Identification of High-Risk Patients With Nonalcoholic Fatty Liver Disease Using Noninvasive Tests From Primary Care and Endocrinology Real-World Practices

Zobair M. Younossi, MD, MPH[1,2], Huong Pham, BS[1], Sean Felix, BS[1], Maria Stepanova, PhD[3], Thomas Jeffers, BS[1,4], Elena Younossi, BS[1], Hussain Allawi, MD[1], Brian Lam, PA-C[1,4], Rebecca Cable, BS[1,4], Mariam Afendy, BS[1,4], Zahra Younoszai, MPH[1,4], Arian Afendy, BS[1,4], Nila Rafiq, MD[1,2,4], Nahrain Alzubaidi, MD[2,4], Yasser Ousman, MD[2], Marc Bailey, MD[2], Zik Chris, MD[2], Maria Castillo-Catoni, MD[2], Pratima Fozdar, MD[2], Maria Ramirez, MD[2], Mehreen Husain, MD[2], Evis Hudson, MD[2], Ingrid Schneider, MD[1], Pegah Golabi, MD[1,2] and Fatema Nader, MSBM[3]

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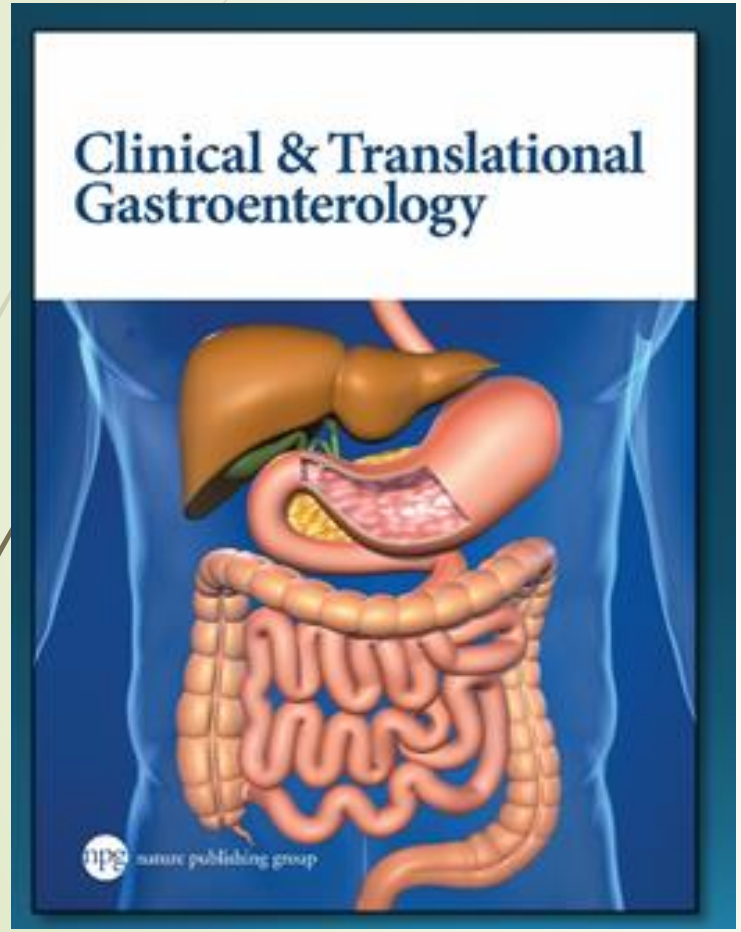
About the Journal



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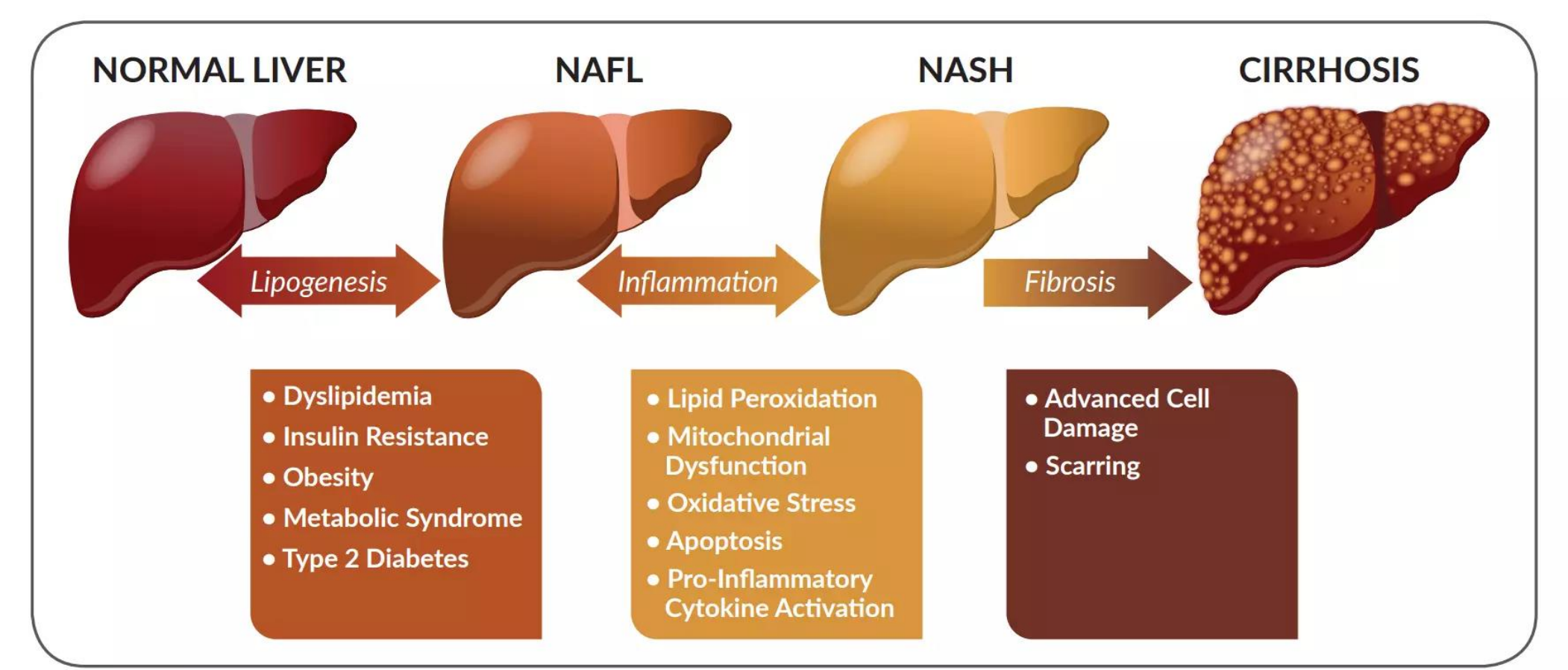
Introduction

Nonalcoholic fatty liver disease (NAFLD) is

- the most common cause of chronic liver disease
- defined as at least 5% fat deposition in the hepatic parenchyma in the absence of other causes of fatty liver or chronic liver disease
- a heterogeneous disease and includes nonalcoholic steatohepatitis (NASH)
- Associated with components of metabolic syndrome



Adapted from : www.caymanchem.com

Introduction

- it is estimated that 15%–20% of patients with NASH can progress to cirrhosis
- NAFLD is now the main driver of cirrhosis, HCC, or being listed for liver transplantation in the United States
- presence of T2DM is the most important clinical driver of mortality in patients with NAFLD

Introduction

- Burden of NAFLD is growing
- identification of these patients and linking those who are at high risk to preventative care and treatment are lacking

Introduction

- Presence of T2DM or other components of metabolic syndrome and
- histologic stage of fibrosis

can provide some clues about patients with NAFLD who are at risk of adverse outcomes

- large volumes of liver biopsies in the clinical practice is impractical
- replacing histologic staging with noninvasive tests (NITs) for fibrosis

Introduction

Noninvasive tests for assessment of fibrosis in NAFLD :

- serum biomarker-based scores :
  e.g APRI, NFS, FIB-4

- imaging-based assessment of liver stiffness :
  transient elastography (TE)

Introduction

- Each single NIT has limited accuracy
- Clinical profiles, serum NITs, and TE can be used in combination to identify high-risk NAFLD patients

- **The aim of the study was to identify patients with NAFLD who are at the highest risk of adverse outcomes and to link them to appropriate care with the aim to optimize their clinical care**

Methods

Study population

- A 2-step screening method was performed. Study inclusion criteria required having 1 of the following:

1. presence of established T2DM and 1 other component of metabolic syndrome (hypertension, hyperlipidemia, BMI > 29.9)
2. T2DM with elevated AST or ALT levels (1.5 x upper limit of normal) or history of fatty liver by any imaging modality
3. in the absence of established T2DM, presence of 3 components of metabolic syndrome

Main exclusion criteria were other causes of chronic liver disease and inability/unwillingness to provide consent.

Methods

Study population

- Study staff screened individuals for the inclusion/ exclusion criteria using their electronic medical record
- Patients were then contacted and invited to participate by telephone
- After informed consent, clinical and demographic data were collected using a pre-specified data collection form
- parameters included age, sex, ethnicity, BMI, comorbidities, and laboratory results.
- Based on these data, NITs were used to determine high-risk patients.

Methods

Detection of high-risk patients and linkage to care

3 NITs (AST-to-platelet ratio [APRI], NAFLD Fibrosis Score [NFS], and FIB-4 index) were calculated

- For **NFS**, 2 cutoff to identify presence (>0.67) and absence (<-1.45) of significant fibrosis

- For the **FIB-4 index** a value <1.45, excludes advanced hepatic fibrosis with 90%–98%certainty

and a threshold value of> 3.25 for the FIB-4 index, leads to a ppv of 53%–75% for advanced fibrosis

- Sensitivity and specificity of an **APRI score**>1 for significant fibrosis is 30% and 92.8%, respectively.

Methods

Detection of high-risk patients and linkage to care

- The criterion for high-risk NAFLD was to have **at least 2 NITs above certain thresholds**
- Participants who fulfilled this criterion were eligible for the linkage-to-care step
- If they agreed, they were referred to a gastroenterology or hepatology clinic
- Medical history was collected followed by physical examination, blood sample collection, and TE

Methods

Patients with **liver stiffness** of

≤ 6 kPa	→	no significant hepatic fibrosis
≥8 kPa	→	clinically significant fibrosis
≥ 12kPa	→	advanced fibrosis or cirrhosis

Results

- A total of 7,555 patients were screened for the study
- 1,707 (22.6%) participants met the initial inclusion criteria
- Among them, 716 (42%) agreed to proceed with the 2nd step of screening by NITs
- 184 patients were eligible for linkage to care
- 103 participants agreed to be linked to GE-HEP for clinical assessment and TE.

Table	Linked	Not linked	Prob	All called
N	103	613		716
Eligible	103 (100.0%)	81 (13.2%)	<0.0001	184 (25.7%)
Age	68.3 ± 9.6	58.3 ± 13.1	<0.0001	59.7 ± 13.1
Male sex	53 (51.5%)	247 (40.3%)	0.0336	300 (41.9%)
Race				
White	60 (58.3%)	325 (53.3%)	0.35	385 (54.0%)
Black	30 (29.1%)	181 (29.7%)	0.91	211 (29.6%)
Hispanic	4 (3.9%)	45 (7.4%)	0.19	49 (6.9%)
Asian	5 (4.9%)	42 (6.9%)	0.44	47 (6.6%)
BMI, kg/m^2	31.4 ± 6.6	33.2 ± 7.7	0.041	33.0 ± 7.5
Diabetes	56 (54.4%)	266 (43.4%)	0.0383	322 (45.0%)
Hyperlipidemia	91 (88.3%)	527 (86.0%)	0.52	618 (86.3%)
Hypertension	85 (82.5%)	507 (82.7%)	0.96	592 (82.7%)
History of myocardial infarction	9 (8.9%)	25 (4.1%)	0.0354	34 (4.8%)
History of stroke	4 (4.0%)	27 (4.4%)	0.83	31 (4.4%)
History of congestive heart failure	1 (1.0%)	14 (2.3%)	0.39	15 (2.1%)
History of cancer	24 (23.5%)	89 (14.5%)	0.0213	113 (15.8%)
APRI	0.419 ± 0.282	0.219 ± 0.108	<0.0001	0.247 ± 0.162
Fibrosis-4 (FIB-4)	2.07 ± 0.80	1.06 ± 0.51	<0.0001	1.20 ± 0.67
NAFLD Fibrosis Score	0.382 ± 0.996	−1.11 ± 1.42	<0.0001	−0.893 ± 1.464

APRI, AST-to-platelet ratio; AST, aspartate aminotransferase; BMI, body mass index; NAFLD, nonalcoholic fatty liver disease.

Results

Table 2. **Distribution of patients based on fibrosis severity by transient elastography**

	All
N	103
Liver stiffness < 6 kPa	62 (60.2%)
Liver stiffness 6–8 kPa	23 (22.3%)
Liver stiffness 8–10 kPa	6 (5.8%)
Liver stiffness 10–12 kPa	4 (3.9%)
Liver stiffness ≥12 kPa	8 (7.8%)

kPa, kilopascal.

Results

Patients with liver stiffness of ≥8 kPa on TE

- were *younger* (mean age 61.3 vs 69.9 years
- had higher mean BMI (36.5 vs 30.5),
- higher controlled attenuation parameter (318 vs 274 dB/m2),
- higher AST (44 vs 25 U/L), ALT (51 vs 23 U/L), and alkaline phosphatase(95 vs 76 U/L) levels
- higher APRI (0.665 vs 0.316) (all $P < 0.05$)

but

- similar FIB-4 index (2.36 vs 1.90)
- and NFS (0.705 vs 0.281) ($P > 0.05$)

Results

- Compared with non-cirrhotic patients (liver stiffness <12 kPa),patients with presumed cirrhosis (liver stiffness ≥12 kPa had higher
- mean BMI (36.4 vs 31.2 years)
- AST (53 vs 26 U/L), ALT (59 vs 26 U/L), and alkaline phosphatase (116 vs 76 U/L) levels
- higher APRI (0.894 vs 0.333), FIB-4 index (3.21 vs 1.88), NFS (1.580 vs 0.252),
- and were more likely to have diabetes (100% vs 51.6%), history of CVD (50% vs 12.8%), and MI (25% vs 4.3%) (all $P < 0.05$).

Discussion

- NAFLD and its progressive form NASH have become the fastest growing causes of chronic liver disease
- most patients with NAFLD have likely not been identified and most of them are being seen in the primary care practices without being diagnosed
- 10%–15% of those with NASH may progress to cirrhosis
- identifying patients with NAFLD who are at risk of adverse outcomes will be critical to address the increasing burden of NAFLD.

Discussion

- The main strength of the current study is the prospective application of a stepwise algorithm in real-world practices for detection of patients who had the highest risk of NAFLD
- liver biopsy remains the gold standard for detecting and grading liver fibrosis but cannot be used in a large scale in the clinical practice
- **this study demonstrates that a stepwise prospective application of an algorithm using NITs and TE in clinical practice setting can lead to identification of patients with high-risk NAFLD**

Thanks for your attention