Incidence and Risk Factors of Acute Rejection in HIV+ Liver Transplant Recipients

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Background

With the advent of combined antiretroviral therapy (cART), patients infected with human immunodeficiency virus type 1 (HIV) are now living longer and dying of illnesses other than acquired immunodeficiency syndrome. Currently, LT can be performed safely in selected HIV-1-infected patients [Miro JM (2012)]. However, a number of issues persist regarding patient selection, postoperative management, treatment of post-LT HCV recurrence and interactions between antiretroviral and immunosuppressive agents. HIV-infected liver transplant (LT) recipients seem to have higher rates of acute rejection than recipients without HIV infection.

Objectives

This study aims to determine the 5-year cumulative incidence of acute rejection in patients with HIV infection who underwent LT and compare it with that observed in HIV-negative LT recipients.

Methods

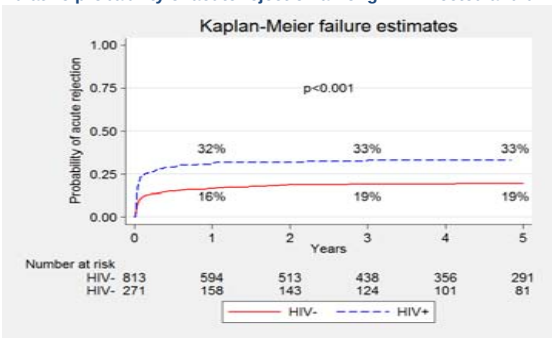
271 consecutive HIV infected patients who underwent LT between 2002-2012 and who were followed until December 2014 were matched with 813 patients without HIV infection (1:3 ratio) who underwent LT during the same period in 22 Spanish institutions. Other matched criteria were age (+/-12 years), gender, calendar year (1 year), and LT indication. All acute rejections were biopsy-proven.

Table 1. Predictors of first biopsy-proven acute rejection in liver transplant recipients

	Non-acute rejection n=848	Acute rejection n=236	Crude HR (95% CI)	p-value	aHR (95% CI)	p-value
Pre-LT characteristics						
Recipient age at LT, years (1-unit increase)*	48 (44;53)	47 (42;52)	0.98 (0.96;0.99)	0.030	0.99 (0.97-1.01)	0.471
Male gender	676 (80)	177 (75)	0.79 (0.59;1.06)	0.116	1.26 (0.94-1.69)	0.127
HIV infection	186 (22)	85 (36)	1.90 (1.45;2.47)	<0.001	1.85 (1.40;2.45)	**<0.001**
HCV infection	801 (94)	223 (94)	1.03 (0.59;1.78)	0.926		
MELD score at enlisting (1-unit increase)*	15 (11;18)	15 (12;17)	0.99 (0.96;1.01)	0.319		
MELD score at LT (1-unit increase)*	15 (12;19)	15 (11;18)	0.98 (0.96;1.00)	0.129		
Hepatocellular carcinoma	252 (30)	63 (27)	1.15 (0.86;1.53)	0.352		
Transplant characteristics						
2008-2012 transplant period	481 (57)	114 (48)	0.75 (0.58;0.96)	0.025	0.75 (0.58;0.98)	**0.035**
Donor age (1-unit increase)*	52 (38;64)	52 (39;65)	1.00 (0.98;1.01)	0.219		
Ciclosporine-based initial immunosuppressive regimen	201 (24)	64 (27)	1.11 (0.83;1.48)	0.476		

*Median and interquartile range; HR, hazard ratio; CI, confidence interval; LT, Liver transplantation

Figure 1: Cumulative probability of acute rejection among HIV-infected and uninfected individuals.



Results

- 85 (36%) HIV-infected and 186 (22%) LT recipients without HIV infection developed biopsy-proven acute rejection during a median of 4.4 (IRQ: 2.1-7.0) years of follow-up. The proportions of late acute rejection (>90 days after LT) were 19% and 29%, respectively (p=0.081).
- In the **univariate analysis**, the only factors associated to AR among HIV-infected individuals were calendar year and MELD score at LT.
- Among HIV-infected LT recipients, HIV infection-related factors, such as history of opportunistic infections, CD4 cell count, serum HIV detectable viremia at LT or raltegravir-based initial post-LT antiretroviral therapy, were not associated with acute rejection.
- **Table 1** shows the **multivariate analysis** for the whole cohort: HIV infection and calendar LT period (2008-2012) were the only two factors independently associated with biopsy-proven acute rejection.
- **Figure 1** shows **cumulative incidence** of acute rejection (95% confidence intervals) rates at 1, 3, and 5 years in LT recipients with and without HIV infection.

Conclusions

HIV-infected LT recipients have a higher incidence of acute rejection. HIV infection is an independently associated factor of acute rejection. In the cohort of HIV-infected LT recipients, HIV infection-related factors were not associated with acute rejection.

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