined parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HOMA-IR&lt;2</th>
<th>HOMA-IR&gt;2</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gluc 0 (mmol/L)</td>
<td>4.91 ± 0.48</td>
<td>4.72 ± 0.42</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Ins 0 (mIU/L)</td>
<td>5.88 ± 1.31</td>
<td>5.11 ± 1.10</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Ins 120 (mIU/L)</td>
<td>22.27 ± 7.45</td>
<td>20.90 ± 5.86</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>HOMA-B (%)</td>
<td>106.28 ± 67.90</td>
<td>103.12 ± 44.34</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>HOMA-S (%)</td>
<td>2.79 ± 0.89</td>
<td>1.12 ± 0.39</td>
<td>p &lt; 0.001</td>
</tr>
</tbody>
</table>

Legend: Gluc 0 and Gluc 120 – plasma glucose level during the 0th and 120th OGT test; Ins 0 and Ins 120 – plasma insulin level during the 0th and 120th OGT test; HOMA-IR - calculated index of insulin resistance (homeostasis model assessment, calculator HOMA 2); HOMA-B - calculated index of insulin secretion (homeostasis model assessment, calculator HOMA 2); HOMA-S - calculated index of insulin sensitivity (homeostasis model assessment, calculator HOMA 2)

Material and Methods

The study included 486 subjects who were examined at the Center for Laboratory Medicine, Clinical Center of Vojvodina, from January 2014 to December 2015.

All the participants have undergone adequate preparation, including eight-hour, overnight fasting, as well as half an hour standstill before blood sampling. Blood was collected in EDTA (venous blood collection tubes) vacutainer tubes, centrifuged at a speed of 4000 rpm for 10 minutes. Glucose and insulin levels were determined from obtained plasma samples.

Glucose determination was done using a specific enzyme, GOD-pap method (reference range from 4.0 to 6.1 mmol/L), while insulin was measured using an automated immunometric system (ADVIA Centaur system XP), based on direct chemiluminescence immunoassay (CLIA). The sensitivity and the range of insulin was 0.5 to 300 mIU/L. The recommended reference value for the basal insulin values was 3.0 – 25.0 mIU/L.

Based on the measured values, exclusion criteria were as follows: fasting glucose during 0th of OGT testing > 6.1 mmol/L; glucose during 120th minute of OGT testing > 7.8 mmol/L. According to the above criteria, the study included only nondiabetic, euglycemic subjects [9].

HOMA indexes were calculated in all participants. According to HOMA2 calculator, the following indexes were determined: HOMA-IR (insulin resistance index), HOMA-S (index of insulin sensitivity %) and HOMA-B (index of β-cells secretory capacity %). HOMA2 calculator was downloaded from the official website of the University of Oxford, Oxford Centre for Diabetes, Endocrinology and Metabolism [10]. The content of the formulas used by the mentioned calculator is not known, but it most certainly represents a perfected model in comparison to previously defined HOMA equations.

The results were statistically analyzed using a Data Analysis program, and then presented in graphical and tabular forms.

Results

The study included 401 (83%) women, and 85 (17%) men. The average age of respondents was 36.84 ± 12.86, the youngest participant was 19 years old, and the oldest 70 years old (Table 1).

In the examined subjects, both average glycemic levels (at 0th and 120th minute) of OGTT were within the euglycemic range (Gluc 0 = 4.76 ± 0.45 mmol/L; Gluc 120 = 5.24 ± 1.17 mmol/L). The mean values of calculated HOMA indexes are presented in Table 1 (HOMA-IR = 1.41 ± 0.82; HOMA-B = 131.54 ± 49.41% and HOMA-S = 91.94 ± 47.32%) (Table 1).

The upper cut-off value for HOMA-IR has been defined to be less than 2 (Table 2).

Based on study results, 84 (17.28%) individuals manifested increased insulin resistance, while 402 participants had HOMA-IR values less than 2.0 and accounting for 82.7% (healthy subjects without insulin resistance) of the total of examined subjects (Table 2). According to the results presented in Graph 1, most subjects (83) had the interval of HOMA-IR values between 0.8 and 1.0 (Graph 1).

The T-test showed a statistically significant difference of all analyzed parameters between the group with initially elevated insulin resistance (HOMA-IR>2) and healthy subjects (HOMA-IR<2) (Table 2).

By definition, HOMA-S index represents the percentage of deviation from the expected, ideal 100% insulin sensitivity. Therefore, only the lowest reference value for HOMA-S less than 50% was set (Table 2).
No overlap in the mean basal insulin values (-1SD < x̄ < +1SD) has been established between the two groups with (5.72 < 8.81 < 11.9 mIU/L) and without (14.82 < 22.27 < 29.72 mIU/L) elevated insulin resistance. With the probability of 66.67% (x̄ ±1SD), basal insulin level under 11.91 mIU/L can be considered to correspond the physiologic level of insulin resistance (Table 3).

Linear correlation analysis revealed a statistically significant connection of a moderate degree between calculated HOMA-IR values and Ins 120 (r = 0.632, p <0.01). A high degree of positive correlation was observed between HOMA-IR and HOMA-B (r = 0.831, p <0.01), while there was a high degree of negative correlation between HOMA-IR and HOMA-S (Table 4).

Discussion

This study included a total of 486 subjects with normal blood glucose levels during the 0th and 120th OGT-test (baseline glucose < 6.1 mmol/L and 120th glucose <7.8 mmol/L, respectively). Since the glucose reference range during OGT testing is independent of gender and age, the study included 83% of women and 17% of men, with an average age of 36.8 years (range - 19–70 years) [11].

Based on the values and results obtained in the study, the recommended cut-off value for HOMA-IR less than 2 was accepted [12]. The adequacy of the defined upper limit has been confirmed by analyzing the calculated value of HOMA-IR in the entire examined population. In the group of participants without insulin resistance, the level of HOMA-B and HOMA-S had the slightest deviation from the optimal values defined according to the euglycemic population (HOMA-S = 103.12%; HOMA-B = 117.05%) [4].

At the same time, the lower reference limit for HOMA-S to less than 50% has been established. HOMA-S represents a very important parameter because it defines condition of insulin resistance in peripheral tissues more closely. This index enables assessment of peripheral tissues insulin sensitivity. Due to lower insulin sensitivity, the insulin resistance is increased. Disturbances of insulin resistance represent the first link in the chain of numerous pathophysiological events leading to disruption of the complex metabolic processes in the body. Initially, higher insulin secretion is compensated with elevated insulin resistance, introducing the system in a vicious circle, until the collapse of glucose regulation and other metabolic homeostasis mechanisms resulting in a permanent expression of hyperglycemia and clinical manifestations of T2DM.

Based on the upper limit for HOMA-IR, 17.28% (84 of 486) of participants presented with elevated insulin resistance. This result is in accordance with numerous results obtained from different studies conducted in various populations. Japanese authors determined the upper limit value for HOMA-IR at 2.4 [13]. Another study established reference value for HOMA-IR at 2.05, and it included adult population in Spain [14]. Similar to our values, Swedish group of authors defined the limit for HOMA-IR at 2.0 [15], while HOMA-IR indexes were higher among Italians (HOMA-IR = 2.77) [16] and the French [17]. The study conducted among the adult population in the USA set a cut off value at 4.39 [18].

Table 3. Basal insulin levels and HOMA-S % in the groups of subjects with and without elevated insulin resistance

<table>
<thead>
<tr>
<th></th>
<th>HOMA-IR &lt; 2</th>
<th>HOMA-IR &gt; 2</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>N = 402</td>
<td>N = 84</td>
</tr>
<tr>
<td>Ins 0 (mIU/L)</td>
<td>5.72</td>
<td>14.82</td>
</tr>
<tr>
<td>HOMA-S (%)</td>
<td>58.78</td>
<td>47.33</td>
</tr>
<tr>
<td>+1 SD</td>
<td>8.81</td>
<td>22.27</td>
</tr>
<tr>
<td></td>
<td>11.91</td>
<td>38.44</td>
</tr>
<tr>
<td></td>
<td>147.47</td>
<td>29.72</td>
</tr>
<tr>
<td></td>
<td>147.47</td>
<td>29.72</td>
</tr>
</tbody>
</table>

Legend: Ins 0 – plasma insulin level during the 0th of OGT test; HOMA-B% - calculated index of insulin secretion (homeostasis model assessment. calculator HOMA 2); x – mean value; SD – standard deviation

Graph 1. Histogram of HOMA-IR distribution in the group of subjects without insulin resistance (HOMA-IR<2)

Table 3. Vrednosti bazalnog insulina i HOMA-S% u grupi zdravih i grupi ispitanika sa povišenom insulinski režistencijom

<table>
<thead>
<tr>
<th></th>
<th>HOMA-IR &lt; 2</th>
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</tr>
<tr>
<td></td>
<td>147.47</td>
<td>29.72</td>
</tr>
</tbody>
</table>

Legend: Ins 0 – koncentracija insulina u toku oralnog testa tolerancije glukoze; HOMA-S% – izračunati indeks insulinske senzitivnosti; x – srednja vrednost; SD – standardna devijacija
The differences between the defined reference values of HOMA indexes can be explained by numerous facts. It is noteworthy that in many studies HOMA indexes have been calculated according to the original equation, using plasma values of glucose and insulin measured in basal conditions (original HOMA model equations). It is known that this original equation is defined based on the earlier generation of insulin tests, and as such underestimates insulin sensitivity and insulin resistance and overestimates the secretory capacity of pancreatic β-cells [4]. In contrast, in this study, HOMA2 computer model was used, which is more reliable and widespread providing the ability of calculating three different HOMA values at the same time (HOMA-IR, HOMA-B and HOMA-S). This model offers a non-linear solution. It is calibrated according to the latest generation of insulin or even c-peptide values as a direct indicator of insulin secretion. HOMA2 calculator is widely used in hyperglycemic states, taking into account the renal glucose loss [4].

Obesity and socioeconomic status are also important factors for the development of insulin resistance, which can explain the significantly higher value of the index among Americans compared to other populations, including our examinees [15]. A Mexican study dealt with the influence of heritage on the level of insulin resistance. The results of that study proved that Mexicans of Indian origin had higher HOMA indexes than those whose origins were European [19]. This is an interesting fact considering that the population of Vojvodina is multi-ethnic and future studies should take into account the ethnicity of the population being tested.

The participants were divided into two groups, based on the set cut-off HOMA-IR and were statistically different in all parameters (plasma glucose and insulin during the 0th and 120th minute of OGTT, HOMA-B and HOMA-S). Both groups had blood glucose levels in the reference range (from 4.0 to 6.1), with significantly higher values in the group with elevated insulin resistance (4.91 mmol/L vs. 4.72 mmol/L (Table 2).

Also, the baseline plasma insulin was significantly lower in the group without elevated insulin resistance (8.81 mIU/L vs. 22.27 mIU/L). These insulin levels may be used in a rough estimation of insulin resistance and increased insulin secretion. Although the reference value of baseline insulin levels is between 3.0 and 25.0 mIU/L (manufacturer’s recommendation), according to this study, with the probability of 66.67% (± 1SD), basal insulin level under 11.91 mIU/L can be considered to correspond to physiologic level of insulin resistance.

Numerous publications were aimed to define the upper limit for insulin levels under basal conditions. McAuley and associates have set the limit at 12 mIU/L [20–22]. Other studies have defined the upper reference range at 16 mIU/L [23]. In this study, we noticed that the limit at 15.0 mIU/L resulted in the absence of false-negative patients (none of the 84 subjects with insulin resistance had the basal insulin level less than 15.0 mIU/L), and only 2 participants were false-positive (only 2 of 403 subjects without insulin resistance had fasting insulin levels above 15.0 mIU/L).

HOMA-B defines a compensatory mechanism which maintains the level of glucose in the optimal range. Since HOMA-B is about the degree of deviation of beta cells activity from the optimal glucose homeostasis, it provides very useful information on the current level of the compensatory mechanism in advanced stages of the disorder.

The study focuses on subjects whose glucose levels did not reflect a realistic insight into the physiological mechanism of glucose regulation, during the period when the pancreatic beta cells were sufficient to maintain glucose in the reference range. Therefore, it is very important to detect elevation of insulin resistance using indirect methods.

### Table 4. Linear correlation

<table>
<thead>
<tr>
<th></th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gluc 0 (mmol/L)</td>
<td>0.311</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Gluc 120 (mmol/L)</td>
<td>0.300</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Ins 0 (mIU/L)</td>
<td>0.998</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Ins 120 (mIU/L)</td>
<td>0.632</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HOMA-B (%)</td>
<td>0.831</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HOMA-S (%)</td>
<td>-0.775</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

**Legend:** r-Pearson's coefficient of correlation; p - statistical significance; Gluc 0 and Gluc 120 – plasma glucose level during the 0th and 120th OGTT test; Ins 0 and Ins 120 – plasma insulin level during the 0th and 120th OGTT test; HOMA-IR - calculated index of insulin resistance (homeostasis model assessment, calculator HOMA 2); HOMA-B % - calculated index of insulin secretion (homeostasis model assessment, calculator HOMA 2); HOMA-S % - calculated index of insulin sensitivity (homeostasis model assessment, calculator HOMA 2)
that can measure the degree of insulin resistance, particularly in people with an increased risk of disruption of glucose regulatory mechanisms, obesity and poor physical activity. For individuals with detected elevated HOMA-IR it is necessary to repeat the testing in order to exclude certain conditions that may compromise the credibility of the obtained results (tests performed in non-standard conditions). After confirming the elevation of HOMA-IR and/or reduction of HOMA-S, it is recommended to monitor these individuals in appropriate time intervals, since it is thought they are at increased risk for developing T2DM. In addition to regular laboratory monitoring of this population and calculation of HOMA indexes, it is very useful to implement education for these persons. However, today there is very little data available on monitoring and taking appropriate measures in non-diabetic population with early established increase in insulin resistance [24]. Therefore, it would be of particular importance to continuously monitor individuals with established insulin resistance, according to set criteria (HOMA-IR >2). Eventually, slightly elevated insulin resistance will cause changes in blood glucose levels. The follow-up of changes in insulin resistance and secretion of pancreatic beta cells, may be useful in assessing the dynamics and severity of disruptions of glucose regulatory mechanisms, as well as in taking adequate therapeutic measures in due time.

**Conclusion**

Continuous monitoring of individuals with elevated insulin resistance will give more precise answers about the efficacy of homeostatic model assessment indexes in early detection of the glucose regulation disturbances. The calculated homeostatic model assessments of insulin sensitivity (%) and of secretory β-cells capacity (%) are useful indicators that provide additional information necessary for proper interpretation of homeostatic model assessment of insulin resistance.

**References**

