Hepatic Steatosis and Fibrosis Diagnosed by Transient Elastography with Controlled Attenuation Parameter in Canadians living with HIV Receiving Antiretroviral Therapy: Results of a Screening Program of 1,033 patients

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Background: Liver disease is emerging as a major health concern in HIV-infected patients. However prospective, large-scale data on hepatic steatosis and fibrosis are lacking.

Methods: We prospectively investigated prevalence and predictors of hepatic steatosis and fibrosis by transient elastography (TE) and associated controlled attenuation parameter (CAP) in a large series of unselected HIV-infected adults as part of a routine screening program. Fatty liver (any grade involving >10% of hepatocytes) was defined as CAP ≥238. Significant liver fibrosis and cirrhosis were defined as TE measurement ≥7.1 and ≥13 kPa, respectively. Predictors of hepatic steatosis and significant liver fibrosis were determined using logistic regression analysis.

Results: 1033 consecutive HIV-infected patients (mean age 50.5±9.9 years, 77.6% men, mean CD4 590±298, 90% on antiretrovirals) were included in 2013-2016. Coinfection with HCV and HBV was found in 35% and 6% of cases, respectively. HCV genotype 3 was present in 19% of HIV/HCV coinfected patients. Hazardous alcohol use was found in 8% of patients. Prevalence of hepatic steatosis, significant liver fibrosis and cirrhosis by TE with CAP was 51%, 31% and 13%, respectively (Figure 1). The results of a

multivariable analysis are shown in the Table. After adjustment, significant liver fibrosis was associated with duration of HIV infection, being overweight, HCV coinfection, ALT>ULN and CD4<200, while black ethnicity was found to be protective. Hepatic steatosis was associated with diabetes, being overweight, low HDL cholesterol and high triglycerides, while HCV coinfection was found to be protective.

Conclusion: Hepatic steatosis and fibrosis are major health comorbidities in Canadians living with HIV. Hepatic steatosis is particularly frequent in HIV mono-infected patients, likely due to high prevalence of metabolic dysfunction. Liver fibrosis is associated with HCV coinfection, while steatosis is less prevalent, likely due to low proportion of HCV genotype 3 and possibly to the high prevalence of cirrhosis, resulting in burned out fatty liver. Non-invasive screening strategies can help early diagnosis and initiation of interventions, including control of weigh loss, optimal glycemic control, treatment of dyslipidemia and antiviral therapy for HCV.

Figure 1. Prevalence (%) of hepatic steatosis, significant liver fibrosis and cirrhosis by coinfection status.

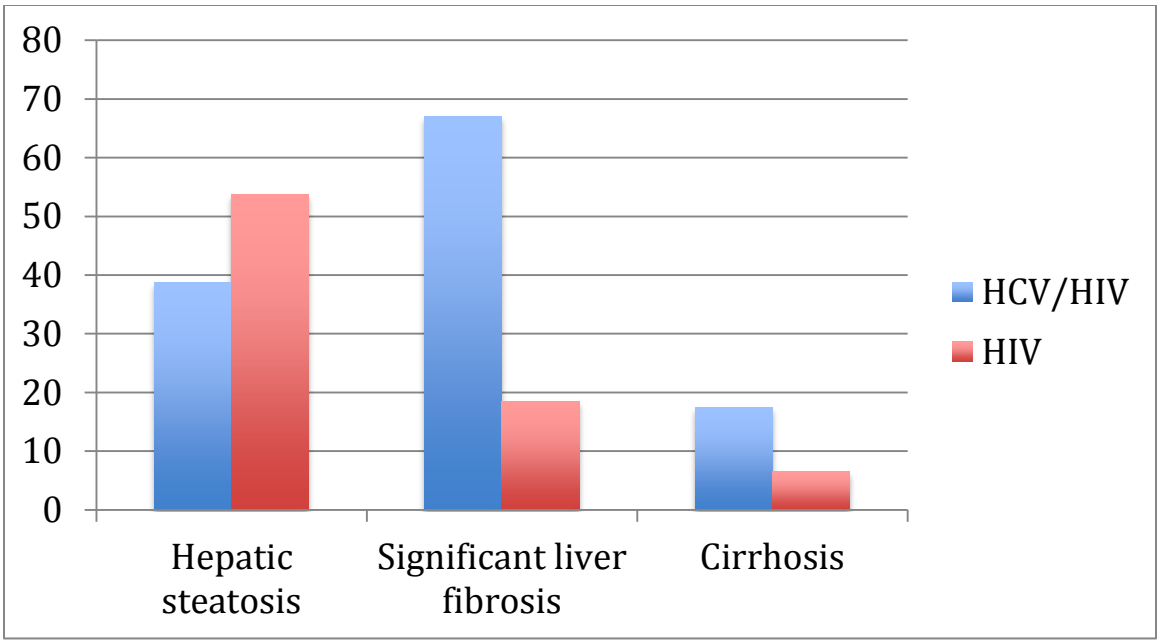
80
70
60
50
40
30
20
10
0
Hepatic steatosis
Significant liver fibrosis
Cirrhosis
HCV/HIV
HIV

Table 1. Multivariable analysis of factors associated with Hepatic steatosis and significant liver fibrosis.

	Significant liver fibrosis		**Hepatic steatosis**	
Variable	**aOR (95% CI)**	**p**	**aOR (95% CI)**	**p**
Black ethnicity	0.40 (0.17-0.92)	0.03	0.99 (0.54-1.83)	0.99
Duration HIV infection (per year)	1.07 (1.03-1.11)	<0.001	1.01 (0.98-1.05)	0.37
Diabetes	1.08 (0.37-3.18)	0.89	4.47 (1.49-13.43)	0.008
BMI>25Kg/m^2	2.29 (1.35-3.90)	<0.001	2.54 (1.59-4.06)	<0.001
HCV	2.95 (1.78-4.90)	<0.001	0.46 (0.29-0.73)	0.001
HBV	0.66 (0.20-2.17)	0.49	0.85 (0.33-2.17)	0.73
Didanosine	1.14 (0.56-2.31)	0.71	1.01 (0.51-2.01)	0.98
ALT>ULN	2.07 (1.25-3.42)	0.005	1.26 (0.77-2.05)	0.36
CD4<200	3.20 (1.41-7.23)	0.005	0.50 (0.21-1.20)	0.12
HDL cholesterol (per unit)	0.67 (0.36-1.26)	0.22	0.36 (0.19-0.69)	0.002
Triglycerides (per unit)	0.98 (0.80-1.19)	0.82	1.28 (1.05-1.55)	0.01