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Survival Benefit of Repeat Liver Transplantation in the US: A Serial MELD analysis by Hepatitis C Status and Donor Risk Index

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Abstract

Survival benefit (SB) for first LT is favorable at MELD ≥ 15. Herein, we identify the MELD threshold for SB from repeat liver transplant (ReLT) by recipient HCV status and donor risk index (DRI). We analyzed lab MELD scores in new UNOS registrants for ReLT from 3/2002–1/2010. Risk of ReLT graft failure ≤1 year versus waitlist mortality was calculated using Cox regression, adjusting for recipient characteristics. Of 3057 ReLT candidates, 54% had HCV and 606 died while listed. There were 1985 ReLT recipients, 52% had HCV and 567 ReLT graft failures by 1 year. Unadjusted waitlist mortality and post-ReLT graft failure rates were 416 (95% CI 384–450) and 375 (95% CI 345–407) per 1000 patient-years, respectively. Waitlist mortality was higher with increasing waitlist MELD ($p<0.001$). The MELD for SB from ReLT overall was 21 (21 in non-HCV and 24 in HCV patients). MELD for SB varied by DRI in HCV patients (MELD 21, 24 and 27 for low, medium and high DRI, respectively) but did not vary for non-HCV patients. Compared to first LT, ReLT requires a higher MELD threshold to achieve a survival benefit resulting in a narrower therapeutic window to optimize the utility of scarce liver grafts.

Introduction

Liver transplantation (LT) can be a lifesaving intervention for patients with acute or chronic liver disease. The need for LT far exceeds the supply of liver grafts[1]. Optimizing the use of available liver grafts is therefore part of a rational approach to decision-making in patient and graft selection. This is particularly important when post-transplant outcomes are known

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to be inferior such as in patients with advanced hepatocellular carcinoma (*i.e.* beyond Milan or UCSF criteria) or repeat liver transplantation (ReLT). Post-transplant outcome is utilized by a predominately urgency-based allocation in the US by limiting the standard Model for End-stage Liver Disease (MELD) exception score for hepatocellular carcinoma by tumor burden to within the Milan criteria to mitigate the risk for post-LT recurrent hepatocellular carcinoma[2, 3]. Although ReLT has inferior outcomes to first LT[1, 4–9], post-ReLT outcome is not explicitly incorporated into current liver graft allocation. For first LT, Merion *et. al.* characterized the survival benefit (when waitlist mortality exceeds post-LT mortality) as occurring when the MELD score at LT is 15 or greater[10]. However, the survival benefit from ReLT has not been characterized. Better understanding of the circumstances where ReLT candidates may achieve a survival benefit from the procedure could improve optimize the use of scarce liver grafts. In this study, we examine the MELD threshold for survival benefit from ReLT and assess the influence of graft quality and hepatitis C (HCV).

Patients and Methods

Data on adult patients receiving a first LT between 1995 and 2009 and newly registered for a second LT between March 1, 2002 and January 31, 2010 were obtained from the United Network for Organ Sharing Standard Transplant Analysis and Research files. We excluded patients with any of the following: 1) Diagnosis of HIV at first LT or at listing for second LT (n=5), 2) final status of listing for ReLT was status 1 (n=834), 3) removed from ReLT waiting list for condition improved, transplant not needed (n=308) or 4) missing initial or final MELD score for ReLT wait list period (n=36).

Indications for ReLT were uniquely classified independent of HCV status as primary non-function (PNF), hepatic artery thrombosis (HAT), other vascular, biliary, rejection or recurrent disease. Separate from these diagnoses, each patient's HCV status was assessed and coded. HCV was defined as either definite (HCV at ReLT or first LT and ReLT) or as probable (HCV at first LT but not ReLT). HCV diagnosis was assessed using coded and text based diagnostic fields. Listings for ReLT were categorized as early (patients listed for ReLT within 90 days of first LT) and late (patients were listed for ReLT greater than 90 days after first LT). The donor risk index (DRI) was calculated for all liver grafts[11].

Characteristics of the study population were summarized for patients on the waiting list for ReLT and patients receiving ReLT, as shown in Tables 1 and 2, respectively. Comparisons between HCV and non-HCV patients were evaluated using the chi-square and Wilcoxon rank sum tests.

Lab MELD categories

Data on lab MELD at listing for ReLT and consecutively updated lab MELD scores while on the waiting list were obtained from the waitlist history file. For unadjusted event rate analysis, patients were categorized according to their MELD score at time of listing for ReLT and MELD score at time of ReLT for calculation of waitlist and post-ReLT mortality, respectively, using two MELD scores per patient for the analysis as shown in Table 3. For adjusted Cox proportional hazards analysis, patients were categorized to their current MELD score while listed for ReLT using all MELD score updates for the analysis as shown in

Table 4. Therefore, patients with changing MELD scores while on the waiting list may contribute follow-up time to multiple MELD categories according to their MELD score at a given follow-up time on the waitlist. MELD categories for estimates for post-ReLT outcome were based on the lab MELD immediately prior to ReLT.

Unadjusted mortality rates

Waiting list mortality and 1-year post-ReLT unadjusted mortality rates with 95% confidence intervals were calculated per 1000 patient-years by lab MELD category. Crude mortality rates were compared for patients with and without HCV, early versus later relisting and by DRI[12] tertile.

ReLT waitlist mortality

Waitlist graft survival was calculated as days from first listing for ReLT to waitlist death. Patients remaining on the waitlist or removed from the waitlist for reasons other than death (retransplanted, refused second transplant, transferred to another center) were censored at the date of last follow-up. Patients with a final waitlist status reported as inactive were censored at the date of last active waitlist follow-up, unless a death was reported within 14 days. Patients reactivated on the waitlist were followed to their final waitlist observation and their waitlist outcome was classified based on this final status. Patients removed from the waitlist due to condition deteriorated, too sick, were recorded as deaths. Of these patients, 86% had a social security death date recorded and the death date was a median of two days before waiting list removal. As these dates were relatively similar, the date of removal from the waiting list was used as the death date. One-year survival from listing for ReLT to death or second ReLT was estimated using the Kaplan-Meier method.

Post-ReLT outcomes

The primary outcome of interest was graft failure after ReLT defined as death or second ReLT. Post-ReLT follow-up status and date were updated with data from the social security death master file for patients reportedly alive or lost to follow-up who also had a valid social security death date (2%). Graft survival time after ReLT was calculated as days from ReLT to death or third liver transplant within 1 year. Patients alive or lost to follow-up were censored at the date of last follow-up or 1 year, whichever occurred first. One and 5 year graft survival from ReLT was estimated using the Kaplan-Meier method.

Threshold for Survival Benefit from ReLT

Cox proportional hazards models adjusted for recipient characteristics (age at relisting, gender and race) compared adjusted hazard ratios for ReLT graft failure versus waitlist mortality (ratio of hazard ratios). Most recent lab MELD score while on the waitlist was modeled as a time-varying covariate as described above, allowing patients to be in different risk sets over time as their MELD changed[13]. We defined a covariate for whether the patient was transplanted by day t, where t represents time. The waiting time for patients at risk of death while on the waitlist, for the MELD category at that time, was compared with survival times for patients who experienced events. We then used appropriate contrast statements to compare the hazard ratios for transplanted patients versus those on the waitlist for each

MELD category. Hazard ratios were estimated by early and late relisting, HCV and non-HCV diagnosis, DRI tertile (<1.15, 1.15–1.45, >1.45) and intervals of post-ReLT follow-up time (0–7, 8–30 and 31–365 days). MELD threshold for survival benefit from ReLT was defined as the lab MELD score on the ReLT waitlist where the ratio of post-ReLT graft failure risk to waitlist mortality risk no longer was statistically significantly greater than 1 (*i.e.* the 95% CI includes value of 1.0).

Results

During the study observation period, there were 3057 patients listed for ReLT of whom 1985 (65%) underwent ReLT and met study criteria. Patient characteristics are listed in Tables 1 and 2. The indication for listing varied by interval from LT1 to listing for ReLT and is shown in Figure 1. As expected, PNF, HAT and other vascular indications were more frequent in the early listing group whereas those with biliary complications, rejection or recurrent disease were more common in the later listing group. Diagnosis of HCV was definitive (n=1265) or probable (n=395) in 54% (1660 of 3057). There were 606 deaths (23.7%) on the waitlist for ReLT with a median (IQR) follow up of 35 (10–133) days. The median (range) number of MELD entries per patient while on the wait list was 6 (1–235). The distributions of MELD scores at initial waitlist registration and at end of wait list observation are presented in Figure 2. As expected, the MELD scores at waitlist removal were higher than at listing and proportion removed without ReLT was highest in the highest MELD categories (35 or greater). In the 1985 patients in the ReLT cohort, 52% had a diagnosis of HCV, the median (IQR) ReLT donor age was 37 (23–50), median (IQR) DRI 1.29 (1.09–1.55) and there were 567 graft failure events within 1 year of ReLT (466 deaths, 101 second ReLTs).

Event rates on waitlist and post-ReLT

Next, we calculated unadjusted event rates per 1000 patient-years as shown in Table 3. The overall waitlist mortality rate (95% CI) was 416 (384–450) per 1000 patient-years, increased concordantly with increasing MELD at listing for ReLT ($p<0.001$) and differed significantly for candidates with and without diagnosis of HCV, 426 (384–472) and 511 (460–568) per 1000 patient-years, respectively ($p=0.01$). Candidates listed early (≤90 days from LT1) versus later had a higher waitlist event rate, 1096 (941–1276) vs 337 (307–370) per 1000 patient-years respectively ($p<0.001$). The overall graft failure rate after ReLT was 375 (345–407) per 1000 patient-years and was higher in recipients with HCV vs without HCV, 472 (425–524) and 283 (248–323) per 1000 patient-years respectively ($p<0.001$). Higher MELD at time of ReLT was associated with higher graft failure rates ($p=0.001$). Early and late listings had similar post-ReLT rates of graft failure, 384 (330–447) and 372 (337–410) ($p=0.07$). Use of lower DRI liver grafts for ReLT was associated with lower post ReLT event rates; lowest DRI tertile (<1.15) vs medium DRI (1.15–1.45) and highest tertile (>1.45) rates were 264 (224–311), 406 (353–466) and 469 (412–535) per 1000 patient-years, respectively ($p<0.001$). Thus, these data indicate that DRI, previously shown to reliably predict graft failure after first LT[11], also provides prognostic information following ReLT.

Graft failure hazard ratios and MELD threshold for survival benefit

One-year Kaplan-Meier survival without event (waitlist death or post -ReLT death or ReLT graft failure) (95% CI) from listing for ReLT was 63.6% (61.8–65.3) with survival lower for HCV (59.0%; 56.5–61.4) compared to non-HCV (69.0%; 66.4–71.4) patients ($p<0.001$). Post-ReLT 1 year graft survival (95% CI) was 71.0% (68.99–73.0) and was reduced among HCV (65.5; 62.5–68.3) compared to non-HCV (76.9%; 74.1–79.5) ReLT recipients ($p<0.001$). Post-ReLT 5-year graft survival (95% CI) was 51.9% (49.2–54.5) and was also reduced among HCV (45.8; 42.2–49.3) compared to non-HCV (58.3%; 54.4–62.0) ReLT recipients ($p<0.001$). Hazard ratios for post-ReLT graft failure versus waitlist mortality by current MELD score adjusted for age, gender and race are shown in Table 4. For the entire cohort, the lab MELD category at ReLT where the hazard for waitlist mortality no longer statistically exceeds the hazard of post-ReLT graft failure was 21–23. That is, recipients in MELD categories < 21 had a statistically significant higher hazard of graft failure with ReLT within 1 year than the hazard of waitlist mortality whereas, those with MELD ≥ 21 did not (Figure 3). When stratified by diagnosis of HCV and DRI of graft used for ReLT, retransplant recipients without HCV had a similar MELD threshold of <21 overall and <21 for low (<1.15), medium (1.15–1.45) DRI and high (>1.45) DRI liver grafts. However, ReLT recipients with HCV had higher MELD threshold of < 24 overall. Retransplant recipients with HCV who received low (<1.15) DRI liver grafts for ReLT had MELD threshold of <21 similar to that of non-HCV ReLT candidates. Conversely, retransplant recipients with HCV receiving medium (1.15–1.45) or high (>1.45) DRI liver grafts had a higher MELD threshold of 24 and 27, respectively.

Hazard ratios within each MELD category decreased as follow-up time increased which influenced the MELD threshold for survival benefit with ReLT. (See Table 5) At MELD 6–20, post-ReLT mortality was higher than waitlist mortality in the first month post-ReLT, whereas recipients with MELD of 27 or higher had survival benefit within the first week post-ReLT. Recipients with MELD 21 or higher had a survival benefit after the first week post-ReLT and recipients with MELD 15 to 18 or higher had a survival benefit after the first month post-ReLT. When stratified by HCV, the early post-ReLT MELD thresholds (within 0–7 days and 8–30 days) were unchanged. Yet, when considering the survival benefit after the first month post-ReLT, recipients with HCV and a MELD 21 or higher had a survival advantage, whereas recipients without HCV only needed MELD of 18 or higher for a survival advantage from ReLT.

Sensitivity analyses

As the physiological consequences of HAT and PNF, are not always accurately reflected by MELD, we performed sensitivity analyses. When we repeated our primary analysis excluding all patients with diagnosis of HAT (n=355) and PNF (n=142), we found the effects on survival benefit in our primary analysis were unchanged. In a separate analysis of the 834 patients excluded from the primary analysis because they had a final listing as Status 1, there were 733 who had both initial and final status as status 1. Using the same MELD categories as the primary analysis, no MELD category had a statistically significant reduced post-ReLT survival compared to the waitlist survival. Although the statistical power to

detect a survival benefit is reduced in this smaller cohort, the finding suggests a survival benefit may exist in all MELD categories for this subgroup.

Discussion

The optimal use of scarce liver grafts is dependent on appropriate candidate and donor liver selection: this is particularly true for candidates for ReLT[14, 15]. In this study, we found that the MELD threshold for survival benefit from ReLT is 21 which is higher than the MELD threshold of 15 for first LT reported previously[10]. Our data show that the risk for death or graft failure after ReLT is 3.5 to 8.3 times greater than risk of death without ReLT for ReLT candidates with MELD < 21. For ReLT candidates with HCV in this era before direct acting antiviral agents, the MELD threshold for survival benefit from ReLT was even higher at MELD of 27. However, use of better quality livers (lower DRI), can lower the MELD threshold for survival benefit with ReLT in HCV recipients to a level similar to non-HCV ReLT recipients. Whether the use of direct acting antiviral agents may reduce the graft failure rates of patients with HCV undergoing ReLT to levels similar to non-HCV individuals is unknown. Yet if this is true, it is reasonable to expect that ReLT with successfully-treated HCV infection either before or after ReLT may be able to have similar MELD threshold for survival benefit as recipients who never had HCV infection.

In our study we found that the risk of early graft failure (at 0–7 days and 8–30 days) after ReLT was similar between recipients with and without HCV across the spectrum of MELD scores at transplant. Graft failure after this early period was more likely to be influenced by HCV during our study timeframe. This finding is similar to that reported in prior studies of retransplant recipients with and without HCV in the UNOS database[8, 9]. Consistent with a prior study by Watt et al, we found that a higher MELD at the time of ReLT was associated with higher rates of death or graft failure after ReLT and this effect was even more pronounced in recipients with HCV when compared to those without HCV[9]. We detected a difference in the MELD threshold for survival benefit between ReLT recipients with and without HCV which was driven by higher rate graft failure occurring 31–365 days after ReLT in recipients with HCV. Therefore, we would expect that future HCV therapies with high efficacy and safety could result in ReLT graft failure rate for HCV infected recipients that are similar to recipients without HCV.

Recipients of ReLT have previously been shown to have higher graft failure rates than recipients of first LT[1, 4–9]. Herein, we demonstrate the influence the higher ReLT graft failure rate has on the MELD threshold for survival benefit. This higher MELD threshold for survival benefit from ReLT (with or without HCV) compared to that previously reported for first LT has several potential implications. Firstly, under an urgency allocation system, additional priority for candidates for ReLT could be granted if waitlist mortality is underestimated by MELD or in case of acute graft failure from primary graft non-function or hepatic artery thrombosis. Yet, if utility measures are considered in an allocation system, the higher threshold for survival benefit from ReLT versus first LT may justify deferring ReLT until MELD score is 21 or greater for patients without HCV or with successful HCV treatment. Secondly, graft quality and early technical complications within the first month after ReLT are influential factors driving the survival benefit. If ReLT is pursued, good

quality (low DRI) liver grafts can lower the MELD threshold for survival benefit from the procedure particularly in patients with HCV. Our study demonstrated that use of lower quality liver grafts can raise MELD threshold for survival benefit to as high as 24 in recipients with HCV. As graft quality has much less of an influence in ReLT recipients without HCV, we would expect that successful HCV treatment either before or after HCV could expand the number of suitable liver grafts for ReLT. Additionally, we found that early graft failure after ReLT (occurring within 0–7 days or 8–30 days) had a significant influence on raising the MELD threshold for survival benefit. Conversely, among patients that avoided graft failure within the first month after ReLT, the risk for graft failure was lowered to near that of recipients of first LT. Unfortunately, the technical complications of retransplantation are difficult to predict and to avoid. Lastly, even though an individual ReLT candidate may achieve a survival benefit from the procedure, given the scarcity of available liver grafts there may be a minimum likelihood of post-ReLT graft survival that is acceptable to the transplant community, our patients and other stakeholders[14]. Therefore, there is a therapeutic window for ReLT where the MELD threshold for survival benefit is achieved for the candidate yet a minimum post-ReLT graft survival is maintained. Much like candidates for first LT candidates, ReLT candidates within this therapeutic window may not have a sufficient priority to obtain a liver graft and may require petitions for additional priority to be competitive for liver grafts while within the therapeutic window. Candidates for ReLT make up approximately 3% liver transplant list US[16]; whether and how to provide additional priority for this minority of liver transplant candidates will be an important issue for the transplant community to address. The findings in our study suggest that the therapeutic window for ReLT is broader with selection of high quality donors and when the patient does not have HCV. Furthermore, we would expect in the era of new HCV direct acting antiviral agents that cure of HCV would improve the therapeutic window for ReLT and allow more flexibility in donor selection.

In conclusion, our analysis expands the seminal work by Merion *et al*[10] of the MELD threshold for survival benefit from first LT to that of ReLT. Compared to first LT, ReLT requires a higher MELD threshold to achieve a survival benefit resulting in a narrower therapeutic window to optimize the utility of scarce liver grafts.

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Abbreviations

SB	survival benefit
LT	Liver Transplantation
ReLT	repeat liver transplantation
HCV	Hepatitis C virus
DRI	donor risk index

UNOS	United Network for Organ Sharing
IQR	interquartile range
MELD	Model for End-stage Liver Disease
PNF	primary non-function
HAT	hepatic artery thrombosis
GF	Graft failure
HR	hazard ratio
CI	confidence interval

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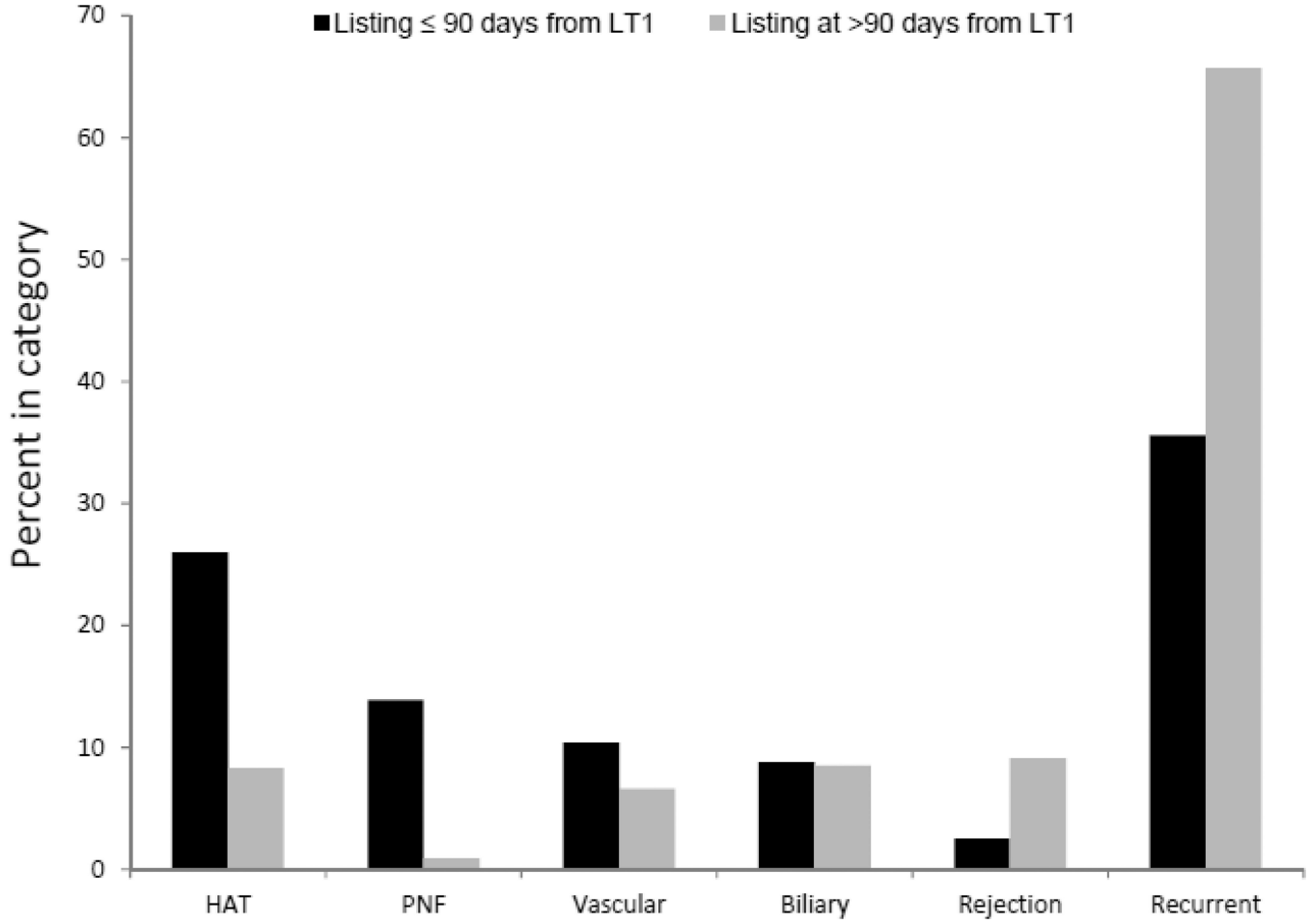

Figure 1.

Percent of retransplant candidates in that indication category by time interval from first transplant. LT1, First liver transplant; HAT, Hepatic artery thrombosis; PNF, Primary non-function; Recurrent, recurrent disease.

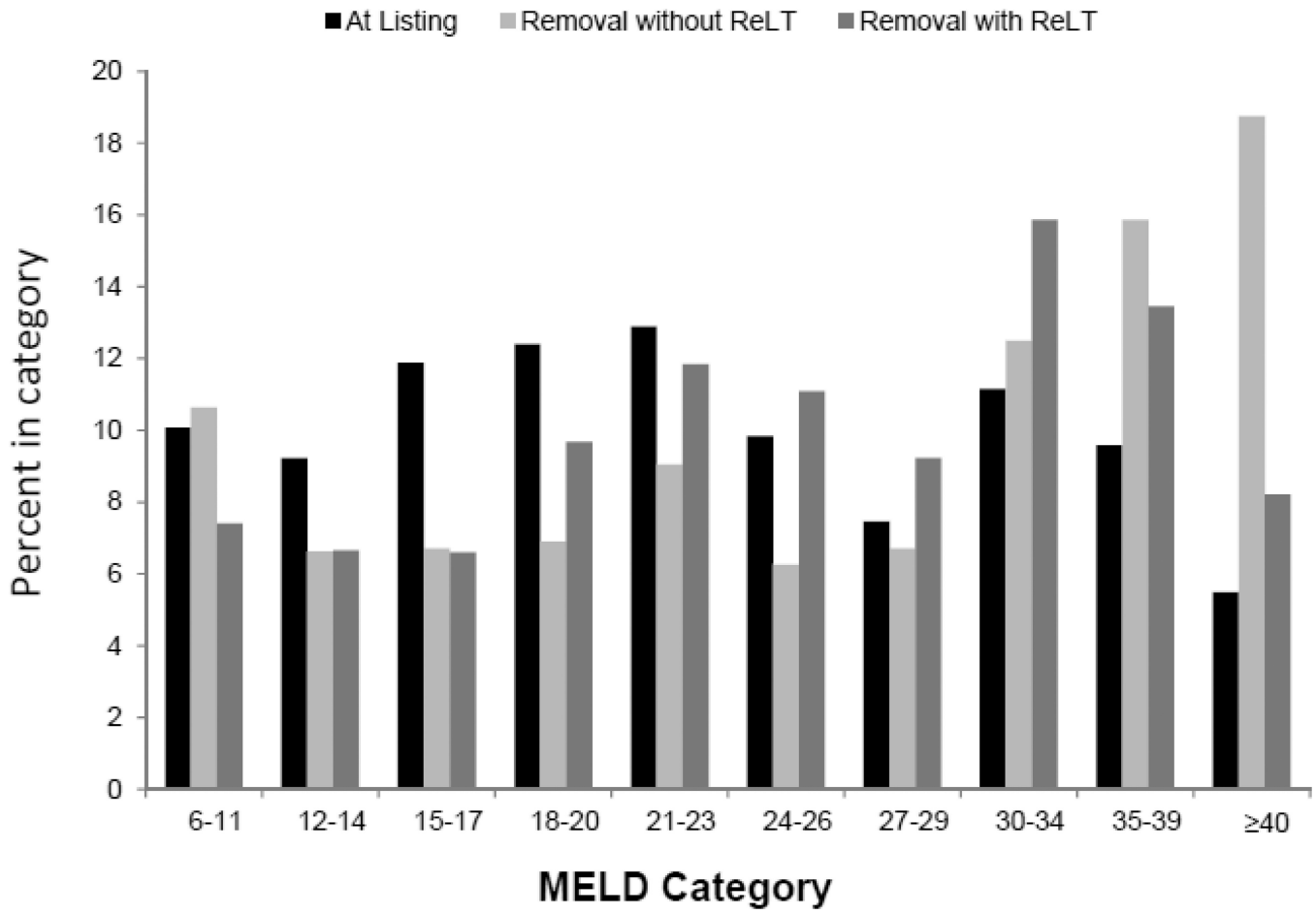

Figure 2.

Percent of patients in lab MELD category at date of listing for retransplant, at date of waitlist removal without retransplant and date of waitlist removal with retransplant.

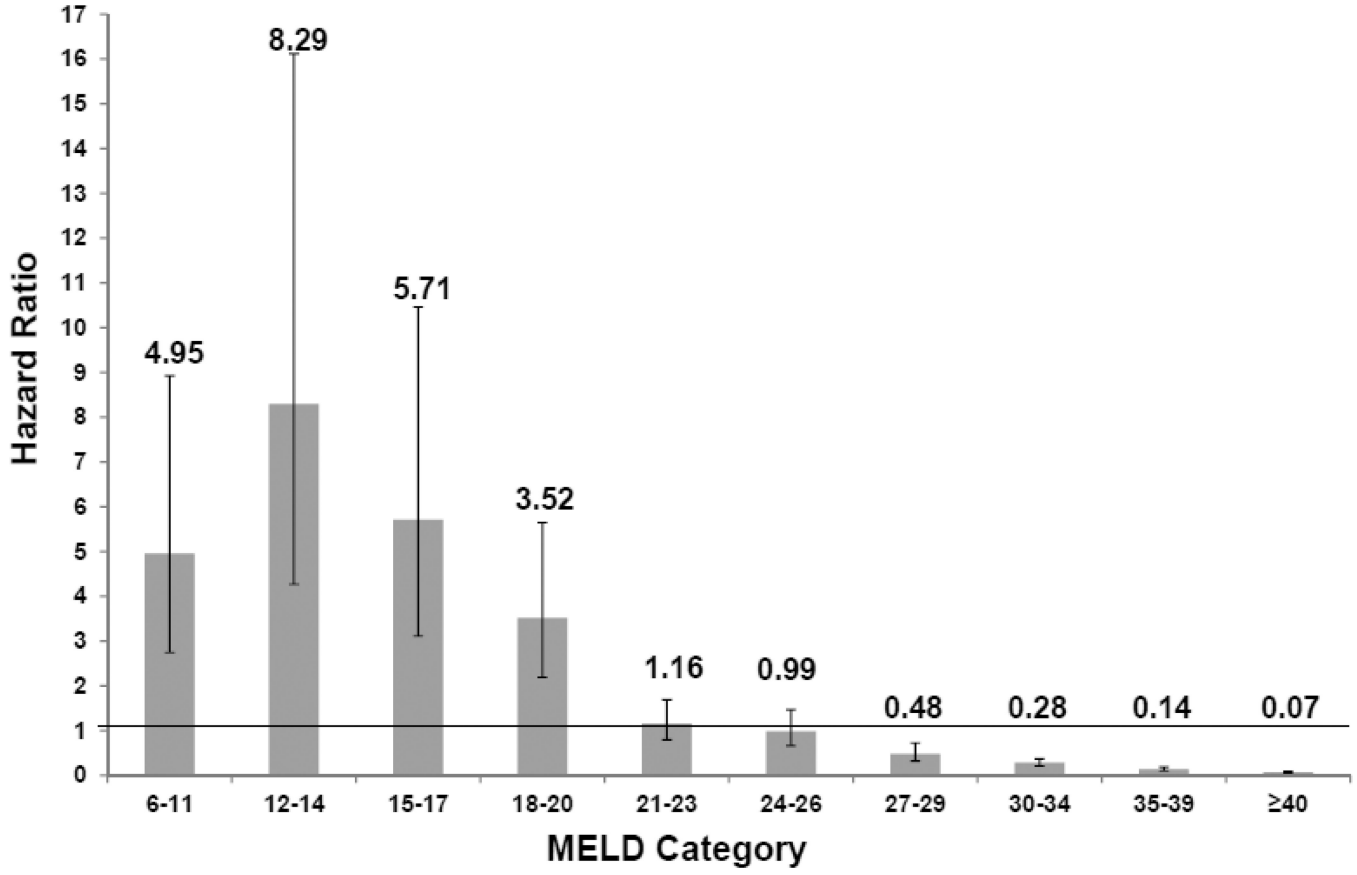

Figure 3.

Adjusted hazard ratios for post-ReLT graft failure versus waitlist mortality by current lab MELD score category.

Table 1

Characteristics of patients on waitlist for ReLT

Characteristic	Total cohort (n=3057)	Non-HCV (n=1397)	HCV (n=1660)	P value
Age at first LT, median (IQR)	49 (43–55)	48 (37–57)	50 (46–54)	<0.001
Age at Listing for ReLT, median (IQR)	52 (46–57)	51 (40–58)	53 (49–57)	<0.001
Male, n (%)	2084 (68)	831 (60)	1253 (76)	<0.001
Race, n (%)				
Caucasian	2172 (71)	1014 (73)	1158 (70)	0.09
AA	374 (12)	182 (13)	192 (12)	0.22
Hispanic	389 (13)	146 (10)	243 (15)	<0.001
Asian	80 (3)	42 (3)	38 (2)	0.22
Other	42 (1)	13 (1)	29 (2)	0.05
Diagnosis, n (%)				
PNF	142 (5)	76 (5)	66 (4)	0.06
Vascular (non-HAT)	40 (1)	28 (2)	12 (1)	0.002
Biliary	234 (8)	136 (10)	98 (6)	<0.001
HAT	355 (12)	222 (16)	133 (8)	<0.001
Rejection	208 (7)	127 (9)	81 (5)	<0.001
Recurrent disease	1804 (59)	643 (46)	1161 (70)	<0.001
Other	274 (9)	165 (12)	109 (7)	<0.001
Early Listing*, n (%)	832 (27)	467 (33)	365 (22)	<0.001
Waitlist Outcome, n (%)				
Death/Removal too Sick	606 (20)	242 (17)	364 (22)	0.002
ReLT	1985 (65)	958 (69)	1027 (62)	<0.001
Still waiting/Other removal reason	466 (15)	197 (14)	269 (16)	0.11
Lab MELD at, median (IQR)				
Listing for ReLT	22 (16–30)	22 (16–30)	22 (16–30)	0.18
Removal with ReLT	25 (19–33)	24 (18–32)	27 (20–34)	<0.001
Removal without ReLT	29 (19–38)	28 (20–38)	30 (18–39)	0.78

* ≤90 days from first LT; ReLT, Repeat liver transplantation; IQR, interquartile range; PNF, primary non-function, HAT, hepatic artery thrombosis

Table 2

Characteristics of patients who underwent ReLT

Characteristic	Total cohort (n=1985)	Non-HCV (n=958)	HCV (n=1027)	p
Age at first LT, median (IQR)	49 (42–55)	47 (37–56)	50 (46–54)	<0.001
Age at Listing for ReLT, median (IQR)	52 (46–57)	50 (40–58)	52 (48–56)	<0.001
Male, n (%)	1401 (71)	601 (63)	800 (78)	<0.001
Race, n (%)				
Caucasian	1422(72)	701(73)	721(70)	0.14
AA	243(12)	121(13)	122(12)	0.61
Hispanic	244(12)	98(10)	146(14)	0.007
Asian	50(3)	31(3)	19(2)	0.049
Other	26(1)	7(1)	19(2)	0.03
Diagnosis, n (%)				
PNF	92 (5)	42 (4)	50 (5)	0.61
Vascular (non-HAT)	26 (1)	20 (2)	6 (1)	0.003
Biliary	171 (9)	105 (11)	66 (6)	<0.001
HAT	266 (13)	166 (17)	100 (10)	<0.001
Rejection	143 (7)	89 (9)	54 (5)	<0.001
Recurrent disease	1134 (57)	444 (46)	690 (67)	<0.001
Other	153 (8)	92 (10)	61 (6)	0.002
Early Listing*, n (%)	567 (28)	320 (33)	247 (24)	<0.001
Donor Age**, median (IQR)	37 (23–50)	36 (22–50)	37 (23–49)	0.75
Donor Risk Index**, median (IQR)	1.29 (1.09–1.55)	1.29 (1.08–1.57)	1.29 (1.09–1.53)	0.98
Post-ReLT Outcome within 1 year n(%)				
GF(Death/second ReLT)	567 (29)	218 (23)	288(34)	<0.001
Death	466 (24)	178 (19)	349(28)	<0.001
Second ReLT	101 (5)	40 (4)	61 (6)	0.07

* ≤90 days after first LT;

** For grafts used for ReLT; ReLT, Repeat liver transplantation; GF, graft failure; IQR, interquartile range; PNF, primary non-function, HAT, hepatic artery thrombosis

Table 3

Unadjusted waitlist mortality and retransplant graft failure rates by MELD score category at Listing for ReLT and at time of ReLT

	MELD at Listing for ReLT					MELD at ReLT						
Lab MELD	Number at risk	Deaths	Pt-yrs	Rate per 1000 Pt-yrs	95% CI	Number at risk	Deaths	Pt-yrs	Rate per 1000 Pt-yrs	95% CI	Post-ReLT/pre-ReLT	95% CI
6–11	308	32	352	91	64–129	147	27	124	217	149–317	2.39	1.44–4.00
12–14	282	47	318	148	111–197	132	34	104	326	233–456	2.21	1.42–3.44
15–17	363	64	278	230	180–294	131	32	102	313	221–442	1.36	0.89–2.08
18–20	379	57	198	288	222–373	192	54	151	357	273–466	1.24	0.86–1.80
21–23	394	56	139	404	311–525	235	60	183	327	254–421	0.81	0.56–1.17
24–26	301	67	69	966	760–1227	220	61	167	365	284–469	0.38	0.26–0.53
27–29	228	53	28	1922	1468–2516	183	52	143	364	278–478	0.19	0.13–0.28
30–34	341	88	43	2062	1673–2541	315	113	224	504	420–606	0.24	0.19–0.32
35–39	293	84	26	3248	2623–4022	267	78	199	391	313–488	0.12	0.09–0.16
≥40	168	58	8	7371	5698–9535	163	56	112	501	386–651	0.07	0.05–0.10
Total	3057	606	1458	416	384–450	1985	567	1511	375	345–407	0.90	0.80–1.01

Table 4

Adjusted* hazard ratios for post-ReLT graft failure versus waitlist mortality by current lab MELD score category (anytime while active on waitlist for ReLT and at time of ReLT) and HCV diagnosis

	Overall			HCV			Non-HCV		
Lab MELD at ReLT	**HR**	**95% CI**	**p value**	**HR**	**95% CI**	**p value**	**HR**	**95% CI**	**p value**
6–11	4.95	2.74–8.93	<0.001	7.44	4.05–13.68	<0.001	5.29	2.93–9.54	<0.001
12–14	8.29	4.27–16.12	<0.001	12.48	6.31–24.65	<0.001	8.86	4.56–17.23	<0.001
15–17	5.71	3.11–10.46	<0.001	8.33	4.47–15.51	<0.001	5.92	3.23–10.85	<0.001
18–20	3.52	2.19–5.65	<0.001	5.08	3.10–8.31	<0.001	3.61	2.25–5.79	<0.001
21–23	1.16	0.80–1.69	0.43	1.67	1.12–2.49	0.012	1.19	0.81–1.73	0.37
24–26	0.99	0.66–1.47	0.94	1.42	0.93–2.17	0.10	1.01	0.68–1.51	0.96
27–29	0.48	0.32–0.72	<0.001	0.69	0.45–1.05	0.08	0.49	0.33–0.73	<0.001
30–34	0.28	0.21–0.37	<0.001	0.39	0.29–0.53	<0.001	0.28	0.21–0.37	<0.001
35–39	0.14	0.10–0.19	<0.001	0.19	0.14–0.27	<0.001	0.14	0.10–0.19	<0.001
≥40	0.07	0.05–0.09	<0.001	0.07	0.05–0.09	<0.001	0.07	0.05–0.09	<0.001

*Adjusted Hazard Ratio, adjusted for age at listing for ReLT, gender, race; CI=Confidence interval

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Table 5

Adjusted* hazard ratios for post-ReLT graft failure versus waitlist mortality by current lab MELD score category (anytime while active on waitlist for ReLT and at time of ReLT) and interval of post-ReLT follow up time.

	0–7 days			8–30 days			31–365 days		
Lab MELD	**HR**	**95%CI**	**p value**	**HR**	**95%CI**	**p value**	**HR**	**95%CI**	**p value**
6–11	22.2	8.2–60.5	<0.001	5.43	2.00–14.8	0.001	2.81	1.48–5.35	0.002
12–14	26.5	8.48–82.8	<0.001	12.7	5.14–31.2	<0.001	4.37	2.14–8.91	<0.001
15–17	33.6	14.1–80.2	<0.001	10.2	4.46–23.1	<0.001	2.05	0.99–4.21	0.05
18–20	16.0	7.69–33.4	<0.001	4.38	2.16–8.91	<0.001	1.60	0.95–2.71	0.08
21–23	4.05	1.99–8.23	0.001	1.20	0.62–2.31	0.58	0.55	0.36–0.84	0.005
24–26	5.92	3.38–10.3	<0.001	1.08	0.58–2.02	0.81	0.34	0.21–0.54	<0.001
27–29	1.24	0.56–2.77	0.59	0.66	0.37–1.19	0.16	0.19	0.12–0.31	<0.001
30–34	0.88	0.54–1.45	0.62	0.26	0.17–0.42	<0.001	0.12	0.08–0.16	<0.001
35–39	0.48	0.28–0.83	0.008	0.15	0.09–0.25	<0.001	0.05	0.03–0.07	<0.001
>=40	0.34	0.20–0.58	<0.001	0.05	0.03–0.10	<0.001	0.02	0.02–0.04	<0.001

*Adjusted Hazard Ratio, adjusted for age at listing for ReLT, gender, race; CI, confidence interval