Published in final edited form as:

Transplantation. 2020 October ; 104(10): 2078–2086. doi:10.1097/TP.0000000000003107.

Temporal Trends and Outcomes in Liver Transplantation for Recipients With HIV Infection in Europe and United States

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Abstract

Background.—We evaluated trends and outcomes of liver transplantation (LT) recipients with/without HIV infection.

Methods.—LT recipients between 2008 and 2015 from the United Network for Organ Sharing and Organ Procurement and Transplantation Network and European Liver Transplant Registry were included. Trends and characteristics related to survival among LT recipients with HIV infection were determined.

Results.—Among 73 206 LT patients, 658 (0.9%) were HIV-infected. The proportion of LT HIV-infected did not change over time (P -trend = 0.16). Hepatitis C virus (HCV) as indication for LT

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Supplemental digital content (SDC) is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.transplantjournal.com).

decreased significantly for HIV-infected and HIV-uninfected patients (P -trends = 0.008 and <0.001). Three-year cumulative graft survival in LT recipients with and without HIV infection was 64.4% and 77.3%, respectively ($P < 0.001$), with improvements over time for both, but with HIV-infected patients having greater improvements (P -trends = 0.02 and 0.03). Adjusted risk of graft loss was 41% higher in HIV-infected versus HIV-uninfected (adjusted hazard ratio [aHR], 1.41; $P < 0.001$). Among HIV-infected, model of end-stage liver disease (aHR, 1.04; $P < 0.001$), body mass index $<21 \text{ kg/m}^2$ (aHR, 1.61; $P = 0.006$), and HCV (aHR, 1.83; $P < 0.001$) were associated with graft loss, whereas more recent period of LT 2012–2015 (aHR, 0.58; $P = 0.001$) and donor with anoxic cause of death (aHR, 0.51; $P = 0.007$) were associated with lower risk of graft loss.

Conclusions.—Patients with HIV infection account for only 1% of LTs in United States and Europe, with fewer LT for HCV disease over time. A static rate of LT among HIV-infected patients may reflect improvements in cirrhosis management and/or persistent barriers to LT. Graft and patient survival among HIV-infected LT recipients have shown improvement over time.

INTRODUCTION

Advances in the care of persons living with HIV, especially the efficacy of antiretroviral therapy (ART), have led to remarkable reductions in HIV-related mortality, but with patients living longer, liver disease has emerged as a major cause of death (COD).¹ In the Data collection on Adverse events of anti-HIV Drugs study, a large cohort of European, US, and Australian HIV-infected persons, 13% of deaths were liver-related, and in the Swiss HIV Cohort Study, 15% of deaths were liver-related, increasing to 18% when hepatocellular carcinoma (HCC) was included in the liver-related deaths.^{1–4} Thus, 1 in every 5–10 persons with HIV infection is at risk of dying from liver disease.⁵

Liver transplantation (LT) is the treatment of choice for patients with complications of cirrhosis, and HIV is no longer a contraindication for LT.^{6–8} Historically, post-LT survival was lower for HIV-infected patients with chronic hepatitis C virus (HCV) compared to other indications,^{6–9} likely reflecting the lack of effective HCV therapy rather than HIV effect per se.¹⁰ In well-selected patients, posttransplant survival was equivalent or higher than patients without HIV infection.^{6,7} However, LT in HIV-infected patients has other complexities related to management of acute rejection, drug–drug interactions, and opportunistic infections.^{6,7,11} Thus, it is unclear how widely LT is used to manage complications of cirrhosis among HIV-infected patients. Using 2 large liver transplant registries from the United States and Europe, we examined trends in LT among HIV-infected patients and whether post-LT outcomes among HIV-infected and HIV-uninfected recipients has changed over time.

MATERIALS AND METHODS

Data Source

HIV-infected and HIV-uninfected LT recipients were identified from the United Network for Organ Sharing (UNOS) and Organ Procurement and Transplantation Network database and the European Liver Transplant Registry (ELITA/ELTR). The list of European countries contributing to the registry and those including HIV-infected patients is provided in Table S1

(SDC, <http://links.lww.com/TP/B864>). The total number of centers included were 133 for the UNOS registry and 140 for the ELTR registry. In each registry, we first identified all adults (>18 y) who received a LT between 2008 and 2015 (before 2008, the number of patients with HIV serostatus missing was >19%). HIV serostatus was recorded as negative, positive, undetermined, unknown, or missing for UNOS and negative, positive, or missing for ELTR. Those with undetermined, unknown, or missing status were considered as missing and excluded from analysis. HCV infection was defined as anti-HCV positive because nucleic acid testing was not available. Patients who received multiorgan transplantation (other than simultaneous liver–kidney [SLK]) or retransplantation were excluded as well as patients missing model of end-stage liver disease (MELD) at transplant. The etiology of cirrhosis was based on disease diagnosis coding in UNOS and ELTR. COD was compared, with hepatitis recurrence as COD including both HCV and hepatitis B virus.

From an extensive list of variables available in each database, common elements for analysis were identified. Some variables such as cold ischemia time and allocation MELD were only available for the UNOS cohort. An extensive list of common and unique variables per registry is provided in Table S2 (SDC, <http://links.lww.com/TP/B864>). For the 5% (n = 65) with out of range MELD values (<6 or >40), the lower MELD quartile by cohort (ELTR or UNOS) was imputed for values <6 and the upper MELD quartile by cohort imputed for values >40. We imputed missing body mass index (BMI) (5% and 17% among HIV uninfected and HIV infected, respectively) with the median value by sex, cohort of origin, and HIV serostatus. Center experience with transplantation of HIV-infected patients was categorized as <1 versus ≥1 HIV-infected transplant per year, transplant era was categorized in 2 periods based on the arrival of the first HCV direct-acting antivirals (DAAs; 2008–2011 versus 2012–2015), and BMI was categorized as <21 kg/m² versus ≥21 kg/m².⁶ Transplant year was first evaluated by individual year of transplant using 2008 as the reference group. Patient death did not differ significantly from year 2008 to 2012. Therefore, we utilized 2012 as our cut-point. BMI was evaluated as a continuous, ordinal, and dichotomous variable and compared using Akaike information criterion with lower values indicating better model fit. For patient death, Akaike information criterion was lowest for BMI dichotomized at 21 kg/m² and with the use of 5 ordinal categories <18.5, 18.5–24.9, 25.0–29.9, 30.0–34.9, and ≥35.0 kg/m². Because the 5 categories added little regarding model fit, we proceeded with the dichotomous form of BMI.

Statistical Analysis

Comparisons between groups used Chi-square test for categorical variables and Wilcoxon rank sum test for continuous variables. Temporal trends in primary indications for LT (HIV, HCV, and HCC) were evaluated using the Cochran–Armitage trend test, whereas other characteristics were evaluated by time period (2008–2011 versus 2012–2015) using the Chi-square test. To confirm that missing HIV serostatus did not introduce bias into the evaluation of temporal trends, a sensitivity analysis was conducted among patients transplanted at centers with <2% missing HIV serostatus data.

The primary study endpoints were post-LT patient death and graft loss. Graft loss was defined as retransplant or death. Graft and patient survival were computed using Kaplan–

Meier methods and compared by HIV serostatus and transplant era using the log-rank test with 95% confidence intervals (CIs) provided. Among the HIV-infected group, Kaplan–Meier survival was also evaluated by (1) cohort of origin and era and (2) HCV infection. Cox proportional hazards regression was performed to identify factors independently associated with the outcome of interest in the total cohort and among HIV-infected patients. Characteristics with $P < 0.1$ in univariate analysis and $<5\%$ missing values were evaluated in multivariable models (except for BMI, which was managed as previously stated). The total cohort model included 94% of patients, and the HIV model included 96% of patients. Backward elimination with $P < 0.05$ was used to select the final multivariable models. All models were adjusted for cohort of origin. Multicollinearity among evaluated variables was ruled out. Interactions between HIV serostatus and recipient age, donor age, and era of LT were assessed. Cox regression models were not performed separately for each cohort of origin due to the limited sample size among the HIV-infected group.

Given the imbalance in population size between the HIV-infected and HIV-uninfected groups, we confirmed the results of Cox modeling using propensity score methods. The propensity score for the probability of being HIV infected was estimated using logistic regression, accounting for key characteristics at LT (sex, age, BMI, HCV infected, and dialysis). Inverse probability of treatment weights (IPTWs) were calculated for each subject from the propensity score and stabilized to avoid extreme weights and reduce variance. We confirmed the propensity score achieved balance between HIV-infected and HIV-uninfected groups by calculating the standard difference (differences $<10\%$ indicate balanced populations). Using the propensity score–stabilized IPTW, weighted Cox regression models for graft and patient survival were generated. Statistical analyses were conducted using SAS v. 9.4 (Cary, NC) and STATA v13 (College Station, TX). This study was approved by the University of California San Francisco Institutional Review Board.

RESULTS

HIV-infected Patients in UNOS and ELTR Cohorts

Among 90 422 LTs during the study period, 8494 were excluded because of previous LT, multiorgan transplantation (other than SLK), or lack of MELD value (Figure S1, SDC, <http://links.lww.com/TP/B864>). Of the remaining 81 928, HIV serostatus was not available for 8722 (10.6%) patients. The proportion with missing HIV serostatus was significantly less frequent over time, ranging from 15.4% in 2008 to 5.3% in 2015 (P -trend <0.001) (Figure S2A, SDC, <http://links.lww.com/TP/B864>). This trend was observed in both US and European cohorts (Figure S2B, C, SDC, <http://links.lww.com/TP/B864>). Among 73 206 LTs with known HIV serostatus, 658 (0.9%) were HIV-infected patients, 200 (0.5%) in the United States and 458 (1.4%) in Europe. The main characteristics per cohort are shown in Table S3 (SDC, <http://links.lww.com/TP/B864>).

Compared to HIV-uninfected patients, HIV-infected patients were more frequently male (80.2% versus 67.6%) and younger (median, 50 versus 56 y) and more frequently had HCV and hepatitis B virus coinfections (63.4% versus 31.8% and 12.2% versus 6.4%, respectively). HIV-infected LT recipients received older donors (median, 50 versus 45 y) and

fewer donors with head trauma as COD (23.6% versus 17.5%) than the HIV-uninfected recipients (Table 1).

Era Differences in HIV-infected and HIV-uninfected LT Recipients

The proportion of LTs with HIV infection did not significantly change over time (Figure 1). In the sensitivity analysis, among centers with <2% of HIV serostatus missing, *P* values remained nonsignificant. Overall, the median number of LTs for HIV-infected recipients per center decreased from a median of 12 in 2008–2011 to 9 in 2012–2015. The proportion of centers with <1 HIV LT/y did not change significantly over time: 38.7% versus 43.5% in the first and second eras (*P* = 0.21) but was higher in the United States compared to European cohort (59.0% versus 33.2%; *P* < 0.001).

From 2008 to 2015, HCV as indication for LT decreased from 76.1% to 52.2% in HIV-infected patients (*P*-trend = 0.008) and from 34.4% to 28.4% in HIV-uninfected patients (*P*-trend < 0.001). HCC as indication for LT increased for both groups from 2008 to 2015 but not significantly in the HIV-infected group 25.4% versus 37.3% (*P*-trend = 0.06), compared to 26.3% versus 31.1% (*P*-trend < 0.001), for the HIV-uninfected group (Figure 2).

In non-HCC patients, MELD was unchanged over time in HIV-infected patients (median MELD 20 for both eras; *P* = 0.62) but increased in HIV-uninfected patients (median MELD 20 versus 22; *P* < 0.001). SLK transplants decreased by half, from 5.3% to 2.5% (*P* = 0.10) for HIV-infected patients, but increased from 4.6% to 6.0% for HIV-uninfected patients (*P* < 0.001). The number of patients receiving a living-donor/ split liver transplant remained stable for HIV-uninfected patients (8.1% versus 8.0%; *P* = 0.54) but decreased for HIV-infected patients (6.8% versus 2.5%; *P* = 0.02). The degree of urgency remained stable for both groups over time (Table 2).

Graft and Patient Survival

Three-year cumulative graft survival was 64.4% (95% CI, 59.9–68.6) and 77.3% (95% CI, 77.0–77.7) for HIV-infected and HIV-uninfected LT recipients (*P* < 0.001). Three-year cumulative patient survival was also lower in HIV-infected versus HIV-uninfected LT recipients: 68.7% (95% CI, 64.1–72.8) versus 81.5% (95% CI, 81.2–81.9) (*P* < 0.001). Over time, graft and patient survival rates improved for both HIV-infected and HIV-uninfected groups (*P* < 0.001) (Figure 3).

In the multivariable Cox regression, HIV infection was independently associated with higher risk of graft loss (adjusted hazard ratio [aHR], 1.41; 95% CI, 1.23–1.63; *P* < 0.001) and patient death (adjusted hazard ratio [aHR], 1.67; 95% CI, 1.43–1.94; *P* < 0.001) (Table 3). However, there was an interaction between HIV status and period of LT. Among HIV-infected LT recipients, graft and patient mortality improved in 2012–2015 versus 2008–2011 (hazard ratio [HR], 0.58 and 0.58; *P* < 0.001 for both). HIV-uninfected graft and patient survival also improved in the recent era but was of lesser magnitude (HR, 0.86 and 0.85; *P* < 0.001 for both) (Table S4, SDC, <http://links.lww.com/TP/B864>). In the latter era (2012–2015), there was a significantly greater reduction in risk of graft loss (HR, 0.58 versus 0.86; *P* = 0.02) and patient death (HR, 0.58 versus 0.85; *P* = 0.03) for HIV-infected versus HIV-uninfected patients.

Infection-related and hepatitis-related deaths were more frequent in HIV-infected recipients than in HIV-uninfected recipients (odds ratio, 2.06; 95% CI, 1.39–3.04; $P < 0.001$; odds ratio, 2.60; 95% CI, 1.58–4.28; $P < 0.001$). There was no difference in rejection-related deaths (1.8% and 1.9% for HIV-infected and HIV-uninfected patients; $P = 1.00$). Only 1 death was HIV related. Over time, there was a significant reduction of deaths due to recurrence of hepatitis among HIV-uninfected patients (P -trend < 0.001), whereas no change was observed for HIV-infected recipients ($P = 0.39$) (Table S5, SDC, <http://links.lww.com/TP/B864>).

Using the propensity score stabilized IPTW, we generated weighted Cox regression models paralleling the unweighted graft and patient survival models. The HR estimates from the weighted models did not meaningfully differ from the unweighted models (Tables S6 and S7, SDC, <http://links.lww.com/TP/B864>).

Survival and Factors Associated With Survival Among HIV-infected LT Recipients

Three-year cumulative graft survival was 58.9% (95% CI, 52.2–64.9) and 62.4% (95% CI, 51.9–71.3) for patients from ELTR and UNOS cohort during the first era (2008–2011) ($P = 0.43$). For the second era (2012–2015), 3-year cumulative graft survival was 72.7% (95% CI, 60.9–81.4) and 73.1% (95% CI, 59.2–82.9) for patients from ELTR and UNOS cohort ($P = 1.00$). Similar results were seen in patient survival (data not shown).

HCV infection was the most common indication for LT among HIV-infected recipients. Three-year graft survival rates among HIV-infected recipients with and without HCV were 55.9% (95% CI, 48.9–62.2) and 67.4% (95% CI, 57.6–75.4) in 2008–2011 ($P = 0.049$) and 62.6% (95% CI, 49.1–73.5) and 84.7% (95% CI, 73.8–91.3) in 2012–2015 ($P = 0.65$). Similar results were seen in patient survival (data not shown).

In the multivariable Cox model, variables related to graft loss in HIV-infected recipients were higher MELD (aHR, 1.04 per 1 unit; 95% CI, 1.02–1.05; $P < 0.001$), lower BMI (aHR, 1.61; 95% CI, 1.15–2.25; $P = 0.006$), and HCV coinfection (aHR, 1.83; 95% CI, 1.32–2.52; $P < 0.001$). More recent period of LT (2012–2015 versus 2008–2011; aHR, 0.58; 95% CI, 0.41–0.80; $P = 0.001$) and receipt of an anoxic COD donor (aHR, 0.51 versus nonanoxic; 95% CI, 0.32–0.83; $P = 0.007$) were associated with lower risk of graft loss (Table 4).

DISCUSSION

This study represents the first comprehensive evaluation of trends in LT for HIV-infected patients in Europe and the United States. HIV remains an uncommon comorbidity among LT recipients, accounting for approximately 1% in both Europe and United States. Moreover, the proportion of LT recipients with HIV infection has not changed over time, a somewhat surprising finding given the reported burden of liver disease among those living with HIV.^{3,4,12,13} Concerns related to poor outcomes among LT recipients with HIV infection may have contributed. In this regard, our study highlights the improvements in survival achieved among those with HIV infection over time. Specifically, the most recent era (2012–2015) of LT has showed a 42% lower rate of graft and patient loss compared with the earlier era (2008–2011). Indeed, the era improvements were more pronounced for HIV-infected LT

recipients than for HIV-uninfected recipients. Thus, with broader recognition of the improved outcomes of LT recipients with HIV, barriers to listing for LT based upon that concern will be removed.

During the most recent era, 3-year graft and patient survival for LT recipients with HIV infection were 70.6% and 75.4%, respectively. There are several factors that have likely contributed to this improved survival over time. Newer antiretroviral drugs make management of drug–drug interactions between ART and immunosuppressive drugs easier. In the earlier era of LT for HIV, protease inhibitors and nonnucleoside reverse transcriptase inhibitors were commonly used and affected cyclosporine, tacrolimus, and mammalian target of rapamycin inhibitors levels.¹⁴ The complexity in achieving optimal immunosuppressive levels may have contributed to the high rates of acute rejection reported in earlier series.^{6,7} HIV treatment regimens have shifted to include integrase inhibitors, such as raltegravir, which do not interact with immunosuppressives, thereby allowing easier management of treatments, even when HCV treatment is coadministered.^{10,15–17}

Earlier cohorts conducted before the availability of DAAs showed worse results for HIV–HCV LT recipients compared to their monoinfected counterparts.^{6–8} As expected, in the era with DAA therapy available (after 2014), HCV recurrence as COD has decreased in HCV monoinfected patients, but this trend is not seen for HIV–HCV coinfecting patients. This might reflect a later application of DAA on HIV-infected LT recipients due to concern about drug–drug interactions with first generation of DAA, a reduced number of HIV-infected LT recipients with HCV in more recent cohorts or presence of more advanced disease among those treated (making achievement of sustained virologic response insufficient to prevent graft loss). These findings support the concept that HCV coinfection has contributed to the differential in patient and graft survival of LT recipients with and without HIV over time.

Other recipient factors associated with reduced survival among HIV-infected recipients in our study were high MELD score and low BMI. Interestingly, MELD at LT has continued to increase for HIV-uninfected patients but remained stable over time among HIV-infected patients, which could be interpreted to reflect a bias against offering LT to HIV-infected patients with very high MELD scores. However, we have to acknowledge that we cannot prove this hypothesis, and other recipient or donors characteristics may contribute to this finding. Low BMI is likely a surrogate marker of sarcopenia and frailty. Sarcopenia has shown to be related to an increased risk of pre- and post-LT mortality in HIV-uninfected patients.^{18,19} This might be a modifiable condition, and future strategies to improve BMI, exercise capacity, and muscle mass are needed in this population. Clearly, there is a need for the LT community to continually assess the factors influencing post-LT survival among HIV-infected patients and adjust selection criteria accordingly.

A major strength of our study is the use of 2 large transplant registries to study an infrequent indication for LT. However, there are some limitations that are inherent with using registry data, including missingness, with variables of interest not captured in the registry, and difficulties to making generalizations, in a database, where details cannot be evaluated. To minimize bias, we excluded patients with unknown HIV serostatus instead of considering them HIV-uninfected. HIV infection–specific factors (viral load and CD4) for transplanting

HIV-infected patients were not captured in either database. We chose to adjust models by cohort of origin, accepting that there might be unmeasured differences between UNOS and ELTR in terms of data collection and completeness. Regrettably, some donor characteristics could not be explored (donor diabetes, infectious risk donors, or donor risk index as an example) because of differences in the variables collected between cohorts. HCV genotype and nucleic acid testing were not available for analysis. Likewise, no data regarding DAA use were available, so we can only hypothesize a relation between their use and survival improvement related to era. Also, some social factors, such as drug and alcohol use, psychiatric illness, or other comorbidities that might limit referral of HIV-infected candidates to LT centers are beyond the scope of both registries. Another limitation is that both registries collect HIV serostatus at LT and not at listing, not allowing to evaluate the relationship between HIV serostatus and waiting list outcomes. However, this combined analysis of UNOS and ELTR registries provides an accurate global snapshot of the HIV experience with LT and helps to identify important trends that should guide practice going forward.

In summary, HIV-infected recipients account for 1% of liver transplants in the United States and Europe, representing 0.5% in the United States and 1.4% in Europe. This proportion may be lower than expected based upon projections of liver disease burden among persons living with HIV.^{2,20–23} Because of the nature of this study, no definitive conclusions can be drawn from this study to explain the stagnant number of transplants among those with HIV infection. Regardless, patient and graft survival have improved significantly over time, and this likely reflects patient selection or advances in management of ART and immunosuppression as well as successes in treatment of post-LT diseases, such as HCV. These positive results support the use of LT for HIV-infected patients with complications of cirrhosis, including HCC.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

The authors thank all the centers that contribute to the European Liver Transplant Registry (list available at www.eltr.org) and the centers that contribute to United Network for Organ Sharing (list available at <https://optn.transplant.hrsa.gov>).

This work was supported in part by Health Resources and Services Administration contract 234–2005-37011C. This research was supported in part by funding to the University of California San Francisco (UCSF) Liver Center (National Institute of Diabetes and Digestive and Kidney Diseases [NIDDK] grant number: P30 DK026743). Ciberehd is partially funded by the Instituto de Salud Carlos III.

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I.C.-V. received travel and conference grant from MSD, Astellas, and Chiesi. M.B. received grant from Gilead. She is a speaker at meetings for Abbvie, Gilead, MSD, Astellas, and Novartis. L.S.B. received fellowship grant from Gilead. C.D. received speaker's honoraria and or research grants from Novartis, Astellas, Chiesi, Sandoz, and Biotest. N.A.T. received institutional grants from Gilead and consulting from Dova Pharmaceuticals. The other authors declare no conflicts of interest.

I.C.-V. participated in the design of the study, data merging and analysis, and writing draft and final version of the manuscript; J.L.D. participated in study design, was the primary data analyst for the study, and participated in manuscript revision; M.B., R.A., D.S., F.D.B., V.K., L.S.B., and C.D. participated in data collection and revision of the manuscript; and N.A.T. participated in study design, data merging an analysis, and drafting first and final versions of the manuscript.

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Entire Cohort	67	68	93	113	86	87	77	67
ELTR	45	48	67	83	67	59	49	40
UNOS	22	20	26	30	19	28	28	27

FIGURE 1.

Proportion (in columns) and total (in table) liver transplant recipients with HIV infection by year in United States and European Cohort. Entire cohort P -trend = 0.16, European Liver Transplant Registry (ELTR) P -trend = 0.34, and United Network for Organ Sharing (UNOS) P -trend = 0.87.

FIGURE 2.

Proportion of liver transplant recipients with hepatocellular carcinoma (HCC) by year, 2008–2015. A, HIV-infected recipients, P -trend = 0.06. B, HIV-uninfected recipients, P -trend <0.001.

FIGURE 3.

Cumulative probability of postliver transplantation (LT) graft and patient survival by HIV status overtime. A, Graft survival: the 1- and 3-year graft survival rates, between 2008 and 2011, were 73.9% (95% CI, 68.9–78.3) and 59.7% (95% CI, 54.1–64.8) for the HIV-infected group and 84.2% (95% CI, 83.8–84.6) and 75.8% (95% CI, 75.3–76.3) for the HIV-uninfected group ($P < 0.001$). Between 2012 and 2015, the 1- and 3-year graft survival rates were 84.3% (95% CI, 79.3–88.2) and 70.6% (95% CI, 60.7–78.5) for the HIV-infected cohort and 87.0% (95% CI, 86.7–87.4) and 78.9% (95% CI, 78.4–79.5) for the HIV-

uninfected group ($P < 0.001$). B, Patient survival: the 1- and 3-year patient survival rates, between 2008 and 2011, were 78.2% (95% CI, 73.3–82.4) and 64.1% (95% CI, 58.4–69.2) for the HIV-infected group and 88.2% (95% CI, 87.8–88.5) and 80.4% (95% CI, 79.9–80.8) for the HIV-uninfected group ($P < 0.001$). Between 2012 and 2015, the 1- and 3-year patient survival rates were 86.2% (95% CI, 81.3–89.9) and 75.4% (95% CI, 65.3–82.9) for the HIV-infected group and 90.3% (95% CI, 89.9–90.6) and 82.9% (95% CI, 82.3–83.4) for the HIV-uninfected group ($P < 0.001$). CI, confidence interval.

TABLE 1.

characteristics of the entire cohort by HIV status

Variable	Total (n = 73 206)	No. of missing values	HIV uninfected (n = 72 548)	HIV infected (n = 658)
Recipient				
Male, n (%)	49 589 (67.7)	4	49 061 (67.6)	528 (80.2)
Age at LT (y), median (IQR)	56 (49–61)	0	56 (49–61)	50 (45–55)
MELD at LT, median (IQR)	18 (12–26)	0	18 (12–26)	18 (11–26)
MELD at LT excluding HCC, median (IQR)	21 (15–29)	0	21 (15–29)	20 (15–29)
MELD at LT (allocation-UNOS only), ^a median (IQR)	25 (22–32)	0	25 (22–33)	25 (22–32)
Height (cm), median (IQR)	172 (165–178)	3004	172 (165–178)	174 (168–179)
Weight (kg), median (IQR)	80 (68–92)	3658	80 (68–92)	73 (64–83)
BMI (kg/m ²), median (IQR)	26.8 (23.6–30.8)	3845	26.8 (23.7–30.8)	23.9 (21.5–26.9)
Bilirubin at LT (mg/dL), median (IQR)	3.2 (1.4–8.6)	2345	3.2 (1.4–8.6)	3.5 (1.3–10.2)
INR, median (IQR)	1.6 (1.3–2.1)	6214	1.6 (1.3–2.1)	1.5 (1.2–2.2)
Creatinine (mg/dL), median (IQR)	1.0 (0.8–1.5)	2320	1.0 (0.8–1.5)	1.0 (0.8–1.5)
Sodium (mEq/L), median (IQR)	137 (133–140)	5324	137 (133–140)	137 (133–140)
HCV diagnosis, n (%)	23 495 (32.1)	0	23 078 (31.8)	417 (63.4)
HBV diagnosis, n (%)	4686 (6.4)	0	4606 (6.4)	80 (12.2)
Hepatocellular carcinoma, n (%)	20 898 (28.5)	0	20 700 (28.5)	198 (30.1)
Split/LDLT, n (%)	5826 (8.0)	447	5790 (8.0)	36 (5.5)
Simultaneous liver-kidney transplant, n (%)	3513 (5.3)	6743	3494 (5.3)	19 (3.9)
Medical urgency, ^b n (%)	2999 (4.5)	6342	2946 (4.4)	53 (10.4)
Blood type, n (%)		68		
A	28 734 (39.3)		28 493 (39.3)	241 (36.6)
AB	3901 (5.3)		3870 (5.3)	31 (4.7)
B	9870 (13.5)		9774 (13.5)	96 (14.6)
O	30 633 (41.8)		30 343 (41.9)	290 (44.1)
Dialysis before LT, n (%)	6259 (8.5)	0	6230 (8.6)	29 (4.4)
Ascites, n (%)	44 458 (66.0)	5891	44 133 (66.2)	325 (53.4)
Encephalopathy, n (%)		5854		

Variable	Total (n = 73 206)	No. of missing values	HIV uninfected (n = 72 548)	HIV infected (n = 658)
Recipient				
None	33 354(49.5)		32 994(49.4)	360 (59.8)
1–2	27 453(40.8)		27 270(40.8)	183 (30.4)
3–4	6244 (9.3)		6185 (9.3)	59 (9.8)
NA	301 (0.4)		301 (0.4)	0 (0.0)
Clinical condition, n (%)		5551		
ICU	7713 (11.4)		7649 (11.4)	64 (10.1)
Hospital	26 070 (38.5)		25 717(38.4)	353 (55.6)
Home	33 872 (50.1)		33 654 (50.2)	218 (34.3)
ICU, n (%)	7713 (11.4)	5551	7649 (11.4)	64 (10.1)
Follow-up (y), median (IQR)	2.0 (0.8–4.2)	721	2.0 (0.8–4.2)	1.7 (0.5–3.3)
Waiting list time (mo), median (IQR)	3.1 (0.7–8.8)	4307	3.0 (0.7–8.8)	3.5 (0.8–9.2)
Era of LT, n (%)		0		
2008–2011	34 844(47.6)		34 503(47.6)	341 (51.8)
2012–2015	38 362 (52.4)		38 045 (52.4)	317 (48.2)

^a Allocation MELD not available in ELTR.

^b Medical urgency; status 1.

BMI, body mass index; ELTR, European Liver Transplant Registry; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; ICU, intensive care unit; INR, international normalized ratio; IQR, interquartile range; LDLT, living-donor liver transplant; LT, liver transplantation; MELD, model of end-stage liver disease; NA, not available; UNOS, United Network for Organ Sharing.

TABLE 2.

Characteristics of the cohort by period of liver transplant and HIV serostatus

Variable	HIV infected			HIV uninfected		
	2008–2011 (N = 341)	2012–2105 (N = 317)	P	2008–2011 (N = 34503)	2012–2105 (N = 38 045)	P
Recipient						
Male, n (%)	259 (76.0)	269 (84.9)	0.004	23 427 (67.9)	25 634 (67.4)	0.14
Age at LT (y), median (IQR)	49 (44–54)	51 (47–56)	<0.001	55 (48–61)	57 (49–62)	<0.001
MELD at LT, median (IQR)	18 (12–26)	18 (11–25)	0.44	18 (12–25)	18 (12–27)	<0.001
MELD at LT excluding HCC, median (IQR)	20 (15–28)	20 (15–29)	0.62	20 (15–28)	22 (15–30)	<0.001
MELD at LT (allocation-UNOS only), ^a median (IQR)	25 (22–32)	28 (22–34)	0.29	24 (22–30)	27 (22–33)	<0.001
BMI (kg/m ²), median (IQR)	23.7 (21.3–26.6)	24.1 (21.6–27.5)	0.14	26.6 (23.6–30.5)	27.0 (23.8–31.0)	<0.001
HCV positive, n (%)	227 (66.6)	190 (59.9)	0.08	11 373 (33.0)	11 705 (30.8)	<0.001
HBV positive, n (%)	39 (11.4)	41 (12.9)	0.56	2423 (7.0)	2183 (5.7)	<0.001
Hepatocellular carcinoma, n (%)	95 (27.9)	103 (32.5)	0.20	9366 (27.2)	11 334 (29.8)	<0.001
Split/LDLT, n (%)	321 (94.1)	300 (94.9)	0.65	2784 (8.1)	3006 (8.0)	0.54
Simultaneous liver-kidney transplant, n (%)	13 (5.3)	6 (2.5)	0.10	1435 (4.6)	2059 (6.0)	<0.001
Urgency, ^b n (%)	24 (9.2)	29 (11.6)	0.39	1423 (4.5)	1523 (4.4)	0.44
Dialysis before LT, n (%)	17 (5.0)	12 (3.8)	0.45	2461 (7.1)	3769 (9.9)	<0.001
Clinical condition, n (%)						
ICU	38 (11.5)	26 (8.5)	0.42	3148 (10.1)	4501 (12.6)	<0.001
Hospital	178 (53.9)	175 (57.4)		11 937 (38.2)	13 780 (38.5)	
Home	114 (34.6)	104 (34.1)		16 184 (51.8)	17 470 (48.9)	
Waiting list time (mo), median (IQR)	3.2 (0.7–8.1)	4.1 (0.9–11.2)	0.02	2.8 (0.6–7.9)	3.3 (0.7–9.7)	<0.001
No. of HIV LT per center, median (IQR)	12 (4–24)	9 (4–15)	0.002	N/A	N/A	N/A
Transplants in centers with <1 HIV LT/y, n (%)	132 (38.7)	138 (43.5)	0.21	N/A	N/A	N/A
Donor						
Male, n (%)	188 (56.0)	164 (52.1)	0.32	19 747 (57.6)	22 000 (58.4)	0.02
Donor age, n (%)	50 (36–62)	49 (34–63)	0.74	46 (29–58)	45 (29–57)	0.003
Donor height (cm), median (IQR)	170 (165–178)	170 (163–176)	0.16	170 (165–179)	171 (165–179)	0.70
Donor cause of death, n (%)						

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Variable	HIV infected			HIV uninfected			P
	2008–2011 (N = 341)	2012–2105 (N = 317)	P	2008–2011 (N = 34503)	2012–2105 (N = 38 045)	P	
Anoxia	44 (13.4)	50 (16.4)	0.55	4604 (14.0)	7306 (20.2)	<0.001	
Stroke	162 (49.4)	156 (51.2)		16 763 (51.2)	16 145 (44.7)		
Head trauma	62 (18.9)	49 (16.1)		8100 (24.7)	8282 (22.9)		
Other	60 (18.3)	50 (16.4)		3302 (10.1)	4406 (12.2)		

^aAllocation MELD not available in ELTR.

^bMedical urgency; status 1.

BMI, body mass index; ELTR, European Liver Transplant Registry; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; ICU, intensive care unit; IQR, interquartile range; LDLT, living-donor liver transplant; LT, liver transplantation; MELD, model of end-stage liver disease; N/A, not applicable; UNOS, United Network for Organ Sharing.

TABLE 3.

Multivariable Cox models of characteristics associated with graft loss and mortality for the entire cohort

Covariates	Graft loss aHR ^a (95% CI)	P	Mortality aHR ^a (95% CI)	P
HIV infection	1.41 (1.23–1.63)	<0.001	1.67 (1.43–1.94)	<0.001
Recipient female sex	0.97 (0.93–1.00)	0.047		
Recipient age (per 10 y)	1.11 (1.09–1.13)	<0.001	1.22 (1.20–1.25)	<0.001
MELD	1.01 (1.01–1.01)	<0.001	1.02 (1.02–1.02)	<0.001
Recipient BMI <21 kg/m ²	1.17 (1.11–1.24)	<0.001	1.20 (1.13–1.28)	<0.001
Recipient hepatitis C	1.29 (1.25–1.34)	<0.001	1.31 (1.26–1.36)	<0.001
Recipient hepatitis B	0.79 (0.73–0.86)	<0.001	0.77 (0.70–0.85)	<0.001
Hepatocellular carcinoma			1.21 (1.16–1.26)	<0.001
LDLT/split	1.15 (1.06–1.25)	<0.001		
Pre-LT dialysis	1.33 (1.26–1.41)	<0.001	1.42 (1.34–1.51)	<0.001
Era 2012–2015 (vs 2008–2011)	0.86 (0.83–0.89)	<0.001	0.84 (0.81–0.88)	<0.001
Donor age (y)				
<40	1		1	
40–49	1.11 (1.06–1.16)	<0.001	1.10 (1.04–1.16)	<0.001
50–59	1.23 (1.18–1.29)	<0.001	1.22 (1.16–1.28)	<0.001
60–69	1.26 (1.20–1.33)	<0.001	1.27 (1.20–1.35)	<0.001
>70	1.37 (1.29–1.45)	<0.001	1.30 (1.21–1.39)	<0.001
Donor COD				
Head trauma	1		1	
Anoxia	1.01 (0.96–1.07)	0.69	1.02 (0.96–1.08)	0.51
Cerebrovascular/stroke	1.16 (1.11–1.21)	<0.001	1.13 (1.08–1.19)	<0.001
Other	1.08 (1.02–1.15)	0.02	1.09 (1.01–1.17)	0.02

^a Adjusted by cohort of origin.

BMI, body mass index; CI, confidence interval; COD, cause of death; HR, hazard ratio; LDLT, living donor-liver transplant; LT, liver transplantation; MELD, model of end-stage liver disease.

TABLE 4.
Multivariable Cox models of characteristics associated with graft loss and mortality in the HIV-infected cohort

Covariates	Graft loss aHR ^a (95% CI)	P	Mortality aHR ^a (95% CI)	P
Era 2012–2015 (vs 2008–2011)	0.58 (0.41–0.80)	0.001	0.56 (0.39–0.80)	0.002
MELD (per 1 unit)	1.04 (1.02–1.05)	<0.001	1.04 (1.03–1.06)	<0.001
Recipient BMI <21 kg/m ²	1.61 (1.15–2.25)	0.006	1.63 (1.13–2.35)	0.009
Recipient hepatitis C coinfection	1.83 (1.32–2.52)	<0.001	1.90 (1.33–2.69)	<0.001
Donor COD anoxia	0.51 (0.32–0.83)	0.007	0.59 (0.36–0.97)	0.04

^aAdjusted by cohort of origin.

BMI, body mass index; CI, confidence interval; COD, cause of death; HR, hazard ratio; MELD, model of end-stage liver disease.