Ospedale Niguarda

Sistema Socio Sanitario Regione Lombardia

Overall survival in HIV-positive liver transplant recipients and the role of DAAs

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BACKGROUND

- Liver transplantation (LT) represents the best therapeutic option for end-stage liver disease (ESLD) and hepatocellular carcinoma (HCC).
- In recent years, LT in HIV+ recipients showed similar survival rates compared to HIV-, even though the risks of rejection and infection seem higher. Few data are available about the impact of direct-acting agents (DAAs) on survival in this special population.
- Aims of this study:
  - o evaluate the rate of overall survival and HCC recurrence;
  - o define the causes of death;
  - o describe the impact of DAAs (largely available in Italy only after 2016) on mortality.

METHODS

- This monocentric, retrospective analysis included all Caucasian subjects with HCV/HBV infection who underwent LT for ESLD or HCC from 2012 to 2019.
- Demographic and clinical features were collected. Patients were stratified according to HIV serostatus.
- Descriptive statistics and non-parametric tests (Chi-square, Fisher's exact and Mann-Whitney U, as appropriate) were used.
- KM probability curves for overall survival and HCC recurrence were calculated.

Table 1. Baseline clinical features of Study population.

		HIV+ (n=31)	HIV- (n=268)	p
Male sex, %		83.9	83.2	.9255
Age (ys), median (IQR)		53 (50-56)	58 (53-63)	**<.0001**
BMI, median (IQR)		23 (21-25)	25 (23-28)	**.0012**
Viral co-infection, %	HBV	16.1	23.9	**.0176**
	HCV-Ab+/ HCV-RNA+	38.7	54.1	
	HCV-Ab+/ HCV-RNA-	45.2	22.0	
HCV Genotype, %	1A	42.3	14.2	**.0036**
	1B	19.2	43.1	
	2	--	6.9	
	3	23.1	27.9	
	4	15.4	7.8	
Alcohol use, %	No	41.9	74.3	**<.0001**
	Moderate	41.9	7.8	
	Abuse	16.2	17.9	
Diabetes, %		12.9	30.6	**.0394**
ECOG Status, %	0	29.0	27.6	**.0306**
	1	25.8	33.6	
	2	9.7	19.8	
	3	22.6	16.4	
	4	12.9	2.6	

Overall survival after Liver Transplantation (LT) is similar among HIV+ and HIV- subjects. The causes of death are comparable in the two populations.
DAAs availability decreased the mortality in the same way in both groups.
The rate of Hepatocellular carcinoma recurrence is higher in HIV+ subjects but it is delayed: imaging monitoring should not decrease despite a long interval from LT.

RESULTS (1)

- 299 individuals, mainly men (83.3%), with a median age of 57 years (IQR 52-63) were included; 31 (10.4%) were HIV+. HCC was the indication for LT in 66.6% of cases.
  - o All HIV+ patients had undetectable viral load; median CD4 cell count was 368 cell/mmc (IQR 220-518).
- Table 1 shows baseline demographic and clinical features: HIV+ subjects were younger, more commonly HCV+ in Sustained Virologic Response and infected by HCV genotype 1a. Alcohol use habits, ECOG status and diabetes were significantly different in the two populations.
- Pre-LT features were similar except for the number of bridging treatments, which were more common (especially TACE) in HIV+ subjects (Table 2).

Figure 1. KM survival curves in HIV-infected and uninfected LT recipients.

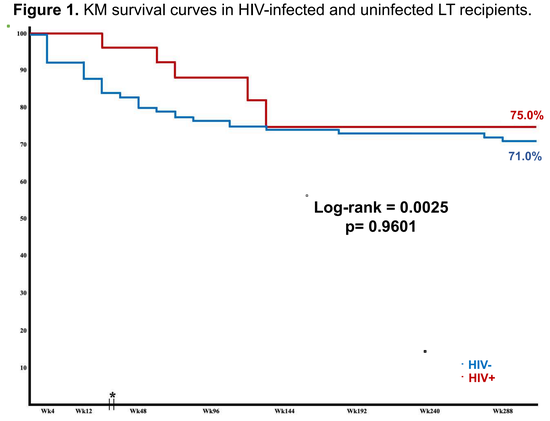


Figure 2. KM curves for the risk of HCC recurrence.

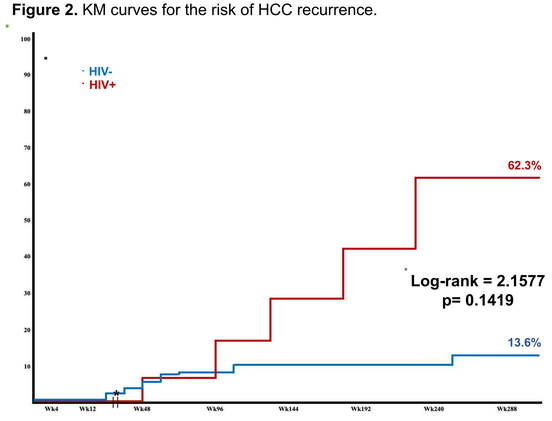


Table 2. LT-related features of Study population.

		HIV+ (n=31)	HIV- (n=268)	p
Reason for LT, %	ESLD	38.7	31.0	.4972
	HCC	58.1	67.5	
	Fulminant hepatitis	3.2	1.5	
Months in waiting list, median (IQR)		18 (7.4-32)	18.1 (7.1-34.9)	.6818
Calendar year of LT, median (IQR)		2016 (2014-2017)	2015 (2013-2017)	.0574
CPT in ESLD, median (IQR)		11 (10-11)	10 (9-11)	.0500
MELD in ESLD, median (IQR)		22 (16-31)	17 (16-24)	.1676
AFP in HCC, median (IQR)		8.7 (4.0-19.5)	7.7 (4.2-24.0)	.4533
Pre-LT Tx for HCC, %	TACE	83.3	58.6	**.0401**
	RFA	33.3	39.8	.5932
	Surgery	--	20.4	.1032
	None	--	17.7	.1568
Number of pre-LT Tx, mean (DS)		2.3 (1.2)	1.8 (0.9)	**.0044**
BCLC Stage, %	A	83.3	54.7	.1061
	B	16.7	22.1	
	C	--	22.7	
	D	--	0.5	
Overall Mortality, %		16.1	19.0	.6951
Cause of Death, %	Infection	20.0	15.7	.9333
	Oncologic	40.0	19.6	
	Liver-related	20.0	29.4	
	Surgery-related	--	13.7	
	Other	20.0	19.6	
HCC relapse, %		26.3	8.8	**.0164**
Days to HCC relapse, median (IQR)		910 (715-1334)	304 (219-415)	**.0067**

RESULTS (2)

- Overall mortality was similar among groups (Figure 1) and no difference was registered about causes of death.
- The overall rate of HCC relapse was higher in HIV+ subjects.
- Of note, time to recurrence was significantly longer in HIV+ than in HIV- individuals.
  - o Even though the risk of recurrence was not different when evaluated with KM (Figure 2) — probably because of the low number of events in HIV+ population — it should be noted that 96 weeks after LT HCC recurrence is rare in HIV-, while the curve continues to increase in HIV+ with no "plateau effect".
- After 2016, the mortality dropped from 26.7% to 9.4% (p=0.0001). DAA availability had no different impact in the two populations, exerting a similar mortality decrease in HIV+ and in HIV- (-33.3% and -72.5%, respectively; p=0.2128).

CONCLUSIONS

- Over a follow up of more than 6 years, HIV+ and HIV- LT recipients showed similar survival rates with a significant decrease in mortality after DAA availability.
- Even if HCC recurrence is more common and delayed in HIV+, the causes of death are similar in the two groups with no distinctive role for infective complications.