

Does the Non-Alcoholic Fatty Liver Disease (NAFLD) Score Predict Liver Fibrosis Progression after HCV Treatment in HIV-HCV Co-infected Patients?

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- ### Background

 - Chronic HCV is associated with NAFLD, through both viral and host (BMI, obesity, insulin resistance) pathways
 - Prevalence of hepatic steatosis is ~40-85% in HCV+ individuals, with a higher prevalence among G3
 - Steatosis accelerates progression of HCV-related liver disease and development of HCC
 - HCV-related “metabolic steatosis” is a negative predictor of response to IFN-based therapy, but little data exists on the impact of steatosis on DAA treatment response
 - Objective:** To determine the role of the NAFLD score in hepatic fibrosis progression following HCV treatment in HIV-HCV co-infected patients
- ### Methods

 - The Canadian Co-infection Cohort (CTN 222) is a prospective multicentre cohort study of 1,693 HIV-HCV co-infected patients from 18 sites in Canada
 - Liver fibrosis progression (regression) was defined as an increase (decrease) of at least one Metavir stage from pre-treatment as determined by FibroScan or aspartate aminotransferase-to-platelet ratio index (APRI)
 - A multivariate LOGISTIC model assessed the association of the NAFLD score (which integrates age, body mass index, hyperglycemia, liver transferases, platelet count and serum albumin) with the odds of liver fibrosis regression
 - A multivariate LINEAR model estimated the relationship between the NAFLD score and the percentage change in APRI (the best available proxy for fibrosis) post-treatment

Results

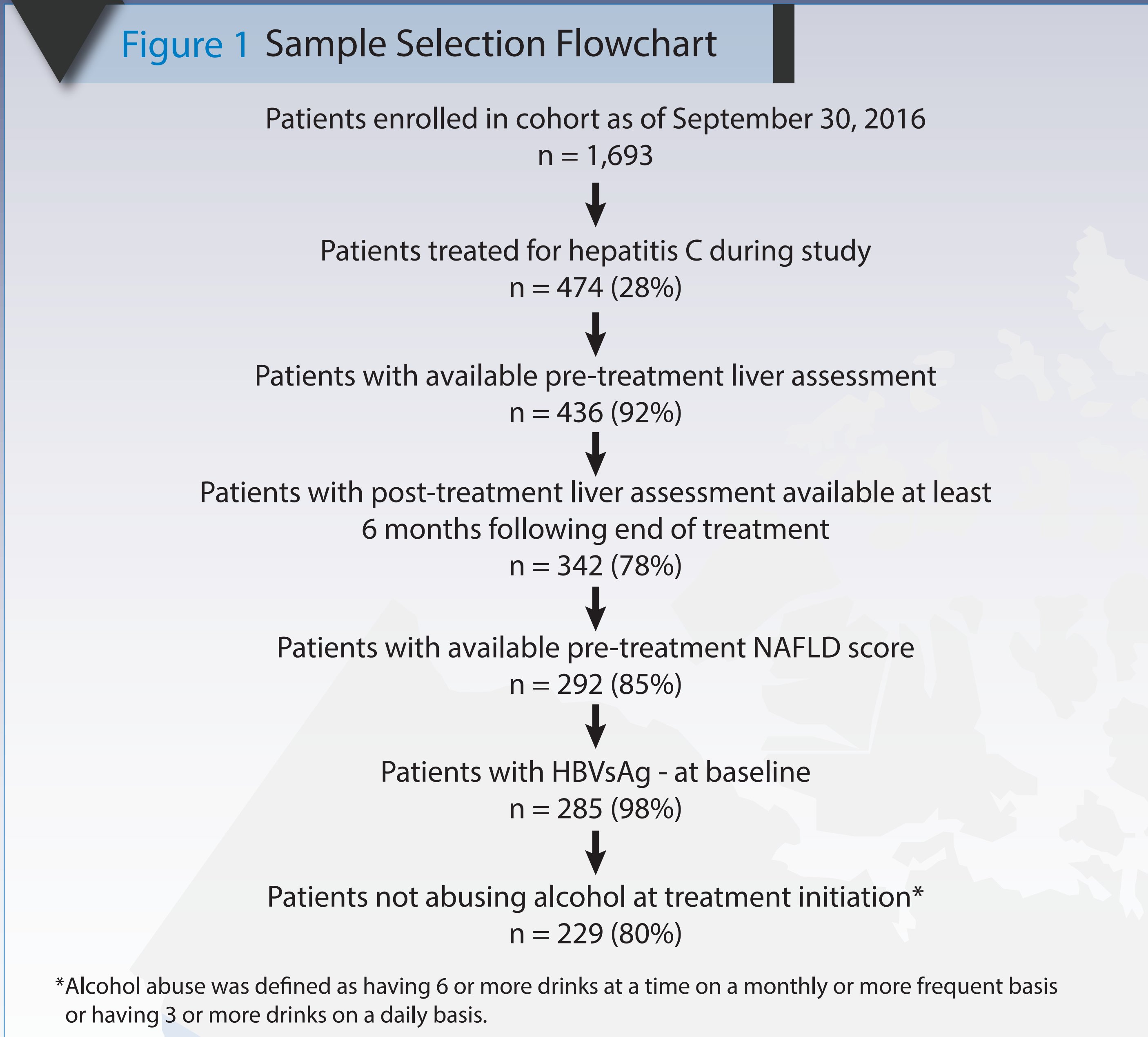


Table 1 Baseline characteristics

Age	49 (44 ; 53)
Ethnicity	
White	193 (84%)
Aboriginal	10 (4%)
Black	12 (5%)
Other	14 (6%)
HIV duration (years)	15 (8 ; 21)
CD4 count (cells/mL)	430 (280 ; 600)
CD4 nadir (cells/mL)	180 (88 ; 290)
HIV RNA (log ₁₀)	1.59 (1.59 ; 1.69)
HCV duration (years)	14 (6 ; 20)
Previous HCV treatment	44 (19%)
Active IDU	95 (41%)
Monthly income ≤ \$1,500	154 (67%)
APRI	0.97 (0.56 ; 1.76)
Platelets	164 (111 ; 209)
NAFLD score	-1.6 (-2.5 ; -0.6)
Note: Results presented as median (Q1 ; Q3) or frequencies with percentages	

- Between 6 and 24 months post-treatment (median 1.4 years), 5% progressed, 25% regressed and 70% remained stable

Table 2 Regression Models

Variable	Odds of liver fibrosis regression*		Percentage change in APRI post-treatment†	
	Odds ratio	95% C.I.	Coefficient	95% C.I.
SVR status post-treatment	3.74	(1.49 ; 10.21)	-0.80	(-0.97 ; -0.62)
Log of pre-treatment NAFLD score	0.47	(0.03 ; 6.70)	1.12	(0.56 ; 1.69)
Log of pre-treatment APRI score	6.23	(3.48 ; 12.05)	-0.58	(-0.69 ; -0.47)
DAA-based treatment	0.88	(0.38 ; 2.02)	-0.10	(-0.28 ; 0.07)
Genotype 3	0.91	(0.32 ; 2.46)	-0.06	(-0.30 ; 0.17)
HCV duration (per 5 years) at initiation	1.05	(0.83 ; 1.33)	0.04	(-0.01 ; 0.08)
CD4 count (per 100 units) at initiation	1.04	(0.92 ; 1.16)	-0.00	(-0.03 ; 0.02)
Lipodystrophy prior to treatment	0.52	(0.14 ; 1.71)	0.06	(-0.18 ; 0.31)
Waist circumference (cm) at initiation	1.01	(0.97 ; 1.04)	-0.00	(-0.01 ; 0.00)
*The dependent variable for this model was a binary indicator for fibrosis regression, based on Metavir stage				
†The dependent variable for this model was the natural log of the percentage change in APRI from pre-treatment to post-treatment				
C.I. = Confidence Interval				

- In the logistic model, the NAFLD score had no effect on fibrosis regression; however, SVR and pre-treatment APRI were associated with regression
- In the linear model, the NAFLD score was associated with increases in APRI post-treatment

Analysis #2

- A second analysis was done with CCC and LIVEHIV cohort participants who had radiographic evidence (CT/MRI/US/CAP) of NAFLD prior to treatment
- Among the 78 patients, 18 (23%) had NAFLD and 60 (77%) did not have NAFLD prior to treatment

Results (median (IQR)):

Pre-treatment APRI	Post-treatment APRI
NAFLD+: 0.9694 (0.7258, 2.6120)	NAFLD+: 0.4383 (0.3289, 0.9769)
NAFLD-: 1.0170 (0.6422, 2.8160)	NAFLD-: 0.4121 (0.3190, 0.7323)

- Change in APRI from pre- to post-treatment
NAFLD+: -0.5833 (-1.6110, -0.1994)
NAFLD-: -0.4721 (-1.4500, -0.1679)
- Percentage change in APRI from pre- to post-treatment
NAFLD+: -58.33 (-65.19, -35.80)
NAFLD-: -58.11 (-73.31, -30.05)

Conclusions

- SVR was strongly associated with fibrosis regression post-treatment
- A high pre-treatment APRI was predictive of recovery, indicating reduction in inflammation or the greater potential for change to the mean
- After controlling for confounders, a higher NAFLD score appeared to be associated with increases in APRI post-treatment
- Management of fatty liver disease following treatment may be essential to achieve optimal liver outcomes after cure