

HIV coinfection shortens the survival of patients with hepatitis C virus-related decompensated cirrhosis

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Background: As survival of human immunodeficiency virus (HIV)-infected persons has improved due to widespread use of highly active antiretroviral therapy, mortality due to hepatitis C virus (HCV)-related liver disease has increased in this setting. Consequently, cirrhosis caused by HCV has become a major cause of death in some areas. These facts have led to some experts to consider liver transplantation as a suitable therapeutic tool in coinfecting patients with HCV-related end stage liver disease. For this reason, it is required to know whether HIV coinfection reduces the survival of coinfecting patients with HCV-related end stage liver disease. This may help us to establish priorities between transplantation candidates rationally.

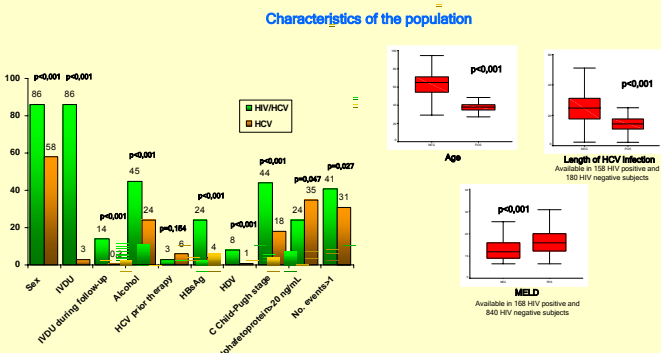
Objective: To compare the survival of HIV-infected and HIV-uninfected patients with decompensated cirrhosis due to HCV.

Results: 1037 HCV monoinfected and 180 HCV/HIV coinfecting patients with decompensated cirrhosis and fulfilling the inclusion criteria attended the participant hospitals during the study period. In 225 (18%) individuals, 13 (7%) HIV-infected and 212 (20%) uninfected, the life status could not be determined at closing the study. Three hundred and eighty-six (37%) patients without HIV infection and 100 (56%) HIV-infected individuals died during the follow-up. Liver disease was the cause of death in 332 (86%) monoinfected individuals and in 81 (81%) coinfecting patients. AIDS accounted for 5% of deaths in the latter group.

Methods: In a retrospective cohort study, we analyzed patients with decompensated liver cirrhosis who were attended in eight hospitals in Andalusia (Southern Spain) from January 1997 to December 2002 and that fulfilled the following inclusion criteria: (1) older than 18 years; (2) positive serum anti-HCV; (3) detectable plasma HCV-RNA; (4) no evidence of metabolic or autoimmune liver disease, according to clinical history, appropriate laboratory tests, and, when available, histological examination; (5) no previous decompensation of liver disease. HIV-infected and HIV-uninfected patients received similar care. Data were censored at the date of death or when the last information on life status was obtained and no later than December 31st, 2002. For patients who underwent liver transplantation, the date of censoring was that of the surgical procedure.

Cirrhosis was diagnosed by histological examination or by the combination of clinical, biochemical and ultrasound imaging data agreeing with such a diagnosis. Cirrhosis cases that presented with ascites, portal hypertensive gastrointestinal bleeding, hepatic encephalopathy, non-obstructive jaundice, spontaneous bacterial peritonitis or hepatocellular carcinoma, were classified as decompensated. The event that led the patient to the hospital was considered as the type of the first hepatic decompensation in the analysis. When more than one complication were present simultaneously, what dominated the clinical picture in the opinion of the attending physician was considered as the first hepatic decompensation.

The survival time was calculated from the date of the first decompensation to death or censoring date. The univariate analysis of survival was performed using the method of Kaplan-Meier. Curves were compared by the log rank test. Independent prognostic factors for survival were identified by a stepwise forward Cox regression model.

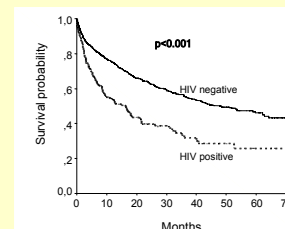


Predictors of mortality in HCV-related cirrhosis after the first decompensation

Variable	Median survival (months)	p univariate	RR* (95% CI)	p multivariate
Age (years) <63	52			
>63	31	0.02	2.25 (1.53-3.31)	<0.001
Source of HCV infection				
Intravenous drug use	21			
Other	44	<0.001	-	0.101
HIV Infection				
No	48			
Yes	16	<0.001	2.26 (1.51-3.38)	<0.001
Child-Pugh stage				
A	>72			
B	42	<0.001	1.95 (1.41-2.68)	<0.001
C	10		2.78 (1.86-4.70)	<0.001
Daily alcohol intake < 50g/dL	42			
≥ 50g/dL	37	0.34	-	-
HBV coinfection				
Yes	38			
No	41	0.42	-	-
Prior HCV therapy				
Yes	>72			
No	42	0.016	-	0.211
Care giver unit				
Hepatology	43			
Other	30	0.005	-	0.901
Serum anti-HDV positive				
Negative	41			
Positive	17	0.08	1.56 (1.12-4.77)	0.05
Active intravenous drug use				
Yes	13			
No	41	0.022	-	0.935
Type of first decompensation				
Gastrointestinal bleeding	>72			
Encephalopathy	19	<0.001	2.03 (1.26-3.10)	0.003
Other	34		1.16 (0.77-1.73)	0.480
No. of events at the first decompensation				
1	51			
>1	26	<0.001	1.23 (1.12-3.37)	0.023
MELD score				
≤ 13	>72			
>13	22	<0.001	1.05 (1.01-1.11)†	<0.001

*RR: relative risk, †For one unit of increase.

Probability of survival according to the HIV serostatus of the patients

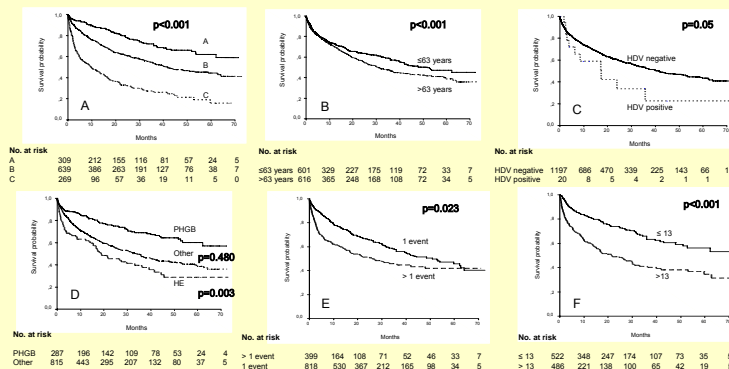


Estimates of survival at different times of the follow-up among HCV-infected individuals with and without HIV coinfection

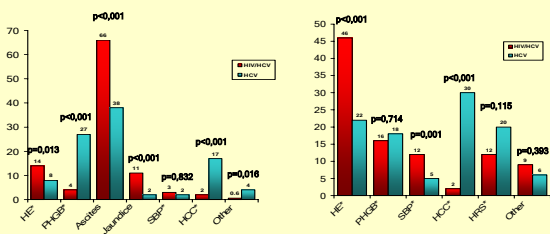
	1-year	2-years	5-years
HCV	74%	61%	44%
HCV/HIV	54%	40%	25%

No. at risk	1037	619	429	313	208	133	62	9
HIV negative	1037	619	429	313	208	133	62	9
HIV positive	180	75	46	30	19	11	5	3

Probability of survival according to predictors of death other than HIV infection. A: Child-Pugh stage. B: Age. C: HDV serostatus. D: Type of first hepatic decompensation. PHGB: portal hypertensive gastrointestinal bleeding. HE: hepatic encephalopathy. E: No. of simultaneous events at the first hepatic decompensation. F: MELD score



Frequency of specific events as first cirrhosis decompensation (left) and cause of death (right)



*HE: hepatic encephalopathy, PHGB: portal hypertensive gastrointestinal bleeding, SBP: spontaneous bacterial peritonitis, HCC: hepatocellular carcinoma, HRS: hepato-renal syndrome.

Conclusions: HIV coinfection reduces considerably the survival of patients with HCV-related liver cirrhosis after the first hepatic decompensation. This effect is independent of other markers of poor prognosis. This fact must be taken into account to establish the adequate timing to consider HIV-coinfecting patients with HCV-related end stage liver diseases as candidates for liver transplantation.