Monitoring Fatty Liver Disease During Pre/Post-Bariatric Surgery With Non-Invasive LIVERFASt™

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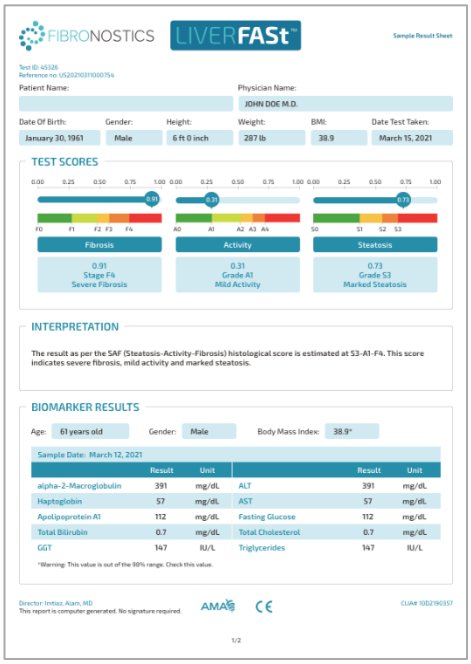
LIVER DISEASE AND BARIATRIC SURGERY

According to the American Society for Metabolic and Bariatric Surgery (ASMBS)[1], non-alcoholic fatty liver disease (NAFLD) is one of the obesity-related co-morbidities that qualifies a patient to undergo a bariatric surgery if BMI> 35. By 2030, it is predicted that nearly half of adults in the USA will have obesity[2]. Over 80% of the patients with obesity submitted to bariatric surgery suffer from (NAFLD), with 25% - 55% resulting in steatohepatitis (NASH) and 2% - 12% liver fibrosis and cirrhosis[3]. Current management of obese patients with NASH consists of lifestyle recommendations as very few therapeutic strategies for NASH are available[4]. Unfortunately, lifestyle interventions, rarely permit more than 10% total body weight loss, the threshold for meaningful improvement in patients with NASH to reduce inflammation and fibrosis[5].

Numerous clinical practice guidelines including AASLD, EASL-EASD-EASO, APASL, and WHO recommend non-invasive serum biomarker-based diagnostic modalities to diagnose NAFLD[6–8].


FIBRONOSTICS LIVERFASt™ Sample Result Sheet

Patient Name: Physician Name: JOHN DOE M.D.

Date Of Birth: January 30, 1961 | Gender: Male | Height: 6 ft 0 inch | Weight: 287 lb | BMI: 38.9 | Date Test Taken: March 15, 2021

TEST SCORES

Fibrosis: 0.91 — Stage F4, Severe Fibrosis

Activity: 0.31 — Grade A1, Mild Activity

Steatosis: 0.73 — Grade S3, Marked Steatosis

INTERPRETATION

The result as per the SAF (Steatosis-Activity-Fibrosis) histological score is estimated at S3-A1-F4. This score indicates severe fibrosis, mild activity and marked steatosis.

BIOMARKER RESULTS

Age: 61 years old | Gender: Male | Body Mass Index: 38.9*

Sample Date: March 12, 2021

	Result	Unit		Result	Unit
alpha-2-Macroglobulin	391	mg/dL	ALT	391	mg/dL
Haptoglobin	57	mg/dL	AST	57	mg/dL
Apolipoprotein A1	112	mg/dL	Fasting Glucose	112	mg/dL
Total Bilirubin	0.7	mg/dL	Total Cholesterol	0.7	mg/dL
GGT	147	IU/L	Triglycerides	147	IU/L

*Warning: This value is out of the 98% range. Check this value.

Director: Imtiaz, Alam, MD. This report is computer generated. No signature required. AMA CE CLIA# 10D2190357

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THE ONLY NON-INVASIVE BIOMARKER TECHNOLOGY APPROVED BY: AMA & CMS

Complete Staging of the Liver
Fibrosis
Inflammation
Steatosis

Stage Liver injury for Common Liver Diseases
HBV
HCV
NAFLD
ALD

Non-Invasive & Cost Effective
Easily repeatable for frequent follow-up & monitoring

10 Biomarkers including
Alpha-2-Macroglobulin
Haptoglobin
Apolipoprotein A1

LIVERFASt™: AN ADVANCED BLOOD BASED TEST FOR LIVER DISEASES

Using the latest available artificial intelligence (AI) technology based on neuronal networking, an advanced algorithm LIVERFASt™ has been developed on multiethnic population as non-invasive clinical tool for staging and grading NAFLD[9]. LIVERFASt™ individual serum biomarkers have been identified as appropriate biomarkers for liver disease evaluation and results from FDA cleared assays[10].

LIVERFASt™ combines anthropometric (age, gender and BMI) and validated serum biomarkers including alpha-2-macroglobulin, haptoglobin, apolipoprotein A1, bilirubin, gamma glutamyl transpeptidase (GGT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), triglycerides, cholesterol (total) and fasting glucose to generate a score and a categorization of steatohepatitis using similar to histology grading and staging of the elementary liver lesions[11–15].

Clinicians overly rely on abnormal liver transaminases alone to identify patients with NAFLD and NASH, although they have insufficient reliability to detect fibrosis[16,17].

LIVERFASt™ Fibrosis score has been greatly optimized that discriminate fibrosis from other liver lesions that occur concomitantly as steatosis and inflammation which is biased by fluctuations in ALT.

LIVERFASt™ Activity score detects the degree of ballooning and lobular inflammation and discriminates from the fibrosis and steatosis liver lesions.

LIVERFASt™ Steatosis score detects lower amounts of steatosis than liver ultrasound (5%) permitting the diagnosis of NAFLD and the monitoring of patients.

To reliably diagnose NASH, a simplified scoring system, the SAF score (steatosis, activity, fibrosis) intended for pathologists has been validated in patients with morbid obesity undergoing bariatric surgery[18,19], LIVERFASt™ is using the cutoffs tightly adapted to NAFLD and as discriminative as the histological SAF classification for steatosis, activity and fibrosis for the non-invasive determination of NAFLD/NASH with a cost-efficient approach.

NAFLD AND NASH DIAGNOSIS PRE AND POST-BARIATRIC SURGERY

The subsequent risk of cirrhosis and hepatocellular carcinoma (HCC) emphasizes an urgent need for effective therapy to reverse fibrosis in morbidly obese patients diagnosed with NASH[20].

Bariatric surgery efficacy has been proven for achieving sustained weight loss in NAFLD and NASH patients and can reverse risk factors that contribute to the pathogenesis of NAFLD, including dyslipidemia, insulin resistance, and hepatic inflammation, making it a promising treatment option for NAFLD[21–23].

Various studies evaluating the histologic impact of bariatric surgery reported the disappearance of NASH in over 80% of cases[24–26].

However, the initial severity of liver disease may affect bariatric surgery outcomes[27], as some

studies have shown that NASH-diagnosed patients have a higher risk of liver-related mortality in the long-term follow-up[28]. Therefore, screening liver damage may help in the decision-making process of high-risk patients.

PRE-BARIATRIC SURGERY: STRATIFYING PATIENT RISK WITH LIVERFASt™

To prevent unwanted post-bariatric surgery events, it is crucial to individualize patient selection and management.

A challenging element of the diagnostic workup of patients with morbid obesity is the NAFLD determination of disease severity. The goals here are double: to identify NASH, among the factors proceeding with bariatric surgery, and to identify those with advanced NAFLD at increased morbidity and mortality.

LIVERFASt™ can evaluate liver damage by stratifying high-risk patients with well-known metabolic comorbidities associated with NAFLD like obesity, type 2 diabetes, hyperlipidemia, hypertension, and metabolic syndrome[4]. LIVERFASt™ simplifies the indication of bariatric surgery by identifying liver diseases and NASH, the final report with patient's stage of liver fibrosis, activity and steatosis will be revised by the physician and communicated appropriately to the patient.

POST-BARIATRIC SURGERY: MONITORING PATIENTS WITH LIVERFASt™

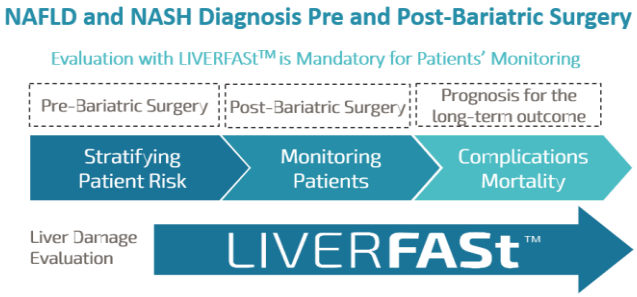
Despite initial concerns about rapid weight loss from bariatric surgery could exacerbate NASH or acute liver failure in morbidly obese patients[29,30], more recent surgical techniques such as Roux-en-Y gastric bypass[31,32] and intragastric balloon[33] have shown improvements in liver histopathologic scoring after 5 years of follow-up evaluation.

Liver biopsy is not adapted to monitoring of high amounts of patients undergoing bariatric surgery.

Besides sample variability, liver biopsy has non-negligible morbidity and mortality, Therefore, LIVERFASt™ provides a surrogate of liver biopsy without risks and bypassing its limits.

LIVERFASt™, a quantitative score, provides more granularity than the categorical liver biopsy to evaluate post-bariatric surgery regression of NASH or even worsening that could be noted in a small subset of patients[34–37].

LIVERFASt™ simplifies liver monitoring in post-bariatric patients being crucial for the appropriate management and prevention of worse outcomes.



ORDERING LIVERFASt™ FOR PATIENTS

A simple blood draw will be performed to obtain the LIVERFASt™ using Fibronostics technology.

In order to obtain a LIVERFASt™ digital assay test report, a healthcare provider must prescribe the LIVERFASt™ and order it through the laboratory with the CPT code. LIVERFASt™ ordering is integrated with laboratory ordering systems and communicate the results to the physician. The serum biomarkers are obtained from a CLIA certified lab and the results are submitted to the LIVERFASt™ algorithm platform.

The LIVERFASt™ report provides scores along with staging of liver disease. The results will guide the physician's medical decisions and, communicated appropriately to the patient, will improve its compliance.

Furthermore, LIVERFASt is the only test able to discriminate fibrosis from steatosis and activity without bias in fibrosis estimation related to the presence of activity or steatosis.

Non-invasive diagnostic tools such as LIVERFASt™ are easy to perform, less expensive, and readily available and aid to the early diagnosis and better prognosis in patients with NAFLD and NASH.

Staging/Grading of three lesions – Fibrosis Activity & Steatosis

	LIVERFASt™	Transient Elastography	MRI	Ultrasound	APRI	ELF	FIB-4
Fibrosis	YES	YES	YES	NO	YES	YES	YES
Activity	YES	NO	NO	NO	NO	NO	NO
Steatosis	YES	YES	YES	YES	NO	NO	NO
# Biomarkers	10	NA	NA	NA	2	3	4

LIVERFASt™ provides complete evaluation and staging of fibrosis, activity and steatosis

(MRI = Magnetic Resonance Imaging, APRI = AST-to-Platelet Ratio Index, ELF = Enhanced Liver Fibrosis, FIB-4 = Index for Liver fibrosis)

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