

# IMPACT OF HIV ON THE SURVIVAL OF HEPATOCELLULAR CARCINOMA IN HCV-INFECTED PATIENTS

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## ABSTRACT

**BACKGROUND:** Previous studies have suggested that hepatocellular carcinoma (HCC) has a more aggressive presentation and lower survival in HIV-infected patients. However, the differences in survival found in older studies may be due to a later diagnosis or to lower rates of treatment against HCC, and not to a specific negative impact of HIV infection. Objective: To assess the impact of HIV infection on the survival of HCC in HCV-infected patients.

**METHODS:** Multicenter cohort study (1999-2017). The GEHEP-002 cohort recruits all the HCC cases diagnosed in HIV-infected patients from 32 centers in Spain. For this study, 339 cases diagnosed in HIV/HCV-infected patients were selected. A control population of 118 HCC cases diagnosed in HCV-monoinfected patients during the study period at the Liver Unit from the Hospital de Valme was used. The survival after HCC diagnosis and its predictors, including HIV infection, were assessed.

**RESULTS:** HCC was diagnosed by surveillance, considered when all scheduled ultrasound had been performed at least within 1 year prior to HCC diagnosis, in 192 (57%) and 73 (62%) HIV+ and HIV- patients, respectively (p=0.3). In spite of similar rates of HCC diagnosis by screening, cases diagnosed in HIV/HCV-coinfected patients were diagnosed at advanced stages. Barcelona-Clinic Liver-Cancer (BCLC) stage at diagnosis was: 0-A 133 (39.6%), B 28 (8.3%), C 118 (35.1%) and D 57 (17%) in HIV+ and 0-A 63 (53.4%), B 21 (17.8%), C 27 (22.9%) and D 7 (5.9%) in HIV- patients (p<0.001). 103 (77%) HIV/HCV-coinfected patients and 4 (70%) HCV-monoinfected patients diagnosed at BCLC stage 0-A underwent curative therapies (p=0.09). 334 (73.1%) patients died, 303 (91%) of them due to HCC. The probability of death at 1-year and 2-year was 53% and 65% in HIV+ and 35% and 57% in HIV- patients (p=0.13). In a Cox model adjusted by age, sex, alcohol consumption, HIV infection and previous SVR, the independent predictors of mortality were BCLC stage at presentation, alfa-fetoprotein levels and lack of previous ultrasound surveillance. HIV infection did not show any trend for an independent association (HR 1.07; 95% CI: 0.74-1.54; p=0.7).

**CONCLUSION:** HIV coinfection has no impact on the survival after the diagnosis of HCC in HCV-infected patients. Although the mortality of HCC is somewhat higher in HIV/HCV-coinfected patients, these differences seem to be related with a later diagnosis of HCC in HIV-infected patients and not with HIV infection itself or a lower access to HCC therapy.

## BACKGROUND

Previous studies have suggested that hepatocellular carcinoma (HCC) has a more aggressive presentation and lower survival in HIV-infected patients.

However, the differences in survival found in older studies may be due to a later diagnosis or to lower rates of treatment against HCC, and not to a specific negative impact of HIV infection.

## OBJECTIVE

To assess the impact of HIV infection on the survival of HCC in HCV-infected patients.

## PATIENTS AND METHODS

### Study design

Multicenter retrospective cohort study (1999-2017).

### Patients

The GEHEP-002 cohort (ClinicalTrials.gov ID: NCT02785835) recruits HCC cases diagnosed in HIV-infected patients from 32 centers from Spain. For this analysis, HCC cases diagnosed in HIV/HCV-infected patients were selected.

A control population of HCC cases diagnosed in HCV-monoinfected patients during the study period at the Liver Unit from the H.U. Valme was used.

### Clinical data and follow-up

Surveillance of HCC was done by the performance of an abdominal ultrasound every 6 months.

HCC staging and treatment were established by the Barcelona-Clinic Liver Cancer (BCLC) staging system. Management of HCC was done according to EASL recommendations.

### Statistical analyses

The survival after HCC diagnosis and its predictors, including HIV infection, were assessed.

## RESULTS

Table 1. Characteristics of the study population (n=457).

Parameter	HIV positive (n = 339)	HIV negative (n = 118)	p
Age (years) <sup>1</sup>	50 (47-53)	66 (55-72)	< 0.001
Male sex, n (%)	306 (90.3)	79 (66.9)	< 0.001
HCV genotype, n (%) <sup>2</sup>			< 0.001
1	135 (47.9)	55 (67.1)	
2	3 (1)	0	
3	104 (36.9)	18 (22)	
4	40 (14.2)	5 (6.1)	
HIV RNA < 50 copies/mL, n (%)	252 (74.3)	-	
CD4 cells/ $\mu$ L <sup>1</sup>	381 (195-557)	-	
Antiretroviral therapy, n (%)	309 (91.2)	-	
MELD <sup>1</sup>	9 (7-13)	10 (8-13)	0.306
Child-Pugh stage A, n (%)	179 (52.8)	64 (54.2)	0.345
HCC diagnosis by surveillance, n (%)	192 (56.6)	73 (61.9)	0.291

<sup>1</sup>Median (Q1-Q3); Available in <sup>2</sup>282 HIV-infected patients.

## RESULTS

Figure 1. BCLC stage at HCC diagnosis by HIV status.

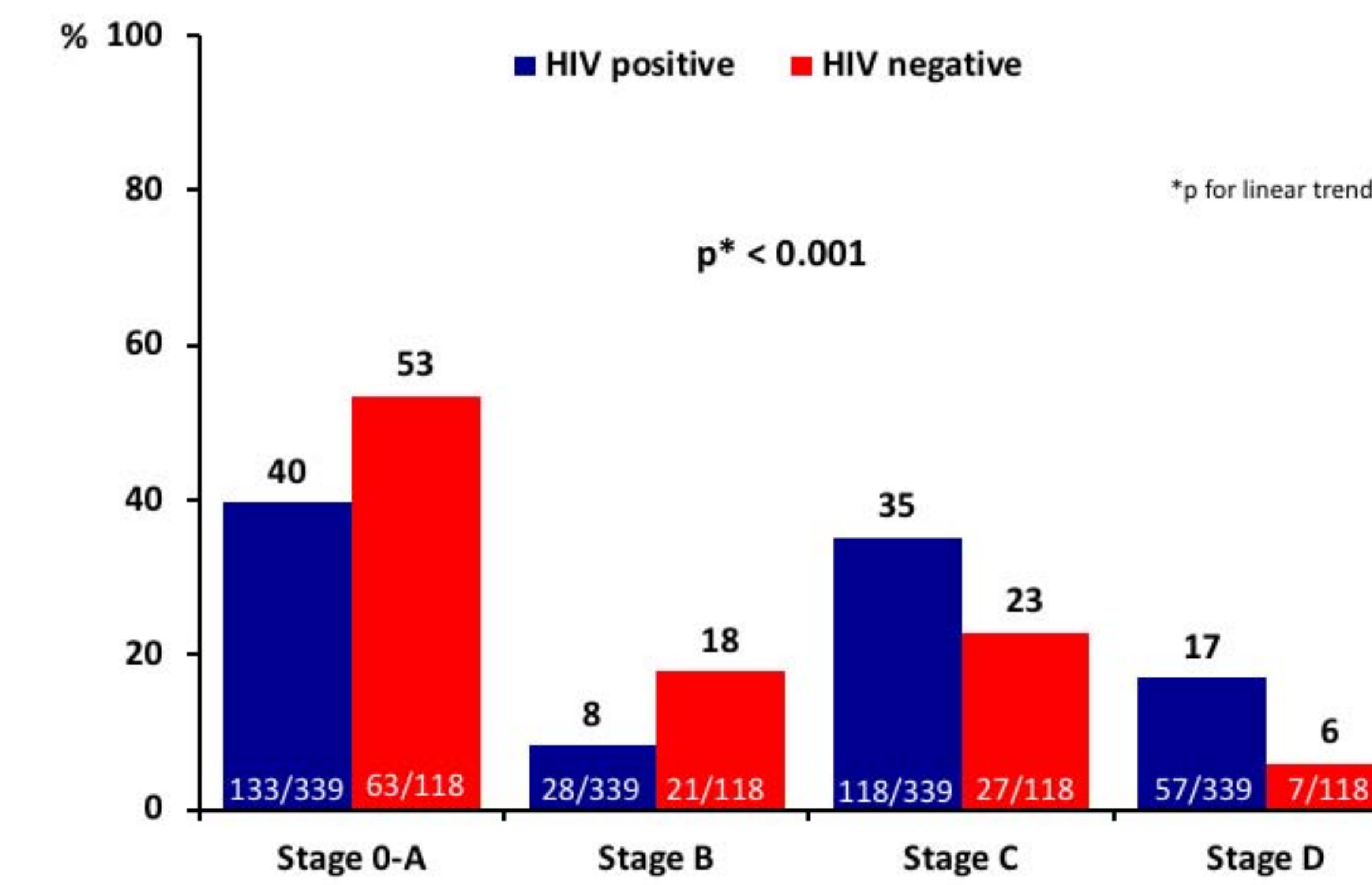
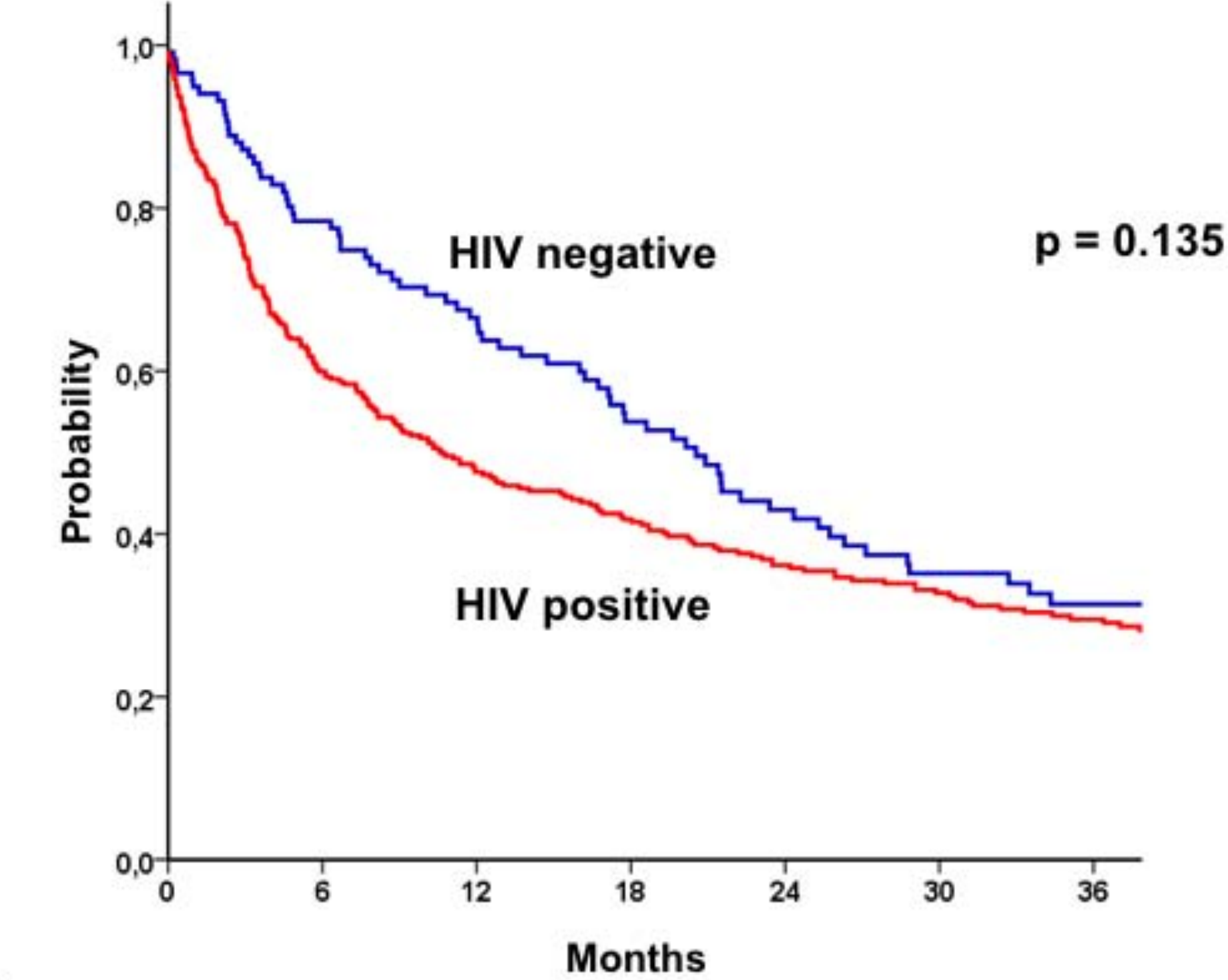


Table 2. Treatment strategies for HCC

Best treatment received	HIV positive (n = 339)	HIV negative (n = 118)
Curative therapies	119 (35%)	48 (41%)
Ablative therapies	60	19
Surgical resection	38	11
Liver transplant	21	18
Non-curative therapies	105 (31%)	28 (24%)
Transarterial chemoembolization	60	22
Sorafenib	45	6
No therapy	115 (34%)	42 (35%)

Figure 3. Probability of survival after HCC diagnosis by HIV status

Globally, 334 (73.1%) patients died after HCC diagnosis. In 303 (90.7%) of them, death was HCC-related.



Patients at risk	0	6	12	18	24	30	36
HIV negative	118	88	71	52	39	29	24
HIV positive	339	193	145	121	100	84	68

Figure 2. Proportion of patients receiving treatment for HCC (as indicated by BCLC stage) according to HIV status.

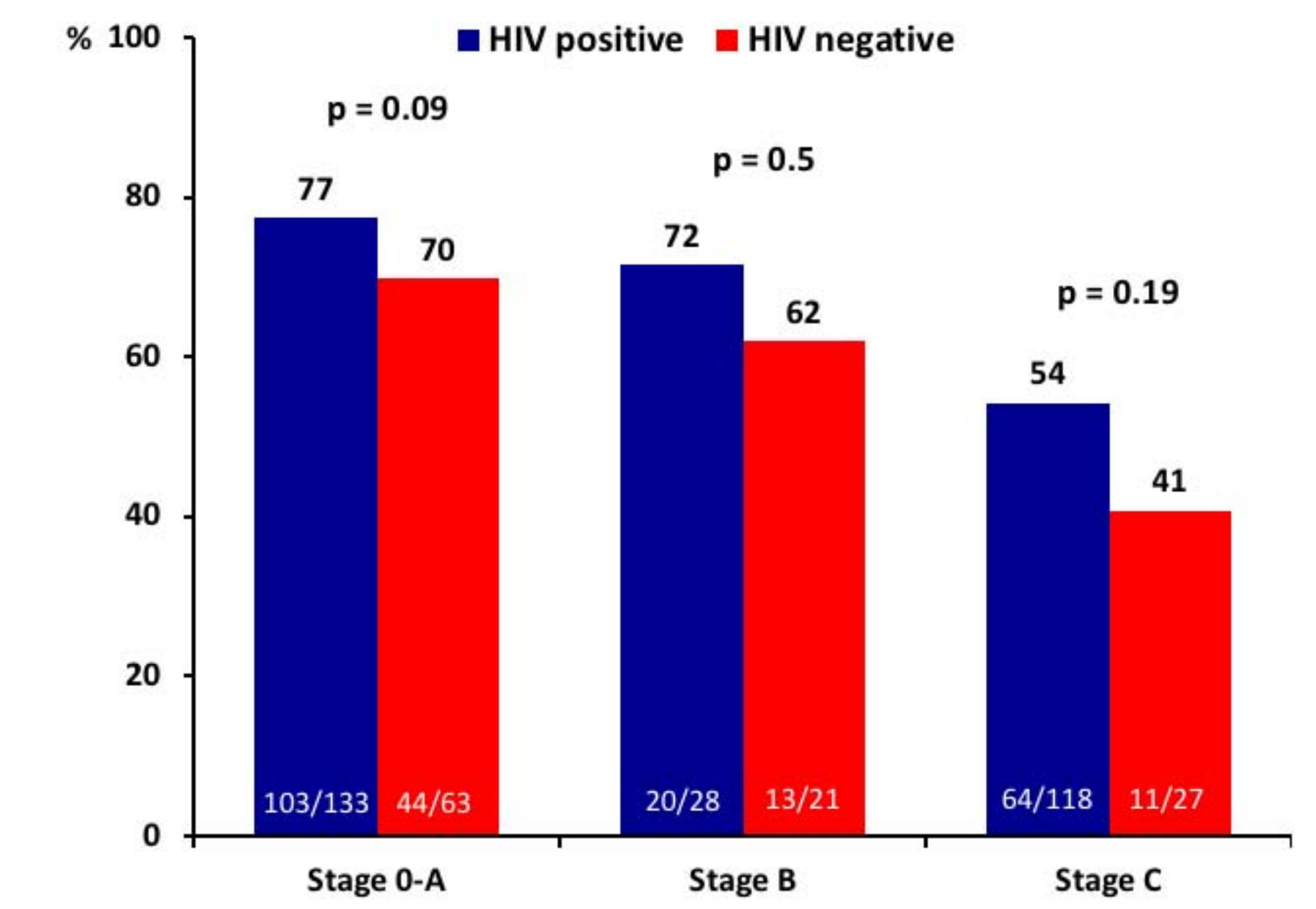


Table 3. Multivariate analysis: Independent predictors of mortality after HCC diagnosis

Factor	Adjusted hazard ratio (95% CI)	p
Age <sup>1</sup>	1.01 (0.99-1.03)	0.2
Male sex	1.08 (0.77-1.52)	0.65
Alcohol intake > 50 g/day	1.06 (0.81-1.39)	0.65
HIV infection	1.07 (0.74-1.54)	0.7
Lack of previous SVR	1.19 (0.82-1.7)	0.36
BCLC stage at diagnosis		<0.001
Stage 0-A	Reference category	
Stage B	3.31 (2.23-4.91)	
Stage C	5.03 (3.74-6.77)	
Stage D	9.35 (6.41-13.64)	
Alfa-phetoprotein > 50 ng/dL	2.15 (1.69-2.73)	<0.001
HCC diagnosis outside of a surveillance program	1.36 (1.06-1.73)	0.01

<sup>1</sup>Considered as a continuous variable.

## CONCLUSIONS

- HIV coinfection has no impact on the survival after the diagnosis of HCC in HCV-infected patients.
- Although the mortality of HCC is somewhat higher in HIV/HCV-coinfected patients, these differences seem to be related with a later diagnosis of HCC in HIV-infected patients and not with HIV infection itself or a lower access to HCC therapy.

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