Assessment of fatty liver disease using a biomarker-based noninvasive algorithm LIVERFASt™ test in South-East Asia

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Background/Aim

Prevalence of NAFLD (Nonalcoholic Fatty Liver Disease) and resulting NASH (Nonalcoholic SteatoHepatitis) are constantly increasing worldwide[1] creating challenges for screening, as the diagnosis for NASH requires invasive liver biopsy. Key issues in NAFLD patients are the differentiation of NASH from simple steatosis and identification of advanced hepatic fibrosis[2].

Noninvasive tests could be used as screening tools to identify patients with NAFLD at high risk of progression[3]. Study aim is to analyze real-world evidence of a non-invasive machine learning algorithm LIVERFASt™ (Figure 1) to diagnose fatty liver disease in patients across South-East Asia.

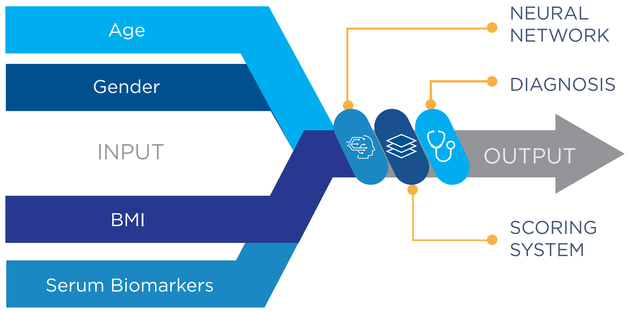
Table 1. Characteristics of the population in South East Asia. SD, standard deviation: BMI, body mass index

Number of patients per Country	Findings
Hong Kong, sample size (%)	205 (1.57%)
Malaysia, sample size (%)	3055 (23.34%)
Philippines, sample size (%)	2435 (18.63%)
Singapore, sample size (%)	2884 (22.07%)
United Arab Emirates, sample size (%)	8 (0.06%)
Total number of subjects	13068
Demographics (Gender, Age)	Findings
Male, sample size (%)	59.90%
Female, sample size (%)	49.10%
Male age mean +-SD, years	49.71 ± 13.21
Female age mean +-SD, years	52.37 ± 13.29
Physical measurements	Findings
BMI (kg/m2)	27.22 ± 8.16

References

1. Estes C, Razavi H, Loomba R, Younossi Z, Sanyal AJ. Hepatology, 2018.
2. Stengel JZ, Harrison SA. Gastroenterol Hepatology 2006.
3. Younossi ZM, Loomba R, Anstee QM, Rinella ME, Bugianesi E, Marchesini G, Neuschwander-Tetri BA, Serfaty L, Negro F, Caldwell SH, Ratziu V, Corey KE, Friedman SL, Abdelmalek MF, Harrison SA, Sanyal AJ, Lavine JE, Mathurin P, Charlton MR, Goodman ZD, Chalasani NP, Kowdley KV, George J, Lindor K. Hepatology 2018.

Figure 1. LIVERFASt™ algorithm



Methods

In this prospective study, the staging of three different lesions of the liver to diagnose fatty liver were analyzed using a proprietary machine learning algorithm LIVERFASt™ (Figure 1) developed with a database of 2862 unique medical assessments of biomarkers & biopsy reports, where 1027 assessments were used to train the algorithm and 1835 constituted the validation set.

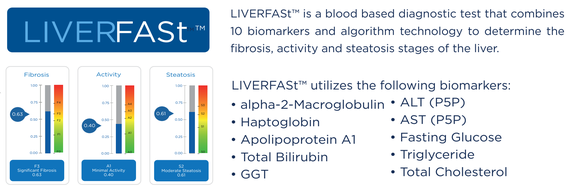
Patients were registered either in ongoing clinical trials or referred diagnostic liver disease test by their doctor during routine clinic visits. Patient data were collected over a period of 3 years from 16 different sites across Asia which included countries like Hong Kong, Malaysia, Philippines, Singapore, Thailand and United Arab Emirates (Table 1).

Table 2. SAF score
SAF score/diagnosis mapping: X, Y, and Z are integers as [0-3], [0-4] and [0-4] respectively.

Estimated SAF score	Diagnosis
$S_0\ A_y\ F_z$	No NAFLD
$S_{x>0}\ A_{y<2}\ F_z$	NAFLD
$Sx<_0\ A_2\ F_z$	NAFLD or NASH
$S_{x<0}\ A_{y>2}\ F_z$	NASH

Table 3. NAFLD and NASH scoring according to machine learning LIVERFAStTM algorithm.

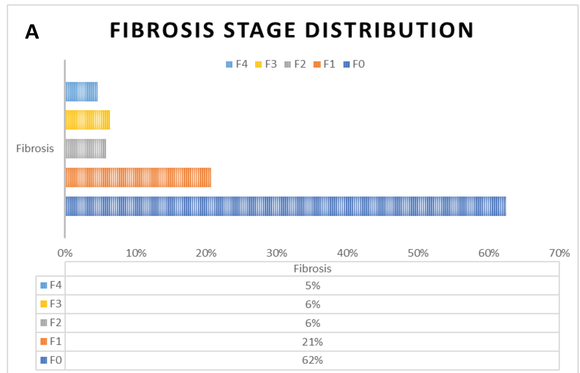
Diagnosis	Diagnostic criteria	Description of diagnosis	% Patients
NAFLD only	Sx>0, Ay<2, Fz>0	Patients with NAFLD	13.41%
NAFLD or Initial NASH	Sx>0, Ay=2, Fz>0	Patients with Inflammation Activity A y=2, possible diagnosis of either NAFLD or NASH	1.91%
Moderate NASH	Sx>0, Ay>2, Fz=1-2	Patients scoring A y>2 indicated NASH condition, not including patients with advanced NASH	1.08%
Advanced NASH	Sx>0, Ay>2, Fz=3-4	Patients with advanced NASH i.e. NASH with advanced Fibrosis F z=3-4	1.49%

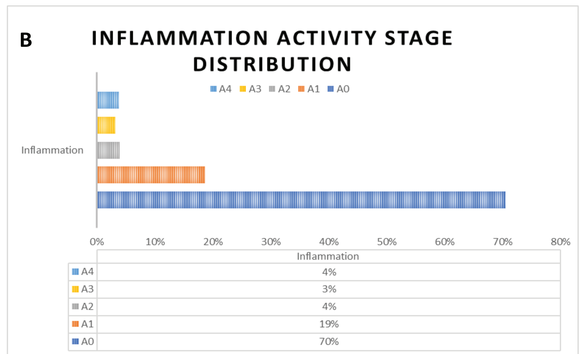


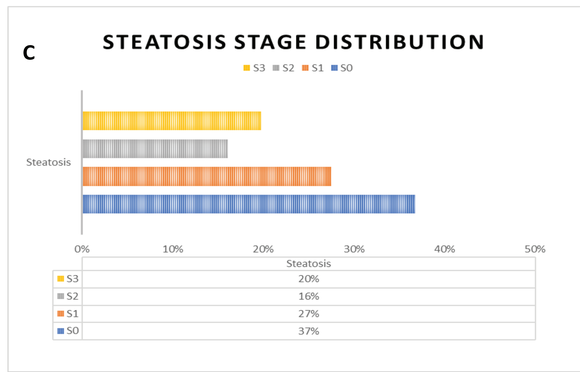
LIVERFASt™ is a blood based diagnostic test that combines 10 biomarkers and algorithm technology to determine the fibrosis, activity and steatosis stages of the liver.

LIVERFASt™ utilizes the following biomarkers:
- alpha-2-Macroglobulin
- Haptoglobin
- Apolipoprotein A1
- Total Bilirubin
- GGT
- ALT (P5P)
- AST (P5P)
- Fasting Glucose
- Triglyceride
- Total Cholesterol

Figure 2.
Machine learning LIVERFASt™ algorithm applied to South Asian population. A) Fibrosis Score; B) Inflammation Activity; C) Steatosis.







Results

Data of 13068 subjects who underwent the LIVERFASt™ test for diagnosis of fatty liver disease was analyzed. As shown in figure 2, data evaluation revealed 11% of the patients exhibited significant fibrosis with fibrosis scores 0.6-1.00 (Figure 2A). Approximately 7% of the population had severe hepatic inflammation (Figure 2B). Steatosis was observed in most patients (63%) whereas severe steatosis S3 was observed in 20% (Figure 2C).

As shown in table 3, using modified SAF (Steatosis, Activity and Fibrosis) scores obtained using machine learning LIVERFASt™ algorithm, NAFLD was detected in 13.41% of the patients (Sx>0, Ay<2, Fz>0).

Approximately 1.91% (Sx>0, Ay=2, Fz>0) of the patients showed NAFLD or NASH scorings while 1.08% had confirmed NASH (Sx>0, Ay>2, Fz=1-2) and 1.49% had advanced NASH (Sx>0, Ay>2, Fz=3-4).

Conclusion

The modified SAF scoring system generated by LIVERFASt™ provides a simple and convenient diagnosis of NAFLD and NASH and staging of the three liver lesions as shown in a cohort of South East Asia.

The use of noninvasive liver tests in extended populations provides an accurate diagnosis of liver pathology, prediction of clinical path of individuals at all stages of liver diseases, and an efficient system for therapeutic interventions.

In accord with the 2016 EASL-EASO-EADO Guidelines, noninvasive markers should aim to: 1) in primary care settings, identify the risk of NAFLD among individuals with increased metabolic risk; 2) in secondary and tertiary care settings, identify those with worse prognosis, e.g. severe NASH; 3) monitor disease progression; 4) predict response to therapeutic interventions. Achieving these objectives could reduce the need for liver biopsy.

The applicability of LIVERFASt™ extends beyond hepatologists and includes primary care providers, as well as endocrinologists, diabetologists and other medical discipline that manage and monitor fatty liver, liver fibrosis and liver activity. LIVERFASt™ test has a potential role in the United States clinical care settings as screening for NAFLD and NASH population at risk.