The concordance of triglyceride glucose index (TyG index) and homeostatic model assessment for insulin resistance (HOMA-IR) in non-diabetic subjects of adult Indonesian males

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ABSTRACT

Background: Recently, an examination with the TyG index has developed as an alternative to the gold standard, by which this measure has a relatively high sensitivity in assessing IR. The measurement with TyG index only requires triglyceride levels and fasting blood glucose and is expected to be an examination instrument used to assess IR available in all health facilities in developing countries, especially in Indonesia. In this study, we analyzed the concordance between the TyG index and HOMA-IR in assessing IR in nondiabetic subjects of adult Indonesian males.

Method: A cross sectional study was conducted at the outpatient installation of Wahidin Sudirohusodo Hospital and Hasanuddin University Hospital during March until June 2019. An examination of FBG, TyG and fasting insulin was performed. The statistical test results were considered significant if the p value was <0.05.

Result: Of the 88 healthy male subjects, the mean age was 51.15 \( \pm \) 6.8 years. The ROC curve showed that the cutoff value of the TyG index in predicting HOMA-IR was 4.66, with the sensitivity of 86.2% and specificity of 44.1%. The OR value revealed that subjects with a TyG index \( \geq \) 4.66 indicated a 5-time greater risk for IR than subjects with a TyG index \(<\) 4.66.

Conclusion: There was a significant concordance between the TyG index and the HOMA-IR in the subjects of adult Indonesian males.

1. Background

Insulin resistance (IR) is broadly defined as a subnormal biological response to normal insulin concentration.\textsuperscript{1} It precedes the development of type 2 diabetes mellitus and cardiovascular disease. Therefore, it is very important to establish a concise and practical method for identifying individuals at high risk of IR.\textsuperscript{2,3}

The gold standard in IR diagnosis is HEC, but this method is invasive, complex, and expensive. Therefore, it is difficult to apply on daily clinical screening and population-based epidemiological studies.\textsuperscript{4,5}

These days, the emerging methods performed for clinical screening are the HOMA-IR, the QUIKI index and the Matsuda index, but each of them is not currently available in all health services.\textsuperscript{6,7} HOMA-IR is and one of the valid inspection instruments and the most common methods used for IR measurement, but this examination requires plasma insulin levels which, however, are currently not available on demand.\textsuperscript{7,8}

In recent years, an examination with the TyG index has developed. This approach has a fairly high sensitivity in assessing IR. The measurement with TyG index only requires triglyceride levels and fasting glucose. Thus, the TyG index can be used as a test instrument to assess IR in all health facilities in developing countries, especially in Indonesia.\textsuperscript{6,9}

However, since.

This study aims to investigate the concordance between TyG index and HOMA-IR in assessing IR in nondiabetic patients.
2. Method

A cross sectional study was performed at the outpatient installation of Wahidin Sudirohusodo Makassar hospital and Hasanuddin University hospital during March 2019–June 2019. This study received the ethical clearance approval from the Ethics Commission of Biomedical Research in Humans, Faculty of Medicine, Universitas Hasanuddin, Makassar, number of 231/UN4.6.4.5.31/PP36/2019. The approval of medical actions and the signing of informed consent were reported by providing the background, objectives and benefits of the study, as well as blood drawings that the study subjects underwent.

Consecutive sampling was performed in this study. 88 nondiabetic subjects who met the inclusion criteria were included in the study. The inclusion criteria were 1 men, 40–65 years old 2 without diabetes or a history of diabetes 3 without consumption of anti-diabetes drugs, antidiyslipidemia, anti-hypertension and/or without consumption of the aforementioned drugs in the period of > 1 month 4 healthy (no signs of sickness), and 5 with an approval of involvement in the study by signing the informed consent. The subjects were diagnosed with DM if the FBG was ≥ 126 mg/dL and categorized as IR if the tertile was 3 HOMA-IR. In addition, healthy subjects were those with a good physical, mental and social condition and were not only determined by the absence of illness or weakness. The HOMA-IR score was resulted from [FBG (mg/dL) x insulin (μU/L)/405], and TyG index was calculated by Ln [TG (mg/dL) x FBG (mg/dL)]/2.

The data were analyzed by using SPSS ver. 22 with descriptive statistical analysis and Chi square statistical test, Pearson’s correlation, ROC curves, kappa and logistic regression. The statistical test results were considered significant if the p value was < 0.05.

3. Results

Table 1 shows the results of the data analysis among 88 healthy male subjects aged 40–65 years. It can be seen that the mean age was 51.15 ± 6.8 years. The characteristics of the study subjects indicated the rate of FBG at 94.92 ± 9.94, TG at 170.69 ± 88.10, fasting insulin at 8.29 ± 7.27, HOMA-IR at 2.0 ± 1.82, and TyG index at 4.79 ± 0.25.

The value of HOMA-IR and TyG index was divided based on tertile because there was no cutoff in assessing IR either from HOMA-IR value or TyG index value. Tertile 1.2 of HOMA-IR was < 2.24, while tertile 3 of HOMA-IR was ≥ 2.24. On the other hand, tertile 1.2 of TyG index was < 4.89, and tertile 3 of TyG index remained at ≥ 4.89.

Fig. 1 illustrates the results of the ROC curve analysis. It showed that the value of Area Under Curve (AUC) was 0.701 (p < 0.05), which indicated that the TyG Index was fairly sensitive in predicting HOMA-IR values with a cutoff value of 4.66.

Table 2 shows that there was a significant concordance between TyG index and HOMA-IR (p < 0.01), with a sensitivity of 86.2% and specificity of 44.1%. OR values indicated that subjects with TyG index at ≥ 4.66 were 5 times more at risk of IR than those with TyG index at < 4.66.

Table 1

<table>
<thead>
<tr>
<th>Variables</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>40</td>
<td>65</td>
<td>51.15</td>
<td>6.83</td>
</tr>
<tr>
<td>FBG</td>
<td>73</td>
<td>125</td>
<td>94.92</td>
<td>9.94</td>
</tr>
<tr>
<td>TG</td>
<td>63</td>
<td>477</td>
<td>170.69</td>
<td>88.10</td>
</tr>
<tr>
<td>Fasting Insulin</td>
<td>2.0</td>
<td>28</td>
<td>8.29</td>
<td>7.27</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>0.36</td>
<td>7.48</td>
<td>2.00</td>
<td>1.82</td>
</tr>
<tr>
<td>TyG Index</td>
<td>4.34</td>
<td>5.50</td>
<td>4.79</td>
<td>0.25</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>TyG Index</th>
<th>HOMA-IR</th>
<th>Total</th>
<th>p</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>OR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 4.66</td>
<td>25</td>
<td>33</td>
<td>0.005</td>
<td>86.2%</td>
<td>44.1%</td>
<td>5.0</td>
</tr>
<tr>
<td>&lt; 4.66</td>
<td>4</td>
<td>26</td>
<td>0.005</td>
<td>86.2%</td>
<td>44.1%</td>
<td>5.0</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>59</td>
<td>0.000</td>
<td>86.2%</td>
<td>44.1%</td>
<td>5.0</td>
</tr>
</tbody>
</table>

* OR: Odds Ratio CI: Confidence Interval. 

95% CI (1.52–15.93).

Table 3

<table>
<thead>
<tr>
<th>Variable</th>
<th>Statistics</th>
<th>Homa-IR</th>
</tr>
</thead>
<tbody>
<tr>
<td>TyG index</td>
<td>Pearson Correlation</td>
<td>0.436</td>
</tr>
<tr>
<td></td>
<td>Sig. (2-tailed)</td>
<td>0.000</td>
</tr>
<tr>
<td>n</td>
<td>88</td>
<td></td>
</tr>
</tbody>
</table>
Table 3 reveals that there is a significant positive correlation between the TyG index and the HOMA-IR: the higher the TyG index, the higher the HOMA-IR \((p < 0.001)\). The result of the correlation test confirms the coefficient value at \(r = 0.436\). Fig. 2 illustrates the positive correlation between the TyG index and the HOMA-IR.

4. Discussion

The study was not conducted in female subjects due to the influence of menstruation on blood glucose. Several studies reported that certain physiological parameters, such as blood glucose, are affected by menstruation. In healthy non diabetic women, some researches indicated a worsening in glucose tolerance, as assessed by the oral glucose tolerance test (OGTT), during the luteal phase (secretory phase)\(^6\). This study shows that the average HOMA-IR value remained at 2.0 ± 1.82. A similar study by Lina Y et al. (2009) in Makassar showed different results with a HOMA-IR value of 1.90 ± 1.10\(^7\). Another study by Ritawaty et al. (2013) found an average HOMA-IR value of 3.2 ± 3.40\(^8\). Gayoza-Diz et al. stated that the value of HOMA-IR differed according to ethnicity, clinical estimation methods, and the condition of the metabolism of the population\(^9\). The average value of the TyG index in this study was 4.79 ± 0.25. In the study by Wongsari MH et al. (2018) in Makassar, however, the value of the TyG index was 4.59 ± 0.22\(^10\). This study shows that there is a significant concordance between the TyG index and the HOMA-IR index. TyG index with a high value indicates a high HOMA-IR value \((p < 0.01)\), with a sensitivity of 86.2%, instead of a low specificity at 44.1% and a cutoff at 4.66. This is in line with a research by Fahimeh et al. (2014) which also found a significant correlation between the TyG and HOMA-IR indices in the population of obese women in Iran\(^11\). This study shows that the average value of the TyG index was 4.79 ± 0.25 in the luteal phase (secretory phase). The study was not conducted in female subjects due to the influence of menstruation on blood glucose. Several studies reported that certain physiological parameters, such as blood glucose, are affected by menstruation. In healthy non diabetic women, some researches indicated a worsening in glucose tolerance, as assessed by the oral glucose tolerance test (OGTT), during the luteal phase (secretory phase). Another study by Ritawaty et al. (2013) found an average HOMA-IR value of 3.2 ± 3.40. Gayoza-Diz et al. stated that the value of HOMA-IR differed according to ethnicity, clinical estimation methods, and the condition of the metabolism of the population. The average value of the TyG index in this study was 4.79 ± 0.25. In the study by Wongsari MH et al. (2018) in Makassar, however, the value of the TyG index was 4.59 ± 0.22. This study shows that there is a significant concordance between the TyG index and the HOMA-IR index. TyG index with a high value indicates a high HOMA-IR value \((p < 0.01)\), with a sensitivity of 86.2%, instead of a low specificity at 44.1% and a cutoff at 4.66. This is in line with a research by Fahimeh et al. (2014) which also found a significant correlation between the TyG and HOMA-IR indices in the population of obese women in Iran. Another study by Guerrero-Romero et al. (2010 and 2016) in Mexico also showed the same result between the TyG index and the HOMA-IR index. The significant concordance between the TyG index and the HOMA-IR index is useful in recognizing insulin resistance among subjects with various grades of body weight and glucose tolerance. There is a remarkable correlation between the TyG index and several obesity factors including BMI, fasting insulin, and LP. This correlation is much greater than that with HOMA-IR\(^9,16\). It also reported that the TyG-Index had a more accurate association with the risk factors for carotid atherosclerosis compared to HOMA-IR\(^17\).

The TyG index has been validated in several populations around the world for use as IR screening\(^8,15\). This study shows that the TyG index has high sensitivity but low specificity. A research by Simental-Mendia et al. (2008) in a healthy population aged 18–65 years in Mexico also showed the same results\(^6\). On the other hand, a study by Guerrero-Romero et al. (2010) shows that the TyG index has high sensitivity and specificity\(^15\). Another study by Bastard et al. (2012) of 163 postmenopausal nondiabetic women suggested that, in a large population, further investigation on TyG index was needed. Furthermore, a cross sectional study of 82 patients in Brazil (2011) showed that the TyG index indicated better results than HOMA-IR\(^5,16\).

High-sensitivity test, such as the TyG index, has fewer false negatives and is useful in identifying subjects with IR on clinical examination. This is very beneficial because fasting insulin measurement is not necessary in the TyG index assessment, so it can be used as an alternative in assessing IR, especially in the first-level public health facilities that improve early detection of IR and suggest early lifestyle changes\(^6\). On the other hand, the TyG index in identifying the proportion of subjects without any disease (specificity) is low, so there are false positives that limit its use for screening purposes. Therefore, this study suggests that subjects with TyG index of < 4.66 are very likely to have IR. Conversely, those with TyG index of ≥ 4.66 indicate the possibility of IR and still require additional examinations, such as HOMA-IR. According to the OR value, the subjects with TyG index of ≥ 4.66 had a 5-time-greater risk of experiencing IR than those with TyG index of < 4.66.

In conclusion, this study shows that there is a significant concordance between the TyG index and the HOMA-IR index for carotid atherosclerosis compared to HOMA-IR\(^17\).

5. Study limitation

The limitation of this study can be identified over the sensitivity and specificity of the TyG index that was compared only with HOMA-IR, which is not the gold standard in diagnosing IR.

Authors’ contribution

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the work to
take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript. Furthermore, each author certifies that this material or similar material has not been and will not be submitted to or published in any other publication.

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Acquisition of data: Dewi Resnawita.
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Authors approval
All authors read and approved the final version of the manuscript.

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References