Abstract P-555

Significance of Alcohol Abuse Diagnosis vs Other Risk Factors for Advanced Fibrosis by FIB-4 in the CNICS Cohort

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BACKGROUND

Liver disease has emerged as a major cause of non-AIDS-related death among patients with HIV. Given the limitations of liver biopsy, noninvasive markers of hepatic fibrosis such as FIB-4, an index derived from age, platelet count and aminotransferase levels (ALT, AST), have been validated and shown to predict both severity of fibrosis and clinical outcomes.[1,2]

We studied current alcohol use as measured systematically across sites by a self-reported clinical assessment, alcohol history as captured by clinician-recorded alcohol diagnoses over time, and clinical factors such as viral hepatitis and evaluated their associations with advanced fibrosis as represented by FIB-4 >3.25 in a large clinical cohort of HIV-infected patients across the U.S.

METHODS

- We examined all 8,220 patients across 6 sites in the Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) cohort who completed self-reported assessments from Sept 2005 to May 2013 as part of routine care and had at least one of FIB-4 labs. The most recent self-reported data and lab values were used.
- FIB-4 formula = (Age [years] x AST [IU/L]) / (Platelets [10^9/L] x (ALT [IU/L])$^{1/2}$). A FIB-4 score >3.25 has an estimated positive predictive value for advanced fibrosis (Ishak fibrosis score 4-6) of 65%.[3]
- Current alcohol use was categorized using AUDIT-C scores with at-risk use defined as AUDIT-C score ≥5 for men, ≥4 for women.
- We defined alcohol diagnosis as having an alcohol abuse and/or dependence diagnosis recorded at least once over time in the cohort.
- Logistic regression was used to analyze possible clinical predictors of FIB-4 score >3.25.

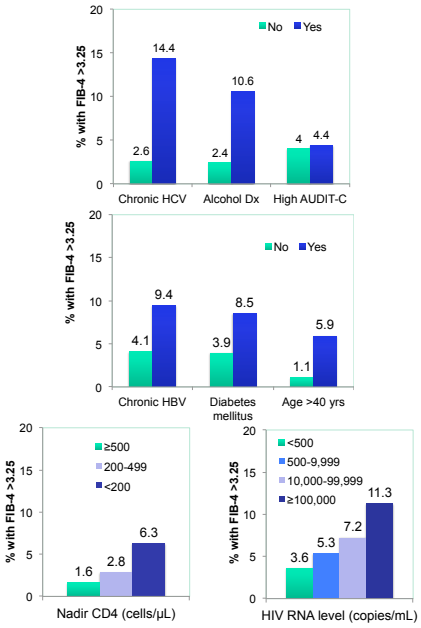
RESULTS

Table 1. Baseline Characteristics

	Total (N=8220)	HIV Monoinfected (n=7054)	HIV-HCV Coinfected (n=1166)
Age, years (median, IQR)	45 (37-51)	45 (37-51)	48 (42-54)
Sex, male	7107 (86)	6149 (87)	958 (82)
Race			
White	4354 (53)	3697 (52)	657 (56)
Black	2050 (25)	1754 (25)	296 (25)
Hispanic	987 (12)	885 (13)	102 (9)
Other	829 (10)	718 (10)	111 (10)
HIV Risk factor			
MSM	5160 (63)	4750 (68)	410 (35)
IDU	1208 (15)	642 (9)	566 (50)
Heterosexual	1618 (20)	1452 (21)	166 (14)
Other	134 (2)	118 (2)	16 (1)
Chronic hepatitis B	360 (4.4)	311 (4.4)	49 (4.2)
Diabetes mellitus	755 (9)	623 (9)	132 (11)
Current CD4§, cells/mm^3			
≥500	4130 (50)	3625 (51)	505 (43)
200-499	3088 (38)	2612 (37)	476 (41)
<200	996 (12)	811 (12)	185 (16)
Nadir CD4, cells/mm^3			
≥500	945 (12)	863 (12)	82 (7)
200-499	3371 (41)	2942 (42)	429 (38)
<200	3895 (47)	3240 (46)	655 (56)
HIV RNA level§, copies/ml			
<500	6664 (81)	5741 (82)	923 (79)
500 to <10,000	623 (8)	531 (7)	92 (8)
10,000 to <100,000	584 (7)	477 (7)	107 (9)
≥100,000	329 (4)	285 (4)	44 (4)
Current HAART	6730 (86)	5828 (87)	902 (83)
Alcohol Dependence/ Abuse Diagnosis	1579 (20)	1129 (17)	450 (42)
Current At-Risk Alcohol Use (AUDIT-C score ≥5 for men, ≥4 for women)	1231 (16)	1082 (16)	149 (14)
FIB-4 score§			
<1.45	6154 (75)	5548 (78)	606 (52)
1.45-3.25	1712 (21)	1320 (19)	392 (34)
>3.25	354 (4)	186 (3)	168 (14)

Values above are number (%) except for age.
§Most recent lab values closest to clinical assessment survey.

DISTRIBUTION of High FIB-4 by Variety of Clinical Factors



P-value <0.001 for all of above except for AUDIT-C, P=0.5.

Table 2. Relative Risk of High FIB-4

	Bivariate Analysis		Multivariable Analysis	
Factor	**OR**	**95% CI**	**aOR**	**95% CI**
Chronic hepatitis C	6.2	5.0-7.7	4.2	3.3-5.4
Age >40 years	5.4	3.7-7.8	4.7	3.2-7.4
HIV viral level, copies/ml §				
500 – 9,999	1.5	1.0-2.2	1.6	1.0-2.4
10,000 – 99,999	2.1	1.5-2.9	2.7	1.8-3.9
≥100,000	3.4	2.3-4.8	4.8	3.1-7.5
CD4 nadir, cells/mm^3 §§				
200-499	1.8	1.0-3.0	1.6	0.9-2.9
<200	4.2	2.5-7.1	2.5	1.4-4.4
Alcohol dependence/abuse	4.8	3.9-6.1	3.1	2.4-3.9
Chronic hepatitis B	2.5	1.7-3.6	2.0	1.3-3.2
Diabetes mellitus	2.3	1.7-3.0	1.8	1.3-2.5

OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval
§ Referent category: HIV RNA <500 copies/mL
§§ Referent category: CD4 nadir ≥500 cells/mm^3

CONCLUSIONS

- In a large diverse population of HIV-infected patients with multiple comorbidities, we identified several independent risk factors for advanced hepatic fibrosis - chronic HCV or HBV, diabetes, HIV viremia, older age and low nadir CD4.
- Alcohol history as measured by diagnoses over time appears to be a more robust predictor of liver fibrosis than current at-risk alcohol use. This highlights the importance of alcohol behavior over time rather than current use in outcomes that require substantial time to develop such as liver fibrosis.

REFERENCES

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