NON-INVASIVE PREDICTION OF HEPATIC DECOMPENSATION IN PATIENTS WITH HIV

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BACKGROUND

People with HIV (PWH) are at high risk for compensated advanced chronic liver disease (cACLD) and hepatic decompensation[1]. While non-invasive tools (NITs) such as liver stiffness measurement (LSM) by transient elastography are used to identify those at risk of hepatic decompensation, these remain not validated and potentially inaccurate in the setting of non-cirrhotic portal hypertension which can occur in PWH[2]. We aimed to identify an optimal strategy to predict any liver event or death by comparing various NITs.

METHODS

This was an international multicenter retrospective cohort study. Overall, 8 centres contributed to this study. Participants were identified from prospectively maintained databases. Participants were included if they were above the age of 18 years, had a diagnosis of HIV, and had available LSM. Those with a previous episode of hepatic decompensation or with an unreliable baseline LSM were excluded. Demographic, behavioural, clinical, biochemical and virological data were retrieved.

Patients were stratified in 4 groups (Gr) based on the presence of thrombocytopenia (defined as Platelets ≤150) and the presence of cACLD (defined as LSM≥10kPa):

Group1= LSM<10kPa, Plt>150;
Group2= LSM<10kPa, Plt≤150;
Group3= LSM≥10kPa, Plt>150;
Group4= LSM≥10kPa, Plt≤150.

Incidence of any event (hepatic decompensation, hepatocellular carcinoma and death) was assessed. NITs evaluated included LSM, LSM to Plt ratio (LPR), LSM-spleen diameter to Plt ratio (LSPS), and Portal Hypertension risk score (PHRS)[3]. NITs were assessed using area under the receiver operating curve (AUROC) analysis to predict any event and thresholds were selected based on Youden's index. Predictors of any event were assessed using Cox-regression analysis. Analysis was performed using R software and SPSS (v24.0, IBM).

RESULTS

Table 1. Baseline characteristics

	Total Cohort (n=1488)
Age, years, SD	48.5 (8.4)
Gender, male, %	1131 (76.0%)
Duration HIV, years	18.5 (8.9)
Infection type, %	
Monoinfected	394 (26.5%)
HIV-HCV	966 (64.9%)
MSM, %	233 (15.7%)
IVDU, %	725 (48.7%)
Hypertension, %	181 (12.2%)
Diabetes, %	122 (8.2%)
Obesity, %	119 (11.6%)
Undetectable HIV viral load (< 40 copies), %	1058 (71.1%)
CD4, cells/mm^3, IQR	498 (397)
Nadir CD4, IQR	193 (234)
INR, SD	1.07 (0.25)
Albumin, g/L, SD	42 (5)
Bilirubin, umol/L, IQR	11.8 (10)
LSM, in kPa, IQR	7.6 (11.7)
cACLD, %	614 (41.3%)
Spleen size, cm, SD	12.1 (2.8)
Splenomegaly, %	153 (33.9%)
Thrombocytopenia, %	479 (32.2%)

Figure 1. Incidence rate of classical hepatic decompensation by LSM and Plt group

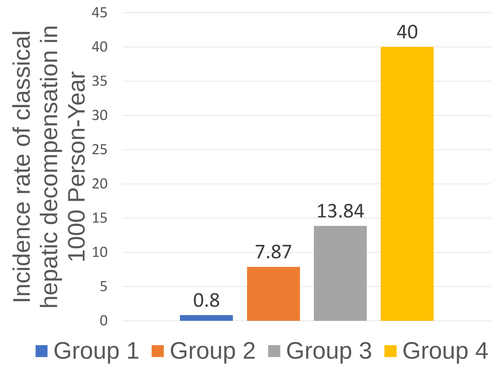

Table 2. Incidence rate ratio of hepatic decompensation by cACLD and Plt group

	Incidence rate ratio (95% CI)
Group 2, ref Group 1	9.8 (2.4-47.7)
Group 3, ref Group 1	17.2 (5.9-73.3)
Group 4, ref Group 1	44.8 (16.7-183.1)
Group 3, ref Group 2	1.8 (0.7-5.3)

Figure 2. ROC curve for NITs and development of any event

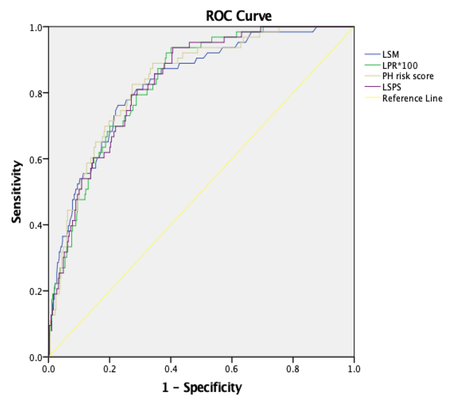

Table 3. Diagnostic accuracy of NITs to predict development of any event

	AUC (95% CI)	Cut-off	Sens	Spec	LR+	LR-
LSM	0.828 (0.776-0.881)	15.9	0.76	0.77	3.35	0.31
LPR100	0.831 (0.784-0.878)	5.49	0.92	0.62	2.39	0.13
LSPS	0.832 (0.785-0.884)	0.60	0.94	0.59	2.30	0.11
PH Risk score	0.835 (0.785-0.879)	0.54	0.83	0.73	3.02	0.24

Table 3. Multivariate Cox regression analysis for development of hepatic decompensation, hepatocellular carcinoma or death.

Variables	HR (95%CI)	p-value
Model 1		
LSM above 15.9kPa	4.09 (1.95-8.54)	<0.001
Gender, ref male	0.89 (0.46-1.73)	0.74
Duration of HIV, per year	1.01 (0.98-1.04)	0.60
Spleen diameter, per cm	1.10 (1.01-1.21)	0.04
Platelets, per unit	0.99 (0.99-1.00)	0.54
Co-infection status, ref HIV-monoinfection	1.38 (0.58-3.28)	0.46
Model 2		
LPR above 5.49	7.28 (2.59-20.50)	<0.001
Gender, ref male	0.81 (0.42-1.58)	0.54
Duration of HIV, per year	1.00 (0.97-1.03)	0.98
Spleen diameter, per cm	1.11 (1.02-1.22)	0.02
Co-infection status, ref HIV-monoinfection	1.26 (0.56-2.82)	0.58
Model 3		
LSPS above 0.60	11.97 (4.00-35.79)	<0.001
Gender, ref male	0.79 (0.41-1.53)	0.49
Duration of HIV, per year	1.00 (0.97-1.03)	0.93
Co-infection status, ref HIV-monoinfection	1.37 (0.62-3.04)	0.44
Model 4		
PHRS above 0.54	5.27 (2.57-10.80)	<0.001
Duration of HIV, per year	1.01 (0.98-1.04)	0.65
Co-infection status, ref HIV-monoinfection	1.71 (0.77-3.84)	0.19

CONCLUSIONS

In PWH, thrombocytopenia identifies patients at risk of liver events even in the absence of cACLD, likely due to non-cirrhotic portal hypertension. Although all NITs performed similarly well, the use of NITs combining Plt and spleen diameter provides a more global assessment of a patient's risk of any event.

ADDITIONAL KEY INFORMATION

References

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