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Chronic HCV Infection Accelerates Non-Liver Mortality in HIV Patients: a Nationwide Cohort Study

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ABSTRACT (Updated)

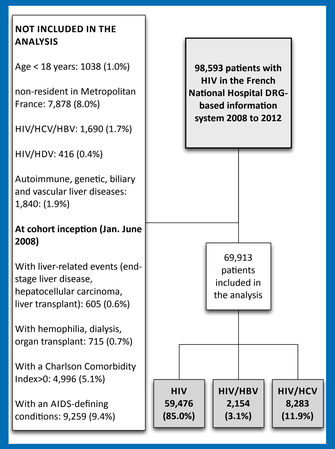
BACKGROUND:HIV worsens the course of HCV infection. Whether HCV infection accelerates HIV progression and non-liver mortality is controversial. HBV treatment guidelines recommend that it be administered to all HIV/HBV patients regardless of liver fibrosis. HCV treatment guidelines recommend that it be administered to HIV/HCV patients with significant (≥F2) liver fibrosis. The aim of this nationwide study was to assess whether HCV hastens overall and non-liver mortality in HIV-infected patients.

METHODOLOGY: We conducted a retrospective, longitudinal analysis of the French National Hospital DRG-based information system. All HIV-infected patients receiving hospital care from January 2008 to December 2012 were included, and their medical trajectory was tracked in all French hospitals with use of the International Classification of Diseases (ICD-10), medical procedures, and in-hospital mortality as recorded per stay. Exclusion criteria involved: age 18 years, non-resident in Metropolitan France; triple infection (HIV/HCV/HBV; HIV/HBV/HDV); autoimmune, genetic, biliary and vascular liver diseases; and patients identified at cohort inception with AIDS-defining conditions, liver-related events (end-stage liver disease, hepatocellular carcinoma, liver transplant), hemophilia, dialysis, organ transplant, and a Charlson Comorbidity Index>0. A Cox model was initially used to estimate the overall risk of death adjusted for gender, age, and alcoholism; time-dependent covariates were then incorporated to control for the competitive risks of liver-related events or AIDS-defining conditions.

RESULTS: Of 69,913 HIV-infected patients (male 71.3%; mean age 42.3 years), 2,366 deaths occurred in 247,484 patient-years. Overall mortality was higher in 8,283 (7.5%) HIV/HCV patients as compared to 59,476 (2.8%) HIV patients (HR 1.79, P<0.0001), while it did not differ in 2,154 (3.9%) HIV/HBV patients (HR 1.21, P=0.09). When competitive risks were taken into account, non-liver-related mortality as well as non-liver, non-AIDS-related mortality remained higher in HIV/HCV coinfected patients (HR 1.36, P<0.0001 and HR 1.43, P<0.0001, respectively).

Conclusion: HCV infection increases overall and non-liver-related mortality in HIV-infected patients. This was not found in HIV/HBV infected patients, suggesting that viral suppression should be recommended for HCV coinfection as it is for HBV coinfection.

FLOWCHART



CHARACTERISTICS OF PATIENTS

Characteristic	HIV	HIV/HBV	HIV/HCV	P Value
Mean age (SD), yr	42.1 (11.9)	41.9 (10.6)	44.2 (7.6)	< 0.0001
Male sex, n (%)	38,258 (64.3)	1,523 (70.7)	5,801 (70.0)	< 0.0001
Alcoholism, n (%)	2,065 (3.5)	107 (5.0)	1,311 (15.8)	< 0.0001
ESLD, n (%)	982 (1.7)	89 (4.1)	669 (8.1)	< 0.0001
HCC, n (%)	49 (0.1)	36 (1.7)	185 (2.2)	< 0.0001
AIDS, n (%)	11,309 (19.0)	578 (26.8)	2,133 (25.8)	< 0.0001
Cancer, n (%)	4,007 (6.7)	194 (9.0)	747 (9.0)	< 0.0001
Ischemic or congestive heart disease, n (%)	2,404 (4.0)	82 (3.81)	416 (5.0)	0.0001
Stroke, n (%)	1,619 (2.72)	70 (3.3)	270 (3.3)	0.001
Other severe condition, n (%)	8,038 (13.5)	307 (14.2)	1,781 (21.5)	< 0.0001
Death, n (%)	1,660 (2.8)	84 (3.9)	622 (7.5)	< 0.0001

RISK FACTORS OF ALL-CAUSE DEATH AMONG 69,913 FRENCH HIV-INFECTED PATIENTS

Characteristic	Hazard Ratio	95% Hazard Ratio Confidence Limits		P Value
MALE	1.257	1.143	1.383	<.0001
AGE (35-39)	1.631	1.327	2.005	<.0001
AGE (40-44)	2.364	1.967	2.84	<.0001
AGE (45-49)	2.941	2.449	3.532	<.0001
AGE (50-54)	3.719	3.069	4.507	<.0001
AGE (55-64)	4.935	4.106	5.932	<.0001
AGE ≥ 65	9.443	7.779	11.463	<.0001
Alcoholism	2.243	2.009	2.504	<.0001
HIV/HBV	1.211	0.972	1.508	0.088
HIV/HCV	1.785	1.616	1.971	<.0001

Reference group: female, age below 35, no chronic alcoholism ,HIV monoinfected

RISK FACTORS OF ALL-CAUSE DEATH AMONG 69,913 FRENCH HIV-INFECTED PATIENTS CONTROLLED FOR THE OCCURENCE OF END-STAGE LIVER DISEASE (ESLD)

Characteristic	Hazard Ratio	95% Hazard Ratio Confidence Limits		P Value
MALE	1.248	1.134	1.373	<.0001
AGE (35-39)	1.59	1.294	1.955	<.0001
AGE (40-44)	2.307	1.919	2.773	<.0001
AGE (45-49)	2.811	2.339	3.38	<.0001
AGE (50-54)	3.459	2.853	4.195	<.0001
AGE (55-64)	4.347	3.614	5.228	<.0001
AGE ≥ 65	7.927	6.526	9.629	<.0001
Alcoholism	1.119	0.994	1.26	0.0627
HIV/HBV	1.031	0.827	1.285	0.7857
HIV/HCV	1.362	1.23	1.508	<.0001
ESLD	18.119	16.332	20.102	<.0001

Reference group: female, age below 35, no chronic alcoholism ,HIV monoinfected, no end-stage liver disease

RISK FACTORS OF ALL-CAUSE DEATH AMONG 69,913 FRENCH HIV-INFECTED PATIENTS CONTROLLED FOR THE OCCURENCE OF END-STAGE LIVER DISEASE (ESLD) AND AIDS

Characteristic	Hazard Ratio	95% Hazard Ratio Confidence Limits		P Value
MALE	1.221	1.109	1.343	<.0001
AGE (35-39)	1.514	1.232	1.861	<.0001
AGE (40-44)	2.186	1.819	2.627	<.0001
AGE (45-49)	2.691	2.239	3.233	<.0001
AGE (50-54)	3.165	2.611	3.838	<.0001
AGE (55-64)	4.024	3.346	4.841	<.0001
Age > 65	7.122	5.864	8.649	<.0001
Alcoholism	1.027	0.914	1.153	0.6554
HIV/HBV	0.982	0.788	1.223	0.8688
HIV/HCV	1.431	1.295	1.583	<.0001
ESLD	10.618	9.574	11.774	<.0001
AIDS	6.448	5.922	7.021	<.0001

Reference group: female, age below 35, no chronic alcoholism ,HIV monoinfected, no end-stage liver disease, no transition to AIDS

CONCLUSION

HCV increases overall mortality in HIV-infected patients, even after controlling for the occurrence of ESLD and AIDS.

This was not found in HIV/HBV infected patients.

Viral suppression should be recommended for HCV coinfection as it is for HBV coinfection.

Presented by Prof Yazdanpanah at CROI 2014. *Contact: Vincent Mallet, Paris, France; e-mail, vincent.mallet@cch.aphp.fr.*