

Outcomes in HIV/HCV Hemophilic vs. Non-Hemophilic Transplant Recipients: HIV Transplant Study HIV-TR



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ABSTRACT

Background: Hepatitis C virus infection is the major cause of end-stage liver disease, and it is the major indication for liver transplantation among HIV-infected individuals. Individuals with hemophilia (H), in contrast to those without hemophilia (NH), acquired HCV at a very young age, specifically with the first transfusion in the first years of life. Thus, we sought to determine whether HIV/HCV co-infected hemophilic men experience poorer OLTx outcomes than those without hemophilia.

Methods: MELD, CD4, HIV VL, HCV VL, HAART therapy, event rates and time-to-events, including transplant, rejection, and mortality, were compared between co-infected H and NH, from the same centers, participating in the multi-center HIV transplant study (HIV-TR). Statistical analysis included Wilcoxon rank-sum test for comparison of continuous variables, Fisher's exact test for comparison of categorical variables, and log-rank test for comparison of time-to-event curves.

Results: Of 100 HIV/HCV enrolled candidates, 33 (33%) underwent liver transplantation, including 8 of 16 (50.0%) H and 25 of 84 (29.8%) NH. Currently fewer H transplant candidates remain alive, 3 (18.8%) than NH, 46 (54.8%); H were more likely to die pre-OLTx, 5 (31.3%), as compared with NH, 13 (15.5%), $p=0.03$, primarily from sepsis and multi-organ failure. Hemophilic candidates reached OLTx ($p=0.06$) and MELD of 25 ($p=0.09$) marginally faster than non-hemophilic subjects. Although H were younger, 42 vs. 48 yr, $p=0.004$, there were no differences between H and NH in BMI, 24 vs. 25, $p=0.54$, CD4, 321 vs. 281 μL , $p=0.57$, detectable HIV RNA, 25.0% vs. 13.1%, $p=0.25$, or detectable HCV VL, 100% vs. 86.9%, $p=0.20$. Time to post-OLTx death ($p=0.67$), graft loss ($p=0.86$), and treated rejection ($p=0.81$) were similar. Rejection rates (95% CI) among H were 27% (7, 72) at 1-yr and 51% (18, 92) at 3-yr; and among NH were 40% (23, 64) at 1-yr and 48% (28, 72) at 3-yr. Post-O OLTx survival (95%CI) among H was 75% (31, 93) at 1-yr and 56% (15, 84) at 3-yr; and among NH was 62% (39, 78) at 1-yr; 56% (33, 74) at 3-yr. Liver cancer was not significant predictor of graft loss or survival.

Conclusion: Among HIV(+) hemophilic men, despite early acquisition of HCV, transplant outcomes appear to be similar to those in co-infected individuals without hemophilia. However, pre-transplant mortality appears higher among co-infected hemophilic men. Whether earlier intervention could reverse this finding is not known.

BACKGROUND

HIV/HCV Co-Infection in Hemophilia

- HCV is the leading cause of chronic liver disease and mortality in individuals with hemophilia.
- HCV acquisition occurred in 90%, via factor therapy with their first exposure, in the first years of life.
- 40% are co-infected with HIV, introduced in 1982, 10+ years after HCV infection.
- Two features distinguish hemophilic men:
 - Longer (life-long) duration HCV infection
 - Phenotypic cure by liver transplantation
- Nearly one-fourth of HCV(+) hemophilic men now have Metavir \geq F3 fibrosis.
- Those undergoing transplantation constitute 10% of co-infected liver transplant recipients.

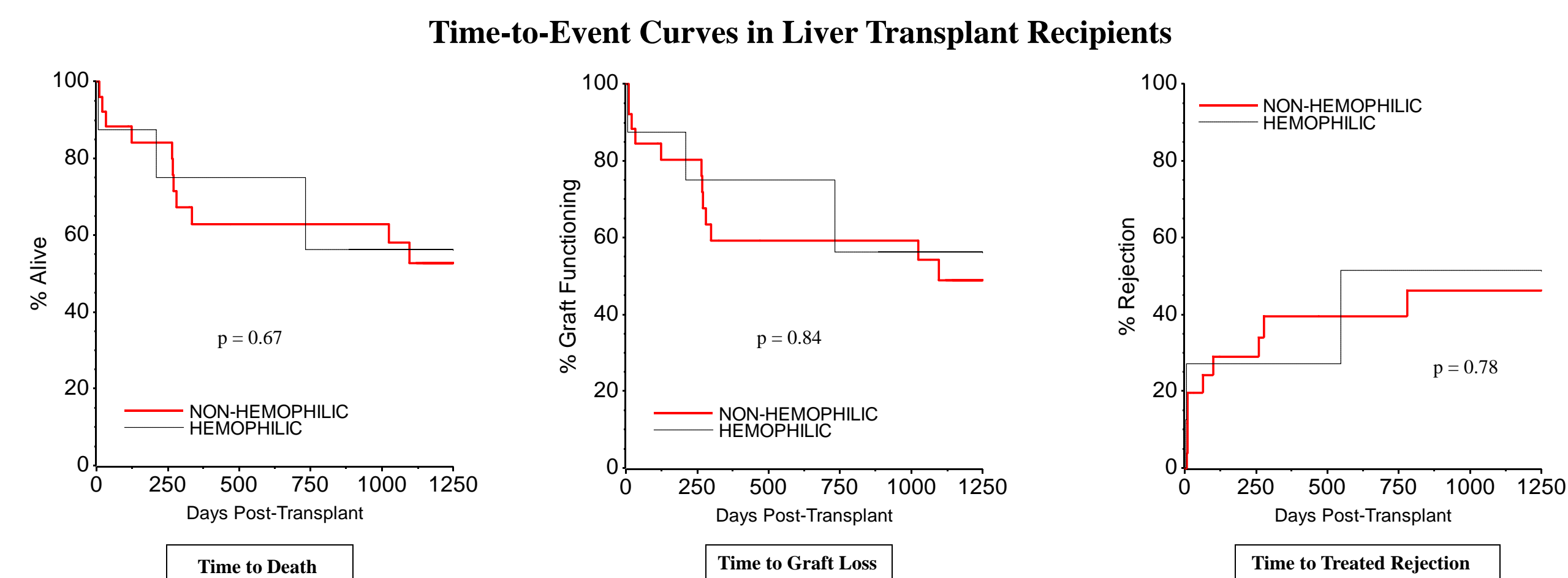
METHODS

Subjects: Hemophilia transplant candidates from 8 centers, and non-hemophilic candidates from the same centers.

Measures: MELD, CD4, HIV-VL, HCV-VL, HAART therapy, event rates, and time-to-events (transplant, rejection, mortality) between co-infected hemophilic and non-hemophilic candidates.

Statistics: Wilcoxon rank-sum test for comparison of continuous variables; Fisher's exact test for comparison of categorical variables; and log-rank test for comparison of time-to-event curves.

RESULTS



CLINICAL CHARACTERISTICS OF THE LIVER TRANSPLANT CANDIDATES

	Hemophilia N=16	Non-Hemophilia N=85	p value	
BASELINE CHARACTERISTICS				
Age Median (yr)	42	48	$p = 0.004^*$	
Gender:	No. Male	61 (71.8%)	$p = 0.01^*$	
Race:	No. Caucasian	58 (68.2%)	$p = 0.29$	
	No. Black	1 (6.3%)		
	No. Other/unknown	10 (11.9%)		
Median BMI	24	25	$p = 0.57$	
Median CD4	No./ μL	321	281	$p = 0.59$
HIVVL:	No. ≥ 48 copies/ml	4 (25.0%)	11 (12.9%)	$p = 0.25$
HCVVL:	No. ≥ 50 copies/ml	16 (100%)	74 (87.1%)	$p = 0.20$

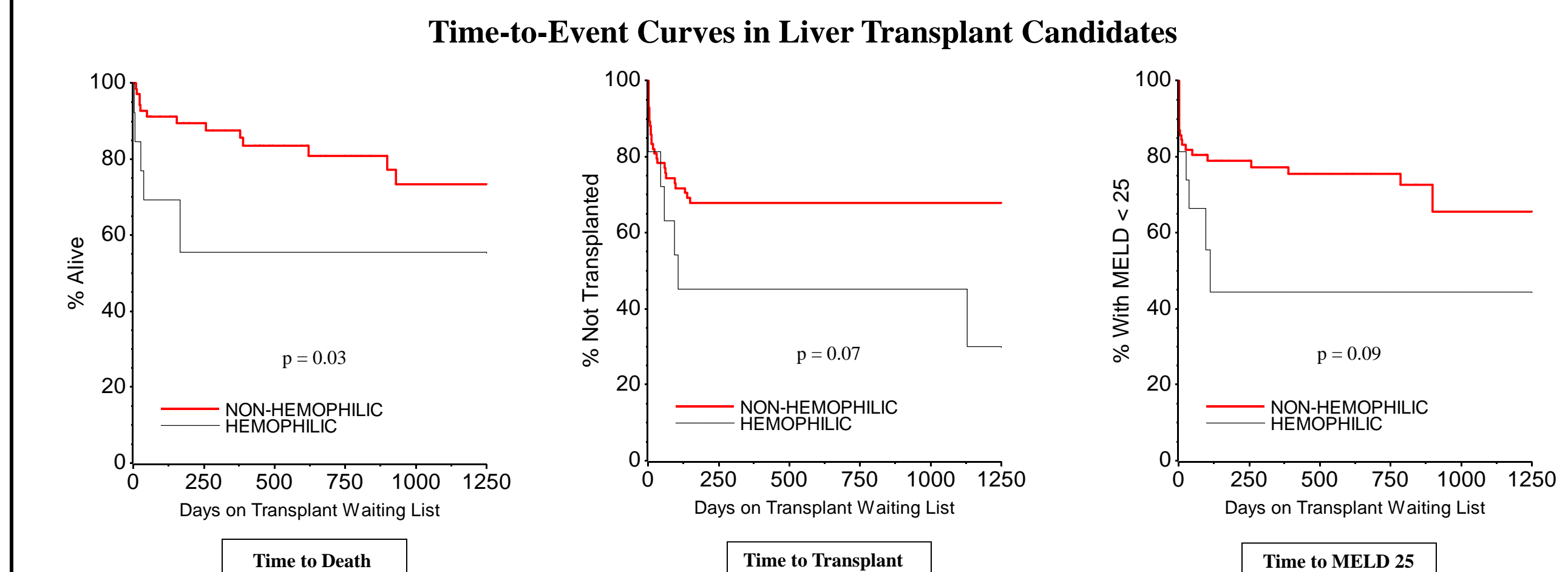
LIVER TRANSPLANT RECIPIENTS

No.	8 (50.0%)	59 (69.4%)	
Median time to death (days)	471	267	$p = 0.67$
Median time to graft loss (days)	471	265	$p = 0.84$
Median time to rx rejection (days)	6	35	$p = 0.78$
1-yr Post-transplant survival (95% CI)	75% (31%, 93%)	63% (41%, 79%)	
3-yr Post-transplant survival (95% CI)	56% (15%, 84%)	53% (31%, 71%)	

LIVER TRANSPLANT CANDIDATES

No.	5 (31.2%)	13 (15.3%)	
Median Time to Death (days)	26	152	$p = 0.03^*$
Median Time to Transplant	51	11	$p = 0.07$
Median Time to MELD=25	26	1	$p = 0.09$

RESULTS



CONCLUSIONS

- Two features distinguish HIV(+) hemophilic men from other HIV(+) liver transplant candidates: #1: early age of HCV acquisition, with first blood product exposure, and #2: phenotypic cure by liver transplantation. This study sought to determine whether the long duration HCV infection had any impact on transplant outcomes in co-infected hemophilic men.
- Despite early acquisition of HCV, and, thus, longer duration HCV infection by the time of transplantation, liver transplant outcomes appear to be similar between HIV/HCV co-infected hemophilic and non-hemophilic transplant recipients, as measured by time to graft loss ($p = 0.84$), treated rejection ($p = 0.78$), or post-transplant death ($p = 0.67$).
- By contrast, pre-transplant mortality among HIV/HCV co-infected hemophilic transplant candidates, however, is higher than among non-hemophilic HIV/HCV co-infected candidates ($p = 0.03$), primarily from sepsis and multi-organ failure.
- As hemophilic candidates reached MELD of 25 ($p = 0.09$) and OLTx ($p = 0.06$) only marginally faster than non-hemophilic candidates, but did not differ in CD4 ($p = 0.57$) or detectable HIV VL ($p = 0.25$) or HCV VL ($p = 0.20$), whether earlier intervention could reverse these findings is not known.

Solid Organ Transplant in HIV: Multi-Site Study



The HIV-TR Study
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