



# LABORATOIRE SION

## BIOLOGICAL ANALYSIS AND MEDICAL IMAGING

Specialized tests – Ultrasound – specimen collection at home or at the office.

**The FIB-4:  
a new, simple and effective tool for  
screening chronic liver diseases.**

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Tuesday 10  
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## Abstract

The Fibrosis-4 (FIB-4) score is a non-invasive diagnostic tool used to assess liver fibrosis, particularly in patients with chronic liver diseases such as hepatitis B and C, and non-alcoholic fatty liver disease (NAFLD). It is calculated from age, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and platelet count, which makes it a cost-effective and accessible alternative to liver biopsy. The FIB-4 score is particularly advantageous in resource-limited countries, such as sub-Saharan Africa, where access to advanced diagnostic tools is limited. However, its application is not without limitations, notably variability in accuracy due to factors such as comorbidities and demographic differences.

**Keywords:** FIB-4; liver fibrosis; liver biopsy

### 1. Introduction

The FIB-4 test, or more precisely the FIB-4 score (Fibrosis-4 Index), is an index developed to assess liver fibrosis, particularly in patients with chronic liver diseases such as hepatitis B and C, and metabolic fatty liver disease. This score is calculated using routine clinical data, including the patient's age, liver enzyme levels (ALT and AST), and platelet count. Because it is simple to calculate and relies on commonly available parameters, the FIB-4 has established itself as a first-line screening tool in the clinical management of patients in resource-limited areas, where more sophisticated methods such as elastography are not readily accessible. One of the main reasons for the importance of the FIB-4 lies in how easily it can be performed. It can be calculated rapidly from routine blood tests, and even during outpatient consultations. This practical advantage makes the tool particularly suited to primary care settings and to developing countries. Moreover, the minimal cost of the FIB-4 makes it an accessible solution, meeting the screening needs of high-risk populations.

### 2. Calculation and interpretation of the FIB-4

#### 2.1. Calculating the FIB-4

The FIB-4 score is calculated using an empirical formula and interpreted according to the table below:

**FIB-4 Interpretation Table: A Practical Clinical Guide**

| FIB-4 result | Category                          | Interpretation                               | Recommended Clinical Action                                      |
|--------------|-----------------------------------|----------------------------------------------|------------------------------------------------------------------|
| < 1.30       | Negative predictive value (>90 %) | Low probability of advanced fibrosis (F3–F4) | No further testing; standard clinical follow-up                  |
| 1.30 – 2.67  | Intermediate zone (uncertainty)   | Indeterminate result                         | Perform an additional test (ELF, elastography, or repeat FIB-4)  |
| > 2.67       | Positive predictive value (>65 %) | Positive predictive value (>65 %)            | Refer for confirmation by elastography and specialist management |
| > 3.48       | Probable cirrhosis                | High probability of cirrhosis (F4)           | Refer for cirrhosis management; screening for complications      |

*Note: The thresholds may require adaptation according to age, sex, BMI, and the aetiology of the liver disease.*

## 2.2. Special considerations and limitations to bear in mind when interpreting the score:

- **Interpretation in the context of liver inflammation.** Since the FIB-4 includes AST (aspartate aminotransferase), a marker of liver inflammation, FIB-4 results may be falsely elevated in patients with substantial inflammation but only minor fibrosis. Conversely, patients with advanced fibrosis but minimal inflammation may have falsely low FIB-4 values.
- **Reduced performance in complex metabolic conditions.** In patients with both chronic hepatitis B and MASLD, the FIB-4 shows reduced diagnostic performance compared with patients with hepatitis B alone. This observation underlines the importance of recognising that the FIB-4 performs less well in complex mixed liver diseases.
- **Limited performance of the FIB-4 in certain specific populations.** Although the FIB-4 is a valuable screening tool, its diagnostic performance is impaired in certain populations. In lean subjects with non-alcoholic fatty liver disease (NAFLD), the FIB-4 has shown acceptable diagnostic performance, but with reduced sensitivity and specificity compared with non-lean patients. Likewise, in extremely obese patients, the FIB-4 failed to discriminate advanced fibrosis, suggesting the use of alternative cut-off values or complementary markers. In elderly patients, the FIB-4 also falls short: it increases naturally with age, which may lead to an overestimation of fibrosis in older people if age-specific cut-off values are not used.
- **Impact of indeterminate results.** One of the significant clinical limitations of the FIB-4 is the large proportion of patients who fall within the intermediate zone. A foundational study illustrating this problem demonstrated that, out of 100 patients, approximately 30–40 fall within the intermediate zone. This indeterminacy makes direct clinical decision-making impossible for a substantial proportion of patients.

## 3. Diagnostic performance of the FIB-4 in selected liver diseases

### 2.2. Special considerations and limitations to bear in mind when interpreting the score:

The FIB-4 score has demonstrated diagnostic performance superior to that of several other non-invasive markers for the detection of advanced fibrosis in patients with non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH). In a comparative study, the FIB-4 showed a sensitivity of 78.5 % and a specificity of 85.9 % for detecting

advanced fibrosis, thereby outperforming the APRI index (Aspartate Aminotransferase-to-Platelet Ratio Index), another simple non-invasive blood score used to assess liver fibrosis. The FIB-4 has also proved effective in assessing the presence and severity of various aspects of NAFLD. In obese patients undergoing bariatric surgery, the FIB-4 showed an overall diagnostic accuracy of 95.4 % for advanced fibrosis. These results suggest that the FIB-4 is an excellent risk-stratification tool in the NAFLD population.

### 2.2. Diagnosis of liver fibrosis in patients with chronic viral liver disease

In patients with chronic hepatitis C, the FIB-4 has shown excellent performance for fibrosis risk stratification. In a meta-analysis including 84 studies with a total of 107,583 participants, the FIB-4 score with a low threshold (1.45) to rule out severe fibrosis achieved a sensitivity of 81.1 % and a specificity of 62.3 %. Likewise, in patients with chronic hepatitis B, the FIB-4 outperformed other non-invasive markers, with studies showing a fairly high sensitivity for the detection of liver fibrosis.

## 4. Conclusion

FIB-4 testing is of considerable clinical value as an accessible and inexpensive non-invasive tool for the initial assessment of liver fibrosis in a variety of chronic liver diseases. Its usefulness is maximised when it is integrated into sequential approaches combined with other non-invasive markers, making it possible to optimise the detection of advanced fibrosis while minimising unnecessary liver biopsies. However, clinicians must remain aware of its limitations, particularly in elderly patients, obese populations, and those with mixed liver disease, where complementary markers or adapted cut-off values may be necessary for better diagnostic performance. Further research and validation in diverse populations, particularly in Africa, are essential to optimise its clinical usefulness.

# References

1. American Association for the Study of Liver Diseases (AASLD). NAFLD diagnostic and management guidelines. 2023.
2. Anderson LS, Clinicians Group. Two-step diagnostic algorithm for NAFLD fibrosis assessment. *Hepatology Communications*. 2023.
3. Ghaniyya WF, Humairah I, Kholili U. Evaluating the accuracy of APRI and FIB-4 scores in chronic HBV-related liver fibrosis: A literature review. *World J Adv Res Rev*. 2024;24(3):3937.
4. Huttman M, Parigi T, Zoncap M, et al. Liver fibrosis stage based on the four factors (FIB-4) score or Forns index in adults with chronic hepatitis C. *Cochrane Database Syst Rev*. 2024;8(13):CD011929.pub2.
5. Indian Diabetes Cohort Study. Adjusted FIB-4 thresholds for fibrosis detection in type 2 diabetes. *Diabetes Care*. 2022.
6. Kim M, Jun D, Park H, et al. Sequential combination of FIB-4 followed by M2BPGi enhanced diagnostic performance for advanced hepatic fibrosis in an average-risk population. *J Clin Med*. 2020;9(4):1119.
7. Lean NAFLD Study. Performance of FIB-4 in lean patients with nonalcoholic fatty liver disease. *Gastroenterology*. 2022.
8. Mzes FE, Lee J, Selvaraj E, et al. Diagnostic accuracy of non-invasive tests for advanced fibrosis in patients with NAFLD: an individual patient data meta-analysis. *Gut*. 2021;70(9):1088-1098.
9. Nordic Reference Interval Project. Age-adjusted FIB-4 reference intervals in healthy populations. *Scand J Clin Lab Invest*. 2020.
10. Obesity and Fibrosis Study. FIB-4 performance in extremely obese NAFLD patients. *Obes Surg*. 2021.
11. Study on CHB-MASLD overlap syndrome. Performance of FIB-4 in chronic hepatitis B with concomitant MASLD. *Hepatol Res*. 2023.