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Combined effects of recipient age and Model for End-Stage Liver Disease score on liver transplantation outcomes

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Abstract

Background—The proportion of older patients awaiting liver transplantation (LT) is rising. While increased age and LT-MELD are known to increase the risk of graft loss, no studies have explored whether there is a synergistic effect between LT-age and LT-MELD.

Methods—All US adult, non-Status 1 recipients of primary deceased donor LT from 2/05–1/10 without MELD exceptions were included (n=15,677). Recipients were categorized by LT-age [18–59y (n=11,966), 60–64y (n=2,181), 65–69y (n=1,177), ≥70y (n=343)] and LT-MELD [low (<20, n=5,290), mid (20–27, n=5,112), high (≥28, n=5,265)]. Adjusted Cox models evaluated the 1) independent and 2) combined effects of LT-age and LT-MELD on graft loss (death or re-LT).

Results—LT-age ≥70y (HR=1.65, 95% CI 1.08–1.82) and LT-MELD ≥28 (HR=1.46, 95% CI 1.02–1.47) were independently associated with increased risk of graft loss (p<0.001). In a model allowing for the interaction between LT-age and LT-MELD, the risk of graft loss for recipients

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≥70y with MELD ≥28 was *higher than predicted* by the additive model (HR=2.38, 95%CI 1.73–3.27, p<0.001) resulting in one-year graft survival of 56%. However, the increased risk of graft loss in recipients ≥70y was attenuated at lower LT-MELD <28. Furthermore, the interaction term was not significant for any other LT-age and LT-MELD combination.

Conclusion—Our analyses suggest that recipients should not be excluded solely based on age, however LT for recipients ≥70y at high LT-MELD scores should be undertaken cautiously.

Keywords

recipient age; MELD; graft loss

Introduction

From 2005 to 2009, the proportion of wait-list candidates for liver transplantation over 60 years of age increased from 27% to 34% (1). As the population with cirrhosis due to chronic hepatitis C (2) and non-alcoholic fatty liver disease ages (3), the proportion of older candidates on the wait-list is anticipated to grow. Exacerbating this problem is stagnant donor availability (1); as the gap between the number in need of transplant and the number of livers procured widens, candidates are waiting longer and undergoing transplant at older ages with higher MELD scores (1).

Older age at the time of transplant (LT-age) has been associated with worse post-transplant outcomes, including increased risk of graft loss (4–8). For this reason, some U.S. centers have set arbitrary maximum age cut-offs for liver transplantation, usually 65 or 70 years of age. However, a few single-center studies have suggested that comparable outcomes can be achieved in well-selected older recipients (9–12). Older candidates arguably undergo more stringent evaluation and consideration prior to transplantation in an effort to select those most appropriate to proceed to transplantation. However, data as to the optimal selection algorithm for older candidates is limited such that currently, consensus as to specific factors that predict favorable or unfavorable post-transplant outcomes are lacking.

The aim of this study was to evaluate post-transplant outcomes based on the combination of LT-age and MELD score at transplant (LT-MELD). We hypothesized that LT-MELD would be associated with a *synergistic* effect on post-transplant outcomes among older recipients. Therefore, we undertook this study to examine the interaction between LT-age and LT-MELD on the outcome of graft loss.

Results

Among the 15,677 liver transplant recipients who comprised our study cohort, 11,966 (76%) were 18–59 years, 2,181 (14%) were 60–64 years, 1,177 (8%) were 65–69 years, and 343 (2%) recipients were ≥70 years (Table 1). As LT-age increased, the proportion of African American recipients decreased while the proportion of Caucasians increased (p<0.001). Older recipients were more frequently transplanted for non-alcoholic fatty liver disease (NAFLD), cholestatic, or other liver diseases, whereas younger recipients were more frequently transplanted for hepatitis C virus (HCV) [p<0.001]. There were no significant differences between LT-age categories in the proportion of recipients on hemodialysis at the time of transplant (p=0.06). Median wait-list times were statistically different but clinically similar, ranging between 43 to 55 days (p<0.001).

Donor and transplant characteristics are listed in Table 2. Median donor age for recipients who were 18–59 years, 60–64 years, 65–69 years, and ≥70 years of age was 43 years, 45 years, 46 years, and 51 years, respectively (p=0.001). The proportion of recipients who received livers from donors who died from cerebrovascular accident (CVA) increased with LT-age (p<0.001). Older recipients were more likely to receive donation after cardiac death (DCD) livers (p=0.007), whereas younger recipients were more likely to receive livers from donor classified as CDC high-risk (p=0.01). Recipient LT-age strata did not exhibit differences in split liver (p=0.70) or cold ischemia time (p=0.78).

Unadjusted and adjusted models evaluating the association of LT-age and LT-MELD on graft loss – independent of the interaction between the two factors – showed that older LT-age was associated with an increased risk of graft loss (Table 3). Specifically, compared to recipients 18–59 years of age, the adjusted hazard ratio for graft loss for recipients 60–64 years, 65–69 years, and ≥70 years of age was 1.26 (95% CI, 1.16–1.37), 1.28 (95% CI, 1.14–1.43), and 1.65 (95% CI, 1.38–1.97), respectively (p<0.001 for all). Similarly, higher LT-MELD was associated with an increased risk of graft loss compared to recipients with LT-MELD <20 (Table 3); the adjusted hazard ratio was 1.19 (95% CI, 1.11–1.29) for MELD 20–27 and 1.46 (95% CI, 1.02–1.46) for MELD ≥28 (p<0.001 for both).

Next, we investigated the *combined* effect of LT-age and LT-MELD on the risk of graft loss. Unadjusted Kaplan-Meier survival curves for each LT-age category are shown for LT-MELD <20 (Figure 1A), 20–27 (Figure 1B), and ≥28 (Figure 1C). One-year graft survival rates for each LT-age and LT-MELD combination are listed in Table 4. Within each LT-MELD stratum, one-year graft survival declines incrementally with increased LT-age category. Graft survival in 60–64 year old recipients was 86%, 83%, and 75% at low (<20), mid (20–27), and high (≥28) LT-MELD group, respectively. For recipients 65–69 years of age, survival was 85%, 83%, and 74% at low (<20), mid (20–27), and high (≥28) LT-MELD group. Within all three LT-MELD categories, graft survival was lowest for the oldest (≥70 year old) cohort. At low LT-MELD (<20) and mid LT-MELD (20–27), graft survival at one year was 85% and 75%; survival was particularly poor at 56% for ≥70 year old recipients with LT-MELD ≥28.

Lastly, we evaluated unadjusted and adjusted models that included the interaction between LT-age *and* LT-MELD, using LT-age <60 years as the reference group (Table 4). Within each LT-MELD category, the hazard ratio for graft loss increased with LT-age. The adjusted hazard ratio for graft loss in 60–64 year old recipients at low, mid, and high LT-MELD was 1.14 (95% CI, 1.01–1.33; p=0.07), 1.28 (95% CI, 1.11–1.48; p=0.001), and 1.36 (95% CI, 1.18–1.57; p<0.001), respectively. For recipients 65–69 years of age, the adjusted hazard ratio for graft loss at low, mid, and high LT-MELD was 1.22 (95% CI, 1.02–1.46; p=0.03), 1.21 (95% CI, 1.01–1.48; p=0.06), and 1.40 (95% CI, 1.15–1.69; p=0.001), respectively. In the oldest cohort, recipients ≥70 years of age, the adjusted hazard ratio for graft loss was 1.41 (95% CI, 1.08–1.82; p=0.02), and 1.51 (95% CI, 1.08–2.09; p=0.01) at low and mid

LT-MELD. However, the adjusted hazard ratio for graft loss in recipients ≥70 years old transplanted at high LT-MELD (≥28) was markedly higher when compared to all other LT-age and LT-MELD strata (HR=2.38, 95% CI 1.73–3.27; p<0.001). This finding was supported by the fact that the interaction term for LT-age and LT-MELD was statistically significant only for recipients with LT-age ≥70 years and LT-MELD ≥28 (p=0.01). No interaction was detected for any other LT-age and LT-MELD combination (Table 4).

Discussion

Although chronologic age alone cannot be used as a sole criterion for liver transplantation for a particular candidate (13), there exists strong selection bias against offering transplantation to older candidates through the application of exclusion criteria – variably applied – such as the presence of multiple medical co-morbidities and poor functional status. As a result, only 10% of liver transplant recipients are ≥65 years old, and 2% are ≥70 years old. However, given the rising age of wait-listed candidates, determining specific factors beyond age alone that are associated with poor – or acceptable – outcomes in the oldest recipients is becoming increasingly more important.

In this study, we specifically evaluated whether the *combined* effect of older LT-age and higher LT-MELD was associated with an increased risk of graft loss. Using national registry data, we found that the risk of graft loss for all but one combination of LT-age and LT-MELD approximated the predictions of the independent models for all recipients (i.e., there was *no* interaction between LT-age and LT-MELD). Only for the unique combination of the oldest (LT-age ≥70 years) and sickest (LT-MELD ≥28) recipients did the risk of graft loss correspond to an unacceptably low one-year graft survival rate of 56%. It is noteworthy that this occurred despite strong selection bias against transplanting older recipients, as evidenced by the fact that this group represented only 0.5% of recipients during the five year study period. In other words, these individuals had been deemed “fit for transplantation” by their clinicians after undergoing rigorous testing, and yet, nearly half of those who underwent transplant at LT-MELD ≥28 died within the first post-transplant year.

What we also found through our analyses is that there were patients within the older LT-age categories who were able to achieve acceptable post-transplant survival rates. For recipients ≥70 years undergoing transplant at LT-MELD <20 and LT-MELD 20–27, there was no significant interaction between LT-age and LT-MELD, with one-year graft survival rates of 85% and 75%, respectively. Furthermore, while recipients 60–64 years and 65–69 years, compared to those <60 years, also experienced an increase in risk of graft loss, this decrement was not synergistic at higher LT-MELD categories.

Our study is limited by characteristics of the UNOS/OPTN registry. First, we were unable to adjust for additional factors that likely impact graft loss particularly among older recipients, such as coronary artery disease, complications of long-standing diabetes, and other medical co-morbidities as these factors are subject to inconsistencies in data definitions from center to center or are not collected at all. However, the evaluation and selection process for liver transplantation is stringent, such that we would anticipate that the prevalence of these conditions was relatively low. This is further supported by the modest number of ≥70 year old liver transplant recipients. The absence of the strong selection bias inherent in our study cohort would, almost certainly, exacerbate the impact of increased age on post-transplant survival for high disease severity candidates.

Despite these limitations, our study, which encompasses the U.S. national experience of liver transplantation for older recipients, has important implications for the consideration of chronologic age in liver transplant decision-making. While recipients 64–69 years of age experienced higher rates of graft loss when compared to younger candidates, one-year graft survival rates remained acceptable regardless of MELD at the time of transplant. Furthermore, recipients ≥70 years of age with lower disease severity (MELD <28) also experienced acceptable rates of graft loss at one year post-transplant. However, our findings urge extreme caution with respect to transplantation for candidates ≥70 years of age with high disease severity. The overall one-year graft survival rate of 56% was sobering, approaching the five year 50% graft survival rates embraced as a minimum threshold of acceptability. The current shortage of deceased donor livers translates into a high opportunity cost for every transplant performed. As such, the broader community will need to grapple with the wisdom of transplanting elderly and sick candidates. Clearly, setting absolute age limits for liver transplant candidacy rings of arbitrariness and thereby engenders disfavor. Our study highlights the need for an accurate and objective assessment of physiologic age to supplement or perhaps even replace chronologic age to optimally select recipients for liver transplantation.

Methods

Study population and data

All adult (≥18 years of age), non-Status 1 recipients of primary deceased donor liver transplants in the United States between February 1, 2005 and January 31, 2010 were included. In order to objectively evaluate the physiologic effect of liver disease severity on transplant outcomes, we excluded recipients who received MELD exception points, including those with hepatocellular carcinoma (HCC). Age at the time of transplant (LT-age) was categorized into four groups: 18–59 years, 60–64 years, 65–69 years, and ≥70 years. These categorizations were chosen based on clinical relevance, as deemed by the investigators. MELD score at the time of transplant (LT-MELD) was categorized into three groups based on LT-MELD tertiles in this cohort: <20 (low), 20–27 (mid), and ≥28 (high). Region risk was defined based on median LT-MELD for all recipients within a region; regions were divided by LT-MELD tertiles: low (LT-MELD 22), mid (LT-MELD 25), and high (LT-MELD 27).

All data were obtained from The United Network for Organ Sharing (UNOS) / Organ Procurement Transplantation Network (OPTN) registry as of April 30, 2012. Approval to perform this research was obtained by the Institutional Review Board at the University of California, San Francisco.

Statistical analysis

Descriptive continuous and dichotomous characteristics were compared using the Kruskall-Wallis and Chi-square tests, respectively. The primary outcome was graft loss, defined as death or re-transplantation. Graft survival curves were calculated using the Kaplan-Meier method. Univariable and multivariable Cox regression models were used to investigate the independent effects of LT-age and LT-MELD on graft loss. Models were then re-run allowing for the interaction between LT-age and LT-MELD categories. All multivariable models were adjusted for recipient (gender, ethnicity, and disease etiology), donor (age, height, cause of death, donation after cardiac death (DCD) status, and split liver), and transplant (cold ischemia time and share region) factors. Given the difference in receipt of DCD grafts by LT-age strata, we performed a sensitivity analysis which did not change our results. Again, recipients ≥70 years of age with LT-MELD>28 were the only group to experience a synergistic effect on graft loss with a hazard ratio of 2.62 (95% CI 1.89–3.62, p value <0.001) and a significant interaction term (p=0.008).

For all tests, statistical significance was defined as a p value ≤ 0.05. Statistical analyses were performed using STATA (SE Version 12.0, College Station, TX).

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None

Abbreviations

DCD	donation after cardiac death
ECD	expanded criteria donor
HBV	hepatitis B virus
HCV	hepatitis C virus
HCC	hepatocellular carcinoma
INR	international normalized ratio
LT	liver transplantation
MELD	Model for End Stage Liver Disease
NAFLD	non-alcoholic fatty liver disease
LT-age	recipient age at time of transplantation
LT-MELD	recipient laboratory MELD at time of transplantation

References

1. Based on UNOS/OPTN data as of July 20, 2012
2. Division of Viral Hepatitis, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945–1965. MMWR Recomm Rep. 2012 Aug 17; 61(RR-4):1–32.

3. Charlton MR, Burns JM, Pedersen RA, Watt KD, Heimbach JK, Dierkhising RA. Frequency and outcomes of liver transplantation for nonalcoholic steatohepatitis in the United States. Gastroenterology. 2011; 141(4):1249. [PubMed: 21726509]

4. Levy MF, Somasundar PS, Jennings LW, et al. The elderly liver transplant recipient: a call for caution. Ann Surg. 2001; 233(1):107. [PubMed: 11141232]

5. Burra P, Martin ED, Gitto S, Villa E. Influence of age and gender before and after liver transplantation. Liver Transpl. 2013; 19(2):122. [PubMed: 23172830]

6. Dutkowski P, Oberkofler CE, Slankamenac K, et al. Are there better guidelines for allocation in liver transplantation? A novel score targeting justice and utility in the model for end-stage liver disease era. Ann Surg. 2011; 254(5):745. [PubMed: 22042468]

7. Herrero JI, Lucena JF, Quiroga J, et al. Liver transplant recipients older than 60 years have lower survival and higher incidence of malignancy. Am J Transplant. 2003; 3(11):1407. [PubMed: 14525602]

8. Keswani RN, Ahmed A, Keeffe EB. Older age and liver transplantation: a review. Liver Transpl. 2004; 10(8):957. [PubMed: 15390320]

9. Cross TJ, Antoniades CG, Muiesan P, et al. Liver transplantation in patients over 60 and 65 years: an evaluation of long-term outcomes and survival. Liver Transpl. 2007; 13(10):1382. [PubMed: 17902123]

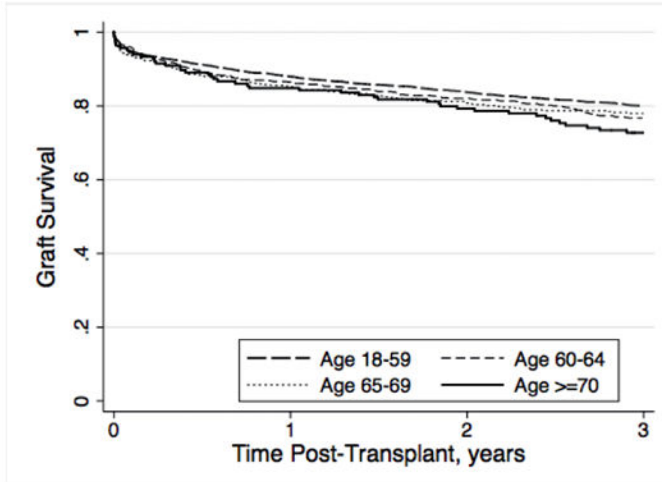
10. Aloia TA, Knight R, Gaber AO, Ghobrial RM, Goss JA. Analysis of liver transplant outcomes for United Network for Organ Sharing recipients 60 years old or older identifies multiple model for end-stage liver disease-independent prognostic factors. Liver Transpl. 2010; 16(8):950. [PubMed: 20589647]

11. Taner CB, Ung RL, Rosser BG, Aranda-Michel J. Age is not a contraindication for orthotopic liver transplantation: a single institution experience with recipients older than 75 years. Hepatol Int. 2011

12. Yoshizumi T, Shirabe K, Soejima Y, et al. Living donor liver transplantation in patients older than 60 years. Transplantation. 2010; 90(4):433. [PubMed: 20588207]

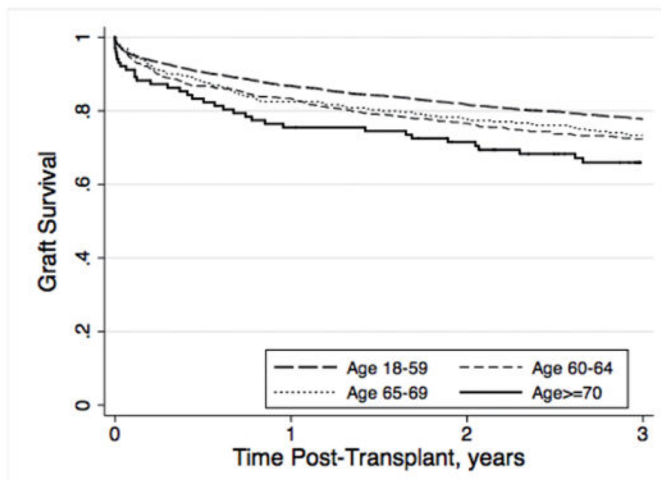
13. OPTN-UNOS. Policy 3.6 – Allocation of Livers. 2012 Jul.:1–25.

A.



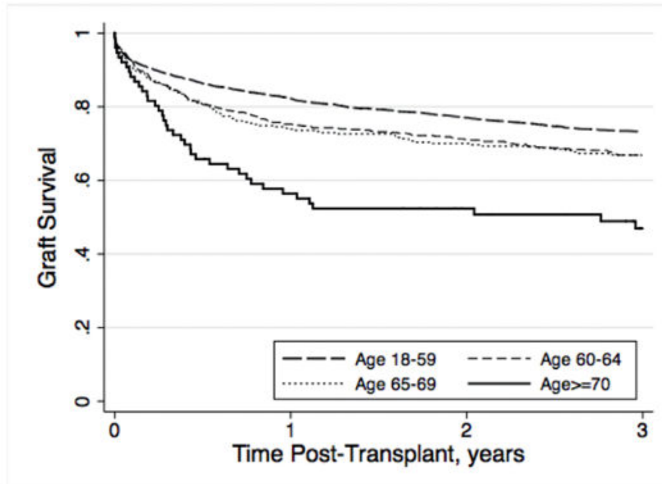
Number at Risk				
Age 18-59	3847	3351	2995	2393
Age 60-64	786	673	596	468
Age 65-69	492	417	283	283
Age >=70	165	139	105	105

B.



Number at Risk				
Age 18-59	3884	3311	2864	2205
Age 60-64	765	623	506	375
Age 65-69	361	296	256	190
Age >=70	102	77	69	46

C.



Number at Risk				
Age 18-59	4235	3415	2845	2105
Age 60-64	630	466	391	275
Age 65-69	324	231	198	138
Age >=70	76	42	32	21

Figure 1.

A. Unadjusted graft survival in recipients with low LT-MELD (<20) by LT-age categories

B. Unadjusted graft survival in recipients with mid LT-MELD (20–27) by LT-age categories

C. Unadjusted graft survival in recipients with high LT-MELD (≥28) by LT-age categories

Table 1

Baseline recipient characteristics by LT-age categories.

Characteristic*		LT-age Categories				p value
		18–59y n=11,966	60–64y n=2,181	65–69y n=1,177	≥70y n=343	
LT-age, years		51 (45–55)	62 (60–63)	66 (65–68)	71 (70–73)	
Female		34%	37%	43%	41%	<0.001
Race/ethnicity	African American	11%	6%	5%	3%	<0.001
	Caucasian	72%	77%	78%	82%	
	Hispanic	13%	12%	12%	9%	
	Asian	3%	3%	4%	4%	
	Other	1%	1%	1%	1%	
Disease etiology	HCV	45%	27%	17%	18%	<0.001
	Alcohol	16%	21%	20%	12%	
	NAFLD	6%	15%	18%	17%	
	HBV	3%	3%	2%	3%	
	Cholestatic	13%	15%	15%	21%	
	Other	17%	20%	28%	28%	
LT-MELD		23 (18–31)	22 (17–29)	21 (17–28)	20 (16–26)	<0.001
INR		1.9 (1.5–2.4)	1.7 (1.4–2.2)	1.7 (1.4–2.1)	1.6 (1.3–2.0)	<0.001
Total bilirubin, mg/dL		5.9 (3.2–14.1)	4.6 (2.6–10.1)	4.2 (2.2–8.9)	3.7 (2.1–6.9)	<0.001
Creatinine, mg/dL		1.2 (0.8–1.8)	1.3 (1.0–1.9)	1.3 (1.0–1.9)	1.3 (1.0–1.8)	<0.001
Hemodialysis at transplant		9%	8%	8%	6%	0.06
Waitlist time, days		43 (9–201)	43 (9–201)	55 (12–211)	46 (11–170)	<0.001

*Median (interquartile range)

Table 2

Donor and transplant characteristics by LT-age categories.

Characteristic*		LT-age Categories				p value
		18–59y n=11,966	**60–64y n=2,181**	**65–69y n=1,177**	**≥70y n=343**	
Donor age, years		43 (25–54)	45 (27–57)	46 (29–60)	51 (33–65)	0.001
DCD		5.2%	5.9%	6.5%	7.5%	0.007
CDC high risk donor		8.2%	7.6%	6.6%	5.5%	0.01
Donor positive HCV antibody		3.1%	2.2%	0.9%	1.7%	<0.001
Partial/split		1%	1%	1%	2%	0.70
Donor cause of death	Trauma	39%	35%	32%	26%	<0.001
	CVA	42%	46%	47%	51%	
	Anoxia	17%	16%	18%	19%	
	Other	2%	3%	3%	4%	
Region (by MELD category)	Low	40%	44%	43%	38%	0.33
	Mid	37%	34%	24%	36%	
	High	23%	22%	23%	26%	
Share region	Local	69%	69%	64%	56%	<0.001
	Regional	25%	23%	25%	26%	
	National	7%	8%	11%	18%	
Cold ischemia time, hours		7.0 (5.1–8.9)	6.9 (5.1–8.7)	6.6 (5.1–8.5)	7.0 (5.5–8.9)	0.78

*Median (interquartile range)

Table 3

Hazard ratios for graft loss from univariable and multivariable models *without* the interaction between LT-age and LT-MELD

Predictor		Univariable			Multivariable*		
		HR	95% CI	p-value	HR	95% CI	p-value
LT-age	<60y	1.0 (reference)			1.0 (reference)		
	60–64y	1.18	1.08–1.28	<0.001	1.26	1.16–1.37	<0.001
	65–69y	1.16	1.04–1.29	<0.001	1.28	1.14–1.43	<0.001
	≥70y	1.60	1.35–1.89	<0.001	1.65	1.38–1.97	<0.001
LT-MELD	<20	1.0 (reference)			1.0 (reference)		
	20–27	1.11	1.03–1.19	0.005	1.19	1.11–1.29	<0.001
	≥28	1.33	1.23–1.43	<0.001	1.46	1.02–1.46	<0.001
Recipient Race/ethnicity	Caucasian	1.0 (reference)			1.0 (reference)		
	African American	1.41	1.29–1.54	<0.001	1.37	1.25–1.50	<0.001
	Hispanic	0.99	0.91–1.08	0.76	0.95	0.86–1.04	0.24
	Asian	0.86	0.71–1.04	0.12	0.90	0.73–1.09	0.28
	Other	1.08	0.80–1.45	0.63	1.05	0.78–1.42	0.74
Recipient disease etiology	Alcohol	1.0 (reference)			1.0 (reference)		
	HCV	1.33	1.22–1.46	<0.001	1.45	1.33–1.59	<0.001
	NAFLD	1.05	0.92–1.20	0.43	1.05	0.92–1.20	0.46
	HBV	0.80	0.65–0.98	0.03	0.80	0.64–0.99	0.04
	Cholestatic	0.89	0.79–1.00	0.05	0.90	0.80–1.20	0.07
	Other	1.14	1.03–1.26	0.01	1.09	0.98–1.21	0.10
Donor age, per year		1.01	1.00–1.01	<0.001	1.01	1.00–1.01	<0.001
Donation after Cardiac Death (DCD)		1.56	1.40–1.75	<0.001	1.79	1.60–2.00	<0.001
Cold ischemia time, per hour		1.03	1.02–1.04	<0.001	1.03	1.02–1.03	<0.001

* Each model is also adjusted for: recipient gender; donor age, height, and cause of death; split liver; and share region

Table 4

One-year graft survival and hazard ratios for graft loss associated with each LT-age and LT-MELD category for univariable and multivariable models *including* the interaction between LT-age and LT-MELD

LT-MELD	LT-age (years)	n (*)	Univariable			Multivariable†			1y Graft Survival
			HR	95% CI	p-value	HR	95% CI	p-value	
<20	18–59	3,847 (24)	1.0 (reference)			1.0 (reference)			88%
	60–64	786 (5)	1.10	0.95–1.28	0.18	1.14	1.01–1.33	0.07	86%
	65–69	492 (4)	1.15	0.97–1.38	0.10	1.22	1.02–1.46	0.03	85%
	≥70	165 (1)	1.53	1.19–1.98	0.001	1.41	1.08–1.82	0.01	85%
20–27	18–59	3,884 (25)	1.0 (reference)			1.0 (reference)			87%
	60–64	765 (5)	1.21	1.05–1.39	0.008	1.28	1.11–1.48	0.001	83%
	65–69	361 (2)	1.13	0.93–1.38	0.21	1.21	1.01–1.48	0.06	83%
	≥70	102 (0.5)	1.46	1.06–2.03	0.02	1.51	1.08–2.09	0.02	75%
≥28	18–59	4,235 (27)	1.0 (reference)			1.0 (reference)			82%
	60–64	630 (4)	1.30	1.13–1.50	<0.001	1.36	1.18–1.57	<0.001	75%
	65–69	324 (2)	1.29	1.07–1.57	0.008	1.40	1.15–1.69	0.001	74%
	≥70‡	***76 (0.5)***	***2.37***	***1.73–3.25***	***<0.001***	***2.38***	***1.73–3.27***	***<0.001***	***56%***

* % of total recipient population

† Adjusted for: recipient gender, ethnicity, and disease etiology; donor age, height, and cause of death; donation after cardiac death (DCD); split liver; cold ischemia time; and share region.

‡ p value for the interaction term = 0.01; no other interaction terms for LT-age and LT-MELD combinations were significant