Clinical Decision Tool Reviews

Updated Review of HOMA-IR (Homeostatic Model Assessment for Insulin Resistance)

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Abstract

HOMA-IR is used to estimate prevalence of insulin resistance in individuals who are at risk of developing metabolic syndrome and diabetes. This review summarizes pearls, pitfalls and practical application of the calculator.

WHEN TO USE

Use the HOMA-IR to estimate the prevalence of insulin resistance in individuals who are at high risk of developing metabolic syndrome and diabetes when direct measurement (i.e., euglycemic clamp) methods are not feasible. High risk individuals include patients with obesity, increased waist circumference, dyslipidemia, and impaired glucose tolerance. It is best used in research settings for large-scale epidemiological studies.[1,2] Clinically, it may be used as an adjunct in patients who need objective numbers to demonstrate the degree of insulin resistance to incentivize lifestyle modifications along with pharmacological treatment and prevent complications of metabolic syndrome.

PEARLS / PITFALLS

This is a simple, non-invasive estimate using fasting glucose and insulin measurements after an eight hour overnight fast. Values are assay-dependent (reference intervals need to be individualized) and also vary by ethnicity, β-cell function, and body mass index.[3] Results typically show reasonable correlation between HOMA-IR and 'clamp' measurement, the gold standard.[4] However, as a fasting test, it predominantly estimates hepatic resistance and does not consider peripheral resistance and early dysglycemia, which are better estimated with dynamic tests such as oral glucose tolerance tests and euglycemic clamp.[5] As a result, it is not recommended for diagnosis or treatment decisions where clinical judgement is prioritized.

HOMA-IR is unreliable in:

- Patients with an established diagnosis of diabetes or patients on exogenous insulin[6]
- Lean individuals or individuals with normal BMI[7]
- Elderly (Age > 60 years)[8]
- Acute illness or stress states[9]

WHY USE

Direct methods (euglycemic clamp) for measuring insulin resistance are resource intensive, invasive, and time consuming, and this score can be a useful non-invasive metric to give patients an indirect measure of their risk of metabolic syndrome.

NEXT STEPS

Advice

- There is no universally accepted single cut-off, **and values between 2.0-3.0** are commonly used in U.S. clinical and research settings, with a **cutoff of ≥2.5** used in NHANES (National Health and Nutrition Examination Survey) to indicate insulin resistance.[10]
- Consider the population and context of use:

- A study of U.S. adults without diabetes (NHANES III) found a HOMA-IR median of 2.2, mean of 2.8, and standard deviation of 2.4.[11]
- A study of U.S. adolescents found a HOMA-IR mean of 2.3 in normal weight and 4.9 in obese individuals (of which >50% had insulin resistance).[12]
- Internationally, cut-offs for metabolic syndrome and dysglycemia are lower in Asian populations, between 1.4-2.5.[13-15]

Management

There are no validated management algorithms or guidelines using the HOMA-IR score.

However, lifestyle modifications are the foundation of reversing early onset insulin resistance.[16,17] High Intensity Interval Training (HIIT) or concurrent resistance training combined with a Mediterranean, or plant-based diet yields the greatest improvement in HOMA-IR, with practical implementation involving 2–3 sessions per week and a diet rich in fiber, whole grains, fruits, vegetables, and unsaturated fats.[18,19] If lifestyle modifications are insufficient, pharmacological therapy focusing on weight loss and cardiovascular comorbidities should be employed. Weight loss of 5–10% can substantially improve insulin sensitivity.[20] For this reason, Glucagon-like peptide-1 (GLP-1) agonists or dual (GLP-1 and Glucose-dependent Insulinotropic Polypeptide) agonists, like tirzepatide, can be prescribed.[21,22] Metformin can also play a role but it is not as effective as the GLP-1 or dual agonists.[23]

EVIDENCE

The HOMA-IR calculator was developed in 1985 via a comparative study using a computer-solved model. The study was a mathematical modeling analysis based on published physiological data, rather than a clinical trial with direct patient enrollment. The estimated insulin resistance obtained by the calculator correlated well with estimates obtained by using the euglycemic clamp (Rs = 0.88, p< 0.0001), the fasting insulin concentration (Rs = 0.81, p < 0.0001), and the hyperglycemic clamp, (Rs = 0.69, p < 0.01) (Rs: Spearman's rank correlation coefficient).[24] The study introduced a novel, non-invasive surrogate for insulin resistance with strong correlations with gold standard measures. However, it was based on a simplified feedback loop, which may not have captured dynamic physiology. Also, the coefficients of variation were high at 31% for insulin resistance and 32% for β-cell function which in turn indicate poor reproducibility and lack of sufficient accuracy for therapeutic decision.

The calculator was validated in a study published in 2000 by Bonora et al.[4] This was a cross-sectional validation study in 53 patients with diabetes and 62 patients without diabetes to evaluate whether the HOMA-IR is a reliable surrogate measure of in vivo insulin sensitivity in humans. Patients on insulin, recent acute illness, clinical evidence of cardiovascular, kidney, or liver disease were excluded. It showed strong correlation between HOMA-IR and clamp-derived glucose disposal with overall r = −0.82, p < 0.0001, and no substantial differences were noted in correlation between patients with and without diabetes. The study concluded that HOMA-IR can be reliably used in large-scale or epidemiological studies. Katsuki et al., using a univariate regression analysis, further validated the calculator by demonstrating a significant correlation between log-transformed HOMA-IR and log-transformed clamp IR before (r = -0.613, p < 0.0001) and after (r = -0.734, p < 0.0001) treatment in 55 Japanese patients with type 2 diabetes.[25] Both Ikeda et al. and Sarafidis et al. came to similar conclusions in patients with diabetes and hypertension.[26,27]

A recent meta-analysis conducted by Otten et al. showed that the log-transformed HOMA-IR had a pooled correlation coefficient of −0.60 (95% CI: −0.66 to −0.53) across 22 studies.[28] Although the correlation was significant, it was still below other fasting indices of insulin resistance like revised QUICKI (r = 0.68) and OGTT-based indices like Matsuda and Stumvoll MCR (r = 0.70).[28]

However, it is important to know that no major clinical guidelines from prominent organizations like the American Diabetes Association or the European Association for the Study of Diabetes endorse HOMA-IR for routine clinical use. An impact analysis done by Wallace et al. demonstrated that HOMA-IR is validated against gold standard methods and useful for large-scale studies, but its reliability depends on input data and interpretation. The authors also caution against using HOMA-IR to assess β-cell function in isolation or in clinical scenarios where dynamic testing is more appropriate.[6]

Of note, a modified version of the calculator called HOMA2-IR was published in 1998. It considers hepatic as well as peripheral glucose resistance, increase in insulin secretion at higher glucose, and the impact of proinsulin. However, this is not a simple equation and requires computer software to run calculations. Currently, a license is required from Oxford University Innovations to run this software, limiting daily use in clinical settings.

FORMULA

Score = (Fasting insulin, uIU/mL)*(Fasting glucose, mg/dL) / 405

FACTS & FIGURES

A HOMA-IR score ≥2.5 is generally considered indicative of insulin resistance, but the optimal cutoff may vary by clinical context and population.

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