

Nonalcoholic Fatty Liver Disease Identified by Intact Insulin



Can intact insulin measured by liquid chromatography/tandem mass spectrometry (LC-MS/MS) accurately detect nonalcoholic fatty liver disease (NAFLD)?

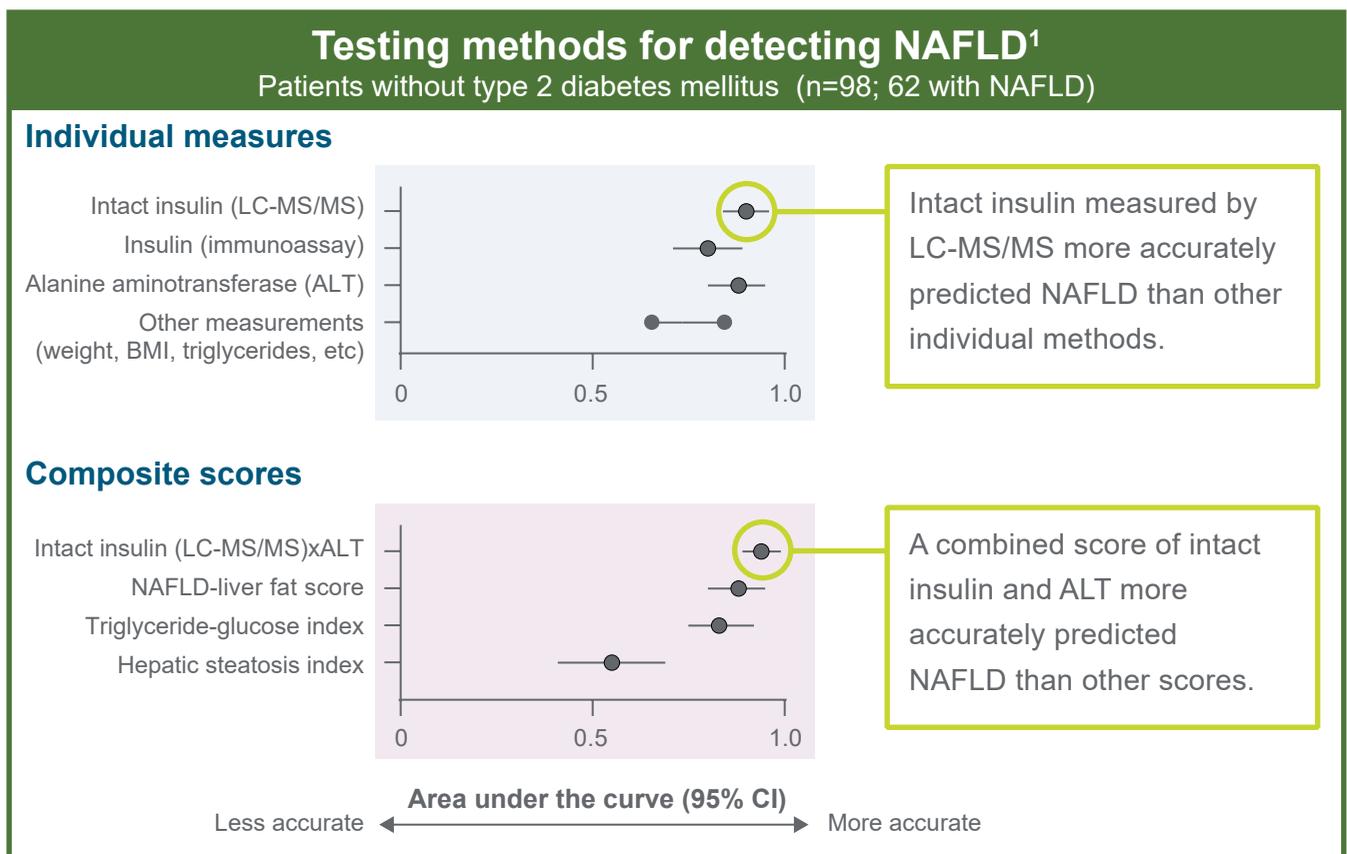


Background

NAFLD and related complications are worldwide public health problems, yet NAFLD remains underdiagnosed. Insulin resistance (IR) is associated with NAFLD, but insulin tests (eg, immunoassays) in past studies have not accurately predicted NAFLD.



Methods and Results



Intact insulin measurement by LC-MS/MS provides a noninvasive approach to accurately predict NAFLD in patients without diabetes, especially when used in conjunction with ALT measurements.

1. Bril F, McPhaul MJ, Kalavalapalli S, et al. *J Clin Endocrinol Metab*. Published online June 30, 2021. doi:10.1210/clinem/dgab417

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Intact Fasting Insulin Identifies Nonalcoholic Fatty Liver Disease in Patients Without Diabetes

Fernando Bril,^{a,b} Michael J McPhaul,^c Srilaxmi Kalavalapalli,^b Romina Lomonaco,^b Diana Barb,^b Megan E Gray,^a Dov Shiffman,^c Charles M Rowland,^c Kenneth Cusi^{b,d}

^aUniversity of Alabama, Birmingham, AL, USA; ^bUniversity of Florida, Gainesville, FL, USA; ^cQuest Diagnostics Nichols Institute, San Juan Capistrano, CA, USA; ^dMalcom Randall, VAMC, Gainesville, FL, USA

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Background

- Identification of nonalcoholic fatty liver disease (NAFLD) may permit the implementation of strategies to prevent progression to advanced liver disease, but NAFLD remains underdiagnosed.¹
- Insulin resistance (IR) is associated with NAFLD,² but methods used to measure IR have not predicted NAFLD in prior studies.^{3,4}
- The discrepancy may be the result of multiple factors: combining patients with and without diabetes in the studies, using assays with low sensitivity for NAFLD (eg, ultrasound, liver enzymes), or measuring insulin with immunoassays, which can be variable.
- **Objective:** This cross-sectional study examined whether measuring intact insulin with a validated multiplexed liquid chromatography-tandem mass spectrometry (LC-MS/MS) method could accurately predict NAFLD.

Methods

- Participants recruited from the general population underwent a 2-hour oral glucose tolerance test (OGTT), with insulin measurements every 30 minutes to determine type 2 diabetes status.
- Liver fat was measured by magnetic resonance spectroscopy (¹H-MRS) to test for NAFLD.
- Fasting plasma levels of intact insulin and C-peptide were measured by the validated LC-MS/MS method; insulin was also measured by radioimmunoassay (RIA).

Results

- Among 180 recruited patients (mean age: 52 years; 67% male), 117 (65%) had NAFLD and 82 (46%) had diabetes.
- Fasting insulin levels were higher among patients with NAFLD (diabetic and non-diabetic) than those without NAFLD.
- Measurement of fasting intact insulin using the LC-MS/MS method predicted NAFLD with high accuracy among patients without diabetes; the area under the receiver operating characteristic curve (AUC) was 0.90 (0.84-0.96), which was greater than that of RIA: 0.80 (0.71-0.89), $P=0.007$.
- For patients without diabetes
 - The LC-MS/MS method (using a cutoff of 10.5 μ U/mL) had a sensitivity of 92.5%, specificity of 71.1%, PPV of 79.0%, and NPV of 88.9% for NAFLD.
 - Intact fasting insulin also predicted NAFLD with greater accuracy than other clinical measurements (eg, ALT, AST, triglycerides, HDL, glucose, hemoglobin A1c, and BMI).
 - However, when measurement of intact fasting insulin was combined with measurement of ALT, the prediction of NAFLD improved (AUC=0.94 [0.89-0.99]; PPV=90.3%; NPV=88.9%).
 - Using both intact fasting insulin and ALT measurements predicted NAFLD better than other previously validated noninvasive scores: NAFLD-liver fat score ($P=0.009$), hepatic steatosis index ($P<0.001$), and triglyceride-glucose index ($P=0.039$).
- Measurement of fasting plasma insulin was less accurate for NAFLD detection in patients with diabetes—the AUC was ≤ 0.75 with either the LC-MS/MS or RIA method.

Conclusions

- The noninvasive LC-MS/MS method of measuring intact fasting insulin accurately predicted NAFLD in patients without diabetes, especially when used in conjunction with ALT measurements.

References

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