Sonora Quest Laboratories™
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Cardio IQ® Insulin Resistance Panel With Score

Test Code: 906974

Specimen Requirements: 0.5 mL refrigerated serum; 0.3 mL minimum

Overnight fasting required

CPT Codes*: 83525, 84681

CLINICAL USE

- Identify insulin resistance

CLINICAL BACKGROUND

In individuals with insulin resistance (IR), cells become less sensitive to the effects of insulin and do not absorb enough glucose from the bloodstream. IR can progress to prediabetes and type 2 diabetes mellitus (DM). IR is also associated with other clinical conditions, including hypertension, cardiovascular disease, stroke, nonalcoholic fatty liver disease, polycystic ovary syndrome, and certain forms of cancer.[1] Early recognition and intervention can help reverse IR or prevent its progression, and thereby reduce the risk of these clinical conditions.[1]

The onset of IR can be gradual and difficult to recognize. In early stages of IR, before prediabetes develops, pancreatic beta-cells may produce high levels of insulin to offset the reduced insulin sensitivity. This increased insulin production can maintain normal levels of blood glucose and hemoglobin A_{1c} (HbA_{1c}). Consequently, monitoring glycemic indices alone will not detect the onset of IR. As insulin sensitivity continues to decline (and insulin resistance increases), the increased insulin production will not be able to maintain normal glucose levels. Glucose levels rise, and prediabetes and type 2 DM can develop.

Methods used in a research setting, such as the hyperinsulinemic euglycemic glucose clamp[2] or the insulin suppression test,[3] can detect IR even in individuals with normal glucose levels. However, these methods are time consuming and labor-intensive, making them impractical for use in a primary-prevention clinic.

Simpler testing methods using surrogate markers of IR are available that correlate with the insulin suppression test.[4] One method, fasting plasma insulin, simply measures insulin. Another method, the homeostatic model assessment of insulin resistance (HOMA-IR), is based on fasting insulin and glucose levels.[5] However, both insulin measurement and the HOMA-IR have shortcomings for assessment of IR. Fasting insulin levels are typically low and fluctuate because of hepatic and renal clearance mechanisms.[6,7] In addition, various immunoassay platforms may yield systematically different results owing to differences in antibody specificity and the procedures used to trace insulin concentration back to reference values.[8,9]

C-peptide, a peptide co-secreted with insulin from the beta-cells, can serve as an indirect marker of IR and has some advantages over insulin for assessing IR.[5] For example, although it is secreted in similar amounts as insulin, C-peptide has a longer half-life in circulation.[5-7] As a result, it is present at 3- to 6-fold higher levels than insulin and exhibits less fluctuation.[6,7] However, C-peptide measurements are not typically performed because of the costs and inconvenience associated with collecting additional samples and performing an additional assay for C-peptide.[5]

The Cardio IQ® Insulin Resistance Score combines fasting insulin and C-peptide measurements to evaluate the likelihood that an individual has IR. Both analytes are simultaneously quantified by liquid chromatography–tandem mass spectrometry (LC/MS/MS). Because the insulin/C-peptide LC/MS/MS assay measures only intact molecules, it eliminates the possibility of cross-reactivity that can affect some immunoassays. In addition, results are traceable, by mass, to the dry weight of pure peptide, avoiding another potential source of variability.[9,10] Finally, because the LC/MS/MS assay measures insulin and C-peptide simultaneously, it does not require multiple samples.

The insulin resistance score was developed in a study of 535 apparently healthy individuals and used to estimate their odds of having IR, as assessed using the insulin suppression test.[11] The association of scores with IR is summarized in the **Table**.

Table. Association Between IR Score and IR Determined During an Insulin Suppression Test[11]

IR Score	Odds of IR (95%CI)
<33	1 (reference)
33 to ≤66	4.4 (2.5 to 7.8)
>66	15.6 (7.5 to 32.4)

CI, confidence interval; IR, insulin resistance

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INDIVIDUALS SUITABLE FOR TESTING

- Individuals at risk for insulin resistance, which may lead to prediabetes or type 2 DM (eg, those who are overweight/obese and/or have a family history of DM, a history of gestational DM, or meet the criteria for metabolic syndrome)
- Individuals with clinical features associated with IR (eg, hypertension, central obesity, and acanthosis nigricans [dark patches of thick, velvety skin on the back of the neck, armpits and groin])

METHOD

- High-throughput immunochemical enrichment of intact insulin and C-peptide from serum
- Liquid chromatography-tandem mass spectrometry (LC/MS/MS)
- Quantitation based on standards traceable by peptide content (including WHO international insulin reference preparation 83/500)
- Analytical sensitivity: 3 µIU/mL (insulin); 0.11 ng/mL (C-peptide)
- Analytical specificity: no cross-reactivity with proinsulin
- Reportable ranges: 3 to 320 µIU/mL (insulin); 0.11 to 27.2 ng/mL (C-peptide); 0 to 100 (insulin resistance score)
- Insulin resistance score:
  - calculated using the insulin and C-peptide concentrations converted to pmol/L
  - expressed as a probability ranking of IR

The panel component Insulin, Intact, LC/MS/MS cannot be ordered separately. The C-peptide LC/MS/MS panel component cannot be ordered separately. C-peptide by immunoassay is not an equivalent test and cannot be used in calculation of the Insulin Risk Score.

REFERENCE RANGES

Insulin:	≤16 µIU/mL
C-peptide:	0.68 to 2.16 ng/mL
Insulin resistance score:	1 to 66

INTERPRETIVE INFORMATION

Individuals with elevated fasting insulin and/or C-peptide levels may have IR,[11] which is reflected in the insulin resistance score.

An insulin resistance score of <33 suggests that an individual has normal insulin sensitivity.

A score of 33 to 66 suggests that an individual is >4-fold more likely to have IR than an individual with a score <33 **(Table)**.

A score >66 suggests that an individual is >15-fold more likely to have IR than an individual with a score <33 **(Table)**.

References

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*The CPT codes provided are based on AMA guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payer being billed.

This test was developed and its analytical performance characteristics have been determined by Quest Diagnostics. It has not been cleared or approved by the U.S. Food and Drug Administration. This assay has been validated pursuant to the CLIA regulations and is used for clinical purposes.