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FAILURE RATE OF ULTRASOUND SURVEILLANCE OF HEPATOCELLULAR CARCINOMA IN HIV+ PATIENTS

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On behalf of Grupo para el Estudio de las Hepatitis Víricas (GEHEP) de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica

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ABSTRACT

BACKGROUND: Surveillance of hepatocellular carcinoma (HCC) by hepatic ultrasound (US) every 6 months is recommended in HIV-infected patients with cirrhosis. However, there are no specific studies addressing the performance of such strategy in this population. As it has been reported that HCC could have a more aggressive course in the HIV-infected patient, the effectiveness of this surveillance policy needs to be evaluated in this specific scenario. The objective of this study was to assess the proportion of HIV-infected patients diagnosed of HCC soon after a normal surveillance US.

METHODS: The GEHEP-002 multicentric cohort (ClinicalTrials.gov ID: NCT02785835) recruits HCC cases diagnosed in HIV-infected patients from 32 centers from Spain. For this analysis, HCC cases diagnosed within an US screening program were selected. Surveillance failure was defined as the diagnosis of an HCC within the first 3 months after a previous surveillance US not showing hepatic nodules. The characteristics of HCC cases after surveillance failure were compared with the remaining HCC cases diagnosed by screening.

RESULTS: 186 (54%) out of 341 HCC cases recruited in the GEHEP-002 have been diagnosed within an US screening program. Of them, 16 had a normal US in the preceding 3 months. Thus, the rate of HCC diagnosis after US surveillance failure was 8.6%. HCC was associated with HCV infection in these 16 cases. HCV genotype 3 infection was responsible for 5 (31%) out of the 16 cases after surveillance failure vs 43 (25%) among the remaining 180 cases diagnosed by screening (p=0.5). Two (12%) cases of those occurring after surveillance failure and 19 (11%) among the remaining cases were diagnosed after the consecution of SVR (p=0.7). There was a trend for a higher frequency of multicentric presentation [9 (60%) vs 74 (44%), p=0.2] and portal thrombosis [6 (37%) vs 40 (23%), p=0.2] among HCC cases after surveillance failure. Thus, 10 (62.5%) of them were diagnosed at advanced stage (BCLC stage C or D) whereas this occurred in 76 (45%) of the remaining cases (p=0.1).

CONCLUSION: A significant proportion of HIV-infected patients are diagnosed of HCC soon after a previous normal surveillance US. HCC cases after US surveillance failure tend to show more advanced presentation at diagnosis. A HCC surveillance policy based on the performance of an US every 6 months might be insufficient in HIV-infected patients with cirrhosis.

BACKGROUND

- Surveillance of hepatocellular carcinoma (HCC) by hepatic ultrasound (US) every 6 months is recommended in HIV-infected patients with cirrhosis.
- However, there are no specific studies addressing the performance of such strategy in this population.
- As it has been reported that HCC could have a more aggressive course in the HIV-infected patient, the effectiveness of this surveillance policy needs to be evaluated in this specific scenario.

OBJECTIVE

- To assess the proportion of HIV-infected patients diagnosed of HCC soon after a normal surveillance US.

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PATIENTS AND METHODS

Study design

- Multicenter retrospective cohort study (1996-2017).

Patients

- The GEHEP-002 cohort (ClinicalTrials.gov ID: NCT02785835) recruits HCC cases diagnosed in HIV-infected patients from 32 centers from Spain.
- HCC diagnosis made by AASLD criteria.
- For this analysis, HCC cases diagnosed within an US screening program were selected.

Statistical analyses

- Surveillance failure was defined as the diagnosis of an HCC within the first 3 months after a previous surveillance US not showing hepatic nodules.
- The characteristics of HCC cases after surveillance failure were compared with the remaining HCC cases diagnosed by screening.

RESULTS

Table 1. Characteristics of the entire cohort (n=346).

Characteristics	Value
Age (years)[1]	49 (46-53)
Male gender, n (%)	313 (90.5)
Etiology of HCC, n (%)	
Hepatitis C	223 (64.5)
Hepatitis B	29 (8.4)
Hepatitis C and B	22 (6.4)
Hepatitis C and alcohol	67 (19.4)
Alcohol	4 (1.2)
Other	1 (0.3)
HCC diagnosis made within screening, n (%)	186 (54)
Alfa-fetoprotein[1]	76.8 (7.5-640)
CDC C stage, n (%)	106 (31)
HIV viral load < 50 copies/mL, n (%)	255 (74)
CD4 cell count (cells/mL)[1]	352 (195-550)
Antiretroviral therapy, n (%)	299 (87)
Child-Turcotte-Pugh stage, n (%)[2]	
A	177 (53)
B	107 (32)
C	51 (15)
MELD score[1]	10 (7-13)
Unicentric HCC, n (%)	173 (50)
Milan criteria, n (%)	123 (35)
Vascular invasion, n (%)	101 (29)
Extra-hepatic metastases, n (%)	41 (12)
Barcelona-Clinic Liver Cancer stage, n (%)[3]	
0	7 (2)
A	121 (36)
B	30 (9)
C	120 (35)
D	63 (18)

[1]Median (Q1-Q3); Available in [2]335 and [3]341 patients.

RESULTS

Figure 1. Proportion of HCC diagnosis after US surveillance failure.

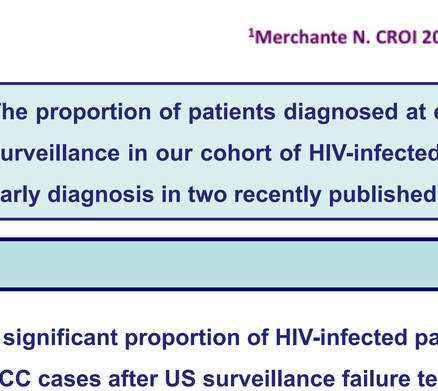
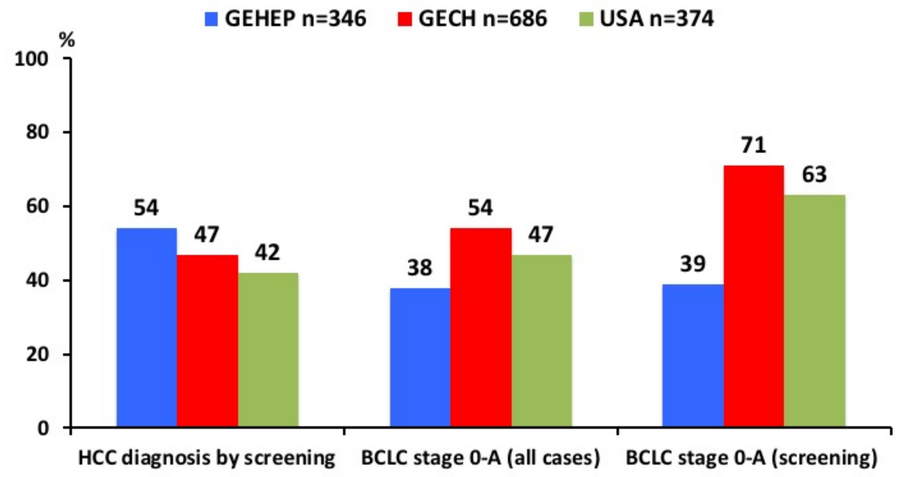


Table 2. Characteristics of HCC cases after surveillance failure and comparisons with the remaining HCC cases diagnosed by surveillance.

Parameter	Surveillance failure (n=16)	No surveillance failure n=170)	*P*
Age (years), median (Q1-Q3)	47 (51-53)	46 (49-52)	0.4
Male sex, n (%)	16 (100)	150 (88)	0.2
HCC etiology, n (%)			
HCV	9 (56)	119 (70)	0.6
Alcohol	0 (0)	2 (1)	
HBV	0 (0)	14 (8)	
HCV-Alcohol	6 (38)	26 (15.5)	
HCV-HBV	1 (6)	5 (5.5)	
HCV Genotype 3, n (%)	5 (31)	43 (25)	0.5
Previous HCV therapy, n (%)	7 (44)	83 (49)	0.7
Previous SVR	2 (12)	19 (11)	0.7
RNA HIV < 50 copies/mL, n (%)	14 (87)	139 (82)	1.0
Alfa-fetoprotein ng/dL, median (Q1-Q3)	31 (6-331)	55 (7-372)	0.9
Child-Turcotte-Pugh stage, n (%)			
A	5 (31)	101 (60)	0.01
B	6 (38)	45 (27)	
C	5 (31)	22 (13)	
Multicentric HCC, n (%)	10 (60)	76 (44)	0.2
Portal thrombosis, n (%)	6 (37)	4 (23)	0.2
BCLC stage, n (%)			
0-A	5 (31)	74 (43)	0.1
B	1 (6)	20 (12)	
C	5 (31)	57 (33)	
D	5 (31)	19 (11)	

Figure 2. Proportion of HCC cases at early stage (BCLC 0-A) according to previous US surveillance. Comparison with previously published data from non-HIV cohorts



[1]Merchante N. CROI 2018; [2]Rodríguez de Lope C. Med Clin 2017; [3]Singal A. Am J Med 2017.

The proportion of patients diagnosed at early stage did not varied according to the performance of previous US surveillance in our cohort of HIV-infected patients. Conversely, surveillance was associated with higher rates of early diagnosis in two recently published cohorts of non-HIV infected patients with HCC.

CONCLUSIONS

- A significant proportion of HIV-infected patients are diagnosed of HCC soon after a previous normal surveillance US.
- HCC cases after US surveillance failure tend to show more advanced presentation at diagnosis.
- US surveillance does not seem to translate into an earlier HCC diagnosis in HIV-infected patients.
- A HCC surveillance policy based on the performance of an US every 6 months might be insufficient in HIV-infected patients with cirrhosis.