Key Summary of Published Article

Use of a Metabolomic Approach to Non-Invasively Diagnose Nonalcoholic Fatty Liver Disease in Patients with Type 2 Diabetes Mellitus

Background

- Nonalcoholic fatty liver disease (NAFLD) is associated with the epidemics of obesity, type 2 diabetes mellitus (T2DM), and metabolic syndrome.[1,2]
- NAFLD can progress to nonalcoholic steatohepatitis (NASH), advanced fibrosis, and even hepatocellular carcinoma.[1,2] It can be difficult to classify, especially in a non-invasive manner.
- Several clinical/metabolic scores have been developed to help assess NAFLD, but they were developed in patients without T2DM and have not been validated in patients with T2DM.
- **Objective:** The investigators evaluated whether metabolomic scores can be applied to patients with T2DM to classify NAFLD.

Methods

- Patients with T2DM (n=220) were recruited in Gainesville, Florida, and San Antonio, Texas, as well as from state university clinics.
- Intrahepatic triglyceride content was measured by proton magnetic resonance spectroscopy (^{1}H-MRS), and insulin resistance/secretion was measured by an oral glucose tolerance test. For patients who had NAFLD diagnosed based on ^{1}H-MRS, a percutaneous liver biopsy was performed to confirm the diagnosis and determine the stage of the disease.
- To determine metabolomic scores, serum specimens were provided to OWL Metabolomics for measurements with the OWLiver® Care and OWLiver tests.
- Scores were evaluated for concordance with biopsy results.

Results

- For the overall cohort of T2DM patients, the OWLiver Care and OWLiver test results had suboptimal performance for detection of biopsy-proven NASH (AUROCs <0.70). This result was inconsistent with previous studies that included mostly Caucasian, non-diabetic patients.
- Because the population in this study was heterogeneous, investigators examined the effects of patient characteristics on test performance. No differences in performance were observed based on age (>65 vs <65 years old), sex, ethnicity (Caucasian vs Hispanic vs other ethnicity), or diabetes control (with or without).
- The investigators found that test performance did improve in subsets of patients that mirrored those used to develop the OWLiver models (ie, European, Caucasian, without T2DM).
  - Patients with good glycemic control (HbA1c<7.0%) and without cirrhosis: AUROC=0.79 (0.68–0.90)
  - Patients with lower insulin resistance and without cirrhosis: AUROC=0.87 (0.76-0.97)

Conclusions

- Metabolomic scores developed for identifying NAFLD and NASH in patients without T2DM cannot be applied to those with T2DM.
- A diabetes-specific, non-invasive test is still needed for patients with T2DM.

Published article in the journal *Diabetes, Obesity, and Metabolism*

Authors

Fernando Bril,[1,2] Laura Millán,[3] Srilaxmi Kalavalpalli,[1] Michael J McPhaul,[4] Michael P Caulfield,[4] Ibon Martinez-Arranz,[3] Cristina Alonso,[3] Pablo Ortiz Betes,[3] José M Mato,[5] Kenneth Cusi[1,2]

Affiliations

[1] Division of Endocrinology, Diabetes and Metabolism, University of Florida, Gainesville, FL
[2] Malcom Randall Veterans Administration Medical Center, Gainesville, FL
[3] OWL Metabolomics, Derio, Spain
[4] Quest Diagnostics Nichols Institute, San Juan Capristano, CA
[5] CIC bioGUNE, CIBERehd, Derio, Spain

Citation

Bril, F, Millán L, Kalavalpalli S, et al. *Diabetes Obes Metab*. 2018; Mar 12. doi: 10.1111/dom.13285.

Webpage

https://www.ncbi.nlm.nih.gov/pubmed/29527789

References

1. Carr RM, Oranu A, Khungar V. *Gastroenterol Clin North Am*. 2016;45:639−652.
2. Pappachan JM, Babu S, Krishnan B, et al. *J Clin Transl Hepatol*. 2017;5:384−393.