



## RETRANSPLANTATION IN HIV-INFECTED PATIENTS AFTER LIVER TRANSPLANTATION: A PROSPECTIVE COHORT STUDY

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**BACKGROUND:** To clarify the role of liver transplantation (LT) to treat end stage liver disease in HIV patients, nationwide prospective studies, such as the Spanish FIPSE/GESIDA 45-05 study or the American Transplant Study for People with HIV, are currently ongoing. Obviously, HIV-patients may suffer from the same complications after LT as the HIV-negative transplanted population some of which may eventually lead to retransplantation (reLT) (graft dysfunction, vascular thrombosis or liver disease recurrence). Published experience in reLT in HIV-patients is scant (Table 4) thus the incidence and outcome of reLT in HIV patients is unknown.

**AIM:** The aim of this study was to describe the incidence and outcome of reLT in HIV-infected patients within the Spanish FIPSE/GESIDA 45-05 study.

**PATIENTS AND METHODS:** The prospective Spanish nationwide study in LT in HIV-infected patients (FIPSE OLT-HIV-05-GESIDA 45-05) was reviewed. From January 2002 to December 2010, 229 transplanted patients had been included in the study. All of the patients fulfilled the Spanish Consensus Document criteria summarized as follows: 1) same criteria than HIV (-) patients relating to liver disease. 2) no opportunistic infection except tuberculosis, esophageal candidiasis and pneumonia due to *P. jirovecii* 3) CD4 lymphocyte count >100 cells/ $\mu$ l 4) Undetectable HIV viral load (<50 copies/ $\mu$ l) under HAART or detectable without HAART but potentially treatable after LTx 5) absence of drug abuse for at least two years.

Seventeen patients were retransplanted although only 12 HIV-positive patients (5.2%) finally underwent reLT and constitute the study cohort. Patients were followed-up until March 31<sup>st</sup> 2011.

**Table 1: Characteristics of the recipients of liver retransplantation**

Case	Age at reLT	Gender	HIV risk factor	Primary liver disease	HCC	HCV genotype	RNA HCV at reLT	Indication for reLT	Indication type
1 (11-13)	37	Male	Heterosexual	Cirrhosis HCV	No	1	Positive	Vascular	Urgent
2 (09-25)	46	Male	IDU	Cirrhosis HCV	No	1	Positive	Vascular	Urgent
3 (10-20)	44	Male	IDU	Cirrhosis HCV+HBV	No	1	Positive	PNF	Urgent
4 (16-23)	45	Male	IDU	Cirrhosis HCV	No	1	Positive	Vascular	Urgent
5 (01-19)	45	Male	IDU	Cirrhosis HCV	No	3	Positive	PNF	Urgent
6 (09-13)	51	Male	IDU	Cirrhosis HBV	NA	NA	NA	Vascular	Urgent
7 (01-26)	44	Male	IDU	Cirrhosis HCV	No	1	Positive	PNF	Urgent
8 (02-01)	41	Male	IDU	Cirrhosis HCV	No	2	Positive	Vascular	Urgent
9 (13-04)	41	Male	IDU	Cirrhosis HCV+HBV	Yes	1	Negative	Vascular	Elective
10 (08-10)	39	Male	IDU	Cirrhosis HCV	No	1	Negative	CDR	Elective
11 (15-46)	52	Male	IDU	Cirrhosis HCV	No	1	Negative	CDR	Elective
12 (14-04)	49	Female	Heterosexual	Cirrhosis HCV	Yes	1	Positive	Cirrhosis/VHC	Elective

NA: Not applicable; IDU: Intravenous drug use; HCV: Hepatitis C virus; HBV: Hepatitis B virus; PNF: Primary biliary cirrhosis; CDR: Chronic ductopenic rejection

**Table 2: Characteristics of the recipients, donors and outcome after liver retransplantation**

Case	Interval (yr mo 2 <sup>o</sup> )	MELD at reLT	Rosan Score (1999)	Rosan Score (2005)	Donor Age	Donor cause of death	Follow-up (months)	Post-reLT complication	Outcomes/cause of death
1 (11-13)	1	32	9.12879	NA	59	CVA	9	CRS; Sepsis; MOF	Death; HCV recurrence; NA
2 (09-25)	3	7	9.14026	NA	35	CVA	1	Not retransplanted	NA
3 (10-20)	3	22	0.41136	NA	73	CET 1	1	Biliary leakage; Postoperative hemorrhage	Death; Sepsis; MOF
4 (16-23)	6	28	0.49977	NA	51	CVA	5	Spontaneous Cholangiolithiasis; Hemorrhagic shock	Death; HCV recurrence
5 (01-19)	10	25	0.66987	NA	51	CVA	37	Patent fibrous vein thrombosis; HAS	Death; CDR
6 (09-13)	11	31	0.76222	NA	63	CVA	0	CRS	Death; CDR
7 (01-26)	12	25	0.61056	NA	55	CVA	3	PCSD; Hemorrhagic shock; HCV recurrence; Empyema; cholangitis; Biliary infection (P. aeruginosa)	Death; CVA
8 (02-01)	18	25	0.34598	14.308	29	CVA	76	Cholangiolithiasis; shock to PNF	Alive
9 (13-04)	22.6	21	0.25152	14.451	24	CVA	72	End-stage liver disease	Alive
10 (08-10)	26.1	26	0.59977	16.292	40	CET 12	12	Biliary stricture; cholangiolithiasis	Alive
11 (15-46)	23.0	24	0.49977	12.772	26	CVA	2	Not retransplanted	Alive
12 (14-04)	11.4	20	0.36204	12.536	46	CVA	11	Cholangiolithiasis; hepatitis; Cholangiolithiasis; Biliary stricture	Death; HCV recurrence

NA: Not applicable; CET: Carcinomatous; CVA: Cardiovascular accident; MOF: Multiple organ failure; CRS: Cardiorespiratory arrest; CDR: Chronic ductopenic rejection; HAS: Hepatic artery stenosis

**Table 3: Characteristics and follow-up of HIV infection**

Case	Pre-LT			Pre-reLT			Last control			
	HIV viral load	CD4 count (cells/ $\mu$ l)	HAART	HIV viral load	CD4 count	HAART	HIV viral load	CD4 count	HAART	
1 (11-13)	<50	369	T-30; 3TC; NVP	ND	ND	ND	<50	403/10	3TC (24W); AZT-3TC	
2 (09-25)	<50	644	ABC/3TC	ND	ND	ND	<50	566	RAL; ATV	
3 (10-20)	<50	277	TDF; 3TC	ND	ND	ND	<50	47	NA	
4 (16-23)	<50	90	TDF; 3TC	ND	ND	ND	<50	32	RAL; ATV	
5 (01-19)	<50	172	TDF; 3TC	<50	406	ND	<50	145 (14.9%)	EFV; 3TC	
6 (09-13)	<50	177	TDF; 3TC	ND	ND	ND	<50	ND	NA	
7 (01-26)	<50	346	RAL	<50	1023	EFV	<50	46	AZT-3TC	
8 (02-01)	<50	108	EFV	<50	NA	ABC/3TC	<50	187	RAL	
9 (13-04)	<50	386	TDF; 3TC	<50	213	ABC/3TC	<50	550	RAL; 3TC	
10 (08-10)	34700	344	TDF; 3TC	<50	288	TDF; 3TC	NA	<50	353	RAL; 3TC
11 (15-46)	<50	252	TDF; 3TC	<50	160	ABC/3TC	<50	239	ABC/3TC	
12 (14-04)	<50	208	FTC; TDF	<50	336	FTC; TDF	<50	27	FTC; TDF	

ND: Not done; NA: Not available; <50: Below detection limit; AZT: Zalcitabine; 3TC: Didanosine; TDF: Tenofovir; RAL: Raltegravir; EFV: Efavirenz; FTC: Emtricitabine; SQV: Saquinavir; TDF: Tenofovir; RAL: Raltegravir; LOPV: Lopinavir; 3TC: Lamivudine; DTG: Dolutegravir; TDF: Tenofovir; MNC: Maraviroc; NVP: Nevirapine; ETV: Etravirine

**Table 4: Literature experience in liver reLT in HIV-infected patients**

Author, year	Number/ Age	Reason of primary LT	Cause of reLT	Interval to reLT	Outcome
Naik, 2005 <sup>1</sup>	1/ 48	HCV cirrhosis	CRS	28 months	Alive 7 months
Prasad, 2005 <sup>2</sup>	1/ 54	HCV cirrhosis	CRS	22 weeks	Alive 6 years
Yoshida, 2005 <sup>3</sup>	1/ 34	HBV cirrhosis	PNF	n.a.	Alive
De Vries, 2006 <sup>4</sup>	1/ 60	HCV cirrhosis	PNF	n.a.	Death 7 years; HCV recurrence
Rezaei, 2008 <sup>5</sup>	n.a.	n.a.	CRS	7 months	Alive 10 months
Rezaei, 2008 <sup>6</sup>	n.a.	n.a.	CRS	49 days	Death 13 months; HCV recurrence
Jan, 2010 <sup>7</sup>	1/ 57	HBV cirrhosis	PNF	7 days	Alive 6 years

<sup>1</sup> HIV infection acquired after primary LT. Liver transplant reLT liver retransplantation. HCV hepatitis C virus; HAART highly active antiretroviral therapy; PNF primary biliary cirrhosis; CRS: Chronic ductopenic rejection; PNF: primary biliary cirrhosis; LCL: living donor liver transplantation; n.a.: not available

**DISCUSSION:** Liver retransplantation rate was 5%. Hepatic artery thrombosis was the most frequent cause for reLT while HCV recurrence was the reason in only one case. HIV disease remained under control at reLT and during the follow-up in all patients except in the last control of those who finally died. 1-year survival was 42% (CI 95%: 13%-68%). Mortality after urgent and elective reLT were 62.5% and 25%, respectively (P=0.20). Survival after elective reLT in patients with negative HCV RNA was 100%. Patient survival after reLT in the non-HIV population (data obtained from the Spanish registry)<sup>8</sup> was 76%, 67% and 58% at 1, 3 and 12 months, respectively.

**CONCLUSIONS:** Incidence and causes of reLT in HIV-infected patients were similar to that already published in the non-HIV population, although one-year survival was lower. Mortality in HIV+ patients was higher after reLT. Survival in HIV-infected patients with negative HCV RNA who needed elective reLT was optimal at mid-term.

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