Comparison of different models of insulin resistance in T2DM: A cross-sectional study.

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Abstract

Introduction: Type 2 diabetes mellitus is a metabolic disease characterized by insulin resistance and defective insulin secretion. Quantification of insulin resistance is essential as it may guide treatment options. The aim of the study was to compare HOMA-IR (both insulin and C-peptide based) and QUICKI in type 2 diabetes mellitus patients.

Methodology: The cross-sectional study included a hundred and fourteen type 2 DM patients diagnosed as per the American Diabetic Association 2017 guidelines. Fasting blood glucose, insulin and C-peptide were assayed. Insulin resistance and beta cell functioning were calculated by HOMA for insulin and C-peptide using suitable formulas. Linear regression analysis was done to correlate insulin and C-peptide based HOMA. ROC curves were constructed to compare different insulin sensitivity indices.

Results: There was a significant correlation (p=0.007) between insulin and C-peptide based HOMA-IR (r=0.3654, r²=0.1335). Insulin and C-peptide based HOMA1% B also had a significant correlation, p=0.0066 (r=0.2975, r²=0.08850). Insulin and C-peptide based HOMA-B cell also had a significant correlation, p=0.0019 (r=0.3223, r²=0.1039). A linear negative correlation was observed between QUICKI and HOMA-IR (p=0.0001) and HOMA-C (p=0.0004) respectively. ROC curve showed that C-peptide based HOMA model had the highest area under the curve, 0.836 with better sensitivity and specificity compared to other insulin resistance/sensitivity models.

Conclusion: Insulin and C-peptide based HOMA-IR are positively correlated. C-peptide based HOMA is a more sensitive and specific marker of insulin resistance compared to insulin based HOMA-IR and QUICKI.

Keywords: HOMA, QUICKI, Insulin, C-peptide.
quantification of insulin sensitivity. Homeostasis model assessment (HOMA) and quantitative insulin sensitivity check index (QUICKI) are two clinically important insulin resistance/sensitivity indices.

HOMA

Homeostatic model assessment (HOMA) is a method used to quantify insulin resistance and beta-cell function from basal (fasting) glucose and insulin or C-peptide concentrations. Simple, minimally invasive predicts fasting steady-state glucose and insulin levels. However, insulin sensitivity in subjects treated with insulin needs further validation. HOMA describes this glucose-insulin homeostasis by means of a set of simple, mathematically-derived nonlinear equations [3,4]. Estimation with the help of the HOMA model parallels equally with that of the euglycemic clamp method [4].

C-peptide, a measure of insulin secretion (not insulin action), can be used in HOMA modeling of both β-cell function and IR. Insulin resistance calculated by the formula, 20/(Fasting C-peptide x FPG) is also a sensitive marker.

QUICKI

It is an empirically derived mathematical transformation of fasting blood glucose and plasma insulin concentrations that provide a consistent and precise insulin sensitivity index with a better positive predictive power [5].

Both HOMA and QUICKI are proved to be clinically important models of quantifying insulin resistance/sensitivity. It is important to quantify IR in diabetics as it may guide in treatment options.

Objectives of our study were to
1. Correlate insulin and C-peptide based homeostatic model assessment for insulin resistance
2. Compare different sensitivity indices like QUICKI and HOMA (both insulin and C-peptide based).

Materials and Methods

Study design

The cross-sectional study was conducted in the Department of Biochemistry, KS Hegde Medical Academy, Mangalore. Institutional ethics committee approval was sought before starting the study. Informed consent was obtained from the subjects.

Inclusion criteria

Subjects: 114 type 2 DM patients (18-65 years), diagnosed as per ADA 2016 guidelines.

Exclusion criteria

Alcoholics, acute and chronic hepatitis, other liver disorders.

Sample collection and analysis

2 ml each of fasting blood sample was collected in fluoride and plain tubes from the antecubital vein, centrifuged at 3000 rpm and plasma was separated. Fasting plasma glucose, insulin, and C-peptide were estimated using fully automated chemistry analyzer, Cobas C-311, and hormone analyzer, Cobas E411, and ELISA respectively.

Insulin resistance was calculated by the homeostasis model assessment (HOMA) (both insulin and C-peptide based) and QUICKI using standard formulae.

Statistical analysis

The data were analysed using Graph Pad Instat version 3. Linear regression analysis was done for the correlation of insulin and C-peptide based HOMA as well as QUICKI. Receiver operator characteristic curves (ROC) were drawn using SPSS version 16 to compare different insulin resistance/sensitivity indices. Insulin-based HOMA-IR was considered as a gold standard to define insulin resistance. HOMA-IR values less than 2.5 were considered normal and more than that were considered as insulin resistant.

Results

There was a significant positive correlation (p=0.007) between insulin and C-peptide based HOMA-IR (correlation coefficient (r)=0.3654, r²=0.133) (Figure 1). Insulin and C-peptide based HOMA1% B also had a significant positive correlation, (p=0.0066) (correlation coefficient (r)=0.2975. r²=0.08850) (Figure 2). A significant positive correlation was observed between Insulin and C-peptide based HOMA-B cell, (p=0.0019) (correlation coefficient (r)=0.3223. r²=0.1039) (Figure 3). A linear negative correlation was observed between QUICKI and insulin based HOMA-IR (p=0.0001) (Figure 4). A similar finding was observed between C-peptide based HOMA (HOMA-C) (p=0.0004) (Figure 5). ROC curve showed that C-peptide based HOMA model had the highest area under the curve, 0.836 with better sensitivity and specificity compared to other insulin resistance/sensitivity models (Figures 6 and 7). ROC curves for log HOMA (insulin based ) and QUICKI revealed that log HOMA is a better model to quantify IR compared to QUICKI with higher AUC (0.787 vs. 0.214).
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Discussion

A significant positive correlation between insulin and C-peptide based HOMA models suggest that C-peptide may be used as an alternative marker to quantify insulin resistance (Figures 1-3). However, ROC studies showed that C-peptide based HOMA-IR had the highest AUC (Figure 6 and Table 1) suggesting that C-peptide based insulin resistance models are superior to that based on insulin. As the normal values for HOMA-IR (insulin based) and QUICKI are well established (<2.5 and 0.382 ± 0.0007), it has been easy to use these indices. As the number of studies on C-peptide based insulin resistance is limited, reference ranges for these are yet to be established.

![Figure 2. Correlation of insulin and C-peptide based HOMA1% B. r=0.297; r^2=0.088; P=0.0066.](image)

![Figure 3. Correlation of insulin and C-peptide based HOMA-B cell. r=0.322; r^2=0.103; P=0.0019.](image)

![Figure 4. Correlation of QUICKI and HOMA-IR. r=-0.665; P=0.0001.](image)

![Figure 5. Correlation of QUICKI and HOMA-C. r=0.565; P=0.0004.](image)

![Figure 6. ROC curves of different insulin resistance/sensitivity model.](image)

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<thead>
<tr>
<th>Insulin resistance models</th>
<th>Area under the curve (AUC)</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>HOMA-IR</td>
<td>0.79</td>
<td>98.70%</td>
<td>80.50%</td>
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<tr>
<td>HOMA-C</td>
<td>0.836</td>
<td>98.70%</td>
<td>91.50%</td>
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<td>CIR</td>
<td>0.414</td>
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<td>52.40%</td>
</tr>
<tr>
<td>QUICKI</td>
<td>0.211</td>
<td>35.50%</td>
<td>6.40%</td>
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<tr>
<td>Log HOMA</td>
<td>0.787</td>
<td>35%</td>
<td>7%</td>
</tr>
<tr>
<td>QUICKI</td>
<td>0.211</td>
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Our findings are in accordance with the study by Kim et al., which suggested a higher area under curve (AUC) for C-peptide based IR models [6]. Fasting C-peptide × fasting glucose was better associated with insulin resistance measured as hyperinsulinemic-euglycemic clamps than HOMA-IR [7]. Meier et al. reported that C-peptide-based index was more closely correlated than an insulin-based index with β-cell mass [8]. Loopstra-Masters et al. report that proinsulin-to-C-peptide ratio was the stronger predictor of diabetes in comparison with proinsulin-to-insulin ratios [9].

C-peptide is may be better index compared to insulin based IR models. C-peptide doesn’t undergo hepatic extraction, so C-peptide may more accurately reflect pre-hepatic β-cell secretion. Pre-hepatic β-cell insulin secretion can be estimated by plasma C-peptide level [10,11]. C-peptides have more steady clearance than insulin [10]. C-peptide has lower within the subject and between-subject variation than insulin, so C-peptides were more reproducible for the determination of β-cell function [12,13]. C-peptide has the insulinomimetic effect and
may also interact synergistically with insulin by disaggregating hexameric insulin into active monomeric form [14,15].

A significant negative linear relationship between QUICKI and both the HOMA models suggest that lower the QUICKI more is the insulin resistance (Figures 4 and 5). ROC analysis shows that log HOMA represents insulin resistance better than QUICKI (Figure 7 and Table 2).

Figure 7. ROC for log HOMA vs. QUICKI.

Conclusion

Insulin and C-peptide based HOMA-IR are positively correlated. C-peptide based HOMA-IR is sensitive (98.7%) and more specific marker (91.5%) of insulin resistance compared to insulin based HOMA-IR (98.7% and 80.5% respectively).

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References


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