Published in final edited form as:

Am J Transplant. 2013 November ; 13(11): . doi:10.1111/ajt.12441.

HCC Patients Suffer Less From Geographic Differences in Organ Availability

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Abstract

It has been suggested that the number of exception model for end-stage liver disease (MELD) points for hepatocellular carcinoma (HCC) overestimates mortality risk. Average MELD at transplant, a measure of organ availability, correlates with mortality on an intent-to-treat basis and varies by donation service area (DSA). We analyzed Scientific Registry of Transplant Recipients data from 2005 to 2010, comparing transplant and death parameters for patients transplanted with HCC exception points to patients without HCC diagnosis (non-HCC), to determine whether the two groups were impacted differentially by DSA organ availability. HCC candidates are transplanted at higher rates than non-HCC candidates and are less likely to die on the waitlist. Overall risk of death trends downward by 1% per MELD point ($p = 0.65$) for HCC, but increases by 7% for non-HCC patients ($p < 0.0001$). The difference in the change of mortality with MELD is statistically significant between HCC and non-HCC candidates $p < 0.0001$. Posttransplant risk of death trends downward by 2% per MELD point ($p = 0.28$) for HCC patients, but increases by 3% per MELD point in non-HCC patients ($p = 0.027$), with the difference being statistically significant with $p < 0.005$. In summary, increasing wait time impacts HCC candidates less than non-HCC candidates and under increased competition for donor organs, HCC candidates' advantage increases.

Keywords

Hepatocellular carcinoma; liver transplantation; MELD score; donation service area; organ allocation

Introduction

Allocation of deceased donor livers for transplantation is based on risk of death, as estimated by the model for end-stage liver disease (MELD) score. Originally developed to predict mortality following transjugular intrahepatic portosystemic shunt placement, MELD score was further validated in end-stage liver disease patients (1), including those on the liver

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Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

Supporting Information

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transplant waitlist (2–7). However, in approximately 15–20% of patients, MELD does not accurately predict risk of death, particularly when hepatocyte failure and portal hypertension are not the primary concern, such as the development of hepatocellular carcinoma (HCC) in the setting of cirrhosis (8,9). To account for the risk of death from malignancy, United Network for Organ Sharing (UNOS) policy grants “exception MELD points” (eMELD) to HCC patients nationally, based on the estimated risk of tumor progression beyond transplantability within the ensuing 3 months (10,11).

HCC characteristics predicting favorable posttransplant outcomes are currently defined by “Milan criteria”: One tumor ≤5 cm in diameter or up to three tumors ≤3 cm each (4). Waitlist candidates meeting these criteria are initially granted 22 points, presumably representing a 15% probability of progressing beyond transplantability in 3 months (12). Candidates that are not transplanted and continue to remain within criteria, receive additional points every 3 months, intended to reflect a 10% increase in mortality risk. While exception points have greatly improved access to transplantation for HCC patients (13), recent studies suggest that the current point scheme inadvertently prioritizes HCC over patients without HCC diagnosis (non-HCC) by overestimating the presumed risk of tumor progression (14–19).

Furthermore, patients progress to a wide range of MELD scores before reaching the top of their donation service area’s (DSA) list, and patients listed in DSAs with higher average MELD at transplant have both a higher risk of waitlist removal and overall death rate (7,20). Because transplant rates differ by DSA, a patient’s risk of death at the same MELD differs from one DSA to another, while eMELD for HCC are granted uniformly nationwide. If HCC points do not accurately represent HCC patients’ risk of death, we hypothesized that their outcomes might be affected less by geographic disparities. We therefore compared transplant and death parameters of HCC and non-HCC candidates by DSA.

Patients and Methods

Study population

Data on candidates listed for liver transplantation (LT) were obtained from the Scientific Registry of Transplant Recipients (SRTR), which collects data on waitlisted patients in the United States through the Organ Procurement and Transplantation Network (OPTN). Our study included adult patients listed between January 1, 2005 [initiation of current eMELD policy (11)] and November 17, 2010 in DSAs with active waitlists over the entire 6-year period. Status 1 and retransplant candidates were excluded from the analysis, as were living donor liver transplant recipients, and registrants who refused transplant were transferred to another center, listed in error or improved and no longer needed a transplant. HCC patients were defined as candidates with a primary or secondary diagnosis of HCC, listed with exception points higher than the laboratory MELD. Non-HCC patients were defined as candidates who did not carry an HCC diagnosis. Removal codes included as “death” encompassed “death,” “medically unsuitable for transplant,” and “too sick for transplant.” This study was declared exempt by the Institutional Review Board of the Massachusetts General Hospital.

Statistical methods

The primary measure of relative organ availability was defined to be MELD at transplant, corrected for censored data as previously described (7). Briefly, a Kaplan–Meier estimate of the mean MELD at transplant for each DSA was calculated, censoring patients that had not received a transplant because of pretransplant death or waitlist removal, or if they remained listed at the date of last follow-up (7).

DSAs were ranked by average MELD at transplant and then divided into four quartiles (Q1–Q4), with Q1 having the lowest and Q4 having the highest average MELD at transplant. The start time for the calculation of transplant and death rate were the first date of receiving eMELD for HCC patients, and the first time MELD reached or exceeded 15 points for non-HCC patients. Demographic and transplant characteristics were compared among quartiles using linear regression for continuous variables and binomial regression for categorical ones. p-Values were obtained from a trend test.

The regression of overall death rate and posttransplant death rate on the average MELD score of their DSA was conducted using random effects Poisson regression models with a log link function and a log person-years offset. The model included two random intercepts, one for each diagnosis group (HCC and non-HCC) within each DSA, with an unstructured covariance matrix to account for the within DSA correlation of these two related observations. The regression of waitinglist death percentage on MELD score was conducted in a similar manner except that the number of deaths was assumed to follow a binomial distribution and the logit link function was used. This model calculates the effect of the average MELD score of a DSA on the risk of death while accounting for the fact that there may be random differences between the death rates at different DSAs. The average death rates and waitlist death percentages by diagnosis were estimated from similar models, excluding the MELD effect.

Results

Patient demographics

A total of 34 730 patients were included in the analysis: 3517 HCC patients and 31 213 non-HCC patients, whose demographic characteristics are summarized by quartile in Table 1. The HCC group includes a lower percentage of females than the non-HCC group (22.5% vs. 34.7%, $p < 0.001$). HCC candidates tend to be slightly older than non-HCC patients (57.3 vs. 52.8 years old, $p < 0.001$). There are slightly more patients with blood group AB ($p < 0.001$) in the HCC group (4.8%) than in the non-HCC group (3.7%). In both groups, there is a higher percentage of patients with AB blood type in quartile 4. There is a slightly lower percentage of Caucasians ($p < 0.001$) in the HCC group (65.5%) than in the non-HCC group (72.2%), while both groups have higher percentages of Caucasians in Q1 than Q4. HCC patients are much more likely to be Asian (10.6%) than non-HCC patients (3.2%; $p < 0.001$) and both groups have a larger proportion of Asians in Q4.

HCC candidates have lower waitlist and overall death rates

HCC candidates' mean waitlist death percentage is only 3.8% while for non-HCC candidates it is over four times higher (18.5%; $p < 0.0001$; Figure 1A). The average overall death rate is lower in HCC (0.114 deaths/patient year) than non-HCC candidates (0.175 deaths/patient year; $p < 0.0001$; Figure 1B). Posttransplant death rates, however, are similar between HCC and non-HCC groups, with 0.104 deaths/patient year in the HCC group, and 0.094 deaths/patient year in the non-HCC group ($p = 0.06$; Figure 1C). Since blood group 0 patients wait the longest for transplant (OPTN), we also compared patients with blood type 0 to non-0 patients (blood groups A, B and AB). Although patients with blood type 0 have a higher waitlist death rate than non-0 patients ($p = 0.018$), the effect of organ availability is the same in both groups (Figure S1A–C, Tables S2 and S3).

HCC candidates' death rate increases less with increasing organ shortage

As a DSA's MELD at transplant increases across quartiles, the percentage of HCC patients receiving a transplant decreases from 96.8% in Q1 to 75.5% in Q4 ($p < 0.001$), and transplant rate decreases from 8.7 to 1.9 per patient year ($p < 0.001$; Table 2). The

percentage of HCC candidates dying on the waitlist increases from 2.1% to 6.8% ($p < 0.001$). However, overall death rate and posttransplant death rate, or posttransplant death rate among patients who survived LT>90 days does not change significantly across quartiles. Interestingly, posttransplant death due to malignancy in HCC recipients is very low overall and not affected by organ shortage (Table 2).

Among non-HCC candidates, the differences are much larger across quartiles. The percentage of transplanted candidates ranges from 79.3% in Q1 to 52% in Q4 ($p < 0.001$). The overall death rate increases significantly (0.15–0.23 per patient year; $p < 0.001$) as well as percent death on the waitlist (13.5–27.1%; $p < 0.001$). The transplant rate is much lower overall compared to HCC candidates and shows a similar decline with increasing organ shortage (2.8 per patient year in Q1 to 0.7 in Q4; $p < 0.001$). In contrast to HCC candidates, the posttransplant death rate for non-HCC candidates increases from 0.09 to 0.11 deaths/patient year ($p = 0.005$), an effect that disappears when we exclude recipients who die in the early postoperative period (Table 2).

Of note, the average MELD at transplant for both groups is the same in Q1, but progressively increases across quartiles in the non-HCC group, so that it is over 3 points higher for non-HCC candidates in Q4. The donor risk index (DRI), a measure of donor liver quality with lower scores indicating better quality (21), does not change across quartiles in either group. In addition, percentage of patients on life support is higher in all quartiles for non-HCC patients, as is the length of hospital admission, and these values increase with increasing MELD at transplant only in the non-HCC group (Table 2).

The survival impact of organ availability differs between diagnoses

To determine whether the apparent differences between HCC and non-HCC candidates' death rate dependence on organ availability are statistically significant, we compared the change in death with MELD score at transplant. Figure 1B shows overall death rate, plotted against the overall MELD score at transplant in each DSA, with regression curves. There is no change in overall death rate in HCC patients with increasing MELD at transplant, with the calculated risk of death decreasing 1% per MELD point ($p = 0.65$). However, in non-HCC patients, the risk of death increases 7% per MELD point ($p < 0.0001$). The difference between these two slopes is significant ($p < 0.0001$). Similarly, posttransplant death rate is not positively correlated with MELD at transplant in HCC patients, as the calculated risk of death decreases 2% per MELD point ($p = 0.28$). However, in non-HCC patients, the risk of death increases 3% per MELD point posttransplant ($p = 0.03$). This inter-group difference is also statistically significant ($p < 0.005$; Figure 1C). The risk of death on the waitlist increased with MELD at transplant similarly in both HCC and non-HCC patients (15% and 14%, respectively, $p < 0.0001$ for both; Figure 1A).

HCC candidates survive longer after removal from the waitlist

To compare outcomes after removal from the waitlist, we assessed the actual time to death for candidates removed for being “medically unsuitable,” “candidate condition deteriorated,” or “too sick for transplant.”

Unfortunately, only 58.5% of HCC patients and 79.6% of non-HCC patients had reported death dates ($p < 0.0001$). The median time to death was 122 days for HCC patients, and 3 days for non-HCC patients ($p < 0.0001$; Wilcoxon rank sum test). A more complete survival analysis is not feasible because the follow-up time for patients who did not have a death time reported is unknown. However, if the time to death was the same in each group and the follow-up protocol was the same for both populations, the percentages with reported death dates and the median death time would be the same in each group.

Discussion

Contrary to the considerable impact of geographic differences in organ availability on the outcomes of liver transplant candidates overall (7,20), we found very modest effect on the subset receiving eMELD points for HCC. While non-HCC patients suffer from increasing waitlist, posttransplant and overall death as their DSA's average MELD at transplant increases, there is no change in posttransplant or overall death rate in HCC patients. Although the percentage of HCC candidates dying on the waitlist increases with MELD at transplant, it is consistently less than for non-HCC candidates. Even in the DSAs with the highest MELD at transplant, waitlist mortality for HCC candidates is half that of non-HCC candidates in the lowest MELD DSAs.

The implication that current exception point allocation leads to preferential transplantation of HCC patients is supported by other recent studies demonstrating that eMELD underestimates the risk of death on the waitlist compared to calculated MELD in non-HCC patients (2,15–17). Our analysis additionally shows that this pretransplant survival advantage does not carry over into better posttransplant or overall survival among HCC candidates, since overall and posttransplant death rates are almost the same in both groups, despite a fourfold higher waitlist mortality in non-HCC candidates.

Furthermore, overall and posttransplant death rates among HCC patients do not change with increasing MELD at transplant, while those of non-HCC patients increase. This suggests that non-HCC patients would do even better than HCC patients posttransplant if they did not have to wait longer in areas of organ shortage. This may be attributed to increases in perioperative deaths (within 90 days of transplant) in non-HCC patients when transplanted at higher MELDs. By the time of transplant, non-HCC patients tend to be in worse health in high MELD DSAs, as indicated by the higher numbers of non-HCC patients on life support at the time of transplant.

Thus, we note that low organ availability magnifies the advantage of HCC over non-HCC patients. MELD at transplant in non-HCC patients exceeds the MELD score of HCC candidates in Q2–Q4 but not in Q1. This may result from a general reluctance to use marginal livers in critically ill recipients (21), potentially allowing HCC patients in better general health to get transplanted before reaching the top of the list, further tempering their waitlist dropout rates. Although there is minimal difference in the DRI of organs allocated to HCC versus non-HCC patients, the DRI calculation does not include factors such as CDC (Centers for Disease Control) high-risk donor, hepatitis B or hepatitis C positivity and steatosis that might affect the decision to offer an organ to an HCC candidate with lower eMELD rather than to a non-HCC candidate with higher MELD.

Our results suggest that HCC patients may not suffer from waiting longer for transplantation. HCC candidates appear to survive almost 40 times longer after removal from the list than non-HCC candidates, since tumor progression kills patients more slowly than multi-organ failure. It remains unclear at what point during that time the patient's posttransplant outcome is truly jeopardized. Favorable outcomes after LT in patients beyond Milan criteria (but within UCSF criteria) further support the notion that current, more restrictive exception underestimate the duration of transplantability in an HCC candidate (22–24). As local and regional therapies for HCC improve (25), tumor progression even within Milan criteria is now slower. In this context, it is particularly noteworthy that posttransplant death from malignancy tends to decline rather than increase with MELD at transplant. It has been hypothesized that longer wait times select candidates with favorable tumor biology for transplant (16). Indeed, although the percentage of patients undergoing

transplantation for HCC is similar in all quartiles, the percentage of HCC patients listed for LT in Q4 is higher than in Q1–Q3 (Table S1).

Decreasing the number of eMELD for HCC in low MELD DSAs to more closely match wait times to those in high MELD DSAs may actually increase the survival benefit of HCC candidates, saving them the months to years of unneeded immunosuppression when transplanted early. Especially with the advent of Regional Share 35 and National Share 15 (11), this could also divert livers to high MELD, non-HCC patients earlier in their disease progression and improve their outcomes. Decreasing the number of eMELD for HCC candidates in high MELD DSAs will also help to equalize mortality and transplant rates between the two groups in those DSAs, but the effect is likely to be muted, as HCC candidates in high MELD DSAs are currently transplanted at lower MELDs than non-HCC candidates, already.

Until a better understanding of tumor biology allows us to more accurately predict outcomes in HCC (5,15,26,27), the current data suggest that decreasing eMELD for HCC overall, and adjusting the number awarded by a DSA's organ availability could increase equity in organ allocation without unduly disadvantaging HCC candidates.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The data reported here have been supplied by the Minneapolis Medical Research Foundation (MMRF) as the contractor for the Scientific Registry of Transplant Recipients (SRTR). The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy of or interpretation by the SRTR or the U.S. Government. This study used data from the SRTR. The SRTR data system includes data on all donor, waitlisted candidates and transplant recipients in the United States, submitted by the members of the Organ Procurement and Transplantation Network (OPTN), and has been described elsewhere. The Health Resources and Services Administration (HRSA), U.S. Department of Health and Human Services provides oversight to the activities of the OPTN and SRTR contractors. This work was conducted with support from Harvard Catalyst (National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health Award 8UL1TR000170-05, and financial contributions from Harvard University and its affiliated academic healthcare centers). The content is solely the responsibility of the authors and does not necessarily represent the official views of Harvard Catalyst, Harvard University and its affiliated academic healthcare centers, or the National Institutes of Health.

Abbreviations

CI	confidence interval
DRI	donor risk index
DSA	donation service area
eMELD	exception MELD points
HCC	hepatocellular carcinoma
LT	liver transplantation
MELD	model for end-stage liver disease
non-HCC	patients without HCC diagnosis
OPTN	Organ Procurement and Transplantation Network
Q1–Q4	Quartiles, defined by MELD at transplant

SRTR	Scientific Registry of Transplant Recipients
UCSF	University of California, San Francisco
UNOS	United Network for Organ Sharing

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Figure 1. Waitlist, posttransplant and overall death percentages by DSA

(A) Percent mortality for candidates on the waitlist is shown for each DSA by average MELD at transplant. (B) Overall death per patient year for each DSA by average MELD at transplant. (C) Posttransplant death is depicted for each DSA by average MELD at transplant. Tables in (A)–(C): The odds ratio and relative risk represent the slope of each curve, or the change in mortality with average MELD at transplant, by DSA. Average mortality is shown for all patients across DSAs in each group. CI, confidence interval; DSA, donation service area; HCC, hepatocellular carcinoma; MELD, model for end-stage liver disease; non-HCC, patients without HCC diagnosis.

Table 1

Candidate demographics by DSA quartile

Characteristic	HCC candidates					non-HCC candidates				
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p
Age	57.1 ± 0.4	57.2 ± 0.3	57.0 ± 0.3	57.6 ± 0.3	0.476	52.8 ± 0.3	52.5 ± 0.2	52.4 ± 0.2	53.0 ± 0.2	0.578
Percent female	22.1 ± 1.7	22.6 ± 2.0	21.1 ± 2.2	23.3 ± 1.6	0.782	34.2 ± 0.8	36.1 ± 1.2	34.0 ± 1.4	34.4 ± 0.8	0.710
Race (%)										
White	70.9 ± 3.2	74.0 ± 2.3	67.9 ± 5.5	56.9 ± 4.5	0.017	78.2 ± 3.5	79.9 ± 2.5	77.8 ± 4.3	63.5 ± 4.2	0.024
Black	11.7 ± 4.4	8.3 ± 2.2	8.1 ± 4.0	18.4 ± 3.6	0.310	10.9 ± 3.3	6.8 ± 2.2	7.9 ± 3.4	22.2 ± 4.4	0.074
Hispanic	9.7 ± 1.7	11.0 ± 2.2	13.5 ± 3.3	7.8 ± 1.3	0.564	8.3 ± 1.1	11.0 ± 1.5	10.9 ± 1.8	8.0 ± 1.5	0.868
Asian	6.7 ± 1.9	5.8 ± 0.9	9.6 ± 2.2	15.6 ± 3.7	0.027	2.0 ± 0.4	1.5 ± 0.2	2.2 ± 0.6	4.9 ± 1.0	0.011
Other	0.9 ± 0.3	0.8 ± 0.2	0.9 ± 0.4	1.3 ± 0.3	0.407	0.6 ± 0.2	0.6 ± 0.2	1.2 ± 0.6	1.3 ± 0.3	0.032
Blood type (%)										
O	48.2 ± 1.0	44.0 ± 2.2	46.2 ± 1.6	42.9 ± 1.6	0.054	47.3 ± 0.4	46.9 ± 1.2	46.3 ± 1.1	46.5 ± 0.9	0.407
A	38.6 ± 1.3	38.9 ± 1.2	38.3 ± 1.5	36.3 ± 1.4	0.232	38.1 ± 0.7	38.0 ± 0.8	38.2 ± 1.2	36.5 ± 0.8	0.189
B	10.3 ± 1.0	12.4 ± 1.8	10.9 ± 1.4	14.9 ± 1.4	0.059	11.7 ± 0.4	11.5 ± 0.8	12.1 ± 0.5	12.8 ± 0.5	0.085
AB	3.0 ± 0.4	4.7 ± 0.6	4.6 ± 0.7	6.0 ± 0.7	0.004	2.9 ± 0.2	3.6 ± 0.3	3.4 ± 0.4	4.2 ± 0.2	0.007
Diagnosis (%)										
Noncholestatic cirrhosis	54.6 ± 8.5	32.6 ± 5.9	43.8 ± 8.0	42.9 ± 6.5	0.487	78.6 ± 1.4	78.2 ± 1.1	77.1 ± 1.7	75.9 ± 3.5	0.420
Malignant neoplasms	43.3 ± 8.8	65.6 ± 6.1	52.1 ± 9.1	53.5 ± 6.6	0.633	0.7 ± 0.1	0.6 ± 0.1	0.5 ± 0.1	0.9 ± 0.5	0.685
Cholestatic liver disease/cirrhosis	0.5 ± 0.4	0.6 ± 0.3	1.2 ± 0.7	0.7 ± 0.3	0.466	9.1 ± 0.8	10.1 ± 0.8	8.9 ± 0.8	6.4 ± 0.6	0.021
Metabolic diseases	0.5 ± 0.4	0.7 ± 0.3	0.2 ± 0.1	0.4 ± 0.2	0.447	2.1 ± 0.2	3.4 ± 0.4	2.5 ± 0.2	2.0 ± 0.3	0.556
Other	1.1 ± 0.6	0.6 ± 0.3	2.7 ± 1.0	2.5 ± 0.5	0.013	9.6 ± 0.9	7.7 ± 0.8	11.0 ± 1.6	14.8 ± 3.6	0.101

Liver transplant candidate characteristics are grouped by DSA into quartiles for HCC and non-HCC candidates separately. The quartiles are stratified by corrected MELD at transplant, with Quartile 4 containing the 12 DSAs with the highest MELD at transplant. The size of a donation service area reflects the mean number of listed patients per DSA. Non-HCC patients were listed in 130 centers, while only 106 centers listed HCC patients. $p < 0.05$ indicates that there is a statistically significant trend across the four quartiles. DSA, donation service area; HCC, hepatocellular carcinoma; MELD, model for end-stage liver disease; non-HCC, patients without HCC diagnosis.

Table 2

Transplant characteristics

Characteristic	HCC candidates					non-HCC candidates				
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p Value	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p Value
Percent transplanted	96.8 ± 0.7	96.3 ± 0.7	93.9 ± 0.8	75.5 ± 2.1	<.001	79.3 ± 2.7	73.9 ± 2.1	63.6 ± 1.9	52.0 ± 1.5	<.001
Transplant rate (per Patient Year = pPY)	8.7 ± 0.3	6.7 ± 0.4	4.7 ± 0.4	1.9 ± 0.3	<.001	2.8 ± 0.2	1.9 ± 0.2	1.2 ± 0.2	0.7 ± 0.1	<.001
Death rate (pPY)	0.12 ± 0.01	0.12 ± 0.01	0.13 ± 0.01	0.12 ± 0.01	0.694	0.15 ± 0.01	0.16 ± 0.01	0.19 ± 0.01	0.23 ± 0.01	<.001
Percent of death while on waitinglist (%)	2.1 ± 0.5	2.8 ± 0.5	4.3 ± 0.6	6.8 ± 0.7	<.001	13.5 ± 1.5	15.1 ± 0.9	20.5 ± 1.0	27.1 ± 0.9	<.001
Waitlist death rate (pPY)	0.17 ± 0.04	0.20 ± 0.04	0.22 ± 0.04	0.16 ± 0.03	0.942	0.43 ± 0.03	0.36 ± 0.03	0.39 ± 0.03	0.38 ± 0.02	0.269
Posttransplantation death rate (pPY)	0.11 ± 0.01	0.11 ± 0.02	0.11 ± 0.02	0.10 ± 0.01	0.690	0.09 ± 0.01	0.09 ± 0.01	0.11 ± 0.01	0.11 ± 0.01	0.005
Death rate in patients who have survived >90 days posttransplant (pPY)	0.09 ± 0.02	0.13 ± 0.02	0.10 ± 0.02	0.07 ± 0.02	0.526	0.06 ± 0.01	0.06 ± 0.01	0.07 ± 0.01	0.07 ± 0.01	0.188
Malignancy death rate in patients who survived >90 days posttransplant (pPY)	0.03 ± 0.01	0.03 ± 0.01	0.02 ± 0.01	0.02 ± 0.01	0.078	0.01 ± 0.00	0.01 ± 0.00	0.01 ± 0.00	0.01 ± 0.00	0.994
MELD										
MELD at transplant or censoring	22.3 ± 0.0	22.5 ± 0.1	23.2 ± 0.2	25.5 ± 0.2	<.001	22.2 ± 0.2	23.2 ± 0.3	24.2 ± 0.2	25.2 ± 0.3	<.001
MELD at transplant	22.3 ± 0.0	22.5 ± 0.1	23.2 ± 0.2	25.3 ± 0.2	<.001	22.4 ± 0.3	24.2 ± 0.1	25.5 ± 0.2	28.8 ± 0.6	<.001
Transplants prior to MELD of 15 (%)	N/A	N/A	N/A	N/A	N/A	5.5 ± 2.4	1.3 ± 0.3	3.5 ± 1.7	3.2 ± 1.2	0.702
MELD at listing (study population)	21.8 ± 0.1	21.8 ± 0.1	21.9 ± 0.0	21.7 ± 0.1	0.924	20.9 ± 0.2	21.2 ± 0.2	21.7 ± 0.2	22.4 ± 0.3	<.001
MELD when added to waitlist	19.5 ± 0.4	19.1 ± 0.6	19.5 ± 0.3	17.3 ± 0.4	0.006	18.3 ± 0.4	18.2 ± 0.5	18.0 ± 0.3	18.0 ± 0.3	0.507
Donation after cardiac death (%)	4.6 ± 1.1	5.0 ± 1.6	6.6 ± 1.4	6.5 ± 1.1	0.171	6.0 ± 2.0	3.7 ± 1.2	6.1 ± 1.6	5.0 ± 0.6	0.968
Ischemia time	7.2 ± 0.2	6.7 ± 0.3	7.2 ± 0.4	7.0 ± 0.3	0.947	7.1 ± 0.2	6.9 ± 0.3	7.6 ± 0.5	7.2 ± 0.3	0.549
Ischemia time: Imported organs	7.7 ± 0.4	8.4 ± 0.5	8.7 ± 0.9	8.5 ± 0.3	0.174	7.7 ± 0.3	8.1 ± 0.5	8.9 ± 0.7	8.7 ± 0.3	0.083
Ischemia Time: Organs within DSA	6.9 ± 0.2	6.4 ± 0.3	6.9 ± 0.4	6.7 ± 0.2	0.831	6.8 ± 0.2	6.7 ± 0.3	7.1 ± 0.4	6.7 ± 0.2	0.794
Relisted within 30 days of transplant	0	0	0	0	N/A	2.6 ± 0.2	3.0 ± 0.3	2.7 ± 0.4	3.5 ± 0.5	0.174
Donor risk index	1.5 ± 0.03	1.5 ± 0.02	1.6 ± 0.04	1.6 ± 0.05	0.116	1.6 ± 0.05	1.5 ± 0.02	1.6 ± 0.04	1.6 ± 0.06	0.547
DRI: Imported organs	1.7 ± 0.05	1.8 ± 0.06	1.8 ± 0.07	1.9 ± 0.06	0.071	1.8 ± 0.04	1.7 ± 0.04	1.9 ± 0.07	1.9 ± 0.07	0.115
DRI: Organs from within DSA	1.4 ± 0.02	1.4 ± 0.01	1.5 ± 0.04	1.5 ± 0.03	0.009	1.4 ± 0.03	1.4 ± 0.01	1.5 ± 0.02	1.5 ± 0.03	0.148
Transplants from living donors (%)	0.1 ± 0.1	0.3 ± 0.2	0.3 ± 0.3	3.0 ± 0.9	0.224	0.4 ± 0.3	2.0 ± 1.0	3.2 ± 2.1	8.2 ± 1.6	0.007
Percent recovered organs exported	22.4 ± 4.3	23.7 ± 7.2	19.0 ± 5.2	6.5 ± 1.6	0.003	27.4 ± 5.0	25.6 ± 6.3	22.6 ± 6.2	8.0 ± 1.3	0.004
Life support at time of transplant (%)	0.1 ± 0.1	0.5 ± 0.2	0.2 ± 0.1	0.6 ± 0.3	0.275	2.0 ± 0.3	2.9 ± 0.5	4.8 ± 0.9	8.6 ± 2.4	0.007

Characteristic	HCC candidates				non-HCC candidates				p Value
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
Length of stay	11.6 ± 1.1	12.6 ± 1.0	11.1 ± 1.0	10.8 ± 0.8	14.5 ± 0.6	16.0 ± 0.7	18.2 ± 2.1	17.9 ± 1.3	0.026

Quartiles are defined as in Table 1. Overall death and waitlist death were analyzed as percentage of all waitlisted candidates, while posttransplant death includes only transplanted patients or transplanted patients that survived at least 90 days posttransplant, as indicated. To account for variations in time spent by each candidate until transplantation or removal from waitlist, the mortality rates were calculated per patient year. The percentage of transplants prior to reaching a MELD of 15 is shown only for non-HCC patients because only patients who received 22 eMELD points were included in the HCC group. No patient in the HCC group was relisted within 30 days of transplant. Bold p-values indicate statistical significance. DSA, donation service area; eMELD, exception MELD points; HCC, hepatocellular carcinoma; MELD, model for end-stage liver disease; N/A, not applicable; non-HCC, patients without HCC diagnosis.