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Lean non-alcoholic fatty liver disease patients from the global NASH registry

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THU068

Postprandial dysfunction in metabolic associated fatty liver disease (MAFLD)

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Background and aims: Fatty liver disease has been associated with metabolic disturbances. MAFLD is defined as hepatic steatosis with either overweight, type 2 diabetes (T2D), or at least two metabolic comorbidities. We hypothesized that metabolic disturbances associated with liver disease are pronounced in the postprandial phase and may be identified by a standardized meal. We therefore aimed to study the fasting and postprandial state in biopsy-proven healthy, MAFLD and cirrhosis.

Method: We included 29 participants, 10 healthy controls (age 23 ± 0 years, BMI 25 ± 1 kg/m^2), 9 patients with non-alcoholic fatty liver disease (NAFLD) (age 50 ± 5 years, BMI 35 ± 2 kg/m^2, no/mild fibrosis) and 10 patients with cirrhosis (age 62 ± 3 years, BMI 32 ± 2 kg/m^2, Child A/B). None of the included participants had T2D. The participants were randomized 1:1 to "fasting" or "postprandial" (Nutridrink, Nutricia, 300 kcal). Blood samples were obtained at baseline and 15, 45, 60, 90 and 120 minutes. At time point 60, blood from the liver vein was collected and a transjugular liver biopsy was performed. Levels of glucose, insulin, C-peptide, glucagon, and fibroblast growth factor 21 (FGF21) were measured in peripheral blood, and glucagon and FGF21 as well in liver vein blood. Results are presented as ± SEM. Peak concentrations were calculated as mean ± SEM of individual peaks. The analyses compared controls versus NAFLD and cirrhosis.

Results: 8/9 patients with NAFLD and 9/10 patients with cirrhosis were classified as MAFLD. Postprandial increase in glucose and C-peptide was significantly greater in NAFLD and cirrhosis compared to controls, with peak glucose of 7 and 10 mmol/L (p = .006), and peak C-peptide of 2675 ± 273 and 3340 ± 1048 pM versus 1689 ± 190 pM. Postprandial iAUC for insulin was greatest in patients with NAFLD (p = .037). Patients with NAFLD and cirrhosis had hyperglucagonemia, a phenotype causally related to prediabetes. FGF21 was significantly increased in NAFLD and cirrhosis and correlated to age (r = .61, p = .001) and fasting glucose (r = .54, p = .006). Glucagon was higher in liver vein compared to peripheral blood while FGF21 levels were similar in liver and peripheral blood.

Conclusion: We found significant metabolic dysfunction after a test meal in patients with MAFLD without diabetes compared to healthy controls and that finding that was pronounced in cirrhosis. Patients with MAFLD had impaired glucose tolerance, hyperinsulinemia and hyperglucagonemia, suggesting MAFLD to be a condition of prediabetes.

THU069

Lean non-alcoholic fatty liver disease patients from the global NASH registry

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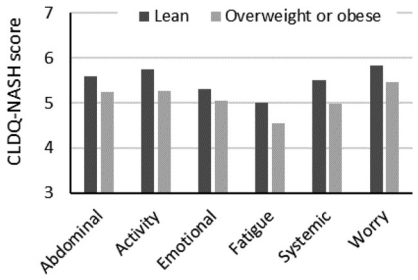
Background and aims: Although vast majority of patients with NAFLD are overweight and obese, NAFLD can be seen among lean individuals. The aim was to assess prevalence of lean NAFLD in different regions of the world.

Method: The Global NASH Registry enrolled patients with an established diagnosis of NAFLD from real-world practices in 18 countries (Australia, China, Cuba, Egypt, Greece, Hong Kong, India, Italy, Japan, Saudi Arabia, Malaysia, Mexico, Pakistan, Russia, Spain, Taiwan, Turkey, USA) in 6 out of 7 Global Burden of Disease (GBD) super-regions. Clinical and patient-reported outcomes (PRO) data (CLDQ-NASH, FACIT-F, WPAI) were collected. Lean NAFLD was defined as NAFLD in patients with BMI <25 kg/m2, or 23 kg/m2 for patients of East Asian origin.

Results: There were 6096 NAFLD patients included (as of November 10, 2021): 48% from High-Income super-region, 24% Middle East and North Africa (MENA), 12% Southeast Asia, 7% Latin America, 6% from Eastern Europe and Central Asia, and 3% South Asia super-region. Of these, 7.3% were lean. The rates of lean NAFLD were the highest in Southeast Asia (12%) and South Asia (31%), the lowest in Eastern Europe and Central Asia (<2%) and MENA (4%) (p < 0.0001). In comparison to overweight/obese patients, lean NAFLD patients were older (mean age 53 vs. 51 years) and predominantly of Asian race (48% vs. 18%) (p < 0.01). Furthermore, lean patients had lower rates of diabetes (28% vs. 41%), hypertension (35% vs. 52%), hyperlipidemia (40% vs. 50%), sleep apnea (8% vs. 33%), clinically overt fatigue (25% vs. 36%), and histologic cirrhosis (10% vs. 15%), but more abdominal pain (25% vs. 18%) and higher FIB-4 scores (mean 1.8 vs. 1.3) (all p ≤0 .02). In multivariate analysis, having lean NAFLD (as opposed to overweight/obese NAFLD) was independently associated with older age (OR = 1.019 (1.008–1.030) per year), enrollment outside of MENA region (OR = 0.43 (0.31–0.58)) and from South Asia (OR = 5.01 (3.42–7.45)) sites (reference: High-Income), absence of type 2 diabetes

(OR = 0.61 (0.46–0.80)) and hypertension (OR = 0.46 (0.35–0.60)), and presence of regular exercise (OR = 1.55 (1.21–2.00)) (all p < 0.01). Lean NAFLD also had higher PRO scores than overweight/obese NAFLD (all domains of CLDQ-NASH and FACIT-F) (all p < 0.01) (Figure). In multivariate analysis, lower total CLDQ-NASH scores (range 1–7) in lean NAFLD patients were independently associated with enrollment from MENA region, history of anxiety, depression, fatigue, and abdominal pain (beta from – 0.40 to – 0.67 for each condition) (p < 0.01).



Conclusion: Lean NAFLD patients seen in real-world practices across the world have different clinical and PRO profiles in comparison to NAFLD patients who are overweight or obese.

THU070

Automated FIB-4 calculator and targeted provider education improved referral of at-risk fibrotic NAFLD patients

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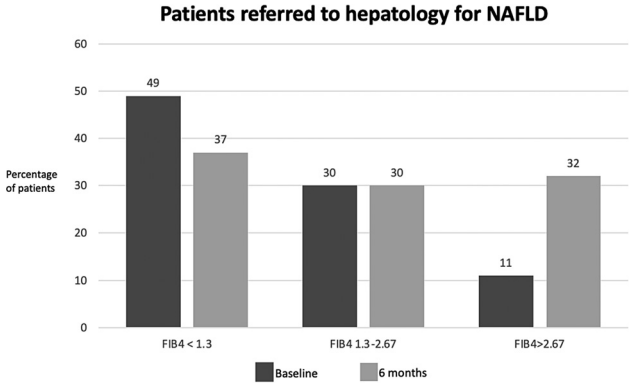
Background and aims: Non-alcoholic fatty liver disease (NAFLD) is the leading cause of chronic liver disease with increasing rates globally. Patients with a higher degree of liver fibrosis in NAFLD are at an increased risk for liver-related mortality but get missed easily during the referral process, based on our[1] and other prior data[2]. Our project aims to improve early detection and linkage-to-care of fibrotic NAFLD patients using a combination of automated electronic health record (EHR)-based FIB-4 score and directed provider education within our tertiary care center, serving a large population of Northern California.
Method: We implemented a health-system wide FIB-4 score calculator, embedded in the EHR that providers can easily add to their workflow for NAFLD patient triaging. Subsequently we provided targeted education to all relevant providers taking care of NAFLD patients. All referrals for NAFLD (defined by specific ICD 9/10 codes), to the hepatology from February 2020- August 2021, were retrieved. Patient characteristics were determined with FIB-4 score being essential for determination of fibrotic NAFLD and comparative analysis with prior data[1].
Results: A total of 303 referrals were placed for NAFLD, of which 62% (n = 188) patients had FIB-4 score at the time of referral. Of the 188 patients, 62 patients with diabetes mellitus and 44% of them had FIB-4 ≥1.3. Compared to prior referrals of 49% with FIB-4 score<1.3, in current referrals after a 6-month post-FIB-4 triage implementation, 37% had FIB-4 <1.3 (Fig 1). This suggested a decrease in unnecessary referrals to hepatology. Primary care doctors referred 73% while endocrinology referred 1% of all patients. We noted higher rates of fibrotic NAFLD patients with FIB-4 ≥1.3 in current referrals compared to prior (63% vs 41%). Furthermore, 32% of current referrals were with severe fibrotic disease defined by FIB-4 >2.67 vs 11% previously (Fig 1). This suggested an increase in appropriate referrals for specialty care. Secondary fibrotic testing using imaging modalities such as ultrasound or magnetic resonance elastography was done in 36% of those with FIB-4 ≥1.3, suggesting room for further refinement.



Conclusion: Automated FIB-4 score in EHR can improve appropriate linkage-to-care for at-risk fibrotic NAFLD, especially when coupled with targeted provider education. The durability of such improvement is essential to study along with the need to increase broad acceptance across health systems.

References

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THU071

Long term outcomes of non-alcoholic fatty liver disease (NAFLD) and metabolic associated fatty liver disease (MAFLD)

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Background and aims: NAFLD and MAFLD are part of the spectrum of fatty liver disease (FLD). Our aim was to compare the outcomes of patients with NAFLD or MAFLD.
Method: Using data from NHANES III and NHANES 2017–2018, FLD was defined as moderate to severe hepatic steatosis by ultrasound (NHANES III) or controlled attenuation parameter (CAP) of ≥285 dB/m (NHANES 2017–2018). Death data were obtained from National Death Index (NDI). NAFLD was defined as FLD without other liver diseases and excessive alcohol consumption (EAC). MAFLD was define as FLD with metabolic dysfunction-one of the following three criteria, overweight/obesity, presence of type 2 diabetes mellitus or metabolic dysregulation (at least two metabolic risk abnormalities).