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# P-177. Prognostic Factors of Mortality in HCV-HIV-Coinfected Liver Transplant Recipients From the FIPSE OLT-HIV-05-GESIDA 45-05 Cohort Study (2002-06)

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**Background**: Recurrent HCV after OLT is a major cause of graft loss and death. Preliminary studies suggest poorer survival in HIV-coinfected patients. This study analyzed the prognostic factors of survival in Spanish HCV-HIV-coinfected recipients.

**Methods**: Prospective multicenter cohort study. One-hundred and two liver transplants in HCV-HIV-infected patients have been performed in Spain since 2002. Prognostic factors of mortality were analyzed in the first 60 patients. Time to death was analyzed using a Cox model, and all covariates with *P*<.2 on univariate testing were used to identify independent predictors of mortality (SAS version 9.1.3).

**Results:** Median (IQR) age was 41 (38;45) years, 77% of recipients were male and former drug use (77%) was the most common HIV risk factor. Genotypes 1/4 or 2/3 were diagnosed in 45 (75%) and 14 (23%) cases, respectively. Pre-OLT MELD and CD4 cell count were 16 (12;19) and 273 (180;420) cells/mm3, respectively. All but 1 patient had undetectable plasma RNA-HIV viral load. Efavirenz-based HAART was the most common post-OLT (59%) treatment. Patients received cyclosporine- or tacrolimus-based regimens in 33% and 67% of cases, respectively. Median (IQR) follow-up was 15 (8;30) months. Two cases required retransplantation. Thirteen patients died (22%). Death was HCV-related in 7 patients (54%), due to post-operative complications in 3 (23%), and other causes in 3 (23%). Survival rates at 1, 2, 3 and 4 years were 87%, 70%, 64% and 64%, respectively. The univariate analysis identified 2 variables independently associated with death: chronic rejection (*P*=.03) and histological criteria of graft cirrhosis (F4)(*P*=.01). There was a trend of higher mortality for patients developing adverse events to HAART (*P*=.12) or immunosuppressive drugs (*P*=.10) and a lower mortality for those patients reaching sustained virological response (SVR) with anti-HCV therapy (*P*=.28). None of the seven patients with SVR died. Baseline CD4 count, MELD score, acute rejection, type of HAART regimen and hepatocellular carcinoma were not associated with death. Multivariate analysis only identified graft cirrhosis (HR [95%CI]: 4.08 [1.36;12.23]) as independently associated with death.

**Conclusions:** OLT is a safe and effective short-term procedure in HCV-HIV-coinfected recipients. Developing graft cirrhosis due to HCV reinfection can compromise mid- and long-term survival. So,new strategies are necessary to improve the outcome of anti-HCV therapy.

Prognostic factors of mortality in Spanish HCV-HIV coinfected LT recipients

# BACKGROUND

Recurrent HCV after orthotopic liver transplantation (OLT) is a major cause of graft loss and death. Preliminary studies suggest poorer survival in HIV-coinfected patients.

# OBJECTIVE

To study the prognostic factors of mortality in Spanish HCV-HIV-coinfected liver transplant recipients.

Prognostic factors of mortality in Spanish HCV-HIV coinfected LT recipients

# PATIENTS & METHODS

- Prospective study of the first 60 HCV/HIV-1-infected patients who underwent OLT in Spain (2002-06).
- The variables used in this study were age of the donor, HIV (stage, CD4 cell count, plasma HIV-1 RNA viral load, cART) & liver disease (MELD, Child) of the recipient, OLT characteristics at baseline and during F/U, type of immunosuppressive regimens and anti-HCV treatment.
- HIV-infected recipients were administered the same immunosuppressive regimens & prophylaxis protocols as HIV-negative patients.

Prognostic factors of mortality in Spanish HCV-HIV coinfected LT recipients

# OLT INCLUSION CRITERIA*

- **Liver criteria:** the same as for the non-HIV-infected population.
- **HIV criteria:**

  **1) Clinical:** no previous C events (CDC, 1993) except some OIs (TB, Can, PCP); and,

  **2) Immunological:** pre-OLT CD4 cell count >100 cells/mm3 for OLT; **and,**

  **3) Virological:** RNA HIV-1 viral load BDL on cART or, if detectable, post-SOT suppression predicted.
- **Drug abuse:** A) No heroin or cocaine abuse for >2 years; B) No alcohol abuse for >6 months.

* Miró JM et al. Enferm Infecc Microbiol Clin. 2005; 23:353-362.

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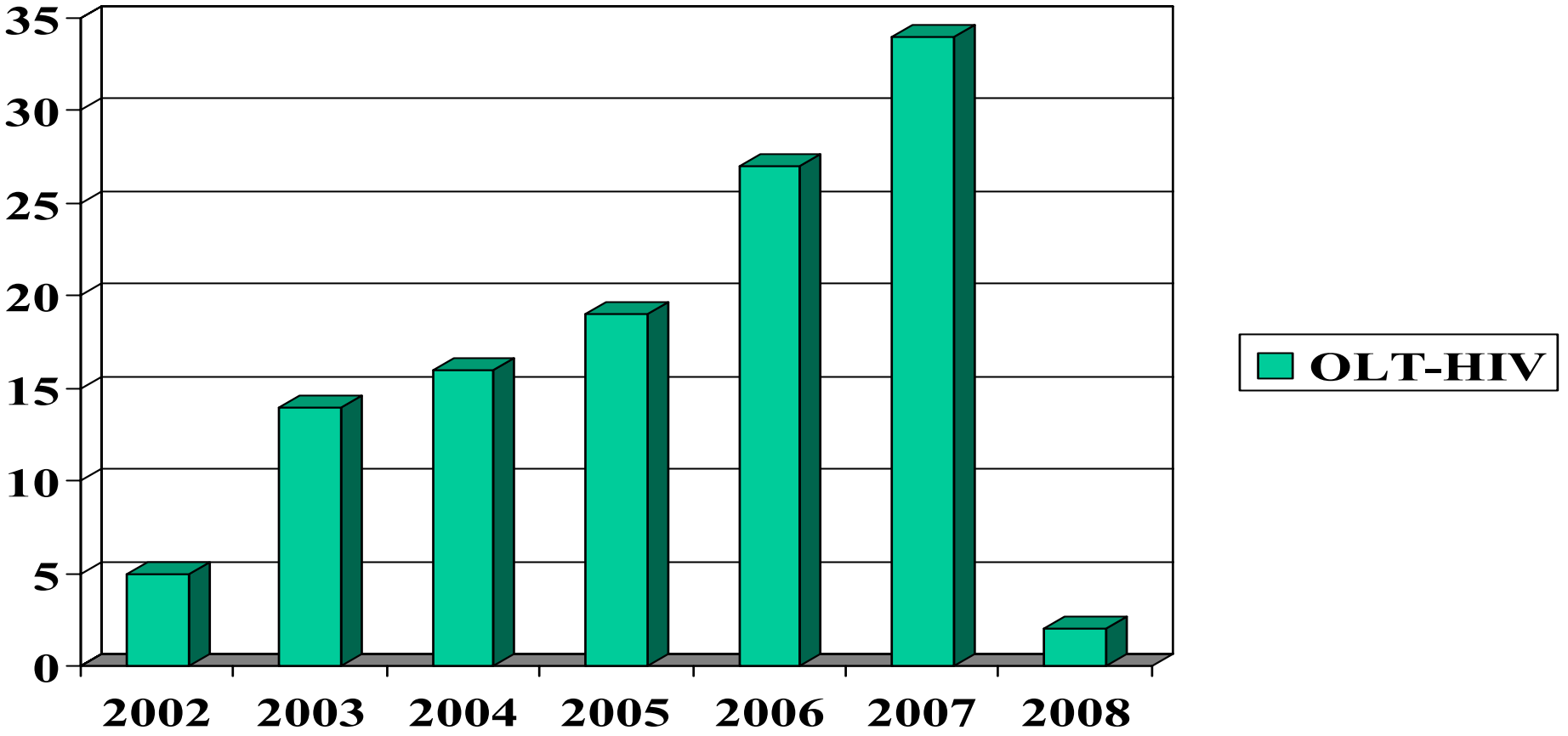
# STATISTICAL ANALYSIS

- Continuous variables were assessed using the *t* test for normally distributed data or the Mann-Whitney U test otherwise, and the Fisher exact test for categorical data.
- The Cox model was used to analyze the time to death, and all covariates with a $P<.2$ on univariate analysis were used to identify independent predictors of mortality.
- The analysis was performed using SAS version 9.1.3 software (SAS Institute, Cary, NC, USA) and the level of significance was established at 0.05 (two-sided).

# Spanish Cohort of OLT in HIV-infected patients (FIPSE OLT-HIV-05 / GESIDA 45-05 )(N=117)



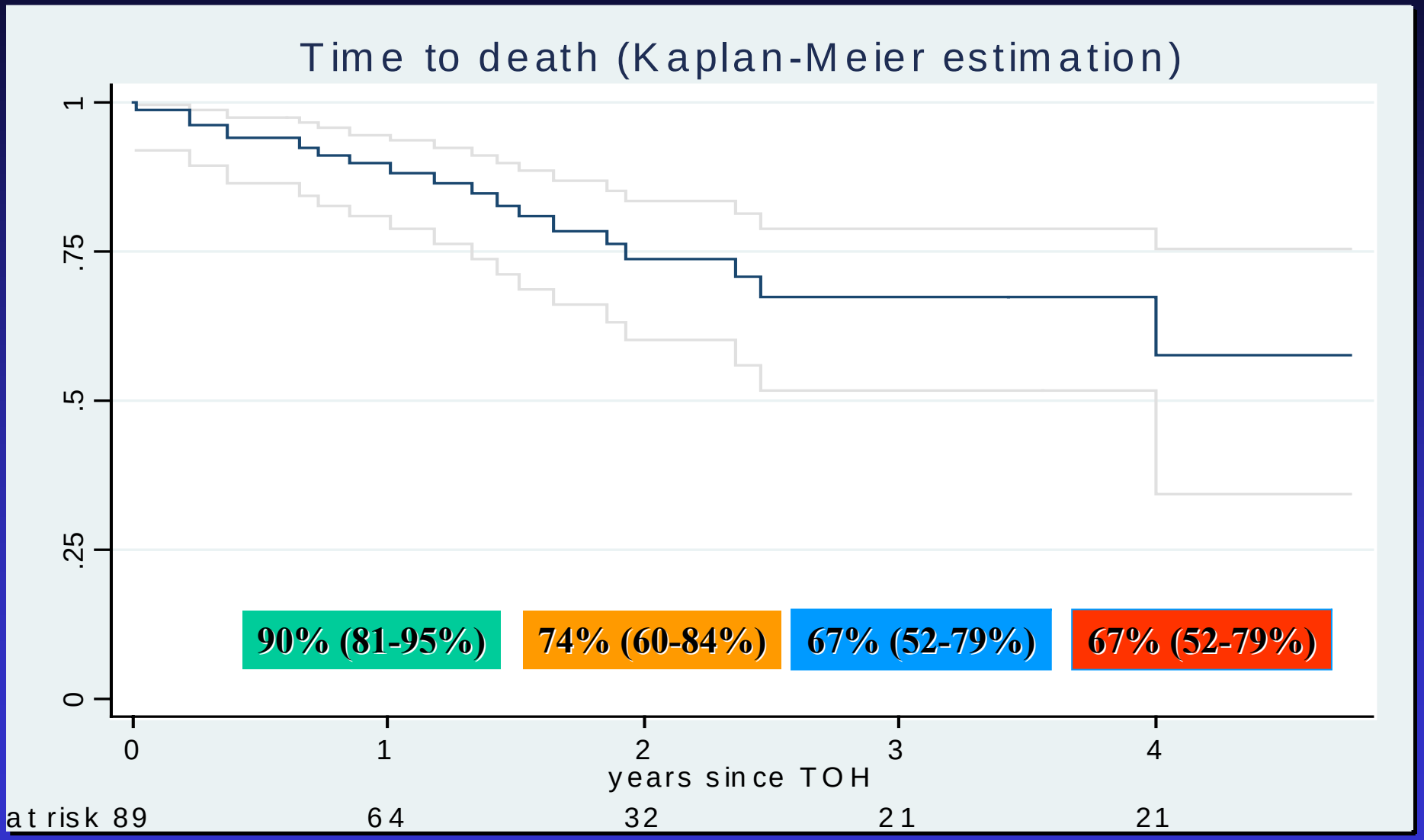

Data updated: January 20, 2008. There were 122 OLT in 117 patients.

# Spanish Cohort of OLT in HIV-infected patients (FIPSE OLT-HIV-05 / GESIDA 45-05 )(N=117)

| | No. cases | No. deaths | No. waiting list |
|---|---|---|---|
| Hosp. Cruces, Bilbao | 20 | 5 | 1 |
| Hosp. Bellvitge, Barcelona | 13 | 2 | 1 |
| Hosp. Vall d'Hebrón, Barcelona | 13 | 3 | 1 |
| Hosp. Clínic, Barcelona | 10 | 2 | 2 |
| Hosp. Ramón y Cajal, Madrid | 9 | 3 | 3 |
| Hosp. 12 de Octubre, Madrid | 12 | 1 | 7 |
| Hosp. Gregorio Marañón, Madrid | 9 | 3 | 1 |
| Hosp. La Fe, Valencia | 11 | 2 | 1 |
| Hosp. Reina Sofía, Cordoba | 6 | 3 | - |
| Hosp. Virgen Arrixaca, Murcia | 2 | 2 | 1 |
| Hosp. Virgen del Rocío, Sevilla | 2 | 1 | 1 |
| Hosp. Juan Canalejo, La Coruña | 3 | 1 | 2 |
| Hosp. Santiago Compostela | 3 | 1 | 1 |
| Hosp. Clinico Lozano Blesa, Zaragoza | 4 | 0 | 1 |
| Hosp. Central de Asturias | 3 | 0 | 1 |
| Hosp. Carlos Haya, Málaga | 1 | 1 | 4 |
| Hosp. Marques Valdecilla, Santander | 1 | 1 | - |
| **Total** | **117** | **31 (26.5%)** | **28** |

# OLT in Spanish HIV-1-infected patients in the HAART era (2002-06)

# Patient Survival (N=89)



Prognostic factors of mortality in Spanish HCV-HIV coinfected LT recipients

# Re-Transplantation & Mortality

| | |
|---|---|
| **Median follow-up** (months) | 15 (8; 30)* |
| **Retransplantation** | 2 (3%) |
| **Mortality** | 13 (22%) |
| - Graft cirrhosis – HCV recurrence | 6 |
| - Post-op. complications | 4 |
| - Other** | 3 |

* Median; IQR; ** Chronic rejection, cancer, and sepsis one case each.

Prognostic factors of mortality in Spanish HCV-HIV coinfected LT recipients

# Pre-OLT characteristics (I)

| | Survivors N=47 | Dead N=13 | *P* value |
|---|---|---|---|
| Age (yr.)* | 42 | 40 | NS |
| Male gender (%) | 77% | 77% | NS |
| IDU | 75% | 85% | NS |
| HBV coinfection | 17% | 8% | NS |
| HCV genotype | | | NS |
| - G1 & G4 | 72% | 69% | |
| - G2 & G3 | 23% | 23% | |
| Plasma HCV-RNA*,** | 0.9 | 0.8 | NS |
| HCC | 13% | 15% | NS |

All patients were Caucasian and none of them had had a previous C event;
IDU= iv drug users; HCC= Hepatocellular carcinoma; * Median; **Units x $10^6$/mL.

Prognostic factors of mortality in Spanish HCV-HIV coinfected LT recipients

# Pre-OLT characteristics (II)

| | Survivors N=47 | Dead N=13 | *P* value |
|---|---|---|---|
| **Child-Pugh class** | | | NS |
| - A | 6% | 8% | |
| - B | 47% | 38% | |
| - C | 47% | 54% | |
| **MELD score*** | 15 | 16 | NS |
| **HAART regimen** | | | NS |
| - PI-based | 17% | 23% | |
| - NNRTI-based | 51% | 38% | |
| - Others | 32% | 39% | |

* Median; NS = non-significant.

Prognostic factors of mortality in Spanish HCV-HIV coinfected LT recipients

# Pre-OLT characteristics (III)

| | Survivors N=47 | Dead N=13 | *P* value |
|---|---|---|---|
| CD4+ cell count | | | |
| - Absolute number* | 270 | 277 | NS |
| - Percentage | 24% | 23% | NS |
| Plasma HIV-RNA | | | |
| - <200 copies/mL | 96% | 92% | NS |
| Time on WL (mo.)* | 3 | 5.5 | NS |
| Creatinine (mg/dL) | .83 | .80 | NS |
| Cadaveric donor | 96% | 100% | NS |
| Donor age (yr.)* | 49 | 64 | .01 |

* Median; WL= Pre-transplant waiting list; NS = non-significant.

Prognostic factors of mortality in Spanish HCV-HIV coinfected LT recipients

# Post-OLT characteristics (I)

| | Survivors N=47 | Dead N=13 | *P* value |
|---|---|---|---|
| Time to restart ART (d.)* | 8 | 7 | NS |
| HAART regimen | | | NS |
| - PI-based | 20% | 17% | |
| - NNRTI-based | 58% | 58% | |
| - Others | 22% | 25% | |
| Immunosuppression | | | NS |
| - CsA-based | 32% | 39% | |
| - Tacrolimus-based | 68% | 61% | |

* Median; NS = non-significant.

Prognostic factors of mortality in Spanish HCV-HIV coinfected LT recipients

# Post-OLT characteristics (II)

| | Survivors N=47 | Dead N=13 | *P* value |
|---|---|---|---|
| HAART toxicity* | 15% | 38% | .11 |
| Immunosuppressive Rx. toxicity* | 34% | 69% | .03 |
| Acute rejection | 45% | 61% | NS |
| Chronic rejection | 4% | 23% | .06 |
| Cirrhosis (F4) | 4% | 46% | <.01 |
| SVR to anti-HCV therapy | 50% (6/12) | 0% (0/6) | .05 |

NS = non-significant. * Grade >2 adverse evens; SVR = Sustained virologicl response.
None of the 6 patients with SVR died during f/u.

Prognostic factors of mortality in Spanish HCV-HIV coinfected LT recipients

# Univariate Analysis of Mortality

| Variable | HR (95%CI) | *P* value |
|---|---|---|
| **Donor age** | | |
| - < 65 years | 1 | |
| - ≥ 65 years | 3.56 (1.08; 11.7) | .04 |
| **Immunosuppressor toxicity** | | |
| - No | 1 | |
| - Yes | 2.69 (0.82; 8.76) | .10 |
| **cART toxicity** | | |
| - No | 1 | |
| - Yes | 2.39 (0.78; 7.33) | .13 |
| **Chronic rejection** | | |
| - No | 1 | |
| - Yes | 4.67 (1.20; 18.2) | .03 |
| **Recurrence of cirrhosis (F4)** | | |
| - No | 1 | |
| - Yes | 4.08 (1.36–12.2) | .01 |

Baseline CD4 count, HCV genotype, MELD or Child scores, acute rejection, type of HAART or immunosuppressive regimen, SVR to anti-HCV Rx and HCC were not associated with death.

Prognostic factors of mortality in Spanish HCV-HIV coinfected LT recipients

# Multivariate Analysis of Mortality

| Variable | HR (95%CI) | *P* value |
|---|---|---|
| **Donor Age** | | |
| - < 65 years | 1 | |
| - ≥ 65 years | 2.91 (0.86;9.88) | .08 |
| **Recurrence of cirrhosis (F4)** | | |
| - No | 1 | |
| - Yes | 3.51 (1.15–10.7) | .03 |

All variables with a *P* value <.2 on univariate analysis were used to identify independent predictors of mortality

# CONCLUSIONS

- OLT is a safe and effective short-term procedure in HCV-HIV-coinfected recipients.
- Advanced donor age and graft cirrhosis (F4) due to HCV recurrence were the two variables associated with death in the multivariate analysis.
- Better donor selection and effective anti-HCV therapies could improve the outcome of HCV OLT in HIV-infected recipients.

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Our patients.