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Correlation between Ultrasound Aspects of Fibrosis and Fibroscan Outcomes of Patients with Chronic Hepatitis B Virus

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Abstract

Background: The assessment of liver fibrosis is an essential part of the follow-up of patients with chronic HBV. Ultrasound and fibroscan are two commonly used non-invasive examinations and the purpose of this study is to assess the correlation between the results of these two examinations in the assessment of liver fibrosis. **Methodology**: This was a descriptive and analytical cross-sectional study with retrospective collection over a period of 30 months from January 01, 2018 to June 30, 2020 on the correlation between the ultrasound aspects and the results of the fibroscan of patients with chronic carriers of Hepatitis B virus at the Teaching Hospital of Bogodogo and at the faith-based health center CANDAF. **Results**: A total of 85 patients with fibrosis were collected. The 30 - 40 age group was the most represented (41.18%), with a male predominance of 52.94%. The patients with a married life were the most represented (77.64%), the social stratum the most represented were the middle managers (32.94%). University level was predominant among education levels (45.64%). The personal history was traditional circumcision (34.12%), excision (21.18%), manicure (16.47%). The circumstances of the findings were blood donation (34.12%), screening (21.18%), fortuitous findings (16.47%). The association between echostructure and fibrosis on the fibroscan scan was significant (homogeneous hyperechoic echostructure p = 0.0028 and granular echostruc-

ture p = 0.0001). Fibrosis on scans had a significant association with liver contour (Regular contours p = 0.0009 and p = 0.0002). Fibrosis on CT scan had a significant association for the diagnosis of fibrosis on ultrasound (p = 0.0002 for hepatic steatosis and cirrhosis and p = 0.0013 for hepatic dysmorphia), on the other hand, no significant association for hepatomegaly (p = 0.8883). **Conclusion**: Detecting the presence of fibrosis and monitoring its progression improves the management of patients with chronic liver disease. Ultrasound scans and fibroscan are complementary in the follow-up of patients with chronic HBV.

Keywords

Fibrosis, HBV, Ultrasound, Fibroscan, Correlation

1. Introduction

Viral hepatitis B (HBV) is a major public health problem in sub-Saharan Africa with approximately 65 million chronic carriers and 56,000 deaths per year [1]. The severity of liver damage conditions both the prognosis and the therapeutic indications during chronic hepatitis [2]. The clinical expression of the natural history of this infection is very variable, ranging from simple inactive carriage to chronic active hepatitis with progressive fibrosis that can lead to cirrhosis, which in its turn can be complicated by hepatocellular carcinoma [2] [3]. In rare situations, hepatocellular carcinoma occurs in a non-cirrhotic liver [4]. Fibrosis is an essential element to monitor in the search for complications of viral hepatitis B [3]. Indeed it is part of the definition of cirrhosis, which is a diffuse process defined by mutilating fibrosis (destroying the normal lobular architecture of the liver), delimiting hepatocyte nodules of abnormal structure called regeneration nodules [5]. Liver biopsy is the gold standard for the diagnosis of liver fibrosis. However, it has the disadvantage of being an invasive procedure with risks of morbidity (0.3% to 0.6%) and mortality (0 to 0.05%) [6] [7]. This invasive examination cannot therefore be repeated in the context of monitoring the evolution of liver fibrosis, hence the development of non-invasive alternatives with blood and morphological tests. Elastometry or fibroscan is a promising and reproducible non-invasive approach to the quantification of fibrosis [8] [9] [10]. Ultrasound is the first-line imaging test used in the follow-up of patients infected with HBV. The advantages of ultrasound are its low cost, reproducibility, non-invasiveness and innocuousness, which can be repeated at will. However, the diagnostic performance of ultrasound for the diagnosis of hepatic fibrosis is insufficient, and its diagnostic accuracy depends on the signs sought [11]. Despite its disadvantages, ultrasound is the most economically and geographically accessible examination in our working context [12]. The aim of our work is to study the correlation between the ultrasound aspects of fibrosis and the results of the fibroscan of chronic carriers of the hepatitis B virus.

2. Material and Methods

This was a descriptive and analytical cross-sectional study with retrospective and prospective collection over a 30-month period from January 1, 2018 to June 30, 2020. Our study population was all chronic HBV infected patients to whom has been done an ultrasound scan during our study period at the teaching hospital of Bogodogo and at the CANDAF faith-based centre and who subsequently underwent a fibroscan. For each patient we noted age, sex, profession, marital status, ultrasound data including right liver, left liver, segment IV and segment I sizes, liver edge and its echotexture, portal vein trunk diameter, permeability and flow direction, splenomegaly and ascites presence or not. We also noted fibrosis score on fibroscan. Data sources were ultrasound reports, fibroscan reports and patient phone calls. Data were collected on an electronic collection form installed on an android smartphone. Data analysis was done on a microcomputer using Stata software version 17. To compare our results, we used the chi-square statistical test; the threshold of $p < 0.05$ was retained as statistically significant.

The following ultrasound signs of cirrhosis and extensive fibrosis were used in this study: hepatomegaly: right liver greater than 150 mm, measured anterior to the right kidney on the medio-clavicular line; diffuse micronodular liver: granular heterogeneous echotexture made up of micronodules less than 3 mm; diffuse macronodular liver: nodular heterogeneous echotexture made up of nodules less than 3 to 20 mm, generally hyperechoic; hepatic dysmorphia: change in hepatic proportions with right liver atrophy (size less than 120 mm), segment IV atrophy (size less than 30 mm), left liver hypertrophy (size greater than 120 mm) and segment I hypertrophy (size greater than 15 mm); portal hypertension: diameter of the portal trunk measured at the hepatic hilum greater than 12 mm +/− hepatofugal flow. Portal hypertension syndrome: dilatation of the portal trunk associated with splenomegaly and/or ascites.

Fibroscan score: Elasticity score > 10 kpa (likely F3-F4: severe fibrosis); 7 kpa < elasticity score ≤ 10 kpa (likely F1-F2: moderate fibrosis); 2.5 kpa ≤ elasticity score ≤ 7 kpa (F0-F1: absent or minimal fibrosis).

The secrecy and confidentiality of the information was respected. The protocol was submitted to the Ethics National Committee of Burkina Faso for biomedical research and was approved by deliberation n° 2021-07-180.

3. Results

A total of 993 ultrasounds were performed in chronic HBV infected patients and 289 ultrasounds were abnormal. Fibrosis was found in 283 ultrasound results but only 85 patients with both ultrasound and fibroscan agreed to participate in the study. Figure 1 shows the flow-chart of the ultrasound and fibroscan results.

Thus we included 85 patients with both ultrasound and fibroscan in this study. The mean age of the patients was 38 years with extremes of 19 and 69 years. The age range 30 - 40 years was represented by 41.18%. There was a male predominance with 45 patients and the sex-ratio was 1.12. Middle managers

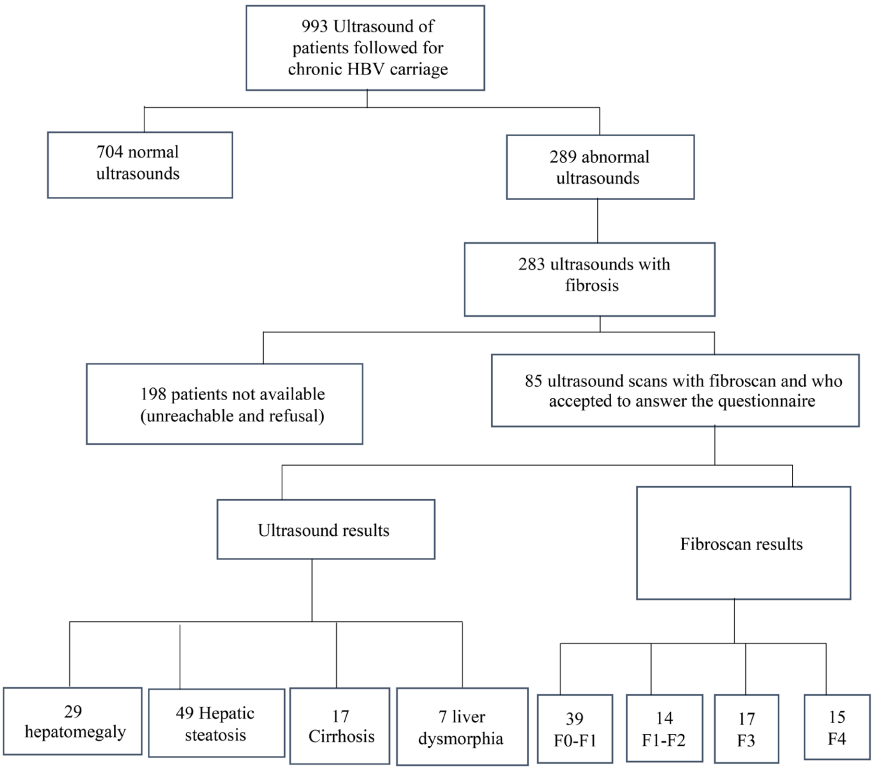


Figure 1. Flow chart of ultrasound and fibroscan results in chronic HBV infected patients.

were represented at 32.94% (N = 85) followed by informal sector actors at 17.65% (N = 85). Patients with a higher education were represented at 45.88% followed by those with secondary education at 28.4%. The majority of patients (85.88% or 73) lived in urban areas and follow-up was mainly carried out in a public facility (44.71%), followed respectively in a religious facility (27.06%), then private facility (22.35%) and the provinces (5.88%). In our study population, all fibroscan examinations were prescribed by a hepato-gastroenterologist (100%). Regarding alcohol consumption as another risk factor for fibrosis, n = 21 patients or 24.71% claimed to be regular consumers of alcohol in unspecified quantities.

According to the quality criteria of the ultrasound reports, some elements had not been filled in. Table 1 gives the distribution of the dimensions of the liver filled in on the different ultrasound reports. Average size of right liver was 137.706 mm with extremes of 45 and 177 mm. That of left liver was 96.417 mm with extremes of 80 and 122 mm. Those of segment 4 and segment 1 were respectively 36.945 and 38 with extremes of 21 and 51 mm and 9 and 55 mm.

Liver edge was recorded in the entire study population. The edge was regular with a frequency of 78.82% (n = 67) and irregular with a frequency of 21.18% (n = 18).

Liver echotexture was homogeneous hyperechoic in 66 patients (77.65%), granular in 18 patients (21.18%) and micronodular in 4 patients (4.71%).

Table 1. Distribution of chronic hepatitis B virus infected patients according to liver size (N = 85).

Variables	effective	Averagesize	Standard deviation	Min	Max
Right liver	85	137.706	19.11	45	177
Left liver	24	96.417	10.521	80	122
Segment IV	73	36.945	7.137	21	51
Segment I	3	38	25.239	9	55

Hepatic steatosis appeared to be the most frequent ultrasound diagnosis (n = 49 or 57.65%) in these patients followed by hepatomegaly (n = 29 or 34.12%), cirrhosis (n = 17 or 20%) and dysmorphia (n = 7 or 0.08%).

The average time interval between ultrasound and fibroscan was 6 days, the maximum was 120 days and the minimum was 1 day for patients who had both examinations.

On fibroscan, 39 patients or 45.88% had a score between F0-F1, 14 patients or 16.47% between F1-F2, 17 patients or 20% had a score at F3 and 15 patients 17.65% had a score at F4. **Figure 2** shows fibroscan score frequency in our study population.

Association tests between liver echotexture findings on ultrasound and fibrosis on fibroscan showed a significant association between hyperechogeneous and granular liver with fibrosis. Respectively p-value was 0.2% and 0.01% and the strength of this association was 8.92 and 19.36.

Table 2 shows the association tests.

Association tests between final diagnosis on ultrasound and fibrosis on fibroscan showed a significant association between steatosis, cirrhosis, dysmorphia and fibrosis with a respective p-value of 0.02%, 0.02% and 0.13%. There was no significant association between hepatomegaly and fibrosis (p-value = 88%). **Table 3** shows the association tests.

The association tests between liver edge on ultrasound and fibrosis on fibroscan showed a positive association between liver edge and the presence of fibrosis. There was significant association between irregular edge of liver on ultrasound and fibrosis with p-value of 0.02%. There was also significant association between regular edge of liver on ultrasound and fibrosis with p-value of 0.09%. The strength of this association was 11 for regular edge and 13 for irregular edge.

Table 4 shows the association tests.

Figure 3 showed correlation between ultrasound diagnosis of cirrhosis and the advanced fibrosis (F4) on fibroscan in a 28-year-old patient with chronic hepatitis.

4. Discussion

The young age of chronic HBV infected patients seen on ultrasound has also been found in several sub-regional [1] [10] and national [13] [14] studies. However,

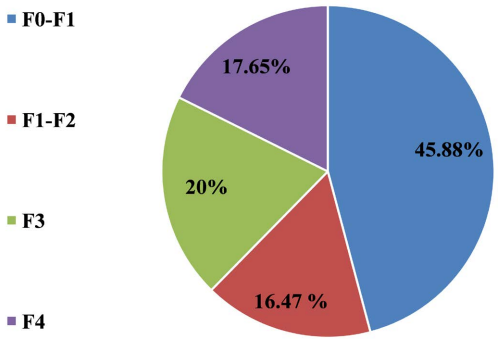


Figure 2. Fibroscan score frequency (N = 85).

Table 2. Correlation between liver echotexture and fibrosis on fibroscan in patients with chronic hepatitis B virus.

Variables	Fibrosis score				
Homogeneous hyperechogenous	**Fibrosis −**	**Fibrosis +**	**Total**	**Odd ratio**	**P-value**
Yes	36	30	66	8.92	0.0028
No	3	16	19		
Granular					
Yes	0	18	18	19.36	0.0001
No	39	28	67		
Micronodular					
Yes	1	3	4	0.74	0.3906
No	38	43	81		

*Fibrosis (+) = F1-F2, F3, F4; *Fibrosis (−) = F0-F1.

Table 3. Correlation between ultrasound diagnoses and fibroscan results of chronic hepatitis B virus infected patients.

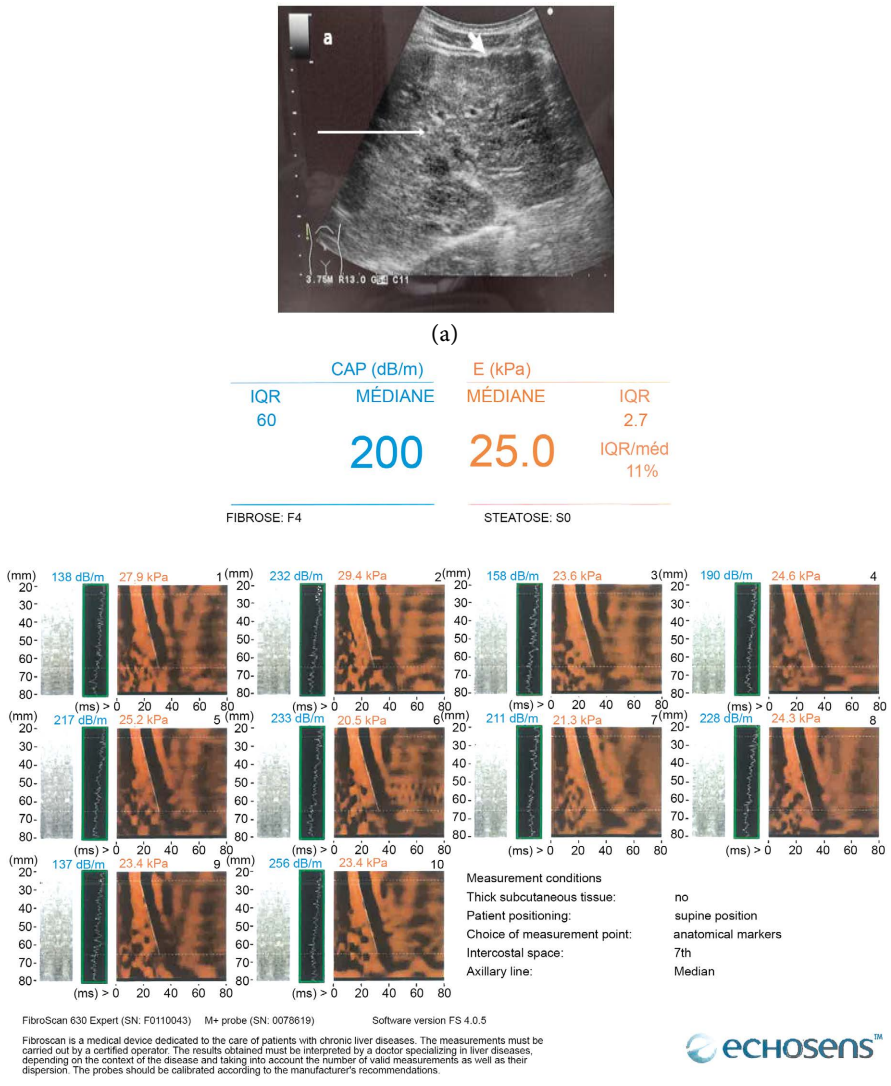
Variables	Fibrosis score				
Hepatomegaly	**Fibrosis −**	**Fibrosis +**	**Total**	**Odd ratio**	**P-value**
Yes	13	16	29	0.02	0.8883
No	26	30	56		
Hepatic steatosis					
Yes	31	18	49	14.08	0.0002
No	8	28	36		
Cirrhosis					
Yes	1	16	17	13.69	0.0002
No	38	30	68		
Dysmorphia					
Yes	3	4	7	11.07	0.0013
No	36	42	78		

*Fibrosis (+) = F1-F2, F3, F4; *Fibrosis (−) = F0-F1.

Table 4. Correlation between the appearance of liver edges on ultrasound and fibroscan findings in chronic hepatitis B virus infected patients.

Variables	Fibrosis score on fibroscan				
Regular edges	**Fibrosis −**	**Fibrosis +**	**Total**	**Coefficient**	**P-value**
Yes	37	30	67	11.12	0.0009
No	2	16	18		
Irregular edges					
Yes	2	16	18	13.69	0.0002
No	38	29	67		

*Fibrosis (+) = F1-F2, F3, F4; *Fibrosis (−) = F0-F1.



(a)

(b)

Figure 3. Cirrhosis diagnosed on ultrasound (a), correlated with severe fibrosis F4 on fibroscan (b) in a 28 years old patient followed for chronic hepatitis B virus carriage. (a): Liver with micronodular echotexture (white arrow) and irregular border (head of arrow); (b): Severe fibrosis F4 on fibroscan.

elsewhere in France, Cassinotto C. *et al*. (France 2016) found an average age of 58 years [15]. This difference could be explained by the low life expectancy of the Burkinabe population in general, which is 60 years [16] and the complications related to the natural evolution of the disease and the comorbidity factors often associated with chronic HBV infected patients in our context. In our study there was a male predominance (52.94%) with a sex ratio of 1.12. Male predominance is the most reported in the literature [1] [10] [14]. Male sex is recognized as a factor in the progression of liver fibrosis, which could partly explain their greater demand for ultrasound monitoring of the evolution of fibrosis. Furthermore, in Burkina Faso it is recognized that the majority of health expenses are supported by men [16] and therefore this could explain why they have more access to paid paraclinical examinations. The schooling rate in our study was 84.28%, other authors found figures close to ours [13] [17] [18]. This high rate of schooling in our population can be explained by the fact that the study took place in the city, where the schooling rate is generally high, but also by a better awareness of the risks among educated and informed patients. 85.88% of our study population lived in urban areas. Chronic HBV infected patients living in urban areas have better access to qualified personnel and technical facilities for their follow-up [13] [19]. All our patients were followed by a gastroenterologist who prescribed both ultrasound and fibroscan. This could be explained by the fact that good practice recommends that follow-up be done by specialists. However, given the high prevalence of HBV infection (9.1%) in the general population [20] in our country and the insufficient number of specialists, it is essential to scale up the care of patients to include general practitioners. Even though the majority of our study population was salaried or had an income-generating activity (80%), it was not possible for all patients to have both ultrasound and fibroscan. This could be explained by the fact that the expenses were supported by the patients and that the fibroscan remains a relatively expensive examination (47.54$) compared to ultrasound (15.85$) in a context where the minimum wage is 49$ in 2022.

The factors influencing the evolution of fibrosis are numerous and often associated in the same patient. In our study, only alcohol consumption was evaluated as a cofactor and 24.7% stated that they were alcohol consumers, which is a frequent phenomenon found in locoregional studies [3] [10] [13] [17] [21]. In our population 45.88% had minimal or non-significant fibrosis, 54.12% had significant fibrosis. The results are variable in the literature depending on the cohorts Diallo I *et al*. (Senegal 2016) found 57.14% of non-significant fibrosis and 42.86% of significant fibrosis [22] while Touré Ps *et al*. (Senegal 2016) found 89.9% of non-significant fibrosis, 10.1% of significant fibrosis [10].

In our study, a non-significant correlation ($p = 0.3906$) for a micronodular structure was found and this could be explained by the small sample size. Further studies with larger sample sizes are still relevant to clarify the issue. Ultrasound assessment of liver edge is a criterion associated with the diagnosis of fibrosis with the irregular type strongly associated with the diagnosis of fibrosis on fibroscan. These results are in agreement with those found in the literature,

Teyssier Y *et al*. (France 2020) found a match between liver edge on ultrasound and fibrosis on fibroscan [23]. The diagnosis of steatosis, cirrhosis and dysmorphia were significantly associated with the presence of fibrosis, while hepatomegaly was not significantly associated with fibrosis. This highlights the non-significant criterion of hepatomegaly which can express several pathologies. There is a significant association between steatosis diagnosed on ultrasound and fibrosis on fibroscan. Ultrasound allows the diagnosis of steatosis with a sensitivity of over 90%. However, the hyperechogenicity of the liver parenchyma may be the expression of a fibrosis that has not progressed very far, and ultrasound cannot make the distinction at this stage [24]. These different tests between ultrasound and fibroscan show us that there is a concordance between the diagnosis of fibrosis on ultrasound and the diagnosis of fibrosis on fibroscan. These results support the use of ultrasound in the periodic follow-up of chronic HBV carriers. It should be noted that hepatic ultrasound is an indispensable means of monitoring, available, accessible, affordable, non-invasive, reliable and adapted to our context, and that access to fibroscan is limited, costly, and not available in the majority of health centres in our settings. These two examinations are complementary and cannot be dissociated in the follow-up of chronic HBV infected patients. For this reason, the new fibroscan devices are coupled with ultrasound and we speak of echo-elastometry. Certain signs should be specified in all ultrasound reports because they may indicate liver fibrosis and guide the management of chronic HBV patients. These are: hyperechoic echotexture of the liver, irregular liver edges, hepatic dysmorphia, granular appearance, hepatic steatosis, cirrhosis (but prior to the diagnosis of cirrhosis, the above signs may point to appropriate management). As our study was carried out without funding, it was subject to limitations and constraints, including the failure to carry out the fibroscan due to a lack of financial resources, the sometimes long delay between the two examinations, incomplete data in the ultrasound reports, and the non-standardization of the data, which required additional data collection via mobile phone. However, we can also consider that these results reflect real life and current practice.

5. Conclusion

Detecting the presence of fibrosis and monitoring its evolution improve the management of patients with chronic liver disease. Our study shows that ultrasound and fibroscan are complementary in the monitoring of chronic HBV infected patients. Ultrasound is a good means of monitoring due to its low cost, reliability, availability and accessibility with precise signs to look for and record in the ultrasound report. Fibroscan becomes totally relevant for those cases of fibrosis not found on ultrasound but detected as early fibrosis on fibroscan.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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