Lean NAFLD patients have lower prevalence of cardiovascular, metabolic and severe liver disease compared to overweight or obese patients with NAFLD

TARGET-NASH

TARGET PharmaSolutions

EASL European Association for the Study of the Liver

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INTRODUCTION

- Nonalcoholic fatty liver disease (NAFLD) is associated with obesity, but it is also seen in patients with a normal BMI (lean NAFLD)
- Lean NAFLD is more common among Asians than other races.
- This study estimated the prevalence and odds of NAFLD cirrhosis, cardiovascular (CV) and metabolic abnormalities by BMI category and race in TARGET-NASH.

METHODS

Cohort

- TARGET-NASH is an ongoing longitudinal, observational cohort of patients with NAFLD managed according to local practice standards at 55 academic and community sites in the United States.
- Participating clinics provided redacted medical records (structured and unstructured data) from consented patients. Patient narratives, laboratory, pathology, and imaging data were extracted and stored in a secured database. Patient reported outcome (PRO) measures were also collected on an annual basis. Patients contributed blood samples to a biospecimen repository for biomarker validation and translational research

Study Population

This analysis included 3,386 adults enrolled in TARGET-NASH between October 4, 2018 and March 4, 2019.

Clinical Case Definitions of NAFLD

NAFLD Cirrhosis	**History of NAFLD with:** **1) Liver biopsy with fibrosis stage = 4 OR** **2) Liver biopsy with fibrosis stage = 3 and 1 ≥ clinical signs of cirrhosis OR** **3) 2 or more clinical signs of cirrhosis OR** **4) FibroScan® elastography result ≥ 11 kPa**
NASH	**Confirmed by biopsy:** • **Steatohepatitis by Brunt criteria OR NAS total score ≥ 4** **Clinical diagnosis:** • **ALT > 19 U/L for adult female (22 child), > 30 U/L for adult male (26 child) and;** • **Hepatic steatoses on biopsy or CT/US/MRI and;** • **1 of the following: BMI ≥ 30, type 2 diabetes, dyslipidemia**
NAFL	**Any participant not meeting criteria for clinical NASH or cirrhosis**

BMI Categories

Patients with NAFLD were stratified into BMI categories based on the World Health Organization (WHO)[1] and "Asian Cutoff" values.[2]

WHO
- Lean (>18.5-25)
- Overweight (>25-30)
- Obese (>30-35)
- Morbid Obesity (>35)

Asian Criteria
- Lean (>18.5-23)
- Overweight (>23-27.5)
- Obese (>27.5)

Patients who were underweight were excluded

Statistical Analysis

- The prevalence of CV and metabolic abnormalities was estimated among patients with NAFLD by BMI category and severity of liver disease.
- The odds of CV and metabolic abnormalities as well as 95 % confidence intervals were estimated adjusting for age and sex. Site type was included as a random effect.

RESULTS

Table 1. Descriptive characteristics of the patients with NAFLD by BMI Category

Patient Characteristics	Lean (N=433) N(%)	Overweight (N=917) N(%)	Obese (N=896) N(%)	Morbid Obsity (N=1140) N(%)	P values (Lean vs Non-Lean)
Age at Study Entry; Mean (SD)	58.5 (13.1)	58.8 (12.6)	57.0 (12.9)	54.7 (12.9)	0.0073
Liver Disease Severity					
NAFLD Cirrhosis	102 (23.6)	334 (36.4)	381 (42.5)	552 (48.4)	
NASH	137 (31.6)	365 (39.8)	406 (45.3)	462 (40.5)	
NAFL	194 (44.8)	218 (23.8)	109 (12.2)	126 (11.1)	
Not Available	–	–	–	–	<0.0001
Sex					
Male	178 (41.1)	452 (49.3)	381 (42.5)	391 (34.3)	
Female	255 (58.9)	465 (50.7)	515 (57.5)	749 (65.7)	
Not Available	–	–	–	–	0.8931
Race					
White	189 (43.6)	643 (70.1)	729 (81.4)	967 (84.8)	
Black	10 (2.3)	38 (4.1)	47 (5.2)	83 (7.3)	
Asian	204 (47.1)	164 (17.8)	43 (4.8)	8 (0.7)	
Other	16 (3.7)	37 (4.0)	36 (4.0)	37 (3.2)	
Not Available	14 (3.2)	35 (3.8)	41 (4.6)	45 (3.9)	<0.0001
Ethnicity					
Hispanic or Latino	29 (6.7)	128 (14.0)	133 (14.8)	126 (11.1)	
Not Hispanic or Latino	387 (91.9)	760 (85.0)	727 (83.6)	975 (88.2)	
Not Available	12 (2.8)	23 (2.5)	26 (2.9)	34 (3.0)	0.0005

CONCLUSIONS

- Lean NAFLD comprised 12.8% of the cohort and was significantly more prevalent among Asians.
- Asians had a significantly lower prevalence of cirrhosis and were 62% less likely to have any history of CV disease compared to Non Asians.
- Asians were also approximately 14% less likely to have HTN or Diabetes.
- Longitudinal follow-up is ongoing to determine if lean patients with NAFLD have slower progression of liver disease, in particular among lean Asians.

ACKNOWLEDGEMENTS

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Figure 1. Distribution of cardiovascular and metabolic disease by BMI category among patients with NAFLD

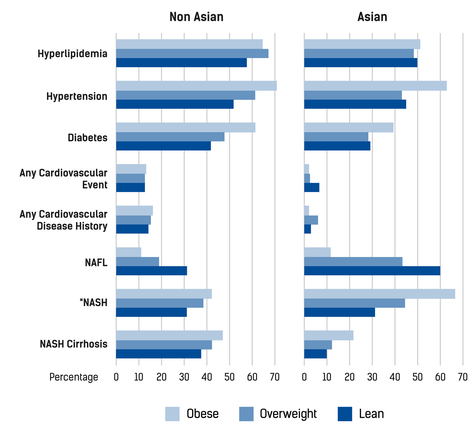
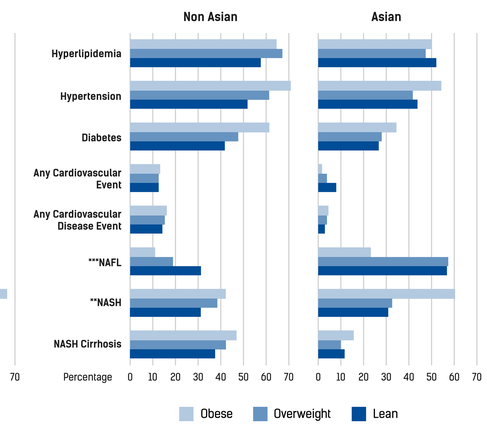


Figure 2. Distribution of cardiovascular and metabolic disease by race specific BMI category among patients with NAFLD



Any Cardiovascular Event: As indicated by medical history, adverse events or procedures.
Diabetes: As indicated by medical history, adverse events, concomitant medications or HbA1c>6.5.
Hypertension/Hyperlipidemia: As indicated by medical history, adverse events or concomitant medications *p=0.0460; **p<0.001; ***p =0.0070

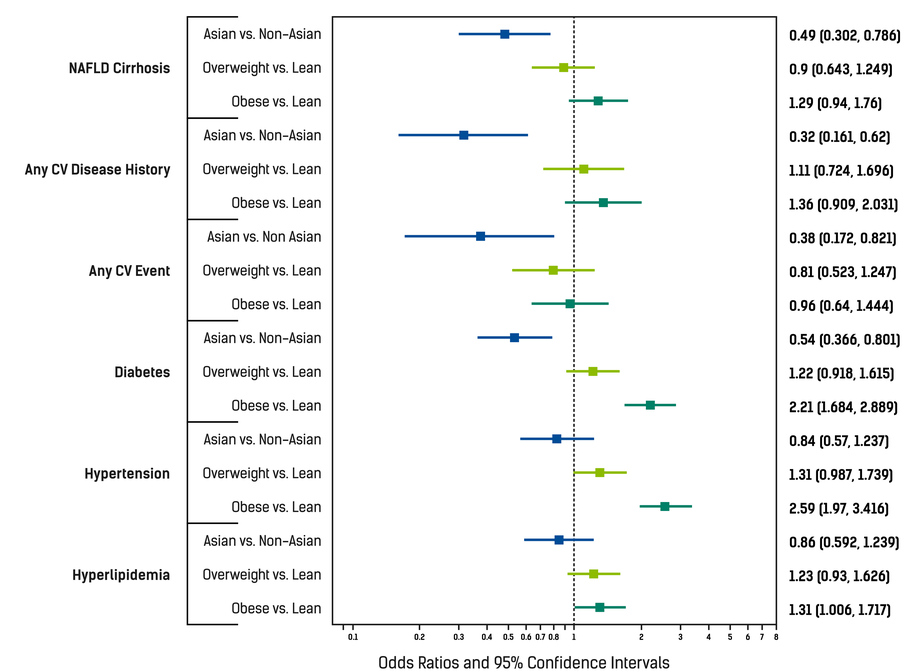



Figure 3. Odds of cardiovascular, metabolic disease, and severity of liver disease among Asians vs Non Asians and by BMI category