Survival Benefit of Liver Transplant Among HIV+ Waitlist Candidates

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Introduction

- Liver failure is the most common cause of non-AIDS related death among HIV-infected (HIV+) individuals, primarily due to high prevalence of co-infection with hepatitis C (HCV) and hepatitis B (HBV) virus.
- Recent prospective clinical trials have demonstrated good outcomes of liver transplantation (LT) in select HIV/HCV co-infected patients with end-stage liver disease (ESLD). The OPTN does not collect HIV status at the time of LT listing.
- Therefore, the survival benefit of LT in HIV+ individuals with ESLD patients on the LT waiting list has not been previously examined.
- Moreover, most prospective studies of LT in HIV+ individuals have focused only on those individuals with hepatitis coinfection.
- Using a unique cohort, we sought to examine the survival benefit of LT in all HIV+ LT candidates.

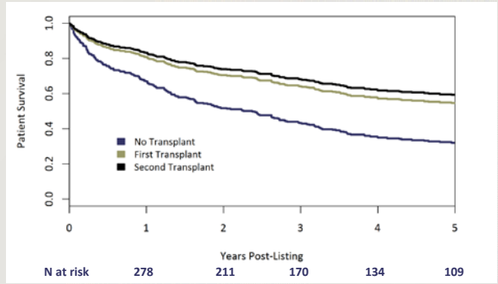
Methods

- IMS Health pharmacy fills (1/1/2001 – 10/1/2012) were linked with SRTR data.
- 437 LT waitlist candidates who filled ≥1 antiretroviral (ARV) medication unique to HIV treatment were identified and followed from the later of date of listing or first known HIV medication fill; simultaneous listings were collapsed.
- Time to event (waitlisting to death or administrative end of study) survival analyses were performed using Cox proportional hazards modeling, adjusted for available waitlist covariates.
- Number of transplants was treated as a time-dependent categorical variable (0, 1, 2).

Results

- Of 437 HIV+ LT waitlist candidates, 93% filled >1 ARV and 31% had a primary diagnosis other than HCV or HBV.
- First-time LT was associated with a 68% lower risk of death versus no transplant (adjusted hazard ratio [AHR] 0.32, 95% CI 0.22-0.46, p<0.0001).
- AHR for second LT suggested reduced mortality risk, but was not statistically significant (0.32, 0.09-1.1, p=0.07). Lack of significance may be due to sample size (n=12 repeat vs. n=199 first LTs).
- All variables are as of list date.
- Other significant predictors for patient survival were Modified End Stage Liver Disease Score (MELD) at listing; Body mass index (BMI) at listing; and physical capacity at listing (Table).
- Primary cause of ESLD was not a significant predictor of survival in the adjusted model or in an unadjusted model.

Figure. Patient survival curves by liver transplant while on the waitlist.



- Other non-significant or marginal adjusters included age, race, ABO type, coronary artery disease, diabetes type, cerebrovascular disease, drug-treated hypertension, education level, sex, prior malignancies, hospitalization or intensive care unit (ICU) status, insurance type, working for income, any dialysis, prior liver transplant, prior kidney transplant, and bilirubin.

Table. Significant predictors for patient survival on the liver waitlist.

Covariate	HR (95 % CI)	P-Value
Transplant (ref, no transplant)		<0.0001
First LT	0.32 (0.22, 0.46)	<0.0001
Re-transplant	0.32 (0.09, 1.2)	0.09
Albumin at listing (linear, per 1 g/dl)	0.67 (0.55, 0.81)	<0.0001
Creatinine at listing (ref, <1 mg/dl)		0.0006
1-< 2 mg/dl	0.91 (0.65, 1.3)	0.59
2-< 3 mg/dl	0.85 (0.50, 1.5)	0.55
≥3 mg/dl	2.6 (1.5, 4.5)	0.0006
Status at listing (ref, MELD 35+)		0.005
MELD 30-34	0.24 (0.08, 0.73)	0.01
MELD 15-29	0.33 (0.15, 0.70)	0.004
MELD <15	0.23 (0.10, 0.52)	0.0004
Other	0.29 (0.11, 0.78)	0.01
INR at listing (linear, per 1 unit)	1. 1 (1.0, 1.2)	0.007
BMI at listing (ref, 20-< 25)		0.01
<20	1.6 (0.96, 2.6)	0.07
25-< 30	0.78 (0.56, 1.1)	0.15
≥30	1.5 (0.92, 2.4)	0.10
Physical capacity (ref, no limitations)		0.04
Hospitalized	4.7 (1.2, 17.6)	0.02
Limited mobility	0.93 (0.51, 1.7)	0.83
Unknown	1.6 (0.94, 2.8)	0.08

Conclusions

- In a large cohort of HIV+ ESLD patients awaiting transplant, survival benefit from first-time LT was significant, resulting in a 68% lower hazard of death. Survival benefit also existed for repeat LT, though it was not statistically significant (p=0.09).
- This survival benefit was not limited to HCV+ or HBV+ recipients, and extended to patients with diverse ESLD etiologies.

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Dr. Durand is the Hopkin's site principal investigator on clinical trials for Gilead (HIV pharma) where funding is received by Hopkins. She has also served on an advisory board for Gilead.

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