Serum hyaluronic acid in chronic B and C viral hepatitis – a biomarker for assessing fibrosis in chronic hemodialysis patients

Olga Hilda Orasan[1], Madalina Sava[2], Mihaela Iancu[3], Angela Cozma[1], Aniela Saplontai-Pop[4], Remus Aurel Orasan[5], Ioan Mihai Patiu[5], Dan Lucian Dumitrascu[6]

[1]University of Medicine and Pharmacy, 4th Medical Department, [2]University of Medicine and Pharmacy, student, [3]University of Medicine and Pharmacy, Medical Informatics and Biostatistics,[4]University of Medicine and Pharmacy, Heart Institute, [5]Nefromed Dialysis Centers, [6]University of Medicine and Pharmacy, 2nd Medical Department, Cluj Napoca, Romania

This paper was published under the frame of the European Social Fund, Human Resources Development Operational Programme 2007-2013, project no. POSDRU/159/1.5/S/138776.

INTRODUCTION

Chronic viral hepatitis / liver cirrhosis B or C in patients with end-stage renal disease treated by hemodialysis are more frequent than in general population and have a more severe evolution, particularly on account of the aggravation of liver fibrosis (F). Liver puncture biopsy, the gold standard for assessing F, has a higher risk of complications in hemodialysis patients-13,2% [1].
Serum hyaluronic acid (HA) is studied as a non-invasive marker of F in chronic B and C viral hepatitis in general population, but less in end-stage renal disease patients undergoing hemodialysis. The aim of our research was the validation by laboratory testing of HA as a biomarker that predicts F in chronic viral liver disease in hemodialysis patients.

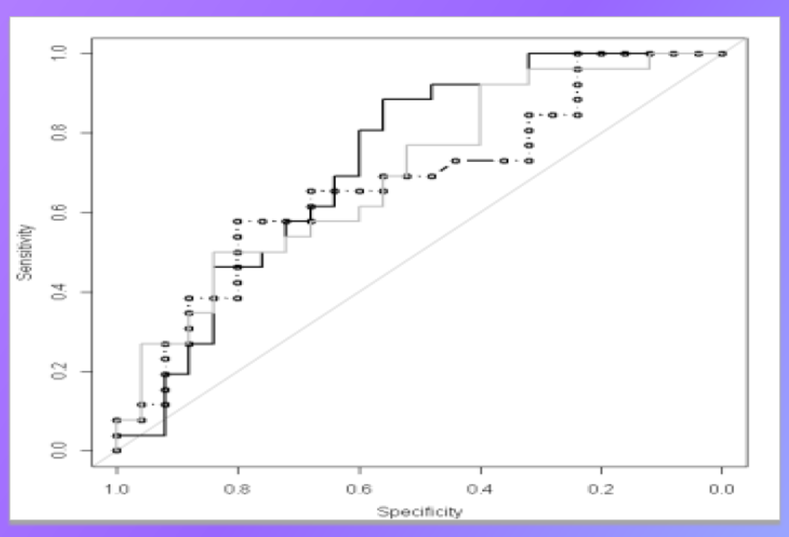
METHODS

This was a multicenter prospective, transversal and observational study which included 52 end-stage renal disease patients with chronic B (14) and C (38) viral hepatitis (age: 55.57±14.46 years, dialysis vintage: 132.59±86.02 months).
We evaluated HA as a non-invasive biomarker of F, compared to Fibroscan, APRI, ASAT/ALAT ratio and FIB4.
Considering Fibroscan as the standard test for the determination of F, we analyzed the possibility of determining HA threshold values to differentiate F in patients with chronic B and C viral hepatitis on hemodialysis.
Threshold values were determined using ROC curve analysis. In the case of a statistically significant ROC analysis result, we also determined the indicators of sensitivity (Se), specificity (Sp), the positive predictive value (VPP), the negative predictive value (VPN), the false positive rate (FP) and the false negative rate (FN). The comparison of HA with APRI, ASAT/ALAT ratio and FIB4 index was performed if these tests were also considered as a marker for determining F, by ROC curve analysis (AUC); multiple comparisons were performed using the de Long test, with a significance level after Bonferroni correction of 0.02.

RESULTS

Of the non-invasive tests analyzed, only HA, APRI and FIB4 were able to differentiate patients with F1 (HA AUC=0.725, 95%CI: 0.58-0.86, p=0.006; APRI AUC=0.686, 95%CI: 0.52-0.82, p=0.031; FIB4 AUC=0.697, 95%CI: 0.55-0.84, p= 0.016). No statistically significant differences were found between HA and APRI, ASAT/ALAT ratio and FIB4 in detecting F1 (de Long test, p>0.02), although in the studied sample, HA seemed to be more efficient than APRI, ASAT/ALAT ratio and FIB4, having the highest estimated AUC value. The HA threshold value for F1 was equal to **33.46 ng/mL**, with the following estimated values of the performance indicators: Se 88.46%, Sp 50%, VPP 64%, VPN 81%, FP 50%, FN 12% (figure 1).
HA was the only non-invasive test of the studied tests that could determine F2 (HA AUC=0.760, 95%CI: 0.62-0.89, p=0.002), with a threshold value of **80.24 ng/ml** (Se 63%, Sp 88%, VPP 75%, VPN 81%, FP 12%, FN 37%) (figure 2), and F3 (HA AUC=0.739, 95%CI: 0.59-0.88, p=0.008), with a threshold value of **88.54 ng/ml** (Se 60%, Sp 84%, VPP 60%, VPN 84%, FP 16%, FN 40%) (figure 3).
None of the studied non-invasive tests could determine F4 (HA p=0.086; APRI p=0.097; ASAT/ALAT ratio p=0.048; FIB4 p=0.097).

Figure 1. ROC curves of three fibrosis indices for the diagnosis of F1 score



Note. Black curve - ROC curve for HA ; dotted curve - ROC curve for APRI and grey curve - ROC curve for FIB4

Figure 2. ROC curve of HA for the diagnosis of F2 score

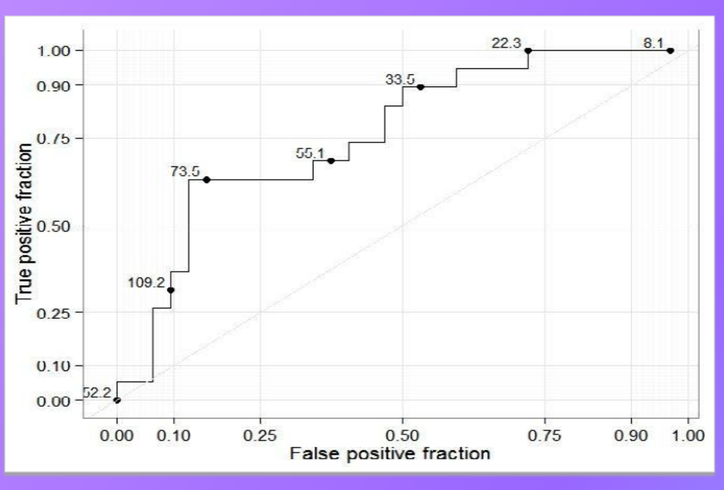
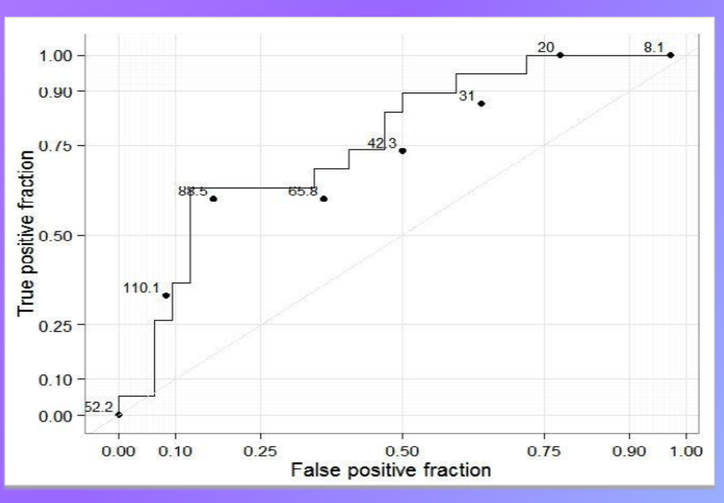


Figure 3. ROC curve of HA for the diagnosis of F3 score



CONCLUSION

In patients with chronic B and C viral hepatitis undergoing hemodialysis HA may be a useful biomarker for the liver fibrosis grades: F1-mild, F2-moderate and F3-severe, but it doesn't differentiate between chronic hepatitis (F1-F3) and liver cirrhosis (F4).

REFERENCE

1. Avila RE, Carmo RA, Farah Kde P et al. (2010) Hyaluronic acid in the evaluation of liver fibrosis in patients with hepatitis C on haemodialysis. Braz J Infect Dis. Jul-Aug;14(4):335-341

DOI: 10.3252/pso.eu.52era.2015