Key Summary of Published Article

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

Background

- Identification of nonalcoholic fatty liver disease (NAFLD) may permit the implementation of strategies to prevent progression to advanced liver disease, but NAFLD is often underdiagnosed.[1]
- Insulin resistance (IR) is associated with NAFLD,[2] but methods often used to measure IR have not accurately 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:** The investigators of this study examined whether measuring intact insulin molecules with a validated multiplexed liquid chromatography-tandem mass spectrometry (LC-MS/MS) method could accurately predict NAFLD.

Methods

- Recruited participants underwent a 2-hour oral glucose tolerance test (OGTT), with insulin measurements every 30 minutes.
- Liver fat was measured by magnetic resonance spectroscopy (^{1}H-MRS) to test for NAFLD, which was confirmed with a liver biopsy.
- Intact fasting insulin molecules and C-peptide levels were measured by the validated LC-MS/MS method.

Results

- Among the 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 intact fasting insulin using the LC-MS/MS method predicted NAFLD with high accuracy among patients without diabetes, with area under the receiver operating characteristic curve (AUC)=0.90 (0.84-0.96), which was better than that of radioimmunoassay (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 µU/mL) had a sensitivity of 92.5%, specificity of 71.1%, PPV of 79.0%, and NPV of 88.9%.
- In patients without diabetes, 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%).
- In patients without diabetes, using both intact fasting insulin and ALT measurements predicted NAFLD better than other previously validated noninvasive scores, including the NAFLD-liver fat score (*P*=0.009), hepatic steatosis index (*P*<0.001), and triglyceride-glucose index (*P*=0.039).
- In patients with diabetes, measurement of intact fasting insulin, either by the LC-MS/MS or RIA methods, had lower accuracy (AUC≤0.75).

Conclusions

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

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