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EVALUATION OF THE DIAGNOSTIC PERFORMANCE OF THE FIB-4 SCORE IN THE DIAGNOSIS OF LIVER FIBROSIS USING FibroTest ® AS A REFERENCE METHOD

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ABSTRACT
Liver fibrosis is a progressive disease that can lead to cirrhosis and hepatocellular carcinoma. Its diagnosis is traditionally based on liver biopsy, an invasive method. In order to avoid the complications and discomfort of repeated biopsies, non-invasive tests such as FibroTest ® and the FIB-4 score have been developed to assess liver fibrosis. The aim of this study is to evaluate the diagnostic performance of the FIB-4 score for the detection of liver fibrosis, comparing it to the FibroTest ®, which is a reference method. The study aims to determine whether the FIB-4 score can be a reliable and accessible alternative, particularly in developing countries.

KEYWORDS: Liver fibrosis, FIB-4, FibroTest.

INTRODUCTION

Liver fibrosis is a serious pathology that can be life-threatening in the long term. It usually progresses to liver cirrhosis and hepatocellular carcinoma. To reduce this burden, it may be essential to identify patients with significant liver disease and treat them as early as possible, including with appropriate antiviral treatment. Thus, the histological assessment of liver fibrosis is a crucial step in identifying the best therapeutic strategy and assessing the prognosis of the disease. Since liver biopsy (LBP), the gold standard for diagnosing fibrosis, is not always feasible due to its invasive nature , high cost, and multiple complications causing discomfort for patients, especially if a repeat examination is necessary for follow-up, non-invasive scores based on biological parameters have been validated by the WHO as alternatives, including FIB-4 and FibroTest ®.

Researchers from the international APRICOT (AIDS Pegasys) trial Ribavirin International Coinfection Trial)[22], a pivotal trial evaluating the efficacy of pegylated interferon and ribavirin in patients co-infected with HIV and HCV, proposed a simple non-invasive test for liver fibrosis, known as FIB-4, a test derived from the APRICOT database, which produces interesting results using the following formula: (age (years) × AST (U/L) / platelets (109 /L) × √ALT (U/L)).[23] The FIB-4 index has an area under the ROC curve of 0.76. A cut-off value of 1.45 has a negative predictive value for the exclusion of extensive fibrosis (F4-F6 in the Ishak classification) of 90%. A cut-off value of 3.25 has a positive predictive value for the diagnosis of extensive fibrosis of 65 %.[23]

Our study aims to evaluate the diagnostic performance of the FIB-4 score to predict liver fibrosis, using FibroTest ® as a reference method and analyzing the contribution of the FIB-4 score.

PATIENTS AND METHODS

This is a retrospective study collecting data from 50 patients over an 18-month period from August 2021 to February 2023, who underwent a FibroTest and a general assessment carried out on the same day to calculate the FIB-4 score (ASAT, ALAT, Platelets).

Serum ASAT and ALAT levels were routinely measured in our laboratory, the usual upper normal values were 50 IU/l for both parameters in both sexes. Platelet count was performed in the same laboratory, normal values were between 150,000 and 400,000/mm3.

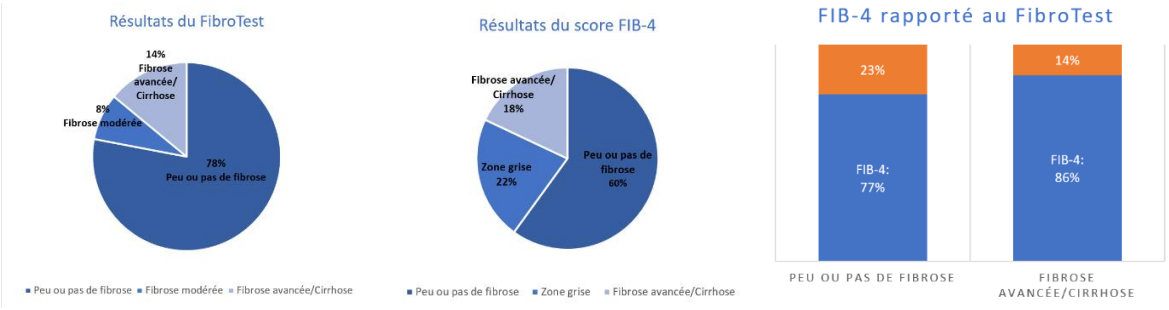
The FIB-4 score was calculated using the following formula:
(Age (years) × ASAT (U/L) / Platelets (10^9 /L) × √ALAT (U/L))
After performing both FibroTest and FIB-4 scores we related their respective results to their equivalents of the METAVIR score of the liver biopsy and then we evaluated the percentage of concordance of the two.

RESULTS

There were 50 patients, 21 women (42%) and 29 men (58%) with a mean age of 53 years [range 18–80 years] Of the 50 scores calculated, 36 (72%) revealed similar results to the FibroTest, 11 scores (22%) were included in the gray zone of the FIB-4 whose fibrosis stage is undetermined and 3 scores (6%) revealed values contradictory with those of the FibroTest.

Among the 11 tests included in the gray zone, only 1 is equivalent to an advanced stage of fibrosis on the FibroTest, compared to 6 advanced fibrosis/cirrhosis on FIB-4 concordant with the same result on the FibroTest , thus providing the FIB-4 with good sensitivity (85.71%) for advanced stages of fibrosis.

The 3 conflicting results were found in 1 patient with profound thrombocytopenia and 2 with thrombocytosis and of extreme ages for the optimal age interval for the FIB-4 score.



DISCUSSION

Non-invasive markers of liver fibrosis can replace liver biopsy in the majority of cases. They have a good positive predictive value for the diagnosis of moderate to severe fibrosis.[9-21] They are also simple, reproducible and accessible.

The FibroTest requires a standardization of methods in order for it to be considered relevant; it assumes, as for the PBF, a risk of over or underestimation of fibrosis.[2]

As for the FIB-4 score, the calculation is simple and does not require standardization, deducible from the results of a standard assessment of any patient at risk of fibrosis, particularly patients suffering from hepatitis, which does not generate additional costs, an important parameter in developing countries.

In the study conducted by Anais Vallet-Pichard et al. the value of the area under the ROC curve for severe fibrosis (F3) was equal to 0.85, while those produced by the APRI, FibroTest and FibroScan techniques were respectively 0.84, 0.90 and 0.90.[10-11-18] The FIB-4 score allowed the correct identification of advanced stages of fibrosis. The FIB-4 index, like other non-invasive tests, could replace 70% of biopsies.[1]

The gold standard for diagnosing liver fibrosis is PBH, the results of non-invasive tests are compared to the latter, however this also carries a risk of over or underestimation of the degree of fibrosis.[2-5-8] It has been suggested that the discrepancies between PBH and FibroTest results could be explained by the technical difficulties related to the examination of PBH samples, which makes this test unreliable. Poynard et al.[2] [4] observed discrepancies in 29% of patients due to marker failure, biopsy failure in 2.4% and both failures in 18% of cases respectively. They showed that diagnostic failures of the biopsy were seven times more frequent than diagnostic failures due to markers. Furthermore, to correctly assess diffuse liver disease in a reliable manner a sample of at least 15 mm would be necessary. Bedossa et al. [8] recently showed that only 65% of biopsies based on 15 mm samples led to correct diagnoses (using the METAVIR score), whereas 75% of biopsies based on 25 mm samples were correct. Since there is no advantage to taking larger samples, the researchers suggested that 25 mm samples are necessary to accurately assess fibrosis.

We performed a comparison of the FIB-4 score with the FibroTest results in the same patients (Figure 3), which revealed a concordance of 85.71% for a FIB-4 score >3.25 and 65.85% for a FIB-4 score <1.25 (Figure 3), 11 patients in our series had FIB-4 score results in the gray zone of the latter (score between 1.45 and 3.25) equivalent to an indeterminate stage of fibrosis not allowing comparison with the FibroTest. The discrepancies between the two scores, noted in 3 of our patients are explained by the failure of the FIB-4 due to advanced age in two patients and unexplained deep thrombocytopenia in a young patient leading to an overestimation of the FIB-4. This is consistent with the results in the literature where discordant results have been found in patients with extreme ages, low platelet count affecting FIB-4 or low haptoglobin levels or Gilbert's disease explaining the failure of the FibroTest.[1]

The FIB-4 score is more easily achievable than the FibroTest because, unlike the latter, it does not require standardization of biochemical values to be used reliably.

CONCLUSION

The FIB-4 score is a new noninvasive way to assess liver fibrosis. A score <1.45 and >3.25 correctly identifies patients with moderate or severe fibrosis and could save

patients from undergoing liver biopsy. The FIB-4 score was found to be consistent with the results of the FibroTest. As the FIB-4 score is readily available, inexpensive, and easily reproducible, it could rapidly replace expensive and/or invasive methods of assessing liver fibrosis, particularly in emerging countries, to detect patients requiring antiviral treatment and to monitor the progression (or regression) of liver fibrosis. Further studies are now needed to validate this new score in combination with other noninvasive tests to improve its diagnostic performance, particularly for patients with intermediate fibrosis or in the gray zone of the score.

DECLARATION OF INTERESTS

The authors declare that they have no competing interest.

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