Concordance between FibroScan® and Aspartate aminotransferase-to-Platelet Ratio Index (APRI) using different cut-off values in 301 Asian adults with chronic HCV with no or compensated cirrhosis in Thailand and Malaysia

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Introduction

Numerous non-invasive fibrosis tests based on blood indices (such as Aspartate aminotransferase-to-Platelet Ratio Index (APRI) and Fibrosis-4 (FIB-4)) and imaging techniques (in particular, transient elastography by FibroScan®, Echosens) are now available and have replaced liver biopsy in the management of viral hepatitis. Nevertheless, the availability of FibroScan® is limited in resource-constrained settings. The use of readily available blood results to calculate APRI and of a reliable cut-off value to diagnose cirrhosis is important for national programs looking for simplification of liver fibrosis assessment without the need for costly investment in equipment. World Health Organization (WHO) recommend 2 cut-offs values for APRI (low > 1 and high > 2) to diagnosis and allocate treatment regimen as cirrhosis [1].

Methods

To determine a reliable APRI cut-off value, we retrospectively analyzed the concordance between FibroScan® and APRI in prospectively collected baseline data in adults with chronic HCV with no or compensated cirrhosis enrolled in an open label phase II/III, multicenter trial to assess the efficacy, safety, tolerance, and pharmacokinetics of ravidasvir plus sofosbuvir [2]. The presence of cirrhosis was determined either by a FibroScan® result >12.5 kPa (with M probe) or by an APRI >2 in the absence of a valid FibroScan® result. FibroScan® was performed by trained operators. Patients with significant cardiovascular and renal diseases were not included in the study. Non-cirrhotic and cirrhotic subjects were assigned to receive 12 and 24 weeks of treatment, respectively. FibroScan® and APRI results were considered concordant if the FibroScan® result was ≤12.5 kPa and the APRI was ≤2, or if the FibroScan® result was >12.5 kPa and the APRI was >2. Similar analyses were performed with APRI cut-off values of 1 and 1.5 and with FIB-4 cut-off values of 1.45 and 3.25.

Results

The baseline characteristics of the 301 patients were: 231 (77%) male gender, median age was 47 years (IQR 40-55), median BMI was 23.5 kg/m^2 (IQR 21.3-26.7), 90 (30%) HIV co-infection, median ALT was 71 U/L (IQR 43-111), median AST was 55 U/L (IQR 37-81), median platelets was 213x10^9/L (IQR 165-260), median HCV RNA was 6.3 Log_{10} IU/mL (IQR 5.8-6.7), HCV genotypes (GT): GT 1a = 98 (33%), GT 1b = 27 (9%), GT 2 = 2 (1%), GT 3 = 158 (52%), GT 6 = 16 (5%).

Of the 301 subjects enrolled, 4 had invalid FibroScan® results. Of the remaining 297 subjects, 241 (81%) had concordant results and 56 (19%) had discordant results: 49 (16%) had FibroScan® >12.5 kPa but APRI ≤2, and 7 (2%) had FibroScan® ≤12.5 kPa but APRI >2 (table 1). The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) are presented in table 2. Results using APRI cut-off values of 1 and 1.5, and FIB-4 cut-off values of 1.45 and 3.25 are given in tables 1 and 2.

Table 1: Concordance between FibroScan® and APRI and FIB-4 at different cut-off values

Fibrosis staging		Total	APRI						FIB-4			
			≤ 2	> 2	≤ 1.5	> 1.5	≤ 1	> 1	≤ 1.45	> 1.45	≤ 3.25	> 3.25
FibroScan	≤ 12.5 kPa	218 (72%)	211 (70%)	7 (2%)	203 (67%)	15 (5%)	179 (59%)	39 (13%)	145 (48%)	73 (24%)	211 (70%)	7 (2%)
	> 12.5 kPa	79 (26%)	49 (16%)	30 (10%)	39 (13%)	40 (13%)	16 (5%)	63 (21%)	7 (2%)	72 (24%)	47 (16%)	32 (11%)
	Invalid result	4 (1%)	3 (1%)	1 (<1%)	3 (1%)	1 (<1%)	2 (<1%)	2 (<1%)	2 (1%)	2 (1%)	2 (1%)	2 (1%)

PS: using blood index patients under-treated, patients correctly treated, patients over-treated

Table 2: Sensitivity, specificity, PPV, NPV of APRI and FIB-4 at different cut-off values

	APRI cut-off value of 2	APRI cut-off value of 1.5	APRI cut-off value of 1	FIB-4 cut-off value of 1.45	FIB-4 cut-off value of 3.25
Sensitivity *=true positive rate*	38% (30/79)	51% (40/79)	80% (63/79)	91% (72/79)	41% (32/79)
Specifity *=true negative rate*	97% (211/218)	93% (203/218)	82% (179/218)	67% (145/218)	97% (211/218)
Positive predictive value *=true positive/(true+false positive)*	81% (30/37)	73% (40/55)	62% (63/102)	50% (72/145)	82% (32/39)
Negative predictive value *=true negative/(true+false negative)*	81% (211/250)	84% (203/242)	92% (179/195)	95% (145/152)	82% (211/258)

Conclusions

In this population of Asian adults with chronic HCV (HCV serology prevalence is 2.5% and 0.9% respectively in Malaysia and Thailand), using a cut-off value of 2 for APRI resulted in good specificity but poor sensitivity as compared to FibroScan®. Had FibroScan® not been available, 49 of 79 (62%) cirrhotic subjects would have been treated for a shorter period than required and thus been at risk of virologic failure. Decreasing the APRI cut-off value to 1 greatly improved sensitivity while maintaining adequate specificity, and therefore may be a better option for countries looking for simplification of cirrhosis assessment and treatment duration assignment. The WHO lower APRI cut-off value for cirrhosis is better suited to our population.

References

[1] *World Health Organization. Guidelines for the Care and Treatment of Persons Diagnosed with Chronic Hepatitis C Virus Infection. Geneva: WHO Document Production Services; 2018.*

[2] *Safety and efficacy of ravidasvir plus sofosbuvir for 12 weeks in non-cirrhotic and 24 weeks in cirrhotic patients with hepatitis C virus genotypes 1, 2, 3 and 6: the STORM-C-1 phase II/III trial stage 1 results. Poster LBP-032 presented during EASL 2018*

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