Acta Scientific Gastrointestinal Disorders (ISSN: 2582-1091)

Volume 4 Issue 4 April 2021

Research Article

APRI Score and Conventional Liver Ultrasonography Accurately Evaluate Liver Fibrosis in Hepatitis C Patients in an African Hospital Setting

Raïssa Nana Sede Mbakop[1], Mathurin Pierre Kowo[1]*, Firmin Ankouane Andoulo[1], Antonin Wilson Ndjitoyap Ndam[1], Jean Roger Mouliom Tapouh[2], Jean Claude Mballa Amougou[2], Patricia Guekam Ouamba[1], Samuel Nko'o Amvene[2] and Oudou Njoya[1]

[1]Department of Internal Medicine and Specialties, Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1, Yaoundé, Cameroon

[2]Department of Radiology, Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1, Yaoundé, Cameroon

***Corresponding Author:** Mathurin Pierre Kowo, Department of Internal Medicine and Specialties, Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1, Yaoundé, Cameroon.

Received: March 11, 2021

Published: March 19, 2021

Abstract

Background: In Cameroon, some non-invasive methods used in the assessment of liver fibrosis in chronic hepatitis C (CHC) such as liver stiffness or biomarker panels such as FibroTest® and Fibrometer ® are expensive and/or not easily accessible. However, the Aspartate aminotransferase-Platelet Ratio Index (APRI) and conventional liver ultrasonography are readily available and can be used in this resource-limited setting.

Aim of the Study: The aim of this study was to evaluate the diagnostic performance of APRI and conventional liver ultrasonography in the assessment of liver fibrosis in patients with CHC in Cameroon.

Materials and Methods: We conducted a retrospective study at the Yaoundé University Teaching Hospital in Cameroon. CHC patients ≥ 18 years seen at this center from January 2015 to December 2017 with available results of FibroTest® were included in this study. APRI was calculated for each patient and liver ultrasonography findings were obtained from patient files. The diagnostic accuracy of APRI and liver ultrasonography was assessed using the area under the receiver operator curve (AUROC). The sensitivities, specificities, and predictive values of various cut-offs of APRI in detecting significant fibrosis and cirrhosis were determined using FibroTest® as the standard.

Results: 81 patients were included with a mean age of 60.3 ± 9.3 years. The mean viral load was 6.02 ± 0.62 logIU/ml. APRI was strongly correlated to FibroTest® ($r = 0.52$, $p < 0.001$). APRI's AUROCs in diagnosing liver fibrosis were 0.766 and 0.774 for significant fibrosis and cirrhosis respectively. Practically, an APRI > 0.5 had a sensitivity of 75.4% and a positive predictive value (PPV) of 88.5% for significant fibrosis. APRI > 2 was 97.7% specific for cirrhosis and had a PPV of 93.8%. An irregular liver surface was highly specific for cirrhosis ($p = 0.004$). The diagnostic accuracy for liver cirrhosis significantly increased when APRI was combined with US liver surface parameters (AUROC 0.802, $p = 0.005$). The combination of irregular liver surface and APRI ≥ 0.73 was 97.7% specific for cirrhosis.

Conclusion: APRI score is useful in identifying patients at the main endpoints of hepatitis C-related fibrosis, especially when combined with ultrasound, and could be a potentially valuable tool in staging and appropriately managing patients with CHC in limited resource settings.

Keywords: Hepatitis C; Liver Fibrosis; APRI Score; FibroTest®; Ultrasonography

Abbreviations

ALD: Alcoholic Liver Disease; ALT: Alanine Aminotransferase; APRI: Aspartate Aminotransferase-to-Platelet Ratio Index; AST: Aspartate Aminotransferase; AUROC: Area Under the Receiver Operator Curve; CHC: Chronic Hepatitis C; CLD: Chronic Liver Disease; EASL: European Association of the Study of Liver Disease; GGT: Gamma Glutamyl Transferase; HBV: Hepatitis B Virus; HCC: Hepatocellular Carcinoma; HCV: Hepatitis C Virus; HIV: Human Immune Deficiency Virus; IU: International Units; mm^3: Millimeters Cube; NAFLD: Non-Alcoholic Fatty Liver Disease; NPV: Negative Predictive Value; PPV: Positive Predictive Value; TE: Transient Elastography; ULN: Upper Limit of Normal; US: Ultrasonography; WHO: World Health Organization

Background

Chronic Hepatitis C virus (HCV) infection is a major public health problem affecting an estimated 71 million individuals globally [1]. In Cameroon, the prevalence is estimated at 6.5% [2]. Since 2015, in collaboration with partners, constant efforts have been made by Cameroonian authorities to get direct antiviral agents (DAA) available at lower prices for patients with chronic hepatitis C (CHC). However, despite the availability of DAA, only a small number of patients still have access to treatment, mainly due to the cost of pretherapeutic work up including staging of hepatic fibrosis and the lack of screening.

Liver fibrosis is a pivotal factor influencing the selection of therapeutic options, the duration of treatment, and in determining the prognosis of patients with chronic liver disease (CLD). To estimate prognosis and guide management decisions, accurate staging of hepatic fibrosis is a clinical and research priority. Although liver biopsy is considered the gold standard for the assessment of fibrosis, it is invasive, associated with significant morbidity, and is often limited by sampling errors and inter- or intraobserver variability [3-5]. In addition, liver biopsy has been shown to yield nearly 25% rate of discordance for fibrosis staging depending on several factors including the length of the specimen biopsy, the level of experience and the specialization of the pathologist [5-8].

In recent years, several noninvasive means have been developed to assess liver fibrosis in patients with CLD, notably in CHC patients. These non-invasive tests comprise of serum tests that are habitually combined with other markers of advanced liver disease in to panels, and imaging tests mostly represented by transient elastography (TE). Some of these panels such as FibroTest® and Fibrometer® [9] are still protected by patents and are commercially available with proprietary bundle assays, whereas others such as the Aspartateaminotransferase-Platelet Ratio Index (APRI) [10] are more readily available. FibroTest® is the most widely validated indirect serum marker panel, extensively studied in CHC [9-12]. It has been shown to have excellent accuracy in identifying cirrhosis and significant fibrosis, the two main endpoints in CHC [12,13]. However, FibroTest® is costly, and in a low-income setting like Cameroon, it is not readily available to most patients both from a financial and geographical standpoint.

With the advent of accessible and highly effective drugs for the treatment of Hepatitis C in our setting, there is an increased demand for treatment from patients and consequently a need for quick, accurate and readily accessible means of evaluation of liver fibrosis in these patients.

Tests accessible and routinely done in these patients include Aspartate aminotransferase and platelet count, from which APRI can be obtained, and conventional liver ultrasonography. These tests have been shown to be relevant in assessing liver fibrosis.

Aim of the Study

The current study aimed at evaluating the diagnostic performance of APRI and conventional liver ultrasonography in the evaluation of liver fibrosis in CHC patients with CLD in a resource limited setting; using FibroTest® as the reference test for assessing liver fibrosis.

Materials and Methods

A retrospective analytical study was carried out at the Yaoundé University Teaching Hospital (YUTH) in Cameroon. YUTH is a reference center for the treatment of viral hepatitis in Cameroon. It offers Gastroenterology consultations weekly on 4 out of 5 business days and holds monthly committees with other Gastroenterologists in the region to review all new files before the initiation of antiviral therapy. Patients consulting for viral hepatitis come from roughly all parts of the country.

The study focused on a three-year period from January 2015 to December 2017. All patients aged 18 years and above, seen at the outpatient consultations for CHC and with available results for aspartate transaminases, platelets count, FibroTest® and liver ultrasonography done within a 6 months period were included. Outpatient consultation registers were used to identify the files of patients who consulted for CHC during the study period. Patients who fit the inclusion criteria were screened for exclusion criteria using clinical and paraclinical data found in the patient's record from the previous 06 months. Clinical and biochemical and radiologic data of retained participants, obtained from their medical records were noted in a preconceived data collection form. Sampling was conse-

cutive and exhaustive. We excluded all patients with liver tumors, acute hepatitis, chronic hepatitis B and HIV co-infection, fatty liver disease, decompensated cirrhosis, and congestive heart failure.

Liver enzymes and APRI

APRI was calculated using the formula = (AST elevation/platelet count) x 100, where AST elevation = AST level/upper limit of the normal (ULN) for the laboratory. The platelet count per mm^3 was divided by 1000.

Among the APRI cut-off points tested were the classical cut-off points of APRI ≤ 0.50 to predict the absence of significant liver fibrosis, APRI > 1.50 to predict the presence of significant fibrosis and APRI >2 to predict cirrhosis [14].

FibroTest®

FibroTest® is not yet done locally in Cameroon and frozen serum samples were therefore sent abroad for the test to be done. A two to three weeks delay was necessary for the results to be available. FibroTest® values and corresponding fibrosis stage according to the Metavir classification ranging from F0 to F4 were obtained from patients' files. Significant fibrosis was defined as a FibroTest® result of F ≥ 2 and cirrhosis was defined as a FibroTest result of F4.

Conventional liver ultrasound

The parameters used for the ultrasound (US) evaluation were:

1. Liver surface; scored 1 for smooth, 2 for irregular.
2. Liver parenchymal texture; scored 1 for homogenous, 2 for heterogeneous 3- Liver size; scored 1 for normal size, 2 for atrophy, 3 for hepatomegaly the sum of these three parameters was defined as the US score.

Statistical analysis

Data were recorded and analyzed using SPSS 23.0 Inc. 2011 Chicago USA software. The mean and standard deviations of continuous variables were reported. Mean distributions were compared using the Mann Whitney U test, and the Spearman rank correlation coefficient was used to assess the correlation between APRI and FibroTest®. The sensitivities, specificities, positive and negative predictive values (PPV and NPV) of several cut-off points of APRI in the detection of significant fibrosis and cirrhosis were evaluated. Areas under the receiver operator curve (AUROC) were used to assess the diagnostic accuracy of APRI and liver ultrasonography. Multivariate analysis was performed for prediction models. Statistically significance was set at $p < 0.05$.

Results

Characteristics of the study population

Overall, 81 patients were included in this study; 45 women and 36 men. The mean age of the patients was 60.3 ± 9.3 years and ranged from 38 years to 82 years. The most common comorbidity was hypertension in 27 patients (33.3%). Diabetes mellitus was found in 15 patients (18.5%). Among the 69 patients who had data on alcohol consumption, 13patients (18.8%) were recorded as being alcohol consumers. 4 out of 51 patients (7.8%) were obese and

2 out of 70 patients (2.9%) were active smokers (Table 1). The mean value of alanine aminotransferase was 66.2 IU/l and the mean value of aspartate aminotransferase was 67.0 IU/l. The mean value for platelet count was 200456.8/mm^3 (range: 23000 - 2240000/mm^3). The APRI index had a median value of 0.66 (Table 2). The mean viral load was 2,621,207.19 ± 4,666,181.56 IU/mL (6.02 ± 0.62 log IU/ml).

Parameter	N (%)
Demographic parameters	
Gender	
Male	45 (55.6%)
Female	36 (44.4%)
Age groups	
< 40	2 (2.5%)
[40-49]	9 (11.1%)
[50-59]	24 (29.6%)
[60-69]	33 (40.7%)
[70-79]	10 (123%)
≥ 80	3 (3.8%)
Mean age (year): 60.3 ± 9.3 (38-22)	
Comorbidities	
High blood pressure	77 (333%)
Diabetes	15 (18.5%)
Alcohol consumption (n = 69)	13 (18.8%)
Obesity (n = 51)	4 (7.8%)
Smoking (n = 70)	2 (2.9%)
Fibrosis stages (according to Fibrotest®)	
FOF1	9 (11.1%)
F2	15 (18.5%)
F3	17 (21%)
F4	40 (49.4%)
Virologic parameters	
Genotype 1	37 (45.7%)
Genotype 2	20 (24.7%)
Genotype 4	24 (29.6%)
Mean viral load: 2621207.19 ± 4666.181.56 IU/ml (6.02 ± 0.62 logIU/ml)	

Table 1: Baseline demographic, histologic and virologic characteristics of the study population.

Data	Minimum	Maximum	Mean	Standard deviation
AST (IU/l)	14	377	67.0	54.5
ALT (IU/l)	1.30	304	66.2	56.0
Platelet count (/mm^3)	23000	2240000	200456.8	239993.1
APRI (Median*)	0.1	15.2	0.66*	
Total Bilirubin (µmol/l)	3.6	47.0	13.2	7.9
Prothrombin ratio (%)	55.1	100	84.1	12.5

Table 2: Biochemical characteristics of study population.
AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase.

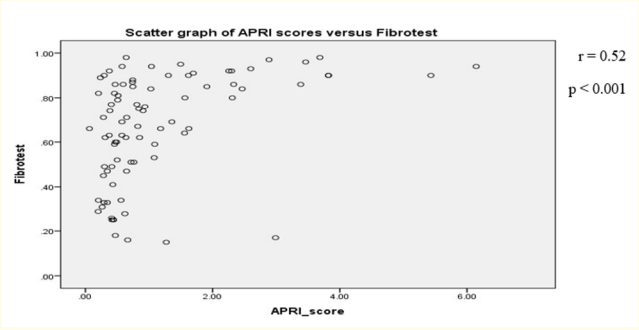

Figure 1: Scatter plot of APRI index against FibroTest®.

Genotype 1 was the most frequent genotype, found in 37 patients (45.7%), followed by genotype 4 in 24 patients (29.6%), then genotype 2 in 20 patients (24.7%).

For the liver ultrasound parameters, the liver surface was regular in 87.7% of patients, the liver ultrasound structure was homogenous in 79% of cases, and its size was normal in 71.6% of cases. Overall, 59.3% of the study population had a normal US score.

The mean FibroTest® value was 0.67 ± 0.24. 70.4% of the patients included had severe fibrosis or cirrhosis according to FibroTest®. Concerning ActiTest®, 27.2% of patients had severe activity.

The APRI mean rank in the group of patients with severe fibrosis or cirrhosis was 47.1 and was significantly higher than that in the group of patients with no-to-significant fibrosis (Table 3).

	F0 F1 F2	F3 F4	p-value
Mean rank	26.5	47.1	0.001
N	24	57	

Table 3: APRI index mean difference between no-to-significant fibrosis versus severe fibrosis.

Correlation between APRI and FibroTest®

The correlation between APRI and FibroTest®, assessed using Spearman's rank coefficient, was positive, strong and significant at 0.520 ($p < 0.001$) (Figure 1).

Diagnostic performance of APRI To detect significant fibrosis

The diagnostic accuracy of APRI for significant fibrosis was evaluated using a ROC curve. The AUROC was 0.766 at $p = 0.001$ (Figure 2). Several cut-offs were used to predict significant fibrosis. The highest sensitivity (75.4%) for the APRI to detect significant fibrosis was obtained at a cut-off of 0.5 with a PPV of 88.5%. As the cut-off increased, the sensitivity decreased while the specificity increased. At the 1.5 cut-off, APRI was 94.4% specific for significant fibrosis with a PPV of 95.5% (Table 4).

Figure 2: Diagnostic accuracy of APRI for significant fibrosis.

F0-F1 vs Significant fibrosis (F≥2)			
APRI Cut-off values	0.5	0.7	1.5
Sens./Specificity (%)	75.4/66.7	60.3/88.9	33.9/94.4
PPV/NPV	88.5/44.4	95/39	95.5/44.4

Table 4: Value of some APRI cut-offs to diagnose significant fibrosis.

To detect cirrhosis

The highest AUROC was that of APRI diagnosing cirrhosis (0.774, $p < 0.01$) (Figure 3). At a cut-off of 2, APRI had a specificity of 97.7% and a PPV of 93.8% for diagnosing cirrhosis, although the sensitivity was low at 39.5% (Table 5).

Figure 3: Diagnostic accuracy of APRI for cirrhosis.

No cirrhosis versus Cirrhosis			
APRI Cutoff values	1	1.5	2
Sens./Specificity	60.5/81.4	51.4/93	39.5/97.7
PPV/NPV	74.2/70	86.4/69	93.8/64.6

Table 5: Value of some APRI cut-offs to diagnose cirrhosis.

Diagnostic performance of liver ultrasonography

There was a poor correlation between liver ultrasonography as assessed by the US score and FibroTest®, $r = 0.24$, $p = 0.03$. The AUROC for diagnosing fibrosis were poor as well; 0.57 for significant fibrosis and 0.58 for cirrhosis.

Liver surface was significantly associated with cirrhosis ($p = 0.004$); although an irregular liver surface was poorly sensitive (23.7%) in detecting cirrhosis, it was highly specific for liver cirrhosis at 97.7%.

Linear regression model for predicting fibrosis as assessed by FibroTest®

APRI score, viral load, prothrombin time and total bilirubin levels were all independent and significant predictors of fibrosis as assessed by FibroTest® (Table 6).

Variable	Beta coefficient	p-value
APRI	0.191	0.001
Prothrombin ratio (sec)	0.007	0.005
US score	-0.38	0.09
Log Viral load (IU/ml)	0.125	0.005
Total bilirubin (µmol/L)	0.008	0.021

Table 6: Predictors of fibrosis as assessed by FibroTest®.

Combined APRI and ultrasound liver surface to detect cirrhosis

The accuracy of the combined APRI and US liver surface was superior to that of APRI alone at diagnosing cirrhosis with an AUROC of 0.802 ($p < 0.001$) (Figure 4). The ROC curve suggested that a subject with an irregular liver surface and an APRI score ≥ 0.73 had a specificity of 97.7% for cirrhosis.

Figure 4: Diagnostic accuracy of combined APRI and US liver surface in detecting cirrhosis.

The sensitivity of liver surface irregularity at detecting cirrhosis also increased from 23% when alone to 47.4% when combined with APRI.

Discussion

This study focused on the potential of APRI and conventional liver ultrasonography to assess liver fibrosis in CHC patients.

APRI is based on routinely performed, inexpensive laboratory parameters, and as such it is potentially the ideal tool for the staging of liver fibrosis in CHC patients and may guide management in these patients in regions with limited health care resources.

This study found APRI to have acceptable diagnostic accuracy in the detection of HCV-related fibrosis, with AUROCs of 0.766 and 0.774 for diagnosing significant fibrosis and cirrhosis respectively. Practically, values of APRI less than 0.5 could permit to 'rule out' significant fibrosis, as well as APRI values of > 2 could 'rule in' cirrhosis. The diagnostic accuracy for liver cirrhosis significantly increased when APRI was combined with US liver surface parameters. A patient with an irregular liver surface and an APRI ≥ 0.73 had 97.7% chances of having cirrhosis.

Association between APRI and FibroTest®

In this study, there was a significant difference in the mean APRI values in different fibrosis stages, namely, between the groups of no-to-significant fibrosis versus severe fibrosis. The mean APRI values increased as fibrosis got worse.

The correlation between APRI and FibroTest® was positive and significant at 0.520, revealing a strong association between APRI and FibroTest®. Also, APRI was found to be accurate in detecting significant fibrosis (≥F2) and cirrhosis (F4); with the AUROC for the diagnosis of cirrhosis being higher than the AUROC for diagnosing significant fibrosis.

These findings are in accord with numerous studies found in literature. Crisan and collaborators in 2012 recruited 446 hepatitis C patients from a clinic in Romania to evaluate the diagnostic accuracy of APRI in predicting fibrosis stages [15]. They obtained an AUROC of 0.727 and 0.741 for APRI to diagnose significant fibrosis (≥F2) and severe fibrosis (≥F3) respectively. These AUROCS are similar to 0.766 and 0.754 for significant and severe fibrosis obtained in this study.

Likewise, Streinu-Cercel., *et al.* in 2013 [16] conducted a similar study in which they included 56 patients with hepatitis C from the National Institute of Infectious Diseases in Bucharest, to evaluate the accuracy of APRI and other non-invasive markers in predicting FibroTest®. The AUROC for APRI to predict FibroTest® was 0.70 for ≥F2 and 0.83 for F4. Also, Wang and colleagues in 2017 recruited 1284 Asian patients with chronic hepatitis C in Taiwan to evaluate non-invasive tests as predictors of liver fibrosis [17]. They obtained an AUROC of 0.747 for APRI to predict cirrhosis (F4). Their optimal cutoff to rule out cirrhosis was 1.3 with a negative predictive value of 92.4%. A meta-analysis by Shaheen AAM., *et al*. [18] in a systematicreview looking at the diagnostic accuracy of APRI for the prediction of Hepatitis C-related fibrosis, obtained an AUROC of 0.76 [95% confidence interval 0.74 - 0.79] in detecting significant fibrosis. The AUROC for the prediction of cirrhosis in the present study was however, lower than theirs, evaluated at 0.82 (95% confidence interval, 0.79 - 0.86). This discrepancy may due to the fact that the percentage of males in all 17 studies included in their analysis was higher than ours, who may have had more established cirrhosis at diagnosis.

In order to draw clinical significance from our findings, we calculated the sensitivity, specificity, PPV and NPV of various cut-offs of APRI in the diagnosis of different stages of liver fibrosis.

To diagnose significant fibrosis

At a cut-off of 0.5, APRI had a 75.4% sensitivity and 66.7 specificity in detecting significant fibrosis. Specificity increased at higher cutoffs at the expense of sensitivity. Crisan D., *et al*. found a similar sensitivity (71.92%) and specificity (66.67%) at a cutoff of 0.44 [15] while Shaheen AAM., *et al*. found a higher sensitivity of 81% and a lower specificity of 50% [18]. An APRI cut-off of 0.5 has been previously suggested to 'rule out' significant fibrosis [19].

To diagnose cirrhosis

A 0.7 cut-off yielded 71.1% sensitivity and 69.8% specificity. The PPV was 67.5% and the NPV reached 73.5%. The moderately high NPV suggested that patients with an APRI less than 0.7 were likely not to have cirrhosis.

As the cut-off of APRI increased to 1.5 and 2, the specificities increased to 93 and 97.7% at the expense of their sensitivities at 51.4% and 39.5% respectively. The PPVs for these cutoffs were 86.4% and 93.8% and the NPVs were 69% and 64.6%, respectively. The World Health Organization (WHO) in its guidelines for the management of CHC patients in 2014 referred to a similar specificity and sensitivity of 94% and 48% at an APRI cut off of 2 [19]. Therefore, the cut-offs found in this study would be appropriate to diagnose cirrhosis and may have important practical implications for the initiation of surveillance programs for hepatocellular carcinoma (HCC).

In Cameroon, FibroTest® and Fibroscan® which are well validated tools for the assessment of fibrosis in CHC patients are not readily accessible because of their unavailability, their high cost and the long delay to obtain the result. In order to attain the WHO objective of eradicating HCV and identify HCV patients with severe disease who need follow-up after successful anti- HCV treatment, it is imperative to have cheap and readily accessible tools for the assessment of fibrosis. The APRI score calculated based only on AST level and platelet count appears to be a good alternative to FibroTest® and FibroScan® to assess fibrosis during chronic hepatitis C in resource limited countries as already recommended by WHO [20].

Association between Liver Ultrasonography and FibroTest®

The association between US score and FibroTest® was poor with a correlation coefficient of 0.24 (p = 0.032), this translated into a poor diagnostic accuracy of liver ultrasonography, with an AUROC of 0.574 for predicting severe fibrosis and 0.584 for predicting cirrhosis.

In 2005, Nishiura T and colleagues [21] found the US score to be a reliable and effective alternative for histological staging in chronic liver disease. They studied 103 patients who had undergone liver biopsy and found a correlation of 0.9524 between US scores and fibrosis stage. The poor correlation observed in the current study may be because ultrasonography, which is known to be operator-dependent, was performed by different radiologists, unlike in their study. On the other hand, liver surface was significantly associated with cirrhosis (p = 0.004). In effect, the reproducibility of this US sign has been proven by several studies [22,23]. In this study, although an irregular liver surface was poorly sensitive (23.7%) in detecting cirrhosis, it was highly specific for liver cirrhosis at 97.7%. Previous studies have also confirmed the specificity of this US feature. In 2003, Colli A., *et al.* [22] studied the accuracy of US for the detection of severe liver fibrosis and cirrhosis as evaluated by liver biopsy; liver surface nodularity had a high diagnostic accuracy with a specificity of 95% for cirrhosis. Similarly, Martin J., *et al.* in 2015 in a hospital-based study in Dallas county found a high specificity of 87.5% in detecting cirrhosis using ultrasound liver surface criteria [24].

APRI-liver ultrasonography to diagnose cirrhosis

The accuracy of the combined APRI and US liver surface was superior to that of APRI alone in diagnosing cirrhosis with an AUROC of 0.802 (p = 0.000). The ROC curve suggested that a subject with an irregular liver surface and an APRI score ≥ 0.73 had a specificity of 97.7% probability of having cirrhosis. In the study carried out by Martin., *et al*. 2015, individual noninvasive markers had low predictive values when used alone, but when combined (for instance, ultrasound with APRI), the predictive values increased by about 40% [24]. In effect, the European Association for the Study of the Liver (EASL) recommends that, where feasible, two noninvasive markers be used to assess liver fibrosis [25]. In our setting, this finding is relevant in that ultrasonography as well serum transaminases and blood count are a routine workup in CHC patients and are usually readily accessible. When used in combination, they could therefore permit to quickly identify those who should be enrolled in a surveillance program for HCC or esophageal varices, as well as guide the selection of antiviral therapy.

Limitation of the Study

The major limitation of our study is its retrospective nature, characterized by possible unmeasured confounders. Furthermore, abdominal ultrasound for various patients was performed by different radiologists, which may have influenced the results. Further studies in this setting involving a single operator for ultrasonography are therefore recommended to validate our results.

Conclusion

In this study, APRI proved to be relevant in identifying patients at the main endpoints of HCV- related fibrosis. An APRI of less than 0.5 could permit to rule out significant fibrosis, whereas an APRI ≥ 2 was highly specific/predictive of liver cirrhosis. An irregular liver surface was highly specific for liver cirrhosis. An APRI ≥ 0.73 associated with an irregular liver surface was 97.7% specific for liver cirrhosis. In resource limited settings, APRI combined toliver ultrasound could reliably be used to assess the severity of liver disease in patients with CHC.

Ethics Approval and Consent to Participate

Ethical clearance for this study was obtained from the Centre Regional Ethics committee for Human Health Research. Number: CE 00827/CRERSHC/2018 Centre Region Cameroon.

Administrative authorization was obtained from the administration of the Yaoundé University Teaching Hospital. Number: 90/AR/CHUY/DG/DGA/CAPRC.

Participant's data were processed using specific unique identifiers for the purpose of confidentiality.

Consent for Publication

Not applicable.

Availability of Data and Material

The datasets generated during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

Funding

None.

Authors Contributions

Authors RNSB, MPK, ON, JRMT, JCMA contributed to the study design, wrote the research protocol, and contributed indata collection, data analysis and editing the first draft of the manuscript. Aut-

hors MPK, FAA, ON contributed to study conception, data analysis, and editing the manuscript. Authors FAA, AWNNN, PGO contributed to data collection, editing the manuscript. Authors JRMT, JCMA, SNA performed the different liver ultrasounds. Author ON supervised all the activities and approved the final version to be submitted for publication. All authors have read and approved the manuscript.

Bibliography

1. Global Hepatitis Report, Geneva: World Health Organization (2017).

2. Bigna JJ., *et al.* "Seroprevalence of hepatitis C virus infection in Cameroon: A systematic review and meta-analysis". *BMJ Open* (2017): 7.

3. Intraobserver and interobserver variations in liver biopsy interpretation in patients with chronic hepatitis C. The French METAVIR Cooperative Study Group". *Hepatology* 20.1 (1994): 15-20.

4. Regev A., *et al.* "Sampling error and intraobserver variation in liver biopsy in patients with chronic HCV infection". *The American Journal of Gastroenterology* 97.10 (2002): 2614-2618.

5. Bedossa P., *et al.* "Sampling variability of liver fibrosis in chronic hepatitis C". *Hepatology* 38.6 (2003): 1449-1457.

6. Skripenova S., *et al.* "Variability of grade and stage in simultaneous paired liver biopsies in patients with hepatitis C". *Journal of Clinical Pathology* 60.3 (2007): 321-324.

7. Siddique I., *et al.* "Sampling variability on percutaneous liver biopsy in patients with chronic hepatitis C virus infection". *Scandinavian Journal of Gastroenterology* 38.4 (203): 427-432.

8. Rousselet MC., *et al.* "Hepatitis Network 49 Sources of variability in histological scoring of chronic viral hepatitis". *Hepatology* 41.2 (2005): 257-264.

9. Papastergiou V., *et al.* "Non-invasive assessment of liver fibrosis". *Annals of Gastroenterology* 25.3 (2012): 218-231.

10. Wai CT., *et al.* "A simple noninvasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C". *Hepatology* 38.2 (2003): 518-526.

11. Poynard T., *et al.* "Overview of the diagnostic value of biochemical markers of liver fibrosis (FibroTest, HCV FibroSure) and necrosis (ActiTest) in patients with chronic hepatitis C". *Comparative Hepatology* 3.1 (2004): 8.

12. Zarski JP., *et al.* "ANRS HCEP 23 Fibrostar Group.Comparison of nine blood tests and transient elastography for liver fibrosis in chronic hepatitis C: the ANRS HCEP-23 study". *Journal of Hepatology* 56.1 (2012): 55-62.

13. Chou R and Wasson N. "Blood tests to diagnose fibrosis or cirrhosis in patients with chronic hepatitis C virus infection: a systematic review". *Annals of Internal Medicine* 158 (2013): 807-820.

14. Lin ZH., *et al.* "Performance of the aspartate aminotransferase-to-platelet ratio index for the staging of hepatitis C-related fibrosis: an updated meta- analysis". *Hepatology* 53 (2011): 726-736.

15. Crisan D., *et al.* "Two or more synchronous combination of noninvasive tests to increase accuracy of liver fibrosis assessement in chronic hepatitis C; results from a cohort of 446 patients". *Hepatitis Monthly* 12.3 (2012): 177-184.

16. Streinu-Cercel O., *et al.* "Correlations between noninvasive tests as predictors of liver fibrosis and of viral response in chronic hepatitis C patients". *BMC Infectious Diseases* 13.1 (2013): P54.

17. Wang HW., *et al.* "New noninvasive index for predicting liver fibrosis in Asian patients with chronic viral hepatitis". *Scientific Reports* 7.1 (2017): 3259.

18. Shaheen AAM and Myers RP. "Diagnostic accuracy of the aspartate aminotransferase- to-platelet ratio index for the prediction of hepatitis C–related fibrosis: A systematic review". *Hepatology* 46.3 (2007): 912-921.

19. World Health Organisation. Guidelines for the screening, care and treatment of persons with Hepatitis C infection. Assessing the degree of liver fibrosis and cirrhosis (2016): 54-58.

20. World Health Organisation 2018. Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection clinical assessment of persons with HCV infection prior to treatment (2018): 34-35.

21. Nishiura T., *et al.* "Ultrasound evaluation of the fibrosis stage in chronic liver disease by the simultaneous use of low and high frequency probes". *The British Institute of Radiology* 78.927 (2005): 189-197.

22. Vigano M., *et al.* "US features of liver surface nodularity as a predictor of severe fibrosis in chronic hepatitis C". *Radiology* 234.2 (2005): 641.

23. Colli A., *et al.* "Severe liver fibrosis or cirrhosis: accuracy of US for detection--analysis of 300 cases". *Radiology* 227.1 (2003): 89-94.

24. Martin J., *et al.* "Accuracy of ultrasound and noninvasive markers of fibrosis to identify patients with cirrhosis". *Digestive Diseases and Sciences* 60.6 (2015): 1841-1847.

25. EASL-ALEH Clinical Practice Guidelines: Non-invasive tests for evaluation of liver disease severity and prognosis". *Journal of Hepatology* 63.1 (2015): 237-264.