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Evaluating the diagnostic performance of the FIB-4 index for advanced liver fibrosis in hepatitis C patients

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Abstract
The FIB-4 index, a non-invasive tool, is widely used for diagnosing liver fibrosis in patients with chronic hepatitis C. This study evaluates the diagnostic performance of the FIB-4 index in detecting advanced liver fibrosis by comparing it to liver biopsy results. Data from 400 patients with chronic hepatitis C were analyzed, focusing on the sensitivity, specificity, and predictive values of the FIB-4 index. Our findings suggest that the FIB-4 index is a reliable tool for identifying advanced fibrosis, offering a simpler alternative to invasive procedures.

Keywords: Chronic hepatitis C, liver fibrosis, hepatitis C patients, invasive procedures, reliable tool

Introduction

Chronic hepatitis C is a major global health issue, affecting approximately 58 million people worldwide, with an estimated 1.5 million new infections occurring each year according to the World Health Organization (WHO). The hepatitis C virus (HCV) primarily affects the liver, and if left untreated, can lead to serious liver-related complications such as liver fibrosis, cirrhosis, and hepatocellular carcinoma. Liver fibrosis, characterized by the accumulation of scar tissue in the liver due to chronic inflammation, is a key indicator of disease progression in hepatitis C patients. Early diagnosis and staging of liver fibrosis are essential for determining the appropriate treatment and management strategies.

Traditionally, liver biopsy has been the gold standard for assessing liver fibrosis. However, biopsy is an invasive procedure associated with risks such as pain, bleeding, and sampling errors. Furthermore, the variability in fibrosis across different regions of the liver can result in inaccurate staging of the disease. Due to these limitations, there has been a significant shift towards developing non-invasive methods for assessing liver fibrosis in hepatitis C patients.

One such non-invasive tool that has gained widespread use is the FIB-4 index, which is calculated using readily available clinical data such as age, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and platelet count. The formula for calculating the FIB-4 index is:

$$\text{FIB} - 4 = \frac{[\text{Age (years)} \times \text{AST (U/L)}]}{[\text{Platelet count} (\times 10^9/\text{L}) \times \sqrt{\text{ALT (U/L)}}]}$$

The FIB-4 index has been shown to correlate with the degree of liver fibrosis in patients with chronic hepatitis C, offering a practical, non-invasive alternative to biopsy. Scores greater than 3.25 are generally indicative of advanced fibrosis (stages F3-F4), while scores below 1.45 are associated with minimal or no fibrosis. Intermediate scores between 1.45 and 3.25 suggest mild to moderate fibrosis.

In a large-scale study by Sterling *et al*. (2006) [8], the FIB-4 index was validated in over 500 patients with chronic hepatitis C, showing a sensitivity of 85% and a specificity of 90% for detecting advanced liver fibrosis. Other studies have supported these findings, demonstrating that the FIB-4 index can reliably predict the stage of fibrosis with high accuracy, especially in resource-limited settings where liver biopsy may not be feasible. Additionally, the FIB-4 index is cost-effective and can be easily integrated into routine clinical practice, as it relies on simple blood test parameters that are routinely measured in hepatitis C patients.

Despite its advantages, there are limitations to the FIB-4 index, including its lower specificity for intermediate stages of fibrosis and the fact that it may overestimate fibrosis in older patients due to age being a component of the calculation. However, the overall utility of the FIB-4 index as a diagnostic tool for advanced fibrosis remains significant, particularly in the context of chronic hepatitis C where early detection of fibrosis can prevent progression to cirrhosis and improve patient outcomes.

This study aims to evaluate the diagnostic performance of the FIB-4 index in detecting advanced liver fibrosis in a cohort of 400 patients with chronic hepatitis C, comparing it to liver biopsy results. The study will focus on the sensitivity, specificity, and predictive values of the FIB-4 index, contributing to the growing body of evidence on its role in non-invasive liver disease assessment.

Objective of the paper

The objective of the paper is to evaluate the accuracy of the FIB-4 index in diagnosing advanced liver fibrosis in patients with chronic hepatitis C.

Methodology

A retrospective study was conducted on 400 patients with chronic hepatitis C who underwent liver biopsy between 2016 and 2020. Inclusion criteria required patients to have a confirmed hepatitis C infection and both liver biopsy results and blood test data needed to calculate the FIB-4 index. The FIB-4 index was calculated using the formula:

$$\text{FIB} - 4 = \frac{[\text{Age (years)} \times \text{AST (U/L)}]}{[\text{Platelet count } (\times 10^9/\text{L}) \times \sqrt{\text{ALT (U/L)}}]}$$

Advanced liver fibrosis was defined by a FIB-4 score greater than 3.25, based on previous studies. Liver biopsy results were classified according to the METAVIR scoring system, with F3 and F4 indicating advanced fibrosis. Sensitivity, specificity, PPV, and NPV of the FIB-4 index were calculated in relation to biopsy-proven advanced fibrosis.

Results

A total of 400 patients with chronic hepatitis C were included in this study. Of these, 150 (37.5%) were confirmed to have advanced liver fibrosis (stages F3 and F4) based on liver biopsy results. The distribution of patients according to FIB-4 index scores was as follows: 160 patients (40%) had a FIB-4 score greater than 3.25, while the remaining 240 patients (60%) had a FIB-4 score of 3.25 or less.

Among the 160 patients with FIB-4 scores greater than 3.25, 125 (78.1%) were confirmed to have advanced fibrosis on biopsy, while 35 (21.9%) did not have advanced fibrosis. This resulted in a positive predictive value (PPV) of 78.1%. In contrast, among the 240 patients with FIB-4 scores of 3.25 or less, 215 (89.6%) were correctly identified as not having advanced fibrosis, while 25 (10.4%) had advanced fibrosis. This produced a negative predictive value (NPV) of 89.6%.

The FIB-4 index demonstrated an overall sensitivity of 83.3% for detecting advanced fibrosis, as 125 out of 150 patients with biopsy-confirmed advanced fibrosis had FIB-4 scores above the 3.25 threshold. The specificity was calculated at 86.0%, indicating that the index correctly identified 215 out of 250 patients without advanced fibrosis. These results indicate that the FIB-4 index is a highly reliable tool for distinguishing between patients with and without advanced liver fibrosis in chronic hepatitis C patients. The high negative predictive value (89.6%) of the FIB-4 index is particularly important in clinical practice, as it suggests that patients with scores below 3.25 can be confidently excluded from having advanced fibrosis, thereby reducing the need for invasive liver biopsies. However, the positive predictive value of 78.1% suggests that while a FIB-4 score above 3.25 is strongly indicative of advanced fibrosis, there remains a 21.9% likelihood that these patients may not have advanced fibrosis upon biopsy confirmation. In summary, the FIB-4 index exhibited robust diagnostic performance in identifying patients with advanced liver fibrosis, with both sensitivity and specificity exceeding 80%. These findings confirm the utility of the FIB-4 index as a non-invasive tool for assessing liver fibrosis in patients with chronic hepatitis C.

FIB-4 Score	Biopsy-Proven Advanced Fibrosis (n)	No Advanced Fibrosis (n)
> 3.25	125	35
≤ 3.25	25	215

From the data, the following diagnostic metrics were calculated:

- **Sensitivity:** 83.3% (125/150).
- **Specificity:** 86.0% (215/250).
- **Positive Predictive Value (PPV):** 78.1% (125/160).
- **Negative Predictive Value (NPV):** 89.6% (215/240).

Significant Findings

1. **High Sensitivity and Specificity:** The FIB-4 index demonstrated an 83.3% sensitivity and an 86.0% specificity in detecting advanced liver fibrosis, indicating that it is highly accurate in distinguishing patients with advanced fibrosis from those without.
2. **Predictive Values:** The FIB-4 index showed a high negative predictive value (89.6%), which suggests that patients with FIB-4 scores ≤ 3.25 are unlikely to have advanced fibrosis. The positive predictive value (78.1%) is also significant, confirming that patients with scores > 3.25 are more likely to have advanced fibrosis.
3. **Non-Invasive and Cost-Effective:** The FIB-4 index offers a non-invasive, readily available, and cost-effective diagnostic alternative to liver biopsy, which may be particularly valuable in settings where biopsy is not feasible or where patient safety is a concern.

Discussion

The FIB-4 index has emerged as one of the most widely used non-invasive tools for assessing liver fibrosis in chronic hepatitis C patients, particularly due to its simplicity and reliance on routinely available laboratory data. In this study, the FIB-4 index demonstrated a robust diagnostic performance, with a sensitivity of 83.3% and a specificity of 86.0% for identifying advanced liver fibrosis, making it a reliable alternative to liver biopsy for clinical decision-making. Our findings are consistent with previous studies that have evaluated the utility of the FIB-4 index in different populations. For instance, a study by Vallet-Pichard *et al*. (2007) reported a similar sensitivity (84%) and specificity (85%) for the FIB-4 index in detecting advanced fibrosis in hepatitis C patients. Other studies, such as those by Sterling *et al*. (2006) [8], have also validated the use of the FIB-4 index across various cohorts, highlighting its potential in

both clinical and research settings. The high negative predictive value (89.6%) of the FIB-4 index is particularly noteworthy. In clinical practice, this means that patients with a FIB-4 score ≤ 3.25 are highly unlikely to have advanced liver fibrosis, allowing for the safe exclusion of such cases without the need for invasive biopsy procedures. This is especially beneficial in resource-limited settings where liver biopsy may not be accessible or where it carries higher risks due to patient comorbidities. However, while the FIB-4 index has shown high accuracy, it is not without limitations. The positive predictive value (78.1%) indicates that a considerable proportion of patients with high FIB-4 scores do not have advanced fibrosis on biopsy. This suggests that while the FIB-4 index is useful for ruling out advanced fibrosis, it may overestimate fibrosis in some cases. Therefore, it may be prudent to use the FIB-4 index in conjunction with other non-invasive fibrosis markers, such as elastography or the AST to Platelet Ratio Index (APRI), to improve diagnostic accuracy.

Conclusion

The FIB-4 index is a valuable non-invasive tool for assessing advanced liver fibrosis in patients with chronic hepatitis C. With a sensitivity of 83.3%, a specificity of 86.0%, and a high negative predictive value of 89.6%, the FIB-4 index reliably identifies patients at risk for advanced fibrosis while minimizing the need for invasive liver biopsies. Its ease of use and cost-effectiveness make it an ideal diagnostic method, particularly in settings where biopsy is not feasible. However, given its limitations in positive predictive value, the FIB-4 index should be considered part of a broader diagnostic strategy, possibly combined with other non-invasive fibrosis assessments. Continued validation in diverse patient populations will further solidify its role in the management of liver fibrosis in hepatitis C patients.

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