POSTER
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CROI 2019

LOW PERFORMANCE OF ULTRASOUND SURVEILLANCE FOR THE DIAGNOSIS OF LIVER CANCER IN HIV

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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 specifically evaluated in the scenario of HIV infection. Objective: To assess the performance of US surveillance for the diagnosis of HCC in HIV-infected patients.

METHODS: The GEHEP-002 cohort recruits HCC cases diagnosed in HIV-infected patients from 32 centers across Spain. The proportion of 'US lack of detection', defined as HCC diagnosed within the first 3 months after a normal surveillance US, and the proportion of 'surveillance failure', defined as cases in which surveillance failed to detect HCC at early stage (BCLC stage 0-A), were assessed. To assess the impact of HIV, a control population of 104 HCC cases diagnosed in HCV-monoinfected patients during the study period was used.

RESULTS: 186 (54%) out of 346 HCC cases in HIV+ patients and 62 (60%) out of 104 cases from the control group were diagnosed within a US surveillance program. US lack of detection occurred in 16 (8.6%) of 186 HIV+ patients diagnosed by surveillance whereas this occurred in 5 (8.6%) in the control group (p=1.0). HCC cases after US lack of detection in HIV+ patients were more frequently at Child-Pugh stage C and had an advanced stage at diagnosis. The performance of US surveillance to achieve an early diagnosis of HCC was significantly lower for HIV+ patients. Thus, US surveillance failure occurred in 107 (57%) out of 186 cases diagnosed by screening in HIV+ patients whereas this occurred in 18 (29%) in the control group (p < 0.0001). Similarly, US surveillance failed to detect HCC within Milan criteria in 104 (56%) out of 186 cases diagnosed by screening in HIV+ patients whereas this occurred in 18 (29%) in the control group (p < 0.0001). The probability of 1-year and 2-year survival after HCC diagnosis among those diagnosed by screening was 56% and 45% in HIV+ patients whereas it was 79% and 64% in HIV-negative patients (p=0.038).

CONCLUSION: The performance of US surveillance of HCC in HIV-infected patients is very poor and worse than that shown outside HIV infection. A HCC surveillance policy based on US examinations every 6 months might be insufficient in HIV-infected patients whit 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 specifically evaluated in the scenario of HIV infection.

OBJECTIVE

- To assess the performance of US surveillance for the diagnosis of HCC in HIV-infected patients.

This study was supported by grants from the Consejería de Salud de la Junta de Andalucía [PI-0014/2014], the Servicio Andaluz de Salud [grant number SAS/111239] and the Fondo de Investigaciones Sanitarias ISCIII [grant number PI13/01621 and PI16/01443]. JAP is the recipient of an intensification grant from the Instituto de Salud Carlos III [grant number Programa-I3SNS]. Besides, this work has been partially funded by the RD12/0017/0012 project as part of the Plan Nacional R + D + I and cofinanced by ISCIII- Subdirección General de Evaluación y el Fondo Europeo de Desarrollo Regional (FEDER).

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 cases diagnosed while being on a US screening program were selected.
    - Diagnosis by surveillance was considered when all scheduled US had been performed at least within 1 year prior to HCC diagnosis.
- Control group: HCC cases diagnosed in HCV-monoinfected patients during the study period (2000-2017) at the Liver Unit from the H.U. Valme.

Main variables of the study

- US lack of detection: HCC cases diagnosed within the first 3 months after a previous surveillance US examination not showing suspicious hepatic nodules.
- US surveillance failure. It was defined by two approaches:
  - HCC diagnosed within the screening program that was classified at Barcelona-Clinic Liver Cancer (BCLC) stage B, C or D at initial presentation (stages not candidates for curative treatments of HCC).
  - HCC cases diagnosed by screening beyond Milan criteria.

Statistical analyses

- The rates of US lack of detection and of US surveillance failure were assessed. To assess the potential impact of HIV, the proportion of US lack of detection and US surveillance failure were compared to that found in the control group.
- The impact of HIV on the survival after HCC diagnosis was assessed by means of the Kaplan-Meier and log-rank test survival analyses.

RESULTS

Table 1. Characteristics of HCC cases of GEHEP-002 cohort (n=346) and of the control group (n=104)

Parameter	HIV positive (n = 346)	HIV negative (n = 104)
Age (years)[1]	49 (46-53)	67 (56-72)
Male sex, n (%)	313 (90)	71 (68)
HCC etiology, n (%)		
Hepatitis C	223 (64.5)	72 (69)
Hepatitis B	29 (8.4)	NA[2]
Hepatitis C and B	22 (6.4)	1 (1)
Hepatitis C and alcohol	67 (19.4)	31 (30)
Alcohol	4 (1.2)	NA[2]
Other	1 (0.3)	NA[2]
Undetectable HIV viral load, n (%)	255 (74)	NA[2]
CD4 cell count (cells/mL)[1]	352 (195-550)	NA[2]
Antiretroviral therapy, n (%)	299 (87)	NA[2]
Child-Pugh stage A, no (%)	177 (53)	55 (54)
Previous US screening, n (%)	186 (54)	62 (60)

[1]Median (Q1-Q3). [2]NA, not applicable.

Proportion of HCC diagnosis after US lack of detection according to HIV status.

16 (8.6%) out of 186 HCC cases in HIV-infected patients diagnosed within an US surveillance program were diagnosed in the first 3 months after a previous US not showing suspicious hepatic nodules; whereas this occurred in 5 (8.6%) out of 58 HCC cases from the control group (p = 1.0).

RESULTS

Figure 1. US surveillance failure rates according to HIV status.

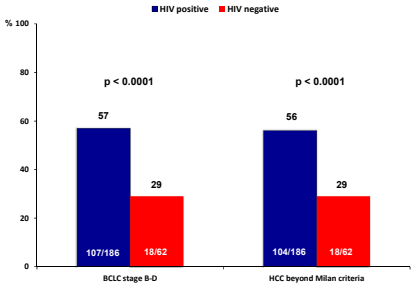


Figure 2. Rates of HCC diagnosis by surveillance and BCLC stage at diagnosis according to surveillance and HIV status.

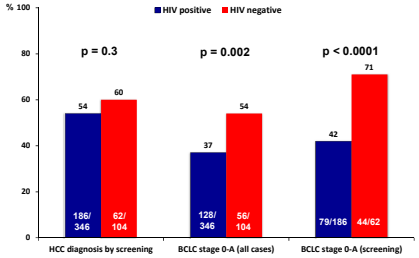
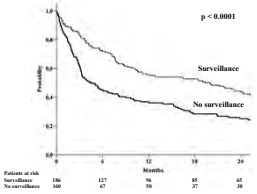


Figure 3. Impact of US surveillance on survival in HIV-infected patients.

Probability of survival according to previous surveillance in HIV-infected patients with HCC (n=346)



Probability of survival according to previous US surveillance failure in HIV-infected patients with HCC diagnosed by screening (n=186)

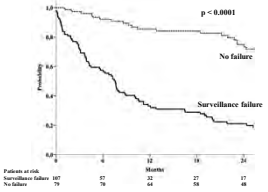
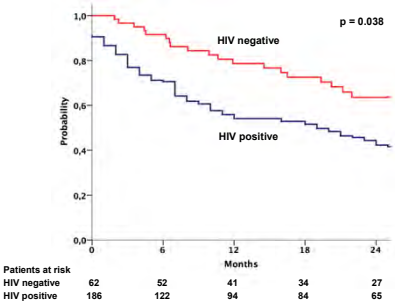


Figure 4. Probability of survival after HCC diagnosed within screening according to HIV status.



CONCLUSIONS

- The performance of US surveillance of HCC in HIV-infected patients is very poor and worse than that shown outside HIV infection.
- In spite of similar rates of HCC diagnosis by surveillance and similar rates of US lack of detection, HIV infected patients are more prone to a late diagnosis of HCC.
- US surveillance does not seem to translate into an earlier HCC diagnosis in HIV-infected patients. As a consequence of this, survival after HCC diagnosis by screening is lower in HIV-infected patients than in those not infected by HIV.
- A HCC surveillance policy based on US examinations every 6 months might be insufficient in HIV-infected patients with cirrhosis.

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