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Performance of APRI and FIB-4 Scores Compared to Fibro Scan in the Assessment of Fibrosis in Chronic Viral Hepatitis in Cote D'Ivoire

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Abstract

Purpose: To compare the performance of APRI and FIB-4 versus FIBROSCAN in the assessment of fibrosis in chronic viral hepatitis.

Methodology: This was a retrospective descriptive and analytical cross-sectional study, carried out in outpatient consultations for hepatogastroenterology at Cocody University Hospital during the period from January 2016 to June 2020. Patients with viral hepatitis chronic B or C were included. APRI and FIB-4 scores were calculated from the respective formulas. Data were analyzed using SPSS and XLSTAT software. The Chi2 test was used to determine the correlation between the different markers. The sensitivity, specificity, positive predictive value and negative predictive value of APRI and FIB-4 were calculated for the different thresholds and the best Se/Sp compromise evaluated by the ROC curve. The Chi 2 test was used to assess statistically significant associations for a significance level was 0.05.

Results: 694 patients were eligible among which we retained 269 divided into 156 men (57.9%) and 113 women (42.1%). There was a male predominance with a sex ratio of 1.38. The mean age was 39.64 ± 10.8 years. 256 (95.16%) had chronic viral hepatitis B, 13 (4.84%) had chronic viral hepatitis C. Non-significant fibrosis (F0F1) was found in patients under 39 years of age and cirrhosis in patients patients over 48 years of age.

Discussion: According to the APRI and FIB-4 scores, 83.29% and 89.7% of patients had non-significant fibrosis versus 72.9% for FIBROSCAN. The significant fibrosis for FIBROSCAN and APRI was 27.1% versus 16.7%. Severe fibrosis for FIBROSCAN and FIB-4 was 8.4% versus 10.3%. There was a statistically significant association between age, cytolysis, thrombocytopenia and the occurrence of significant fibrosis according to the APRI score and severe fibrosis according to the FIB-4 score. There was a positive correlation between FIBROSCAN and biological fibrosis scores with coefficients of 2.09 for APRI and 0.43 for FIB4 (p-value < 0.005). APRI and FIB-4 scores had high specificities (92.35% and 98.85% respectively) and high negative predictive values (80.8% and 89.12% respectively) for the prediction of significant fibrosis in course of chronic viral hepatitis B and C. The AUROC for detecting significant fibrosis was 0.71 for APRI with a better discriminating threshold of 0.48 (Se: 56.2%, Sp: 85.2%). The AUROC for detecting severe fibrosis was 0.70 for FIB-4 with a best discriminatory cutoff of 3.65 (Se: 70%, Sp: 94.5%).

Conclusion: APRI and FIB-4 scores are powerful markers for detecting fibrosis in chronic viral hepatitis B and C and can be included in recommendations for patient follow up in low income countries.

Keywords: APRI; Fibrosis; FIBROSCAN; FIB-4; Viral hepatitis B and C

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Introduction

The evaluation of hepatic fibrosis during chronic viral hepatitis is essential for patient management because in addition to guiding treatment decisions and screening for complications, it also makes it possible to monitor the evolution of the lesions [1]. The gold standard for fibrosis assessment is liver biopsy (PBH), which uses standardized semi-quantitative scores [2]. However, this method being invasive has drawbacks and is associated with often fatal complications [3]. Additionally, its diagnostic accuracy has been questioned due to sampling errors and intra and inter-operator variability [4,5]. Several non-invasive markers were then validated, including pulse elastography or FIBROSCAN, validated in a large number of studies mainly in patients with chronic viral hepatitis B and C [6,7]. Biochemical scores have also been developed to estimate the stage of fibrosis, some of which are based on the biochemical examinations carried out routinely in our hospitals, in particular the APRI and FIB-4 scores. The objective of our study was to compare the performance of APRI and FIB-4 scores against FIBROSCAN in the assessment of fibrosis in chronic viral hepatitis.

Materials and Methods

This was a retrospective descriptive and analytical cross-sectional study on the files of patients seen in outpatient Hepato-Gastroenterology consultations at the Cocody Hospital and University Center (CHU) during the period from January 1, 2016 to January 30, 2016. June 2020. Were included: all patients followed for chronic viral hepatitis B or C or compensated cirrhosis of aetiology B or C, having performed in the same month, a FIBROSCAN and the laboratory tests necessary for calculating the APRI and FIB-4 scores during the study period. Parameters studied: demographic (age, sex); biological (HVB, HVC, HVD, HIV viral markers; complete blood count and transaminase levels) and radiological (FIBROSCAN, abdominal ultrasound). The APRI score was calculated from the formula of Wai, et al. and the FIB-4 score was calculated from the formula of Sterling [8,9]. The interpretation of the Fibroscan results was made on the basis of the recommendations of a multicenter study published in the "Expert Medecine Device 2012" which, depending on the viral etiology B or C, made it possible to classify the different F0F1, F2F3, F3F4, F4 fibrosis stages [10]. The different groups to be compared were then:

-Group 1: non-significant fibrosis (F0F1)

-Group 2: significant fibrosis (F2F3, F3F4 and F4) or severe fibrosis (F3F4 and F4)

For APRI and FIB-4, predefined thresholds were used [11]:

-APRI <0.66 corresponding to non-significant fibrosis (F0F1) and ≥ 0.66 to significant fibrosis (F2F3 to F4);

-FIB-4 ≤ 1.45 corresponding to non-significant fibrosis (F0F1) and ≥ 3.25 to severe fibrosis (F3F4 to F4).

Data were analyzed using SPSS and XLSTAT software. The Chi2 test was used to determine the correlation between the different markers. The sensitivity, specificity, positive predictive value and negative predictive value of APRI and FIB-4 were calculated for the different thresholds and the best Se/Sp compromise evaluated by the ROC curve. The Chi 2 test was used to assess statistically significant associations for a significance level was 0.05.

694 patients were eligible among which we retained 269 divided into 156 men (57.9%) and 113 women (42.1%). There was a male predominance with a sex ratio of 1.38. The mean age was 39.64 ± 10.8 years. 256 (95.16%) had chronic viral hepatitis B, 13 (4.84%) had chronic viral hepatitis C. Non-significant fibrosis (F0F1) was found in patients under 39 years of age and cirrhosis in patients patients over 48 years of age. According to the APRI and FIB-4 scores, 83.29% and 89.7% of patients had non-significant fibrosis versus 72.9% for FIBROSCAN. The significant fibrosis for FIBROSCAN and APRI was 27.1% versus 16.7%. Severe fibrosis for FIBROSCAN and FIB-4 was 8.4% versus 10.3%. There was a statistically significant association between age, cytolysis, thrombocytopenia and the occurrence of significant fibrosis according to the APRI score and severe fibrosis according to the FIB-4 score. There was a positive correlation between FIBROSCAN and biological fibrosis scores with coefficients of 2.09 for APRI and 0.43 for FIB4 (p<0.005). APRI and FIB-4 scores had high specificities (92.35% and 98.85% respectively) and high negative predictive values (80.8% and 89.12% respectively) for the prediction of significant fibrosis in course of chronic viral hepatitis B and C. The AUROC for detecting significant fibrosis was 0.71 for APRI with a better discriminating threshold of 0.48 (Se: 56.2%, Sp: 85.2%) (**Figure 1**).

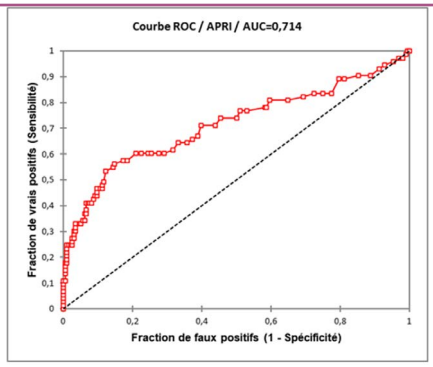

Figure 1 Courbe ROC du score APRI pour la prédiction de fibrose significative

The AUROC for detecting severe fibrosis was 0.70 for FIB-4 with a best discriminatory cutoff of 3.65 (Se: 70%, Sp: 94.5%) (**Figure 2**).

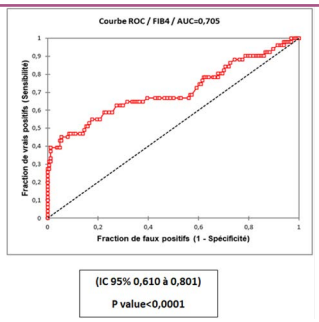

Figure 2 Courbe ROC du score FIB-4 pour la prédiction de la fibrose sévère

Discussion

The mean pulse elastometry (FIBROSCAN) value in our patients was 7.26 kPa ± 5.65 kPa with values between 3.3 and 63 kPa. In Senegal, Touré Ps, et al. reported in 2017, a comparable means value of 7.59 kPa with extremes of 2.3 kPa and 75 kPa [12]. In our study, non-significant fibrosis was found more by APRI (83.29%) and FIB-4 (84.4%) scores than by FIBROSCAN (72.3%). Our results were comparable to those of Touré Ps et al. in Senegal who, in a population of 404 patients, found non-significant fibrosis of 83.7% and 84.4% with APRI and FIB-4 scores respectively and in 59.9% of patients with FIBROSCAN (12). Significant fibrosis was found in 27.1% of our patients with the FIBROSCAN and 16.7% with the APRI score. The FIB-4 score and the FIBROSCAN found severe fibrosis in 10.3% and 8.4% of our patients, respectively. Touré Ps et al. in their study also found more significant fibrosis with the FIBROSCAN (40.1%) than with the APRI score (17.3%); they found severe fibrosis in 17.1% and 14.6% of patients with the FIBROSCAN and the FIB-4 score respectively. The similarity between our results and those of Touré Ps et al. then testified to the low sensitivity and the high specificity of the APRI and FIB-4 scores for the prediction of significant and severe fibrosis. Wai, et al. who defined this marker, also noted this average sensitivity (41%) and high specificity (95%) [8]. The APRI score had low sensitivity (41.1%) for predicting significant fibrosis. Nevertheless, we found a high specificity and a good negative predictive value of 92.35% and 80.8% respectively. Our results were comparable to those of Touré Ps et al. who found a lower sensitivity of the APRI score (27.8%) and high specificity and VPN rates (91.3% and 91.3% respectively). On the other hand, Lemoine, et al. in a multicenter study in West Africa found an average sensitivity of the APRI score with 64% in the Gambia, 42% in Senegal; they also had specificities and relatively average NPVs of 64% and 73% in The Gambia and 70% and 72% in Senegal [13]. Ren, et al. in China, in a population of 160 patients, also found an average sensitivity of the APRI score (66%), a specificity and NPV of 86% and 62% respectively [14]. This variability between the different studies is probably due to the difference in the upper limit values of the ASAT standard which vary from one country to another [15]. The FIB-4 score also had a low sensitivity (48.78%) for the diagnosis of severe fibrosis with high specificity and NPV of 98.85% and 89.12% respectively. Similar results were found by Toure Ps, et al. who reported in their series low sensitivity (21.6%), and high specificity and NPV (88.4% and 88.4% respectively). Lemoine, et al. found a sensitivity of 63% in The Gambia and 43% in Senegal, a specificity and NPV of 98% and 70% respectively in The Gambia and 83% and 92% in Senegal. In China, Ren et al. reported a sensitivity of 59%, a specificity of 95% and a NPV of 75%. Our study found agreement in terms of diagnostic performance between the APRI and FIB4 fibrosis scores and the FIBROSCAN (reference examination) as shown by the Chi2 correlation test with $p<0.005$. The APRI score appeared to be a good non-invasive fibrosis marker with an AUROC of 0.71 (95% CI: 0.63-0.79), very high specificity and a high negative predictive value (NPV). Our results were comparable to those of Lemoine, et al. who found AUROCs for an APRI score of 0.66 (95% CI: 0.57-0.76); 0.77 (95% CI: 0.65-0.89); 0.62 (95% CI: 0.48-0.76) respectively in Gambia, France and Senegal [13]. Ren, et al. in China found an AUROC of 0.63 (95% CI: 0.54–0.72) [14]. The variability between the AUROCs would probably be due to the differences in the cut-off values used in the different studies. In our study, an APRI score <0.66 corresponded to non-significant fibrosis and an APRI score ≥ 0.66 corresponded to significant fibrosis. This value allowed us to classify all our patients, which is not the case for the other studies which used APRI score thresholds ≤ 0.50 for non-significant fibrosis and ≥ 1.5 for significant fibrosis, thus eliminating patients with an intermediate APRI score since they could not be classified. The FIB-4 score appeared to be a good non-invasive marker for predicting severe fibrosis with an AUROC of 0.70 (95% CI: 0, 61-0.80), very high specificity and high NPV. Our results were comparable to those of Lemoine, et al. who found AUROCs for an FIB-4 score of 0.68 (95% CI: 0.57-0.78); 0.86 (95% CI: 0.77-0.95); 0.71 (95% CI: 0.53-0.89) respectively in Gambia, France and Senegal. Likewise, Ren, et al. in China found an AUROC of 0.68 (95% CI: 0.59–0.78). Touré Ps, et al. in Senegal found a weak AUROC: 0.59 (95% CI: 0.53-0.54). The best cut-off for the APRI score for the detection of significant fibrosis in our study was 0.48 with a sensitivity of 56.2% and a specificity of 85.2%. Our results were different from those of Huang D, et al. in China who, in a population of 91 patients, found a cut-off value of 0.58 with a sensitivity of 62.38% and a specificity of 71.29%, for an average APRI score of 1.40 ± 0.96 [16]. These variations were probably due to the difference in sampling. In fact, in our study for a population of 269 patients, the mean APRI score was 0.53 ± 0.69. The best cut-off value found for the FIB-4 score was 3.65 with a sensitivity of 70% and a specificity of 94.5%. Our results were different from those of Huang D, et al. in China who found a cut-off value of 5.76 with a sensitivity of 64.48% and a specificity of 63.19% for an average FIB-4 score of 6.70 ± 2.14. These variations were probably due to the difference in sampling.

Conclusion

FIBROSCAN Is one of the tests validated for the prediction of fibrosis in chronic viral hepatitis and is used as a replacement for PBH. APRI and FIB-4 scores, compared to FIBROSCAN have good performance in predicting fibrosis in chronic viral hepatitis B and C. These scores being accessible could be widely used in our clinical practice as a replacement for FIBROSCAN. Further multicenter studies are needed to definitively assess the performance of APRI and FIB-4 scores on a larger workforce in our African context.

Acknowledgement

None

Conflict of Interest

None

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