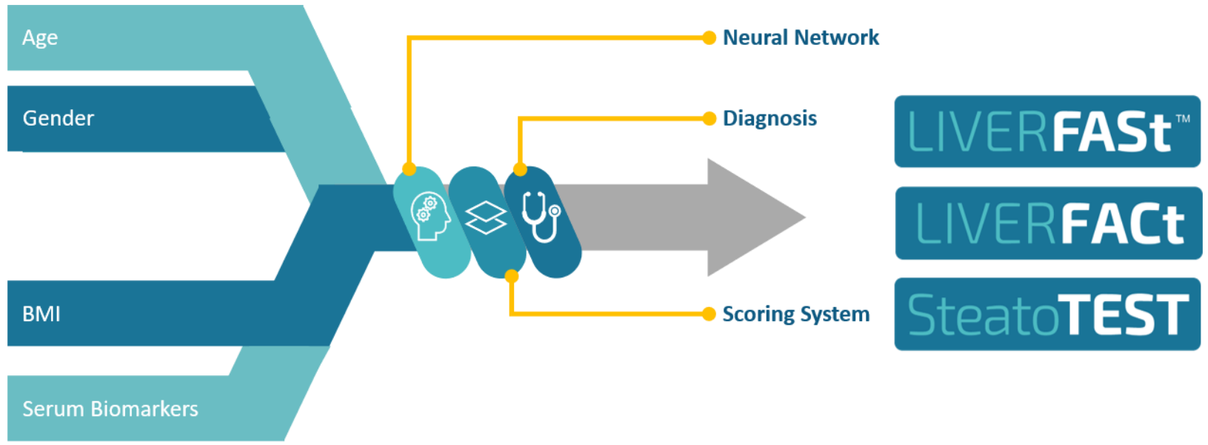
Assessment Of Fatty Liver Disease Using A Biomarker-based Non-invasive Algorithm LIVERFASt™ Test In South-east Asia

Avinash Bahirvani[a], Abhishek Aravind[a], Ronald Quiambao[a], Nelly Conus[b] and Teresa Gonzalo*
[a]Fibronostics Pte Ltd., 79 Science Park Drive #06-01/08 Cintech IV, Singapore 118264, SG b Fibronostics Sàrl, Av du Tourbillon 100, 1950 Sion, Switzerland c Fibronostics US, Inc., 3452 Lake Lynda Drive, Building 100, Suite151, Orlando, FL 32817, US.
* Corresponding author: teresa.gonzalo@fibronostics.com

BACKGROUND

Prevalence of NAFLD (Nonalcoholic fatty liver disease) and resulting NASH (nonalcoholic steatohepatitis) are constantly increasing worldwide 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.

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



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™ 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. 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%)
Thailand, sample size (%)	4481 (35.29%)
United Arab Emirates, sample size (%)	8 (0.06%)
Total number of subjects	13068
Demographic (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 ± 13.39
Physical measurements	**Findings**
BMI (kg/m2)	27.22 ± 8.16

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
$S_{x>0}\ A_2\ F_z$	NAFLD or NASH
$S_{x>0}\ A_{y>2}\ F_z$	NASH

LIVERFASt™

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

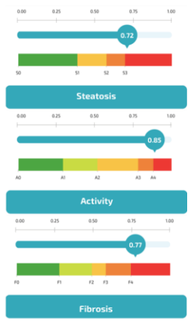
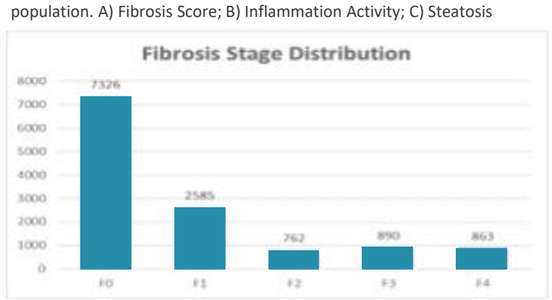
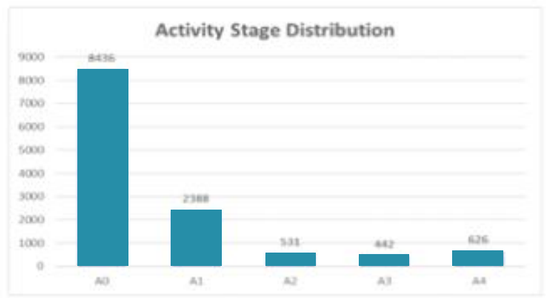


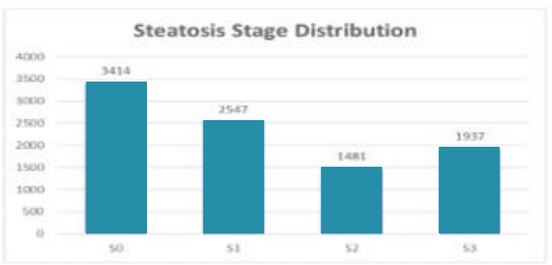
Table 3. Diagnosis of NAFLD and NASH based on LIVERFASt™ algorithm

Diagnosis	Diagnostic criteria	Description of diagnosis	No. of patients
NAFL+NASH	s>0,a>0,f>0	Total number of all afflicted by either NAFL or NASH	8.92%
NAFL only	s>0,a=1,f>0	Patients with NAFL only, no NASH	4.49%
NAFL or NASH	s>0,a=2,f>0	Patients with a=2, possible diagnosis of either NAFL or NASH	1.91%
Confirmed NASH	s>0,a>2,f=1/2	Patients with a>2, confirmed NASH diagnosis, not including patients with advanced NASH	1.08%
Adv NASH	s>0,a>2,f=3/4	Patients with advanced NASH i.e. NASH with f=3/4	1.49%

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 analysed. Data evaluation revealed 14.03% of the patients exhibited significant fibrosis with fibrosis scores 0.6-1.00. Approx. 6.13% had severe hepatic inflammation. Steatosis was observed in most patients (74.58%) whereas severe steatosis was observed in 28.73%. Using modified SAF (Steatosis, Activity and Fibrosis) scores obtained using LIVERFASt™, NAFLD and NASH were diagnosed in 8.92% of the patients (s>0,a>0,f>0). Approx. 4.49% (s>0,a=1,f>0) of the patients had NAFL only while 1.08% had confirmed NASH and 1.49% (s>0,a>2,f=1/2) had advanced NASH (s>0,a>2,f=3/4).

CONCLUSION

The modified SAF scoring system generated by LIVERFASt™ provides a simple and convenient diagnosis of NAFLD and NASH in a cohort of South East Asia. This may lead to the use of noninvasive liver tests in extended populations for more accurate diagnosis of liver pathology, prediction of clinical path of individuals at all stages of liver diseases, and provision of an efficient system for therapeutic interventions. LIVERFASt™ applicability extends beyond hepatologists to more primary care providers, which should facilitate its implementation outside of leading tertiary care centers, and should be tailored according to the setting (primary health care, tertiary referral center, trial) and clinical needs (screening, staging of fibrosis, follow-up).Diagnose fatty liver disease in patients across 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.

FIBRONOSTICS